TANZANIA
JOURNAL OF HEALTH RESEARCH

TANZANIA JOURNAL OF HEALTH RESEARCH

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CONTENTS

ORIGINAL RESEARCH ARTICLES

Antimicrobial resistance among neonates with neonatal sepsis Morogoro Tanzania

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Abstract

Background: Neonatal sepsis increases neonatal morbidity and mortality in low- and middle-income nations. however, the prevalence of neonatal sepsis, the etiological agents, and antimicrobial resistance patterns have not been documented in areas with the highest neonatal mortality rates in Tanzania.

Aim: This study aimed to investigate the prevalence of neonatal sepsis, identify the primary causative agents, and understand their resistance patterns at Morogoro Regional Hospital.

Methods: The study involved 252 admitted neonates at Morogoro Regional Hospital and was carried out between March and June 2019. Clinical and demographic information for each neonate was collected using a standardized questionnaire. Blood samples were obtained from all 252 neonates, and 50 swabs were randomly taken from neonates with umbilical pus discharge. The samples were cultured using aseptic techniques on blood, chocolate, and MacConkey agar. The identification of the causative agents relied on the characteristics of colony morphology, gram staining, and biochemical tests. Antimicrobial resistance patterns were determined using the disc diffusion method with Muller Hinton agar against Ampiclox, Erythromycin, Gentamycin, Nalidixic acid, Ciprofloxacin, Norfloxacin, Ofloxacin, Kanamycin, Co-trimoxazole, Cephalexin, Ceftriaxone, and Amikacin.

Results: The prevalence of neonatal sepsis, as determined through blood culture, was 40 % (102 /252). The predominant bacteria isolated from blood cultures were *E. coli* 31 %, *Staphylococcus aureus* 23 %, and *Citrobacter* spp 16%. Around 50% of the gram-negative bacteria resisted Ceftriaxone, a third-generation cephalosporin. Both gram-negative bacteria and *Staphylococcus aureus* displayed resistance to Ampiclox.

Conclusion: *E. coli, Staphylococcus aureus*, and Citrobacter spp. were shown to be the most frequent bacteria in neonatal sepsis in Morogoro. Many isolates were Ampicillin-resistant. Neonatal sepsis is common in Morogoro, highlighting the need for innovative neonatal care and preventative techniques.

Keywords: Neonatal sepsis, antimicrobial resistance, Tanzania

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Introduction

Children in Low- and Middle-Income countries are 18 times more likely to die before the age of five than those in developed countries (Chan and Lake, 2013, WHO 2018). Among the numerous health challenges affecting neonates in LMICs, neonatal sepsis emerges as a predominant cause of hospital admissions (Shitaye et al., 2010). As a result, sepsis causes nearly 2 million newborn deaths in Africa (UNICEF, 2017).

In Tanzania, neonatal sepsis is responsible for a significant portion, ranging from 29% to 38.9% of neonatal deaths (Manji, 2009; Kayange et al., 2010; Mhada et al., 2012). Neonatal sepsis is a life-threatening clinical syndrome characterized by dysregulated host immune responses due to infection, often leading to organ dysfunction (Pop-Begun et al., 2014). While the prevalence of neonatal sepsis varies from country to country (Kaistha et al., 2009), its profound impact is prominently observed in developing countries. In contrast, sepsis in adults has been extensively studied and documented worldwide (WHO, 2018), whereas neonatal sepsis remains a relatively underexplored area (*Ibid*.).

The sustainable development goal (SDG) 3.2 targets newborn and child mortality by 2030 is to end preventable deaths of newborns and children under five years of age. All countries shall aim to reduce neonatal mortality to as low as 12 per 1,000 live births and under-five mortality as low as 25 per 1,000 live births(https://www.undp.org/sustainable-development-goals/good-health).

The diagnosis and treatment of neonatal sepsis pose substantial challenges in many LMICs, partly due to inadequate healthcare personnel and the absence of essential laboratory facilities (Lawn et al., 2009). The need for appropriate laboratory resources hinders the identification of causative agents, and their drug sensitivity profiles, resulting in limited data regarding the incidence, prevalence, and etiological factors associated with neonatal sepsis in developing nations like Tanzania.

Furthermore, research has indicated dynamic changes in the susceptibility patterns of bacteria causing sepsis (Thapa and Sapkota, 2019). This has led to the absence of a one-size-fits-all antibiotic recommendation (Kayange et al., 2010; Mhada et al., 2012; Thapa and Sapkota, 2019). Most etiological agents responsible for neonatal sepsis have developed multiple resistances to antimicrobial therapies, resulting in high mortality rates, increased healthcare costs, and clinical failures (Iqbal, 2013; Friedman et al., 2016). The variation in etiological agents and drug susceptibility patterns among bacteria causing neonatal sepsis underscores the need for regular antimicrobial resistance monitoring programs.

Studies on neonatal sepsis in Tanzania have focused on regions such as Mwanza and Dar es Salaam (Mshana et al., 2009; Jabiri et al., 2016). The Tanzania Demographic Health Surveillance estimates the infant mortality rate at Morogoro Regional Hospital to be 82 per 1000 live births (DHS, 2015 – 2016). However, updated information on the causes of neonatal deaths in the region is required. This study determined neonatal sepsis's prevalence, identified the associated etiological agents, and assessed the susceptibility status to commonly used antimicrobial agents among neonates

admitted to Morogoro Regional Hospital.

Materials and Method
Study Area and Design

The study was conducted in Morogoro Region Hospital, in the eastern part of mainland Tanzania, from January to July 2019. The region is characterized by a high infant mortality rate, with approximately 82 deaths per 1000 live births (DHS, 2015). Data were collected from neonates admitted to Morogoro Regional Hospital, a referral hospital for the region's eight districts. All laboratory work was conducted at Morogoro National Institute of Medical Research laboratories.

The study involved cross-sectional and cohort study designs involving neonates aged from 0 to 30 days after delivery who were admitted to the neonatal ward at Morogoro Regional Hospital and were suspected to have sepsis. Demographic data such as age, sex, and area of residence were obtained from consented parents or guardians. Clinical information, including the neonates' weight, gestational age, premature rupture of membranes, fever, breathing rate, delivery mode, cyanosis, convulsions, feeding ability, jaundice, and umbilical redness were sourced from hospital records.

Inclusion Criteria and Informed Consent

The selection of neonates for the study was based on findings from physical and clinical examinations. Enrollment included all neonates who were admitted to the Morogoro Regional Referral Hospital's neonatal ward, aged between 0 and 30 days of postpartum and who were clinically suspected of having sepsis, with parents available. Informed consent was obtained from the parents of the neonates.

Sample Size Estimation

The sample size was calculated using Fisher's formula, based on research conducted at Muhimbili National Hospital, which showed a prevalence of neonatal sepsis of 24% (Mhada et al., 2012). Using the formula $N = Z^2P(1-P)/\delta^2$, N is the minimum sample size, Z is the standard average deviation (1.96 for the 95% confidence interval), and P is the expected prevalence. Δ is the acceptable margin of error; a minimum sample size of 280 neonates was anticipated to be used.

Ethical permit

The ethical approval was obtained from the National Health Research Committee (NatHREC) of the National Institute of MedicalResearch (NIMR/HQ/R.8a/Vol.IX/1896).

Neonatal Blood and Swab Samples Collection

Structured and semi-structured questionnaires were used to obtain demographic and clinical information from admitted neonates. This included physical examinations, neonate weight, and information about premature rupture of membranes, fever, breathing rate, delivery mode, cyanosis, convulsions, feeding ability, jaundice, and umbilical redness. Blood and pus samples were collected from all neonates suspected of having sepsis and admitted to Morogoro Regional Hospital with the consent of their parents. Blood collection was aseptically done, with 2 to

3 ml of intravenous blood taken from each suspected neonate. The blood samples were coded and transferred to the microbiology laboratory for storage, culturing, identifying, and determining antimicrobial resistance patterns. Neonates positive for sepsis were monitored to assess their health outcomes (El-Halik et al, 2018).

Microbial analysis: Sub-culturing of neonatal blood and swab samples
The collected blood samples and swabs were mixed with sterile 10mls of Brain Heart Infusion broth under aseptic environmental conditions. The mixture was then incubated at 37°C for 24 hours to allow maximum multiplication of pathogens in the given swab and blood samples. The mixture was sub-cultured using a sterile inoculating wire loop into a dry and clean surface of blood agar, chocolate agar and MacConkey agar. Then the inoculated petri dishes were incubated at 37°C overnight, followed by observation for 24, 48,72 96 hours until there was no growth of colonies. The colony morphologies were recorded based on the colour, texture, forms, shape, and reaction on blood agar whether the colonies had undergone β, α or no hemolysis. Also, the reaction of the isolates on MacConkey agar and gram staining were recorded. Microscopic observations of the slides were done using an objective lens with 100x at medium lighting using immersion oil. After identifying gram-positive and gram-negative bacteria, biochemical tests were set depending on the staining nature of the isolates. Gram-negative bacteria were put into the triple iron sugar agar reaction test (TSI), SIM test (involving motility, hydrogen sulphide test and Indole test), citrate, and urease tests. In contrast, Gram-positive bacteria were set into catalase reaction, coagulase activity, and haemolytic activity on horse blood agar plates.

Susceptibility testing
To identify the extent to which isolates were resistant or susceptible to the standard antibiotics used in the treatment of bacterial infections, a sensitivity test was carried out using the Kirby-Baeur disc diffusion susceptibility method. Muller Hinton agar was employed as a growth medium because it supports the growth of most non-fastidious pathogens satisfactorily and exhibits acceptable batch-to-batch reproducibility for susceptibility testing. It also has low concentrations of sulfonamide, trimethoprim, and tetracycline inhibitors. (Clinical and Laboratory Standard institute 2017).To ascertain the isolates' susceptibility, the following antibiotics were used: Ampiclox 30 µg (LOT 110714054), Erythromycin with 15µg (LOT 327996), Gentamycin with 30µg (LOT 2856439), Nalidixic acid 30µ (LOT 0000322969), Ciprofloxacin 30µg (LOT 320778), Norfloxacin 10µg (LOT 327289), Ofloxacin with five µg (LOT 325442), Kanamycin 30µg (LOT 321894), Clo-Trimoxazole with 25µg (LOT326434), Cephalexin 30µg, Ceftriaxone 30µg (LOT 2855442), and Amikacin with 30µg (LOT 2440768). Susceptibility testing followed Ruangpan, 2004, and Wayne, 2017.

Data analysis
Early onset neonatal sepsis was defined as the onset of symptoms 0-72 hours after birth, and late onset was more than 72 hours after birth. The prevalence of early-onset was compared to that of late-onset using the Chi-Squire test. Neonatal

death due to sepsis was calculated from the number of neonates who died due to sepsis over the total number of neonates with positive blood culture sepsis.

Fisher's exact test compared the etiological agents of early and late-onset newborn sepsis. A statistical significance was defined as a P value of less than 0.05.

Results

Sub-culturing blood and swabs on Brain Heart Infusion Broth revealed that 40.5% (102 out of 252) had positive blood culture results among the tested neonates, while 59.5% (150 out of 252) showed negative blood culture results. Of the neonate samples with positive blood culture results, 74.5% (78 out of 102) grew on MacConkey agar, while 24.5% (24 out of 102) did not. In addition, 80% (40 out of 50) of the swab samples collected showed growth on MacConkey agar, with 20% not exhibiting any growth. Gram Staining Results indicated that 23.5% (24 out of 102) of the bacterial isolates were gram-positive bacteria, while 76.5% (78 out of 102) were gram-negative bacteria. Among the gram-positive bacteria, 96% (23 out of 24) were gram-positive cocci in clusters, and 4% (1 out of 24) were gram-positive diplococci in chains. All isolated gram-negative bacteria had a rod-shaped morphology.

Biochemical characterization of gram-positive bacteria, including colony morphology on blood agar and hemolytic reaction, revealed that 96% of gram-positive bacteria from pure growth exhibited β-hemolysis colonies, which were large, convex, and wet. In comparison, 4% displayed α-hemolysis on blood agar with transparent and mucoid colonies. In the Catalase test, 96% (23 out of 24) of gram-positive bacteria tested positive for catalase, while 4% (1 out of 24) tested negative for catalase. Furthermore, the catalase-positive samples (23) were subjected to the coagulase test, and all of them exhibited a positive coagulase test by forming clumps on the glass slide after inoculation.

Biochemical characterization of gram-negative bacteria showed that about 78% (78 out of the total) of the gram-negative bacteria grown on MacConkey agar were lactose-fermenting, leading to pinkish colonies. The remaining 22% (17 out of 78) were non-lactose-fermenting and had clear colonies (see Table 1 for details).

Table 1Summary of biochemical characterization of gram-negative bacteria

Total samples	Morphology on BA	Morphology on CA	Morphology on MCA	Gram stain test	TSI test			SIM test			Ureastest	Simon citrate test	Probable isolate
					Butt	slant	Gas	Sulphur	Indole	Motility			
14	Pure growth of non-hemolytic, circular in shape, convex, opaque colons.	Pure growth of whitish colons, circular in shape, opaque in opacity.	- Pure growth of non-lactose ferment colons, whitish in colour and circular in shape.	Gram-negative rod	Red	red	negative	Negative	Negative	Positive	Positive	Positive	Pseudomonas spp
06	Pure growth of non-hemolytic colons, medium in size, circular and opaque.	Pure growth of whitish colons, circular and opaque.	Pure growth of lactose fermenting colons, pink in colour and opaque	Gram-negative rod	Yellow	yellow	positive	Negative	Negative	Positive	Negative	Positive	Enterobacter spp
32	Pure growth of non-hemolysis colons, circular in shape, entire and opaque colons.	Pure growth of circular colons, opaque in opacity.	Pure growth of lactose fermenting colons, pinkish in colour and circular in shape.	Gram-negative rod	yellow	yellow	positive	negative	positive	Positive	Negative	Negative	E. coli
16	Pure growth of non-hemolysis colons, medium in size, convex, opaque and circular.	Pure growth of whitish colons, circular opaque in opacity.	Pure growth of lactose fermenting colons, pinkish in colour and convex in shape.	Gram-negative rod	Yellow	red	positive	positive	Negative	Positive	Positive	Positive	Citrobacter spp
07	Pure growth of non-hemolytic mucoid colons,	Pure growth of mucoid colons	Pure growth of lactose fermenting pinkish colons with	Gram-negative rod	Yellow	yellow	positiv	Negative	Positiv	Negative	Positive	Positive	*Klebsiella spp*

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Total samples	Morphology on BA	Morphology on CA	Morphology on MCA	Gram stain test	TSI test			SIM test			Ureastest	Simon citrate test	Probable isolate
					Butt	slant	Gas	Sulphur	Indole	Motility			
	flat on the surface	whitish in colour.	mucoid and irregular shape										
02	Pure growth of entire, pale-whitish, flat swarming the blood agar		Pure growth of non-lactose fermenting colons with flat entire irregular shape	gram-negative rod	Yellow	red	positive	positive	negative	Positive	Positive	Positive	Proteus Spp
01	Pure growth of non-hemolysis colons with whitish colour, circular and raised.	Pure growth of whitish colons, convex and circular	Pure growth of non-lactose fermenting colons with a whitish colour.	Gram-negative rod	Yellow	red	negative	positive	negative	Positive	Negative	Negative	Salmonella spp

Prevalence of Neonatal Sepsis at Morogoro Regional Hospital

This study found that 40% (102 out of 252) of the admitted neonates had positive blood cultures indicating sepsis. Notably, late-onset sepsis accounted for 58% (59 out of 102) of these cases, while early neonatal sepsis represented 42% (43 out of 102) ($\chi2$=2.46, df = 1, p = 0.005). Additionally, 38% (19 out of 50) of premature neonates included in the study tested positive for sepsis in blood cultures.

The predominant bacteria responsible for neonatal bacterial sepsis in Morogoro were Gram-negative bacteria, accounting for 76% (78 out of 102) of all isolates. Gram-positive bacteria constituted only 24% (24 out of 102) ($\chi2$ = 28.58, d f= 1, p = 0.005). Among the bacterial isolates identified in blood samples, *Escherichia coli* was the most common, making up 31% (32 out of 102) of the cases, followed by *Staphylococcus aureus* at 23% (23 out of 102), *Citrobacter* spp at 16% (16 out of 102), and *Pseudomonas* spp at 14% (14 out of 102). Other less common isolates included *Klebsiella* spp (7 out of 102, 7%), *Enterobacter* spp (6 out of 102, 6%), *Proteus* spp (2 out of 102, 2%), *Salmonella* spp (1 out of 102, 1%), and *Streptococcus* spp (1 out of 102, 1%). The distribution of etiological agents in the early and late onset of sepsis is depicted in Figure 1.
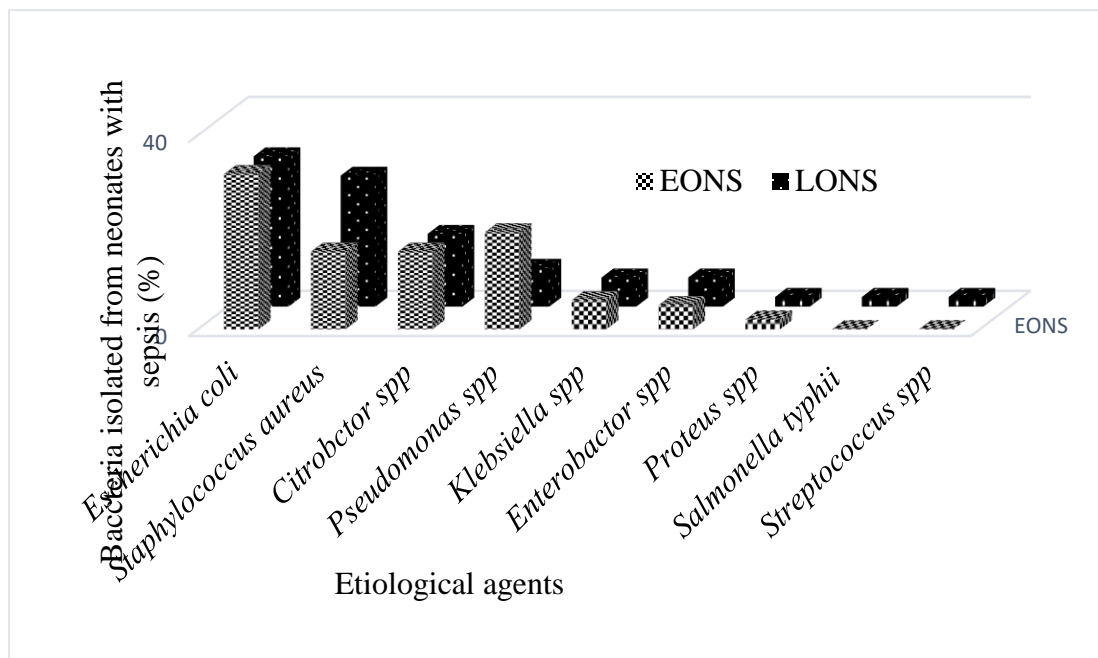
Figure 1 Etiology of neonatal sepsis among neonates admitted in Morogoro Regional Hospital

Common pathogens were isolated from swabs taken from the discharging umbilical cords of selected neonates admitted to Morogoro Hospital. The predominant bacteria found in these swabs included *E. coli* at 40% (20 out of 50 samples), *Citrobacter* spp at 28% (14 out of 50 samples), Staphylococcus aureus at 21% (10 out of 50 samples), and *Klebsiella* spp at 12% (6 out of 50 samples) (see Table 2).

Table 3 Common Pathogens Isolated from Neonatal Swabs in neonates admitted in Morogoro Hospital

Organism	EONS	LONS	Total N (%)
Escherichia coli	07	13	20(40.0)
Citrobactor spp	06	08	14(27.5)
Staphylococcus aureus	04	06	10(20.5)
Klebsiella spp	02	04	06(12.0)
Total	**19**	**31**	**50(100)**

Antibiotic Sensitivity Pattern in Neonates with Neonatal Sepsis at Morogoro Regional Hospital

The antibiotic sensitivity test followed the 2020 Clinical and Laboratory Standards Institute guidelines. The diameters of the zones of inhibition were recorded as Sensitive (S), Intermediate (I), and Resistant (R), with Intermediate (I) considered as Resistant (R). The gram-positive bacteria *S. aureus* isolates were resistant to Ampiclox and Erythromycin, while all Streptococcus isolates were susceptible to all antibiotics.

Most gram-negative bacteria showed high resistance to Ampiclox and Nalidixic acid and moderate resistance to Ceftriaxone. At the same time, most gram-negative bacteria were less resistant to Gentamicin, Cephalexin, Ciprofloxacin, Norfloxacin, and Ofloxacin. All gram-negative bacteria were sensitive to Amikacin.

Seventy-six per cent of *E. coli* were resistant to Ampiclox, 87% to Nalidixic acid, 45% to ceftriaxone and highly sensitive to Gentamicin, Ciprofloxacin, Cephalexin, Ofloxacin, Norfloxacin and Amikacin

Table 3 Sensitivity Pattern of Gram-Positive Bacteria to the Common Antibiotics used in Tanzania

	Staphylococcus aureus		*Streptococcus spp*	
	S	R	S	R
Ampiclox	0	**100**	100	0
Erythromycin	9.5	**90.5**	100	0
Gentamycin	85.7	14.3	100	0
Vancomycin	61.9	38.1	100	0
Kanamycin	57.1	42.5	100	0
Clo-Trimoxazole	57.1	42.5	100	0
Ciprofloxacin	100	0	100	0
Norfloflaxin	100	0	100	0
Amikacin	100	0	100	0

Citrobacter spp isolates from both blood and swab were 100% resistant to Ampiclox, 33.3% to ceftriaxone, 8.3% Gentamicin, 8.3% Ciprofloxacin and sensitive to the rest of the antibiotics. *Klebsiella* isolates showed resistance to Ampiclox, Nalidixic acid, Gentamicin and Ceftriaxone. Enterobacter *spp* isolates were resistant to Ampiclox and Nalidixic acid and susceptible to Gentamicin, Ciprofloxacin, Ofloxacin, Norfloxacin, Cephalexin and Amikacin (Table 4). *Pseudomonas spp* were 100% sensitive to ceftriaxone, cephalexin, amikacin, Ofloxacin, and Ciprofloxacin and slightly resistant to Norfloxacin. *Proteus spp* and *Salmonella typhii* isolates from blood were sensitive to all antibiotics, including Gentamicin, Ceftriaxone, Ciprofloxacin, Norfloxacin and amikacin.

Table 4 Sensitivity Pattern of Gram-Negative Bacteria Isolates to the Common Antibiotics Used in Tanzania.

	Escherichia coli		*Citrobacter*		*Enterobacter*		*Klebsiella*		*Proteus*		*Salmonera typhi*		*Pseudomonas*	
	S	R	S	R	S	R	S	R	S	R	S	R	S	R
APL	23.6	**76.4**	00.0	**100**	00.0	**100**	00.0	**100**	NA	NA	00.0	**100**	NA	NA
GEN	87.5	12.5	91.7	08.3	100	00.0	73.3	26.7	100	00.0	100	00.0	100	00.0
CEFT	56.2	**43.8**	66.7	**33.3**	50.0	**50.0**	73.3	**26.7**	100	00.0	100	00.0	100	00.0
CIP	91.2	18.8	91.7	08.3	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0
NX	94.1	05.9	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0	76.0	**14.0**
OF	91.2	18.8	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0
CL	90.5	09.5	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0
AK	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0	100	00.0
NAL	12.0	**56.0**	NA	NA	33.5	**66.5**	NA	NA	NA	NA	NA	NA	NA	NA

APL* Ampiclox, GEN* Gentamicin, CEFT* Ceftriaxone, NAL*Nalidixic acid, CIP* Ciprofloxacin, NX*Norfloxacin, OF*Ofloxacin, CL*Cephalexin, AK*Amikacin, S*Sensitive, R*Resistant, NA* Not applied.

Clinical Outcomes among Neonates with Sepsis at Morogoro Regional Hospital

Sixteen per cent of the neonates whose sepsis was confirmed by a positive blood culture passed away from their illness. *Escherichia coli,* which was the most common isolate found in blood and swabs, was linked to 31% (5 out of 16) of the deaths that occurred in neonates, followed by *Citrobacter* spp at 25%, *S. aureus* at 19% (3 out of 16), *Pseudomonas* spp at 13%, *S. typhii* at 6%, and *Proteus* spp at 6%. Bacterial sepsis caused by gram-negative bacteria resulted in a higher mortality rate than gram-positive bacteria (χ^2 =1.12, df =1, p < 0.05).

Discussion

The prevalence of neonatal sepsis in Morogoro is notably high. Among the neonates admitted to Morogoro Hospital, late-onset neonatal sepsis surpassed early-onset cases. This higher incidence of late-onset neonatal sepsis suggests a greater prevalence of substandard neonatal care environments. Blood cultures from neonatal sepsis cases revealed that *E. coli* was the most common pathogen, followed by *S. aureus* and *Citrobacter* spp. Similarly, neonatal swab samples predominantly featured *E. coli*, Citrobacter, and *S. aureus*. An unexpected rise in *Pseudomonas* spp. cases were noted, although it is an uncommon cause of blood infection. In this study, gram-positive bacteria, particularly. *S. aureus* exhibited significant resistance to Ampiclox and erythromycin, with moderate resistance to Clo-trimoxazole. Ceftriaxone resistance was more common among gram-negative bacteria. Mortality from gram-negative bacterial infections remained higher than that from gram-positive infections, consistent with findings in other Tanzanian hospitals.

Both early and late-onset neonatal sepsis in Morogoro was primarily attributed to *E. coli*, followed by *S. aureus*, *Citrobacter* spp, and other isolates, which contrasts with studies in Mwanza that reported similar rates of early and late sepsis among neonates (Kayange et al. 2010). Furthermore, *E. coli*, *S. aureus*, and *Citrobacter* spp. were the predominant causes of neonatal sepsis in blood samples, aligning with findings in Tanzania and other low-income countries where *S. aureus*, *Klebsiella* spp, and *E. coli* were the leading culprits (Mhada et al. 2012, Fuchs et al. 2016). An increase in *E. coli* infections as the primary bacteria in both early and late-onset sepsis from both blood and swab samples may be attributed to antibiotic selective pressure. Gram-negative bacteria outnumbered gram-positive bacteria in this study, consistent with earlier studies that emphasized the predominance of gram-negative bacteria as the primary etiological agent of neonatal sepsis in various hospitals throughout Tanzania.

Surprisingly, this study identified a rise in neonatal sepsis cases caused by *Pseudomonas* spp. Although *Pseudomonas* typically causes infrequent blood infections and outbreaks in developed nations (Harnein et al. 2015), it was found to be the second most common bacteria causing early onset neonatal sepsis, following *E. coli,* which was more prevalent in early sepsis than late sepsis. These findings suggest maternal risk factors might have contributed to *Pseudomonas* infections among neonates. However, the study could not establish a causal link between

specific environmental and maternal factors in either early or late sepsis. In addition to *E. coli*, *Klebsiella* spp, *Proteus* spp, *Salmonella* spp, and *Streptococcus* spp were also associated with neonatal sepsis. The current findings emphasize the need for further research to determine and assess the risk factors for neonatal sepsis.

The study findings revealed that most gram-positive and gram-negative bacteria isolates from blood and swab samples were susceptible to Amikacin, Norfloxacin, Ofloxacin, and Ciprofloxacin. The infrequent use of these antibiotics, considered second or third-line drugs for neonatal sepsis treatment, may explain the lack of antibiotic resistance. *Staphylococcus aureus* isolates from this study exhibited high resistance to Ampiclox and erythromycin, along with moderate resistance to Clo-Trimoxazole, consistent with similar findings at Muhimbili Hospital in Tanzania (Mhada et al. 2012). Erythromycin resistance by *S. aureus* has also been reported in Uganda, where 72.4% of all Staphylococci tested were resistant (Tumuhamye et al. 2020). The increasing antibiotic resistance among gram-positive bacteria challenges the standard protocol for neonatal sepsis treatment that relies on these drugs in the current setting.

On the other hand, gram-negative bacteria displayed high sensitivity to Amikacin, Cephalexin, Norfloxacin, Ofloxacin, and Ciprofloxacin, which might be due to their limited use, reserved for neonates with multidrug-resistant sepsis strains. Despite the observed sensitivities, most gram-negative bacterial isolates in this study resisted Ampiclox, a common antibiotic for bacterial infections in this setting. Additionally, *Klebsiella*, *Citrobacter*, *E. coli*, and *Enterobacter* demonstrated resistance to Ceftriaxone, consistent with previous research indicating widespread Ampicillin, Cloxacillin, Erythromycin, and Ceftriaxone resistance among bacteria (Amir et al. 2015, Tumuhamye et al. 2020, Shehab et al. 2015, Kayange et al. 2010). These observations emphasize the need for routine susceptibility tests to reassess the use of these antibiotics in neonatal sepsis treatment.

In contrast to other studies in Tanzania and various countries, the findings from this setting showed low resistance to Gentamycin, ranging from 0 to 17%. Conversely, a study in a tertiary hospital in India found up to a 70% Gentamycin resistance rate among gram-negative bacteria (Shah et al. 2016). The median percentage of antimicrobial resistance for gram-negative bacteria in neonates in low- and low-middle-income countries in Africa and Asia varied widely, indicating that resistance patterns to specific antibiotics differ from one setting to another. Therefore, the judicious use of Gentamycin in this setting remains recommended.

Mortality due to gram-negative bacterial infections exceeded those due to gram-positive infections. This is in line with findings in other Tanzanian hospitals (Kayange et al. 2010, Mhada et al. 2012) but in contrast with studies by Tumuhamye et al. (2020) where gram-positive bacteria were associated with more fatalities than gram-negative bacteria. Gram-negative bacteria's higher mortality rate can be attributed to their primary role in inducing a potent systemic inflammatory response, resulting in multiple organ dysfunction and a more severe form of sepsis. This

necessitates early detection and reduction of risk factors associated with neonatal sepsis.

Conclusion

Late-onset newborn sepsis outnumbers early-onset cases in Morogoro hospitals, indicating poor neonatal care and the urgent need for improved standards. The most common pathogens identified in neonatal sepsis cases were *E. coli, S. aureus*, and *Citrobacter* spp, with *E. coli* being the predominant bacterium. Notably, there was an unexpected increase in cases of neonatal sepsis caused by *Pseudomonas* spp., which is typically infrequent in causing blood infections. Gram-positive bacteria, particularly *S. aureus*, were resistant to common antibiotics like Ampiclox and Erythromycin. Gram-negative bacteria were more sensitive to Amikacin, Cephalexin, Norfloxacin, Ofloxacin, and Ciprofloxacin but showed Ampiclox and Ceftriaxone resistance. Gram-negative bacteria-induced newborn sepsis with a higher fatality rate than gram-positive bacteria. This study underscores the critical need for improved neonatal care, increased awareness of antibiotic resistance, and the importance of tailored antibiotic treatment regimens to combat neonatal sepsis effectively. The findings stressed the significance of frequent susceptibility testing for antibiotic treatment guidance.

Conflict of Interest

All authors declare that they have no conflicts of interest that could potentially influence the integrity, objectivity, or credibility of the research findings presented in this paper.

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Patterns of head and neck lesions among HIV/AIDS patients on highly active antiretroviral therapy at Dodoma Regional Referral Hospital in Tanzania

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Abstract
Introduction: Head and neck lesions associated with Human Immunodeficiency Virus are considered to occur in over 50% of HIV- positive patients and occur in nearly 80% of all patients with acquired immunodeficiency syndrome. The introduction of highly active antiretroviral therapy has led to a remarkable reduction in the global burden of such lesions. Suppose such lesions are undiagnosed or untreated on a prompt basis. In that case, they may cause morbidity and mortality since some lesions, for example, head and neck cancers may interfere with vital functions of life such as respiration, deglutition, and speech. This study determined head and neck lesions among HIV/AIDS patients in Tanzania.
Methods: This was a hospital-based descriptive cross-sectional study that recruited 222 HIV/AIDS patients at a care and treatment clinic at Dodoma Regional Referral Hospital. Physical examination and laboratory investigations (histopathology, viral load and CD4 counts) were collected and data was analyzed using Statistical Package for Social Sciences (SPSS) version 23. P-value<0.05 was statistically significant.
Results: Of all the 222 patients recruited in this study, 26 (11.7%) had head and neck lesions. Most patients with head and neck lesions were females (57.6%). Half of the patients (50.0%) were between 40 and 59 years old. About 21 (80.8%) patients were diagnosed with HIV/AIDS within two years, and 22 (84.6%) were initially diagnosed with CD4 counts less than 200 cells/μL. The most common head and neck lesion was oral candidiasis (46.2%) and others were cervicofacial lymphadenitis (15.4%), head and neck squamous cell carcinoma (laryngeal and hypopharyngeal) (11.5%), sinonasal Kaposi's sarcoma (7.7%), odontogenic abscess (7.7%) and aphthous ulcers (7.7%) and the least encountered head and neck lesion was a ranula in 3.8% of patients. Similarly, a significant association was found between the occurrence of head and neck lesions with viral load, CD4 counts, duration since a patient was diagnosed with HIV/AIDS, presence of comorbid illness, alcohol consumption and cigarette smoking.
Conclusions: The prevalence of head and neck lesions among HIV/AIDS patients on HAART was low. Females outnumbered males in terms of being affected by head and neck lesions. Oral candidiasis was the most common head and neck lesion. Head and neck (laryngeal and hypopharyngeal) squamous cell carcinoma was the predominant subtype of malignant lesions in HIV/AIDS patients on HAART.

Keywords: Patterns; head and neck; lesions; HIV; AIDS; Tanzania

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Introduction

Head and neck lesions (H&N) occur more commonly in HIV-infected individuals and can predict the progression of HIV infection to AIDS (Masele et al., 2020). Regarding infection, oral candidiasis is the most common oral manifestation of AIDS with a prevalence of more than 70% among all head and neck lesions. Kaposi's sarcoma and non-Hodgkin's lymphoma have been classified as AIDS-related malignancies. However, with the introduction of highly active antiretroviral therapy (HAART), there has been a global reduction in the burden of head and neck lesions in adults and children (Tefera et al., 2019).

The introduction and recommendation of treatment for HIV/AIDS in the form of Antiretroviral Therapy especially combination therapy commonly known as Highly Active Antiretroviral Therapy, at least three antiviral drugs two of them are Nucleoside Reverse Transcriptase Inhibitors (NRTIs) with either a protease inhibitor or a Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) have decreased the occurrence of head and neck lesions. They also help decrease viral load and increase CD4 count, which provides immunity against developing head and neck lesions (Ramirez-Crabtree et al., 2010).

In Tanzania, it was estimated that about 1.7 million people were living with HIV/AIDS (PLWH) with annual new HIV infections projected to be 68,000 cases(*UNAIDS Data 2021*).

HIV/AIDS has been the most typical cause of immunosuppression globally thus predisposing affected individuals to various diseases including head and neck cancers which are sometimes deleterious as they may interfere with vital functions of life such as respiration, phonation, and deglutition (Masele et al.,2020; Abraham et al., 2020; Abraham et al., 2018).

Another study from India found the following oral lesions in patients with HIV/AIDS; pseudomembranous candidiasis (34.6%), erythematous candidiasis (15.4%), oral herpes (13.5%), oral hairy leukoplakia (7.7%), gingivitis (15.4%), hyperpigmentation (17.3%) and dry mouth (23.1%) (Rajan & Kannan, 2019).

A study done in Dar es Salaam at a counselling and treatment centre showed that 29% of the participants had at least one oral lesion associated with HIV/AIDS where 11.5% was herpes simplex, 7.5% for oral candidiasis, 4% for oral hairy leukoplakia, 3.5% for Kaposi's sarcoma and 0.5% for angular cheilitis (Mwangosi & Tillya, 2012).

A study that was conducted in the Department of Oral and Maxillofacial Surgery at Muhimbili National Hospital in Tanzania found the following oral lesions; oral candidiasis (25.5%), osteomyelitis of the jaw (5.5%), odontogenic abscess (3.6%), oropharyngeal squamous cell carcinoma (14.5%), aphthous ulcers (3.6%), ranula (3.6%). Other head and neck lesions in HIV/AIDS patients in this study included Kaposi's sarcoma (10.9%), non-Hodgkin lymphoma (10.9%), mucoepidermoid carcinoma (3.6%), fibrosarcoma (1.8%), osteomyelitis of the jaw (5.5%), cervicofacial lymphadenitis (9.1%), ossifying fibroma (1.8%) and lipoma (1.8%) (Masele et al., 2020). On the other hand, a study done at the same national hospital in the department of otorhinolaryngology found the following sinonasal lesions; adenoid hypertrophy (1.5%), nasopharyngeal cancer (2.3%) and sinonasal cancer (3.8%). Other head and neck lesions included chronic suppurative otitis media (22.1%) and necrotizing otitis externa (2.3%) (Swai, 2011).

A study done in Tanzania found HIV/AIDS patients to be at an increased risk of developing various viral-induced cancers, including Kaposi's sarcoma, Burkitt's lymphoma, and primary central nervous system lymphoma. Kaposi's sarcoma was the most common cancer, occurring in 10% to 20% of people with HIV/AIDS. The second-most common cancer is lymphoma, which is the cause of death in nearly 16% of people with

AIDS and is the initial sign of AIDS in 3% to 4% of people living with HIV/AIDS. Both cancers are associated with Human Herpesvirus 8 (HHV-8) (Kapesa et al., 2018).

A study from Northwestern Tanzania at Kilimanjaro Medical Christian Centre, which is the largest zonal hospital in the Western zone, found the following ontological lesions: chronic suppurative otitis media (3%) and otitis externa (1%), adenoid hypertrophy (1%) (Shija et al., 2020).

Determining head and neck lesions in patients with HIV/AIDS is of paramount importance since prompt diagnosis and consequent management of such lesions have a remarkable role in improving the quality of life of HIV/AIDS patients. Suppose such lesions are undiagnosed or untreated on a prompt basis. In that case, they may cause significant morbidity and mortality since some lesions, for example, head and neck cancers may interfere with vital functions of life such as respiration, deglutition, and speech. (Abraham et al., 2018; Abraham et al., 2020)

So far head and neck lesions among patients with HIV/AIDS on HAART have not been adequately studied. Thus, this study aimed to address such an existing gap by determining the prevalence and characterization of head and neck lesions among HIV/AIDS patients on HAART attending the care and treatment clinic at Dodoma Regional Referral Hospital.

Methods
Study design and study duration.
It was a hospital-based cross-sectional study underpinned with a quantitative approach to determine the patterns of head and neck lesions among HIV/AIDS patients on HAART attending the care and treatment clinic (CTC) at Dodoma Regional Referral Hospital. Data was collected from November 2022 to March 2023.

Sampling technique, sample size and study population
Consecutive sampling techniques were utilized to recruit two hundred and twenty-two patients upon consenting to participate. In this sampling technique, every subject who met the inclusion criteria was selected until the desired sample size was achieved. The study population was patients aged 1-69 years.

The study sample size was estimated using Kish Leslie formula (1965) for a cross-sectional study considering the proportion of HIV/AIDS patients with head and neck lesions as 15.9% in a study that was conducted at Muhimbili National Hospital, Tanzania (Masele et al., 2020). The minimum sample size was 205 participants; considering the 5% non-response rate, we obtained a sample of 228 participants though only 222 were recruited in this study.

Inclusion criteria
HIV/AIDS patients on HAART attended care and treatment clinics and consented to participate.

Exclusion criteria
Those who were mentally unfit to consent to participation and those aged under 18 years whose caregivers/parents were not ready to consent on their behalf so that they could be recruited.

Recruitment methods
The principal investigator was positioned at the selected CTC, and patients attended on an outpatient basis were selected until the desired sample size of 222 patients was attained.

Data collection tools
A structured questionnaire adapted from previously published studies and modified to fit the current study was used to collect data (Masele et al., 2020; Shija et al., 2020). The first version was prepared in English and the final draft was translated to Swahili since the study participants in the chosen study area were more conversant with Kiswahili. The questionnaire comprised the following parts:

(i) Socio-demographic characteristics of study participants, (ii) Information on HIV/AIDS status and associated factors, and (iii) Occurrence of head and neck lesions among HIV/AIDS patients on HAART. The questionnaire comprised both open and closed-ended questions. When participants encountered difficulties interpreting the set questions the principal investigator assisted them. The procedure included self-introduction by the principal researcher, introduction of the topic and purpose of the study. The researcher then requested their participation in the study. Participants were assured of free participation and withdrawal from the study at any time if they wished to do so. Validity was ensured by reviewing the literature and pilot testing the instrument prior to the study by involving 10% of the sample size from the health facility and those excluded during the commencement of actual data collection.

Measurement of variables

Dependent variables: The dependent variable for the study was (i) Head and neck lesions among HIV/AIDS patients on HAART.

Independent variables: The independent variables for the study were the socio-demographic characteristics and HIV/AIDS status of the study participants.

Data processing and analysis

Results

Socio-demographic characteristics and disease duration profile of the study participants

222 patients were recruited in this study, most of whom were from urban areas (n=128,57.7%) while those from rural areas were (n=94,42.3%). Females (n=122, 55.0%) predominated the study than males (n=100,45.0%) with a male-to-female ratio of 1:2.5. Over 86% (n=191) of the patients were aged between 20 and 59 years and the last age

The collected data were cleaned and analyzed using the SPSS version 23 software package. Categorical variables were expressed as frequencies and proportions, continuous variables as means, and standard mean error. The Chi-square test was used to ascertain the association between independent (socio-demographic characteristics and HIV/AIDS status of the study participants) and dependent factors (occurrence of head and neck lesions). All the independent variables with p-values <0.05 were considered statistically significant.

Ethical considerations

The Directorate of Research, Publication and Consultancy of the University of Dodoma approved ethical clearance dated 26th September 2022, with an approval number MA.84/261/02/. Furthermore, permission to collect data at the selected health facility was obtained from the District Medical Officer. Both verbal and written individual informed consent was obtained from the study participants after they were fully informed about the study goals and the involved process. Participants were assured privacy and confidentiality. Anonymity was maintained using code numbers on the questionnaire instead of the participant's name. The participant had absolute freedom and the right to withdraw from the study anytime.

group was of <20 years (n=11,5%) with the mean age of 40.94 years. Most (n=119, 56.3%) of the patients were self-employed and about (n=50,22.5%) had no employment. Also, most participants had a primary level of education (n=72,32.4%), and only (n=34, 19.3%) had a university/college level of education. More than half of them (n=140,63.1%) were married. About 55.9% (n=124) were diagnosed with HIV/AIDS for less than two years by the time of the study. More than half of the participants (n=171,79.7%) were initially diagnosed to have

CD4 counts of more than 200 cells/µL, and also 92,3%(n=205) had a viral load of more than 1000 copies at diagnosis. **(Table 1)**

Table 1: Socio-demographic characteristics of the participants and disease duration profile (N= 222)

	Sub variable	**Frequency/n (%)**
Gender	Male	100 (45.0)
	Female	122 (55.0)
Age (years)	0-19	11 (5.0)
	20-39	95 (42.8)
	40-59	96 (43.2)
	60-79	20 (9.0)
Marital status	Married,	140 (63.1)
	Widowed,	23 (10.4)
	Divorced,	11 (5.0)
	Cohabiting	5 (2.3)
	Single	38 (17.1)
	Others	5 (2.3)
Educational level	Non-formal	47 (21.2)
	Primary	72 (32.4)
	Secondary	69 (31.1)
	University/college	34 (19.3)
Occupation	Employed	53 (23.9)
	Self employed	119 (53.6)
	Unemployed	50 (22.5)
Residence	Urban area	128 (57.7)
	Rural area	94 (42.3)
Duration since being diagnosed to have HIV/AIDS (years)	>2	98 (44.1)
	<2	124 (55.9)
CD4 count when diagnosed to have HIV/AIDS (cells/µL)	>200	177 (79.7)
	<200	45 (20.3)
Viral load when diagnosed with HIV/AIDS	>1000	205 (92.3)
	<1000	17 (7.7)

Prevalence of head and neck lesions, socio-demographic characteristics, and disease duration profile of HIV/AIDS patients on HAART and with head and neck lesions

A total of 26 (11.7%) patients had head and neck lesions. **(Figure 1)** Among patients with head and neck lesions, 15 females (57.6%) had H&N lesions than 11 males (42.4%). Half of them, 13 (50%), were aged 40 to 59 years, with the less affected age group being 0 to 19 years, 2 (7. 7%). On the other hand, 15 (57.7%) of the patients with H&N were from rural areas, and 13 (50%) had partners. On the other hand, 21 (80.8%) of the patients with H&N lesions were diagnosed to have HIV/AIDS within two years by the time the study was conducted, and 22 (84.6%) patients were initially diagnosed to have CD4 counts less than 200 cells/μL. **(Table 2)**

Figure 1: Prevalence of head and neck lesions among HIV/AIDS patients on HAART

HIV/AIDS patients without head and neck lesions
HIV/AIDS patients with head and neck lesions
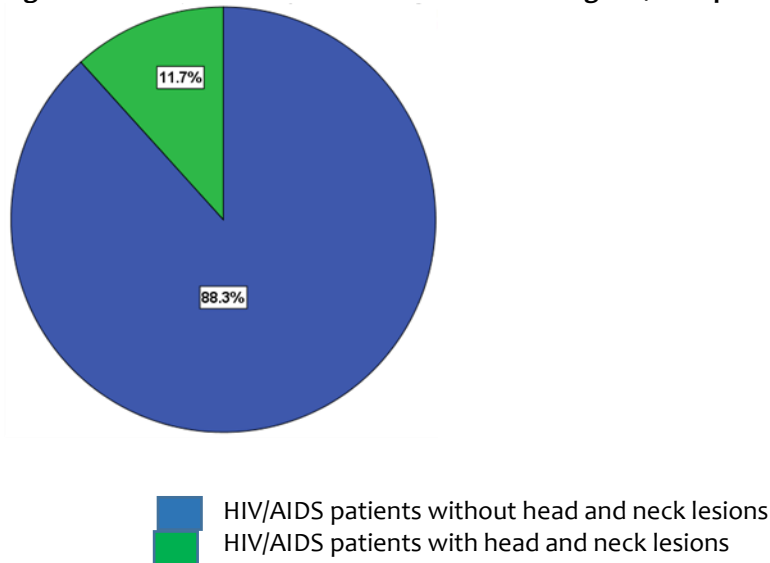
Table 2: Socio-demographic characteristics and disease duration profile of HIV/AIDS patients with head and neck lesions and on HAART, (N=26)

Variable	Sub- variable	Frequency, n(%)
Sex	Female	15 (57.6)
	Male	11 (42.4)
Age (years)	0-19	2 (7.7)
	20-39	7 (26.9)
	40-59	13 (50.0)
	60-79	4 (15.4)
Residence	Urban area	11 (42.3)
	Rural area	15 (57.7)
Marital status	With partner	13 (50.0)
	Without partner	13 (50.0)
Duration since diagnosis of HIV/AIDS (years)	>2	5 (19.2)
	<2	21 (80,8)
CD4 count when diagnosed with HIV/AIDS (cells/μL)	<200	22 (84.6)
	>200	4 (15.4)

Anatomical location for head and neck lesions and their specified aetiology among HIV/AIDS patients on HAART

About 20 (77%) of head and neck lesions were found in the mouth/oral cavity, 5 (19.2%) around the neck and 1 (3.8%) lesion was found in the oropharynx. There were 14 (53.8%) patients

with infectious processes as the predominant specified aetiology for head and neck lesions, 5 (19.3%) had malignant lesions, 5 (19.3%) had inflammatory lesions, and 1 (3.8%) had benign lesions. **(Table 3)**

Table 3: Anatomical location for head and neck lesions and their specified aetiology among HIV/AIDS patients on HAART, N=26

Anatomical location for the lesion	Frequency, n (%)	Specified aetiology for head and neck lesions	Frequency, n (%)
Oral cavity (mouth) Neck(larynx+hypopharynx) Oropharynx	20 (77) 5 (19.2) 1 (3.8)	Infectious process Malignant lesions Inflammatory conditions Benign lesions Others	14 (53.8) 5 (19.3) 5 (19.3) 1 (3.8) 1 (3.8)
Total	26 (100)		
		Total	26 (100)

Specific head and neck lesions among HIV/AIDS patients on HAART

Regarding specific head and neck lesions among HIV/AIDS patients on HAART, 12 (46.2%) patients had oral candidiasis, and it was the predominant head and neck lesion, and the least encountered lesion was ranula and was found in 1 (3.8%) patient. **(Table 4).**

Table 4: Specific head and neck lesions among HIV/AIDS patients on HAART, N=26

Specific head and neck lesions	Frequency, n (%)
Oral candidiasis	12 (46.2)
Cervicofacial lymphadenitis	4 (15.4)
Head and neck squamous cell carcinoma (larynx+hypopharynx)	3 (11.5)
Sinonasal Kaposi's sarcoma	2 (7.7)
Odontogenic abscess	2 (7.7)
Aphthous ulcers	2 (7.7)
Ranula	1 (3.8)

The association between occurrence of head and neck lesions and socio-demographic characteristics of HIV/AIDS patients on HAART

There is a statistically significant association between the occurrence of head and neck lesions and some socio-demographic characteristics of the study participants, such as level of education (P value=0.000) and occupation (P=0.026). On the other hand, there was no statistically significant association between the occurrence of head and neck lesions and patients' age, gender, marital status and type of residence (p-value>0.05) **(Table 5).**

Table 5: Association between sociodemographic characteristics and occurrence of head and neck lesions among HIV/AIDS patients on HAART

Variable	Sub-variables	Occurrence of H&N lesions		p-value
		No (n=196) (%)	Yes (n=26) (%)	

Gender	Female	107 (87.7)	15 (12.3)	0.765
	Male	89 (89.0)	11 (11.0)	
Age (years)	0-19	9 (81.8)	2 (18.2)	
	20-39	89 (90.6)	7 (9.4)	
	40-59	82 (86.3)	13 (13.7)	0.267
	60-79	16 (80.0)	4 (20.0)	
Marital status	Married	127 (90.7)	13 (9.3)	0.555
	Widowed	19 (82.6)	4 (17.3)	
	Divorced	9 (81.8)	2 (18.2)	
	Cohabiting	5 (100.0)	0 (0.0)	
	Single	32 (84.2)	6 (15.8)	
	Others	4 (80.0)	1 (20.0)	
Level of education	Non-formal	36 (76.6)	11 (23.4)	0.000
	Primary	60 (83.3)	12 (16.3)	
	Secondary	66 (95.7)	3 (4.3)	
	University/college	34 (100)	0 (0.0)	
	Self-employed	103(86.6)	16 (13.4)	
	Unemployed	41(82.0)	9(18)	
Residence	Urban	117(69.4)	11(30.6)	0.092
	Rural	79(81.8)	15 (18.2)	

Association between the occurrence of head and neck lesions and associated factors among HIV/AIDS patients on HAART

There was a statistically significant association between the occurrence of head and neck lesions and various associated factors. Among the factors is the CD4 count of HIV/AIDS patients on diagnosis with (a p-value of 0.000). Another association of significance was the duration since being diagnosed with HIV/AIDS (p-value of 0.005), which mainly occurred in those diagnosed with HIV/AIDS in less than two years by the time the study was conducted. Other factors associated were viral load on diagnosis, alcohol consumption, cigarette smoking and frequency of using ARTs (P-values < 0.05) **(Table 6)**

Table 6: Association between the occurrence of head and neck lesions and other associated factors among HIV/AIDS patients

Variable	Sub-variables	Occurrence of H&N lesions		p-value
		No(n=196) (%)	Yes(n=26)(%)	

CD4 count on diagnosis of HIV/AIDS (cells/μL)	<200 >200	23 (51.1) 173 (97.7)	22 (48.9) 4 2.3)	0.000
Duration since being diagnosed with HIV/AIDS (years)	<2 >2	103 (83.0) 93 (94.9)	21 (17.0) 5 (5.1)	0.0 5
Viral load on diagnosis of HIV/AIDS	<1000 >1000	192 (93.7) 4 (23.5)	13 (6.3) 13 (76.5)	0.000
Presence of other comorbid illness/chronic illness	No Yes	181 (91.4) 15 (62.5)	17 (8.6) 9 (37.5)	0.000
Alcohol consumption	No Yes	151 (96.2) 45 (69.2)	6 (3.8) 20 (30.8)	0.000
Cigarette smoking	No Yes	181 (90.5) 15 (68.2)	19 (9.5) 7 (31.8)	0.002
Having treatment partner	No Yes	12 (66.7) 184 (90.2)	6 (33.3) 20 (9.8)	0.009
Frequency of using ART	Everyday Some days	167 (94.4) 29 (64.4)	10 (5.6) 16 (35.6)	0.000

Discussion

Head and neck lesions are commonly encountered in HIV/AIDS patients and the advent of HAART is expected to reduce the burden and manifestation of such lesions. Data remains scarce on whether patients with HIV/AIDS on HAART remain susceptible to head and neck lesions. There is not any study on head and neck lesions that has been conducted in central Tanzania despite the significant number of HIV/AIDS patients attending various care and treatment clinics to receive ARTs. This study aimed to address such a gap by being the first study of its type in central Tanzania.

In this study, most participants were females (55%) aged between 1 and 69. Most participants (86%) were aged 20 to 59 years. These findings were like those reported in the study from Tanzania in which 71.1% of participants were females and over 92.5% were aged between 20 to 59 years (Masele et al., 2020). The mean age of patients was 40.94 years, higher than reported in Nigeria, where the mean age was 35 (Eweka et al., 2012). Another study from Kenya reported the mean age of participants being 37 years (Butt et al., 2008). The similarity in the findings may be due to the same study design utilized in the studies under comparison.

In our study, 11.7% of patients with HIV/AIDS had lesions in the head and neck region. These findings were much lower than what was depicted in a study done in Tanzania where the prevalence was 16% (Masele et al., 2020); in Kenya, the reported prevalence of head and neck lesions was 27% (Butt et al., 2008) and

another study that was conducted in Venezuela reported 85% of the study participants to be affected by head and neck lesions (Bravo et al., 2006). The lower prevalence of head and neck lesions among HIV/AIDS patients in this study may be due to the use of HAART by our study participants, which provides the benefit of decreasing plasma viral load and increasing CD4 counts, thus reducing the prevalence of head and neck lesions.

Most of the participants in this study with head and neck lesions (86.4%) and considerably low CD4 counts (less than 200 cells/µL) were more susceptible to developing head and neck lesions than those with CD4 counts greater than 200 cells/µL. These findings were like those from the study done in Tanzania where more than 60% of patients with head and neck lesions had CD4 count <200 cells/µL (Masele et al., 2020). On the other hand, these findings were contrary to those reported in a study from Iran, which reported 95% of the lesions to have occurred in participants with a CD4 count of less than 350 cells/µl (Saravani et al., 2017). Patients with such lower CD4 counts are severely immune-compromised, and thus, there is an increased risk and severity of opportunistic infections and AIDS-defining malignancies (Cobucci et al., 2015).

About the anatomical location of head and neck lesions among HIV/AIDS patients on HAART, the most standard site noted in this study was the oral cavity/mouth in about 77% of the study participants and this was similar to what has been reported in the study conducted in Ghana where the mouth/oral cavity was the most everyday involved site in 48.2% of the cases (Opoku-Buabeng & Dompreh, 2012) contrary to another study conducted in Europe which reported the most familiar location to be the oropharynx in 19.38% of cases (Haase et al.,2021).
On the other hand, about 53.7% of the lesions in patients recruited in this study were of

infectious cause. These findings were dissimilar to those from another study in Tanzania, where the typical group of head and neck lesions was the malignant process in 44.8% of cases (Masele et al., 2020).

The most common lesion in this study was oral candidiasis occurring in 46.2% of the patients with head and neck lesions and was also observed in 84.6% of patients with CD4 counts <200 cells/µL. The above study findings were similar to a study done in Tanzania, whereby 78% had oral candidiasis (Masele et al., 2020) and also similar to another study conducted in Iran that reported the most joint lesions to be oral candidiasis by 48% (Saravani et al., 2017). Similar findings can be depicted from the study done in Nigeria that reported about 47.7% of participants had oral candidiasis, which was the typical lesion (Eweka et al., 2012). Such resemblance in the studies under comparison may be because oral candidiasis is one of the most common opportunistic infections associated with HIV infection, whose manifestations are related to the depressed level of immunity (Qanche et al., 2021).

The most common head and neck malignancy in this study was head and neck squamous cell carcinoma (11.5%), which does not belong to the group of AIDS-defining illnesses that includes Kaposi's sarcoma (Cobucci et al., 2015). This has been linked to low immunity (immunosuppression) in the patients. Also, it can be explained by the role played by Human Papillomavirus (HPV) in causing HNSCC since its prevalence is increased in patients with HIV/ AIDS (Beachler & D'Souza, 2013). However, the above findings were similar to those from the study done in America, where about 50% of patients with HIV/AIDS had head and neck squamous cell carcinoma, and the typical site was the oropharynx (Haase et al., 2021).

Dissimilar findings can be depicted from the study done in New York where Kaposi's sarcoma was the most familiar head

and neck cancer in 49.7% of cases (Singh, 1999) and another study in Kenya which reported Kaposi's sarcoma to be the most joint head and neck cancer in 68% of studied patients (Butt et al., 2008). Such similarity may be due to Human herpesvirus-8 (HHV-8) being the most ordinarily implicated virus in cancer causation in immunocompromised patients. It has been reported that oral, craniofacial and cutaneous manifestations of AIDS-related Kaposi's sarcoma are relatively common, occurring in around 20% of patients affected by the disease (Agaimy et al., 2017). This is contrary to the findings from this study, which found that the prevalence of KS was relatively low (7.7%). The low prevalence of KS in this study may be attributed to the use of HAART, as randomized clinical trials have shown a protective effect of HAART against the development of KS, even in patients with relatively low immune status (Hoffman et al., 2017).

Moreover, several factors were reported to be associated with the occurrence of head and neck lesions including the duration since one is diagnosed to have HIV/AIDS. In this study from Dodoma, Tanzania, the duration since patients were diagnosed with HIV/AIDS was found to exhibit a similar relationship with the occurrence of head and neck lesions where 80.8% of these lesions occurred in those diagnosed to have HIV/AIDS in less than two years and 84.6% of the lesions occurred in those diagnosed to have CD4 counts less than 200 cells/µL and also 76.5% of the lesions occurred in patients with viral load greater than 1000 copies on diagnosis. The above findings were similar to those reported in a study from Tanzania, which reported age, CD4 count and duration since being diagnosed with HIV/AIDS were the risk factors that influence the occurrence of head and neck lesions among patients with HIV/AIDS (Masele et al., 2020). Other factors that were found to increase the occurrence of head and neck lesions in this study were the presence of comorbid illnesses such as diabetes mellitus,

alcohol consumption and cigarette smoking, frequency of ART consumption and those without treatment partners. These findings were similar to those reported in various studies which reported alcohol consumption and cigarette smoking to be fundamental in causing the severity of the disease (Mmbaga, 2013) and also similar to what was reported in a study from China which reported the presence of comorbid illnesses like diabetes mellitus to increase susceptibility to the occurrence of head and neck lesions by 76.5% (Chen et al., 2015).

Regarding the study limitation, the study was conducted at a single health facility, and therefore, results cannot be generalizable to HIV/AIDS patients countrywide.

Conclusion
The prevalence of head and neck lesions among HIV/AIDS patients on HAART in this study was low. The low prevalence may have been attributed to the use of highly active antiretroviral therapy by all the study participants, which decreased plasma viral load and increased plasma CD4 counts. Oral candidiasis was the most joint head and neck lesions that belonged to the group of opportunistic infections and was in line with what was expected among patients with remarkably lower CD4 counts and higher viral load since most patients with head and neck lesions had CD4 levels below 200 cells/µL and viral load of greater than 1000copies. Pertaining head and neck cancers, head, and neck squamous cell carcinoma (laryngeal and hypopharyngeal cancers) was the predominant subtype of the malignant lesions. On the other hand, a significant association was found between the occurrence of head and neck lesions with viral load, CD4 counts, duration since a patient was diagnosed with HIV/AIDS, presence of comorbid illness, alcohol consumption and cigarette smoking.

Authors' contributions

ZSA, IYD and AAK contributed to the conceptualization, data collection, and analysis study. ZSA, IYD and AAK were involved in manuscript preparation. ZSA and AAK profoundly reviewed the manuscript.

Declaration of competing interests

The authors declare no further conflicts of interest.

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Maternal Psychosocial care and Child feeding practices

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Abstract
Introduction: Psychosocial care is the process by which caregivers meet the needs of infants in terms of adequate nutrition, emotional, social, mental, and healthcare to promote healthy growth and development. This study, therefore, aimed to assess the influence of psychosocial care during complementary feeding among mothers.
Methodology: It was a cross-sectional design, and the sample size was statistically calculated to arrive at 385 mothers. A structured and self-administered questionnaire collected information on socio-economic status and psychosocial care during complementary feeding practices. WHO feeding indicators were used to assess the feeding practices of the mothers. Data were analysed using both descriptive statistics and inferential statistics.
Results: The study showed that 52.1% of respondents were between 20 and 29 years old, 88.1% were married, and others were single or divorced mothers. The feeding indicator showed that 21.5% of respondents met the Minimum Adequate Diet. Half of the respondents (50%) monitored the amount of food consumed by the children, while 12.4% encouraged the children to finish the food served. There was an insignificant relationship between maternal psychosocial care and complementary feeding practices ($\chi2$; p>0.05), whereas there was a significant association between maternal psychosocial care and maternal age (χ^2; $p=0.043$) as well as religion (χ^2; $p=0.031$).
Conclusion: The study concluded that mothers who had advanced in age had better maternal psychosocial care during complementary feeding than the younger mothers. Therefore, maternal nutrition education on complementary feeding and care during infants' feeding should be encouraged during antenatal and post-natal clinics.

Keywords: Infant, Complementary feeding, Maternal, Psychosocial care, Nutrition Education

Introduction

Good complementary feeding knowledge and practices among mothers of under-five children would prevent the consequences of undernutrition, enabling average growth and cognitive development in children. Lack of adequate nutrition and poor psychosocial care among mothers has been identified as the main factors responsible for Severe-Acute-Malnutrition (SAM) in children (Mahmoodianfard & Haghighat, 2021). The average growth and development of infants and young children require care that adequately meets their basic physical needs, such as nutrition, health, clothing, and socio-emotional or psychological needs (Engle& Ricciuti, 1995).

The psychosocial care that meets these needs includes the caregiver's responsiveness and sensitivity, affection and warmth, psychological involvement with the child, and encouragement of learning and development.

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Psychosocial care is defined as a process by which caregivers (mothers, siblings, fathers and childcare providers) meet the needs of infants in terms of adequate nutrition, emotional, social, mental and healthcare for promoting healthy growth and development (Ogunba, 2010). Appropriate psychosocial care exhibited by nursing mothers during complementary feeding periods usually goes a long way to improve the nutritional and health well-being of weaning-aged children.

In order to improve complementary feeding among infants, psychosocial care during the period of complementary feeding must be carefully handled and taken into account (Barrett *et al.*, 2016). Hence, maternal psychosocial factors impact feeding during the complementary feeding period, necessitating intensive psychological care (UNICEF, 2022a). Maternal psychosocial care integrates the availability of food and medical resources into the well-being of a child (WHO, 2020). It is not only about the procedures but also about how psychosocial treatment is delivered. In order to promote the growth and development of children, this should be done with love and consideration for the children (Huynh *et al.*, 2019). Adequate nutrition and wellness of infants may be influenced by the mother's psychosocial care, according to the report of Nagel*et al.* (2022).

Mothers' feeding techniques that incorporate the principles of psychosocial care come in third among the eight principles governing complementary feeding of children (WHO, 2021). Caregiving behaviours have been found to promote development and growth (LaVela *et al.*, 2021). Various psychological elements affect how well infants consume food and thrive during the period of complementary feeding, and these include feeding the young child actively or interactively as opposed to passively presenting food to the children (Shoup, 2018); choosing foods that are appropriate for their developing motor skills and taste preferences (DeJesus, 2022); feeding in response to their hunger cues (USDA, 2021); and feeding in a distract-free, safe environment (Delacey *et al.*, 2022). The children's development is facilitated by feeding in a calm, secure setting, conversing, and playing with the infant while eating (Hu *et al.*, 2021).

Several studies on infant and child feeding have discovered that maternal psychological traits may affect the results of feeding styles. Despite the importance of psychosocial care during infant feeding, little is known about this among nursing mothers of under-five children in Ogun State; hence, this study aimed to determine complementary feeding practices and psychosocial care levels of nursing mothers of under-five children in Ogun State.

Materials and methods
Study location.
The study location was the Basic Health Centres (BHCs) in Ifo Local Government Area in Ogun State, Nigeria. Ifo Local Government Area has its headquarters in Ifo town with an area of 521 km² (201 sq.m) and a population of 698,837 at the 2019 National Population Commission (NPC) [Nigeria] and ICF. 2019.

Results
Socio-Demographic and Economic Characteristics of the Respondents
The socio-demographic characteristics of the respondents, as indicated in Table 1, showed that the highest proportion (50.9%) were within the age range of 20 to 29 years. The marital status of respondents showed that a large proportion of the nursing mothers were living together with their husbands, while the remaining were either separated or single parents. The educational background of the nursing mothers indicated that three-quarters of the nursing mothers had elementary and secondary school education, while 22.1% and 7.8% attained tertiary and no formal education, respectively.

Table 1: Socio-Demographic and Economic Characteristics of the Respondents

Variables	Frequency (385)	Percentage (%)
Age (years)		
<20	6	1.6
20-29	196	50.9
30-39	154	40.0
40-49	29	7.5
Marital Status		
Single	40	10.4
Married	322	83.6
Divorced	21	5.5
Religion		
Christianity	224	58.2
Islam	141	36.6
Traditional	12	3.1
Others	8	2.1
Ethnicity		
Hausa	40	10.4
Ibo	70	18.2
Yoruba	265	68.8
Others	10	2.6
Level of Education		
Primary	117	30.4
Secondary	153	39.7
Tertiary	85	22.1
None	30	7.8
Occupation		
Full Housewife	77	20.0
Business	199	51.7
Civil Servant	49	12.7
Artisans	57	14.8
None	3	0.8

Psychosocial Care Practices of Respondents in Complementary Feeding

The psychosocial care practice of nursing mothers during complementary feeding of infants is presented in Table 2. In Table 2, mothers were concerned about how much their children ate from the meals served. According to this study, mothers experimented with various foods when their children refused to eat. This was done to determine which foods would be the most acceptable by the children and encourage the children to eat more. The present study established that most nursing mothers did not make their children's meals more colourful or serve them on colourful plates that were attractive to children. Besides, many force-feed their children instead of encouraging them to complete their meals.

Table 2: Psychosocial Care Practices of Respondents in Complementary Feeding

Variables	Never(%)	Seldom (%)	Often (%)	Always (%)
Interacting with the child during meal	114(29.6)	71 (18.4)	90 (23.4)	110 (28.6)
Sitting with my child while eating	69 (17.9)	85 (22.1)	58 (15.1)	173(44.9)
Not looking at child's face during meal	52 (13.5)	66 (17.1)	106 (27.5)	161 (41.8)
Eulogize the child while eating	106 (27.5)	56 (14.5)	62(16.1)	161 (41.8)
Encouraging the child to feed him/herself	144(37.4)	85 (22.1)	87 (22.6)	69 (17.9)
Feeding the child only when he/she is hungry	93(24.2)	116 (30.1)	81 (21.0)	95 (24.7)
Giving the child time to finish the food	66(17.1)	68 (17.7)	94 (24.4)	157 (40.8)
Scolding the child if s/he refuses to eat	42 (10.9)	52 (13.5)	132 (34.3)	159 (41.3)
Monitoring how much the child eat	43(11.2)	57 (14.8)	103 (26.8)	182 (47.3)
Not paying attention child's hunger cue	152 (39.5)	36 (9.4)	43 (11.2)	154(40.0)
Making sure the child is satisfied with food	42 (10.9)	49 (12.7)	98 (25.5)	196(50.9)
Force-feeding the child	93 (24.2)	79 (20.5)	58 (15.1)	155 (40.3)
Experimenting with different food and methods of encouragement	82 (21.3)	114 (29.6)	71 (18.4)	118 (30.6)
Not presenting the food in attractive plates	142 (36.9)	68 (17.7)	63 (16.4)	112(29.1)
Putting off the TV when the child is eating	130 (33.8)	104 (27.0)	83 (21.6)	68 (17.7)
Not making the food appealing and colourful	158 (41.0)	58 (15.1)	56 (14.5)	113 (29.4)

Relationship between Practices of Psychosocial care and Complementary Feeding

The relationship between practices of psychosocial care and complementary feeding practices is shown in Table 3. The result establishes no significant (p>0.05) relationship between MAD and psychosocial care in this study. For the Minimum Dietary Diversity (MDD), fewer children received the Minimum Dietary Diversity (≥ four food groups) which accounts for the lower percentage of MAD attainment in this study.

In addition, it was observed in this present study that during infants' complementary feeding, there was no significant relationship between psychological care and MDD. The nursing Mothers in this present study were observed to introduce complementary food early between the ages of 6 and 8 months to their infants. However, there was no significant (*p*>0.05) relationship between psychosocial care and the start of complementary feeding. Besides, there was no significant relationship between the mothers' psychosocial care and the MMF.

Table 3: Relationship between Practices of Psychosocial care and Complementary Feeding

Parameters	Psychosocial care Practices						P-value
	n	%	n	%	N	%	
Commencement of Complementary Feeding							
<6 months	12	3.1	12	3.1	0	0	
6-11 months	66	17.1	219	56.9	16	4.2	0.214
12-17 months	12	3.1	17	4.4	11	2.9	
18-23 months	0	0	9	2.3	11	2.9	
Minimum Dietary Diversity (MDD)							
Not met	57	20.9	203	77.4	13	4.4	0.487
Met	21	20.8	78	73.6	13	5.7	
Minimum Feeding Frequency(MFF)							
Not met	14	13.6	66	64.1	23	22.3	0.332
Met	54	19.1	216	76.6	12	4.3	
Minimum Acceptable Diet (MAD)							
Not met	58	19.1	214	78.1	22	2.7	0.525
Met	19	25.0	58	70.0	14	5.0	
Timely Introduction of Complementary Feeding							
Timely introduced	51	18.21	205	73.2	24	8.5	0.553
Not timely introduced	26	24.8	67	63.8	12	11.4	
Appropriate Complementary Feeding Practices							
Inappropriate	52	18.4	215	76.2	15	5.3	0.913
Appropriate	23	22.3	69	66.9	11	10.8	

Relationship between Socio-Demographic Characteristics and Maternal Psychosocial Care Practices

The relationship between socio-demographic characteristics and maternal psychosocial care practices, as stated in Table 4, showed that mothers' age is related to psychosocial care practices. The p-value showed a positive relationship (0.043). As the maternal age advances, there is a reduction in bad psychosocial practices. Type of religion impacted the psychosocial care provided to the children during complementary feeding (0.031). Meanwhile, marital status (p=0.96), educational level (p=0.163) and ethnicity (p=0.187) had no relationship with the

maternal psychosocial care practices of the mothers during complementary feeding.

Table 4: Relationship between Socio-Demographic Characteristics and Maternal Psychosocial Care Practices

Parameters	Psychosocial Care Practices						
	Bad		Average		Good		p-value
	N	%	N	%	N	%	
Age group							
<20	0	0	4	66.7	2	33.3	
20-29	52	26.5	142	72.4	2	1.1	0.043**
30-39	6	3.9	72	46.8	76	49.3	
40-49	1	3.1	8	27.5	20	69.0	
Marital Status							
Single	13	32.5	27	67.5	0	0	
Married	54	16.7	224	69..6	44	13.7	
Divorced	7	63.0	2	18.5	18.5	0	0.960
Separated	7	70.0	3	30.0	0	0	
Widow	0	0	0	0	0	0	
Educational Level							
Primary	30	30	85	66	2	3.8	
Secondary	19	12.4	121	79.1	13	8.4	0.163
Tertiary	8	9.4	72	84.7	5	5.9	
None	6	20.0	21	70.0	3	10.0	
Religion							
Christianity	12	5.3	179	79.9	33	14.7	
Islam	18	12.7	111	78.7	12	8.5	0.031**
Traditional	1	8.3	11	91.7	0	0	
Others	5	62.5	3	37.5	0	0	
Ethnicity							
Hausa	10	25.0	29	72.5	1	2.5	
Ibo	16	22.9	49	70.0	5	7.1	0.187
Yoruba	50	18.8	199	75.2	16	6.0	
Others	2	20.0	7	70.0	1	10.0	

* means significance at p<0.05

Discussion

The socio-demographic characteristics of the respondents, as indicated in this present study, showed that the highest proportion (50.9%) of the respondents was within the age range of 20 to 29 years, and this observation agrees with the report of Ogunba (2010). This finding implies that the reproductive age of Nigerian women is between the ages of 20 and 29. The marital status of respondents shows that a large proportion of the nursing mothers were living together with their husbands, while the remaining were either separated or single parents. The educational background of the nursing mothers indicates that three-

quarters of the nursing mothers had elementary and secondary school education, while the remaining attained tertiary (22.1%) and no formal education (7.8%).

The psychosocial care practice of nursing mothers during complementary feeding of infants showed that mothers were concerned about how much their children ate from the meal served (Table 2). According to this study, mothers experiment with various foods when their children refuse to eat. This was done to determine which foods would be the most acceptable by the children and encourage the children to eat more. The present study established that most nursing mothers did not make their children's meals more colourful or serve them on colourful plates that were attractive to children. Meanwhile, feeding the children coloured foods had the dual objectives of providing nutrition and promoting good taste (Brown, 2021). Most mothers in the study area choose to force-feed their children instead of encouraging them to complete their meals. This was in line with Akinrinmade *et al.* (2019), *who reported that the majority of mothers in Ondo State, South-West Nigeria,* force-feed their children during complementary feeding. There have been reports of mothers scolding and force-feeding their children while they are resisting eating, and this is not a proper method of feeding (Prabha, 2021). The amount of food consumed and the nutritional health of children were influenced by psychosocial care for children during complementary feeding (WHO, 2020).

The present study indicated that 26.5% of mothers aged 20-29 had bad psychosocial practices during complementary feeding. This same age group had 72.4% of the average complementary feeding practice. Meanwhile, mothers between the ages of 30 and 39 had just 3.9% of bad complementary feeding practices, and mothers between 40 and 49 had only 1% of harmful practices, according to Table 4. This shows that maternal age is related to psychosocial care practices during complementary feeding. Shagaro et al. (2021) reported that maternal

experience with previous children influences complementary feeding practices in Ethiopia. Psychosocial care during complementary feeding could enhance the food intake of infants during complementary feeding. It is well established that psychosocial care exhibited by nursing mothers or caregivers encourages adequate child food and nutrient-dense intakes, facilitating children's growth and development (Ogunba, 2010).

The mothers' psychosocial care practices are essential for establishing a Minimum Adequate Diet during complementary feeding (Bimpong *et al.,* 2020). A study (UNICEF, 2022a) reported that children's nutritional status is influenced by the quantity and quality of food intake and psychosocial care rendered by the parents or caregivers. Masuke *et al.* (2021), who examined the impact of improper complementary feeding practices in Tanzania showed poor compliance of the mothers to complementary feeding guidelines.

The relationship between maternal psychosocial care and complementary feeding practices is shown in Table 3. The result establishes no significant (*p*>0.05) relationship between MAD and psychosocial care in this study. The complementary feeding practices and psychological care during complementary feeding among the mothers in the study population might lead to a lower percentage of MAD achieved. However, fewer children received the Minimum Dietary Diversity (≥ four food groups), accounting for the lower percentage of MAD attainment in this study. A study (Samuel&Ibidapo, 2020) had previously noted this among mothers in South-West Nigeria. The main issue with mothers' complementary feeding practices in developing countries is the low rate of MAD achieved (Kang *et al.*, 2022; Kebede *et al.*, 2022). Similarly, Jacquier *et al.*, (2020) reported on the lack of variation in the complementary feeding practices of Filipino children, particularly those from low-income families.

In addition, it was observed in this present study that during infants' complementary feeding, there was no significant relationship between psychological care and MDD. This finding is similar to the report of Samuel & Ibidapo (2020) in Southwestern Nigeria, Asmare *et al.* (2020) in Northeast Ethiopia, and Ben*et al.* (2021) in Russia. It is worth noting that if mothers could provide their infants with at least four different food groups daily, MDD might be achieved (WHO, 2020). The nursing Mothers in this study were observed to introduce complementary food early, between 6 and 8 months, to their infants. However, there was no significant ($p>0.05$) relationship between psychosocial care and the start of complementary feeding. Besides, no significant relationship was observed between the mothers' psychosocial care and the MMF. The relationship between socio-demographic characteristics and maternal psychosocial care practices (Table 4) indicates that mothers' age and type of religion impacted the psychosocial care provided to the children during complementary feeding, and this finding agrees with the report of Bushaw *et al.*, (2020).

The study recommends further research on the influence of nutrition education on psychosocial care during complementary feeding. This may improve psychosocial care awareness and practices among nursing mothers and caregivers.

Conclusion: The study established that the psychosocial care of mothers has no significant relationship with complementary feeding practices. However, age and religion influenced the psychosocial care of nursing mothers or caregivers. Further study is required to substantiate the findings in this present study.

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Food Environment Facing the School Children in Public Primary Schools in Morogoro Municipality

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Abstract

Introduction: The study focused on examining the overall food environment influencing the dietary choices of school children in public primary schools in Morogoro Municipality. Four primary schools—Magadu, SUA, Mlimani, and Kikundi—were purposively sampled to represent the broader school landscape in the municipality. SUA and Mlimani were in urban and peri-urban areas, Magadu represented peri-urban settings, and Kikundi was in the town center. Data collection involved administering a structured questionnaire to 97 school childrenselected through convenient sampling based on their availability on the day of data collection. **Results** showed that most children were aware of healthy foods (62.9%) but demonstrated lower awareness of unhealthy foods (52.6%). Only 52% of children brought food from home, while the majority purchased items from vendors around the school premises. The most consumed junk foods included biscuits (83.5%), chips (75.3%), chocolates (74.2%), and fried buns (72.2%). Notably, school regulations or bylaws governing the sale of food to children were absent.

Discussion: The findings suggested that children were more conscious of healthy foods than unhealthy options, possibly leading them to consume the latter unknowingly. The study emphasized the prevalence of unhealthy food consumption among school children and highlighted the absence of regulatory measures in place. Addressing these issues could promote healthier dietary habits among school children in Morogoro Municipality.

Keywords- Food, environment, children, regulations, choice

Introduction

The food environment refers to locational access to food in a community, a person's proximity to food store locations, consumer choices inside food outlets, distribution of food stores, food service, and any physical entity by which food may be obtained (Rideout et al., 2015). The school food environment involves all the spaces, infrastructure, and conditions within and beyond the school premises where food is available, obtained or purchased and consumed (roadside shops, kiosks, canteens, food vendors, packed food from home) and the composition of those foods FAO (2019). It also involves the information available about food and nutrition and the promotion and pricing of foods and food products (marketing, advertisements, branding, food labels, packages, and promotions.

The food environment shapes how accessible, affordable, desirable, and convenient a specific food is. All these aspects are taken into consideration in mapping the school food environment. The food environment has been a primary global concern that exposes people to unhealthy foods due to globalisation and the advancement of technologies, which have made the foods convenient to access and consume (UNICEF, 2019).

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Food choice refers to the selection and consumption of various kinds of foods and beverages as well as other aspects of food and eating behaviours (Shepherd & Raats, 2006). The food choice is contributed by the environment in which food is obtained, thus leading to unhealthy eating behaviours, which the school children much postulate. The food environment is essential because it creates and facilitates the continuation of food systems or chains from the producer or supplier to the final consumer. It also plays a crucial role in symbolic and social functions in society, which can be linked to their influence on food selection (Shepherd & Raats, 2006).

According to UNICEF (2019), the trends of technological advancements in the world have been shaping the food options of people, particularly children, and about 77% of processed foods have been on sale thus contributing to poor health options. Unhealthy food choices have been associated with the development of a triple burden of malnutrition. UNICEF (2019) noted that children who are not consuming healthy diets are associated with poor cognition and poor performance at school. Governments, therefore, must play an essential role in ensuring the provision and supply of healthy foods in school environments and discourage the marketing of unhealthy foods, including sugar-sweetened beverages, to improve the wise choice of foods (UNICEF, 2019). Many children in the world, especially those from low social profiles, suffer from malnutrition (whether underweight or overweight) because of the few options of not being able to access healthy foods (UNSCN, 2017). The school environment can influence healthy food options by building a good foundation for the children to change themselves and their homes (UNSCN, 2017).

Problem Statement

The food environment surrounding the school children is a potential problem contributing to poor children's growth and development due to what the children consume while at school. A study by Villiers and Faber (2015) postulates that the current food environment can exploit a child's biological, psychological, social and economic vulnerabilities, making it easier to eat unhealthy food. Also, a study by Wongboonsin et al. (2018) reported that the primary determinant of food choice is mostly the taste followed by the cost of the food. The tastier the food is, the more likely it will be chosen. The child chooses the food depending on what is available on the school premises (Villiers & Faber, 2015). Poor food environment can influence a child's poor food selections. In that respect, fatty or sweet foods are more likely to be chosen by children because such foods are usually tastier (Werle et al., 2013). This study intended to assess the food environment in school children towards poor choices of food items found in school as a significant contributing factor to such choices.

Methodology
Description of the Study Area

The study was conducted in Morogoro Municipality, the urban part of the Morogoro District where most administrative activities are implemented. The main economic activities include industries, subsistence and commercial farming, small-scale enterprises, and trade (Ernest et al., 2017). Administratively, Morogoro Municipality has one division, 29 Wards and 272 streets, popularly known as *"Mitaa"*, with a population estimate of 387 945 people (MMC, 2012). Morogoro Municipality has various road networks; some are trunk and feeder roads, and some are tarmacked (URT, 1997). A central railway line passes through Morogoro town, connecting Dodoma with Dar es Salaam (URT, 1997). There is also the Standard Gauge Railway (SGR) project, which is in progress. It contributes to the improvement of the socioeconomic profile of the municipality. The project focuses on building the railway line described as *"mwendo-kasi"* (literally speed train). The social services provided in Morogoro Municipality include health, education, policy research and food supply services. Morogoro Municipality is surrounded by various primary schools that educate the children. The study involved four selected primary schools located in Morogoro Municipality.

Study Design and Study Population
This study used a cross-sectional design involving a one-point collection of primary data. The participants of this study were children from four primary schools and the food providers who supply food items for these children while at school. The sampling frame included children in four primary schools: Mlimani, SUA, Magadu, and Kikundi.

Sampling Procedure and Sample Size
Four primary schools (Mlimani, SUA, Magadu and Kikundi) were purposively selected to represent the other public schools in Morogoro Municipality. Magadu Primary School was selected to represent the peri-urban part of the Morogoro, while Kikundi Primary School was in the town centre. On the other hand, SUA and Mlimani schools involved families from low, middle, and high-income levels. Then within each of the selected schools, only children from standards 5, 6 and 7 were involved in the study. Using experience in public schools in Tanzania, as well as after consulting the teachers, it was noted that children in the lower classes (i.e., from standards 1 to 4) may need help understanding and answering the questions in the interview questionnaire. Each child in standards 5, 6 and 7 who was in school on the interview day, was included in the study.

According to the school education guidelines for Tanzania, each classroom is supposed to consist of at most 35 children. In that respect, the sample size for the proposed study was expected to include about 280 children (i.e. 35 x 2 x 4 schools) but only 97 children were recruited for this study. On the other hand, convenient sampling was also used to obtain a sample of individuals involved in selling or providing different food items to the children within the selected schools. The logic was followed to obtain at least one individual for each type of food item or seller involved.

Methods of Data Collection
The primary school children of the selected schools were provided with a questionnaire that contained a list of questions; some were open-ended, and some were close-ended. Open-ended questions allowed the children to explain themselves in detail to quench the demands of that particular question. The questionnaire was developed in English but translated into Kiswahili to better understand the respondents. A list of healthy and junk foods was developed which was included in the questionnaire. The list was validated by sharing the information with the nutrition experts, members of staff and fellow nutrition students. On the other hand, food vendors (and food providers) were interviewed face-to-face using semi-structured open-ended questions.

Data Analysis
Data collected from the respondents was entered and analysed by SPSS (Statistical Package for the Social Sciences version 20). Descriptive analysis was performed using frequencies and percentages where categorical variables were involved, while mean and standard deviations were computed for continuous variables. The results were presented using tables.

Ethical Consideration
Permission to conduct this research was obtained from the Sokoine University of Agriculture and the authority in Morogoro Municipality. The participants were asked to give verbal consent to participate in this study. The participants were informed about the benefits of this study. The participants were allowed to withdraw at any time during the study if they wished to do so. The confidentiality of the data collected was considered.
Results

About three-quarters of all surveyed school children (73.2%) were going to school on foot (Table 3), while the rest of the school children were using bicycles (17.5%) and the least used motorcycles (9.3%) (Table 3).

Socio-demographic Characteristics of the Surveyed Respondents
School children and their parents or caregivers in Morogoro Municipality were the targets of this study. Their socio-demographic characteristics included age, sex, class level and means of transport used by the child to reach school, as well as marital status, sex and occupation of the parent or caregiver.

Table 1: Distribution of the surveyed school children according to their sex and age***

Age category	Sex of the child		Total
	Boys (n = 42) (%)	Girls (n = 55) (%)	(N = 97) (%)
10 – 13 years	64.3	81.8	74.2
Above 13 years	35.7	18.2	25.8
Total	100.0	100.0	100.0

*** Mean Age (12.8±1.15)

Age, sex and class level of school children
The average age of the surveyed school children was 12.8 years (12.8±1.15) as shown in Table 1. About three-quarters of all surveyed children were between 10 and 13 (Table 1). The sample included 42 boys and 55 girls. In terms of class grade, more than 60% (Table 2) were in standard seven, followed by standard six, who were about 30%, while standard five was the least (7.2%).

Table 2: Distribution of the surveyed school children according to their sex and class grade

Class grade	Sex of the child		Total
	Boys (n = 42) (%)	Girls (n = 55) (%)	(N = 97) (%)
5	7.1	7.4	7.2
6	35.7	25.5	29.9
7	57.1	67.3	62.9
Total	100.0	100.0	100.0

Means of transport used by children.
About three-quarters of all surveyed school children (73.2%) were going to school on foot (Table 3), while the rest of the school children were using bicycles (17.5%) and the least used motorcycles (9.3%) (Table 3).

Table 3: Distribution of the surveyed school children according to their sex and means of transport used to go to school

Means of transport used to go to school	Sex of the child		Total
	Boys (n = 42) (%)	Girls (n = 55) (%)	(N = 97) (%)
On foot	69.0	76.4	73.2
By bicycle	26.2	10.9	17.5
Motorcycle or vehicle	4.8	12.7	9.3
Total	100.0	100.0	100.0

Parental, marital status and occupation of parents or caregivers
Most surveyed schoolchildren stayed with their parents (87.6%), and few stayed with their guardians (Table 4). Almost all the parents of the surveyed schoolchildren were married (95.9%), while few reported being single. On the other hand, more than thirty per cent of the parents (38.1%) were businessmen and women followed by farmers (29.9%), employed in the informal sector (18.6%) and formal sector (13.4%).

Table 4: Demographic Characteristics of the surveyed parents

Variables	N	%
Status of caregivers		
Parents	85	87.6
Guardian	12	12.4
Marital status of the parents of the pupils		
Single	4	4.1
Married	93	95.9
Occupation of parents or guardians		
Business	37	38.1
Farmer	29	29.9
Employed in the formal sector	13	13.4
Employed in the informal sector	18	18.6

Participation in school lunch programs
About sixty-two per cent (61.9%) of the surveyed children reported being involved in a school lunch program while 38.1% were not (Table 5).

Table 5: Participation in school lunch programs

Participation of children in the school lunch program	N	%
Yes	60	61.9
No	37	38.1

Awareness of Healthy and Unhealthy Foods
 The awareness of healthy and unhealthy foods was assessed by scoring the number of correct answers given by a respondent (school children). The highest score was 6 (mentioned all correct answers) and the lowest was 0 (for not getting any correct answers). To assess excellent and poor performance in awareness, scores ranging from 0 – 3 were categorized as 'poor' while 4 – 6 were categorized as 'good'. Two tests were used to assess the awareness of the school children about healthy and unhealthy foods. The tests were the Chi-square test and the T-test. The results of each test are reported below.

Differences in awareness concerning sex and age category
Chi-square was used to test for differences in awareness among the sampled school children concerning their sex and age category. Results are summarized in Table 6. More than sixty per cent (62.9%) of all the surveyed children had high awareness scores on healthy foods whereas few children had low awareness. According to the results, no statistically significant difference in the awareness of healthy foods between boys and girls P ≤ 0.05). On the other hand, more than half (52.6%) of the surveyed school children had low awareness about unhealthy foods (Table 7) whereby, again, there is no significant difference between girls and boys at P ≤ 0.05.

Results for the tests of the relationship between awareness about healthy foods and age categories of school children are shown in Table 8. Accordingly, there is no significant difference among the included age categories at P ≤ 0.05. However, results for the tests of awareness about unhealthy foods (Table 9) are different whereby there is a significant difference between girls and boys (P ≤ 0.024). It appears that girls performed poorly compared to boys. While more than half of the boys (54.2%) were in the high-awareness category, this was achieved by only 28% of the girls.

Table 6: Chi-square test results for the relationship between categories of awareness about healthy foods and the sex of a child

Awareness of healthy foods (scoring category)	Sex of the child		
	Boys (n = 42) (%)	Girls (n = 55) (%)	Total (N = 97) (%)
High awareness of healthy foods score	52.4	70.9	62.9
Low awareness of healthy foods score	47.6	29.1	37.1
Total	100.0	100.0	100.0

Pearson Chi-square = 3.503; d.f = 1; Asymp. Sig. (2-sided) = .061

Table 7: Chi-square test results for the relationship between categories of awareness about unhealthy foods and the sex of a child

Awareness of unhealthy foods (scoring category)	Sex of the child		
	Boys (n = 42) (%)	Girls (n = 55) (%)	Total (N = 97) (%)
High awareness of unhealthy foods score	50.0	45.5	47.4
Low awareness of unhealthy foods score	50.0	54.5	52.6
Total	100.0	100.0	100.0

Pearson Chi-square = .197; d.f = 1; Asymp. Sig. (2-sided) = .657

Table 8: Chi-square test results for the relationship between categories of awareness about healthy foods and age category of a child

Awareness of healthy foods (scoring category)	Age of the child		
	10-13 years (n = 72) (%)	Above 13 years (n = 25) (%)	Total (N = 97) (%)
High awareness of unhealthy foods score	59.7	72.0	62.9
Low awareness of unhealthy foods score	40.3	28.0	37.1
Total	100.0	100.0	100.0

Pearson Chi-square = 1.199; d.f = 1; Asymp. Sig. (2-sided) =.274

Table 9: Chi-square test results for the relationship between categories of awareness about unhealthy foods and age category of a child

Awareness of unhealthy foods (scoring category)	Age of the child		
	Boys (n = 72) (%)	Girls (n = 25) (%)	Total (N = 97) (%)
	10-13 years	Above 13 years	
High awareness of unhealthy foods score	54.2	28.0	47.4
Low awareness of unhealthy foods score	45.8	72.0	52.6
Total	100.0	100.0	100.0

Pearson Chi-square value = 5.096; df =1; Asymp. Sig. (2-sided) = .024

T-testing for differences in awareness of healthy and unhealthy foods
T-testing was used to compare awareness mean scores on the healthy and unhealthy foods for school children from class five to seven. P-values of equal or less than 0.05 were used to imply a statistically significant difference in the awareness levels. Summarized results of the T-test of the surveyed school children are given in Table 10. Accordingly, there is no statistically significant difference in awareness about healthy foods between class 5 and class 7 children. Similarly, in Table 11, the results show no statistically significant difference in the awareness of unhealthy foods between these two groups of school children.

Table 10: T-test results for comparison of mean scores of awareness on healthy foods between class 5 and class 7 children

Class grade	N	Mean score
Class 5	7	3.1429
Class 7	61	4.2295

T-value= -1.101; Sig (2-tailed) = .275

Table 11: T-test results for comparison of mean scores of awareness on unhealthy foods between class 5 and class 7 children

Class grade	N	Mean
Class 5	7	1.2857
Class 7	61	2.3770

T-value= -1.205; Sig (2-tailed) =.232

Summarised results of the T-test of the surveyed school children are given in Table 12. Accordingly, there is no statistically significant difference in awareness about healthy foods between class 6 and class 7 children. Similarly, in Table 13, the results show no statistically significant difference in the awareness of unhealthy foods between these two groups of school children.

Table 12: T-test results for comparison of mean scores of awareness on healthy foods between class 6 and class 7 children

Class grade	N	Mean
6	29	4.1034
7	61	4.2295

T-value= -.22; Sig (2-tailed) =.823

Table 13: T-test results for comparison of mean scores of awareness on unhealthy foods between class 6 and class 7 children

Class grade	N	Mean
6	29	1.4483
7	61	2.3770

T-value= -1.88; Sig (2-tailed) =.063

Summarized results of the T-test of the surveyed school children are given in Table 14. Accordingly, no statistically significant difference exists in awareness about healthy foods between children of class

and class 6. Similarly, in Table 15, the results show no statistically significant difference in the awareness of unhealthy foods between these two groups of school children.

Table 14: T-test results for comparison of mean scores of awareness on healthy foods between class 5 and class 6 children

Class grade	N	Mean
6	29	4.1034
5	7	3.1429

T-value= .845; Sig (2-tailed) =.404

Table 15: T-test results for comparison of mean scores of awareness on unhealthy foods between class 5 and class 6 children

Class grade	N	Mean
6	29	1.4483
5	7	1.2857

T-value= .845; Sig (2-tailed) =.855

Standard Junk or Un-Healthy Foods Mostly Consumed by School Children
The junk foods consumed by the school children were identified by asking the children to mention the foods or snacks they commonly consume while at school. The criteria used to categorize the food items or drinks as junk or unhealthy foods include food items that are deep fried such as rice buns, white buns, chips, samosa, and crisps. Also included are food items which contain high amounts of salt and/or sugar such as biscuits, chocolate, crisps, sausages, sweets, lollies, and ice cream.
More than eighty per cent of the surveyed girls were reported to consume biscuits (85.5%) compared to 81% of the boys (Table 16). Chocolate was also reported to be consumed more by the surveyed school children after biscuits, where the proportion of boys and girls who consumed chocolate was 71.4% and 76.4%, respectively, followed by white buns. The least consumed food items were *Kalmat* and sausages (Table 16).
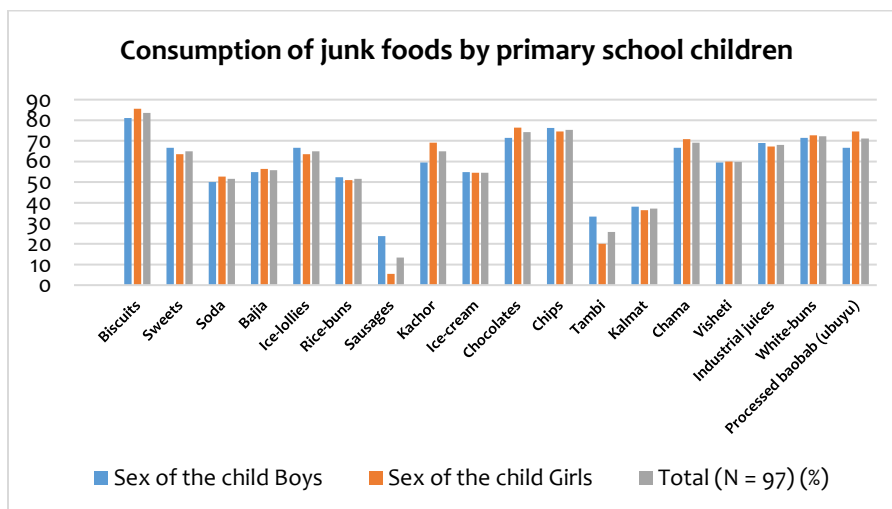
Fig 1. Reported junk foods or drinks consumed by the schoolchildren

Discussion

Common Junk Foods Consumed by the Primary School Children at School

Three criteria were used to identify junk or unhealthy foods namely, those food items that contained much sugar, those that contained much salt and those which were deep fried. The results showed that many of these school children consumed junk foods as part of their daily consumption, whereas biscuits ranked with the most significant percentage (83.5%), followed by chips, chocolates, and buns (more than 70%). A study conducted in Ohio, USA, reported similar results on school children's consumption of junk foods. In contrast, children could come with their packed lunch from home, which is healthy but could still buy the energy-dense foods found at the school compound (Neely, 2011). It appeared that the availability of competitive foods in the school environment was what the children kept on choosing rather than fruits and vegetables. The reasons why school children would consume unhealthy foods, mainly when they are at school, could be that junk foods are readily available and sold at the lowest price around the school premises, they are also tastier as compared to the healthy ones' example, sweets which most children prefer (Neely, 2011).

Awareness of Children about Healthy and Unhealthy Foods

Most of the schoolchildren were aware of healthy foods but not of unhealthy foods. There was also no statistically significant difference in awareness of healthy and unhealthy foods between girls and boys of various age groups. The poor awareness about unhealthy foods was likely because most children might consume junk foods without knowing if they are unhealthy. On the other hand, awareness of healthy foods was high probably due to the common foods that are consumed at home and thus most children are aware of. Food habits are usually shaped during the early years of a child's schooling and form the basis of future eating habits (Sultana, 2017). This central role is played by the parents or the guardians who live with the children. From the reports of the surveyed children, most of them live with their parents who are legally married. Also, the parents are used to instructing their children on what to buy or eat. For this to be effective, parents must be aware of healthy foods to guide their children appropriately (Sultana, 2017). Primary school children observe and look at what their parents do and imitate; with that respect, they can learn and adopt good dietary habits.

The Food Access Environment Where School Children Get the Foods They Consume at School

In assessing the food access environment where school children get their food, several issues were considered namely, the source of the foods, school regulations about the selling of foods in school compounds and conditions in which the foods are sold or consumed.

Source of the foods that school children consume.

Accessibility to food would mean the ability of an individual or a household to purchase food, i.e. the purchasing power of an individual or a household (Napoli, 2011). At times, the food can be accessed because of the purchasing power one has, but the surrounding food or the available food may not be favouring (that is not healthy). Unhealthy foods surround the food access environment of most of the school children. Also, the amount of money which these school children are given by their parents can only be sufficient to access junk foods. The average amount of money which the surveyed school children reported being given by their parents was about 800Tshs/= (Villiers & Faber, 2015) suggesting that the food environment presently has influenced the school children to eat unhealthy foods where they would opt to consume foods of poor nutritional quality for the food environment that surrounds them is dominated by nutrient-poor and energy-dense foods, ultra-processed, large portion sized with attractive packaging.

School regulations about the selling of food in school compounds

The availability of nutrition guidelines and standards in schools can help to ensure the adequacy and quality of the meals provided at school that align with the school children's nutritional requirements (FAO, 2019). From the surveyed schools, there were no problematic regulations against food items sold around the school, for some items were sold by the teachers. The concern of how the foods were prepared and served to the children could have been more pleasing as hygiene behind the preparation of the foods was not observed. Food items like chips were served in plastic bags while hot which is dangerous to the health of the school children.

Conditions in which the foods are sold or consumed

The consumption of unsafe foods and subsequent food-borne illness or food poisoning poses significant threats to nutrition and health status, especially for vulnerable populations such as school children (FAO, 2019). This, in turn, affects the child's learning process since the child cannot concentrate while sick. The food sellers could have adequate knowledge of how to prepare the foods hygienically, but their negligence can pose the children at a higher risk (Losasso et al., 2012). The children also rarely wash their hands before eating the food items they buy, which can increase their risk of developing food-borne diseases.

The junk foods that children consume most of the time at school are not hygienically prepared, therefore putting their health at risk. Food items that are deep fried, such as chips, crisps, buns and others, could compromise the health status of children, for most food sellers usually use the cooking oil many times to the extent that cooking oil loses its quality (becomes rancid). The health concern about using rancid oil is that it could cause cancer later in the day, and it could affect many processes in body metabolism, which in turn affects the health status of school children (Farrokhzadeh et al., 2013).

Study Limitations

The coronavirus pandemic (COVID-19) in 2020 delayed data collection because the Government restricted all unnecessary movements and crowd gatherings. This led to the closure of all schools and universities in Tanzania, which caused difficulty in finding the children for data collection. Because of this, the proposed sample size of 280 respondents could not be reached. Thus, only 97 respondents were included in this study.

Conclusion and recommendations

From the findings, it can be concluded that school children were more aware of healthy foods than unhealthy foods, which could be due to unknowingly consuming these food items. Unhealthy foods were more available on the school premises which contributed to influencing children to consume them. The study also revealed that the common source of the food items consumed by the school children was purchased from food sellers because their parents or guardians gave them some money to spend at school.

The study recommends that The Government of Tanzania enact food safety laws which would protect the health of these children by enforcing that only healthy and safe foods should be available and accessible in schools. All school levels should consider having a school lunch program for children to eat healthy meals and avoid eating unhealthy foods because of hunger.

There should be policies to discourage unhealthy foods, such as special taxation, which will raise the prices of such foods.

Data availability
Data is available upon reasonable request from the authors.

Conflict of interest
The authors declare that they have no conflict of interest.

Authors' contributions
Anna Peter Mamiro: Conceptualization, Writing – original draft. John MSUYA: Conceptualization, Formal Analysis, Methodology, Project administration, Supervision, Validation, Visualization, Writing – review & editing.

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Clinical profile, treatment modalities and outcomes among patients with upper aero-digestive tract emergencies at Bugando Medical Centre, Mwanza, Tanzania

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Abstract

Background: Upper aero-digestive tract emergencies (UADTEs) are common in our setting and can be life-threatening and challenging to otolaryngologists. However, there is a paucity of clinical studies on these emergencies. This study aimed to determine the clinical profile, treatment modalities and outcomes of upper aero-digestive tract emergencies at Bugando Medical Centre (BMC), Mwanza, Tanzania.

Methods: Between January and May 2019, a cross-sectional study involving patients presenting with a clinical diagnosis of UADTEs was conducted at BMC.

Results: Of 487 ENT emergencies seen during the study period, 128 (26.3%) patients had UADTEs. Males outnumbered females by a ratio of 1.5: 1. Their median age at presentation was 5 [range, 2-40] years. The major causes of UADTEs were foreign body ingestion, head and neck tumours, foreign body aspiration and cut-throat injuries that were seen in 56(43.8%), 33(25.8%), 25(19.5%) and (3.9%), respectively. The most frequent presentations were dysphagia 81(63.3%), difficulty in breathing 61(47.7%) and odynophagia 56(43.8). Age ≤ 40 years (p=0.02), prolonged duration to treatment (p=0.04) and low blood oxygen saturation (SPO2) (p=0.04) were significantly associated with poor outcomes following esophagoscopy. In addition, delayed duration to treatment (p=0.01) and foreign body ingestion (p=0.001) were significantly associated with prolonged hospital stay.

Conclusion: UADTEs are common at BMC and constitute a significant cause of otorhinolaryngological admission with foreign bodies in the aerodigestive tract, which is the most typical cause of these emergencies. Most of these injuries can be prevented through public enlightenment campaigns. Early detection and management of UADTEs is essential to reduce morbidity and mortality associated with these emergencies.

Keywords: Upper aerodigestive tract emergencies, clinical profile, treatment modalities, outcomes, Tanzania

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Background

Emergencies of the upper aerodigestive tract are not uncommon in clinical practice and constitute a significant cause of morbidity and mortality worldwide (Furtado *et al.*, 2011; Salih *et al.*, 2016). Diseases causing upper aero-digestive tract emergencies (UADTEs) range from those that can be effectively and efficiently managed by the duty physician with an excellent prognosis to the complex ones that require prompt diagnosis and intervention by the otolaryngologists (Onotai & Ibegwe., 2012). In resource-limited countries like Tanzania, UADTEs are among the most common and potentially life-threatening conditions that need urgent assessment and aggressive management (Gilyoma& Chalya., 2011; Gilyoma & Chalya., 2013; Kirfi*et al.*, 2014). At Bugando Medical Centre (BMC), UADTEs are the most common causes of otolaryngological admissions and contribute significantly to high morbidity and occasional mortality (Gilyoma & Chalya., 2011; Gilyoma & Chalya., 2013; Gilyoma & Chalya., 2014).

The clinical profile and treatment modalities of UADTEs differ worldwide, reflecting geographical differences in standard disease states (Kirfi*et al.*, 2014). The causative factors also differ according to age groups in adults and children (Perez *et al.*, 1995). In children and elderly patients, UADTEs are commonly caused by foreign bodies (FBs) in the larynx and oesophagus and have high rates of morbidity and mortality (Gilyoma& Chalya., 2013). Moreover, the children's population has the potential for aspiration and ingestion of FBs (Onotai& Ebong., 2011; Ibegwe*et al.,* 2012). In adults, the most standard emergencies seen are blunt and penetrating traumas to the neck following road traffic accidents, and cutthroat and gunshot injuries. These conditions can result in life-threatening situations that require immediate intervention by the duty doctor in the emergency department before referring the patients to otolaryngologists (Rathlev &Medzon., 2007; Mohammad *et al.*, 2011).

Cut throat injuries pose a significant challenge because of multiple vital structures that are vulnerable in small, confined and unprotected areas (Bhattacharjee *et al.,* 1997; Okoye & Oteri., 2001; Manilal *et al.*, 2011; Gilyoma & Chalya., 2014) . Other causes of UADTEs include corrosive ingestion, thermal burns, obstructive tonsillitis with its complications and head and neck tumours (laryngeal cancers, thyroid tumours & pharyngeal tumours) (Offer *et al.*, 1995; Onotai & Nwogbo., 2010). Usually, the clinical features of UADTEs depend upon the etiological factor and time of presentation to the hospital. For instance, a large FB occluding the upper airway or esophagus may lead to severe symptoms like severe respiratory distress, dysphagia and even sudden death (Bleach *et al.*, 1994; Lasis *et al.*, 2006), while injuries of long-standing duration may be associated with complications such as mucosal ulcerations, esophageal obstruction, laryngeal stenosis and esophageal diverticulum (Brady., 1991). Either way, early diagnosis and treatment of these emergencies is an essential strategy to prevent morbidity and mortality.

The management of UADTEs poses diagnostic and therapeutic challenges to Otolaryngologists practicing in resource-limited countries. Late presentation of the disease, late diagnosis and late referral to hospital coupled with a lack of modern diagnostic and therapeutic facilities are among the hallmarks of the disease in developing countries (Lasis *et al.*, 2006; Gilyoma & Chalya., 2011; Ibegwe et al., 2012; Gilyoma & Chalya., 2013; Gilyoma & Chalya., 2014; Nakku *et al.*, 2016). It has been reported that UADTEs continue to be associated with significant morbidity and mortality despite recent advances in both pre-operative diagnosis and postoperative care (Singh *et al.*, 2014; Shetty & Gangadhar., 2015). Understanding the factors responsible for increased morbidity and mortality in these patients will better guide appropriate management and improve survival (Majori*et al.*, 2011; Showkat*et al.*, 2015). This study aimed to describe our experience regarding the clinical profile, treatment modalities and outcomes among patients with UADTEs at BMC, a tertiary care hospital in northwestern Tanzania.

Methods and Patients
Study design and setting.
This cross-sectional study involved patients presenting with a clinical diagnosis of UADTEs conducted at the EMD, ICU, OT, Otolaryngological wards and clinics of Bugando Medical Centre from January to May 2019. Bugando medical Centre is a consultant and teaching hospital located in Mwanza City in the Lake Zone, North-Western Tanzania, serving approximately 18 million people. It is a tertiary care and teaching hospital for the Catholic University of Health and Allied Sciences (CUHAS) – Bugando. The hospital has a bed capacity of 1060 and handles most of the otolaryngological cases from eight Lake Zone regions (Mwanza et al.). About 15-20 patients with various otolaryngology conditions attended daily in the EMD at BMC, and among them, 4-6 present with UADTE (BMC-Medical Records database 2019/2020, unpublished).

Study population.
The study population included all patients diagnosed with UADTEs and treated at BMC during the study period and those who consented to the study. Patients known to have any chronic condition of the UADT (e.g. Tumors, chronic laryngitis) and those who died while in admission before completing the intervention were excluded from the study. The sample size was calculated using the Yamane Taro (1967) formula, whereby a total of 128 patients with UADTs were recruited in the study. Sampling of eligible patients was performed serially until the sample size was reached. Independent (predictor) variables included demographic data (age, sex, residence), clinical presentation, duration of symptoms, the time interval between admission, intervention and/or discharge, diagnosis of UADTEs on admission (etiologies of UADTEs) and Intervention done (esophagoscopy, tracheostomy, Fogarty catheter). The dependent variables included post-operative complications (like haemorrhage, surgical site infections, hemorrhagic shock, aspiration pneumonia, pulmonary embolism, deep venous thrombosis (DVT), reactional anaesthesia, pyrexia etc.), length of hospital stay, and-hospital mortality. This information was collected using a pre-tested questionnaire.

Recruitment of patients to participate in the study was conducted at the Emergency Department, Otolaryngological ward ENT clinic, and other wards of BMC, which are the main entry points for potential patients with UADTEs. The principal investigator, together with fellow residents, screened all arriving patients. Patients were recruited after meeting the eligibility criteria and obtaining written informed consent from patients themselves and/or parents/caregivers.

Evaluation of patients was predominantly clinical, supported by laboratory tests and radiological investigation. A detailed history regarding demographic data (age, sex, area of residence, occupation), clinical presentation, duration of symptoms, diagnosis on admission clinical, laboratory or imaging), the treatment offered, type of surgical intervention, the time interval between admission and surgery and outcome of management was obtained from the patients, parents or caregivers.

Resuscitation was administered according to the hospital protocol before recruiting eligible patients. Patients were then taken to the operating theatre for emergency surgery or admitted to Otolaryngological wards. Necessary investigations were completed, and further treatment was instituted. Patients who required ventilator support were admitted to the ICU. In the operating theatre, a consultant otolaryngological surgeon or a senior resident in otolaryngology performs operations under the direct supervision of a consultant surgeon. Postoperatively, patients were managed appropriately in the Otolaryngological ward or the ICU, depending on their clinical condition and the departmental standard operating procedures. Follow-up of each patient until after 30 days post-discharge was done.

Statistical data analysis

Statistical data analysis used SPSS software version 22.0 (SPSS et al., Ill, USA). Data were summarized in proportions and frequency tables for categorical variables. Continuous variables were summarized using median, mean and range. P-values were computed using the Chi-square ($\chi2$) test and Fisher's exact test was used for categorical variables. The Wilcoxon Rank-sum (Mann-Whitney) test was used for continuous variables because the distribution of variables was not expected. Univariate analysis was used to determine factors associated with length of hospital stay. Multivariate logistic regression analysis was employed for the factors with a P value less than 0.05. A factor with a p-value less than 0.05 was considered statistically significant.

Results

During the study period, 487 patients were presented to Bugando Medical Centre with different otolaryngological emergencies. Of these, 128(26.3%) had upper aerodigestive tract emergencies (UADTEs). Out of 128 studied patients, 76 (59.6%) were males, and 52 (40.4%) were females, giving a male-to-female ratio of 1.5: 1. The youngest patient was six months old, and the oldest was 67. The average age of patients at presentation was 8 [IQR: 6-14] years. The modal age group at presentation was 0-10 years, accounting for 40.6% of cases. One hundred and ten (85.9%) patients were 40 years and below (Figure 1). The elderly population of more than 65 years old is comprised of the minority 6(4.7%)(Figure 1). Most patients, 79(61.7%) came from rural areas.
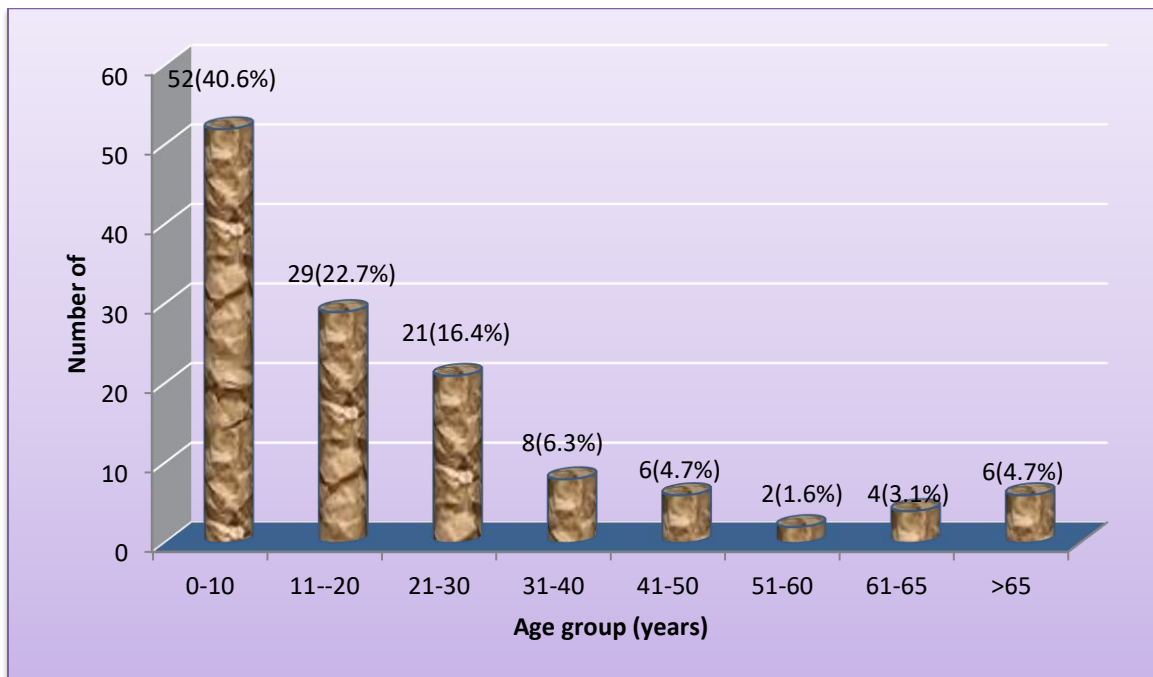
Figure 1: Age group distribution among patients with UADTEs at BMC

Etiologies of upper aerodigestive tract emergencies (UADTEs)
The common etiologies of UADTE among attended patients were foreign body ingestion, head and

neck tumours and foreign body aspiration, which were seen in 56(43.8%), 33(25.8%) and 25(19.5%) patients, respectively. Corrosive ingestion and facial trauma were the minor causes of UADTE that were each seen in 1(0.8%) patient (Figure 2). Regarding gender distribution, male patients were the predominant group in most of the UADTE etiologies compared to their female counterparts. Cut-throat injury and corrosive ingestion were exclusively seen in male patients while vocal cord paralysis was only presented in female patients.
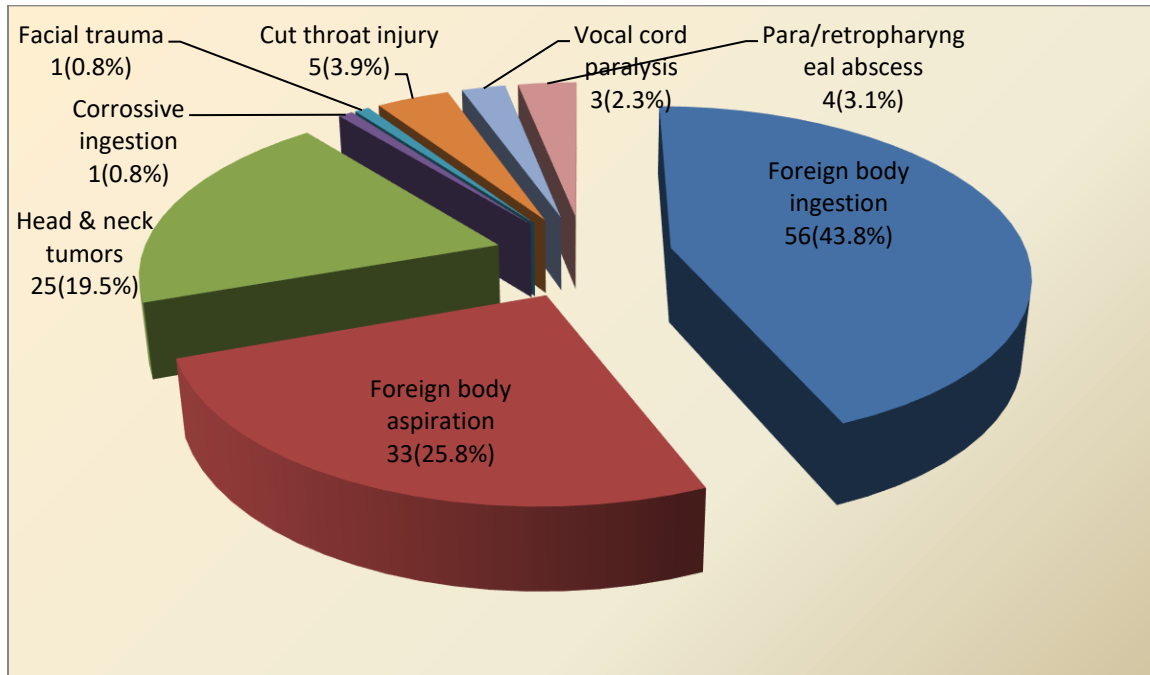
Figure 2: Distribution of patients according to UADTEs

Clinical presentation of upper aerodigestive tract emergencies (UADTEs)
Generally, in this study, dysphagia was the most common presentation, as illustrated in Figure 3 below.
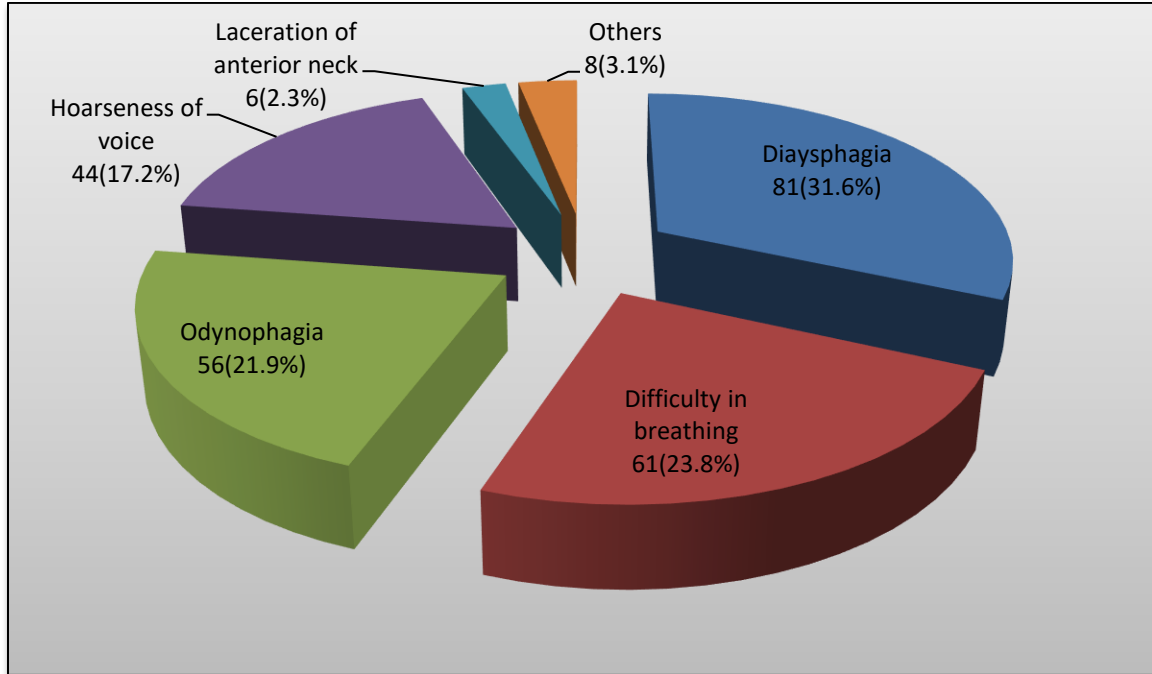
Figure 3: Clinical presentation among patients with UADTEs

Treatment modalities among patients with UADTEs at BMC

In this study, esophagoscopy was the most common endoscopic procedure for the removal of foreign bodies in the aerodigestive tract accounting for 43.0% of cases (**Figure 4**).
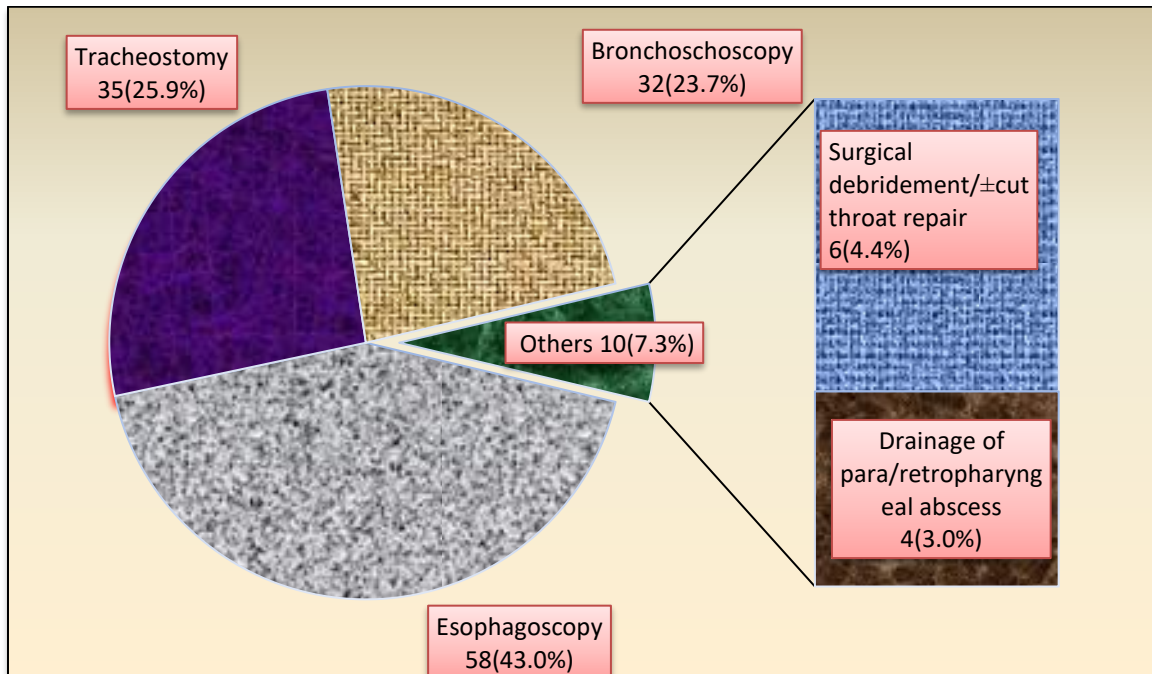
Figure 4: Treatment modalities among patients with UADTEs at BMC

Factors associated with poor clinical outcomes of UADTE treatment

a. Postoperative complications

i. Post-esophagoscopy:

Out of 58 patients who underwent esophagoscopy, five (8.6%) had poor outcomes. These included perforation in 2/5(40%), oesophagal stenosis in 2/5 (40%) and another injury in 1/5 (20%). Patients aged ≤40 years (p=0.02), long duration before the commencement of treatment from the time of insult [7(4-21) v/s2(1-3) days (p=0.04) and lower saturation of oxygen [96(95-96)] %v/s [98(96-98)] %were found to be significantly associated with poor outcomes (**Table 1**).

Table 1: Factors associated with poor outcome post-esophagoscopy at BMC (N= 58)

Independent valuables	Poor outcomes		p-value
	Yes (n=5)	No (n= 53)	
Age			
≤40	1(2.3)	43(97.7)	
>40	4(28.6)	10(71.4)	**0.020**
Sex			
Male	3(9.7)	28(90.3)	
Female	2(7.4)	25(92.6)	0.967
Area of residence			
Rural	4(8.3)	44(91.7)	
Urban	1(10.0)	9(90.0)	
Timing of treatment (days)	7[4-21]	2[1-3]	**0.040**
The rank of the attending surgeon			
Junior doctor	4(8.5)	43(91.5)	
Senior doctor	1(9.1)	10(90.1)	0.986
SPO$_2$	96(95-96)	98(96-98)	**0.040**

Variableswerecompared byFisher'sexacttest

ii. Post-tracheostomy complications

A total of 35 patients underwent tracheostomy, whereby the majority, 29/35 (82.9%) of them, presented with head and neck tumours as the main aetiology of UADTEs. Of these patients, 10/35(28.5%) had at least one poor outcome from the procedure. Four patients (40%) developed post-operative infection, 4/10(40%) developed tracheal stenosis, 2/10(10%) developed post-operative bleeding and1/10(10%) had perforation. None of the factors was associated with poor outcomes in this group of patients.

Table2: Factors associated with poor outcome post-tracheostomy (N=35)

Independent valuables	Poor outcomes		p-value
	Yes (n=10)	No (n= 25)	
Age			
≤40	1(33.3)	3(66.7)	
>40	9(29.0)	22(71.0)	0.581
Sex			
Male	8(30.8)	18(69.2)	
Female	2(22.2)	7(77.8)	0.267
Area of residence			
Rural	9(29.0)	22(71.0)	
Urban	1(25.0)	3(75.0)	0.892
Timing of treatment (days)	1.5[1.0-5]	3[2-6]	0.080
Rank of the attending surgeon			
Junior doctor	10(31.3)	22(68.7)	
Senior doctor	0(0.0)	3(100.0)	0.540
SPO$_2$	93.5(90-95)	94(90-95)	0.940

Fisher's exact test compared variables.

ii. post-bronchoscopy complications

During the study period, 32/128 (25.0%) patients underwent bronchoscopy, and out of these,7(21.9%) patients had poor outcomes, which included Electrolyte imbalance 7(100%), Infection2(28.6%), and perforation 1(14.3%). Using Fisher's exact test, none of the factors below was associated with poor outcomes among patients who underwent bronchoscopy (**Table 3).**

Table 3: Factors associated with poor outcome post-bronchoscopy (N=32)

Independent valuables	Poor outcomes		p-value
	Yes (n=7)	No (n= 25)	
Age			
≤40	5(20.8)	19(79.2)	
>40	2(22.2)	7(77.8)	0.990
Sex			
Male	6(23.1)	20(76.9)	
Female	1(20.0)	5(80.0)	0.732
Area of residence			
Rural	7(24.1)	22(75.9)	
Urban	0(0.0)	3(100.0)	0.112
Timing of treatment (days)	3[2-7]	2[1-3]	0.140
Rank of the attending surgeon			
Junior doctor	7(21.9)	25(78.1)	
Senior doctor	0(0.0)	0(100.0)	
SPO$_2$	93(88-95)	94(90-95)	0.464

Variableswerecompared byFisher'sexacttest

b. Length of hospital stay.
In this study, the overall length of hospital stay ranged from 1 to 15 days, with a median (IQR) age of 2.5 (1-11) days. Delayed duration to treatment (p=0.010) and foreign body ingestion (p=0.001) were significantly associated with prolonged hospital stay.

c. Mortality
No death was recorded in the current study.

Discussion
In this study, the prevalence of UADT among all ENT emergencies at BMC during the study period was 26.3%. This figure is higher than the 4.9% and 3.1% reported in California (Vassiliu et al., 2001) and Nigeria (Onotai & Ibegwe., 2012), respectively. These differences in the prevalence of UADTEs in these studies reflect differences in the prevalence of risk factors for developing UADTEs among different study settings. The author could not establish the reasons for this study's high prevalence of UADTEs. Upper aerodigestive tract emergencies can occur in all age groups (Onotai & Ibegwe., 2012).

In the present study, most patients were in the 1st and 2nd decade of life and comprised approximately two-thirds of the study population. Similar age distribution has been reported in other studies (Sunil & Achal, 1999; Khan & Arif, 2005; Sogebi*et al.,* 2006; Onotai&Ibegwe., 2012). There was no obvious explanation for the high prevalence of UADEs in this age group; however, this can be explained by the fact that an active age group engaging in high-risk activities predisposing them to UADEs. In this study, male patients were more affected than females. The male preponderance in this study agrees with what was reported elsewhere (Sunil & Achal., 1999; Kitcher *et al.*, 2007). However, other researchers found an equal male-to-female ratio (Bleach et al., 1994). The male preponderance in our series may be attributed to the males' overactive nature compared to their female counterparts.

The prevalence of UADTE's different etiologies varies considerably worldwide. In one study from Nigeria, for instance, it was reported that epistaxis was the most frequent emergency that was presented in the ENT emergency department in 16.1%, followed by nasal/facial trauma in14.7%, pharyngo-esophageal foreign bodies in13.3%andairwayobstruction in 8.1% (Shraga *et al*., 1980). Another Nigerian study that involved more than 5000 patients, reported that foreign body aspiration/ingestion or insertion were the most typical causes of UADTE in 41.7% of the patients (Adedeji *et al.,* 2015).

 A previous study done at BMC to assess the causes of ENT injuries showed that foreign bodies in the throat were the most frequent aetiology (18.0%) which was followed by foreign bodies in the nasal pharynx at8.8% (Gilyoma & Chalya., 2013). In the present study, foreign body ingestion was the most common aetiology of UADTEs, followed by head and neck tumors. These findings suggest that there might be a higher prevalence of these tumours in our setting, and most of them probably present in late stages where the patient is already having severe UADTEs symptoms. These tumours' pathological patterns were beyond this study's scope, but our findings have raised an important area of focus for further studies. In previous studies, male subjects have been reported to outnumber their female counterparts in the presentation of cut-throat injuries and corrosive ingestion. In India, more than eighty per cent of patients with cut-throat injuries were males in their third and fourth decade of life (Chakraborty *et al.*, 2017).

 Likewise, in a Nigerian study, it was reported that all patients (100%) who were admitted with cut-throat injuries were males, and the most expected age group was 30-35 years (Onotai & Ibengwe., 2010). Gilyoma *et al. (2014) also reported similar findings in Tanzania, where male subjects with cut-throat injuries outnumbered the females by 2.4:1,* and the median age was 26 years. The most familiar reasons that were reported were suicidal attempts and accidental injuries. The reason males in their youth are more susceptible to cut-throat injuries than females is probably due to the nature of their work, which is related to a risky environment and curiosity. Sex predilection on corrosive ingestion is variable. Other studies have reported male predominance (Hashmi et al., 2018), while others reported female predominance (Swain *et al.*, 2016). In the current study, only one male patient presented with corrosive ingestion; hence, it is difficult to comment on that.

 Clinical presentations in patients with UADE depend on the etiologies. For example, a study in India showed that the most common presentation in patients with head and neck tumors was hoarseness of the voice with difficulty breathing (Swarma *et al.*, 2013). In another study conducted in Nigeria, the most common clinical presentations seen in patients with UADTEs were difficulty in breathing, odynophagia and dysphagia (Onotai & Ibegwe., 2012). A Tanzanian study by Gilyoma *et al* (2011) showed that the most common presentations were dysphagia and difficulty breathing. In the current study, the most common clinical presentations were dysphagia, difficulty in breathing, odynophagia and hoarseness of the voice.

 The modality of treatment of UADTEs depends upon the etiological factors (Onotai &Ibegwe., 2012). Endoscopic removal of foreign bodies in the aerodigestive tract using rigid scopes under general anaesthesia has been reported to be a golden standard procedure (Gilyoma& Chalya., 2011). In the present study, rigid endoscopy (oesophagoscopy and bronchoscopy) with aerodigestive foreign bodies removal under general anaesthesia, cut-throat repair and surgical wound debridement ± tracheostomy were the most common treatment modalities performed. Others have also reported this treatment pattern elsewhere (Onotai &Ibegwe., 2012; Gilyoma& Chalya., 2013).

The presence of complications impacts the outcome of patients presenting with UADTEs as supported by the present study (Onotai & Ibegwe., 2012; Gilyoma & Chalya., 2013). In our study, complications following esophagoscopy included esophageal perforation and esophageal stenosis. The pattern of complications in the present study is similar to what was reported by others (Onotai & Ibegwe., 2012; Gilyoma & Chalya., 2013). In a previous study conducted in China among 519 patients who underwent

rigid esophagoscopy, the significant complications developed included oesophagal perforations and retropharyngeal abscesses (Lam *et al.*, 2003). Also, one study in Nigeria revealed that the most typical complication encountered following esophagoscopy was oesophagal stenosis due to prolonged impacted foreign body in the oesophagus. In another study by Gilyoma *et al. (2011), among 98 patients who underwent esophagoscopy, the complication rate was 7.1%,* and bronchial pneumonia was the commonest. In the current study, the age ≤ 40 was significantly associated with poor outcomes following esophagoscopy. Moreover, increased duration before the intervention of treatment from the time of insult was significantly associated with an increased rate of poor outcomes. Nevertheless, lower oxygen saturation was highly associated with adverse outcomes among patients who underwent esophagoscopy.

A previous study of 100 patients that was done in India encountered surgical site infection around the stoma, hemorrhage, tracheostomy tube obstruction and displacement as the most common complications of tracheostomy. These results were not associated with poor outcomes (Mehta & Chamyal., 1999). Another study done in Nigeria found that the complications of tracheostomy were tracheal stenosis, subcutaneous emphysema and bleeding. This study showed no association between poor outcomes and complications (Alabi *et al.*, 2018). The present study's post-tracheostomy development included post-operative infection, tracheal stenosis, post-operative bleeding and perforation. None of the factors was associated with poor outcomes.

In a previous study by Li *et al. (2020) in China, preoperative pulmonary disease, need for lung assistance, history of ineffective rigid bronchoscopy and prolonged length of bronchoscopy of more than 30 minutes were associated with postoperative poor outcomes.* In the current study, no factors were associated with poor outcomes.

A study done in China by Li *et al.* (2020) stated that prolonged duration between the assault of the UADTEs and treatment was a significant predictor of prolonged length of hospital stay. Another study by Zhang *et al. (2017) showed the predictors of prolonged length of hospital stay to patients with UADTEs to be prolonged duration of the incidence > 24 hours* to the time of intervention. In the current study by multivariate analysis, the only predictor for prolonged length of hospital stay was late presentation to the hospital from the onset of UADTEs. However, foreign body ingestion, as a cause of UADTE, was found to be a strong predictor for short hospital stays. This could be explained by fewer complications encountered pre- and post-management of foreign bodies in the oesophagus.

In conclusion, UADTEs are not uncommon at BMC and constitute a significant cause of otorhinolaryngological admission at BMC, with foreign bodies in the aerodigestive tract as the most typical cause of these emergencies. Children aged ten years and below and young adults are commonly affected. Rigid endoscopic procedures under general anesthesia are the primary treatment modalities performed. Patients aged ≤40 years, long duration before the commencement of treatment from the time of insult and lower saturation of oxygen were found to be significantly associated with poor outcomes after esophagoscopy. Most of these injuries can be prevented through public enlightenment campaigns. Early detection and management of UADTEs is essential in order to reduce morbidity and mortality associated with these emergencies.

Ethical clearance

The research proposal was presented and reviewed by the Department of Surgery and thereafter to the CUHAS / BMC ethical review committee for approval and ethical clearance with research clearance certificate No: CREC/353/2019

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Knowledge of the Risk Factors for Diabetic Foot Syndrome and Self-Foot Care Practices among Diabetic Patients at Muhimbili National Hospital in Dar es Salaam, Tanzania: A Cross-Sectional Study

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Abstract

Background: Evidence indicates diabetic patients have more than 15 times increased risk of non-traumatic foot disabilities. Patients' knowledge of the potential risk factors and self-care practices anticipate better self-management.

Objective: This study aimed to assess patients' knowledge of the risk factors for diabetic foot syndromes and reported self-foot care practices at Muhimbili National Hospital.

Methods: A hospital-based quantitative cross-sectional study design was conducted in June and December 2022. A random sampling technique was applied to recruit 140 diabetic patients at an outpatient clinic. The Guided Interview questionnaire was used to obtain data. Data were analyzed using SPSS version 25.

Result: The reported history of foot ulceration was 42(30%). Participants did not identify Smoking 106 (78.4%), foot soring/fungus 101(72.1%), and toenail ingrowth 96(68.3%) as potential contributors/risks for foot ulceration. Participants 93(66.4%) had an Inadequate knowledge score on the risk factors for Diabetic Foot Syndrome. The gender(male) (AOR: 3.71, 95%CI, 1.513-9.114, P=0.004169), education (secondary level) (AOR: 0.179, 95%CI: 0.045-0.70, P=0.0139), and history of foot ulceration (have not experienced foot ulcer) (AOR: 5.5, 95%CI: 2.14-14.165, P=0.000403) were significant associated to Inadequate knowledge score. Washing the foot with warm water and drying between the toes [daily] 84(60.4%) received poor response. Of the participants, 97(69.3%) had Good self-foot care practices. The duration of Diabetic illness (more than five months and less than one year) (AOR: 19.025, 95%CI: 2.716-133.293, P=0.003) and history of foot ulceration (have not experienced foot ulcer) (AOR: 3.377, 95%CI: 1.218-9.366, P=0.019) were significantly associated to Poor self-foot care practices.

Conclusion: The finding reveals inadequate knowledge of risk factors for diabetic foot syndromes and poor self-care practices. It gives insight into the respective authorities to develop a comprehensive rehabilitative therapy, focusing on foot health education and addressing every aspect affecting their quality of life.

Keywords: Diabetes, Diabetic Foot, Risk factor, Self-Foot Care, Tanzania.

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Introduction

Globally, up to 2021, 537 million people were reported to be living with Diabetes Mellitus (DM), making the prevalence of DM to become 10.5% of all adults aged 20-79 years(IDF et al.., 2021). Diabetes foot (ulcer) remained an outstanding potential DM complication, which makes a global prevalence of 6.3%, which is predominantly burdened in Lower Middle-Income Countries (LMIC) (IDF et al.., 2021; Pengzi Zhang *et al.*, 2017). Evidence indicates that within 30 seconds, one leg is amputated elsewhere in the world due to a Diabetic Foot Ulcer (DFU) (IDF Diabetes Atlas. Evidence has depicted that 15% of DM patients develop foot ulcers during their diabetic lifetime, and have a 2.5 risk of dying within five years due to diabetic foot complications(Walsh et al., 2016). Africa has 24 million diabetic patients, with a 13% prevalence of diabetic foot ulcers, which is two times higher than the global prevalence (IDF Diabetes Atlas. In Africa, 15% of diabetic patients undergo foot amputation, and 14.2% die during the period of hospitalization(Mauro Rigato *et al.*, 2018). In Tanzania, A study done at Muhimbili National Hospital (MNH) and three Municipal Hospitals (Mwananyamala, Temeke, and Amana) in Dar es Salaam region indicates the prevalence of diabetic foot was 15% among diabetic patients(Chiwanga & Njelekela, 2015).

Diabetic foot syndrome is a "constellation of neuropathy, ischemia and several foot infections", It`s associated with lesions in deep tissue and neuropathy(Tuttolomondo et al., 2015). It led to non-traumatic disability, morbidity, and loss of quality of life among diabetic patients(Jeyaraman *et al.*, 2019; Rubio, Jim, & Luis, 2020). Meanwhile, it's a preventable diabetic foot complication, which can be addressed through different perspectives, from patients(self-motivation) to clinical bases (attributes of care) (Amin & Doupis, 2016). The International Working Group on the Diabetic Foot (IWGDF) provides evidence in dealing with diabetic foot care in different approaches and categories (Monteiro-Soares. Crucial evidence demands healthcare providers periodic foot assessments according to the risk of stratification category, deliver foot health education and insist on other accompanying self-management support to diabetic patients depending on their needs (Monteiro-Soares et al., 2020; Morey-Vargas.

Diabetic foot syndrome is attributed to two major risk factors, namely loss of protective foot sensation peripheral neuropathy and peripheral artery disease (PAD)(Monteiro-Soares et al., 2020). However, other factors like walking barefoot, Charcot joint, dry foot skin, toenail ingrowth, onychomycosis, smoking, tight footwear, and poor foot hygiene are equally significant in causing foot ulcers (Monteiro-Soares. The study done in Tanzania reported that dry skin and toenail ingrowth are four times more likely to increase future foot ulceration(Naemi *et al.*, 2020). Meanwhile, these are modifiable risk factors through early recognition and intervention to prevent the likelihood of foot ulceration through integrated clinical and self-management efforts (Hjelm & Beebwa, 2013; IDF et al.., 2021; Monteiro-Soares).

Although health education on self-management and support has been put into clinical evidence of diabetic patients, knowledge and the self-foot care practices for patients have previously been reported poor (Chiwanga & Njelekela, 2015; Muhammad-Lutfi et al., 2014; Solan, Kheir, Salih, & Al-fairy. Previous evidence supports that poor practices and low foot care knowledge among diabetic patients are anticipated by limited health information and teaching about diabetic foot care (Chiwanga & Njelekela, 2015; Rubio et al., 2020; Seid & Tsige, 2015). A study at MNH report that only 48% of the diabetic patients received information for diabetic foot care, although teaching program daily conducted at a clinic (Chiwanga & Njelekela, 2015). Assessment of knowledge on the risk factors for diabetic foot and the foot care practices to patients is a pivotal cornerstone toward

planning and implementation of their integrated care and prevention of foot complication (Morey-vargas & Smith, 2015; Tuha *et al.*, 2021).

Hence there's limited quantitative evidence concerning diabetic foot syndrome knowledge on the risk factors and the self-foot care practices among DM patients. The study aimed to assess the knowledge on the potential risk factors for foot ulceration and the self-foot care practices among diabetic patients at the Muhimbili National Hospital in Tanzania.

Materials and methods
Study design and setting.
A hospital based descriptive cross-sectional study design was employed in this study to assess the knowledge on the potential risk factors for foot ulceration and the self-foot care practices among diabetic patients attending the Diabetic clinic at MNH. The hospital is in Dar es Salaam, Tanzania. The hospital serves as a national referral hospital while simultaneously functioning as a teaching hospital for the Muhimbili University of Health and Allied Sciences. The hospital has a bed capacity of 1,500 and attends about 2,000 outpatients per day. The diabetic clinic is one of the clinics in the MNH and delivers services to both insured and non-insured diabetes patients. The clinic receives both adult and pediatric diabetes patients from within and outside of Dar es Salaam. The clinic provides routine diabetic services such as monitoring of body mass index, glucose monitoring, medication prescriptions, nutritional review, and consultation sessions.

Study population and eligibility criteria.
This study involved a population of diabetic patients attending the Diabetic clinic at Muhimbili National Hospital**.** All adult diabetic patients attending the Diabetic clinic at MNH were included in this study. Patients who had cognitive impairment were excluded from this study because they could introduce recall bias due to distorted memory and concentration. Also, all patients who had communication problems like hearing and speaking problems were excluded from the current study.

Sample size and sampling procedure.
We used the single population proportion formula to estimate the minimum required sample size given as [N=(Z)2×p(1–p)/e2], where *N* is the minimum required sample size, and *p* is the estimated prevalence of diabetic foot ulcers (9.04%) based on a previous study conducted in Kenya (Maingi, Kikuvi, & Matheri, 2020). Furthermore, *e* is the margin of error or precision (5%), and Z is the standard normal value (1.96) corresponding to a 95% CI. After adding a 10% proportion of non-response, the estimated sample size was 140 diabetic patients.

A simple random sampling technique was applied to select participants from patients whose visited at a clinic and registered for consultation.

Data collection tool
An interviewer-administered questionnaire was used as a data collection tool in this study. The tool was adopted from previous related studies (Monteiro-soares et al., 2020; Morey-vargas & Smith, 2015; Naemi et al., 2020) and modified to suit the specific objectives of this study. The questionnaire was prepared in English language and then translated into the Swahili language, the Tanzania national language to enhance better understanding by the study participants. The translation of the questionnaire was done by the principal investigators of this study (EJ and EZC) who are fluent in both languages (English and Swahili language). The questionnaire was divided into three parts, first part comprised of questions on socio-demographic characteristics, the second part comprised of questions

concerning knowledge on the risk factors for diabetic foot syndrome and third part contained questions on participants' self-foot care practices.

Validity and reliability of the questionnaire
As part of quality control, a pilot study was done on 10% of the sample size (14 diabetic patients) who were finally excluded from the actual study sample. A reliability test was performed by calculating the reliability coefficient (Cronbach's alpha), and its values for knowledge on risk factors for diabetic foot syndromes and self-foot care practices parts were 0.717 and 0.792 respectively. These findings indicate a good reliability level for the tool with the studied sample.

Data collection procedure
Data collection was conducted in June 2022 and December 2022 by the principal investigators (EJ and EZC) of this study with the assistance of 1 trained research assistant who had completed 2 days of intensive training at the data collection site. Patients waiting for their consultation at the waiting area were approached by the principal investigators and research assistant and invited to participate in the study. All participants provided written informed consent and completed a background information sheet to obtain the demographic information. Data collection was conducted in Swahili (the national language) to enhance a better understanding to participants of this study. Each participant spent an average of 15 to 20 minutes responding to items of an interviewer-administered questionnaire employed as a data collection tool in the current study.

Data management and analysis
After data collection, the response was coded and entered the computer using Epi-info software version 7.2, and the data were analyzed using IBM SPSS version 25.0. Descriptive analyses were performed to present the demographic characteristics of the participants. Descriptive statistics using frequencies, percentages, means, and standard deviations were computed, and data were then presented in tables. The knowledge on the risk factors for diabetic foot syndrome was measured based on 9 parameters. Of which it contained 9 principal questions, patients were supposed to respond by choosing "Yes/No or I don't know", where "correct answer" as "Yes" was principal accounted as 1 to all question except 2 of which "Yes" was counted as 0 or null and "No" was counted as 1 (**getting asleep and experiencing body weakness**). The knowledge was categorized as Inadequate Knowledge if participants scored 0-5 (55% and below) out of 9 identified questions, and Adequate Knowledge if participants scored above 6-9 (more than 55%).

The self-foot care practices were measured based on the six parameter questions. The participants were supposed to respond "Yes/No or I don't know", where "Yes" was a correct answer, it was counted as 1 and "No or I don't know" counted as 0. Therefore, the foot practices were categorized based on half of the maximum parameters as Poor self-foot care practices scoring 0-3 (50% or below), Good self-foot care practices scoring 4-6(more than 50%). A bivariate analysis was performed to determine the associated factors and variables that showed association, p<0.2 were candidates for multivariate logistic regression. In a multivariate logistic regression model by adjusting for potential confounding variables, the test of significance was performed using a 95% confidence interval, and the level of significance was set at a p-value < 0.05.

Ethical considerations
This study received ethical approval from the Institutional Review Board in the Directorate of Research and Publications of the Muhimbili University of Health and Allied Sciences (Ref. DA. 25/111/01B/117). Permission to conduct the study was obtained from MNH administration

with (Ref. No: MNH/TRCU/Perm/2022/033). Written informed consent was sought and obtained from all participants before data collection. Anonymity and confidentiality of the participants' information were strictly maintained by removing any personal identifiers from the data. Moreover, participation was fully voluntary, and the participants were informed of their full right to skip or ignore any question or withdraw from their participation at any stage without undesirable consequences.

Results
The Social-Demographic characteristics of the Participants.

One hundred forty adult participants aged (20-100 years) were enrolled in the study, it was equal to 40% of 350 encountered during the data collection period. The mean age (±SD) (57.8±14.7). Majority of participants were female 87(62.1%), aged between 41-65, 98(70%) and below/primary education 69(49.3%). 42(30%) of the participants reported to have history of foot ulceration, statistically indicates that in every 3 Diabetic patients 1 have history of foot ulceration among encountered study participants (Table 1).

Table 1: The social-demographic characteristics of the participants (N=140)

Variable		Frequency(N)	Percent's (N) %
Gender	Male	53	37.9
	Female	87	62.1
Age	20-40	11	7.9
	41-65	98	70.0
	66-100	31	22.1
Marital status	Married	119	85.0
	Divorced	10	7.1
	Not married	11	7.9
Education level	Below/primary	69	49.3
	Secondary	38	27.1
	Collage/University	33	23.6
Occupation	Employed	25	17.9
	Self-employed	56	40.0
	Retired	32	22.9
	No job	27	19.3
Residences	Out of Dar es salaam	35	25.0
	Dar es salaam	105	75.0
Duration of DM	>5 months ago	9	6.4
	1-5year	46	32.9
	>5-10 year	32	22.9
	>10 year	53	37.9

| History of diabetic foot ulcer. | No | 98 | 70.0 |
| | Yes | 42 | 30.0 |

Source: Research data base of diabetes 2022

Knowledge on the risk factors for diabetic foot syndromes.

As in (*Table 2*), Majority of participants were unaware on the Smoking 109(78.4%) and Toenail ingrowth 96(68.3%) as potential risk to diabetic foot ulceration. Furthermore, sore/foot fungus is also a potential risk factors for diabetic foot, but minority of participants 39(27.9%) shows attention in observing it as the potential risk factors. However, other factors were not as real potential risk factors but were incorporated as destructors like sleeping and body weakness. The knowledge on the risk factors was computed out of 9 maximum score, majority of the participants 93(66.4%) have overall Inadequate knowledge on the risk factors for diabetic foot syndromes. The mean score of knowledge on the Risk Factors for Diabetic Foot Syndromes was 5.1±1.52, out of maximum score of 9 (Table 4).

Table 2: Participants responses on the risk factors for diabetic foot syndromes, [multiple choice] (N=140).

Knowledge assessments Items	Correct response N(%)	Incorrect response N(%)
Losing protective foot sensation is a risk for your feet to develop ulcers.	92(65.7%)	48(34.3%)
Emerging foot fungus (between the toe) is a risk factor for your feet to develop ulcers.	39(27.9%)	101(72.1%)
Walking barefoot indoor and outdoor, you are at risk of getting foot ulcer.	102(73.4%)	37(26.6%)
Having Charcot joint/limited ankle mobility, you are at risk of getting foot ulcer	75(55.0%)	62(45.0%)
Wearing tight shoes is putting yourself at higher risk of developing foo ulcer.	116(83.5%)	23(16.5%)
Smoking reduces blood flow to the feet, which is a risk for foot ulcer.	30(21.6%)	109(78.4%)
If you are diabetic getting normal asleep is a risk cause of foot ulcer.	19(13.7%)	120(86.3%)
If you are diabetic experiencing body weakness is a risk for foot ulcer.	42(30.4%)	96(69.6%)
If you're diabetic, foot toenail ingrowth is a potential risk for developing foot ulcer.	44(31.7%)	96(68.3%)

Source: research data base of diabetes 2022

Self-Foot care practices

In (Table 3), Majority of participants 84(60.4%) reported poorest foot wash with warm water and dry with a clean dry towel. However, taking medication for glycemic control was among of the practices that was best done by the patients 118(84.9%), it seems that emphasis has been on proper taking hypoglycemic drugs or

insulin than other potential factors to diabetic patients.

The self-foot care practices were computed out of 6 maximum score factors, majority of the participants 97(69.3%) has good self-foot care practices (Table 4). The mean practices score of self-foot care practices was 4.02±1.9 out of 6 maximum score.

Table 3: The distribution of self-foot care practices responses among the patients.

Self-foot care practices assessments Items	Correct response N(%)	Incorrect response N(%)
Inspecting foot [every day]	97(69.8%)	42(30.2%)
Washing foot with warm water dry between the toe by clean towel	55(39.6%)	84(60.4%)
Lifestyle changing [exercising, stop smoking, alcohol and dieting]	97(69.8%)	42(30.2%)
Taking medication for glucose control [every day]	118(84.9%)	21(15.1%)
Following order and guideline for foot care given in each clinic visit	94(67.6%)	45(32.4%)
Wearing soft and non-tight shoes [every day]	102(73.4%)	38(26.6%)

Source: **Research data of diabetes 2022**

Table 4: **Classification of knowledge on the risk factor for diabetic foot syndrome and the self-foot care practices.**

	Knowledge on risk factor for DFS.		Self-Foot Care Practices.	
	Inadequate	Adequate	Poor	Good
Scores	93(66.4%)	47(33.6%)	43(30.7%)	97(69.3%)

Source: **Research data on diabetes 2022**

Association between the knowledge on the risk factors and the self-foot care practices.
After all possible confounders were controlled using multivariate logistic regression analysis. Gender(male) were three more likely associated with Inadequate knowledge on the risk factor for DFS (AOR: 3.71, 95%CI, 1.513-9.114, P=0.004169). Participants with history of foot ulceration (didn't experienced foot ulcer) was five-time more likely associated with Inadequate knowledge score for diabetic foot syndrome (AOR: 5.5, 95%CI: 2.14-14.165, P=0.000403) and duration of DM (>5months and less than 1year) was six times more likely to have Inadequate knowledge score (AOR:6.933, 95%CI: 0.69-68.97, P=0.098). on other hand the secondary education level was 0.179 times less associated with Inadequate knowledge score on the risk factors (AOR: 0.179, 95%CI: 0.045-0.70, P=0.0139). However, other independent and covariate variable was not significant correlated (**Error! Reference source not found.**).

Concerning the self-foot care practices, participants with >5months and less than 1 year from DM diagnosis were nineteen more likely associated with Poor self-foot care practice (AOR: 19.025, 95%CI: 2.716-133.293, *P*=0.003). History of foot ulceration (haven't experienced foot ulcer) were five times more likely associated with Poor self-foot care practices (AOR: 3.377, 95%CI: 1.218-9.366, *P*=0.019). furthermore, participants with primary education level were three times more likely to have Poor self-foot care practices (AOR: 3.33, 95%CI: 0.881-12.63, *p*= 0.0759). Other participants characteristics was not significant associated (**Error! Reference source not found.**).

Table 5: The factors associated with the knowledge on the risk factor for Diabetic Foot Syndromes (DFS)

Variable	Level of Knowledge on DFS					
	Inadequate	**Adequate**	COR(95%CI)	p-value	AOR(95%CI)	P-value
Gender						
Male	26(49.1%)	27(50.9%)	3.391(1.48-7.783)	0.007	3.71(1.513-9.114)	0.004169
Female	59(67.8%)	22(32.2%)	I			
Age						
20-40	4(36.4%)	7(63.6%)	4.965(0.69-35.40)	0.109	0.201(0.028- 1.4)	0.1098
41-65	59(60.2%)	39(39.8%)	1.085(0.31- 3.73)	0.896		
66-100	22(71.0%)	9(29.0%)	I			
Marital status						
Married	71(59.7%)	48(40.3%)	I			
Divorced	6(60%)	4(40%)	0.830(0.13- 4.98)	0.839		
Not married	8(72.7%)	3(27.3%)	0.924(0.08-3.93)	0.890		
Education level						
Below/primary	42(60.9%)	27(39.1%)	3.293(0.82-13.08)	0.090	0.303(0.076- 1.2)	0.0903
Secondary	17(44.7%)	21(55.3%)	5.975(1.49-23.87)	0.011	0.179(0.045-0.70)	0.0139
Collage	26(78.8%)	7(21.2%)	I			
Occupation						
Employed	19(76.0%)	6(24.0%)	I			
Self-employed	30(53.6%)	26(46.4%)	0.663(0.11- 3.69)	0.639		
Retired	21(65.6%)	11(34.4%)	0.523(0.15-1.72)	0.286		

No job	15(55.6%)	12(44.4%)	0.795(0.16-3.75)	0.772		
Residence						
Dar es salaam	60(57.1%)	45(42.9%)	I			
Off Country	25(71.4%)	10(28.6%)	1.157(0.35-3.83)	0.810		
Duration of DM						
>5monthes	6(66.7%)	3(33.3%)	0.147(0.014-1.46)	0.102	6.93(0.69-68.97)	0.098
1-5year	30(65.2%)	16(34.8%)	0.631(0.22-1.77)	0.383		
>5year-10year	19(59.4%)	13(40.6%)	1.154(0.38-3.46)	0.797		
>10year.	30(56.6%)	23(43.4%)	I			
History of foot ulceration.						
Yes	24(57.1%)	18(42.9%)	I			
No	61(62.2%)	37(37.8%)	6.44(2.40-17.29)	0.0002	5.5(2.14-14.164)	0.000403

COR: Crude odds ratio; CI: confidence interval; I, reference category, AOR: Advanced Odds Ratio.

Table 6: The association between the self-foot care practices and the social-demographic characteristics of the participants.

		Self-foot care practices					
		Poor	**Good**	COR (95%CI)	*P-value*	AOR(95%CI)	*P-value*
Sex	Male	16(30.2%)	37(69.8%)	1.051(0.42-2.58)	0.912		
	Female	27(31.0%)	60(69.0%)	I			
Age	20-40	3(27.3%)	8(72.7%)	1.984(0.27-14.5)	0.498		
	41-65	30(30.6%)	68(69.4%)	1.763(0.53-5.76)	0.347		
	66-100	10(32.3%)	21(67.7%)	I			
Marital Status	Married	40(33.6%)	79(66.4%)	I			
	Divorced	2(20.0%)	8(80.0%)	0.191(0.01-1.86)	0.154	1.719(0.086- 34.2)	0.722
	Not Married	1(9.1%)	10(90.9%)	0.581(0.02-11.6)	0.722		
Education Level	Primary	27(39.1%)	42(60.9%)	0.295(0.07-1.12)	0.073	3.33(0.881-12.63)	0.0759
	Secondary	10(26.3%)	28(73.7%)	0.699(0.18-2.70)	0.604		
	Collage/University	6(18.2%)	27(81.8%)	I			
Occupation	Employed	9(36.0%)	16(64.0%)	I			
	Self-Employed	18(32.1%)	38(67.9%)	0.528(0.10-2.62)	0.435		
	Retired	6(18.8%)	26(81.3%)	0.917(0.27-3.01)	0.886		
	No Job	10(37.0%)	17(63.0%)	1.189(0.22-6.33)	0.838		
Residences	Off country	13(37.1%)	22(62.9%)	0.690(0.24-1.97)	0.489		
	Dar es salaam	30(28.6%)	75(71.4%)	I			
Duration of DM	>5 months ago	7(77.8%)	2(22.2%)	0.052(0.007-0.3)	0.0029	19.02(2.71-133.2)	0.003
	1-5years	17(37.0%)	29(63.0%)	0.496(0.17-1.40)	0.186	2.013(0.712- 5.68)	0.186
	>5-10 years	8(25.0%)	24(75.0%)	0.863(0.28-2.64)	0.797		

	>10 years	11(20.8%)	42(79.2%)		I		
History of foot ulceration.	No	35(35.7%)	63(64.3%)	3.229(1.13-9.15)	0.0274	3.37(1.21-9.365)	0.0193
	Yes	8(19.0%)	34(81.0%)		I		

COR: Crude odds ratio; CI: confidence interval; I, reference category, AOR: Advanced Odds Ratio.

Discussion

This study assessed the knowledge on the risk factors for diabetic foot syndrome (ulcer) and the self-foot caring among diabetic patients attending the outpatient's clinic at The Muhimbili National Hospital in Dar es Salaam Tanzania. The current study has found 30% of participants had experienced foot ulcer during diabetic lifetime. A decade ago, a study done at Bugando Medical Center (BMC), an history of foot ulceration was 10.3% among diabetic, statistically its equal to threefold increase within a decade(Chalya et al., 2011). This finding resemble the previously reported history of foot ulceration in the different previous studies done in different setting in LMICs(Goweda et al., 2017; Seid & Tsige, 2015). The study conducted in Saudi Arabia indicated slightly higher (35%) reported history of foot ulceration among diabetic patients at Makkah Hospital(Goweda et al., 2017). The lower finding on history of foot ulcer was obtained from previous study done in South Africa, from which only 9.3% had previously history of foot ulceration (Goie, 2016). The finding reveals the growing burden of diabetic foot ulcer in the limited resource and low middle income countries. Its suitable call for the preparedness of the health facilities and respective authorities for resource and expertise in tackling outcome and demand of care.

The diabetic foot ulcer is anticipated by major two risk factors, the peripheral artery disease and loose of protective foot sensation(Monteiro-soares et al., 2020). Participants were knowledgeable on loose of protective foot sensation (65.7%) as the crucial risk factor for diabetic foot syndrome/ulcer. Studies done in South Africa and India reported only 38.2% and 39.0% respectively, were knowledgeable on loosing of protective foot sensation as a potential risk factor, contrasting to our current finding(Goie, 2016; John, John, Raj, & Fathima, 2019). However, participants lack knowledge on smoking (21.6%), developing foot fungus between the toe (27.7%) and toenail ingrowth (31.7%) to be potential risk

factors for DFS. According to WHO Regional Office for Africa 2015, smoking has tremendous increasing among different ethnic in LMIC Tanzania inclusively(WHO Africa, 2015). Smoking itself known to precipitate reduction on blood flowing to peripheral capillaries, posing risk for foot ulcer(WHO Africa, 2015). Previous studies done in India and Nigeria reported that 30% and 25% respectively, participants lack knowledge on smoking as a potential risk for DFS which was similar to our current finding(Desalu, Salawu, Jimoh, Adekoya, & Busari, 2011; John et al., 2019). Higher finding was reported from the study done in Kuwait which reported (75.6%) were aware with smoking as the potential risk factors for foot ulceration(Alsaleh, Albassam, Alsairafi, & Naser, 2021). Furthermore, the overall knowledge score on the risk factors for the diabetic foot syndrome was Inadequate (66.4%). This was slightly consistence with a study done at Rabat Hospital, Morocco, reported that over 50% of participants were overall unaware on the risk factors for diabetic foot(Lamchahab et al., 2011).

We found gender (male) were three times more likely associated to have Inadequate knowledge for DFS, the finding was not in agreements with the study done Kenya(Maingi, Kikuvi, & Matheri, 2020). History of foot ulcer (haven't experienced foot ulcer) were five time associated with Inadequate knowledge on the risk factor for DFS. Education level (secondary) was significantly associated with inadequate knowledge on the risk factor for DFS. Considerable limited access to health information concerning of diabetic foot risk factors and influence of belief contributes to this association(Hjelm & Beebwa, 2013; Mwangome, Geubbels, Klatser, & Dieleman, 2017). However, The knowledge gap and lack of knowledge on smoking, toe nail ingrowth and foot fungus risk factors has paved the way for increased rate of foot ulceration and hamper the individual glycemic control and improving the quality of life, It led to increased rate of readmission, amputation

and demands of resource in provision of care to patients at family level and National at large(Hertz et al., 2019; Mwangome et al., 2017; Naemi et al., 2020). This finding call for health care provider and the respective authorities on establishing and developing of an urgency foot care programs which promote the compliance and delivering holistic individualized foot care health education(Chiwanga & Njelekela, 2015). Our findings reveal poorest practices of washing foot with warm water and drying between toes with a clean dry towel (39.6%). The finding was in consistence with the study done in Saudi Arabia by which only 39.1% practices drying well between the toes(Goweda et al., 2017), other studies also elucidated the similar finding(John et al., 2019; Muhammad-lutfi et al., 2014).

It can be considered that, the influence of the social economic factors, belief, insufficient information received from the health care personnel and ignorance distort the individual self-esteem and motivation toward self-directed managements of the problems(Hjelm & Beebwa, 2013; Mwangome et al., 2017). Meanwhile, daily taking medication to control hyperglycemia was highly practiced (84.9%) compared to others self-foot care parameter. It's clearly an indication that insistence has been on the controlling hyperglycemia (curative therapy) with minor consideration of other associative factor that must be practiced together to reduce the risk of foot ulceration. Furthermore, the self-foot care practices score was Good (69.3%), the good self-foot care practices could be anticipated by productive educational program carried at a diabetic clinic. The finding was in accordance with the study done in Ethiopia, northern west which indicates 54% had a good self-foot care practices(Seid & Tsige, 2015).

The finding was inconsistence to the study done in Malaysia which reported 61.8% had poor self-foot care practices(Muhammad-lutfi et al., 2014). The poor self-foot care practice was significantly associated to the duration of DM (>5monthes to less than 1 year) and the history of foot ulceration (haven't experienced the foot ulcer) which was in agreement with the study done in Ethiopia(Tuha abdu, Abebe Getie Faris, Ababil Andualem, AMohammed, 2021). Newly diagnosed patients considered to have lower self-esteem and not adherence on the treatments and self-care practices is a possible explanation of this association. Although, the self-foot care practice score was Good, ongoing health education intervention should focus on adherence/compliance of patients to foot care.

Study limitation.
This study considered to be limited on inadequate sample size and study done at only single tertiary relocated National Hospital. Therefore, this finding might not reflect the real knowledge and the self-foot care practices in the community and is very weak to generalize. The cross-sectional nature of a study design poses a difficulty in establishment of cause effect relationship, this challenge or biases a study.

Conclusion and recommendations
The finding reveals knowledge gap on risk factors for diabetic foot syndromes and Adequate (good) self-foot care practices. The finding gives an insight in relation to the health education provided, the need of developing comprehensive rehabilitative therapy that addresses all aspect, focusing on individual needs, diabetic lifetime (duration) and history of foot ulceration.

Abbreviations

DFU	Diabetic foot ulcer.
DM	Diabetes mellitus
DFS	Diabetic foot syndromes
IDF	International Diabetes Federation,
IWGDF	International Working Group on Diabetic Foot
LMIC	Low Middle-Income Country
WHO	World Health Organization

Reference

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Nutritional Status Among Head and Neck Cancer Patients, Tanzania

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Abstract
Background: Nutrition in cancer patients is a challenge as various mechanisms can lead to poor nutrition status, and this contributes to poor prognosis and quality of life. In developing countries, before one concludes that cancer is the culprit to malnutrition, one has to rule out access to food. The Head and Neck region is involved with the intake and initial processing of the food. Therefore, the presence of a tumor in any subsite directly affects nutritional status.
Aim: This study aimed to establish nutritional adequacy among Head and Neck Cancer patients accessing services at a tertiary hospital in Tanzania.
Method: The study was cross-sectional descriptive. Patients with head and neck cancer attended from 1st August 2022 to 31st January 2023 were recruited. Information about access to food and nutrition was collected through anthropometric measurements and biochemical tests (serum albumin levels). After data collection, the correctness was checked by running frequency tables and analyzed by Statistical Package for the Social Sciences (SPSS) version 26.
Results: The study involved a total of 113 participants aged from 15 to 93 years with a mean age of 51.81+/-17.439 years. There were 74 males and 39 females, making a ratio of 1.9:1. Most participants had laryngeal tumours (46%). 85.6% of patients had advanced disease, stage IV (52.2%).17% of patients had pre-existing dietary risk, and 36.3% had severe malnourishment at presentation. In this study,75% of patients with oropharyngeal tumours had malnutrition, followed by hypopharyngeal and nasopharyngeal tumours, each with 66.7%. Stage IV patients were severely malnourished (57.6%) which was statistically significant.
Conclusion and recommendation: Laryngeal tumours are common in men and are related to advanced age. Most of the patients with Head and Neck Cancer (HNC) had severe malnourishment. Management of head and neck cancer should also address malnutrition which contributes to poor prognosis and quality of life.

Keywords: Nutritional status; head and neck; cancer

Background

The subject of nutrition in cancer patients is essential as the findings from the study can add value to the management of this group of patients and improve the prognosis and quality of life. Some factors affecting patients' nutrition are related to socioeconomic status, which influences access to food. Therefore, now that the patient is battling with the disease, his/her nutritional status may also be affected by accessibility factors.

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The presence of cancer has been incriminated for potentiating cachexia in patients. This is attributed to factors grouped as either pro-inflammatory or pro-cachexia. Pro-inflammatory factors released by tumours include IL-1, IL-6, and TNF-α. TNF-α is a cell-signalling protein responsible for several metabolic derangements. Activated macrophages and many other types of cells, such as CD4+, neutrophils, mast cells, eosinophils, and neurons, release TNF-α. TNF-α has a direct catabolic effect on skeletal muscles and acts by induction of the Ubiquitin Proteasome System (UPS). UPS is the primary intracellular protein degradation system. TNF-α.has been shown to increase gluconeogenesis, proteolysis, and loss of adipose tissues, which decreases glycogen synthesis, protein, and lipid (Patel et al.,2016).

A study by Llovera showed that TNF-α doubles the expression of the ubiquitin gene, leading to increased activity of the Ubiquitin Proteasome system in skeletal muscles, which leads to protein degradation and wasting (Witte et al.,2006). Another perspective on nutrition for head and neck cancer is the anatomical location of the disease. The head and neck region is involved with food intake and initial processing. The presence of a tumor in any of its subsites significantly influences the patient's nutritional status.

Nutritional assessment in cancer patients poses a unique challenge, especially for those who are bedridden, as anthropometric measurements such as height and weight require a patient to be in a standing position. However, different alternatives to these measurements are available, as highlighted in the methodology section. This study employed biochemical measurement as an alternative parameter to nutritional assessment. This study used a combination of biochemical and anthropometric measurements as the minimum recommended for assessing nutrition.

Malnutrition in head and neck cancer patients has been shown to have undesired outcomes, such as poor immunity, which result in prolonged morbidity and mortality in these patients (Britton et al., 2012). The same study also revealed poor treatment responses in malnourished patients. The nutritional status of cancer patients is a crucial parameter in influencing issues like length of hospital stay, prognosis, and the course of disease. Malnutrition in cancer patients is significant in some literature. It is reported to be present in 35-60% of all head and neck cancer patients at the time of presentation (Alshadwi et al.,2012). Malnutrition in head and neck cancer is a result of most cancers in the region impairing the ability of oral intake. Therefore, due to the debilitating effects of the disease, cancer patients often succumb to socioeconomic difficulties leading to poor access to food. This also affects the course of disease and overall nutrition of head and neck cancer patients.

There is an existing vacuum of knowledge on how malnutrition affects head and neck cancer patients at the time they present to health facilities regardless of its cause. There is also evidence of how nutritional assessment in head and neck cancer is often neglected, seen as inappropriate, or performed too late in the course of illness (Magnano et al.,2014). The relationship between HNC cancer stage, site, and how they affect the nutrition status of patients is scarcely mentioned not only in local but also global literature (Righini et al.,2012; Gosak et al.,2020; Capuano et al.,2010; Amaral et al.,2008; Kubrak et al.,2010; Takenaka et al.,2014). This study will help responsible authorities and the ENT

fraternity at large to address the customized needs of head and neck cancer patients and, therefore, provide room for tailored therapies that address nutritional needs. It will also enlighten us about the influence of tumor stages on nutritional status.

Methods
Study setting, sampling, and population.
The study was a cross-sectional descriptive study. All head and neck cancer patients aged 15 years and above who attended a tertiary hospital in Tanzania from 1st August 2022 to 31st January 2023 were recruited. The sample size was obtained by estimations based on the computation proposed by the Fischer sampling formula, and the estimated sample size was 120. A convenient sampling technique was used.

Inclusion Criteria
All patients with HNC attended with the identified primary site of malignancy and those who have been staged clinically and the diagnosis confirmed by histopathology.

Exclusion Criteria
Patients with Gastrostomy Feeding tube and Nasogastric tube Feeding were excluded from the study. Another excluded group was those patients with a history of treatment during the study period.

Data collection methods
Data collection was through clinical interviews, physical examination, and laboratory workup. In the clinical interview, a dietary screening tool (DST) was used, this tool is a simplified assessment tool that captures the main dietary components, and it has been assigned a score of 100 points; the weight of each food category was assigned by dietary principal components analysis done in previous studies by (Kang et al.,2016; Cotogni et al.,2021; Krejcie et al.,1970; Bailey

et al.,2009).In each food category questions have been allotted scores based on factor load for each question. The total score for each patient was computed. The patients were categorized as having nutritional risk if they had a DST score of less than 60, possible risk if they had a DST score from 60-75, and those who scored above 75 were categorized as not having nutritional risk. This tool helped to distinguish the malnourishment attributed to poor access/dietary behaviour as contrasted to that due to disease process.

In the clinical interview reference, the patient's weight was sought by establishing a patient's weight six months before the diagnosis of cancer (Righini et al.,2012). For those who did not recall their weight, the expected usual weight of a person was used instead. This was compared to the current weight to get the percentage of weight drop. Later, the results of this assessment were subjected to the **Nutritional Risk Screening tool**. This tool computed the overall nutritional risk to determine whether the patient was at low, medium, or high nutritional risk, and specific recommendations were made. Other information sought for completion of nutrition risk screening was illness status, which could cause the patient to be unable to eat for more than five days.

In physical examination, parameters that were assessed included anthropometric measurements. The latter included measurement of body weight and height which were used to compute Body Mass Index (BMI). BMI was computed by dividing body weight (in Kg) by the square of the

height (in meters) and classified for adults: underweight if BMI ≤18.4 kg/m2; average weight if 18.5 ≤BMI ≤24.9 kg/m2; pre-obese if 25.0 ≤BMI ≤29.9 kg/m2 and obese if BMI ≥30.0 kg/m, for those patients who were unable to stand recumbent height was measured, backed by Lee & Nieman as cited in a study by (Amaral et al.,2008).

Laboratory workup involved assessment of serum albumin. This biochemical parameter was used to compute the nutritional risk Index using the formula Nutritional Risk Index= (1.519 X serum albumin, g/L) + 0.417 X (present weight/usual weight x 100). The nutritional risk index is a powerful screening tool validated in various clinical settings for screening malnutrition in cancer patients (Cotogni et al.,2021). A Nutritional Risk Index>100 indicates that the patient is not malnourished, 97.5–100 indicates mild malnourishment, 83.5-<97.5 indicates moderate malnourishment and <83.5 indicates severe malnourishment. Serum albumin was measured from fasting blood levels as the serum albumin test is affordable and accessible in the study area compared to other biomarkers.

Data validity and reliability

The validity of this study is drawn from the choice of instrument for measuring variables, which are BMI and NRI, which have been inferred to a patient with different nutritional disorders with high accuracy. The reliability of the data was tested by inter-tester variability as the data was collected by the principal investigator and an assistant who was trained on the study protocol using the same instruments. Again, reliability was tested by the Test-retests technique, in which variables such as the height of a patient were tested and retested on the same patient by the same investigator to monitor the consistency of the results.

Data management and analysis

The data collected was handled with confidentiality and was analyzed using computer software SPSS version 26. Cross tabulations were plotted for the Nutritional status of HNC versus the anatomical site of the tumor, tumor stage, status at presentation, and pre-existing nutritional risk. Chi-square tests tested the relationship of the variables.

Ethical Issues

Ethical clearance to conduct this study was sought from Muhimbili University of Health and Allied Sciences Institutional Review Board (IRB) and assigned the reference number MUHAS-09-2022-32.

Results

Table 1: Age and Sex distribution of participants (N=113)

Variable	n(%)
A. Age group(years)	
15-47Young adults	40(35.4)
48-63 Middle Aged	47(41.6)
>64 Elderly	26(23)
B.Sex	
Male	74(65.5)
Female	39(34.5)

The study categorized patients into three age groups based on WHO stratification i.e. 15-47 years (young adults), 48-63years (middle-aged), and above 64 (elderly people). The study involved a total of 113 participants. Age ranged from 15 to 93 years old with a mean age of 51.81+/-17.439 years. Most participants were in the age group 48-63 years, making up 41.6% of all participants. There were 74 males and 39 females making a ratio of 1.9:1.

Figure 1: Tumor site distribution.
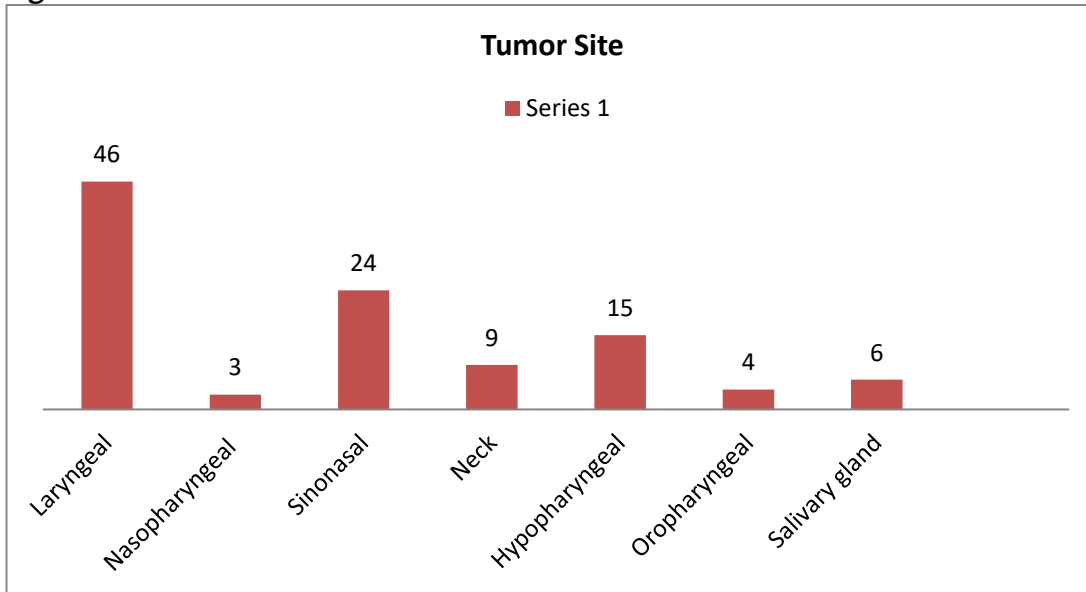
The majority of participants had laryngeal tumors (46%), followed by sino-nasal and hypopharyngeal tumors which made up 24% and 15% respectively. Nasopharyngeal tumors were composed of the least participants (3%).

Figure 2: Tumor stage Distribution.
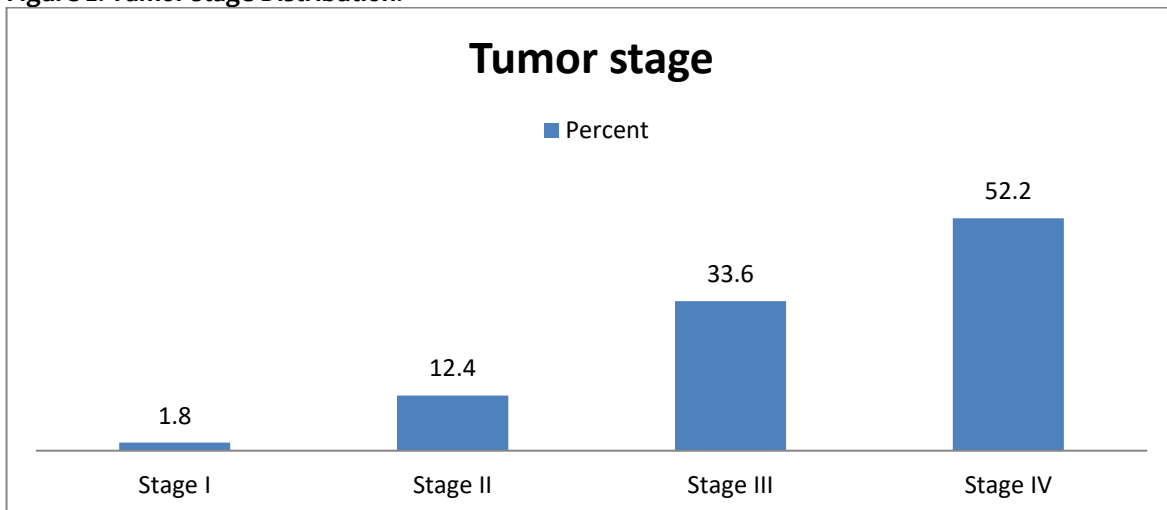
Advanced stages (III and IV) composed most of the patients in the study,85.6%, with stage IV revealed in half of the participants (52.2%).

Stage I disease was revealed in 1.8% of participants.

Figure 3: DST score
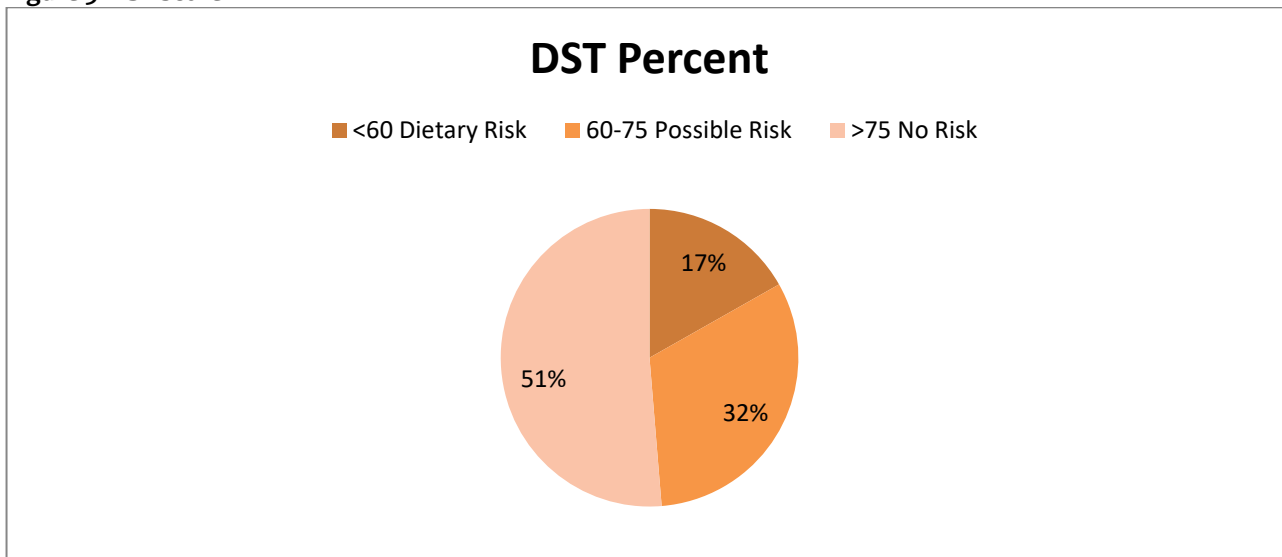
Seventeen per cent of patients were presented with a pre-existing dietary risk, i.e., a DST score of fewer than 60 points. A good proportion of patients presented with no nutritional risk based on their diet i.e.51%.

Figure 4: NRI score
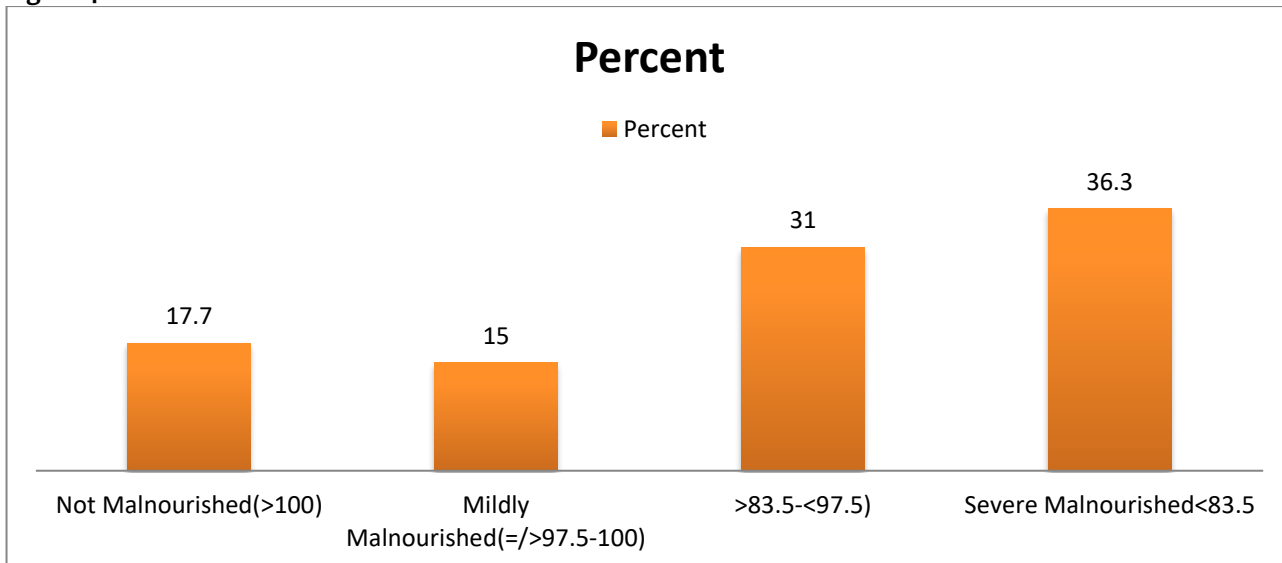
This study found that 36.3% of patients were presented with severe malnourishment as they scored less than 83.5 points based on NRI ratings, moderately malnourished patients made 31%of participants. Well-nourished patients were 17.7%.

Figure 5: BMI score
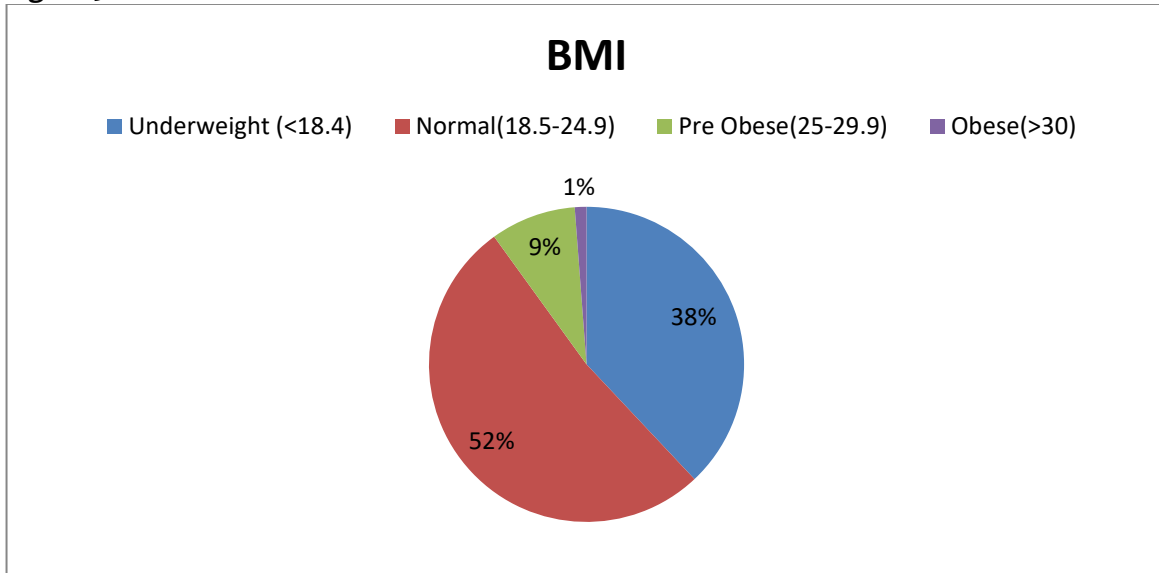
Based on the BMI scale 38% of participants were underweight (BMI score of equal or less than 18.4 points). In this scale, it was noted that 1% of patients had obesity.

Table 2: Age/Sex and Tumor Site

	Laryngeal	Nasopharyngeal	Sinonasal	Neck	Hypopharyngeal	Oropharyngeal	Salivary gland	Total
A: Age group								
15-47	14(35)	2(5)	14(35)	5(12.5)	3(7.5)	1(2.5)	1(2.5)	40(100)
48-63	21(44.7)	1(2.1)	7(14.9)	3(6.4)	7(14.9)	3(6.4)	5(10.6)	47(100)
=/>64	17(65.4)	0(0)	3(11.5)	1(3.8)	5(19.2)	0(0)	0(0)	26(100)
B: Sex Distribution								
Male	44(59.5)	3(4.1)	16(21.6)	3(4.1)	6(8.1)	1(1.4)	1(1.4)	74(100)
Female	8(20.5)	0(0.0)	8(20.5)	6(15.4)	9(23.1)	3(7.7)	5(12.8)	39(100)
Total	52(46)	3(2.7)	24(21.2)	9(8)	15(13.3)	4(3.5)	6(5.3)	113(100)

Laryngeal tumours were more common than any other HNC in the elderly and middle-aged groups, with 65.4% and 44.1%, respectively. However, this difference was not significant (χ^2=20.5 P= .058). It was noted that the laryngeal tumour was more common in men than all other HNC, and the difference was significant ($\chi2$=27.67 P= .000). In females; the hypopharyngeal tumour was much more common than the rest of the HN tumours with the same level of significance (23.1%).

Table 3: Age/Sex and Tumor Stage

	I	II	III	IV	Total
Age groups	**n(%)**				
15-47Young adults	1(2.5)	7(17.5)	14(35)	18(45)	40(100)
48-63 Middle Aged	1(2.1)	4(8.5)	17(36.2)	25(53.2)	47(100)
=/>64 Elderly	0(0)	3(11.5)	7(26.9)	16(**61.5**)	26(100)
Sex Distribution					
Male	2(2.7)	8(10.8)	24(32.4)	40(54.1)	74(100)
Female	0(0)	6(15.4)	14(35.9)	19(48.7)	39(100)

Elderly patients presented late to health care, with 88.4% of them presenting with stage III and IV disease, though the difference was not significant (χ^2=3.34　P= .765). Among male patients, the majority presented at an advanced disease stage (86.5%) χ^2=1.716 P= .633.

Table 4: Tumor site/stage and Nutritional status

	Not malnourished(>100)	Mild malnourished(=/>97.5-100)	Moderately malnourished(=/>83.5-<97.5)	Severe malnourished<83.5	Total
A: Tumor site					
Laryngeal	13(25)	10(19.2)	14(26.9)	15(28.8)	52(100)
Nasopharyngeal	1(33)	0(0)	0(0)	2(66.7)	3(100)
Sinonasal	4(16.7)	6(25)	10(41.7)	4(16.7)	24(100)
Neck	1(14.3)	0(0)	3(42.9)	5(55.6)	7(100)
Hypopharyngeal	0(0)	0(0)	5(33.3)	10(66.7)	15(100)
Oropharyngeal	**0(0)**	**1(25)**	**0(0)**	**3(75)**	**4(100)**
Salivary gland	1(16.7)	0(0)	3(50)	2(33.3)	6(100)
B: Tumor Stage					
I	1(50)	0(0)	1(50)	0(0)	2(100)
II	11(78.6)	0(0)	1(7.1)	2(14.3)	14(100)
III	6(15.8)	10(26.3)	17(44.7)	5(13.2)	38(100)
IV	**2(3.4)**	**7(11.9)**	**16(27.1)**	**34(57.6)**	**59(100)**
Total	**20(17.7)**	**17(15)**	**35(31)**	**41(36.3)**	**113(100)**

The highest percentage of malnutrition was found in oropharyngeal tumours (75%), followed closely by hypopharyngeal and nasopharyngeal tumours, each with 66.7%. The difference was, however, not significant (χ^2 =27.577 P=.069). Stage IV patients were severely malnourished in most excellent percentages and this finding was significant (57.6%) χ^2 =64.414 P=.000.

Table 5: DST score and NRI score

	Not malnourished(>100)	Mild malnourished(=/>97.5-100)	Moderately malnourished(=/>83.5-<97.5)	Severe malnourished<83.5	Total
DST score					
<60	1(5.3)	1(5.3)	7(36.8)	10(52.6)	19(100)
60-75	8(22.2)	6(16.7)	6(16.7)	16(44.4)	36(100)
>75	11(19)	10(17.2)	22(37.9)	15(25.9)	58(100)
Total	**20(17.7)**	**17(15)**	**35(31)**	**41(36.3)**	**113(100)**

Patients with the highest dietary risk had the highest proportion of severe malnourishment at presentation (52.6) χ^2=10.879 P=0.092.

Discussion

This study found that most head and neck cancers were in patients aged 48-63years, classified as middle-aged, with a mean of 51.8 years; this finding is close to that by (Righini et al.,2012), who found that the mean age in head and neck cancer patients to be 59 years. (Amaral et al.2008) found a similar pattern of head and neck cancer patients with a mean age of 57.1 years. A local study done at a cancer institute in Tanzania by Nundu found a similar age distribution for head and neck cancer with a mean age of 51 years (Britton et al.,2012). The sex distribution of participants showed male predominance with 65.5%. This finding is in congruence with the study by Nundu et al.,2020) in a cancer institute in which 58.7% of HNC patients were male.

This study revealed that 36.3% of patients presented for the first time with severe malnourishment according to NRI score (<83.5 points). Based on BMI score 38.1% of HNC presented at the ENT department as underweight. However, it should be noted that some patients had pre-existing nutritional risk based on their dietary intake, which was assessed using the Dietary Screening Tool pioneered initially by (Bailey et al.,2009). According to DST categorization, this study found that 16.8% of patients had prior nutritional risk which could explain the high proportion of malnutrition at presentation. Critical Weight Loss (CWL) is a common phenomenon in HNC, defined as involuntary weight loss of ≥5% in one month or ≥10% in six months, which is present in around (30-55%) of HNC patients (Jager-Wittenaar et al.,2007). CWL phenomenon can explain the presentation of severe malnourishment at a high rate in this study.

A study by (Jager-Wittenaar et al.,2007) found that 19% of patients with HNC had CWL at presentation which is a slightly

lower rate than ours. The difference with our study could be explained by late presentation as most patients had advanced stage (II&IV) i.e. 88.6%.

Oropharyngeal tumour patients were presented with severe malnourishment at the highest rate of all HNC tumours assessed (75%) χ^2 =30.079 P=.090. This finding differed from the study of CWL by (Jager-Wittenaar et al.,2007), which showed that the highest proportion of weight loss in patients with HNC was seen in hypopharyngeal tumours (43%). This difference can be explained by the different tools used to assess nutritional status; our study used NRI while Jager's used CWL. A study in Japan by (Takenaka et al.,2014) had findings that were like the study by (Jager-Wittenaar et al.,2007), showing the highest proportion of malnutrition in head and neck cancer linked to hypopharyngeal tumours; however, this finding was not statistically significant.

Oropharyngeal cancer is incriminated in severe malnutrition due to two mechanisms which are systemic effect which occurs due to the involvement of CNS by the regulation of satiety and sense of taste by the action of cytokines produced by host monocytes and tumour cells (Van Cutsem et al.,2005). The second mechanism is that the local effects of the oropharyngeal tumour may impinge food intake and predispose a patient to severe malnourishment. These effects include odynophagia and dysphagia.

It was also noted that nasopharyngeal tumours had a higher malnutrition rate than laryngeal tumours (66.7% vs 28.8 respectively). This finding is explained by the fact that the majority of nasopharyngeal tumour patients presented with a relatively higher proportion of advanced disease (66.7% vs 44.2% had stage IV disease, χ^2=16.39, P=.565), which contributed to their poor nutritional state at presentation.

A different finding was in a study by (Jager-Wittenaar et al.,2007), who found overall malnutrition to be 16%; however, his study was limited to cancer in the oral cavity and oropharynx, which may explain the lower incidence as compared to this study.

Severe malnourishment was present in stage IV patients for about (57.6%) χ^2 =64.414 P=.000. The advanced stage of the tumour was associated with a large size tumour, which has a mechanical effect of obstructing the food passage, e.g. and hypopharyngeal tumour. Another feature of the advanced-stage disease is the involvement of multiple anatomical sites, e.g., an advanced sinonasal tumour may present with an oral involvement by palatal extension, which may end up causing dysphagia. This finding agreed with the study by (Takenaka et al.,2014), which found that advanced tumour staging in HNC had a significant association with severe malnourishment (56%).

In our study, it was noted that 16.8% of patients with HNC had nutritional risk which could have predisposed them to malnutrition regardless of disease. These findings were comparable to the study by (Esfahani et al.,2017) in Iran, who studied the nutritional risk in inoperable gastric adenocarcinoma; however, in his study, he found 87% of patients had moderate to severe nutritional risk. The cancer type might explain this large discrepancy. Their study included gastric tumours, which directly affect food uptake.

On the contrary, our study assessed multiple upper aerodigestive tumours. Some are not directly involved with dietary intake, like sinonasal tumours. Furthermore, the study by (Esfahani et al.,2017) used a different methodological approach by employing the Patient-Generated Subjective Global Assessment (PG-SGA) tool, and they clustered patients into moderate and severe malnutrition risk.

In this study, the majority had laryngeal tumours, which were followed by sinonasal and hypopharyngeal tumours with 46%, 19.5%, and 13 respectively; our study differed from the study by (Magnano et al.,2014) oropharyngeal and oral tumours predominated over laryngeal and hypopharyngeal tumour with 56.5% vs 46.5% respectively. The discrepancy might be explained by the methodological difference in which Magnano's study followed patients over four years (2009-2013). A similar pattern of HNC was found in (Righini et al.,2012) study in which oropharyngeal tumours were high on the list. This study also had a similar methodological approach to ours, i.e., they used NRI and BMI as nutritional criteria. However, they added an extra criterion of Weight Loss (WL) of more than/less than 10% to categorize malnutrition.

The finding in our study corresponded to a local study by (Abdulshakoor et al.,2020) in a cancer institute in Tanzania, which found that laryngeal tumours were high on the list with 19.7% of all HNC tumours. The lower percentage in his study is explained by the lower sample size, which was 66, compared to our study, which involved 113 participants. Another local study by (Nundu et al.,2020), which studied the effect of chemo-radiotherapy in HNC, also found laryngeal tumour as a leading pathology with 17.3%. The lower percentage in his study is explained by the source of patients who were not just from the ENT department but also from Oro-maxillofacial surgery (OMFS) and General surgery departments, which consisted of other tumours like oral cavity tumours, facial, maxillary and mandibular tumours.

This study found that 85.6% of patients were presented with advanced disease i.e. Stages III and IV, stage IV alone involving more than half of participants (52.2%). The finding in our study differed from an Italian study (Magnano et al.,2014) which found a slightly lower proportion of advanced disease. (Righini et al.,2012) in France had a finding corresponding to (Magnano et al.,2014), but his study categorized patients into two groups based on weight loss of >/= 10%. For those who were less malnourished (WL<10%), the advanced disease was found in 35%, and for those who were severely malnourished, 60% of patients had an advanced disease. Geographical differences explain the differences seen as the two studies were done in Europe and it is documented that cancers in Africa are diagnosed at an advanced stage and with relatively higher levels of malnutrition (Kaduka et al.,2017).

Based on this scale it was noted that 38% of patients were underweight at presentation. It also revealed that 1% had obesity. The finding of obesity in these patients is supported by literature, which shows that obesity alone is an independent risk factor for about 20% of all cancers (Hurria et al.,2012). In the head and neck region obesity has been linked to Thyroid tumours and non-Hodgkin lymphomas. The mechanism for this relationship is the presence of low-grade inflammation (esp.IL-6 cytokine) in obese people which promotes malignant cell growth and progression (Hurria et al.,2012). These findings were contrary to those by (Kaduka et al.,2017) in Kenya who found malnutrition at presentation was present in only 13.4% of participants, with male dominance. The difference is explained by the later study, which involved tumours other than HNC, such as digestive system tumours, breast, hematopoietic, etc.

It was found in this study that among middle-aged and the elderly, the laryngeal tumour was the most familiar pathology, with 44.1% and 65.4%, respectively. This finding concurred with most of the literature on HNC, where tumors commence in the 6th to 7th

decades. The finding that most laryngeal tumours occur in males cannot be overemphasized as most literature links it to the use of alcohol and smoking, which have synergistic effects of carcinogenesis. The two risk factors are common in men (Ellis et al.,2012).

It was revealed that 88.4% of elderly patients were presented with stage III and IV disease though the difference was not significant. This finding is explained by the fact that the majority of HNC patients who show up in health facilities are aged >/= 50yrs (Takenaka et al.,2014) and they present with advanced disease (Kaduka et al.,2017)

This study evidenced an alarming rate of malnutrition in HNC. The highest proportion of malnutrition was found in oropharyngeal tumours, followed by hypopharyngeal and nasopharyngeal tumours, each with 66.7%. A whole body of evidence supports the high rates, (Kaduka et al.,2017) in Kenya found the prevalence of malnutrition in HNC was 17.6% in lip oral cavity and pharyngeal tumour combined, however in their study, they used BMI as a sole criterion for nutritional assessment which some authors incriminate it for its poor sensitivity in overweight and obese patients (Magnano et al.,2014). In the study by (Nundu et al.,2020) in ORCI found that the majority of patients with hypopharyngeal cancer had malnutrition at 85.7% followed by oropharyngeal cancer at 60%, however in his study, he just used BMI as a nutritional assessment tool, and he assessed nutrition after the use of radiotherapy

This study found that patients with the highest dietary risk had the highest proportion of severe malnourishment at presentation (52.6%) χ^2=10.879 P=0.092. It is evidenced that malnutrition is a common feature associated with predisposing patients with HNC to poor prognostic outcomes (Takenaka et al.,2014).

Conclusion and recommendations
The laryngeal tumour is more common in men and strongly related to advanced age. Most of the patients with HNC had severe malnourishment at presentation. The oropharyngeal tumour had the highest rate of severe malnourishment compared to other anatomical sites in the head and neck. Hypopharyngeal and nasopharyngeal tumours ranked second in causing severe malnourishment.

There should be a paradigm shift towards health-seeking behaviour in the Tanzanian community. The latter should be educated more on avoiding risky practices related to cancer aetiology. Healthcare practitioners should address patients with hypopharyngeal tumours with care by providing adequate nutritional support as required.

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Compliance to Recommended Prevention and Management Practices among Type 2 Diabetes Patients in Morogoro Municipality, Tanzania

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Abstract
Introduction: Diabetes-related complications are the significant causes of morbidity and mortality among type 2 diabetes patients. The complications can be reduced by practising and maintaining several preventive measures. The present study aimed to assess compliance and factors associated with recommended management practices and prevention of complications among type 2 diabetes patients in selected health facilities in Morogoro Municipality, Tanzania.
Methods: A hospital-based cross-sectional study was conducted from February to May 2023 among 140 patients diagnosed with diabetes for at least three months before the study. Data were collected through face-to-face interviews using a structured questionnaire, which included patients' characteristics and a previously validated Summary of Diabetes Self-care Activities questionnaire to assess patients' compliance with recommended practices. A multivariable regression analysis was employed to identify factors associated with compliance with recommended practices.
Results: The mean age of the respondents was 59 ±12.08 years and 65% were females. Among 140 patients, 91.4% (n=128) had poor or unsatisfactory self-care practices with an overall mean of 3.81± 2.08 days per week for diabetes management. The recommended practices with good or satisfactory performance were non-smoking, non-alcohol drinking and prescribed medication. In contrast, unsatisfactory performance was observed for self-monitoring blood glucose and physical activities. Multiple regression analysis showed that co-morbidity (AOR 4.5; 95% CI: 1.14-18.02) and being employed (AOR 4.4; 95% CI: 1.25-15.44) independently predict self-care practices.
Conclusion and recommendation: Compliance with self-monitoring of blood glucose, physical exercise and dietary practices were found to be low among type 2 diabetes patients, which could increase the risk of complications. Nutritional and lifestyle counselling and the use of peer groups should be emphasized to improve compliance with recommended practices.

Keywords: Type 2 diabetes, compliance, prevention and management practices, Tanzania.

Introduction

Globally, type 2 diabetes mellitus (T2DM) is considered one of the major public health epidemics, with a considerable number of premature deaths, disabilities, and high morbidity and mortality rates (Khan *et al.,* 2020). The prevalence has been on the increase mainly due to the increasing prevalence of risk factors such as sedentary lifestyles and unhealthy eating habits resulting in overweight and obesity (Motala *et al.,* 2022). Tanzania is one of the top five Sub-Saharan African (SSA) countries where the high prevalence of T2DM has a significant effect (IDF, 2021). The International Diabetes Federation [IDF] (2021) reported that more than two million Tanzanian adults have diabetes, primarily found in urban areas.

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Complications of T2DM can be costly due to its chronic nature and multi-organ involvement which can cause damage to small blood vessels (micro-vascular) such as kidney diseases (nephropathy), eye damage (retinopathy) and nerve damage (neuropathy) and macro-vascular such as blood vessels which lead to heart attack, stroke, or leg amputation (WHO, 2019). People with diabetes are at risk of mental health, such as anxiety, that can result from the stress of managing their conditions (Kalra *et al.,* 2018). Furthermore, it tends to affect individual functional capacities and quality of life, leading to significant morbidity and premature mortality. This is associated with an economic burden to the patients, families, and national and health systems because of the frequent visits to the healthcare care providers and admission to health facilities (Riddle & Herman, 2018).

Even though diabetes can have several impacts on health, its early detection and adherence to a healthy lifestyle change can positively impact the course of the disease (American Diabetes Association [ADA], 2018). Secondary prevention aims to reduce disease impacts on those who already have diabetes or prevent the development of long-term complications (Bali *et al.,* 2018). The complications of the disease can be reduced by several preventive measures including maintaining body weight, limiting alcohol consumption, smoking cessation, and preventive medications (Alouki *et al.,* 2016). In addition, effective management of T2DM requires the patients to learn and practice healthy self-care and lifestyle behaviours like blood glucose monitoring, taking medications, diet and exercise, proper counselling and compliance to these self-care practices and healthy lifestyle behaviour to control blood glucose levels and other complications associated with diabetes (Aschner, 2017).

Numerous studies that assessed compliance and adherence to recommended practices reported varied results. The study done in Saudi Arabia reported that adherence to self-care activities, including diet, exercise, blood glucose monitoring and foot care, was relatively poor. However, medication intake was strictly followed (Alhaiti *et al.,* 2020). A study done by Bonger and Tariku (2018), revealed that the extent to which individuals adhere to the recommended management of T2DM is substantially low whereby about 80% of diabetes patients did not adhere to the recommended diet management and self-monitoring of blood glucose level, while a majority (96%) of the respondents adhere to the prescribed medications. A study done by Rijal *et al.* (2022), to assess compliance of diabetes patients to diet and exercise revealed that compliance on diet was reasonable compared to exercise aspects. Several studies indicated that demographic and socioeconomic, clinical, and health-related characteristics such as age, religion, employment status, sex, family support, duration of T2DM, presence of comorbidities and diabetes-related complications influence compliance to recommended management practices (Ayele *et al.,* 2018; Zarei *et al.,* 2022; Zewdie *et al.,* 2022).

In Tanzania, most studies on T2DM have focused on prevalence and risk factors, diabetes-related complications, knowledge, and awareness (Chiwanga et *al.,* 2016; Stanifer *et al.,* 2016; Damian *et al.,* 2017). However, more information is needed about compliance with recommended prevention and management practices (Rwegerera, 2014; Mwanri *et al.,* 2018). Thus, this study assessed compliance with the recommended management practice and identified factors associated with compliance among T2DM patients. The results will help plan interventions targeting secondary prevention among T2DM patients to improve their quality of life and reduce the burden on the health system.

Methodology
Study area, design, and population.
The cross-sectional study was carried out in urban areas of the Morogoro region between February and May 2023. Morogoro municipality was selected purposively due to limited information on diabetes and being a fast-growing area as it is a central connection to the Southern Highlands and central and

Lake zones. This study included patients diagnosed with T2DM within three months or more and receiving healthcare services in selected diabetes clinics. Type 2 diabetes patients who had hearing or speech problems and those who were critically ill to respond to the questions were excluded from the study.

Sample size and sampling procedures.
A sample was estimated using the formula adopted from Kothari (2004). Based on the prevalence of T2DM in Tanzania (STEP-SURVEY) of 9.1% (Mayige & Kagaruki, 2013), the standard normal distribution of 95% and absolute error of 5% were used to obtain the sample size of 127 T2DM and after adjusting the non-response rate of 10% the total sample size was 140. The two health facilities with diabetes clinics, Sabasaba Health Center, and Morogoro Regional Referral Hospital, were purposively selected to involve public health facilities with diabetes clinics and accommodate most patients. About 15 patients attended the diabetes clinic per day at Morogoro Regional Referral Hospital and about five patients at Sabasaba Health Center. Based on this, a simple random sampling technique was used to select participants from the register list. About 15 patients from the two hospitals who met inclusion criteria and consented to participate were interviewed daily. A proportionate sampling technique was applied to acquire a total sample of 140 T2DM patients in two hospitals. About 80% of the T2DM patients were selected from Morogoro Regional Referral Hospital and 20% from Sabasaba Health Center.

Data collection tool and procedure
Researchers visited the outpatient diabetes clinic weekly on Thursday. Patients were approached to introduce the study to them and seek their consent to participate while they waited for their consultation. Data were collected using a structured questionnaire, which took an average of 45 minutes to complete. Face-to-face interviews were done to collect information on the respondents' sociodemographic details, clinical characteristics, and a Summary of Diabetes Self-Care Activities (SDSCA) questionnaire (Toobert *et al.,* 2000). This questionnaire was adapted and modified to elicit information on patients' frequency to comply with recommended prevention and management practices. The questionnaire consisted of items on the general diet, specific diet, physical activity, blood-glucose testing, foot care and items for smoking. Also, items concerning alcohol consumption and medication were added to capture all recommended practices for the prevention and management of T2DM.

      Each item in SDSCA asks the respondents to mark the number of days the patients performed and adhered to the indicated self-care behaviour related to diabetes care within the last week on an eight-point scale ranging from (0-7), with 0 being the least desirable. Therefore, to maintain this standardization in results interpretation, one item of the specific diet dimension, which asks about intake of fat-rich foods, had their score inverted (7=0, 6=1, 5=2, 4=3, 3=4, 2=5, 1=6, 0=7) and vice versa as recommended by the revised SDSCA. The overall mean score of adherence was generated for each item of recommended practices by summating the mean score for self-care practices of all items and dividing it by the sum of some questions on each scale of the items. Final classification was done as having satisfactory or good self-care practices if the score was above or equal to 5 and poor or unsatisfactory for scores below 5.

Statistical analysis
The Statistical Package for Social Science IBM (SPSS) for Windows version 25 was used for data analysis. Descriptive statistics such as means, and standard deviation (SD) were used for numerical or continuous variables to describe self-care practices. Univariate logistics regression (analysis of a single

variable) was used to determine the strength of association between the dependent (self-care practices) and independent variables (socio-demographic and clinical characteristics). All variables that were significant at a p-value of ≤0.05 in univariate analysis were selected for multivariate analysis (analysis of multiple variables) to adjust the effect of confounders. A backward stepwise procedure was used to ascertain the suitable variables whereby all variables with a p-value of ≤0.05 were retained in a model. Both crude odds ratio (COR) and adjusted odds ratio (AOR) with 95% CI were reported.

Ethical approval
The study commenced upon ethical approval from the National Health Research Committee of the National Institute for Medical Research (NatHREC) with a reference number NIMR/HQ/R.8a/Vol.IX/4239. Also, permission to conduct this study was obtained from the President's Office of Regional Authority and Local Government (PORALG) and respective regional, district and health facility authorities. The aim, procedures, benefits and possible risks of the study were explained and all participants who agreed to participate in this study and met the eligibility criteria were enrolled. Informed written consent was sought from the respondents to ensure voluntary participation in the study. The participants were assured of confidentiality and anonymity concerning the collected information by using numbers to represent patients' names during data handling.

Results
Socio-demographic characteristics of the respondents
The mean age of respondents was 59 years; 65% (n=91) were females, 60.7% (n=85) were married, 7.9% (n=11) had college or university education, and only 7.9% (n=11) were employed in the formal sector. The mean duration of diabetes was 8 ±7.13 years. About half of the respondents, 48% (n=67), had a family history of diabetes, and 42% (n=59) had comorbidities. Out of those with comorbidities, 35.7% (n=50) were hypertensive. About 66% (n=92) of respondents had diabetes-related complications. Of those with complications, 22.9 % (n=32) had retinopathy (Table 1).

Table: Socio-demographic and clinical characteristics of the respondents

Variable	Frequency	Per cent	Mean (SD)
Age			58.84±12.08
18-49 years	35	25	
>50 years	105	75	
Sex			
Male	49	35	
Female	91	65	
Marital status			
Married	85	60.7	
Single (Separated/Divorced/Widowed)	55	39.3	
Education level			
No formal schooling	9	6.4	
Not completed primary school	16	11.4	
Primary school completed	85	60.7	
Not completed secondary school	2	1.4	
Completed secondary school	17	12.1	
College/university	11	7.9	
Source of income			
Formal employment	10	7.1	
Self-employed	44	31.4	

Retired officer	19	13.6	
Unemployed	52	37.1	
Farmer	15	10.7	
Duration of T2DM	140		8.18±7.13
Family history of diabetes			
Yes	67	47.9	
No	73	52.1	
Presence of co-morbidity (Chronic disease)			
Yes	59	42.1	
No	81	57.9	
Type of comorbidity			
Hypertension	50	35.7	
Heart disease	6	4.3	
Cancer	3	2.1	
Presence of diabetes-related complications			
Yes	92	65.7	
No	48	34.3	
Type of complications			
Retinopathy	32	22.9	
Hypertension	29	20.7	
Nephropathy	1	0.7	
Stroke	2	1.4	
Lower extremities amputation	6	4.3	
Retinopathy, Hypertension	14	10	
Hypertension, lower extremities amputation	2	1.4	
Lower extremities amputation and retinopathy	6	4.3	

Frequency of Adherence to Recommended Practices

Table 2 presents the mean number of days participants performed self-care practices for the last seven days. Most participants (91.4%, n=128) reported poor compliance with an overall mean score of 3.81 ± 2.08 days. Only 8.6% of respondents (n=12) reported good compliance. The most performed self-care practice was non-smoking, where almost all respondents (98.6%, n=138) had never smoked, 95% (n=133) of participants had never taken a drink containing alcohol, and the least was self-monitoring of blood glucose with a mean of 2.22±2.05 days per week. About 22% (n=31) of respondents perform physical activities with a mean of 3.04 days per week in five days or more.

Table 2: Frequency of Adherence to Recommended Practices

Self-care behaviour	Poor < 5 days n (%)	Good ≥ 5 days n (%)	Mean (SD)
Diet	93 (66.4)	(47 (33.6)	4.44 (1.81)
General diet			4.33 (1.67)
Follows a healthful eating plan	87 (62.1)	53 (37.8)	4.31 (1.62)
Follows eating plan	79 (56.4)	61 (43.6)	4.36 (1.72)
Specific diet			4.55 (1.95)
Eat five or more servings of fruits and vegetables.	74 (52.9)	66 (47.1)	4.42 (1.95)

Eats high-fat foods (red meat or full-fat dairy products)	60 (42.9)	80 (57.1)	4.68 (1.96)
Exercise	**109 (77.9)**	**31(22.1)**	**3.04 (2.44)**
Participate in at least 30 minutes of physical activity	85 (60.7)	55 (39.3)	3.79 (2.41)
Participate in specific exercise sessions	106 (75.7)	34 (24.3)	2.29 (2.47)
Self-monitoring of blood glucose	**121 (86.4)**	**19 (13.6)**	**2.22 (2.05)**
Tests blood sugar level	107 (76.4)	33 (23.6)	2.51 (2.09)
Tests blood sugar the number of times recommended by health care provider	121 (86.4)	19 (13.6)	1.94 (2.0)
Foot Care	**88 (62.9)**	**52 (37.1)**	**3.78 (2.41)**
Checks feet	84 (60)	56 (40)	3.83 (2.37)
Inspect inside of the shoes.	82 (58.6)	58 (41.4)	3.74 (2.45)
Medication Took the prescribed medication	**15 (10.7)**	**125 (89.3)**	**6.09 (1.83)**
Total Mean	**128 (91.4)**	**12 (8.6)**	**3.81 (2.08)**
	Yes n (%)	No n (%)	
Smoking	2 (1.4)	138 (98.6)	
Alcohol	7 (5.0)	133 (95)	

Factors associated with compliance to recommended practices among Type 2 Diabetes Patients
Univariate analysis revealed that age, sex, education level, family history of diabetes and duration of diabetes were not significantly related to self-care practices and, therefore, were removed from the model. The selected factors, the primary source of income, co-morbidity, and complications, were analysed using multiple logistic regression with a stepwise backward selection procedure to determine their association with self-care practices. A significant association was observed in the presence of co-morbidity (AOR 4.5, 95% CI: 1.14-18.02) and primary source of income (employed patients) (AOR 4.4, 95% CI: 1.25-15.44) (Table 3).

Table 3: Odds ratio of select factors for recommended practices among T2DM Patients

Variables	Good self-care practices		Poor self-care practice		COR (95% CI)	P value
	n	%	n	%		
Age (Years)					0.98 (0.94-1.036)	0.581
Sex						
Male	6	4.3	43	30.7	1	0.262
Female	6	4.3	85	60.7	0.506 (0.154-1.662)	

Education level						
Primary or lower	8	5.7	104	74.3	1	0.3
Secondary or higher	4	2.9	24	17.1	0.51 (0.142-1.825)	
Main source of income	6	4.3	23	16.4	4.56 (1.35-15.436)	**0.015***
Employed	6	4.3	105	7.5	1	
Unemployed						
Family history of T2DM	5	3.6	62	44.3	0.76 (0.229-2.522)	0.654
Yes	7	5.0	66		1	
No				47.1		
						0.727
Duration of T2DM					0.98 (0.899-1.077)	
Presence of co-morbidity						
No	3	2.1	78	55.7	1	
Yes	9	6.4	50	35.7	4.68 (1.208-18.126)	**0.025***
Presence of complications						
No	8	5.7	41	29.3	1	
Yes	4	2.9	87	62.1	0.236 (0.067-0.828)	**0.024***
		Multivariate analysis			**AOR (95% CI)**	
Presence of co-morbidity						
No	3	2.1	78	55.7	1	
Yes	9	6.4	50	35.7	4.5 (1.14-18.02)	**0.032***
Main source of income						
Employed	6	4.3	23	16.4	4.4 (1.25-15.44)	**0.021***
Unemployed	6	4.3	105	7.5	1	

Note: The abbreviation 95% CI =confidence interval, AOR=Adjusted odds ratio, COR =Crude odds ratio number 1 indicates reference in categorical variables at *significance at p<0.05; multivariate analysis also includes the presence of complications with no significant association.

Discussion

The present study aimed to determine the compliance of T2DM patients to recommended prevention and management practices in Morogoro municipality, Tanzania. The study results indicated that most patients performed poorly on recommended practices. This finding can be explained by the low level of education among study participants, as most of them had a primary level of education. It might also be due to a need for more health education regarding recommended self-care practices.

In Tanzania, there needs to be more information on adherence to self-care practices and the factors associated; however, the study done in Brazil supports the current findings that most respondents had poor adherence to self-care practices (Macedo *et al.,* 2022). This could be due to similarities between the standard tool and methodology. The findings of the current study are higher than those of the study conducted in Addis Ababa by Gemeda & Woldemariam, (2022) (52%) and in Northern Ethiopia (49.7%) (Zewdie *et al.,* 2022). The possible reason for this discrepancy could be the differences in methodology, study design, socio-economic and cultural factors, and variation in sample

size across the study. It might also be related to using different numbers of items in SDSCA to assess self-care practices.

In all diabetes domains, self-care practices, such as self-monitoring blood glucose (SMBG) and physical exercise, were the least practiced. Similar results have been reported in other hospital-based studies conducted in Ethiopia (Dedefo *et al.,* 2019; Katema *et al.,* 2020; Jemal *et al.,* 2022). The poor performance of SMBG practices is probably related to socio-economic variation. Some patients could not afford to undergo a checkup at a nearby health facility every day as recommended by healthcare providers or to purchase glucometer and strips for self-blood glucose tests. It might as well be related to discomfort from frequent finger pricking. Contrasting results have been shown by other studies with a very high rate of adhering to regular SMBG compared to other practices, for example, the study done by Al-Ozairi *et al.* (2023) in Arab population and a systematic review conducted by Paudel *et al.* (2022). The variation in knowledge and awareness of the importance of understanding the glycemic status, which helps to adopt appropriate action to cope with the glycemic status, may also explain the observed differences (Mercado, 2019).

In the current study, only 22% of participants adhered to physical activities, which is a higher rate than the findings from a study in South Africa. In contrast, only 9% reported good adherence to physical activity practices (Mutyambizi *et al.,* 2022). The possible reason for relatively low adherence to physical activities could be the presence of comorbidities or diabetes-related complications, which were relatively high in our study. A much better physical activity behaviour was reported in a study from Nepal (90%) (Adhikari & Baral, 2021) and (88%) from a study in Vietnam (Van Loi *et al.,* 2023). This variation may be due to methodological differences, and the tools used in the South African study are the Global Physical Activity Questionnaire (GPAQ) to assess adherence to physical activity.

Regarding recommended moderation of alcohol consumption and cessation of smoking, very few respondents reported having smoked or drunk alcohol in the previous week. The low rate of smoking status and alcohol consumption in the current study were attributed to the fact that after being diagnosed with T2DM, the individuals quit smoking and abstained from alcohol use to prevent the occurrence of diabetes-related complications (Wu et al., 2021; Campagna, 2019). Contrary to the current findings, higher rates of smoking and alcohol status were observed in a systematic review conducted by Paudel et al. (2022) and a study from China (Hu *et al.,* 2022). Approximately, 95% of the respondents in the current study abstained from alcohol consumption. This finding is similar to a study at public healthcare facilities in Gauteng, South Africa, which found that 99% of T2DM patients abstained from alcohol consumption (Mutyambizi *et al.,* 2020).

Only one-third of respondents adhered to diet management practices regarding the diet dimension. It is always difficult to change established eating habits and social influence. This finding is consistent with a study in India which reported that 35.2% of participants had a satisfactory performance on dietary behaviours (Karthik *et al.,* 2020). The current study's findings are lower than those conducted in Ethiopia and South Africa, revealing that more than two-thirds of participants had good dietary practices (Gemeda & Woldemariam, 2022; Mutyambizi *et al.,* 2020). This discrepancy might be attributed to the differences in eating habits, availability of food options, socioeconomics and cultural factors, study population, and the study tool used as other studies used Diabetes Self-Management Questionnaire (DSMQ), 24-hour food recall and Dietary Diversity Score (DDS) whereas our study used SDSCA.

Considering the medication dimension, most patients behaved well when taking diabetes medications (insulin or pills) as recommended. The reason for higher compliance to medication could be a fear of worsening health conditions among patients with comorbidities and diabetes-related complications, which motivated them to adhere to their medication regimen. Another reason could be that patients might have perceived medication as more critical than other recommended ways to

control diabetes (Lim *et al.,* 2022). The findings of the current study are almost comparable to studies done in Ghana (84.5%) by Afaya *et al.* (2020), Ethiopia (82.3%) by Zewdie *et al.* (2022), India (81.6%) by Syed *et al.* (2022). This could be due to similarities between the standard tool and methodology.

According to the multivariate analysis, co-morbidities and being employed were strongly associated with compliance with recommended prevention and management practices. A possible reason for high compliance among those with comorbidities might be that other co-morbidities and their multiple burdens may encourage patients to improve their practices based on the recommendations. Also, it might be due to frequent visits to healthcare facilities, continued counselling and health education; hence, they tend to pay more attention to their health condition. This finding was supported by studies in Kakamega County, Kenya (Mbunya, 2022) and Adama town, Ethiopia (Gemeda & Woldemariam, 2022), which reported that the odds of being adherent to recommended practices were higher among patients with comorbidities. Nevertheless, patients with no comorbidities were less likely to adhere to the recommended practices than their counterparts because they might need to pay more attention to the importance of self-care practices. After all, they have not experienced the burden of managing multiple health conditions.

Furthermore, unemployment was also an essential factor affecting compliance with recommended prevention and management practices. This might be due to financial difficulties limiting a person's ability to engage in self-care practices such as healthy eating and medication. Also, unemployment can have a significant impact on mental health challenges such as stress and anxiety, which can make it difficult to prioritize self-care practices. A job can provide financial stability, improving access to healthcare services and diabetes management resources. Consistent with a study done in Addis Ababa, Ethiopia (Wolderufael & Dereje, 2021) and Debre Markos, Ethiopia (Bayable et al., 2022), the present study revealed that being employed was four times more likely to practice self-care practice compared to their counterparts.

Conclusion and Recommendations

The overall compliance rate with recommended prevention and management practices among T2DM patients was low, with self-monitoring of blood glucose, physical exercise, and dietary practices being the least performed, which could increase the risk of complications. Having diabetes-related comorbidities and being employed were significant variables associated with compliance with recommended prevention and management practices. Therefore, nutritional and lifestyle counselling and the use of peer groups should be emphasized to improve compliance with recommended practices.

Strengths and Limitations of the Study

The major strength of this study is the use of standardized tools to measure frequency to comply with recommended practices, which allowed the findings to be comparable with previous studies. The main limitations of this study were the small sample size and the use of a self-report method to evaluate patients' compliance with recommended practices, which could have resulted in overestimation or underestimation of the level of compliance. The other limitation was that many variables had tiny observations during analysis, which caused low precision. Further research should incorporate qualitative methods to understand better patients' perspectives and experiences on adherence to recommended practices and explore contextual factors influencing compliance to recommended practices.

Conflicts of Interest
The authors declared no conflicts of interest.

Authors contribution
HB conceived the idea, developed the proposal, designed the study, participated in data collection, management, analysis and interpretation of the results, and drafted the manuscript. AWM and SSM assisted in the design and the proposal development, supervised the study procedures, and revised subsequent manuscript drafts. All authors read and approved the final version of the manuscript.

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Risk factors of delayed developmental milestones among infants attending RCH clinics in Dodoma region: A cross-sectional study

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Abstract
Background: Delayed Developmental Milestones are defined as slow to attain typical developmental milestones in one or more developmental areas. This study aimed to assess risk factors of delayed developmental milestones among infants in the Dodoma Region.
Methods: We conducted a health facility-based cross-sectional descriptive study using the pathways developmental screening tool. A total of 262 mothers and their children were enrolled, and the study population consisted of neonates delivered at the study sites during the study period. Three data collection methods were utilized to obtain information for this study: observation, interviewer-administered questionnaires, and documentary review. Ethical approval was obtained from the Ethical Review Board of the University of Dodoma SAS version 9.4, which was used for data analysis. The association between developmental status and factors was assessed using Chi-square and binomial logistic regression.
Results: Notably, infants born with birth asphyxia were more likely three times to develop delayed developmental milestones as opposed to those without birth asphyxia [adjusted risk ratio =3.22, 95%, [1.97, 5.46], probability value= <.0001]. Birth weight was significantly associated with delayed developmental milestones; infants who were born with a birth weight of ≥4000gm had more risk of developing delayed developmental milestones compared to those with a birth weight of 2500-3999gm [adjusted risk ratio 0.48, 95%, [0.26, 0.92], probability value = 0.0256]. Regarding mode of delivery, the risk of developing delayed developmental milestones was less among infants born via caesarean section compared to those who were born via spontaneous vaginal delivery [adjusted risk ratio 0.47[0.18, 0.99], probability value = 0.0461].
Conclusion: Delayed developmental milestones are a burden in developing countries. The risk factors are known, and they are based on the individual to the community level; birth asphyxia was identified as a possible risk factor that has been reported in many studies and has an impact on children's development.

Keywords: Delayed developmental milestones, birth asphyxia, infants, factors, Apgar score

Introduction
Delayed Developmental Milestones (DDM) are defined as slow to attain or not reaching normal developmental milestones in one or more developmental areas such as (communication, sensory-motor, personal-social, cognitive, vision & hearing and activities in daily living) in the expected ways for a child's age (Balica et al., 2014; Nguefack et al., 2015; Habibullah et al., 2020; WHO, n.d.).

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The prevalence of DDM is increasing worldwide over time (Kim., 2022), and more than 250 million children below five years of age do not reach their expected milestones due to this condition (WHO & UNICEF, 2017). The rate of DDM increased from 8% to 15% from 2003 to 2017; this is more than 4 times (from 0.6 to 2.5). boys had a higher incidence than girls. The gap increased from 19.1% to 31.4% (Kim., 2022). According to (Gil et al., 2020) the incidence of DDM varied by region, ranging from 10% in Europe and Central Asia to 42% in West and Central Africa (Padayachee & Ballot, 2013; Shirima, 2013; Oluwafemi et al., 2018; Abdel et al., 2018; Sunderajan & Kanhere, 2020; Saleem et al., 2020). The situation is worse for children born under a variation of medical conditions, including BA (WHO, 2011;Shaahmadi et al., 2015; Boskabadi et al., 2015 ; Lee et al., 2019 ;Lancaster et al., 2018). Delayed developmental milestones was prevalent in African nations in the range of 10% to 38.9%. Mostly severity of these disabilities were noted among infants with neurodevelopmental delay in three or four domains(Namazzi et al., 2019; Meshesha et al., 2020). A study in Uganda showed that of 62 infants with DDM, nine (14.5%) developed long-term disability (Namazzi et al., 2019). Another study in Malawi revealed that 109 out of 933 (11.7%) children were regarded as having DDM, 41 (4.4%) in "language" and 77 (8·3%) in "social" domains (Murphy et al., 2020).

In Tanzania, there has been an upsurge in morbidity among children, such as DDM. (Sepeku & Kohi, 2011; Mangu et al., 2021) the prevalence rate of DDM was 2.3%; among children aged five years and above, overall 7.8% of females had DDM compared to 5.7% of males (Murphy et al., 2020). The frequency of newborns with cognitive developmental delay, on the other hand, was found to be 12.3% in a Dar es Salaam (Shirima., 2013). Studies conducted in Morogoro and Manyara also revealed that the main factors of DDM in cognitive, communication and motor domains were poverty malnutrition and inadequate skills among health care providers in primary health care level (Sudfeld et al., 2015; Ribe et al., 2018; MOHCDGEC., 2022).

Higher understanding of key factors associated with DDM is therefore mandatory and to make sure that all children may achieve their normal developmental milestones within expected time. Children who are exposed to multiple risk factors have a greater chance of having DDM (Ann et al., 2019;Kantar, 2020). However, very little of this work has been done in developing countries like Tanzania, where there are multiple factors including medical, physical, psychosocial, and environmental factors to interact in complex ways and to which children may be at higher risk in different ways.

There is lack of data from Tanzania that widely examine the factors associated with DDM among children. Even though recently there have been some studies examining risk factors for development (Abdel et al., 2018), Child development is one of the transformative agenda to 2030, Sustainable Development Goal (SDG) 4 states that all children should have the equal chance to reach their full developmental potentials (Gil et al., 2020; UNICEF, 2018). Because of inadequate data directly assessing these factors in developing countries, therefore there is a need to conduct the study on the risk factors of DDM among infants in Dodoma region, to raise our understanding about the prominent risk factors leading to DDM particularly in low income countries(Ann et al., 2019). Therefore, this study aimed to assess the range of risk factors of DDM among infants in Dodoma region.

Methods and materials

Study design and population; This was a health facility-based cross-sectional study to determine factors associated with DDM in infants who attended at Bahi, Mundemu, Mlali, Ugogoni, Hombolo and Makole health centers, St Gemma districts designated, Kongwa and Bahi ditricts hospitals. The data was collected from September to December 2022. As per census 2022, the total population for Dodoma region was 2,083,588 (NBS, 2022). The Region has a total of 12 hospitals. Eight of these hospitals are Government owned. These are

Inclusion and exclusion criteria

Children of 9-12 months of age residing continually in the study area for the last three months before data collection and the infants who were born and attended RCH clinical at the study sites were involved. Infants with congenital abnormality, metabolic disorders, infants with parents who did not wish to participate in the study, children below 9 months of age and children who were not born in the study sites were excluded.

Sample size and sampling procedure.

Based on 19 % the prevalence of suspected delayed developmental milestones in a similar study in low middle income countries (Gil et al., Among 7 districts in Dodoma region three were chosen for this study by using simple random sampling. These were Dodoma City Council, Bahi and Kongwa districts. Total of 9 health care facilities were involved in the study. The selected health care facilities were, Kongwa, Bahi Districts Hospitals and St Gemma Districts Designated Hospital. The health centers form Dodoma City Council were Makole and

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Data collection and assessment

A structured questionnaire which was adopted from various African nations (Ilah et al., 2015; Fauste & Olive, 2017; Muluneh, & Denis, 2019). Were used to collect the following information: (mothers) age in years, level of education, marital status, Occupation tribe, body weight,

Dodoma Regional Referral Hospital (DRRH), Benjamin Mkapa Hospital (BMH), Mirembe National Mental Health Hospital, Kondoa, Kongwa and Mpwapwa, Bahi and Chemba, Districts Hospitals and 2 are private hospitals; St. Gemma Hospital owned by Roman Catholic Church and Mvumi Mission Hospital owned by the Anglican Church. There are 26 health centers owned by the government and 6 health centers privately owned. There are 284 dispensaries in the region.

2020) 95% confidence interval (CI), 5% relative error, design effect 2 and 5% non-response rate, the minimum sample came to be 262.

$$\frac{Z^2{}_{\alpha/_2}P(1-P)}{e^2}.$$

Where:

n = Minimum sample size

Z = Standard normal deviation of 1.96 corresponding to 95% confidence interval.

P= The proportion of suspected DDM in low middle income countries which is 19%

e= Degree of accuracy of the results, was 0.05.

$$\frac{1.96^2 \times 0.19 \times (1-0.19)}{0.05^2} = 236.488896 \approx 237$$

Adding attrition rate of 10% we get 261. Hence the minimum sample size was 261 ≈ 262.

Hombolo, from Kongwa district were Ugogoni and Mlali health centers and from Bahi were Mundemu and Bahi health center. Infants from each health care facility were chosen randomly. Three methods of data collection were utilized to obtain information for this study, the observation, interviewer-administered questionnaire and documentary review.

gestational age, sex of a child antenatal care attendance, mode of delivery, Bad obstetric history and complications during labor and delivery. Developmental delay in children was assessed by using Pathways Developmental Screening Tool (PDST). The tool was developed by Paediatric Specialist with the intention of

monitoring any noticeable delays, collecting data from parents, and referring all suspected cases for early detection and treatment.(*Overview of Pediatric Therapy*, 2022), the tool was validated and standardized by American Academy of Paediatrics (AAP), and it has 97 items in total, with four domains: motor, sensory, communication, and feeding domains. In this tool delayed developmental milestones were measured in binary scale on whether a child achieved normal developmental milestones. If a child achieved any items within each domain was given a score of 1 and failure to achieve was scored 0. All scores were summed up, if the child passed a total of 3 items in each domain was regarded as having normal developmental milestones if scores less than that was regarded as having delayed developmental milestones.

Data analysis

Data was entered to statistical package for social science (SPSS) version 25, Data were cleaned and checked for errors to enhance the reliability and consistency, this was done before analysis Statistical Analysis System (SAS) version 9.4 was used for the data analysis and significance of all statistical tests was determined at 5% level. The results of the model were presented in the form of a regression parameter estimate and estimated risk ratios (RR). The estimated RR shows the increase or decrease in the risk of the outcome at a given level of the independent variable compared to those in the reference category. An estimate of RR > 1 indicates that the risk of having DDM at a given level of the independent variable is greater than that for the reference category. Similarly, an estimate of RR <1 specifies that the chance of having DDM at a given level of independent variable is less than that for the reference category. Moreover, adjusted risk ratio (ARR), 95% confidence interval (CI) and probability value (p value) were presented.

Results

Demographic characteristics of study participants among non-exposed and exposed neonates.

The mothers' ages ranged from 18 to 44 years, with a mean age of 26.59 ± 6.63, while the

Ethical considerations

Ethical clearance was attained from the University of Dodoma Ethical Review Board with a Ref no (MA.84/261/141/134). Permission was sought from the Vice Chancellor of the University of Dodoma, Regional Administrative Secretary of Dodoma Region. On the day verbal consent was obtained from each participant to get involved in the study. The participants were informed about the purpose of the study and the duration, how data will be collected and that they were involved voluntarily. Ethical approval from the ethical committee has been acquired September 2022.

The participants were informed about the purpose of the study and the duration, how data will be collected and that they were involved voluntarily. Participants were also informed that they were free to withdraw from studying at any time if they wished to. Participants were assured of anonymity that their names would not be included in the questionnaires.

infants had an average birth weight of 3.227 ± 0.55. Out of all the mothers, 165 were below the age of 25, In terms of gender distribution among the children in the study, more than half were female (148)56.47% and the rest were male. Concerning birth weight, the majority (190 or 59.94%) were born with birth weight of less than 3000g, (Table 1).

Table 1: Demographic Characteristics of the Study Participants among unexposed and exposed (N=262)

Variable	Frequency	Percentage

Age		
<25	125	47.71
26-35	105	40.08
>35	32	12.21
Education		
Not attended	47	17.94
Primary	123	46.95
Secondary	66	25.19
Above secondary	26	9.92
Place of resident		
Urban	141	53.82
Rural	121	46.18
Marital status		
Married	241	91.98
Single	21	8.02
Occupation		
Famer	105	40.08
Formal job	157	59.92
Tribe		
Gogo	120	45.80
Rangi	53	20.23
Others	89	33.97
Birth weight of a child		
<3000	156	59.54
=>3999	106	40.46
UPGAR score at 5min		
<7	178	67.96
7+	84	32.06
Sex of child		
Male	114	43.51
Female	148	56.49

Prevalence of delayed developmental milestones

Out of the 262 infants, 45 infants had delayed developmental milestones giving a prevalence of 17.18% while 217 (82.82%) infants had no DDM.
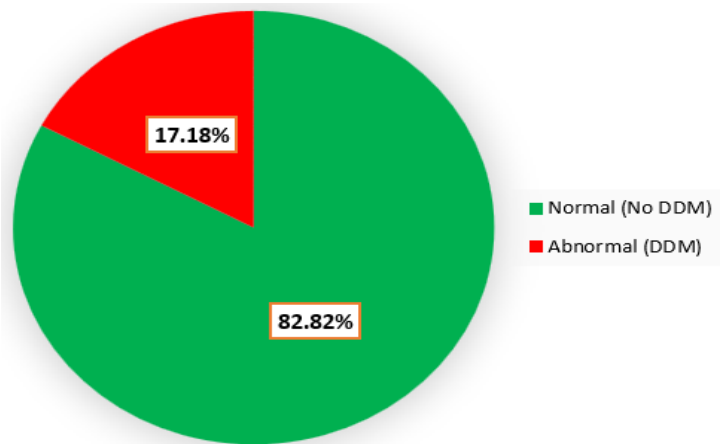
Figure 1: The prevalence of DDM among respondents

Risk factors associated with DDM by using tool 2 PDST

Binomial logistic regression was used to assess other factors associated with DDM among infants. The results showed a strong relationship between DDM and BA (p= 0.0001), and infants who were born with BA had higher risks 3.22 of developing DDM compared to those without BA [RR=2.88,95%, [1.69, 4.91] p= 0.0001]. Other risk factor associated with DDM was birth weight. Regarding birth weight results showed that infants who had birth weight of ≥4000gm had 1.76 more risk of developing DDM than those with birth weight of 2500-3999gm [RR= 1.76, 95% [1.04, 3.00], p value= 0.0365. Other factors such as occupation, place of residence, marital status, mode of delivery, sex of a child and gestational age were not significantly associated with DDM. More details are found in Table 2.

In multiple logistic regression infants born with BA were more likely three times to develop DDM as opposed to those without BA [ARR =3.22, 95%, [1.97, 5.46], p value= <.0001]. Birth weight was significantly associated with DDM, infants who were born with birth weight of ≥4000gm had more risk of developing DDM compared to those with birth weight of 2500-3999gm [ARR 0.48, 95%, [0.26, 0.92], p value = 0.0256]. Regarding mode of delivery, the risk of developing DDM among infants was less among infants born via caesarean section compared to those who were born via spontaneous vaginal delivery [ARR 0.47[0.18, 0.99], p value = 0.0461]. Other factors such as occupation, place of residence, marital status, sex of a child and gestational age were not significantly associated with DDM. More details found in table 2.

Table 2: Factors Associated with DDM 12 Months Using PDST (n=262)

Variable	Normal (No DDM) 217(82.82) n (%)	Abnormal (DDM) 45(17.18) n (%)	Unadjusted analysis RR [95%CI]	p-value	Adjusted analysis ARR [95%CI]	p-value
BA						
Normal (No BA)	159(89.33)	19(10.67)	ref		ref	
Abnormal (BA)	58(69.05)	26(30.95)	2.88[1.69, 4.91]	0.0001	3.22[1.97, 5.46]	<.0001
Occupation						
Farmer	91(86.67)	14(13.33)	ref		ref	
Formal job	126(80.25)	31(19.75)	1.46[0.82, 2.61]	0.1851	1.54[0.87, 2.74]	0.1367

Place of residence						
Urban	118(82.52)	25(17.48)	ref			
Rural	104(83.87)	20(16.13)	0.92[0.54, 1.58]	0.7685		
Marital status						
Married	202(83.82)	25(17.73)	ref			
Single	15(71.43)	6(28.57)	1.77[0.85, 3.68]	0.1294	1.53[0.56, 3.17]	0.2493
Mode of delivery						
SVD	163(81.09)	38(18.91)	ref		ref	
Caesarean section	54(88.52)	7(11.48)	0.61[0.29, 1.29]	0.1941	0.47[0.18, 0.99]	0.0461
Sex of the child						
Male	92(80.70)	22(19.30)	1.05[0.93, 1.17]	0.4311		
Female	125(84.46)	23(15.54)	ref			
Birth weight						
2500-3999gm	95(89.62)	11(10.38)	ref		ref	
4000+gm	122(78.21)	34(21.79)	1.76[1.04, 3.00]	0.0365	1.48[1.26, 2.92]	0.0256
GA						
	37(16.44)	188(83.56)	ref			
	8(21.62)	29(78.38)	0.93[0.78,1.12]	0.4834		
Presentation of the foetus						
	44(17.81)	203(82.19)	ref			
	1(6.67)	14(93.33)	1.14[0.98, 1.32]	0.2103		

Discussion

The current study indicated that the leading risk factor for DDM was BA, this is the main predictor for the occurrence of DDM which can lead to severe consequences of permanent disabilities. The findings showed that the children who were born with BA were at higher risks of having DDM compared to those who were born without BA.

The prevalence of BA was high in study area the risk factors are known, The similar findings were observed by Halloran, Mwakyusa, Nguefack, Oluwafemi and Adeniyi.(Halloran et al., 2009; Mwakyusa et al., 2009; Nguefack et al., 2015; Oluwafemi et al., 2018; Adeniyi; Asinobia & Idowua, 2022) This problem is high in many developing countries than developed countries due limited obstetric care, lack of health care facilities, social cultural norms, low literacy levels and shortage of health care workers (Workineh et al., 2020)

Demographic factors like birth weight, place of residence, sex of a child, mode of delivery etc. were regarded as other factors for the occurrence of DDM in this study. These factors have both positive and negative effect on child development. The similar study form India observed that socioeconomic status, parenting, social environment and interactions as a the strongest risks for poor cognitive performance in children (Zhang et al., 2020). Therefore, therefore is important to consider the aetiology and risk factors in the evaluation of morbidity in these children (Vafaee-Shahi et al., 2020). These could show the importance of these networks surrounding the children, safeguarding the wellbeing and the optimal child growth.

Gender was also noted as one of the prominent factor for occurrence of DDM, it was observed that majority of the study participants were female 179 (56.47%) compared to male 138 (43.53%) (Gemuhay et al., 2023), but it has been noted that male gender is at higher risk 45(32.61%) than female 56(31.28%). This finding concur with the study

conducted in Nigeria and Pakistan (Oluwafemi et al., 2018), (Aghai et al., 2020) these studies reported that male gender was significantly associated with poor neonatal outcome (OR= 3.24, 95% CI = 1.02-10.35). Gender has been found to be a main predictor of BA because boys are more vulnerable than girls and they tend to have poor neonatal outcome, boys are heavier than girls at birth this contribute to higher rates of complications like BA.

Body weight was also regarded as one of the prominent features for the occurrence of BA Gemuhay et al., 2023). A large proportion of asphyxiated babies were those who had birth weight of more than 3999 compared to those without abnormal body weight. These findings are similar to the study conducted in Ethiopia where 83 (23.2%) neonates who were overweight had DDM (Admasu et al., 2022). This is because any difficulties like overweight can create abnormal heart rhythms that cause oxygen deprivation to baby which can lead to HIE.

This study showed that mode of delivery was one of the risk factors for DDM. Most of the infants were born through spontaneous vaginal delivery and this mode of delivery was considered as one of the factors associated with DDM, infants who were born through caesarean section were less likely to have DDM. This results contradict the findings of the study conducted in China (Zhou et al., 2019) the prevalence of DDM was 23.4% in the cesarean section group, compared with 21.3% in the vaginal delivered group, yet without statistical difference (p < 0.05). This portrays that there are some delays in decision making among health care providers to do caesarean section when it is necessary. According to (Waniala et al., 2020) caesarean section is considered a curse, marriage-breaker, misfortune, money-maker and a sign of incompetent health workers, and being for the lazy women and the rich civil servants among some communities.

It is interesting to note that antenatal care attendance, occupation, place of residence, mode of delivery, sex of a child and gestational age were not significantly associated with DDM. These findings are comparable to WHO, which reported that women who attended ANC might have little or no effect on perinatal mortality (2 trials, 713 women; RR: 0.77, 95% CI:0.17–3.48) (Tongkumchum P, 2005; WHO, 2016).

Majority of infants who developed DDM were BA survivors, so those children are likely to develop long-term disabilities (Eblovi et al., 2017; Shaahmadi et al., 2015; Abdel et al., 2018). BA has serious long-term impacts and causes potentially fatal condition among infants in developing countries. Its effects were also observed by Ahearne that majority of these children end up with irreversible permanent disabilities which burdens the child health and wellbeing (Ahearne, 2016). Therefore comprehensive care should be given to women of child bearing age before and after pregnancy to reduce long-term effects (Admasu et al., 2022).

Conclusion and rrecommendations

The DDM is a burden in developing countries, the risk factors are known and they base from individual to community level. These factors are modifiable and needs to be addressed accordingly, when developing and implementing policies for reproductive and child health care, in the aspects of preconception, pregnancy, and early childhood in the context of families and communities. The findings of this study can be applied in developing countries, but they might not apply in developed countries due to the differences in social structures, health care systems, and availability of resources between those nations. It is therefore recommended that health care facilities should include physiotherapy, occupational therapy, speech and language therapy, and early special education because these are frequently beneficial for children with DDM. It is also important to use of both HIE

scoring system and Apgar score for all infants born with BA in order to identify infants who are at higher risk to develop DDM.

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Perception of Health Workers on the Integration of Mental Health Care with HIV Services in Primary Health Care Centres in Ogun East Senatorial District, Nigeria: A Qualitative Study

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Abstract
Background: People Living with HIV/AIDS have an increased incidence of mental health disorders as compared to the general population, and there exists an enormous gap between the demand and supply of mental health services, particularly in low- and middle-income countries.
Aim/Objective: This study aimed to assess the association between HIV and mental health and the knowledge and perception of health workers on their integration in Primary Health Care Services in Ogun East Senatorial District, Nigeria
Methodology: Four Focused Group Discussions were conducted among 27 PHC workers in Highly Active Antiretroviral Therapy (HAART)-enabled centres of Ogun East senatorial district, Nigeria using a focused group guide designed according to study objectives. Data were analyzed using a thematic analysis approach.
Result: Six important themes were extracted from the data in this study (Table 2); "Integration of PHC services", "Multiple mental/psychological health challenges", "Multiple factors as causes of mental illness", "Diverse manifestations of mental illness", "Necessity of incorporating HIV and Mental Healthcare into PHC services", and "Challenges of incorporating HIV and Mental Healthcare into PHC services."
Conclusion and Recommendation: The primary health workers identified the need to integrate mental health care into HIV care in PHCs. However, there is a need to scale up the capacity of PHCs for optimal performance in this regard.

Keywords: Knowledge; Perception; Primary Health Workers; HIV; Mental Disorders

Introduction

In 2019, 12.5% of the global population was reported to be living with mental illness, anxiety and depression being the commonest of these illnesses, affecting 301.4 million and 279.6 million people, respectively. (World Health Organization, 2022) One out of every 4 Nigerians is documented to be

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living with one form of mental illness or the other. (Africa Polling Institute & EpiAFRIC, 2020) Several other morbidities have contributed to the rising incidence of mental illness.

For instance, People Living with HIV/AIDS (PLWHA) have an increased incidence of mental health disorders. (Duffy et al., 2017) This association has also been reported in southwest Nigeria where this study was conducted. (Obadeji et al., 2014) and in some instances, mental health is left untreated among PLWHA in the country. (Ezeanolue et al., 2015) Besides the general population of PLWHA, the burden of mental health has also been shown to be particularly higher in some groups living with the disease such as adolescents (Vreeman et al., 2017) and women. (Waldron et al., 2021) Furthermore, mortality from mental illness among these people is high nullifying the gains of decreased mortality from HIV as a result of efficient antiretroviral therapy over the years. Moreover, mental illness is grossly under-diagnosed and undertreated among PLWHA.(Carvalhal et al., 2012)

A multifaceted association exists between HIV and mental disorders. First, people with mental disorders may underutilize HIV and other medical care, leading to poor HIV treatment outcomes, which may further worsen the psychiatric condition.(Ciesla & Roberts, 2001; Dos Santos & Wolvaardt, 2016) Mental illness can increase an individual's chances of risky behaviours with subsequently increased vulnerability of getting infected with HIV. (Gomez et al., 1999) PLWHA also are faced with mental health stressors due to the protracted nature of HIV, fear of complications and death, and various forms of stigmatization. (Gomez et al., 1999). Lastly, psychiatric illnesses may mimic the early stage of HIV.(Dos Santos & Wolvaardt, 2016)

Primary health care (PHC) is the entry point of the health system. It offers accessible essential health services to people. A direct relationship exists between access to PHC services and positive health outcomes. (Smith, 2017) The PHC system offers people more opportunities to access adequate health care irrespective of socio-economic status. These, among others, include HIV and mental care, which are also common complaints at this level of healthcare. A higher proportion of PHC patients living with HIV is documented to have mental illness as compared to HIV-negative patients. (Dodds et al., 2004)

There exists an enormous gap between the demand and supply of mental health services particularly in low-and-middle-income countries. (Wang et al., 2007) This may partially be due to the shortage of mental health care providers. Mental health disorders are managed by psychiatrists and other mental health specialists who are primarily found in tertiary hospitals(Gm et al., 2020) leading to a shortage of these personnel in Nigeria. (Abang, 2019; Ugochukwu et al., 2020) There is, therefore, a need to explore other alternatives for the provision of mental health services, particularly for individuals like PLWHA who have high risks of mental disorders.

The Nigerian National Mental Health Policy acknowledges the need for integrating mental health services into all levels of care with the responsibility of this integration at the primary level to be shouldered by PHCs and the local governments. (Abdulmalik et al., 2013, 2016; Federal Ministry of Health Abuja Nigeria, 2013) Also, Ezeanolue highlighted areas of possible integration of HIV and mental care services. These include developing health facilities where HIV services are offered, employing the services of standing human resources in HIV programmes giving attention to the importance of existing cultural and social structures in this integration such as building on the roles the community, religious and traditional infrastructures. (Ezeanolue et al., 2015) Nevertheless, there has been poor implementation of this policy. (World Health Organization, 2014) and this has been ascribed to lack of human expertise, deficient screening procedures, insufficient resources for treatment and vertical nature of HIV care.(Remien et al., 2019).

Although PHC workers have been shown in developing countries to have poor knowledge (Cele & Mhlongo, 2020b) and perceptions concerning integrating mental health services into HIV care and also the relationship between these two conditions, (Cele & Mhlongo, 2020a) the feasibility of

scaling up mental health services in PHC settings have been established in Nigeria.(Gureje et al., 2015) Appropriate exposure of PHC workers can lead to significant improvement in their knowledge, diagnostic competence, and apt referral of mental disorders. (Gureje et al., 2015). This study aimed to assess the association between HIV and mental health and the knowledge and perception of health workers on their integration in Primary Health Care Services in Ogun East Senatorial District, Nigeria.

Materials and methods
Study site and design.
This research was a qualitative study conducted in Ogun East Senatorial District, Nigeria which is made up of 9 Local Government Areas (LGAs). In Nigeria, an LGA is an administrative division of a state, often headed by a chairman. It is the first tier of government in the country. Each of these LGAs has a PHC Department which is headed by a Medical Officer of Health. Ikenne and Sagamu Local Government Areas were purposively selected in the senatorial district because they had facilities for HIV care. These were Ogijo PHC and Makun PHC for Sagamu LGA and Ogere PHC and Ilishan PHC for Ikenne LGA. Therefore, a total of 4 Focused Group Discussions (FGDs) were carried out.

Study Population
The study was conducted among PHC workers in the selected facilities.

Inclusion Criteria: All consenting PHC workers who were at least 18 years old **and h**ealth workers who had worked for at least 3 months in their respective health centres.

Sample Size Determination
Nine health workers participated in Ilishan PHC while 6 health workers each participated in Ogere, Ogijo, and Makun PHCs giving a total sample size of 27 health workers (Table 1).

Sampling Method
The participants were selected among health workers in the HAART-enabled Primary Health Care Centres who volunteered to participate in the study. Where there were many volunteers in a facility, purposive sampling was used to select the required number of eligible participants for the FGD (6-12 participants). Purposive method was used so as to select the participants the researcher felt could offer sufficient information concerning the study objective. A range of 6-9 people participated in this study across health facilities. There was a line listing of all the participants selected for the study (this included their names, health centres, and phone numbers). It served as a register used as a quality assurance tool that ensured only those selected participated in the study.

Data collection instrument
A FGD guide was designed according to the objectives of the study with sections including consent process, introduction and establishment of ground rules and the main study questions.

Method of Data Collection
FGDs were done for this study so as to include as many health workers as possible since only a few PHCs offered HIV care and there may not be enough clinic managers to offer enough information for interviews. The FGDs were conducted by the authors of this study, all of which were Public Health or Mental Health physicians. Each FGD lasted about one hour with the participants sitting in a roundtable format and all of them were encouraged to speak freely according to the FGD guide. To ensure this, each participant was assigned a number from one to the last person, so they would not feel uneasy about their real names being mentioned which may affect the quality of their contributions. The

participants were permitted to speak in any of the three languages which were commonly spoken in the study area – English, Yoruba, and Pidgin English. Ground rules were established after which an icebreaker was introduced. Questions were asked on HIV, mental disorders, the association between HIV and mental disorders, and possibility of including them in primary healthcare settings. The moderator was neutral during the discussion. The clerk took notes and also used a voice recorder to capture all issues raised by the participants. All the FGDs were conducted in the respective PHCs.

Data management and analysis: The recorded FGD sessions were transcribed manually. All the comments and opinions of the participants were noted even if such comment(s) were made by just one participant. All similar remarks (themes) were grouped and stated according to the relative number of participants that made them, such that they were stated as being said e.g. 'unanimous or all', 'most of', 'some' or ' a few'. Any reported remarks(s) by the participants in their terms or words were written in italics. Thematic analysis was done for the study.

Ethical consideration
Ethical approval for the study was obtained from the Ogun State Health Research and Ethics Committee (OGHREC/467/36). Approval was also gotten from the MOHs of the two LGAs that were used for this study and from the heads of all the selected facilities. Informed consents were obtained from all the participants and no names or personal identifiers were used for the participants during the focused group discussions. Participation was entirely voluntary.

Results
Socio-demographic Characteristics of Participants
The majority (70.4%) of the participants were in the age group 40-49 years while almost all (96.3%) of them were females. The commonest occupation was nursing (26.0%) and over three-quarters had worked for more than 10 years. Six important themes were extracted from the data in this study (Table 2); "Knowledge of health workers", "Integration of PHC services", "Multiple mental/psychological health challenges", "Multiple factors as causes of mental illness", "Diverse manifestations of mental illness", "Necessity of incorporating HIV and Mental Healthcare into PHC services", and "Challenges of incorporating HIV and Mental Healthcare into PHC services."

Integration of PHC services
The participants believed that various services rendered in PHCs will be more efficiently delivered when the services are integrated instead of each service being offered in isolation. They opined that vertical programmes may not be the best for a typical PHC. According to a 46-year-old CHEW ***"It will be good if we combine our services and efforts in our health centres because the services, we rendered are many. Our patients will benefit better from it".*** In the same vein, a 58-year-old Chief Nursing officer opined ***"Primary Health Services involve different aspects of health and some of them can be integrated."***

PLWHA are faced with multiple Mental/Psychological Health Challenges
Many of the participants believed that a strong association exists between HIV and mental disorders. The negative perceptions the society attached to HIV predisposes PLWHA to a lot of mental health and other related issues. This manifests in different ways

Public Stigmatization

Almost all the participants in this study believed stigmatization is a major challenge that is faced by PLWHA. According to them, stigmatization may be from family, friends, colleagues, or strangers. The following excerpts from the study attest to this

"PLWHA always face stigmatization in the public" (A 40-year-old nurse and a 41-year-old pharmacy technician) *"What I know about their challenges especially when people know that they have HIV is that they run from them they don't want to relate with them thinking they might contract it from them. They keep avoiding them"*. (43-year-old pharmacy technician)

Self-Stigmatization

The participants discussed self-stigmatization as more of a problem among PLWHA as compared to stigmatization from other people. They believe since awareness about HIV has improved over the years, more and more people have come to accept PLWHA. However, many of these individuals feel so bad about their conditions and tend to stigmatize themselves as they refuse to relate freely with others.

According to a 42-year-old assistant chief nursing officer, *"Whenever you test a patient and it turns out that the patient has HIV, they think it is a death warrant. It is left for the health care provider to explain to them that it is not a death warrant that whenever they are using their drugs, they will be okay…. some may even feel so bad about themselves that they will not use their drugs as you recommend it for them, and it will make them more sick and their condition may lead to AIDS"*

According to a 41-year-old pharmacy technician, *"Once some people know that they are HIV positive, then they will feel ashamed to relate with other people."*

Depression

Many participants in this study asserted that HIV patients are prone to having depression irrespective of their socio-demographic status. Depression then contributes negatively to several areas of their lives. In the view of a 42-year-old nurse, *"Once they know they are positive, they feel depressed and due to that, they withdraw from society. This includes withdrawing from performing their normal day-to-day activities…"*

Abandonment and neglect

This was shown as a major issue among PLWHA. It was described that this may however be more common among women by their spouses. A 27-year-old Community Health Extension Worker (CHEW) opined, *"Abandonment of their partners when they find out about their HIV status is common among men, they run away from their partners that have HIV. This can lead to mental health illness in the woman"*.

Issues with Disclosure

Some of the participants believed that PLWHA has issues with disclosing their status to their partners and other people. This is partly due to the fear of possible stigmatization and neglect which may occur once people know their status. According to a 47-year-old Health Assistant, *"They cannot share the nature of their illness with their partner, or anyone else. This particularly worsens depression in them. They cannot share it, even with their pastor or even with their children…"*

Nevertheless, the participants in this study showed that the relationship between HIV and mental health may be 2-way. While PLWHA may have high tendencies of having mental disorder, mentally ill people particularly women and girls on the other end may be exposed to HIV infection when people sexually assault them because of their mental ill-health. In the words of a 58-year-old Chief Nursing

Officer, *"Those mentally ill people because they aren't doing well anymore, people can take advantage of them and have sexual intercourse with them. From there, they can get infected with HIV."*
Mental illness among PLWHA is an interplay of multiple factors.
The participants asserted that there are several factors militating against the mental health of PLWHA. The factors discussed by the participants included.

Social Factor
The participating health workers believed that the social system many of the PLWHA find themselves contribute to mental disorder among them. According to a 48-year-old Medical Laboratory Scientist *"When people join bad gangs and begin to take drugs and alcohol, this can cause mental issues"*. Social issues like disappointments by a partner in a relationship were also a factor that was noted to cause mental disorders. According to a 46-year-old Principal-CHEW *"When people divorce and experience scattered marriage and the person does not have a strong mind, it may result into the mental problem"*.

Economic Factor
Economic condition was also pointed out as a factor that may contribute to the development of mental illness among PLWHA. This may occur because of ill-health leading to loss of job by PLWHA. Mental illness among PLWHA was also noted by the participants to be due to economic reasons. This may result from loss of job or catastrophic expenditure from the cost of care for the disease. According to a 50-year-old Health Assistant *"Other things that may cause mental illness include someone who had a good job and thereafter, suddenly lost it. So, along the line, it can cause mental issues particularly if he or she does not get someone that can assist and he/she begins to brood excessively"*.

Spiritual Factor
Some of the participants believed that spiritual factors could cause or contribute to the development of mental illness. According to a 47-year-old Health Assistant, *"Spiritual attack can come in many ways …. Most especially the foundation someone came from, if there are traces of madness or mental issues in the lineage someone comes from, lo and behold, if prayer is not enough, before he or she knows, he will develop mental illness."*
Other causes of mental illness that were emphasized by participants included accidents with a head injury and puerperal psychosis.

Mental Disorder is Associated with Diverse Manifestations
The participants had various perceptions of how mental illness could manifest ranging from mild to severe manifestation. These include poor personal hygiene, talking alone or having an irrational talk, loss of memory, becoming violent, having hallucinations, poor concentration, having mood swings, suicidal ideation or attempt. Some excerpts below show the views of participants about the manifestation of mental illness
"The signs we can see in them are talking to oneself wherever he is, suddenly talking to someone while the person is wondering what is been said to him or her. Things like these, are the signs". (50-year-old Health Attendant)
"First thing you will observe is that the person will look unkempt with bushy hair and mouth odor…(42-year old nurse)
"Some of these patients may have suicidal ideations thinking of killing themselves…" (47-year-old Health Assistant)

The Necessity of Integrating HIV and Mental Health Care into Primary Health Setting
Participants believed that though mental health should be handled by psychiatrist experts, yet PHC workers have a role to play in mental health care. According to them, there will be an overburden of the tertiary setting for mental health care particularly for minor cases and other responsibilities that need less specialized care. According to a 42-year-old nurse, *"I think with proper training, every nurse in PHCs should be able to manage someone with a psychological problem. At least we can counsel, observe the person, and talk to the relative. Instead of the patients going to the psychiatrist hospital in Abeokuta (Ogun State Capital in Nigeria), they can get their medications here. Though the mental doctors should treat them, but we can always support them in instances like this".*
Another participant, a 46-year-old Principal-CHEW opined *"Early stages of mental illness such as looking lost, brooding about something can be handled in PHCs alongside HIV care. The patients can be given medications here once we have trained personnel, but the serious ones (mental health disorders) cannot be accepted here".*

Yet another respondent, a 27-year-old CHEW said *"From my experience, by the time they are given prescriptions from psychiatric hospitals, they come to the PHCs, and we administer the injections... Therefore, we in PHC settings have a good role to play not only in HIV care but also in mental health care."*

However, many of the participants felt PHC workers should get some level of training that is adequate to identify early stages of mental illness among HIV and other patients and be able to make prompt referrals to specialists. According to a 58-year-old Chief Nursing Officer, *"We may not be able to handle mental illness because we are not trained. We should receive training so that when we see people with mental health problems, we can call the psychiatrists and inform them about the patient….."*
Challenges of integrating Mental Health Care into HIV Services in PHC Settings

While it may be good to incorporate HIV and mental care in PHC, participants believed there are attending challenges to this. First is the shortage of staff which many of the workers pointed out. All the facilities where the FGDs were conducted complained of inadequate personnel. Besides, they also complained of inadequate training and facility space to handle the integration because both mental health and HIV patients need enough privacy and there may be confidentiality issues.
According to a 47-year old Pharmacy Technician. *"One of the bottlenecks that we face in HIV care is a shortage of staff. If only we can have more hands, it will be easy to care for HIV patients in our health centers".* According to a 48-year-old Medical Laboratory Scientist *"An important challenge to care is that the patients (HIV/mental health) do not like to mix with other patients. It starts even from not wanting others to know what type of laboratory investigations they wish to do and therefore they need a facility large enough to offer adequate privacy"* According to some of the participants in this study, not providing enough privacy can cause some of the patients to miss their appointments.
Other challenges involved in care are poor political will, inadequate provisions of drugs, and other resources like test kits. A 41-year-old Pharmacy Technician opined *"in the past 2 months, we have not had enough. We tell the patients to use their drugs to reduce the viral load, but we are not able to make the drugs available in some days… So, we need whatever the government can do about it".*

Discussion

Six important themes were extracted from the data in this study (Table 2); "Integration of PHC services", "Multiple mental/psychological health challenges", "Multiple factors as causes of mental illness", "Diverse manifestations of mental illness", "Necessity of incorporating HIV and Mental Healthcare into PHC services", and "Challenges of incorporating HIV and Mental Healthcare into PHC services". The participants believed that the PHC structure as it cannot accommodate any HIV and mental health care integration. They opined that the PHC professionals lacked the proficiency to handle this important incorporation.

In consonance with the submissions of many of the health workers in this study, various other studies have established a direct relationship between living with HIV and developing mental illness.(Bing et al., 2001; Duffy et al., 2017) In a study, Duko (Duko et al., 2019) proposed several factors that may be positively associated with the development of mental disorders among PLWHA. Such include being a female, being widowed, having poor social support, having poor history of psychiatric illness and HIV-related perceived stigma.

It is not surprising that many participants of this study indicated stigmatization as a major mental-health issue militating against the well-being of HIV patients. This is because stigma and discrimination are two major problems often faced by PLWHA in many developing countries, including Nigeria.(Federal Ministry of Health Nigeria, 2013; Olatunji & Babatunde, 2014) Stigma and discrimination shown to PLWHA can worsen the spread and impact of the HIV/AIDS epidemic. As a result of fear of discrimination and stigma, many individuals are afraid of seeking HIV testing to know their HIV status while PLWHA may be less inclined to declare and openly acknowledge their HIV serostatus. This can lead to continued under-reporting of the epidemic, increased transmission, and limited access to treatment, care, and support programmes. Moreover, stigma and discrimination violate the human rights and dignity of people living with HIV and AIDS and those affected by the epidemic.(Federal Ministry of Health Nigeria, 2013) Similarly, self –stigmatization is a major contributor to mental ill health among PLWHA(Bennett et al., 2016) and it is as dangerous as public stigma.(van der Kooij et al., 2021)

Implementation of the Mental Health Gap Action Programme (mhGAP) has been documented as an effective strategy to scale-up mental health care. The programme is essentially designed to enable non-specialists and improve their proficiency in identifying and managing mental illnesses.(WHO, 2008) In agreement to the goal of this programme, almost all the participants in this current study were of the opinion that mental health care and HIV care should be provided in primary health centres. This assertion by the PHC workers is also in consonance with the report of the study by Gureje which showed that it was possible to scale up mental health services in primary health care centres.(Gureje et al., 2015) It also agreed with the study by Carvalhal (Carvalhal, 2015) which showed mental health care should be integrated with HIV care. This integration has been shown to have several advantages including improved adherence to anti-retroviral therapy.(Carvalhal, 2015). In a scoping review, Conteh reported reduced psychiatric manifestations among PLWHA who received care in facilities where integration of both services was practiced. Furthermore, this review reported that health workers in such facilities were more comfortable discussing mental health issues.(Conteh et al., 2023) According to Remien, this integration would strengthen HIV prevention and care and also facilitated global accessibility to mental health services.(Remien et al., 2019)

One of the themes that emerged from this current study was that integrating mental care into HIV services has associated challenges. The sub-themes included inadequate medicine, poor political will, and shortage of staff. This finding was similar to another Nigerian study which reported that integrating mental and HIV care has inherent challenges such as limited human resources and policy and structural related issues.(Ezeanolue et al., 2015) This finding issues a clarion call to policy makers

and stakeholders in health care particularly concerning mental health and HIV care to ensure provision of more human, material and financial resources if an efficient service integration would be pursued. The use of qualitative approach to elicit data from PHC workers offered the opportunity to adequately explore the views of the participants concerning the subject matter. However, the study does have some limitations. The study area should have been expanded, for instance to include the whole of Ogun State or the southwest region of Nigeria so that more health facilities providing HIV care could have been captured, hence more FGDs conducted with a larger sample size. Moreover, a more robust mixed-method study could have been done with a quantitative component using questionnaires to elicit data not only from health workers but also from PLWHA. This will offer a wholesome assessment of perception from both the providers and the consumers' perspective as regards integration of HIV care and mental health services in PHCs. Future research opportunities may therefore consider such mixed-method studies. According to Wasti et al; 2022, mixed method studies are important and they have increasing relevance in health.(Wasti et al., 2022).

Conclusion and recommendation: This study shows a good perception as regards integrating mental health care into HIV services. However, the participants opined that the setting lacked the capacity to accommodate this integration. Effort, therefore, should be made to improve the capacity of PHCs to perform optimally in caring for HIV and mental health patients. There is a need for infrastructure and system expansion including training and re-training of health care workers to facilitate their competency in both HIV and mental health care.

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Table 1: Socio-demographic Characteristics of Participants

Variable	Frequency	Percentage
Age		
≤39	4	14.8
40-49	19	70.4
≥50	4	14.8
Sex		
Female	26	96.3
Male	1	3.7
Profession		
Nursing	7	26.0
Pharmacy Technician	6	22.2
Laboratory Scientist	5	18.5
Community Extension Worker	4	14.8
Health Attendant/Assistant	2	7.4
Medical Record Officer	2	7.4
Health volunteer	1	3.7
Duration of service (years)		
≤10	6	22.2
>10	21	77.8

Table 2: Themes, Sub-themes and codes from analysis

Theme	Sub-theme(s)	Code	Sub-code	Definition
Integration of PHC services	Understanding of PHC services	Knowledge of PHC services		How knowledgeable are participants on the various types of PHC services that are available
Integration of PHC services	Familiarity with PHC services	Conversant with PHC services		Participants response on how well they are up-to-date on the various PHC services that are available
Integration of PHC services	Awareness of PHC services	Conscious of existing PHC services		Participants thoughts on how mindful they are of the existing PHC services
Integration of PHC services	Information of types of PHC services	Data on PHC services	Evidence. Facts. Figures.	Statistics, records and documentation on the types of PHC services that are available
Multiple mental/psychological health challenges	Public stigmatization	Stigma displayed by family members	Spoiled identity	Participants response to the expression of stigma towards them from family members
Multiple mental/psychological health challenges	Public stigmatization	Stigma displayed by friends		Participants thoughts on stigma towards them from their friends
Multiple mental/psychological health challenges	Public stigmatization	Stigma displayed by their colleagues		Participants opinions on stigma towards them from their colleagues
Multiple mental/psychological health challenges	Public stigmatization	Stigma displayed by strangers		Participants response to the expression of stigma towards them from strangers that learn about their health condition

Multiple mental/psychological health challenges	Self-stigmatization	Internal negative thoughts	Negative emotions	Participants views on them stigmatizing themselves
Multiple mental/psychological health challenges	Self-stigmatization	Disassociation from others	Negative self-perception	Participants feelings on them stigmatizing themselves
Multiple mental/psychological health challenges	Depression	Self-withdrawal		Participants judgments of themselves leading to non-performance of daily activities
Multiple mental/psychological health challenges	Abandonment and neglect	Rejection by family members and friends		Participants beliefs that family members and friends tend to abandon, neglect and leave these people
Multiple mental/psychological health challenges	Issues with Disclosure	Fear of possible neglect	Choosing to be secretive	Participant's opinion that PLWHA prefer not to tell others about their HIV status
Multiple factors as causes of mental illness	Social factors	Social system/societal structure		Participants thoughts on the societal structure not being supportive towards PLWHA
Multiple factors as causes of mental illness	Social factors	Social relationships	Disappointments	Participants feelings on the breakdown of social relations in marriage or in a social arrangement
Multiple factors as causes of mental illness	Social factors	Social connectedness		Participants views on the loss of social connection, social networks or social support
Multiple factors as causes of mental illness	Social factors	Living circumstances/arrangements		Participants understandings of a sudden change in living arrangements
Multiple factors as causes of mental illness	Economic factors	Loss of job	Unemployed	Participants' opinion of being unemployed as a PLWHA due to ill-health
Multiple factors as causes of mental illness	Economic factors	No Income		Participants' thoughts on lack of income for everyday living among PLWHA
Multiple factors as causes of mental illness	Spiritual factors	Belief in unseen forces		Participants response on their acceptance that certain unseen forces are at work and manifesting
Multiple factors as causes of mental illness	Spiritual factors	Workings of the supernatural		Participant's views that beyond the physical world; there is a supernatural power at work.
Diverse manifestations of mental illness	Mild	Poor personal hygiene	Often dirty	Participants response on how unkempt and dirty PLWHA with mental illness look
Diverse manifestations of mental illness	Mild	Poor concentration		Participants reply that PLWHA with mental illness often lack concentration in their daily activities
Diverse manifestations of mental illness	Mild	Mood swings		Participants answers on some PLWHA displaying change in their moods as circumstances and situations persist
Diverse manifestations of mental illness	Mild	Hallucinations		Participants observations of some PLWHA sometimes fantasizing with themselves

Diverse manifestations of mental illness	Severe	Hallucinations		Participants answers on the fact that some PLWHA are delirium and regular hallucinate
Diverse manifestations of mental illness	Severe	Talking alone or having insensible conversations		Participants feedback on the fact that some PLWHA are seen talking to themselves and not to another person. That is, they often have self-conversations that is obvious to other people
Diverse manifestations of mental illness	Severe	Becoming violent		Participants opinion that these people are showing signs of violent behaviour
Diverse manifestations of mental illness	Severe	Suicidal ideation/attempts	Suicidal thoughts	Participants answers that some of these persons are having negative thoughts about themselves and life in general. That is, they lack interest in living their lives
Necessity of incorporating HIV and Mental Healthcare into PHC services	Training	Health workers require training		Participants reply that health workers still need to be trained in the area of basic psychiatry
Necessity of incorporating HIV and Mental Healthcare into PHC services	Drug administration	Health workers intervene		Participants feedback that often times the health workers take up the responsibility of administering the drugs as many PLWHA require proper guidance
Challenges of incorporating HIV and Mental Healthcare into PHC services	Shortage of health workers	Inadequate staff		Participants thoughts on their lack of sufficient workers
Challenges of incorporating HIV and Mental Healthcare into PHC services	Poor political will	Lack of governmental commitment		Participants opinion on poor attention received from the government towards PLWHA
Challenges of incorporating HIV and Mental Healthcare into PHC services	Inadequate medicine	Lack of essential drugs		Participant's opinion on the non-availability of drugs for patients

Factors Affecting the Availability of Essential Health Commodities in Tanzania with a Special Focus on the Tracer Commodities

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Abstract
Background: Access to essential health commodities is fundamental to healthcare system efficacy. These commodities are vital in delivering health services and form integral elements within the World Health Organization's strengthening framework, encompassing the six foundational building blocks. Regrettably, there has been a global increase in shortages and stockouts of essential health commodities in recent years.
Objective: The study aimed to identify factors influencing the availability of essential health commodities throughout all levels of the supply chain in Tanzania.
Methods: A cross-sectional convergent parallel mixed method study that employed both qualitative and quantitative data collection techniques was conducted. Quantitative data were analyzed using STATA version 16, while qualitative data were thematically analyzed.
Results: Factors contributing to stockouts of essential commodities at the national level included increased demand, delayed shipments from donors, decreased funding commitments, delayed disbursement of funds, global shortages, inadequate governance, debt within the Medical Stores Department, donor dependency for vertical programme commodities, and long lead times by Medical Stores Department's suppliers. At the regional and district levels, such factors include a shortage of human resources, lack of electronic medical records, limited interoperability of information systems, poor quality of logistics data, inadequate use of data for decision-making, and poor inventory management. At the healthcare facility level, factors included; an overwhelming number of exempted clients, which reduces facility revenues.
Conclusion: More efforts are still needed to address both the upstream and downstream challenges required to ensure sustainable access and availability of essential health commodities at service delivery points, as a pathway for improving health sector performance.

Keywords: Tracer commodities, essential commodities, availability, access, Tanzania

Background

Stockouts, which refer to the complete absence of a specific formulation and dosage of medicine at a given healthcare facility, are recognized as an essential measure of health service readiness (Prinja et

al., 2015; Bigdeli et al., 2015). They can have significant consequences for the provision of quality health services. When stockouts occur in the healthcare system, consumers may use over-the-counter medicines or products from unqualified sources, increasing the risks of counterfeit or substandard products (Leung et al., 2016).

Even the stockouts of a limited number of health commodities can have widespread implications for delivering high-quality health services. Consequently, stockouts serve as a critical indicator of the preparedness of health services. The prevalence of essential health commodities stockouts at healthcare facility levels in sub-Saharan Africa presents a significant public health challenge. This issue is recognized for its adverse impact on data utilized for performance analysis and continuous transformation and its influence on morbidity, mortality, and disease epidemiology (Koomen et al., 2019; Hwang et al., 2019).

Looking at the financing of healthcare commodities, many medicines are paid out-of-pocket, potentially exposing households to financial hardship (Mahler et al., 2011). To avoid stockouts of healthcare products, ensuring that all supply chain management system components are performing effectively is crucial. Furthermore, examining the logistics cycle within supply chain management can illuminate essential components crucial for guaranteeing access to and availability of health commodities. This analysis also underscores the pivotal factors positioned at the core of the supply chain cycle (Jia et al., 2017). In light of this, a well-functioning supply chain cycle ensures seamless management of health commodities, thereby facilitating effective healthcare delivery (WHO & World Bank, 2018).

The Government of Tanzania, in partnership with development and implementing partners, has made significant efforts to tackle the challenges associated with stockouts of healthcare commodities. A key focus has been to guarantee uninterrupted health services by ensuring service delivery points have access to essential health commodities. This commitment is evident through a dedicated and collaborative funding approach. For instance, there has been a significant increase in the national budget for medicines and related medical supplies from TZS 31 billion during the Financial Year 2015/16 to TZS 258.4 billion during the Financial Year 2022/23 (Luiza et al., 2016). Similarly, the 2018 Global Fund Audit, revealed that funds allocated to Tanzania are predominantly focused on commodity procurement, with 73% of the current grant earmarked for the procurement and distribution of health commodities. These endeavours signify that the government and development partners prioritise health commodities, with a substantial portion of the budget dedicated to ensuring their availability. Despite these promising efforts, supply chain challenges persist in the country (Pronyk et al., 2016). This study aimed to identify the factors influencing the availability of essential health commodities at all levels of the supply chain in Tanzania.

Methods
Study Design and setting
A cross-sectional convergent parallel mixed-method assessment was undertaken to gather information using quantitative and qualitative methodologies. To complement this, a desk review was also conducted. The study was conducted between August and September 2021 within selected healthcare facilities, encompassing district, regional, and national levels. The study was conducted in ten regions including Mtwara; Tabora, Dodoma, Tanga, Iringa, Kilimanjaro, Mbeya; Dar-es-Salaam, Kagera, and Mwanza which represent the Medical Stores Department (MSD) Zonal Strategic Business Units. The choice of districts and healthcare facilities in these regions was guided by considering the levels (hospital, health centre, and dispensary) and geography (rural or urban). The selection of facilities ensured that two dispensaries, two health centres, and one hospital were included in each district. The regional hospitals were purposefully included in the study. Generally, this resulted in 104

facilities included in this assessment (36 dispensaries, 40 health centres, 20 district hospitals, and 10 regional hospitals).

Participants recruitment

The individuals involved in the supply chain of health commodities were selected using purposive sampling. Specifically, four key informants were chosen from each sampled facility and district, Health Management Team representatives from the ten regions, and staff at the Medical Stores Department (MSD) zones. At the national level, key informants were drawn from various organizations, including the Ministry of Health, President's Office - Regional Administration and Local Government, Medical Stores Department central warehouse, Council Health Management Team, Programmes – National AIDS Control Programme, National Malaria Control Programme, National TB and Leprosy Programme, Immunization and Vaccine Development Programme, Reproductive and Child Health Section, Tanzania Medicines and Medical Devices Authority, and the Global Health Supply Chain Technical Assistance Project. To recruit these stakeholders for key informant interviews (KIIs), their contact information was obtained from the Ministry of Health through peer referrals. A list of all participating stakeholders and their phone contacts was generated. Subsequently, research assistants initiated contact with these individuals via telephone, and those who expressed interest were selected to participate in the interviews, considering their preferences regarding interview modality (phone or face-to-face) and scheduling availability.

Data collection

Data collection strategies included the following: (1) Desk review: This involved reviewing several documents, including stock status reports from central agencies of the Ministry of Health, to capture information on essential health commodities and the overall supply chain. (2) Quantitative site audits: These were conducted at health facilities using tools adapted from the Logistics cycle. (3) In-depth interviews: Key informants were purposefully selected and interviewed using a semi-structured interview guide through either phone-based or face-to-face strategies. All qualitative interviews were audio-recorded, transcribed, and translated from Swahili to English. The interviews typically lasted about 30-60 minutes per individual.

Data management and analysis

The quantitative data collected was entered into Microsoft Excel and analyzed using STATA version 16. On the other hand, the qualitative data was analyzed thematically, following the approach described by Braun and Clarke (2006). The transcribing and translating of the key informant interview (KII) data was conducted simultaneously by research assistants and verified by the research team. All interview transcripts were de-identified following transcription and translation, and pseudonyms were assigned to each participant. The data was then imported into NVivo 12 software (QSR International, Australia) for data management and deductive thematic coding. To begin with, the research questions were thoroughly examined, leading to the collaborative generation of an initial analytical matrix consisting of themes and subthemes. Subsequently, individual transcripts were analyzed, and relevant phrases (codes) representing participants' responses to the researchers' inquiries were extracted and linked to the appropriate themes and subthemes using NVivo software (QSR International Version 12). Throughout the coding process, ongoing peer engagement was maintained, employing a consensus-based approach within the research team to determine the inclusion or exclusion of codes that did not align with the developed subthemes and themes. Codes subjectively or objectively deemed to hold little value to the study were either retained or discarded. Lastly, the coded data were exported to Microsoft Word to create the research report.

Ethical considerations

Ethical considerations were ensured throughout the study. The research obtained ethical clearance from Tanzania's National Health Research Ethics Review Committee with the reference number NIMR/HQ/R.8a/VOl.IX/3739. Moreover, the appropriate authorities in the selected regions, districts, and healthcare facilities sought permission to conduct the study. Informed consent procedures were strictly followed, and written informed consent was obtained from all participants. This ensured that participants were provided with clear information about the study's purpose, procedures, potential risks and benefits, confidentiality measures, and their right to withdraw from the study at any time without consequences. Participants could ask questions and seek clarification before voluntarily signing the informed consent forms. By obtaining ethical clearance, seeking permission, and obtaining informed consent, the study protected participants' rights, welfare, and confidentiality, and adhered to ethical guidelines and regulations governing research conduct.

Findings

Acknowledging that all visited hospitals have assigned personnel to manage essential health commodities is crucial. Nevertheless, it is noteworthy that these personnel may not possess pharmacy or laboratory sciences backgrounds, which are paramount for effectively managing essential commodities. For instance, among the visited facilities, 47% had pharmaceutical personnel and 2% had laboratory personnel managing health commodities. This indicates that in 51% of the visited facilities, commodities were overseen by staff lacking pharmaceutical and laboratory backgrounds, which are technically relevant to health commodities management. A detailed examination of individuals managing health commodities in 51% of the health facilities is as follows; 18% were nurses, 15% were medical attendants, 14% were clinicians, 3% were material managers, and one was an accountant (Table 1). Participants' level of education ranged from certificate to bachelor in their respective fields.

Table 1: Professionals managing health commodity stores

Profession	Number	Percentage
Pharmaceutical Personnel	50	47%
Nurses	17	18%
Medical Attendants	16	15%
Clinicians	15	14%
Storekeeper (No title recorded)	3	3%
Lab. Technologist/Assistant	2	2%
Accountant	1	1%
Grand Total	104	100%

Overview

The factors contributing to stockouts of tracer items at the national level included: increased demand, delayed shipments from donors, decreased funding commitments, delayed disbursement of funds and global shortages, inadequate governance, MSD debt, donor dependency for vertical programme commodities, and long lead times by MSD suppliers. The factors contributing to stockouts at the

regional and district levels included: a shortage of human resources, lack of electronic medical records, non-interoperability of information systems, poor quality of logistics data, inadequate use of data for decision-making as well and poor inventory management. Contributors at the healthcare facility level included: an enormous number of exempted clients who reduce the facility revenues, the absence of reliable electronic systems to monitor health commodity consumption, and inadequate capacity in stores for health commodities' management. Concerns about inadequate vehicles and fuel budget to carry out health commodities to healthcare facilities related supervisory visits surfaced at the regional and district levels. Some participants directly linked stockouts to the fluctuating availability of these commodities at the MSD.

The magnitude and frequency of stockouts of essential health commodities including tracer commodities.

Facility audits indicated that the availability of tracer commodities is directly linked to facility level and location. All the 30 tracer commodities with their respective types were more available in urban settings than rural ones. This was because urban settings are more privileged with fair infrastructure and sound systems, enabling adherence to storage measures compared to facilities in rural settings (Figure 1).
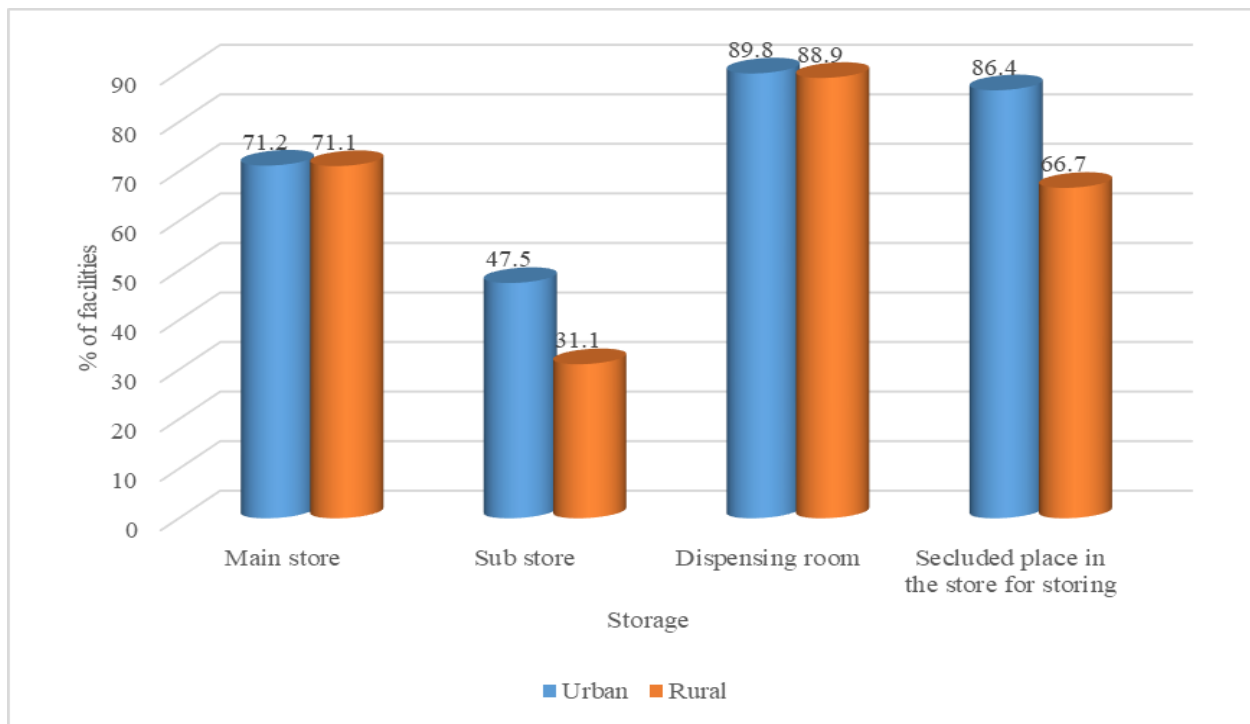
Fig 1: Comparison of availability of all the 30 tracer commodities between urban and rural settings

At the health facility level, there were variations in the availability of tracer items in hospitals, health centres and dispensaries. For example, the Pentavalent vaccine was more available at health centres than at other health facility levels. There were variations in the four presentations of Artemether Lumefantrine (ALU), with ALU 1x6 and ALU 4x6 more available at the dispensary level. At the same time, ALU 2x6 and ALU 3x6 were more available at health centres and hospital levels, respectively. Both amoxicillin caps and dispersible tablets for adults and children, respectively, were more available

at the dispensary level. At the same time, both co-trimoxazole suspension and tabs were more available at the hospital level.

Regarding anthelmintics, Albendazole was more available at the dispensary while Mebendazole was more available at the hospital level. For maternal health commodities for PPH and labour induction, Misoprostol was more available at the hospital level, while Ergometrine was more available at the health centre level. Looking at contraceptives, Depo-Provera was more available at the hospital level, while Microgynon was more available at both the health centres and the dispensary level.

Tracer commodities in the category of supplies, such as syringes, vary across the three levels, with 5cc syringes more available at the dispensary level, 10 cc syringes more available at the health centre level, and 2 cc syringes more available at the hospital level. Relatedly, gloves were more available at the hospital than at other levels. Considering antibiotics, Benzylpenicillin Ceftriaxone 250 mg and I g injections were more available at the health centre than at other levels. For HIV/AIDS commodities namely ARVs and Rapid test kits, variations were also seen across the levels. Considering Antiretroviral drugs (ARVs), Tenofovir, Lamivudine, and Efavirenz were more available at the hospital level, while Tenofovir, Lamivudine, and Dolutegravir were more available at the health centre level. As for Rapid test kits for HIV, SD BIOLINE was more available at the hospital and health centre level while UNIGOLD was more available at the dispensary level (Figure 2).
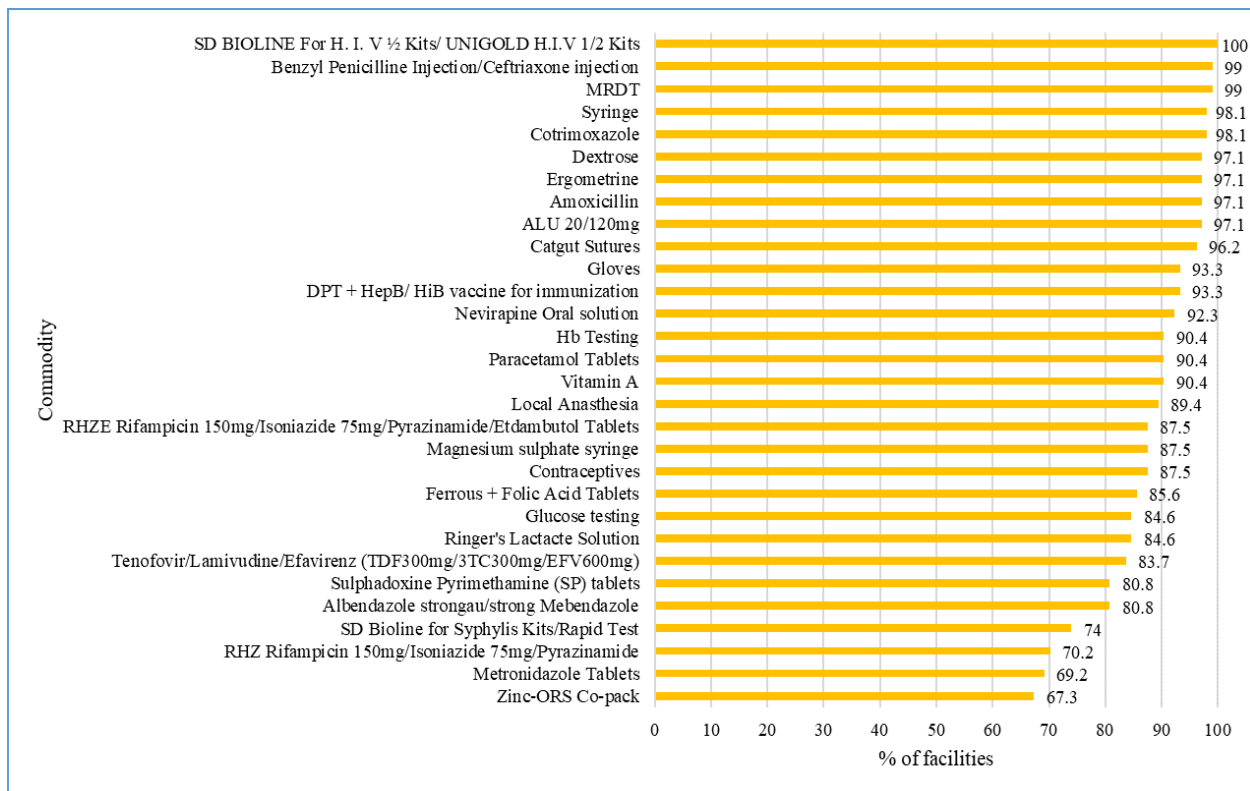
Figure 2: Tracer commodities availability at the facilities.

The findings indicated that the availability of tracer commodities at facilities highly depends on delivery from the Medical Stores Department. However, some indicated availability of commodities up to 90%. Where essential commodities were unavailable, concerns of budgetary limitations dominated as Information was mobilized for performance analysis and continuously transforming the facility's

capacity to purchase some essential health commodities, including tracer items, which were out of stock at MSD.

During qualitative interviews, participants expressed mixed views on the availability of tracer items with most suggesting misalignment on the availability and supply of tracer commodities in the past six months. One group of respondents affirmed that the availability was good although concerns of increasing stockouts in recent months dominated. Another group of respondents affirmed that the availability of commodities at the MSD was not good in previous months and there has been much improvement in recent months.

Relatedly, disagreement emerged during qualitative interviews on the stock of tracer commodities in health facilities. One group of central government respondents suggested that stockouts never happened except for 'intermittent stockouts' in some facilities. Another group comprising respondents from the facilities, districts, regions and development partners affirmed frequent stockouts. The contributing factors to stockouts included facility-level problems, such as errors in forecasting and ordering, a sudden increase in demand from facilities; and stockouts at the national level due to decreased minimum stock levels, delayed shipments from donors, decreased funding commitments, delayed disbursement of funds, and global shortages. One participant commented:

> *"For now, we have improved availability and no major challenges. We purchased health commodities, and only a few are missing, but almost 90% of commodities are available, for example, TB medications. Only Metronidazole tablets have not been available since last month because we ordered them at the MSD"* (Facility in-charge, Mwanza)*.*

The capacity of institutions in the selection, quantification, procurement, management, and distribution of essential health commodities

During qualitative interviews, it was pointed out that pharmacists at the district and regional levels are responsible for ensuring the availability of essential commodities. They conduct health commodity audits and ensure timely ordering, distribution, redistribution, and reporting. Budget expenditure monitoring and capacity building through training and supportive supervision comprise other responsibilities. Pharmacists at the national level affirmed involvement in ensuring the availability, quality, and safety of health commodities entering the country.

Regarding procurement, it was pointed out that ordering essential health commodities involves discussing the available resources at the facility level, preparing Report and Requisition forms, and submitting them through the Electronic Logistics Management Information System. They are then reviewed and approved at the district and regional levels before being sent to the MSD. The MSD and prime vendors dominated the place where procurement is done. However, procurement at the prime vendor was said to require evidence of stockouts of such commodities from MSD. The procurement challenges mentioned by some participants included: delayed updates on the order status even for emergency orders; delayed supply, frequent stocks of health commodities; supplying health commodities not ordered; absence of a guideline on procurement; and inadequate funds for procurement of essential health commodities. One participant commented:

> *"Sometimes they delay delivery because if we ordered at the beginning of July and we write a report in August, it means they need to have brought the medicines, but sometimes a month can end without having them delivered. We need to start manufacturing the medications here at home and I know some industries have started doing that. We have a functional industry making masks. An industry in Keko is making Paracetamol tablets with 70% government and 30% private ownership. Some industries plan to begin producing gloves and tablets in Njombe and creams and*

syrups in Dar es Salaam. This will reduce the time and cost of procurement of commodities. It will also ensure quality because we will manufacture ourselves" (Facility in-charge, Mtwara).

Regarding health commodity management, Facility audits indicated different techniques at all facility levels. The techniques used at the hospital, health centres, and dispensaries included good storage practices, Standard Operating Procedures (SOPs), and energy backup systems. Geographically, facilities in rural areas had a significantly lower number (91.1%) of inventory management tools (prescriptions, bin cards, and ledgers) as compared to those in urban areas (100%). Rural and urban variations were also seen, with urban regions performing better in all aspects of inventory management, including having tools, systems, and equipment in place to enable good storage practices.

Furthermore, many hospitals have SOPs, inventory management tools, and store ledgers. Store ledgers were seen in all visited hospitals, while more bin cards were available at the health centre level (100% of all visited health centres). Regarding the First Expire, First Out (FEFO) application, all levels of health facilities practice it very well. From the facilities visited, the availability of ledgers was 99% but only 74% of the available ledgers were updated. Similarly, bin cards were available to 99% with 78% of the available bin cards updated. Moreover, regarding dispensing registers, the one for ARVs was available to 91% with 83% of the available ones updated.

In comparison, the new Integrated Logistics System (ILS) dispensing register was available to 66% with 90% updated. Lastly, the registers for rapid test kits were available to 80% with 94% updated. However, there is still a challenge with the availability of the tools, especially the ILS dispensing register for essential medicines and registers for record test kits (RTKs). However, updating the tools is a much more significant challenge, leading to reported poor data quality. To prevent the expiry of health commodities, the dominant strategies emerging during

qualitative interviews were supply inspection and refusal of commodities with a short shelf life; ordering commodities based on the demand, and redistribution of near-expiry commodities between facilities. One participant commented:

"We work with Tanzania Medicines and Medical Devices Authority; we know the guidelines. The last time we destroyed expired health commodities was in 2016. We collect and evaluate all expired medicines and prepare for destruction. Another strategy is refusing medications that expire in the next three months. They also order medications considering the three-month demand" (CHMT member, Iringa).

Additionally, most qualitative participants mentioned that the MSD uses a direct delivery system to supply health commodities to the facility. The distribution time ranged between 14 and 28 days upon receiving the order. Almost all MSD officials confirmed the presence of enough vehicles for distribution. Most stakeholders acknowledged being involved in ensuring the availability of sufficient quantities of essential health commodities and capacity building, especially vaccines. However, an electronic system for prime vendor order management was pointed out as the leading solution to inadequate resources for distributing health commodities.

Public sector policies and strategies for the supply chain of essential health commodities including tracer commodities

The desk review examined eleven policy and programmatic documents, including Health Sector Strategic Plan IV (2015-2020), and it was designed to examine progress and challenges regarding the availability of essential health commodities involving 30 tracer commodities. The findings affirmed the

presence of policy documents that emphasized the availability of essential health commodities to facilitate the provision of quality health services at service delivery points.

Key issues that most of the documents showed were increased allocation of funds for the procurement of health commodities to improve the availability of essential health commodities, development of bottom-up quantification guidelines to guide the selection and quantification of essential health commodities, and the availability of management information systems that facilitate reporting of logistics information.

The review, however, indicated several challenges to the availability of essential health commodities. They include human resource shortages, outstanding MSD debt; donor dependency, especially for vertical programme commodities; delayed disbursement of funds; long lead times by Medical Stores Department suppliers and Vertical programmes' commodities suppliers, inadequate coordination and communication between Vertical programmes and MSD, absence of the national oversight body for quantification of all essential health commodities, delayed release of out-of-stock notification by MSD for timely procurement of essential health commodities from prime vendors, lack of interoperability of information systems and delayed distribution of standard treatment guidelines to health facilities.

Discussion

This paper presents factors affecting the supply chain for critical essential commodities in health facilities and selected medical stores in ten regions of Tanzania. The focus was on identifying the institutional factors that affect the availability of health commodities at all levels of the supply chains.

The findings revealed a spectrum of factors influencing the availability of essential health commodities. Challenges include outstanding debts with the MSD, reliance on donors, and delayed fund disbursement. Other key issues include a lack of out-of-stock notifications from MSD for timely procurement from prime vendors, information system interoperability issues, delayed distribution of standard treatment guidelines to health facilities, inadequate tracer commodity lists, disparities between reported availability via District Health Information System 2 and the actual situation on the ground, suboptimal inventory management practices, absence of logistics management information system tools for effective inventory management, and inadequate documentation of inventory management tools leading to poor data quality reported by health facilities regarding essential health commodities and subsequent stock imbalances, including under-stocks and stockouts.

It is important to note that most of these challenges have been widely documented in both Tanzania and Sub-Saharan Africa (Demessie et al., 2020 Githendu et al., 2020). Consequently, these challenges became central to the qualitative inquiry during this study.

More specifically, our findings indicate that at the facility level, challenges include insufficient capacity in health commodities management, a significant number of exempted clients reducing facility revenue, and the absence of reliable electronic systems for monitoring commodity consumption. There was a strong plea for the government to review the exemption policy or find ways to cover medications used by these groups to ensure facilities have adequate financial capacity for tracer item availability.

Furthermore, at the district and regional levels, concerns about inadequate vehicles and fuel budgets have surfaced with some linking the non-availability at facility levels to the fluctuating availability at the MSD. To address challenges in the availability of tracer commodities, suggestions included improving the availability of tracer commodities at the MSD and enhancing the overall functionality of the MSD, with some proposing an overall improvement in work performance. There was also a notable emphasis on building local manufacturing capacity instead of relying on external

suppliers. It is crucial to note that many of these challenges have been previously reported (The Global Fund, 2015 Lee & Tarimo, 2018), indicating a need for the Ministry of Health to develop a comprehensive medicine policy guiding the availability, management, and use of medicines in the country.

The absence of a supply chain strategy to guide the implementation of health commodity-related plans is highlighted. Moreover, the Ministry of Health, particularly the President's Office - Regional Administration and Local Government, is urged to recruit and deploy pharmaceutical and laboratory personnel, especially at lower-level health facilities. This recommendation stems from the significant finding that only 47% of visited health facilities had personnel with a pharmaceutical background managing the stores.

This study uncovered several recommendations for increasing funds for commodity procurement at the facility level. These encompass the Ministry of Health's consideration of measures such as reducing overconsumption by exempted groups through a review of exemption policies and exploring funding avenues for essential health commodities used by these groups through the Medical Store Department. Additionally, facilities, districts, regions, and the Ministry of Health are encouraged to contemplate budget increments, diversify funding sources, and enhance payment systems to boost facility revenues. Furthermore, there is a call to facilitate health facility governing committees overseeing proper fund management. The Government of Tanzania is urged to ensure adherence to Health Commodity Revolving Fund guidelines, with reports prepared by health facility personnel, validated by governing committees, and submitted to relevant authorities for increased awareness, advocacy, and community sensitization to encourage more clients to join the National Health Insurance Fund and Community Health Fund. Implementing these recommendations has the potential to boost the availability of funds for financing tracer commodities across various levels and enhance their accessibility within the healthcare system at different tiers.

In light of our findings, we advocate for facilitating effective and efficient utilization of electronic systems at the facility level. Based on our results, we propose that the Ministry of Health, the President's Office - Local Government and Regional Administration, and the Medical Stores Department (MSD) consider enhancing facility electronic systems to capture patient information accurately, spanning from arrival to departure, to aid in correct quantification.

There is a recommendation to develop a system for monitoring the alignment between facility orders and deliveries from prime vendors. We suggest linking the Government of Tanzania Health Operation Management Information System (GoTHOMIS) data with the Electronic Logistics Management Information System and aligning reporting periods between District Health Information System 2 and Electronic Logistics Management Information System data. It is advised to revise how health commodities availability is reported via District Health Information System 2, moving beyond a binary "Yes" or "No" to indicate the quantity available and its expected duration.

Moreover, there is a call for capacity building for healthcare workers responsible for inputting data into these systems, focusing on proper filing and data triangulation techniques to ensure accuracy before submission to higher levels. The establishment of facility-level Information Mobilized for Performance Analysis and Continuous Transformation teams is recommended, along with efforts by MSD to align essential health commodities costs across various information systems.

Our findings have brought to light critical challenges associated with using prime vendors. To address these issues effectively, we recommend that the Ministry of Health, the President's Office - Local Government and Regional Administration, take the following steps: review and enhance contracts with prime vendors, promptly ensuring strict adherence to stipulated deliverables. Contract improvements may involve incorporating the direct delivery of commodities to health facilities. Developing an electronic system to monitor procurement processes involving facilities and vendors is also advised. Considering the apparent strain on current prime vendors leading to frequent delays, it

is recommended to explore the possibility of increasing their number. It is crucial to uphold contractual agreements, particularly ensuring timely payments and conducting frequent reviews of contractual prices. Furthermore, a review of prime vendors' health commodity catalogues should be conducted to include frequently missing items, thereby enabling them to fulfil orders from health facilities adequately.

Study limitation

This study focused on the issue of stockouts at various levels of the healthcare system. However, we recognize the crucial role of a diverse range of healthcare commodities in ensuring optimal healthcare service delivery. Given the challenges posed by stockouts of these tracer commodities, future studies may benefit from broadening their scope to examine all health commodities. Furthermore, our investigation focused solely on stakeholders' perspectives on the supply side. Recognizing the importance of understanding the demand side, future studies need to explore the views of end users. Future research endeavours should incorporate clients' perspectives to provide a more comprehensive understanding of the issue in examining stockouts.

Conclusion

Continuity in service delivery relies heavily on the consistent availability of health commodities. There remains a critical need for increased efforts to tackle upstream and downstream challenges in the supply chain, aiming to ensure enduring access and availability of essential health commodities at service delivery points. This comprehensive approach is essential as a pathway to enhance overall health sector performance.

Acknowledgement

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Breastfeeding and non-nutritive sucking habits as covariates of malocclusion in the primary dentition among Tanzanian children: A cross-sectional study

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Abstract
Introduction: Studies on the effect of feeding practices and sucking habits on malocclusion traits in the primary dentition of pre-schoolchildren from developing countries are scarce.
Purpose: Assessing the association of feeding and sucking habits with malocclusion traits, and the association of malocclusion traits with observed oral functional problems.
Methods: It was a cross-sectional survey of children aged 3-5 years residing in Kinondoni and Temeke Districts of Dar es Salaam region in Tanzania. Data was analyzed using Statistical Package for Social Scientists, SPSS version 21.0. Univariate analysis was applied to generate frequencies of different variables. Cross tabulations and Chi-square statistics were used to assess bivariate relationships and multivariate analyses were performed by multiple logistic regression.
Results: Most pre-schoolchildren (82.5%) were breastfed for less than two years. A history of non-nutritive sucking habits was reported in 28.1% of the children, mostly in boys than girls (33.6% versus 21.8%, respectively. The current non-nutritive sucking habits were reported in 17.8% of the participants. Overall, malocclusion traits were most significantly seen in children who were breastfed for less than two years, compared with those who were breastfed for two years or more (48.5% versus 27.3%, respectively). The presence of various malocclusion traits was significantly found among most of the children who had a history of non-nutritive sucking habits, compared with those who had never performed the habits (65.9% versus 38.6 %, respectively). In the logistic regression analyses, children who were breastfed for a shorter duration (<2 years), their probability of being found with different traits of malocclusion in the primary dentition was almost three times that for those who were breastfed for a longer duration (≥ two years). Also, children who were not actively performing non-nutritive sucking habits were less likely to have an open bite compared with those who were actively performing non-nutritive sucking habits. An open bite in children was significantly associated with speech problems (p<0.01) and swallowing with tongue thrusting (p=0.000).
Conclusion and recommendations: Most of the children who were breastfed for a shorter duration and children who had non-nutritive sucking habits were found with various malocclusion, compared with those who were breastfed for a longer duration and those who had no non-nutritive sucking habits. It is crucial to recommend exclusive breastfeeding for up to 6 months and continuation of breastfeeding practice, possibly for up to 2 years of age due to its nutritional, immunological, and stomato-gnathic system developmental benefits.

Keywords: Breastfeeding, non-nutritive sucking, habits, malocclusions, primary dentition, pre-schoolchildren

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Introduction

Literature has described sucking habits in children as being either nutritive or non-nutritive (Ling et al., 2018). The nutritive sucking habits include breastfeeding and bottle-feeding (Lopes-Freire et al., 2015). Breastfeeding has several advantages for children, including nutritional, psychological, immunological, orofacial-developmental and general health benefits (Jackson & Nazar, 2006). It was formerly mentioned that breastfeeding promotes oro-facial muscle exercise while activating breathing, swallowing, mastication and phonation (Freire et al., 2015; Roscoe et al., 2018). In bottle feeding, children are fed using a bottle that expels milk through an artificial rubbery nipple-like object (Orimadegun & Obokon, 2015).

A prior study noted that replacing breastfeeding with bottle feeding can have unfavourable oral effects in children (Carrascoza et al., 2006). Notably, the World Health Organization (WHO) recommends that children be breastfed exclusively during the earliest six months of their lives (WHO, 2021). In some instances, children are breastfed for up to two years of age (Peres et al., 2007; WHO, 2021). Turgeon-O'Brien et al. (1996) suggested that when infants are not sufficiently breastfed, they may develop some sucking habits. Concerning the non-nutritive sucking habits, these are numerous, comprising habits such as finger sucking, thumb sucking and pacifier or dummy sucking (Moimaz et al., 2014).

Non-nutritive sucking habits are used to soothe, comfort or calm infants and children (Benis, 2002). Nevertheless, the habits are considered significant factors for altered occlusion in primary dentition/teeth

(Bishara et al., 2006; Frazão et al., 2002; Proffit et al., 2007; Warren & Bishara, 2002). More studies (Capsi Pires et al., 2012; Viggiano et al., 2004) supported the fact that non-nutritive sucking habits are among environmental factors related to the occurrence of malocclusion in children. On the other hand, appropriate breastfeeding practices were suggested to be protective against malocclusion development (Moimaz et al., 2014; Narbutytė et al., 2013).

Malocclusion is growth and developmental deviations involving the muscles and jaw bones during childhood (Moimaz et al., 2014). As regards the specific types of malocclusion, studies found posterior crossbite, open bite, deep bite, Class II molar relation and increased overjet to be malocclusion which may develop due to non-nutritive sucking habits and prolonged bottle-feeding in children (Moimaz et al., 2014; Ling et al., 2018).

Existing African literature shows that limited studies have addressed the effect of the duration or frequency of performing the habits. Moreover, some studies could not confirm the association between specific types of malocclusion and bottle-feeding, as well as the duration of breastfeeding or non-nutritive sucking habits (Ling et al., 2018). Notably, there are some conflicting conclusions in studies which have reported the association between feeding practices, non-nutritive sucking and malocclusion development (Pegoraro et al., 2021; Roscoe et al., 2018; Warren & Bishara, 2002). This study thus aimed to assess the association between breastfeeding practices and non-nutritive sucking as covariates of malocclusion in the primary dentition of Tanzanian pre-schoolchildren.

Methods

Study area and design.

This cross-sectional study was conducted in pre-schools of Kinondoni and Temeke districts in the Dar es Salaam region. Dar es Salaam is the most socially and culturally heterogeneous region in Tanzania. According to the 2012 population and housing survey in Tanzania (NBS, 2016), Dar es Salaam was

Tanzania's most highly populated region. It is divided into five districts: Kinondoni, Ilala, Ubungo, Temeke and Kigamboni. Kinondoni and Temeke were somewhat diverse districts in their socio-demographic profile, with the former having higher employment and literacy rates (NBS, 2016).

Study sample

Study participants were obtained from 8 selected pre-schools in Kinondoni district (5 pre-schools) and Temeke district (3 pre-schools). A census of 3-5-year-olds attending the schools was utilized for the study, where all 3-5-year-olds and their parents/caregivers were invited to participate. All consenting parents of the 3-5-year-olds were given specific days to be present for the study. 253 of 305 eligible preschool children and their parents participated in the survey, making the response rate 83%.

Survey instrument!

Two trained research assistants administered A structured interview schedule and responded by parents/caregivers of the 3-5-year-old preschool children in face-to-face interviews in a classroom setting. The questionnaire was translated from English to Kiswahili and included questions on socio-demographic characteristics, breastfeeding/feeding modalities, and children's sucking habits. The questionnaire was pilot-tested and adjusted accordingly before being used in the field.

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Clinical examination

One trained and calibrated researcher (the Principal Investigator, PI) conducted all clinical examinations in a classroom setting with natural daylight as the source of illumination and a trained assistant was recording the findings. The clinical examination occurred in a private space for this study. Pre-school children were clinically examined in the presence of their parents/caregivers (after their parents had completed the interview). All preschool children who participated were clinically examined for the presence/absence of malocclusion. The registration criterion was according to Björk et al. (1964) with some modifications by al-Emran et al. (1990). For specific malocclusion, the molar relationship was assessed and classified as Angle Class I, II or III when the distal plane of the second deciduous molars in centric occlusion was straight, distal (distal step) or had a mesial (mesial step) discrepancy, respectively.

Socio-demographics were assessed regarding location (Kinondoni/Temeke), gender, age, and parental education. The history of sucking was assessed by asking the parents whether their children had ever sucked their thumb/finger, tongue, or lip. Response categories were given as (1) 'yes' and (2) 'no'. These were then recoded into (0) 'no' and (1) 'yes' for use in further analyses. Current sucking habits were assessed by asking the parents if their children had any sucking habits currently. Response categories were given as (1) 'yes' and (2) 'no'; these were then recoded into (0) 'no' and (1) 'yes'. Parental education was constructed into (0) 'high' and (1) 'low' levels of education. The feeding methods were assessed by asking the parents whether they breastfed or bottle-fed their infants, and the duration was assessed and categorized into (0) 'Breastfeed for ≥2 years' and (1) 'Breastfeed for <2 years'. Tongue thrust swallowing and speech problems in children were recorded and scored as (1) 'presence' and (0) 'absence'.

Similarly, the deciduous canine was in a Class I relationship when the tip of the maxillary deciduous canine occluded in the embrasure of the mandibular deciduous canine and the first deciduous molar, Class II when the tip of the maxillary deciduous canine was anterior to Class I relationship and Class III when it was posterior to Class I relationship. Absence (0)/ presence (1) of the following recordings was also examined; a maxillary overjet, a mandibular overjet, a Class II/Class III molar occlusion, an open bite, a deep bite, a lateral crossbite, a midline shift, crowding and spacing.

Occlusion in the anterior segment could not always be determined in preschool children due to the shedding of their primary incisors. Such cases were excluded from overjet and overbite analyses but included in other malocclusion analyses. A sum score of malocclusion (SMO) was constructed to provide the overall prevalence of malocclusion, based on the diagnosis of absence (0)/ presence (1) of the following

recordings: a maxillary overjet, a mandibular overjet, a Class II/Class III molar occlusion, an open bite, a deep bite, a lateral crossbite, a midline shift, crowding and spacing. Speech and thrusting problems were also assessed.

Data analysis
Data was analysed using the Statistical Package for Social Sciences version 21.0 (SPSS et al., Illinois, USA). Frequencies were generated to assess percentage distribution/prevalence of different variables. Cross tabulations and Chi-square statistics were used to assess bivariate relationships. Multivariate analysis was conducted using multiple logistic regression analysis. The *p-value* for statistical significance was set at *p<0.05,* with 95% Confidence Interval.

Ethical considerations
Ethical clearance was obtained from the Research and Publication Committee of the Muhimbili University of Health and Allied Sciences, MUHAS. Permission to work with pre-school children was obtained from Kinondoni and Temeke municipalities, their respective educational authorities, schools administrations and parents. Only those pre-school children whose parents provided consent participated in the study. The informed verbal and written consent were thus obtained from all pre-school children's parents/caregivers who were involved in the survey.

Results
Table 1. Socio-demographics and behavioral characteristics of children 3-5 years.

Variable	Boys % (n)	Girls % (n)	Total % (n)
Age			
3/4 years	19.4 (26)	26.9 (32)	22.9 (58)
5 years	80.6 (108)	73.1 (87)	77.1 (195)
District			
Kinondoni	70.9 (95)	68.9 (82)	70.0 (177)
Temeke	29.1 (39)	31.1 (37)	30.0 (76)
Parents' education			
At least primary school	88.8 (119)	82.4 (98)	85.8 (217)
Above primary school	11.2 (15)	17.6 (21)	14.2 (36)
Breastfeeding duration			
≥ 2 years	17.4 (23)	17.6 (21)	17.5 (44)
< 2 years	82.6 (109)	82.4 (98)	82.5 (207)
Feeding method			
Bottle/cup	64.9 (87)	64.7 (77)	64.8 (164)
Breast	35.1 (47)	35.3 (42)	35.2 (89)
Ever sucking			
Yes	33.6 (45)	21.8 (26)	28.1 (71)
No	66.4 (89)	78.2 (93) *	71.9 (182)
Current sucking			
Yes	17.2 (23)	18.5 (22)	17.8 (45)
No	82.8 (111)	81.5 (97)	82.2 (208)
Swallowing			
Normal	90.3 (121)	92.4 (110)	91.3 (231)
Tongue thrusting	9.7 (13)	7.6 (9)	8.7 (22)
Speech problem			
No	90.3 (121)	95.0 (113)	92.5 (234)
Yes	9.7 (13)	5.0 (6)	7.5 (19)

*=p<0.05.

In Table 1, most of the pre-school children were above 5 years of age (77.1%). Majority were from Kinondoni district (70.9%). A greater proportion of the pre-school children's parents (85.8%) were educated at the level of primary school or below; few had a higher level of education of above primary school (14.2%). Regarding breastfeeding practices, few children (17.5%) were breastfed for up to 2 years or more. Bottle and cup feeding were the feeding methods utilized by most parents (64.8%); few parents practiced only breastfeeding (35.2%). Concerning sucking habits, a history of non-nutritive sucking was reported in 28.1 % of the children and was mostly among boys compared with girls (33.6% versus 21.8%, $p<0.05$). Whereas 17.8% of the children had active non-nutritive sucking habits. Tongue thrust swallowing was observed in 8.7% of the pre-school children and 7.5% had speech problems, mainly in form of lisping.

Table 2. Percentage (n) of children with malocclusions by feeding modalities and breastfeeding duration.

Malocclusion	Breastfeeding % (n)	Bottle feeding. % (n)	Breastfeed ≥2 years. % (n)	Breastfeed <2 years % (n)
Maxillary overjet	0.0 (0)	2.8 (3)	3.0 (1)	1.5 (2)
Mandibular overjet	3.4 (3)	6.7 (11)	0.0 (0)	6.8 (14)
Angle's Class II or III	3.4 (3)	12.2 (20) *	2.3 (1)	10.6 (22) *
Open bite	13.5 (12)	21.3 (35)	15.9 (7)	18.8 (39)
Cross bite	3.4 (3)	0.0 (0) *	0.0 (0)	1.4 (3)
Midline shift	10.1 (9)	6.7 (11)	6.8 (3)	8.2 (17)
Scissors bite	23.6 (21)	14.0 (23) *	11.4 (5)	18.4 (38)
Crowding	1.1 (1)	0.6 (1)	0.0 (0)	1.0 (2)
Spacing	14.6 (13)	22.6 (37)	18.2 (8)	20.3 (42)
Total malocclusion score	45.9 (28)	43.5 (47)	27.3 (9)	48.5 (66) *

=p<0.05.

Angle's Class II or III was recorded in a significantly greater proportion of children who were bottle-fed compared to those who were breastfed (12.2% versus 3.4%, $p<0.05$); and was significantly most frequently recorded in children who were breastfed for a lesser duration compared with those who were breastfed for >2 years (10.6% versus 2.3%, $p<0.05$). But scissors bite was found in significantly most of those who were breastfed compared with those who were bottle-fed (23.6% versus 14.0%, $p<0.05$); and was found in the majority of those who were breastfed for shorter duration (18.4% versus 11.4%, but not statistically significant). Overall, the total malocclusion score was found in a significantly greater percentage of those who were breastfed for <2 years compared with those who were breastfed for a longer duration (48.5% versus 27.3%, $p<0.05$) (Table 2).

Table 3. Angle's Class II or III malocclusion, scissors bite and total malocclusion score above 0 regressed on feeding methods at first 6 months and breastfeeding duration. Adjusted for age, gender, parents' education, ever sucking and current sucking behaviors.

Malocclusion	Feeding methods	Categories	Adjusted OR	95% CI
Angle's Class II or III	*Feeding first 6 months*	Bottle/cup	1	
		Breast	0.25	0.1-0.8
	Breastfeeding duration	≥ 2 years	1	
		< 2 years	5.2	0.6-40.2
Scissors bite	*Feeding first 6 months*	Bottle /cup	1	
		Breast	1.9	1.0-3.7
Total malocclusion	*Breastfeeding duration*	≥ 2 years	1	
		< 2 years	2.7	1.2-6.8

OR=Odds Ratio; CI= Confidence interval.

In Table 3, compared with those who were bottlefed, children who were breastfed for the first 6 months of life were less likely to be found with Angle's Class II or III malocclusion (OR=0.25, CI=0.1-0.8). But those who were breastfed were more likely to have Scissors bite than those who were bottle fed (OR=1.9, CI=1.0-3.7). Regarding breastfeeding duration, children who were breastfed for <2years were more likely to have a total malocclusion score of >0, than those who were breastfed for a longer duration (≥2years) (OR=2.7, CI=1.2-6.8).

Table 4. Percentage (n) of children with malocclusion by ever sucking and current sucking habits.

Malocclusion	Ever sucking % (n)	Never sucking % (n)	Current sucking % (n)	No current sucking % (n)
Maxillary overjet	5.4 (2)	0.8 (1)	0.0 (0)	1.9 (3)
Mandibular overjet	2.8 (2)	6.6 (12)	2.2 (1)	6.3 (13)
Angle's Class II or III	5.6 (4)	10.4 (19)	4.4 (2)	10.1 (21)
Open bite	38.0 (27)	11.0 (20) **	57.8 (26)	10.1 (21) **
Cross bite	1.4 (1)	1.1 (2)	2.2 (1)	1.0 (2)
Midline shift	12.7 (9)	6.0 (11)	11.1 (5)	7.2 (15)
Scissors bite	21.1 (15)	15.9 (29)	24.4 (11)	15.9 (33)
Crowding	15.9 (29)	1.1 (2)	0.0 (0)	1.0 (2)
Spacing	26.8 (19)	17.0 (31)	20.0 (9)	19.7 (41)
Total malocclusion	65.9 (24)	38.6 (51) **	60.0 (9)	42.9 (66)

**=p<0.01.

Table 4 depicts that; open bite was found in many of those (children) who ever performed non-nutritive sucking habit (38%) compared with those who never performed the habit (11%, p<0.01). Similarly, open bite was found in majority of children who had active non-nutritive-sucking habit (57.8%) as opposed to those who had no current non-nutritive sucking habit (10.1%, p<0.01). Also, a greater percentage (65.9%) of children who ever performed non-nutritive sucking habit had a total malocclusion score >0 compared with those who never had non-nutritive sucking habit (38.6%, p<0.01).

Table 5. Open bite regressed on ever sucking, current sucking (adjusted for age, gender, parental education), total malocclusion regressed on current sucking (adjusted for age, gender, parental education and breast-feeding duration).

Malocclusion	Sucking habit	Categories	Adjusted OR	95% CI
Open bite	Ever sucking	Yes	1	
		No	0.15	0.07-0.31
Total malocclusion	Current sucking	yes	1	
		No	3.0	1.3-6.7
Open bite	Current sucking	Yes	1	
		No	0.07	0.03-0.16

OR=Odds Ratio; CI= Confidence interval.

Table 5 shows that open bite was less likely to be found in children who never performed non-nutritive sucking habits compared with those who ever performed the habits (OR=0.15, OR=0.07-0.31). Also, children who did not have current non-nutritive sucking habits were less likely to have an open bite, compared with those who were performing current non-nutritive sucking habits (OR=0.07, OR=0.03-0.16). But children who had no current non-nutritive sucking habits were more likely to have a total malocclusion score of >0 than those who had current sucking habits (OR=3.0, OR=1.3-6.7).

Table 6. Open bite regressed on swallowing, speech problem (adjusted for age, gender, parental education and sucking habits).

Malocclusion	Normal swallowing % (n)	Thrust swallowing % (n)	Adjusted Model OR (95% CI)	No speech problem % (n)	Speech problem % (n)	Adjusted model OR (95% CI)
Open bite	13.4 (31)	72.7 (16) ***	20.3 (7.1-58.6)	14.5 (34)	68.4 (13) **	16.6 (5.5-49.6)

***=p=0.000, **=p<0.01; OR=Odds Ratio; CI= Confidence interval.

It was shown in Table 6 that children who had an open bite were more likely to thrust while swallowing and to have speech problems than their counterparts who did not have an open bite (OR=20.3; CI=7.1-58.6 and OR=16.6; CI=5.5-49.6, respectively) (p=0.000 and p<0.01, respectively).

Discussion
Socio-demographic characteristics of the participants, breastfeeding, and bottle-feeding practices
A cross-sectional survey was used to collect data from a sample of 3-5-year-old pre-schoolchildren (and their parents), from two districts of the Dar es Salaam region in Tanzania. At this age, most of the children would be having fully erupted primary dentition (Proffit and Fields, 2000). Regarding the parents' education, few parents (14.2%) in the present study had an education of above primary school level. One of the importance of enquiring about the parents' level of education is that it could reflect on the mothers' breastfeeding practices (Heck et al., 2006.; Tang et al., 2019). Hence, considering the parents' breastfeeding practices, in this study the majority (82.5%) of the mothers reported breastfeeding their children for less than two years.

In one Chinese study, the rate of exclusive breastfeeding practice was higher since the parents involved in the study were highly educated (Chen et al., 2015), but it was lower in a lesser educated group of participants in another study among rural Chinese residents (Qu et al., 2015). This implies that the rate of exclusive breast feeding may improve with advancement of the parents' education level. Furthermore, a substantial proportion (64.8%) of parents in the present study reported to have used a bottle-feeding method to feed their infants. Chen et al., (2015) documented that a shorter duration or lack of breastfeeding, may be associated with a longer duration of bottle-feeding.

Thus, past studies have recommended interventions to promote breastfeeding to increase its duration (Marks et al., 2018). This encourages parents to prolong breastfeeding and shorten bottle-feeding duration as much as possible (Orengul et al., 2018). The recommendations are essential for children's correct growth and development.

Malocclusion is related to feeding modalities and duration.
Angle's Class II or III was currently recorded in a significant proportion of bottle-fed children compared to breastfed children (12.2% versus 3.4%, respectively). This finding is comparable to that reported in an earlier study, where bottle-fed children were found to have a high risk of developing a nonmesial step occlusion (Chen et al., 2015). Breastfeeding was further reported to be protective against developing skeletal Class II and distoclusion in children (Abate et al., 2020).

Moreover, breastfeeding has been considered a factor for proper oro-facial development by promoting muscle exercise, which stimulates oro-facial structures (Ling et al., 2018). On the other hand, bottle-feeding practices have been reported to have lesser muscular activities (Cotrim et al., 2002) to promote harmonious orofacial growth. Regarding breastfeeding duration, as it relates to Angle's Class II or III malocclusion, this study found an altered molar relationship

in most children who were breastfed for a lesser duration (below two years) compared with those who were breastfed for a longer duration (2 years and above).

The observation supports what was concluded in a systematic review by Boronat-Catalá et al. (2017), who indicated that breastfeeding for longer duration decreases the risk of being found with Class II malocclusion. In addition, Sánchez-Molins et al. (2010) indicated that breastfed children are likely to have a more correct sagittal mandibular relationship with maxilla and the cranial base. As regards a transverse jaw relationship, scissors bite was currently found in most of those who were breastfed compared with those who were bottle-fed (23.6% versus 14.0%, respectively).

Contrary to this finding, previous workers documented that artificial teat (as those used to bottle-feed) may cause malalignment of teeth by restricting transverse growth of the palate (Viggiano et al., 2004; Peres et al., 2007). This is because the teats usually have a specific shape and rigidity, which is different from the human breast tissue (Peres et al., 2007). Generally, a combined presence of various malocclusion was higher among children who were breastfed for less than 2 years, compared with those who were breastfed for a longer duration (48.5% versus 27.3%, respectively). This finding supports what was reported by previous studies, that breastfeeding determines proper craniofacial development, which may counteract occlusal deviations (Sánchez-Molins et al., 2010).

Regression analysis of the relationship between malocclusion and feeding methods

In a regression analysis between presence of malocclusion and the feeding methods, it was presently found that children who were breastfed were less likely to be found with Angle's Class II or III malocclusion, compared with those who were bottle-fed. The finding is in concordance with earlier reports which found a greater distocclusion among children who were breastfed for a shorter duration (Feldens et al., 2016), and more mesial occlusion among bottlefed children (Wójcik et al., 2011). Other reports found longer breastfeeding duration associated with recording less Class II incisor or molar relationship (Boronat-Catalá et al., 2017; Sum et al., 2015, respectively).

Besides, the regression analysis in this study showed that children who were breastfed for less than two years were about thrice as likely to have various malocclusion than their counterparts (who were breastfed for two years or greater). Suggestions were made by Labbok and Hendershot (1987) that increased breastfeeding duration is associated with a drop in the proportion of malocclusion in children. However, the current study showed that breastfed children were more likely to be seen with scissors bites than bottle-fed children. In contrast to this finding, a study by Moimaz et al. (2014) showed a higher prevalence of transverse malocclusion among bottle-fed children.

Relationship between malocclusion and past/present non-nutritive sucking habits

The present research found an open bite in a more significant number of children who had a history of non-nutritive sucking habits, compared with those who never had the habits. Similarly, open bite was currently found in most children with active non-nutritive-sucking habits, compared with those who did not have the habits. The findings conform to that reported in a study of Chen et al. (2015), who found digit sucking habit to be associated with anterior open bite. The mechanism through which an open bite occurs in people with non-nutritive sucking habits has been explained earlier (Bishara et al., 2006; Dawood, 2004; Fukuta et al., 1996).

The explanation includes that thumb/pacifier pressure prevents the downward maxillary base growth and delays the eruption of anterior teeth while allowing the posterior teeth to erupt. This causes an overeruption of posterior teeth and the formation of an anterior open bite (Chen et al., 2015). Also, this study found a more significant percentage (65.9%) of various malocclusion in children who ever performed non-nutritive sucking habits, compared with a

lesser percentage (38.6%) of various malocclusion in children who never had the habits. This finding is in line with the findings of former researchers who reported an association between the presence of malocclusion in children and non-nutritive sucking habits. (Capsi Pires et al., 2012; Peres et al., 2007).

Regression analysis of the relationship between sucking habits, open bite and other malocclusion

In the present regressing analysis, it was shown that an open bite was less likely to be found in children who never performed non-nutritive sucking habits, compared with those who ever performed the habits. Also, children who did not have active non-nutritive sucking habits were less likely to have an open bite, compared with those who were actively performing the habits. The findings agree with those of Ling et al. (2018) and Belitz et al. (2022), who found the presence of non-nutritive sucking habits to be associated with a higher prevalence of anterior open bite.

In this study reported overall presence of malocclusion (other malocclusion than an open bite) in a higher proportion of children who did not have active sucking habits, compared to those who had active sucking habits. This could be explained by the fact that some of those who were actively performing the habits might have just recently started to perform the habits. Hence, it could have been too early for them to present with some other dental-alveolar alteration/s. On the contrary, other past studies (Montaldo et al., 2011; Viggiano et al., 2004; Warren & Bishara, 2002) reported differently, where they reported that pacifier- and digit-sucking are associated with the occurrence of various malocclusion in children.

Relationship between malocclusion (open bite), swallowing pattern and speech problem.

Because of having an open bite, the current study revealed an association between presence of the condition (open bite) and observing swallowing by thrusting and speech problems among the participants (children). Specifically, children who had an open bite were many times more likely to thrust while swallowing and to have speech problems than their counterparts who did not have the condition. This finding agrees with what was earlier reported, where atypical swallowing was found to have a significant relationship with the presence of anterior open bite (Sahad et al., 2008).

Moreover, a study by Amr-Rey et al. (2022) found a significant association between an anterior open bite and an alteration of the fricative phonemes (s,ch,z) and the affricate (ch). The study further explained that the alteration could be due to a defective air outlet since the anterior teeth do not occlude. Another explanation for the presence of swallowing and speech problems among the present participants is that, since most of the children were breastfed for a shorter duration, they might have been subjected to early weaning. A previous study explained the possibility of early weaning to cause negative consequences such as swallowing, breathing, speaking and malocclusion development (Neiva et al., 2003). Therefore, the appropriate children's feeding modalities should be encouraged and supported.

Study limitations: Few parents might have been unable to provide accurate answers, causing a recall bias. Additionally, this was a cross- sectional study, where it is possible only to establish associations between the predictors and the outcomes, but no causal relations could be determined. Issues like effects of heredity and other detrimental habits as aetiological factors for malocclusion, were beyond the reach of this study.

Conclusion and recommendations

Most of the children who were breastfed for a shorter duration and children who had non-nutritive sucking habits were found with various malocclusion, compared with those who were breastfed for a longer duration and those who had no non-nutritive sucking habits. Exclusive breastfeeding for up to 6

months and continuing breastfeeding practice for possibly up to 2 years of age is recommended due to its nutritional, immunological, and stomato-gnathic system developmental benefits. It is also important to develop public health programs to encourage good behaviours related to oral health and to discourage prolonged children's deleterious habits.

Competing interests

Acknowledgements

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Metastatic patterns and hormone receptor status among breast cancer patients in Tanzania

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Abstract

Introduction: Metastatic breast cancer is a common presentation in Tanzania. Estrogen-receptor (ER)-positive tumors are known to metastasize to the bones and require hormonal treatment as first-line therapy. Challenges with accessing immunohistochemistry services can delay information on breast cancer subtypes, further delaying treatment with effective hormonal therapy.

Objectives: This study aimed to assess the pattern of distribution of metastatic lesions in patients with metastatic breast cancer and evaluate its association with their hormone and HER-2 status, which could help provide recommendations on the use of front-line hormone therapy in areas where access to immunohistochemistry is a challenge.

Methods: A retrospective study covering histologically confirmed breast cancer patients in 2020 with metastatic lesions and complete medical records at Ocean Road Cancer Institute. Clinical information on the number, state and sites of metastasis, presence of symptoms and treatment received, and pathological variables, including histology, ER, PR and HER-2 status, were documented.

Results: Forty-nine (96.1%) of 51 patients analysed were female, with a mean age of 49.5 years. 47% presented with up-front metastatic disease. Lung was the most common metastatic site (76.5%) followed by bone/spine (53%). About half the patients had multiple sites involved. ER-positive tumors accounted for 47%, PR positive for 31% and HER-2 positive 39.2%. ER-positive tumors were more likely to present as a recurrence than up-front metastasis. ER-positive tumors were significantly more likely to be associated with bone and spine metastasis (59%) compared to ER-negative tumors (29%)

Conclusion: The clinical and pathological features of MBC in Tanzanian women are similar in many ways to those in other African regions. However, the ER positivity rate is lower. This study found a significant association between ER-positive tumours and skeletal metastasis, which has implications for the up-front treatment of these patients, especially where access to immunohistochemistry can be a challenge.

Keywords: Breast cancer, metastasis, subtypes, hormone status, HER-2

Introduction

Breast cancer (BC) is the most frequently diagnosed cancer globally, affecting 2.3 million women and causing 685,000 deaths in 2020. It is also the world's most prevalent cancer, with 7.8 million women alive at the end of 2020 who were diagnosed with cancer in the past five years (World Health Organization, 2021). In Tanzania, breast cancer (BC) is the second most common cancer in women, and the number of new cases of BC diagnosed is expected to increase by 82% by the year 2030 (Ministry of Health, Community Development, Gender, Elderly and Children, 2017). According to Globocan estimates, BC accounted for 9.9% of cancer cases and 7.3% of cancer deaths in 2020 (Globocan, 2020).

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A large proportion of women in Tanzania present with advanced (stage 3 and 4) disease, with a significant number having metastatic breast cancer (MBC) on presentation, i.e. Denovo MBC (dnMBC) or developing the metastatic disease during treatment and follow-up. A meta-analysis of studies done in sub–Saharan Africa shows that between 4% to 70% of patients present with metastatic disease at first presentation. A single-centre study done in north-western Tanzania in 2012 demonstrated that 21.4% of women presented with metastatic disease at first presentation., (Jedy-alba et al., 2016; Nabawanuka et al., 2013; Mabula et al., 2012) Information on the clinical characteristics of women presenting with MBC is scarce, and there has been little documentation of the relationship between the hormonal and HER-2 status of these women with the distribution of metastatic sites.

Metastatic breast cancer (MBC) is defined as a tumor spreading beyond the confines of the breast, chest wall and the ipsilateral regional lymph nodes. Typically, breast tumors spread to the bones, lungs, liver or brain, with bones being the most common site of metastatic site recurrence and the first site of metastasis in the majority of patients. The hormone receptor status of MBC is strongly related to the metastatic pattern. Hormone-receptor-positive (estrogen receptor [ER] and progesterone receptor [PR]) tumors are more likely to spread to bones as their primary site of metastases and have better survival outcomes; whereas hormone receptor-negative or human epidermal growth factor receptor 2 (HER2 - neu) positive tumors tend to develop as

Materials and methods

A retrospective study was conducted at Ocean Road Cancer Institute (ORCI), Tanzania's National Cancer Referral Centre which provides oncology services to patients from around the country. At ORCI patients with breast cancer are treated with chemotherapy and radiotherapy after referral from other treatment centres. Nearly two-thirds of patients present with advanced breast cancer, some of whom are found with

visceral metastasis (Pareek et al, 2019; Hou et al, 2021; Tao et al, 2016).

Current recommendations for treating metastatic disease involve the use of first-line hormonal therapy for ER and PR-positive tumors. Hormonal therapy is effective and much better tolerated than chemotherapy, making it a treatment of choice for patients in whom the quality of life is of paramount importance (Kumar et al., 2024). Testing the primary tumour site and the site of metastasis for ER and PR positivity is required but is often a challenge in Tanzania, where immunohistochemistry (IHC) services used to perform these tests are only available in a few large national hospitals, resulting in a long waiting time before patients begin treatment. Sometimes oncologists may begin treating such women with conventional chemotherapy, which is a waste of scarce resources and results in unnecessary side effects. To avoid this, studies have recommended the use of empirical hormonal therapy in patients presenting with clinical features suggestive of hormone-positive disease (Nabawanuka et al., 2013).

Therefore, this study aimed to assess the distribution pattern of metastatic lesions in patients with MBC and evaluate its association with their hormone and HER-2 status. The results of this study may help provide recommendations on the use of front-line hormone therapy in areas where access to immunohistochemistry is a challenge.

metastatic disease at diagnosis, (dnMBC), while others present with recurrence after initial treatment and are found to have developed distant metastasis upon work-up. This study included patients presenting with histologically confirmed BC who have metastatic lesions (confirmed by imaging and/or biopsy) whether newly diagnosed or on follow-up, in the year 2020. Patients who had unconfirmed histology or missing data were excluded. Medical records of breast cancer patients treated in 2020 were

searched to identify patients diagnosed with metastatic disease, including both dnMBC patients and those who developed metastatic lesions as a recurrence.

A data abstraction form was used to document information on sociodemographic, clinical and pathological variables of interest; these included age, sex, education and marital status, age at diagnosis of BC, state of MBC- whether denovo or recurrent, and time between diagnosis of BC and development of metastasis if the initial diagnosis was not MBC. Pathological variables included histopathology and ER, PR and HER-2 status. Number and sites of metastasis, presence of symptoms, and treatment given was documented. Sixty-two records of patients that fit the inclusion criteria were retrieved. After further evaluation, 11 records were excluded:

- o 9 did not have complete information on hormonal status.

- o 1 had significant missing data on several variables.
- o 1 had only lymphnode metastasis and not distant metastasis.
- o Eventually 51 patients' records were entered into the analysis.

Data were analyzed using SPSS Version 23 by summarizing demographic and clinical characteristics, distribution, and frequency of metastatic lesions, and exploring the relationship between ER, PR and HER-2 status and distribution of metastatic sites (skeletal, lung or liver) using chi-squared test. We hypothesized that women with ER positive tumors would have lower proportions of dnMBC compared to ER negative tumors, and that the distribution of metastatic sites would be significantly different, with ER positive tumors presenting more with metastasis to the bones and spine, and ER negative and HER-2 positive tumors with greater visceral metastasis. Permission to conduct this study was obtained from ORCIs ethical review committee.

Results

Of 51 patients whose results were analysed, 49 (96.1%) were female, and two were male. The mean age of patients was 49.5 years (range 26-72 years). For patients who presented with MBC as a recurrence, the median time from diagnosis to development of metastatic disease was 9 months, with a mean time of 16.23 months (SD 24.3, range 1 to 116 months).

Table 1 summarizes the clinical and pathological characteristics. 24 (47%) presented with dnMBC, 26 (51%) with recurrent disease. Lung was the most common metastatic site (76.5%) followed by bone/spine (53%). Nearly half of the patients had more than one metastatic site. The most common documented symptom was dyspnea, with Chest X-rays revealing metastatic lesions in 32 (63%) patients. The remaining 7 patients were diagnosed with lung metastasis through CT scans. Infiltrating ductal carcinoma (IDC) was the most reported histology. 24 (47.1%) of patients were ER positive, 16 (31.4%) were PR positive and 20 (39.2%) were HER-2 positive.

Table 1: Summary of clinical and pathological characteristics

Characteristic		Frequency	Percentage
State of MBC	Denovo	24	47.1
	Recurrence	26	51.0
	Missing	1	1.9
Metastatic sites			
	Bone/spine	27	52.9
	Lung	39	76.5
	Liver	10	19.6
	Brain	11	21.6
No. of metastatic sites			

	1	27	52.9
	2	18	35.3
	3	4	7.8
	>3	2	4.0
Presence of significant symptoms			
	Cough	6	11.8
	Pain	20	39.2
	Dyspnea	29	56.9
Chest Xray findings			
	Pulmonary Metastasis	32	62.7
	Pleural Effusion	15	29.4
Histology			
	IDC	42	82.4
	BC-NST	4	7.8
	Clear Cell	1	2.0
	Missing	4	7.8
Hormonal Status			
	ER Positive	24	47.1
	ER Negative	27	52.9
	PR Positive	16	31.4
	PR Negative	35	68.6
HER-2 Status			
	HER-2 Positive	20	39.2
	HER-2 Negative	29	56.9
	Missing	2	3.9

*IDC = Infiltrating Ductal Carcinoma
*BC-NST = Breast Cancer of No Special Type

A summary of treatment received is presented in Table 2. Information on surgery was available for 47 patients; 41% of these had no surgery done. Modified radical mastectomy (MRM) was the most common surgical procedure. 39 (76.5%) of patients received combination chemotherapy, while only 14 (27.5%) received hormonal therapy. Bisphosphonates (in all cases Zoledronic Acid) was given to 33% of the population, and 86% received analgesics.

Table 2: Summary of treatment received.

Treatment type		Frequency	Percentage
Surgery			
	Not done	21	41.2
	MRM	22	43.1
	Simple Mastectomy	3	5.9
	Lumpectomy	1	2.0
	Missing	4	7.8
Treatment Received			
	Combination chemotherapy	39	76.5
	Hormonal Treatment	14	27.5
	Trastuzamab	3	5.9
	Bisphosphanates	17	33.3
	Analgesics	44	86.3

Table 3 summarizes the bivariate analysis of hormone and HER-2 status against metastatic status. The analysis shows a statistically significant distribution of ER status with state of MBC at presentation, with significantly more patients with ER

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positive tumors presenting with metastatic disease as a recurrence rather than denovo (P value 0.049). PR status and HER-2 status were not statistically associated with the state of MBC at presentation.

Table 3: Bivariate analysis of Hormone and HER-2 status with status of MBC at presentation

Characteristic	Status of MBC at presentation		P-value
	Denovo MBC	**Recurrence**	
ER status			
Positive	9 (35%)	17 (65%)	**0.049**
Negative	15 (62.5%)	9 (37.5%)	
PR status			
Positive	7 (43.8%)	9 (56.2%)	0.680
Negative	17 (50%)	17 (50%)	
HER-2 status			
Positive	10 (50%)	10 (50%)	1.000
Negative	14 (50%)	14 (50%)	

Table 4 summarizes the bivariate analysis of hormone and HER-2 status against distribution of metastatic sites. From this analysis, ER positive tumors are significantly more likely to be associated with bone and spine metastasis (59%) compared to ER negative tumors (29%), P value 0.031. No other significant association was found between ER, PR and HER-2 status and site of metastasis.

Table 4: Summary of bivariate analysis of hormone/HER-2 status Vs metastatic site

Characteristic	Metastatic site							
	Bone/ Spine		**Lung**		**Liver**		**Brain**	
	N (%)	P Value	N (%)	P Value	N (%)	P Value	N (%)	P Value
ER status								
Positive	16 (59)		19 (70)		5 (19)		5 (19)	
Negative	7 (29)	**0.031**	20 (83)	0.276	5 (21)	0.835	6 (25)	0.574
PR status								
Positive	9 (56)		11(69)		4 (25)		4 (25)	
Negative	14 (40)	0.279	28 (80)	0.379	6 (17)	0.512	7 (20)	0.687
HER-2 status								
Positive	8 (40)		16 (80)		4 (20)		4 (20)	
Negative	13 (45)	0.737	23 (79)	0.953	5 (17)	0.806	7 (24)	0.733

*ER = Estrogen Receptor
*PR = Progesterone Receptor
*HER-2 = Human Epidermal Growth Factor 2 Receptor

Discussion

The mean age of patients at diagnosis in this study was 48.1 years. This is consistent with a study of breast tissue samples analysed at Muhimbili National Hospital in Dar es Salaam in 2013 where the mean age was 48.3 years (Mwakigonja et al, 2017). Although in the West, breast cancer is typically a disease of older women, younger ages at presentation of MBC have been documented in several non-white populations such as in India (47 years) and Uganda (45 years) (Pareek et al, 2019; Nabawanuka et al., 2013).

In this study almost half the patients presented with dnMBC. Late stage at diagnosis is a common occurrence in Sub-Saharan African countries; a systematic review by Jedy-Egba et al documented late

stage presentation at 74.7% (range 30.3-100%) (Jedy-agba et al. 2016). This is in contrast with high income countries where most cases of MBC arise as a recurrence of a previously treated BC (Daily et al., 2021). The distribution of metastatic sites also varies across studies; in our study lung metastasis was the most common (76.5%), followed by bone/spine (53%), with dyspneoa being the predominant symptom, whereas many studies in both low and high-income countries have found spine and bone metastasis to be the most prevalent (Bartmann et al., 2017; Carty et al,1995; Ekpe et al, 2019).

Observed differences could be due to the routine use of scintigraphy/bone scan for MBC patients in high resource settings which would allow early identification of bone metastasis, while at our centre due to cost issues scintigraphy is usually requested only when a physician suspects bone metastasis. On the other hand, chest x-rays are easily available and affordable and routinely used for staging patients, allowing early diagnosis of pulmonary metastasis. Around half of the patients in our study presented with more than one metastatic site. Multiple site involvement is common in MBC. A study in India showed metastasis involving a single organ was present in 188 (50.1%), two organs in 92 (24.5%), and more than two organs in 95 (25.4%) patients, with the most common site of metastasis being visceral metastasis (219 [58.4%] lung, liver, and both [lung plus liver] in 117 [31.2%], 53 [14.13%], and 49 [13.1%], respectively), followed by bone-only metastasis in 100 (26.7%) (Gogia et al, 2019).

In our study, ER positive tumors accounted for 47.1%, There are varying results for hormone receptor status across studies; Sayed et al showed that breast cancer in Kenya had comparable receptor status positivity (72%) to that in the West (Sayed et al., 2014); while more recent Kenyan and Indian studies documented this at 70% and 62% respectively (Gogia et al., 2019; Nabawanuka et al., 2013). It is known that immunohistochemistry (IHC) testing for receptors in breast cancer can be affected by many factors including optimal fixation and type of antibody used (Gown, 2008),

however the results may also be a true reflection of receptor positivity in the population and warrant further study. Similarly, 39.2% of this population were HER-2 positive, which is significantly higher than patients in the Kenyan study (19%) but like the Indian study.

Bivariate analysis showed a positive association of ER status with recurrence as compared to ER negative tumours, meaning that patients with ER positive tumours are more likely to present as local disease and then develop metastasis during follow up. There was a statistically significant association between ER positivity and metastasis to the bones and spine, as compared to metastasis to the lung, liver, or brain.

These findings have been discussed previously and shown to be true in many studies, as ER-positive tumors are considered less aggressive than ER- negative tumors (Nabawanuka et al., 2013; Pareek et al, 2019; Hou et al., 2021; Lin et al., 2021). Hence patients with ER positive tumors will typically present with bone metastasis which responds well to palliative treatment. These findings have potential implications for treatment guidelines; when patients present with denovo metastatic disease involving the bones, there may be a role for empirical hormone therapy in previously untreated patients where facilities do not exist for performing hormone receptor tests as is the case in many Sub-Saharan African countries (Vanderpuye, Olopade, & Huo, 2017). A recent study in Northern Tanzania documented that 91% of reviewed cases did not undergo hormone receptor testing, which formed the most frequent reason for failure to treat according to guidelines (Sood et al., 2021)

Our study failed to show association between PR and HER-2 status and MBC state at presentation. It also did not find a statistically significant association between PR and HER-2 status and distribution of metastatic site. These findings would need corroboration with larger studies.

Limitations

This was a retrospective study which depended on extraction of medical records. In some cases, information was unavailable or poorly documented which led to the exclusion of the patient or missing data.

Conclusion

The clinical and pathological features of MBC in Tanzanian women are similar in many ways to those in other regions, with a mean age of 48 years, and nearly half the patients presenting with denovo disease. The ER positivity of tumors in these patients is however lower than that found elsewhere. This study found a significant association between ER negative tumors and denovo presentation, as well as ER positive tumors and skeletal metastasis, which has implications for treatment. Larger cross-sectional and prospective studies would help to acquire better information on the presentation of these patients, and the use of bone scintigraphy to work up all patients presenting with MBC would help to capture asymptomatic bone disease before it involves other organs.

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Dietary diversity and Anthropometric status of students at universities in Dodoma and Morogoro Regions, Tanzania

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Abstract

Background: Young adulthood is a transitional period that provides an opportunity to influence immediate and future eating behavior and good nutritional status. As diets evolve during young adulthood due to changes in circumstances and the introduction of new influences, young adults are a significant population group that influences future eating behaviours and prevents the development of NCDS. There is scanty information on the relationship between dietary diversity and the nutritional status of university students in Tanzania. This study aimed to find the synergy between university students' anthropometric status and dietary diversity in Morogoro and Dodoma regions of Tanzania.

Methods: This cross-sectional study involved 247 University students in Morogoro and Dodoma regions (130 from Mzumbe University and 117 from Saint John's University) respectively. The two Universities were purposively selected from each region. Data on Dietary diversity was collected using food groups from DDS to obtain the dietary score of each student. Anthropometric measures such as weight, height and waist circumference were done to obtain the anthropometric status of the University students.

Results: The descriptive cross-sectional study involved 247 University students. In comparative chi-square analysis, the association was found among different socio-demographic characteristics of the University students. The p-value < 0.05 was used to determine the association among the variables.

Conclusion: In conclusion, university students are a vulnerable group in developing obesity/overweight due to the transitional stage. Being overweight and obese was associated with being female, increased age and being married. High dietary diversity was also linked with abdominal obesity. Factors that can help describe and understand the anthropometric status of university students have also been identified. These include years of study, religion, and university location. Therefore, efforts to adopt good lifestyle behaviours should be sensitized amongst this sub-population to reduce the risk of developing chronic diseases in the long run.

Keywords: dietary diversity, anthropometric status, university students

Introduction

Nearly a third of the world's population is affected by the incidence of overweight and obesity, which has doubled since 1980 whereby it is becoming more of a public health concern, especially among university students in developing nations(Quiliche Castañeda *et al.*, 2021). According to (2018), university represents a fundamental transition into adulthood whereby concerns about lifestyle changes, such as selecting poor-quality diets, have potential implications for body weight and long-term health.

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The overall nutritional status of an individual can be assessed by anthropometry, biochemical tests and evaluation of dietary intake which establishes normal status or risk of malnutrition (Pimentel *et al*., 2019). The fundamental elements of anthropometry are height, weight, body circumference (waist, hip, and head), and skinfold thickness (Kayode & Oshineye, 2022). Malnutrition is characterized by the simultaneous presence of undernutrition, overweight, and obesity linked to diet within populations (Bhati *et al.*, 2022).

The Food and Agriculture organization defines dietary diversity as a measure of the number of individual foods or food groups consumed in a given period of time (Ansari *et a*l., 2020). Food diversity has long been recognized as a key element of high-quality diet, based on the principle that no single food can provide the right amount of nutrients necessary to maintain optimal health (Verger *et al.*, 2021).

Unhealthy dietary habits are common among university students and are associated with increased incidence of lifestyle and chronic illnesses. Studies have reported poor dietary practices among university students for example Tok *et al*., (2018) reported consumption of less than 3 meals per day among (33.3%) of university students. Globally, the literature suggests that during the transitional period from secondary level to graduate level, students often engage in unhealthy dietary habits and poor nutritional intake (Kabir *et al.*, 2018). For this reason, University years are also a potential period of intervention.

The central cause of overweight and obesity is imbalance between energy consumed and calories expended, and reports show a global increase in intake of energy dense-foods that are high in fat (Munyogwa & Mtumwa, 2018). The World Health Organization has linked overweight and obesity to more death worldwide whereby more people are obese in parts of sub-Saharan Africa (WHO, 2020).

Tanzania is one of the sub-Saharan African (SSA) countries facing both undernutrition and obesity problems, where limited dietary diversity is a major challenge (Minja *et al.*, 2021). The recent national nutrition survey reported that the prevalence of overweight or obesity among adult females has nearly tripled from 11.3% in 1991 to 31.7% in 2018 (TNNS, 2018). They are characterized by abnormal eating behaviors, a preoccupation with food and an obsession with weight and body shape.

Studies in Tanzania have shown the association of obesity and dietary diversity in other populations such as women, children, and pastoralist societies. Although there is extensive literature on the association between dietary diversity and anthropometric status of university students in developed countries, there appears to be a scarcity of research on university students in Tanzania.

Due to the rapid global nutrition shift and growing number of people who are directly affected by the double burden of malnutrition and their exposure to various forms of malnutrition throughout their lives (Wells *et al.*, 2020) it is important to know what factors are associated with these risks. The need to focus on this subpopulation is due to the healthy risky behaviors that start in young people.

Considering the scant information this study aims to understand the synergy between dietary diversity and anthropometric status in university students in Tanzanian regions that have contrasting characteristics.

Findings from this study will therefore be important to public health experts in Tanzania and help to work towards the Sustainable Development Goal-3 (SDG-3), which aims to ensure healthy lives and promote wellbeing for all at all ages (United Nations, 2015).

Methodology
Study design.
The study used a cross sectional research design, which .is appropriate for descriptive research and was chosen because of the nature of the investigation, which included collecting and analyzing data from a sample of a large population at a specific point in time.

Description of the study area
The study was conducted in universities located in Morogoro and Dodoma Regions. Morogoro region is in the eastern zone of Tanzania. With 29 wards and 260 square miles of land, Morogoro Municipality, one of Morogoro Region's nine districts, serves as the region's capital which represents 0.74% of the region's total land area. (Pori *et al.*, 2022). The recently estimated population of Morogoro urban is approximate to 440109 with the growth rate of 3.85%. In the case of Morogoro Municipal, linear and nucleated settlements have been the dominant form of urban development, with a few cases of scattered settlements, and population growth go hand in hand with urban

expansion and human development, which may take numerous forms. (Sumari *et al.*, 2020). Morogoro experiences bimodal rainfall seasons. Heavy rain seasons are locally called Masika dominating late March to early May and the light rain seasons are locally called Vuli normally between November to December (Pori *et al.*,2022).

Dodoma is the region found in the central part of Tanzania mainland. With 41.311 km2, it has seven districts: Dodoma urban, Chamwino, Bahi, Kondoa, Kongwa, Mpwapwa, and Chemba. It is the 12th largest area in Tanzania. Movement of people to the region as it became the host of the capital city has resulted in increasing population growth, within the Dodoma region, including its metropolitan environment, having 3,085,625 people in 2022 (NBS, 2022). Dodoma is one of the semi-arid regions with annual rainfall that ranges from 550 to 660 millimetres and a lengthy dry season. The region receives between 550 and 3690 mm of rainfall annually (World Bank, 2022). There is just one rainy season there, which is a crucial climate component for agricultural activity.

Description of the study population
The cross-sectional study included full-time registered students who gave consent in the selected universities in Morogoro and Dodoma region which were Mzumbe University and Saint Johns' University respectively. Students who were on diet or weight management programs, those pregnant and those having physical limitations were excluded from the study**.**

Sample size and sampling procedure.
Students were randomly selected into the sample to ensure fairness, males and females were given an equal opportunity to be included in the sample.
 Morogoro and Dodoma regions were purposively selected due to differences in climatic conditions, food systems, agro-ecological zones, and having a large population of university students.
Purposive sampling was also used to select one public university in Morogoro and one

private University in the Dodoma region (Mzumbe university and Saint John's university respectively).
The total number of university students who participated in the study was determined by using the formula by Kothari (2004) which is used to calculate sample size.

$$n = \frac{z^2 p\,(1-p)}{d^2}$$

whereby.
n = desired sample size
z = standard normal deviation, set at 1.96 corresponding to 95 % confidence interval
P = proportion in the intended population estimated to have a particular characteristic (0.192) among university students. Prevalence of obesity in community studies in urban Tanzania revealed obesity rate to be 19.2% (Pallangyo *et al.*, 2020).
q = (1-p) proportion of the population who are estimated to not have the characteristics (0.192) d = degree of accuracy desired (0.05) therefore

n = (1.96)2 ×0.192 (1-0.192)/0.05^2
n = 238
Allowance for attrition/non-response, which is 10% will be added,
Therefore 10% of 238=23.8
23.8 + 238 =262
The sample size is approximately 262 students. A total of 247 university students participated in this study. 130 students from Mzumbe University participated in the study 117 students from Saint John's participated in the study.

Data Collection
Pre-testing was carried out in one university in Morogoro region (Sokoine University of Agriculture) and another University in Dodoma (University of Dodoma) region after the completion of formal training of research assistants**.** Data was then collected by the help of research assistants at Mzumbe and Saint John's University in Morogoro and Dodoma regions respectively.

Information on socio-demographics
Age of university students, gender, degree type, year of study, marital status, religion, living arrangements, chronic disease situation, smoking status, primary source of nutritional information, total hours spent for sleeping, scholarship status were collected using pretested questionnaire with structured questions which was administered to the students by trained research assistants in the selected Universities in Morogoro and Dodoma regions (Mzumbe and Saint John's respectively).

Anthropometry Measurements
Weight, height, and waist circumference were measured to determine the anthropometric status of the students.
Weight was measured using a standard weighing scale (digital electronic SECA scale;(Model 8811021659, Germany) that was kept on a firm horizontal surface. The participant was measured without shoes and with light clothing by ensuring the removal of heavy-worn clothing such as coats and scarfs as well as personal items such as wallets, phones, and watches. Weight was then recorded to the nearest 0.1kg. The scale reading was always allowed to return to zero before the subject was asked to stand on it. Height was measured using a stadiometer (Model No PE-AIM-101-USA) and recorded to the nearest 0.1 cm. Participants were requested to stand upright without shoes on with their back kept against the wall and heels put together in a V-shape while looking forward.

The body mass index (BMI) was calculated by dividing weight (in kilograms) over their height (in meters square). Nutritional status was classified according to the WHO classification of Body mass index. Students were classified as underweight, normal, overweight and obese if they have a Body mass index of below **18.5 (underweight), 18.5-24.9 (normal weight), 25.0-29.9 (overweight)** and.**≥30.0 above (obese)** (Weir and Jan 2022).

The waist circumference (WC) was measured using a non-stretchable tape on the upper lateral border of the right ilium in the midaxillary line at the navel level without skin compression to the nearest 0.1 cm. The waist circumference was used to identify individuals with possible health risks based upon threshold values of **≥ 82 cm for women** and **≥ 91 cm for men** identified from adults in Sub Saharan Africa population (Tladi *et al.,* 2020).

Dietary Consumption.
Participants were required to recall food groups, number of meals per day during the past 7-days prior to survey. They were also asked on how they accessed their diets during different mealtimes.

Dietary Diversity
Individual dietary diversity was collected by using a dietary diversity score questionnaire. Participants were asked on whether or not certain food groups were consumed during the past 7-days prior to survey to assess their variety in diets on the food groups consumed. (Kolliesuah *et al.,* (2023) reported the 7-day reference period presents a better

understanding on nutrient adequacy which is a proxy measure of nutritional status.

The individual dietary diversity was adapted from United Nations' Food and Agriculture Organization (FAO, 2010) and modified to include foods present in Tanzanian setting.

To calculate the Dietary diversity score (DDS), reported food items were categorized into 16 food groups which are (i) cereals (ii) Vitamin A-rich vegetables and tubers (iii) Other roots and tubers (iv) Green leafy vegetables (v) Vitamin A-rich fruits (vi) Other vegetables and fruits (vii) Legumes (viii) Nuts and oil seeds (ix) Animal milk and milk products (x) Eggs (xi) Organ meats (xii) flesh meats (xiii) fish, sardines and other sea foods (xiv) Oil, fat, ghee and butter used for cooking (xv) Sugars, honey, sugary products, sweetened sodas (xvi) spices, condiments, beverages.

Consumption of each food group was transformed into binary variables (1=yes, 0=No) to indicate whether food items from a particular group was eaten or not. Total score was the sum scores of the sixteen food groups and the maximum score was 16.

The sixteen (16) food groups were then aggregated into nine (9) food groups adapted from (FAO,2010). Individual dietary diversity was determined by aggregating the sixteen (16) food groups into nine (9) food groups present in the Women's dietary diversity questionnaire. Women's dietary diversity questionnaire can be used to assess dietary diversity at individual level on individuals in other age/sex groups (FAO,2010). The food groups aggregated include (i) Starch staples (ii) Dark green leafy vegetables (iii) Other vitamin A rich fruits and vegetables (iv) Other fruits and Vegetables (v) Organ meats (vi) Meat and Fish (vii) Eggs (viii) Legumes, nuts and seeds (ix) Milk and Milk products. Cut off values were established by determining the distribution of the dietary diversity scores by measures of central tendencies (mean and median) of the participants. The points were then summed to generate a DDS for each participant. A dietary diversity scored <7 was regarded as inadequate dietary diversity and ≥ 7 was regarded as adequate dietary diversity.

Dietary habits
Participants were required to recall the number of meals consumed per day i.e. Breakfast Lunch and dinner and how often they consumed these meals during the past 7-days prior to the survey. They were also asked if they skipped meals (yes/no) and reasons for meal skipping.

Dietary access during various mealtimes
Participants were asked on how they access their diets throughout their day. The questionnaire included four options adapted for university settings (i) Purchasing cooked meals at university canteens (ii) Purchasing food out of university (iii) Self-cooking (iv) Group cooking.

Data Analysis
The data was entered, cleaned and analyzed using Statistical Package for Social Sciences (SPSS™) version 26 software. Descriptive statistical measures such as percentage and frequencies of variables were computed to summarize the data. Chi square (X^2) test at 5% level of significance was used to examine the relationship between dependent variables (Anthropometric status) and other independent variables such as socio-demographic factors.

Ethical Considerations
The study was approved by the National Institute for Medical Research (NIMR/HQ/R.8a/Vol.IX/4363) and Sokoine University of Agriculture (SUA/MHN/D/2019/0009). Permission to conduct the study was also sought from respective universities from the administration offices through the dean of students. Students were informed about the study and consent forms were given for signing. Confidentiality of the information was ensured where all participants were identified by numbers.

Results

Socio-demographic characteristics of University Students

The socio-demographic characteristics of the University students are presented in Table 2.1. A total of 247 university students participated in this study whereby about half 131(53%) were males and 116 (47%) were females. More than half females at Mzumbe University participated in the study 70 (53.8%) when compared to Saint John's 46 (39.3%). More than half of the males at Saint John's University participated in the study 71 (60.7%) when compared to Mzumbe University 60 (46.2%).

More than half of the participants 155 (62.8%) were between 20-24 years old. About half 137 (55%) of the participants in this study were on their second year of university. Most of the study participants were single 230 (93.1%). Majority 201 (81.4%) of the university students were Christians. There was a significant difference in gender, years of study, religion and place of residence between the University students in Mzumbe and Saint John's University.

Table 2.1: Demographic characteristics of study population (n=247)

Characteristics	Overall	Mzumbe University	St.John's University	P-Value
Sex				0.022*
Female	116 (47%)	70 (53.8%)	46 (39.3%)	
Male	131(53%)	60 (46.2%)	71 (60.7%)	
Age				0.221
20-24 Years	155 (62.8%)	85 (65.4%)	70 (59.8%)	
≥25 Years	92 (37.2%)	45 (34.6%)	47 (40.2%)	
Study Year				0.045*
Second Year	137 (55.5%)	65 (50%)	72 (61.5%)	
>Second Year	110 (44.5%)	65 (50%)	45 (38.5%)	
Marital Status				0.301
Single	230 (93.1%)	119 (91.5%)	111 (94.9%)	
Married	17 (6.9%)	11 (8.5%)	6 (5.1%)	
Religion				0.001*
Christian	201 (81.4%)	96 (73.8%)	105 (89.7%)	
Muslim	46 (18.6%)	34 (26.2%)	12 (10.3%)	
Presence of Chronic diseases				0.858
Yes	9 (3.6%)	5 (3.8%)	4 (3.4%)	
No	238 (96.4%)	125 (96.2%)	113 (96.6%)	
Sleeping hours				0.373
<8 hours	124 (50.2%)	69 (53.1%)	55 (47%)	
≥ 8 hours	123 (49.8%)	61 (46.9%)	62 (53%)	
Place of residence				0.000*
Off campus	192 (77.7%)	85 (65.4%)	107 (91.5%)	
In campus	55 (22.3%)	45 (34.6%)	10 (8.5%)	
Smoking status				0.079
Non-smoker	240 (97.2%)	124 (95.4%)	116 (99.1%)	
Smoker	7 (2.8%)	6 (4.6%)	1 (0.9%)	
Primary source of nutritional Information				0.893
Offline	83 (33.6%)	43 (33.1%)	40 (34.2%)	
Online	164 (66.4%)	87 (66.9%)	77 (65.8%)	
Scholarship status				0.006
No	124 (50.2%)	76 (58.5%)	48 (41%)	
Yes	123 (49.8%)	54 (41.5%)	69 (59%)	
Type of scholarship				0.087
Partial	25 (20.3%)	9 (16.7%)	16 (23.2%)	
Full	98 (79.7%)	45 (83.3%)	53 (76.8%)	

***Significant at P< 0.05**

Food access during various meal times

Majority 100 (79.9%) of the participants eat breakfast and purchase them at University Canteens. The proportion of students that purchase breakfast at university canteens in Mzumbe university is slightly higher 65 (50%) than Saint Johns' University 35 (29.9%). More than half 89 (72%) of the university students purchase their lunch out of the University premises. The proportion of students that purchase lunch out of the university premises

in Mzumbe university is slightly higher 48 (37%) than Saint John's University 41 (35%). A large proportion 91 (76%) of participants in this study cook their dinner. More than half 70 (59.8%) of Saint Johns' students cook their dinner compared to Mzumbe university students 21 (16.2%). There was a significant difference in ways of accessing food during all the mealtimes.

Dietary habits of University Students

The dietary habits of the University Students are as shown in Table 2.3. Majority 167 (67.6%) of the study participants ate two meals per day. The proportion of students who ate two meals per day was slightly higher 88 (67.7%) in Mzumbe university when compared to Saint John's University 79 (67.5%). Skipping of

meals due to being busy with studies was common 144 (58.3%) and was significantly higher in Mzumbe University 87 (66.9%) than Saint John's University 57 (48.7%). There was a significant difference in reasons for meal skipping in Mzumbe and Saint Johns' university.

Table 2.3 Dietary habits of University Students

VARIABLES	OVERALL	MZUMBE UNIVERSITY	ST JOHNS' UNIVERSITY	P-VALUE
Number of meals per day				
One meal	17 (6.9)	9(6.9)	8(6.8)	0.999
Two meals	167 (67.6)	88(67.7)	79(67.5)	
Three meals	63 (25.5)	33(25.4)	30(25.7)	
Meal Skipping				
No	63 (25.5)	33(25.4)	30(25.6)	0.963
Yes	184 (74.5)	97(74.6)	87(74.4)	
Reasons for meal skipping				
Busy with studies	144 (58.3)	87(66.9)	57(48.7)	0.001*
Financial constraints	20 (8.1)	4(3.1)	16(13.7)	
Less priority	12 (4.9)	3(2.3)	9(7.7)	
Not applicable	71 (28.7)	36(27.7)	35(29.9)	
Often take breakfast				
No	176 (71.3)	94(72.3)	82(70.1)	0.779
Yes	71 (28.7)	36(27.7)	35(29.9)	
Often take Lunch				
No	66 (26.7)	41(31.5)	25(21.4)	0.071
Yes	181(73.3)	89(68.5)	92(78.6)	
Often take dinner				
No	37(15)	24(18.5)	13(11.1)	0.106
Yes	210 (85)	106(81.5)	104(88.9)	

*Significant at   P<0.05

Association between Dietary diversity score and Anthropometric status

The association between dietary diversity score and Anthropometric status of university students are as shown in Table 2.4. The proportion of Mzumbe university students in consuming a diverse diet was slightly higher 79 (60.8%) than students in Saint John's University 75 (64.1%). The study revealed that more than half 119 (59.2%) of the Christian students had a diversified diet. There was a significant difference in Religion and waist circumferences in the dietary diversity of the university students.

Table 2.4 Association between Dietary Diversity Score and Anthropometric status

VARIABLES	Less than 7 food groups	At least 7 food groups	P-Value
Name of university			
Mzumbe university	51 (39.2)	79 (60.8)	
St. John's University	42 (35.9)	75 (64.1)	0.602
Sex of respondents			
Female	39 (33.6)	77 (66.4)	0.219
Male	54 (41.2)	77 (58.8)	
Age_categories			
20 to 24 years old	58 (37.4)	97 (62.6)	0.922
≥25 years old	35 (38)	57 (62)	
Marital status of respondents			
Single	88 (38.3)	142 (61.7)	0.467
Married	5 (29.4)	12 (70.6)	
Religion			
Muslim	11 (23.9)	35 (76.1)	0.033*
Christian	82 (40.8)	119 (59.2)	
Place of residence			
Off-campus	74 (38.5)	118 (61.5)	0.59
Within students' residence	19 (34.5)	36 (65.5)	
Scholarship Status			
No	43 (34.7)	81 (65.3)	0.333
Yes	50 (40.7)	73 (59.3)	
Scholarship Type			
Partial	54 (36.2)	95 (63.8)	0.573
Full	39 (39.8)	59 (60.2)	
Anthropometric profile			
Underweight (BMI < 18.5)	9 (50)	9 (50)	
Normal weight (18.5≤BMI<25)	65 (40.4)	96 (59.6)	
Overweight (25≤BMI<30)	15 (27.8)	39 (72.2)	
Obesity (BMI ≥ 30)	4 (28.6)	10 (71.4)	0.22
WAIST CIRCUMFERENCE			
Risk of morbidity (≥91 cm male ≥82cm female)	7 (21.9)	25 (78.1)	
None risk of morbidity (Normal fat distribution)	86 (40)	129 (60)	0.048*
Suffering from of chronic disease			
No	91 (38.2)	147 (61.8)	
Yes	2 (22.2)	7 (77.8)	0.33
Total number of hours spent for sleeping per night			
Less than 8 hours	49 (39.8)	74 (60.2)	
8 hours and above	44 (35.5)	80 (64.5)	0.48
Currently smoking status			
Non-smoker	89 (37.1)	151 (62.9)	
Ex-smoker/smoker	89 (37.1)	151 (62.9)	0.28
Source of nutrition information			
Offline (family, friends and others)	32 (38.6)	51 (61.4)	
Online (TV, internet, news)	61 (37.2)	103 (62.8)	
			0.835

Anthropometric status of university students

Body mass index (BMI) and Waist circumference (WC) were used to assess the anthropometric status of the University students. Body mass index was used to identify general obesity while waist circumference was used to identify central obesity.

Waist Circumference

The waist circumference of study respondents is as shown in Tables 2.5. The study revealed that a larger proportion 125 (95.4%) of male participants not in a risk of morbidity when compared to female participants 90 (77.6%). There was a significant difference on Sex, Age and Marital status.

Table 2.5 Socio- demographic characteristics and Waist Circumference

VARIABLES	Risk of morbidity (≥91 cm male ≥82cm female)	None risk of morbidity (Normal fat distribution)	P-VALUE
Name of university			
Mzumbe	18(13.8)	112(86.2)	0.707
St. John's	14 (12)	103(88)	
Sex			
Female	26 (22.4)	90 (77.6)	0.000*
Male	6(4.6)	125 (95.4)	
Age categories			
20 to 24 years old	11 (7.1)	144 (92.9)	0.001*
≥25 years old	21 (22.8)	71 (77.2)	
Years study			
Second year	18 (13.1)	119 (86.9)	0.924
>Second year	14 (12.7)	96 (87.3)	
Marital status			
Single	22 (9.6)	108 (90.4)	0.000*
Married	10 (58.8)	7 (41.2)	
Religion			
Muslim	7 (15.2)	39 (84.8)	0.613
Christian	25 (12.4)	176 (87.6)	
Place of residence			
Off campus	23 (12)	169 (88)	0.393
Within students' residence	9 (16.4)	46 (83.6)	
Presence of Chronic disease			
No	32 (13.4)	206 (86.6)	0.238
Yes	0	9 (100)	
Hours spent for sleeping			
Less than 8hours	18 (14.6)	105 (85.4)	0.434
More than 8hours	14 (11.3)	110 (88.7)	
Smoking status			
Non-smoker	31 (12.9)	109 (87.1)	0.915

Smoker	1 (14.3)	6 (85.7)		
Source of nutrition information				
Offline (family, friends and others)	15 (18.1)	68 (81.9)	0.088	
Online (TV, internet, news)	17 (10.4)	147 (89.6)		
Scholarship status				
No	19 (15.3)	105(84.7)	0.266	
Yes	13 (10.6)	110 (89.4)		
Type of scholarship				
Partial	21 (14.1)	128 (85.9)	0.511	
Full	11 (11.2)	87 (88.8)		

*Significant at P<0.05

Body Mass Index

The Body mass index of study respondents is as shown in Tables 2.6. This study shows that Saint Johns' University students had a slightly higher proportion 33 (28.2%) of overweight when compared to Mzumbe University students 21 (16.2%). The study revealed that the proportion of overweight and obesity 37 (31.9%) ;12 (10.3%) respectively in female university students was slightly higher when compared to male university students 17 (13%) for overweight and 2 (1.5%) for obesity.

Overweight in students from third year and above was slightly higher 31 (28.2%) when compared to students in the second year 23 (16.8%). This study also showed that Students who were enrolled in their second year had higher proportion 11 (8%) of obesity than students in higher years of enrolment 3 (2.7%). There was a significant difference on university type Sex, Age, year of study and marital status.

Table 2.6 Socio- demographic characteristics and Body Mass Index (BMI)

VARIABLES	Underweight (BMI < 18.5)	Normal weight (18.5≤BMI<25)	Overweight (25≤BMI<30)	Obesity (BMI ≥ 30)	P-VALUE
Nameof university					
Mzumbe	13 (10)	86 (66.2)	21 (16.2)	10 (7.7)	0.031*
St. John's	5 (4.3)	75 (64.1)	33 (28.2)	4 (3.4)	
Sex					
Female	4 (3.4)	63 (54.3)	37 (31.9)	12 (10.3)	0.000*
Male	14 (10.7)	98 (74.8)	17 (13)	2(1.5)	
Age categories					
20 to 24 years old	15 (9.7)	106 (68.4)	30 (19.4)	4 (2.6)	0.007
≥25 years old	3 (3.3)	55 (59.8)	24 (26.1)	10 (10.9)	
Years_study					
Second year	8 (5.8)	95(69.3)	23 (16.8)	11(8)	0.039*
>Second year	10(9.1)	66(60.0)	31 (28.2)	3 (2.7)	
Marital status					
Single	17 (7.4)	156 (67.8)	47 (20.4)	10 (4.3)	0.001*
Married	1 (5.9)	5(29.4)	7 (41.2)	4 (23.5)	
Religion					

Muslim	3 (6.5)	28 (60.9)	11(23.9)	4(8.7)	0.746
Christian	15 (7.5)	133(66.2)	43 (21.4)	10 (5)	
Place of residence					
Off campus	14 (7.3)	123(64.1)	46(24)	9 (4.7)	0.339
With in students' residence	4 (7.3)	38 (69.1)	8 (14.5)	5 (9.1)	
Presence of chronic diseases					
No	17 (7.1)	154(64.7)	53(22.3)	14 5.9	0.697
Yes	1 (11.1)	7 (77.8)	1 (11.1)	0	
Total number of hours spent for sleeping per night					
Less than 8hours	11 (8.9)	81(65.9)	23 (18.7)	8 (6.5)	0.501
More than 8hours	7 (5.6)	80 (64.5)	31(25)	6 (4.8)	
Smoking status					
Non-smoker	16 (6.7)	158(65.8)	52 (21.7)	14 (5.8)	0.134
Smoker	2 (28.6)	3 (42.9)	2(28.6)		
Source of nutrition information					
Offline (family, friends and others)	7 (8.4)	56 (67.5)	16 (19.3)	4 (4.8)	0.833
Online (TV, internet, news)	11 (6.7)	105 (64)	38(23.2)	10(6.1)	
Scholarship status					
No	5 (4)	82(66.1)	29 (23.4)	8 (6.5)	0.242
Yes	13(10.6)	79 (64.2)	25 (20.3)	6 (4.9)	
Type of Scholarship					
Partial	7 (4.7)	95 (63.8)	38 (25.5)	9(6)	0.115
Full	11 (11.2)	66 (67.3)	16 (16.3)	5 (5.1)	

*Significant at P   <0.05

Discussions
Dietary diversity and anthropometric status of university students.

This study reports the association between dietary diversity scores and characteristics of university students as well as their Anthropometric status. Generally, high levels of dietary diversity are frequently linked to better nutritional status, whereas low levels are strongly thought to contribute to inadequate nutrient intake.

In this study the religion of the university students was associated significantly with dietary diversity scores. Whereby Muslim students had a high dietary diversity (76.1%) when compared to Christian students. This means that the intake of a diverse diet may be attributed with religion in university students. The possible explanation could be the difference in the agro-ecological zones. However, this could perhaps be due to the fact that majority of respondents in this study were Christians. According to a study conducted in Ethiopia the odds of having inadequate dietary diversity were 70% lower among Muslim adolescents when compared to Christians due to difference in residence (Gonete et al., 2020). Furthermore, a study done in Tanzania suggested that dietary diversity can also be attributed by agriculture, agrobiodiversity, landscape

heteroginty personality and family traditions (Powell *et al.*,2017).

The findings of the current study showed that there was a significant difference between waist circumference and dietary diversity. According to this study high dietary diversity is linked with increased risk of central obesity in university students due to excessive consumption of selected food groups which are mostly-energy dense. Respondents that had low dietary diversity

Anthropometric status of university students.
Central Obesity among University students.
The study reported that risk of morbidity was associated with sex of the respondents. The finding shows that female university students were at a higher risk of developing central obesity compared to their male counterparts. The possible explanation for this could be due to high dietary diversity in the female students; selection of meals compared to their male counterparts. These findings are in line with the study done by (Mogeni & Ouma, 2022) who reported females embraced greater dietary diversity in their eating habits compared to males.

The possible variations in the obesity prevalence could be justified by the use of different cutoff values for waist circumference (Tekalegn *et al.*, 2022).

Moreover, the findings of this study corroborate with (Molla *et al.*, 2020)mthe odds of being centrally obese was 9.62 times higher among female study participants compared to their counterparts. Furthermore, Maila *et al.*, (2021) reported a study done in Verulam, South Africa that indicated 68.4% of women and 25% of men were at risk of central obesity.

The study also found that age was associated with risk of abdominal obesity, whereby participants aged twenty-five and above (≥25 years of age) where at a higher risk of morbidity compared to participants aged between 20-24 years. The possible

Overweight and Obesity among University students.

were at a low risk of developing central obesity. This study corroborates with similar study done in the southwest of China which showed adults with medium and high Dietary diversity score were at higher risk of central obesity (Zhang *et al.*, 2017). However, using waist circumference, a study of pastoralists in Tanzania revealed no connection between dietary diversification and central obesity for both male and female (Khamis *et al.*, 2021).

reasons are higher dietary diversity of individuals aged 20-24 when compared to individuals of ≥25 years of age. The findings of this study are in line with Molla *et al.*, (2020) that found an increase in age was statistically associated with central obesity. Tekalegn *et al.*, (2022) also revealed that the odds of central obesity tend to increase as age increases. Similarly, a study by (Munyogwa *et al.*, 2021) in Dodoma City reported respondents with an increased age were associated with development of abdominal obesity.

Furthermore, in this study married people were reported to have a risk of morbidity compared to Single people. This could be due to the difference in dietary diversity where married people have a higher dietary diversity which is believed to be linked with higher intake of energy dense foods. However, this could perhaps be due to the fact that majority of respondents in this study were single. The findings of this study go in line with a study done by (Ntimana & Choma, 2023) whereby Bivariate correlation analysis showed that married participants correlated positively and significantly with central obesity. Similarly, a study Bakir *et al.*, (2017) reported that the mean Body mass indexes and other anthropometric measurements such as Waist circumference were significantly higher in married women. Furthermore, Cisse *et al.*, (2021) reported that main predictors of abdominal obesity were associated with being married.

The findings showed that students in Saint John's University were overweight when

compared to Students in Mzumbe University. The possible reason for this could be due to difference of agro-ecological zones, since Saint John's is located in Dodoma a semi-arid area and Mzumbe University is located in Morogoro characterized by bi- modal rainfall patterns. The increase in urbanization in Dodoma could also justify the prevalence of overweight in the region. (Munyogwa & Mtumwa, 2018) reported prevalence of overweight to be higher in urban areas in Tanzania and other countries worldwide. A study revealed that Overweight and obesity are common in private schools and urban settings (Mosha *et al.*,2021).

It is important to take into consideration difference in agro-ecological zones since they differ in climate soil as well as economic activities, all this can have influence in the overall nutritional status of an individual. A study reported that household dietary diversity differed from different regions in rural and urban Tanzania, regions such as Morogoro contributes to high diversity due to food availability while regions like Dodoma import most foods due to experiencing one season rainfall per annum (Borrego, 2021). Bailey *et al.*, (2022) reported that students in the Midwest had higher BMIS compared to students in the Northeast.

This study reports that female University students were more likely to be Overweight and Obese when compared to their male counterparts. This could be influenced with the differences between the dietary diversity among the genders. Because females often have less lean mass and more fat mass, biological factors may account for the gender differences in overweight or obesity.

Dietary diversity has been reported to positively affect obesity through higher energy intake. A study reported that the probability of overweight/obesity was increased as tertiles of dietary diversity score increased (Golpour-Hamedani *et al.*, 2020). In contrast to these findings Tok *et al.*, (2018) reported the prevalence of overweight/obesity was similar among male

and female students with a difference of only 0.3%.

In our study students that were ≥ 25 years of age were more susceptible to Overweight and obesity when compared to students that were 20-24 years of age. It was noted that individuals that were ≥ 25 years of age had a lower dietary diversity which can affect the overall nutritional status due to lack of diversified foods that complement each other. The study is in line with Al-Ghamdi *et al.*, (2018) who reported that there was a linear positive association (trend) of increasing BMI with older age groups. In the same context a study done in Tanzania reported that older women (35-49 vs 15-24 years) of a reproductive age where at a higher risk to develop obesity/overweight (Mosha *et al.*,2021). Quiliche Castañeda *et al.*, (2021) reported that being older than 27 years old significantly predicted overweight/obesity (OR$_B$= 2.07;95% CI=1.19-3.6).

The current study reported that years of studies was associated with Overweight and Obesity. Whereby Students that where in their 3rd year and above were associated with Overweight when compared to second year students. The possible explanation for this could be the difference in dietary diversity and selection of food among the second-year students and students that are in their 3rd year and above. These findings are in line with Ahmed *et al.*, (2015) who reported a significant association between students of their first year of study and second year of study. In contrast Bailey *et al.*, (2022) reported that being a second-year student had higher BMI$_s$ compared to four-year students.

In our study we also found that Married people were Overweight when compared to single people. This study revealed that married individuals had a high dietary diversity when compared to single individuals which could lead to the consumption of high energy foods and affect the overall nutritional status. However, we noted that majority of the study participants were single this could also be a possible explanation. These findings are similar with

(Liu *et al.*, (2021) who reported that married individuals were at a higher risk of being overweight/obese than never-married individuals. In the same context being married was a significant predictor of overweight/obesity whereby it was suggested that companionship after marriage may encourage an individual to avoid obesity or even contribute towards it (Al-Ghamdi *et al.*, 2018).

Conclusions and Recommendations

The study concludes that University students are at a risk of general obesity and central obesity which could be a baseline for developing chronic illnesses in the long run. The study also shows that University students have different access to meals in and out of the University campus and tend to skip meals due to being busy with studies. This study suggests that female university students, Increased age and Married individuals are at a higher risk of developing central and general obesity. The study also implicates that high dietary diversity is linked with central obesity. This study builds insight on dietary diversity and anthropometric status on university students. It shows that Body max index in itself is not sufficient to evaluate the overall nutritional status. Dietary diversity can be associated with factors like Religion and waist circumference which is an indicator of abdominal obesity. Factors that can help describe and understand the Anthropometric status of university students have also been identified these include; gender, year of study, marital status, age, location of university.

Recommendation

Due to the risks that University students face due to their newly adapted independency, there is a need for sustained health and nutrition education initiatives to help them adjust to lifestyle changes that affects their overall health. There should be educational initiatives promoting healthier diets, lifestyles, and weight control which may have a positive impact on university student's health.

Competing Interests

The authors declare that they have no competing interests

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Complete genome sequences and multidrug resistance genotypes of nontuberculous mycobacteria isolates from the Central Tuberculosis Reference Laboratory Muhimbili Tanzania

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Abstract
Background: Nontuberculous mycobacteria (NTM) usually comprise a group of environmental bacteria, with emerging but elusive coinfection with tuberculous mycobacteria, causing pulmonary tuberculosis. Whole genome sequencing may give insight into potential antimicrobial resistance genotypes, giving clinicians and policymakers proper directions in clinical applications and management regimens.
Methods: WGS was performed on twenty-four gDNA isolates from archival samples at the Central Tuberculosis Reference Laboratory using the MinION Oxford Nanopore Sequencing approach. Out of twenty-four, two were confirmed to belong to the NTM group. Further analysis was done to resolve the complete genomes of two nontuberculous mycobacteria strains isolated from tuberculosis patients. We then combined phylogenomics, reference-based scaffolding and average nucleotide identity (ANI) analysis to delineate each strain's taxonomic position and corresponding features.
Results: Our findings reveal that the two strains fit into the genus Mycolicibacterium, and the closest relative is ***Mycolicibacterium novocastrense***. Coupling BacAnt and CARD-based antibiotic resistance analyses revealed multidrug-resistant genotypes of diverse spectra and mechanisms. While the BC02 strain is genetically resistant to beta-lactams, macrolides and rifamycins, the BC05 strain portrays an extended drug resistance genotype encompassing beta-lactams, macrolides, polyamines, and aminoglycosides. Both strains possess a single nucleotide polymorphism (SNP) of the RNA polymerase beta-subunit (rpoB), representing resistance to the first-line rifampicin. Additionally, the BC05 strain genetically portrays resistance to ethambutol, isoniazid and fosfomycin through mechanisms involving target alteration through SNPs, drug inactivation and efflux.
Conclusion: Our findings strongly suggest the potential implication of multidrug-resistant NTM clinical isolates in the pathogenesis of pulmonary tuberculosis.

Keywords: Genomics; whole genome sequencing; NTM; phylogenomics; phylogenetics; antimicrobial resistance

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Introduction

Non-tuberculous mycobacteria (NTM) usually comprise a group of environmental *Mycobacterium* species (spp) with potential health risks considerably thought to pose a risk to pulmonary health. There are more than 160 NTM species worldwide apart from the Mycobacterium tuberculosis complex living in water and soil (Ratnatunga *et al.,* 2020). Previously, these organisms were considered non-dangerous to humans with immune competence and affected only immunocompromised individuals. However, evidence is increasing of their importance in pulmonary disease in both immune-competent and immunocompromised individuals (Griffith *et al.,* 2007).

In addition, the emergence of co-infection is alarming, suggesting a link between Mycobacterium tuberculosis (MTB) and NTM in the pathogenesis of pulmonary disease. With increased complications of pulmonary disease, evidence is accumulating pointing to the overwhelming phenomenon of antimicrobial resistance among respiratory pathogens. Draft-to-complete genomes of various *Mycobacterium tuberculosis* complex (MTBC) strains are flooding the databases. This contributes to a better understanding of the genetics underlying virulence, host-pathogen interaction features, and antimicrobial resistance patterns among MTBC strains.

However, despite this globally evident achievement, whole genome sequencing technology in the sub-Saharan African Region is in its infancy, with most infectious and noninfectious bacteria being sequenced. Except for a few MTBC sequencing studies in East African settings (Ssengooba *et al.,* 2016; Kanyerezi & Nabisubi, 2020; Katale *et al.,* 2020; Mbelele *et al.,* 2022), evidence shows that even MTBC strains are yet to be sequenced at the genomic level from East and Central Africa. This calls for attention and emphasis on the need for whole genome sequencing of MTB and NTM strains to track the possible epidemiological trend of pulmonary disease associated with *Mycobacterium* species. In addition, even the current research interest has been skewed towards the analysis of MTBC strains, whose infection, pathogenesis, and clinical implications are elucidated to a significant level.

On the contrary, little is explored about the genomics of NTM. The increase in multidrug-resistant strains of the MTB complex has been substantially established (Al-Mutairi *et al.,* 2019; Katale *et al.* 2020; Senghore *et al.,* 2020). Evidence of co-infection between MTBC and NTM is emerging, with speculations increasing about their role in the pathogenesis of TB as well as antimicrobial resistance (Kotwal *et al.,* 2017). In Tanzania, a recent combination of microscopy and molecular markers, entailing rRNA and hsp65 gene sequences, identified over 16 NTM strains, including M. *gordonae*, M. interjectum, and *M. intracellular. M. kumamotonense/hiberniae, and M. flavescens/novocastrense,* among others (Hoza et al. 2016).

A case study conducted in Dar es Salaam, Tanzania, identified a strain *M. yongonense* (Mnyambwa et al. 2018) adding to the previously identified strains. However, these results were based on partial sequences, which are of low resolution, recovering only taxonomic identities to the level of genus. This work focused on establishing whole genomic information including potential antimicrobial resistance genotypes from high throughput sequencing via Oxford Nanopore technology. Therefore, the current study reports *Mycolicibacterium novocastrense*UDSM-BC02 and *Mycolicibacterium novocastrense*UDSM BC05 as NTM strains from Tanzania with genomic characteristics potentially representing multidrug resistance and TB pathogenic potential, accounting for symptoms of pulmonary tuberculosis in TB patients.

Materials and Methods
Sampling and sample preparation
In this project, Ethical approval was sought from the National Health Research Review Committee and granted ethical clearance number HQ/R.84/VOLII/853. Our study involved analysis of 24 mycobacterial samples archived at the central TB reference laboratory (CTRL) in Dar es Salaam which were collected from selected cross border regions of Tanzania. The samples used for this study were received from the East African Public Health Laboratory Network (EAPHLN) project satellite (using GeneXpert MTB/RIF assay (Cepheid, USA)) hospitals namely Kibong'oto (Kilimanjaro), Mnazimmoja (Unguja), Musoma referral hospital (Mara), St Benedict Ndanda referral hospital (Mtwara), Sumbawanga referral

DNA Extraction and sequencing
The genomic DNA was extracted from twenty four heat-killed *Mycobacteria* isolates by the cetyltrimethylammonium bromide (CTAB) method as previously described (van Soolingen *et al.,* 1991). Briefly, sterile loops were used to lift bacterial isolates from LJ medium slants. The isolates were added into tubes containing 1X TE (Tris–ethylenediaminetetraacetic acid) buffer, pH 8.0, and then heat-killed in a water bath at 80°C for 20

Library preparation and sequencing
Library construction and sequencing were done using the Oxford Nanopore ligation sequencing kit (LSK 109) without fragmentation according to manufacturer's instructions. Twenty-four samples were end-prepped by adenylating the 3' end and phosphorylating the 5' end, followed by attaching barcodes for multiple sample sequencing. The end-prepped DNA was washed with a long fragment buffer to select only long fragments of

Genome annotation and establishment of basic features for each sample strain
To predict the possible taxonomic placement of each strain, assembled genomes for all the strains were first annotated with Microbial Genome Atlas (*MiGA*) (Rodriguez-R *et al.,* 2018) and then with the comprehensive genome analysis service at PATRIC (Wattam *et al.,* 2014). Annotation was also

hospital (Rukwa) and Kigoma referral hospital (Kigoma).

In addition, the study utilized samples from the EAPHLN project non-satellite (without Xpert MTB/RIF assay) sites of Nyamagana district hospital in Mwanza, Levolosi, and St Vicent health centers in Arusha and Pwani regions respectively. These selected areas for sample collection were from the cross-border regions except for St Vicent Health center. The inclusion criteria were all tuberculosis patients with positive smear consented to participate in the study. However, presumptive tuberculosis cases not willing to participate in the study were excluded as well as tuberculosis patients who were already on anti-tuberculosis treatment.

min followed by the addition of 10 mg/ml lysozyme in each tube and incubated at 37 °C overnight. On the following day, the DNA was extracted with chloroform–isoamyl alcohol (24:1), and the pellets of genomic DNA were rehydrated in 80 µl TE and left overnight at 4 °C. The quality and quantity of gDNA were confirmed using a Qubit 2.0 fluorometer (Thermal Fisher Scientific, Waltham, MA USA). The gDNA was eventually stored at -20 °C before sequencing.

more than 3kb. Sequencing adapters were added to these long fragments of DNA and incubated for 20 minutes at room temperature. Libraries were sequenced using MinION MK1C for 48 hours generating a total of 6.45 gb reads, which were base called using Guppy as the device was sequencing and the mean read length was 2.43kb, while *de novo* assembly was accomplished with Flye (v2.8).

accomplished with Rapid Annotation by Subsystems Technology (RAST).
Taxonomic insight: Approach from Genomic Data and 16S rRNA genes to determine possible closest strain
To predict the possible closest strains, the 16S rRNA genes were extracted using the ContEst16S algorithm (Lee et *al.,* 2017) and used for BLASTn

against the NCBI nucleotide database. Alternatively, the entire genomes from MiGA were used to identify the closest strains based on automated average nucleotide identity (ANI). Thereafter, the closest relative genome sequences were downloaded from GenBank for detailed comparison. The genomes were analyzed by the

Type (Strain) Genome Server (TYGS), for whole genome-based taxonomic identities (Meier-Kolthoff & Göker 2019), also integrating the latest updates for the most appropriate features (Meier-Kolthoff *et al.,* 2022). The TYGS analysis was subdivided into the following steps:

Determination of closely related type strains

Determination of closest type strain genomes was achieved in two complementary ways: First, all user genomes were compared against all type strain genomes available in the TYGS database via the MASH algorithm, a fast approximation of intergenomic relatedness (Ondov *et al.,* 2016) and, the ten type strains with the smallest MASH distances chosen per user genome. Second, an additional set of ten closely related type strains was determined via the 16S rRNA gene sequences. These were extracted from the user genomes using RNAmmer (Lagesen *et al.,* 2007) and each sequence was subsequently subjected to BLAST analysis against the 16S rRNA gene sequence of each of the currently 15679 type strains available in the TYGS database. This was used as a proxy to find the best 50 matching type strains (according to the bitscore) for each user genome and to subsequently calculate precise distances using the Genome BLAST Distance Phylogeny approach (GBDP) under the algorithm 'coverage' and distance formula d5 (Meier-Kolthoff *et al.,* 2013). These distances were finally used to determine the 10 closest type strain genomes for each of the user genomes.

Scaffolding and chromosome-level assembly to deduce full genomes.

The closest relatives identified via genome PATRIC annotation and blind phylogenic reconstructions from TYGS were selected as reference genomes. Then contigs from each strain genome were mapped to these selected reference genomes using CONTIGuator v2.27 (Galardini *et al.,* 2015). The scaffolds from the best matches were used as a reference for further remapping of the contigs to enhance recovery. This process of reference-guided assembly was repeated four times for each strain genome and the ultimately recovered sequence was considered a chromosome, relative to the chromosome sizes of reference and other closely related strains from genome and assembly databases in the National Center for Biotechnology Information (NCBI).

Genomic screening of antimicrobial resistance genes

Antimicrobial resistance genes analysis was done using the PATRIC annotation pipeline for the identification of antimicrobial resistance genes and mechanisms (Antonopoulos *et al.,* 2019). Then the genome sequences were alternatively scanned by the comprehensive antimicrobial resistance database (CARD) (Alcock *et al.,* 2020) and, using default parameters, the BacAnt: a combinatorial pipeline for concomitant identification of antimicrobial resistance genes with integrons and transposable elements (Hua *et al.,* 2021).

Results
Demographic and clinical features of the patients

Among all 24 samples isolated as Mycobacteria, 2 (8.3%) samples were identified as NTM and labeled as BC02 and BC05. The patient with a code BC02 was a male aged 23 years living in Kilimanjaro with

a history of TB relapse in the year 2015 and HIV negative. He was referred to a regional Hospital (Kibong'oto) after relapse with the following clinical features: coughing (60 days), fever (7 days), chest pain (7 days), fatigue (14 days), and loss of appetite (21 days). The second patient,

coded as BC05, was a male living in Arusha aged 32 years with the following clinical characteristics; HIV positive, with typical TB relapse symptoms including coughing for 58 days, fever (30 days), weight loss (53 days), breathing difficulties (30 days) and fatigue (30 days). He was previously treated with anti-Tb first-line drugs in the same facility.

Assembly of NTM strains genomic features
The results of the assembled genome for Myc_UDSM_BC02 contained 108 contigs, a total of

5958338 bp (GC 66.72%), 7263 protein-coding sequences (CDS), 49 RNAs with 3 rRNA genes from PATRIC annotation. On the other hand, the Myc_UDSM_BC05 genome comprised 80 contigs, equivalent to 9197165 bp (GC 66.63%), 11,370 protein CDS, 90 transfer RNA (tRNA) genes, and 9 rRNA genes. Based on the annotation statistics and a comparison to other genomes in PATRIC within this same species, both genomes appeared to be of good quality. Details of the analysis, including predicted functions, and phylogenetic positions are shown (Figures 1, 2).
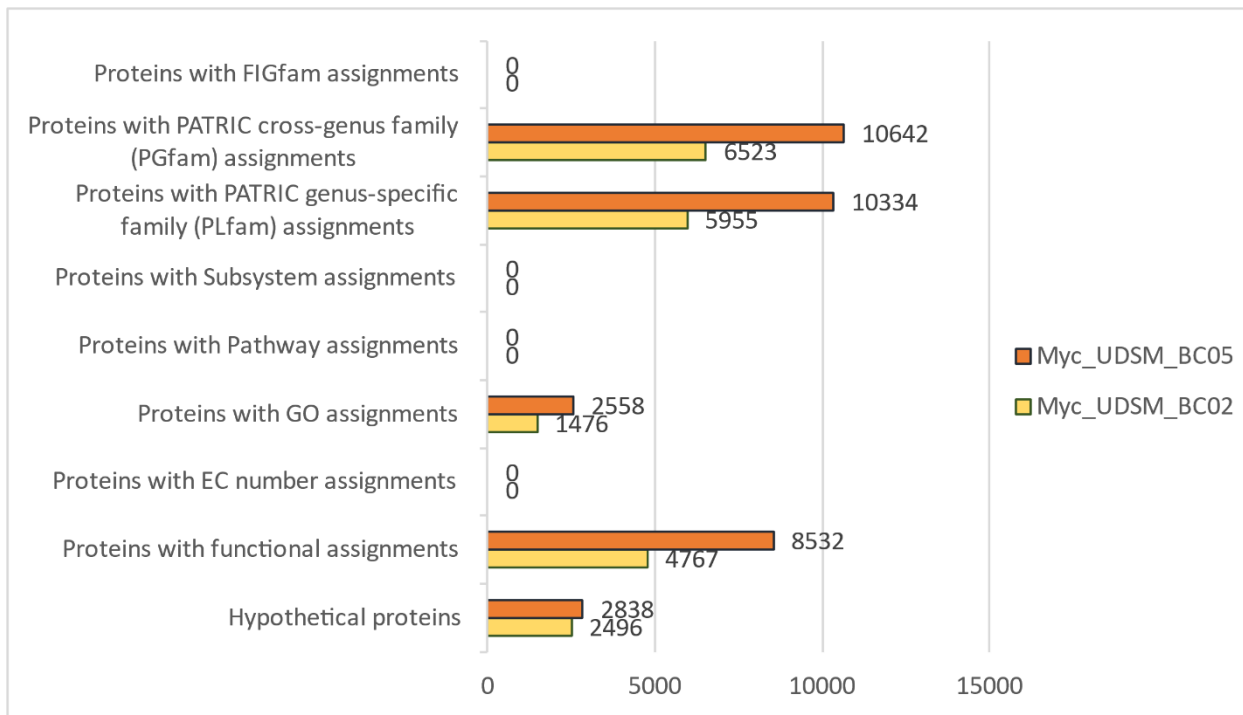
Figure 1. Functional characteristic features of coding sequences from the PATRIC annotation pipeline.
Numbers at the end of each bar indicate the proteins that are functionally assigned according to corresponding functions and database.

Phylogenetic analysis of NTM strain genome from comprehensive annotation by PATRIC
Further annotation was done using PATRIC platform using reference genomes from the National Center of Biotechnology Information (NCBI) and includes them in the phylogenetic analysis as part of the comprehensive genome analysis process. The closest reference and representative genomes were identified by

Mash/MinHash (Ondov *et al.,* 2016). PATRIC global protein families (PGFams) *(Davis et al.,* 2016) were selected from these genomes to determine the phylogenetic placement of the study genomes. The protein sequences from the predicted families were aligned with MUSCLE (Edgar 2004), and the nucleotides for each of those sequences were mapped to the protein alignment. The joint set of amino acid and nucleotide alignments were

concatenated into a data matrix, and RaxML (Stamatakis 2014) was used to analyze this matrix, with fast bootstrapping (Stamatakis *et al.,* 2008) was used to generate the support values in the trees.

PATRIC global protein families (PGFams) (Davis et al. 2016) were selected from these genomes to determine the phylogenetic placement of the study genomes. The PATRIC platform retrieves high-quality and appropriate representative reference genomes from the National Center for Biotechnology Information (NCBI) and includes them in the phylogenetic analysis as part of the comprehensive genome analysis process. The closest reference and representative genomes were identified by Mash/MinHash (Ondov *et al.,* 2016). PATRIC global protein families (PGFams) (Davis *et al.,* 2016) were selected from these genomes to determine the phylogenetic placement of the study genomes. The protein sequences from the predicted families were aligned with MUSCLE (Edgar 2004), and the nucleotides for each of those sequences were mapped to the protein alignment. The joint set of amino acid and nucleotide alignments were concatenated into a data matrix, and RaxML (Stamatakis 2014) was used to analyze this matrix, with fast bootstrapping (Stamatakis *et al.,* 2008) was used to generate the support values in the trees. The initial prediction of the phylogenetic placement of each strain is indicated in Figure 2. Each of the strains forms a cluster with *Mycolicibacterium acapulense,* suggesting a close relationship between them. However, other members of the genus *Mycolicibacterium* are missing from this automated phylogenetic tree analysis. This shortfall accounts for the need to incorporate other phylogenomic approaches with the most recent and up-to-date databases.
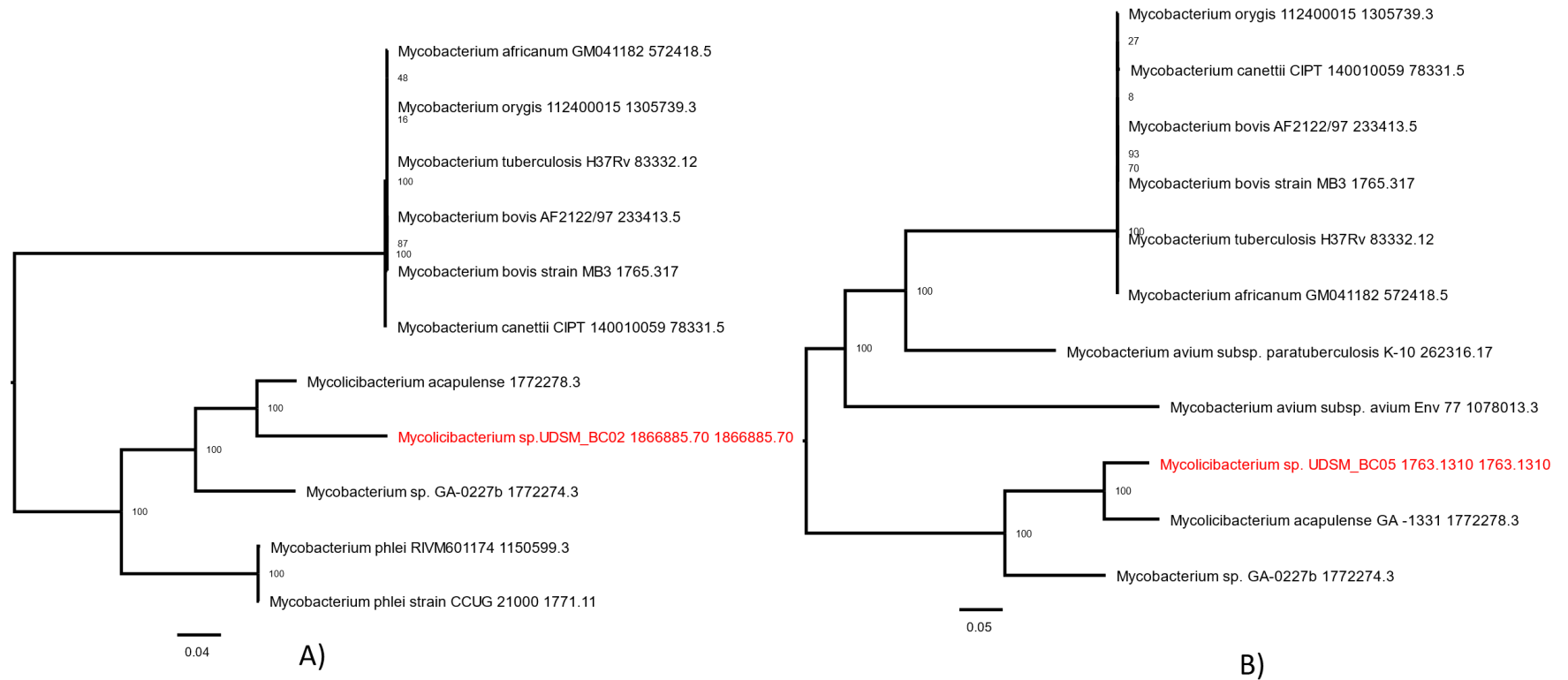
Figure 2. Codon phylogenetic trees generated from PATRIC annotation: A) the position of Myc_UDSM_BC02, B) the position of Myc_UDSM_BC05 based on PATRIC database search for close strains. Numbers above branches are bootstrap values for 1000 replicates automatically generated by RAxML.

Phylogenetic position of BC02 and BC05 based on 16S rRNA gene sequences.

To reassess the quality of genome sequences before rRNA analysis, screening for contigs contamination was approached using ContEst16S (Lee *et al.,* 2017). The genomes were both found to be clean, i.e., devoid of intra-genus contaminant sequences. The BC02 genome contained one 16S rRNA gene, which upon BLASTn against the NCBI database showed a percentage identity of 98.43 – 99.19 % with *Mycolicibacterium* spp exclusively *M. novocastrense* (GenBank accession no. **HM807280.1**) and *M. flavescens* (GenBank accession no. **AF174289.1**). On the other hand, the BC05 strain contained three 16S rRNA genes. The BLASTn algorithm in ContEst16S predicted *Mycobacterium*/LQIX as the closest strain. Based on 16S rRNA phylogeny (Figure 3) annotation results revealed that the strains of the two isolates BC02 and BC05 were closer to each other than to the reference genomes. The results of phylogenetic position analysis of each isolate inferred from genome-based distance phylogeny (GBDP) calculated from 16S rRNA revealed that the two isolates lies within the genus Mycolicibacterium (Figure 4). Their possible difference is suggestive of further genomic differences and potential virulence and antibiotic resistance features, described in the next parts of this work.
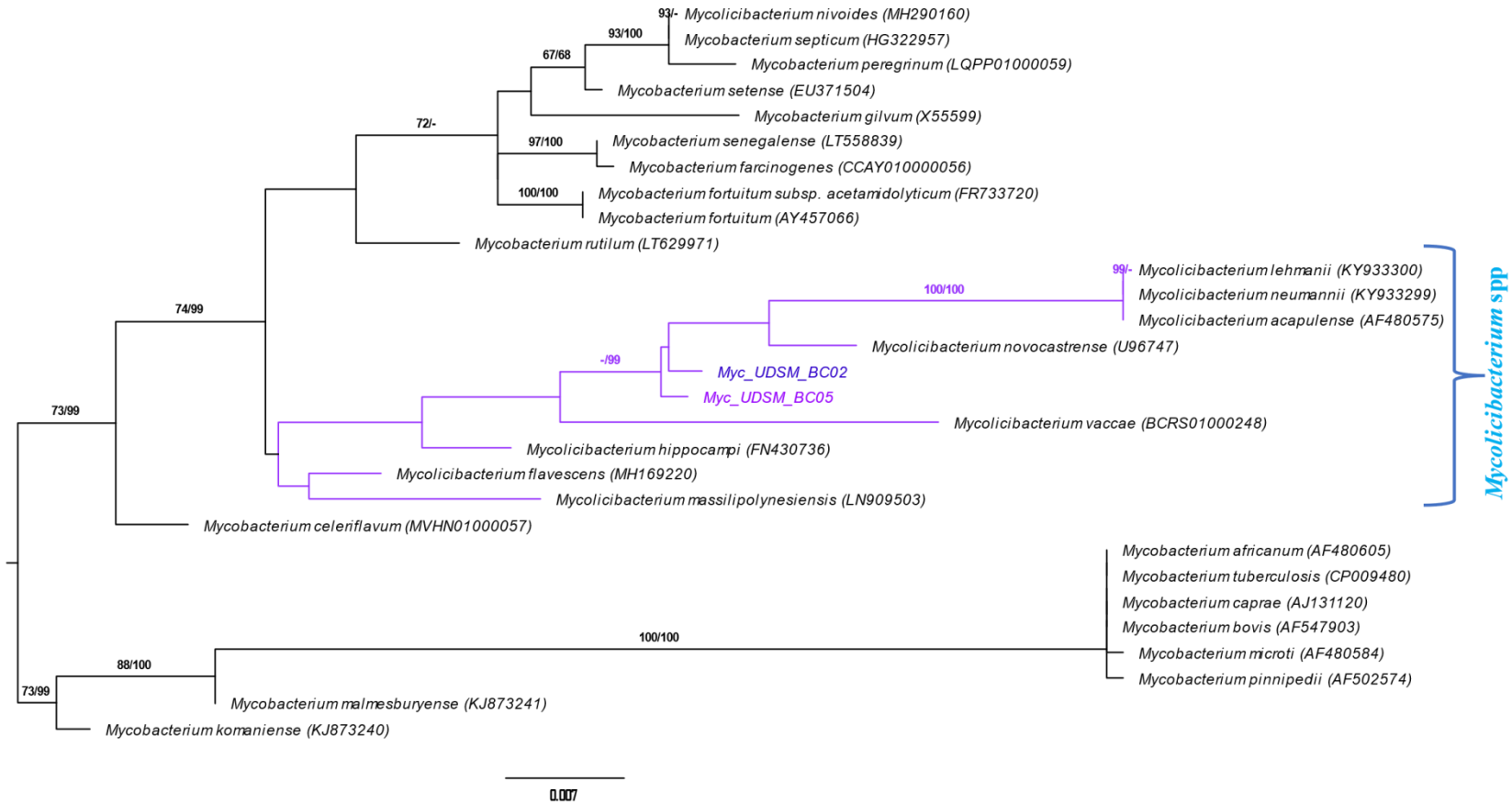
Figure 3. Tree inferred with FastME 2.1.6.1 from GBDP distances calculated from 16S rRNA gene sequences. The branch lengths are scaled in terms of GBDP distance formula d5. The numbers above branches are GBDP pseudo-bootstrap support values > 60 % from 100 replications, with an average branch support of 52.6 %. The tree was rooted at the midpoint.

Whole genome-based phylogenetics and taxonomic placement of BC02 and BC BC05 strains

The two strains were further subjected to other approaches to be able to discriminate the two strains. Based on whole genome phylogenetic and taxonomic placement, the two strains BC02 and BC BC05 were first subjected to the TYGS database for fast classification (Meier-Kolthoff *et al.,* 2022). The TYGS database can retrieve the most closely and distant related strains based on several computations integrating ANI and genome-genome distance calculation (GGDC). The results of this annotation as presented in Figure 4, revealed that the two study strains form a separate clade from MTBC such as *M. tuberculosis* H37Rv, *M. africanum* ATTC 25420, and *M. caprae* ATTCC BAA-824 or *M. microti* ATTCC 19422, which are well-established strains of the MTBC.
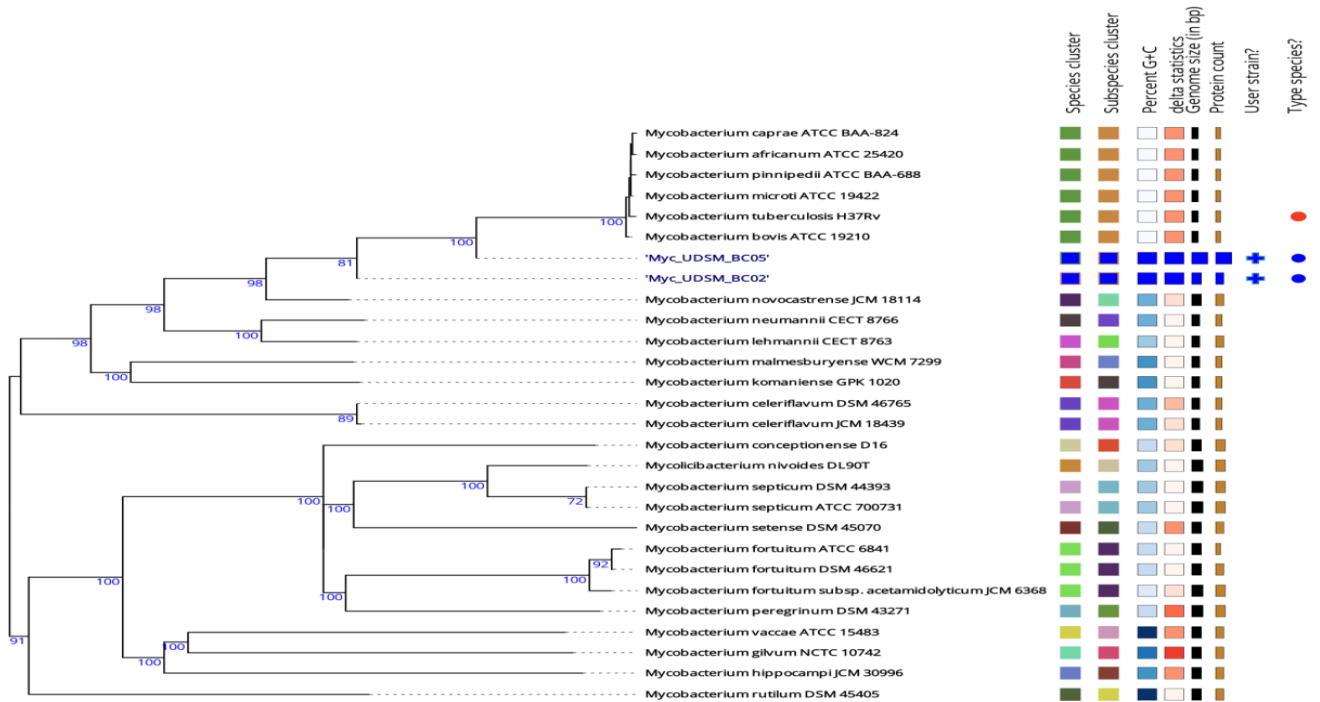
Figure 4. Genome-based phylogenetic tree inferred with FastME 2.1.6.1 from GBDP distances Calculated from genome sequences. The branch lengths are scaled in terms of the GBDP distance formula d5. The numbers above branches are GBDP pseudo-bootstrap support values > 60 % from 100 replications, with an average branch support of 79.7 %. The tree was rooted at the midpoint.

Assembled chromosomes.
It is usually ideal to decrease the number of contigs as much as possible to generate a chromosomal genomic DNA and enhance the resolution of extrachromosomal sequences if any. Following the identification of phylogenetically close strains, the latter genome sequences were downloaded from the NCBI database and used as references against which the contigs for the study genomes were mapped using CONTIGuator 2.27 (Galardini *et al.,* 2015). The scaffold size and corresponding percentage recovery generated from each mapping are indicated in Figure 5. The final recovered genome for the strain BC02 can be accessed via accessed via accession no. **CP097264** while that of BC05 is under the NCBI processing but can be shared upon request..
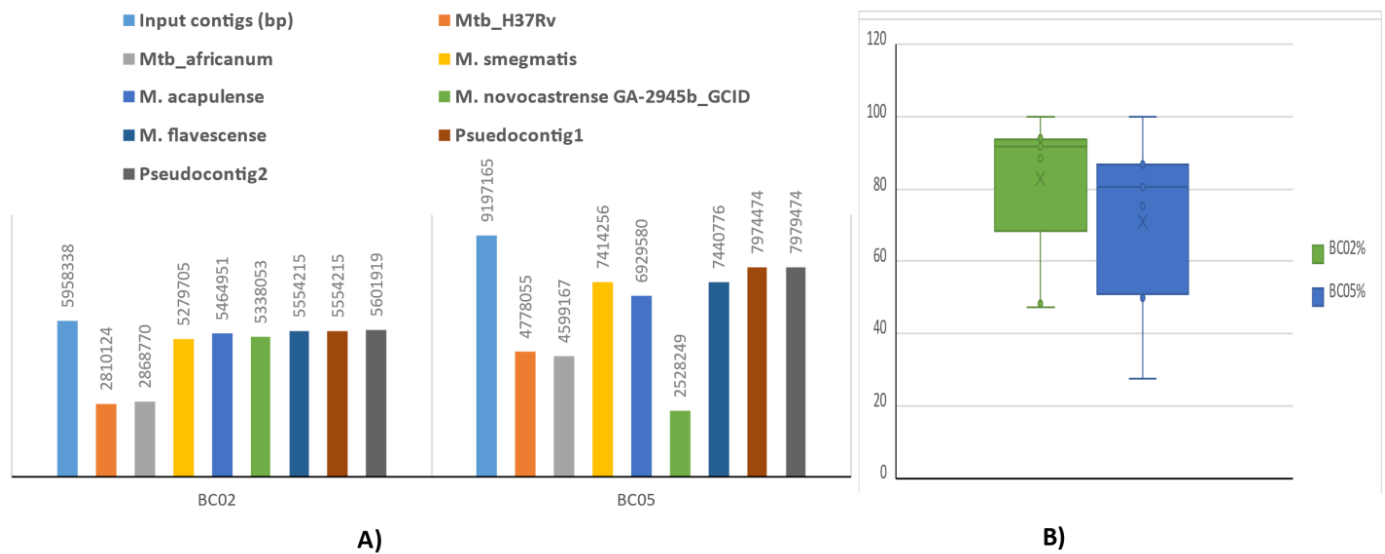

Figure 5. Chromosome recovery profiles obtained from reference-based assembly via CONTIGuator scaffolding pipeline. A) Genome size for each reference mapping, numbers above bars indicate the recovered chromosome against the corresponding reference genomes. B) Mapping percentage corresponding to each recovered genome.

Analysis based on Average nucleotide identity of BC02 and BC05
To enhance the power of inference, the genomes were compared with other NTM in the genus *Mycolicibacterium* as well as standard strains from the MTBC complex based on their average nucleotide identity. Average nucleotide identity (ANI) was calculated using the enve-omics algorithm (Kim *et al.,* 2014). The values of ANI analysis are presented in Tables 1. From these results a distance matrix was generated and the corresponding comparative heatmap is shown in Figure 6.

Table 1. Average nucleotide identities of each strain compared to reference genome sequences

| Reference sequence	BC02		BC05	
	ANI	SD	ANI	SD
Mtb. kansasii ATCC 12478 (CP006835.1)	78.38	4.45	80.17	4.12
Mtb H37Rv (NC_018143.2)	88.34	11.09	88.35	11.04
M. acapsulence (NZ_LT592249.1)	90.02	3.61	90.03	3.72
M. acapulense CSURP1424 (NZ_LT592249.1)	90.02	3.61	90.03	3.72
M. flavescens NCTC10271 (LR134353.1)	89.89	3.38	89.91	3.48
M. moriokaense JCM 6375	80.06	4.26	79.88	4.35
M. nivoides strain DL90	78.72	4.49	78.54	4.53
M. novocastrense GA-2945b GCID (NZ_LQIJ01000001NZ)	95.51	3.19	95.56	3.15
M. novocastrense JCM18114 (NZ_BCTA01000119.1)	95.63	3.36	95.67	3.38
M. pulveris JCM 6370	80.94	4.42	80.87	4.45
M. smegmatis FDAARGOS 679 (CP054795.1)	79.19	4.61	79.08	4.70
Myc_UDSM BC02	100.00	0.00	99.81	0.66
Myc_UDSM_BC05	99.81	0.66	100.00	0.00
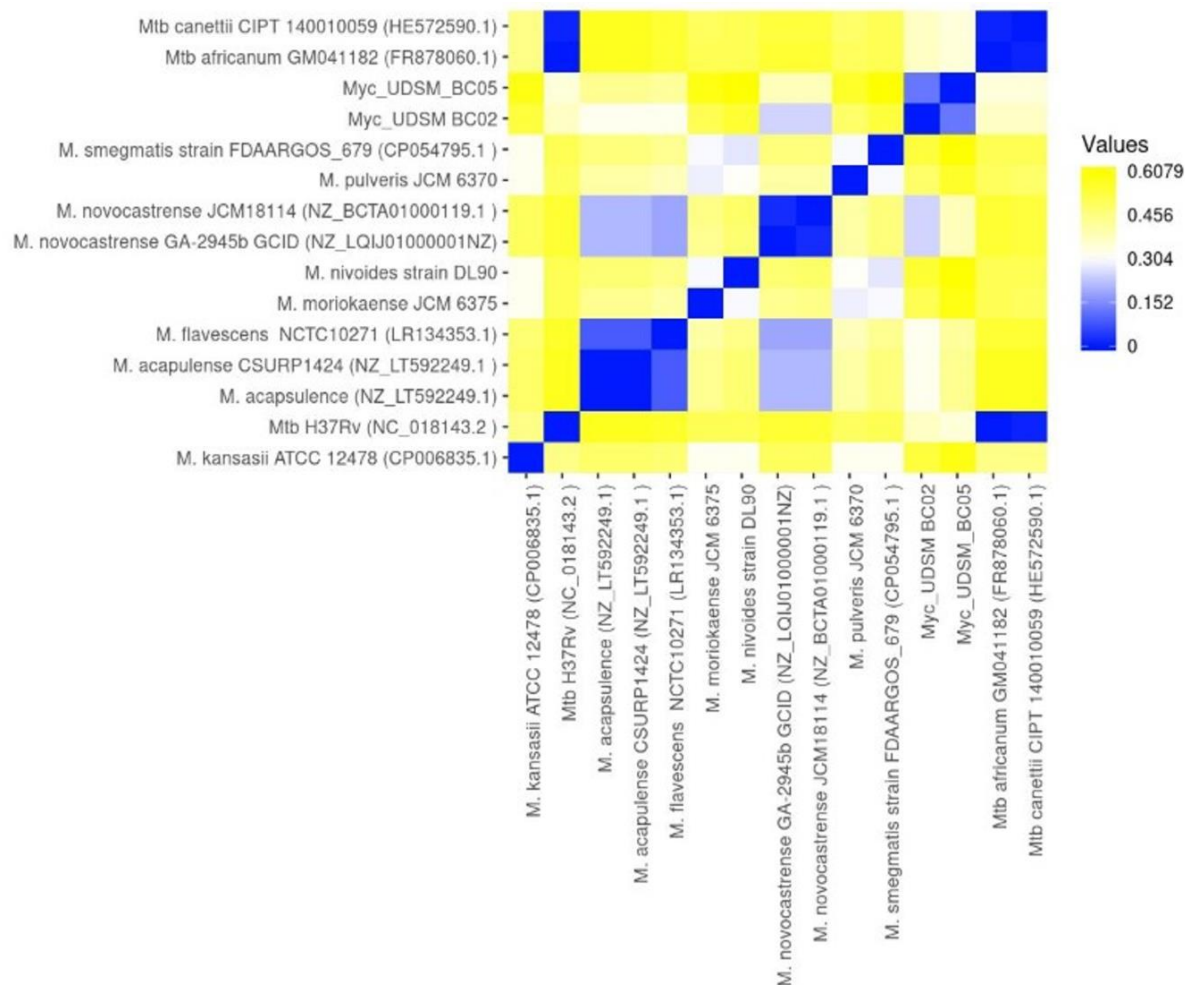
Figure 6. A heatmap representing pairwise comparison of BC02 and BC05 strains against NTM and standard MTBC strains. The correlation was inferred using Euclidean distance measurement method.

Results from RAST annotation

To enhance precision in the description of these two genomes the assembled chromosomes were reannotated with the RAST server (Aziz *et al.,* 2008) using the RASTk pipeline (Brettin *et al.,* 2015). Default minimum gene length was used, with the minimum identity being adjusted to 70%. From this annotation, the BC02 genome (with 5,624,151 bp in size and 66.9 GC %) was found to contain 6657 CDS with 50 RNA genes and 301 subsystems. These genomic features are coherent with most members of the genus *Mycolicibacterium* reported from recent genomic studies (Sánchez *et al.,* 2019; Vatlin *et al.,* 2019).

Out of the 301 subsystems (Figure 7), the richest in features is that for amino acid metabolism followed by those for carbohydrate metabolism and then fatty acids, lipids, and isoprenoids. The most remarkable feature of *Mycolicibacterium* spp is their genomic richness in the genes for biosynthesis of membrane lipids, which have been implicated in fatty acid accumulation and biofilm formation, among other adaptive mechanisms to harsh conditions (Chen *et al.,* 2020). On the other hand, the BC05 genome 7,979,474 bp and GC 66.5%) contained 9590 CDS and 90 rRNAs with 833 subsystems with various functional categorizations indicated in Figure 8. These annotation features are consistent in terms of values with genomic size and are more coherent with *Mycolicibacterium* spp genomes from other studies (Sánchez *et al.,* 2019) than *Mycobacterium* spp (Advani *et al.,* 2019). Detailed analysis of virulence factors showed that both BC02 and BC05 strains possess genes for invasion and intracellular resistance, i.e., 51 gene features for BC02 and 519

for BC05, suggesting that the strains can potentially infect and cause disease.

The BC02 genome also possesses resistance to fluoroquinolones (2 genes). All these features are indicative of their potential virulence and antibiotic resistance. In the BC05 genome, other antibiotic resistance features identified via RAST annotation include resistance to vancomycin (9 genes), tetracycline resistance, ribosome protection type (45 genes), aminoglycoside adenylyl-transferases (2 genes), and tetracycline resistance, ribosome protection type, too (45

In addition, while BC02 possesses a single, potentially class A beta-lactamase gene, BC05 contains up to 105 beta-lactamase genes. genes), among others. This pattern of genotypic antimicrobial resistance is a strong indicator of multidrug resistance, characterized in the vast majority of Mycobacteria including the *Mycobacterium tuberculosis* H37Rv, *M. tuberculosis var africanum*, *M. tuberculosis var kansasii* (Katale *et al.,* 2020; Al-Mutairi *et al.,* 2019), and other MTBC species (Joean *et al.,* 2020; Parthasarathy *et al.,* 2016).

Figure 7. Metabolic subsystems recovered from RASTk annotation of the BC02 chromosome. The bar in the left represents the percentage of each subsystem coverage and the legend on the right indicates the counts for each subsystem feature.
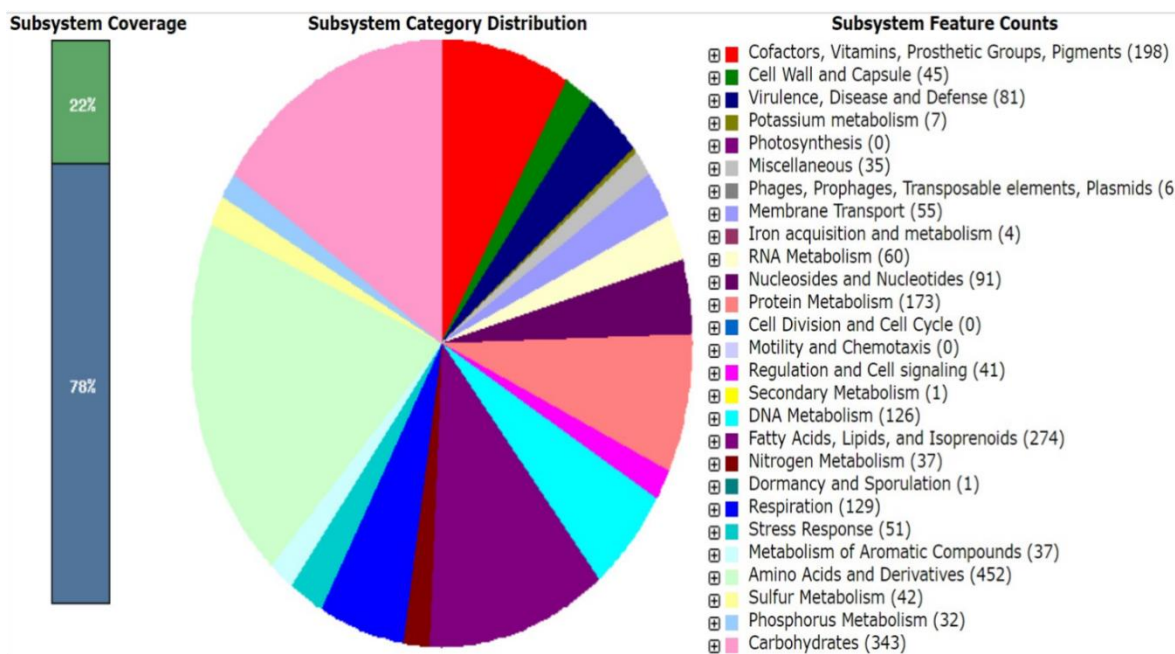
Figure 8. Metabolic subsystems recovered from RASTk annotation of the BC05 chromosome. The bar in the left represents the percentage of each subsystem coverage and the legend on the right indicates the counts for each subsystem feature.
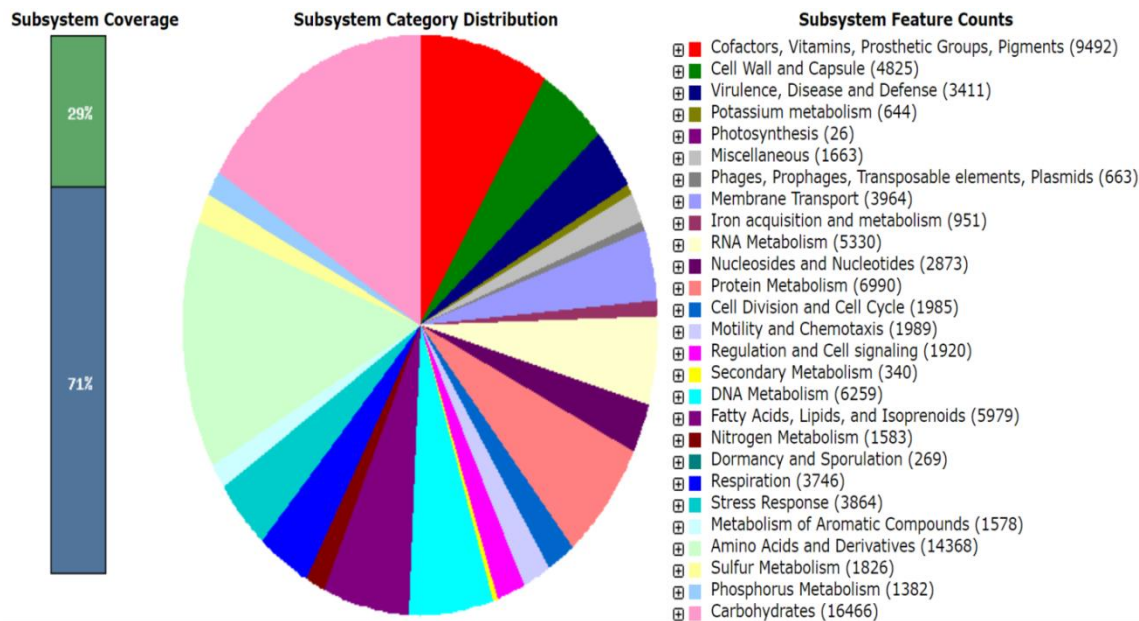
Orthologous clusters

From Orthovenn2 analysis, BC02 and BC05 together with the most closely related NTM species and reference MTBC strains form 7769 clusters, 6559 orthologous clusters (at least contains two species) and 1210 single-copy gene clusters (Table 2). This indicates that most of the gene families and clusters are shared among *Mycolicibacterium* spp as contrasted to the

Mycobacterium representative strains. The number of singletons (genes not conforming to a cluster) is consistently dependent upon the genome size and the number of inherent CDS. It appears that, the BC02 genome (1316 singletons) has fewer singletons than the BC05. Genome (2646 singletons) Likewise, the genome of *Mycolicibacterium smegmatis* LN831039 (6847 CDS) contains 1928 singletons.

Table 2. Clusters of orthologous recovered from Orthovenn2 analysis and annotation. The proteome of each genome is presented against the clusters and corresponding singletons.

Species	Proteins	Clusters	Singletons
Myc_UDSM_BC02	6657	5108	1316
Myc_UDSM_BC05	9590	5950	2646
Myc_novocastrense_JCM_BCTA01000119	5336	4794	411
Myc_flavescens_NTC10271_LR134353	5698	4762	674
Myc_smegmatis__LN831039	6847	4427	1928
Mtb_africanum_GM041182	4269	4070	129
Mtb_H37Rv_NC018143	4302	4092	124

Shown in Figure 9 the members of *Mycolicibacterium* share 1537 protein families. While protein families shared between BC02 and *M. novocastrense* could not be resolved, 35 families are shared between BC05 and *M. novocastrense*.
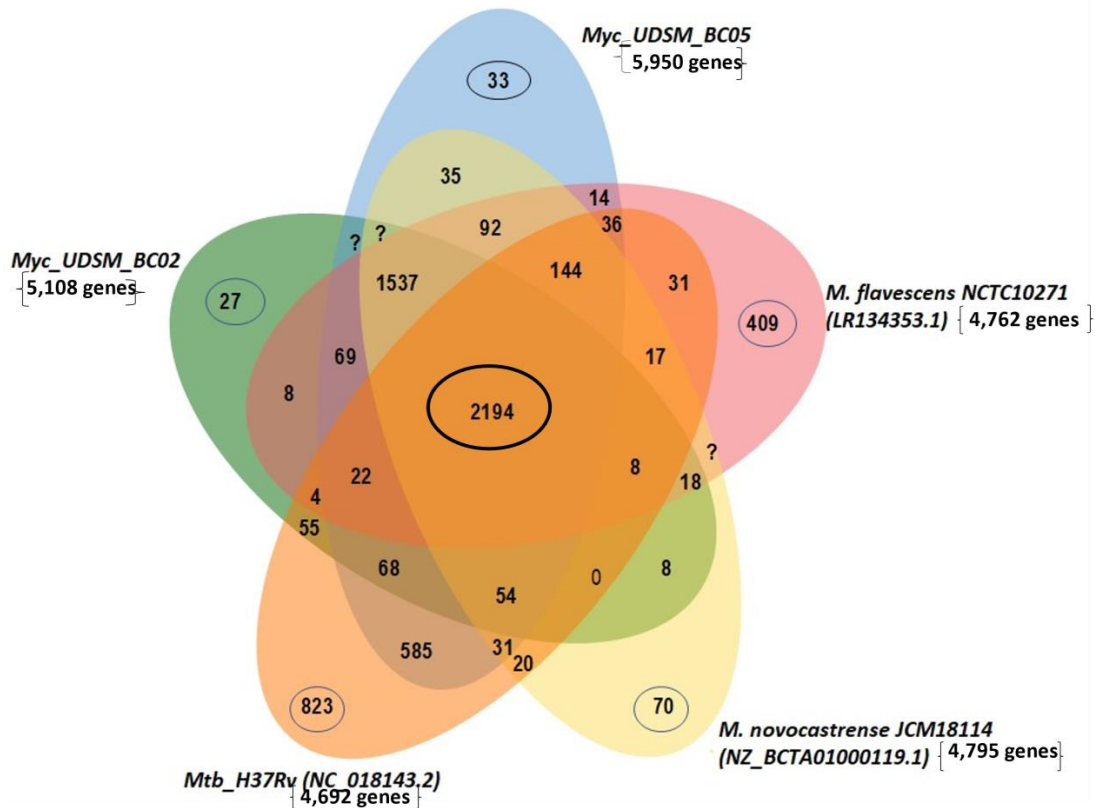
Figure 9. A Venn representation of the distribution of unique, group-specific, and core gene families among the Mycolicibacterium spp as compared with M. tuberculosis H37Rv. The selected closest scaffolds with at least a single one-to-one ortholog shared among the genomes were compared using OrthoVenn2. The core genome is shown in the central circle. Each colored intersect segment represents the number of gene families shared among the respective overlapping genomes, and the outermost circled numbers represent unique gene families for individual genomes.

Analysis of mutations associated with antimicrobial resistance genotypes in BC02 and BC05 strains of NTM to anti-TB drugs.

PATRIC database offers an opportunity to analyze genes related to antimicrobial resistance (specialty genes), including a count of virulence factors, drug targets, and antimicrobial resistance genes. As indicated in Table 3, again specialty genes for the BC05 are more than two-fold those of BC02, possibly due to larger genome size, also attributable to repetitive sequences in the BC05 genome. To better define the antimicrobial resistance potential of each strain, the FASTA files were first analyzed with BacAnt v3.3.3, which provides a database (BacAnt-database v2.0) to scan for resistance genes, insertion elements, and transposon regions from the genome sequences (Hua *et al.,* 2021). Results from this scanning revealed neither insertion elements nor transposons but a class A beta-lactamase (BlaA) gene flanked between 2605222 and 2605896 of the BC02 chromosomal DNA sequence, which covers 73.26% with 99.56% identity to the reference gene in the resistance database (resDB).

In the case of the BC05 chromosome, the antimicrobial resistance genotype could not be resolved with BacAnt. Thus alternative reannotation was approached using the comprehensive antimicrobial resistance database, (CARD) retaining default parameters (Alcock *et al.,* 2020). Based on CARD analysis, nucleotide sequences undergo ORF calling to generate predicted protein sequences (Alcock *et al.,* 2020). 2020). From this analysis (Table 3), the BC02 genome was found with three strict hits, relevant to genes conferring resistance against macrolides

and rifamycin as defined by efflux, drug inactivation, and target alteration/replacement respectively. On the other hand, results show that the strain BC05 contains one perfect and 10 strict hits for a wide range of antibiotic resistance genes (Table 5). The perfect hit presents efflux-mediated antibiotic resistance against first-line anti-TB drugs, rifamycin, and isoniazid. The rest of the hits include efflux, and target alteration against rifamycin, macrolide, penam, disinfectants, polyamine, and fosfomycin antibiotics. These resistance genotypes in the BC05 are strongly suggestive of the emergence of a multidrug-resistant NTM strain associated with MTBC coinfection, which underlies exacerbated pulmonary tuberculosis pathogenesis.

Table 3. Antimicrobial resistance genes for BC02 and BC05 strains as recovered from the PATRIC annotation pipeline. The annotation entails virulence factors, transporter genes and drug targets from different databases accessible to the PATRIC database.

Specialty Genes	Source	Myc_UDSM_BC02	Myc_UDSM_BC05
Virulence Factor	PATRIC_VF	171	548
Virulence Factor	Victors	113	315
Virulence Factor	VFDB	31	76
Transporter	TCDB	51	127
Drug Target	DrugBank	38	82
Drug Target	TTD	14	35

Table 4. **Myc_UDSM_BC02 antibiotic drug resistance genotypes annotated via the CARD pipelines. Models for detection criteria, antimicrobial resistance gene families, drug class and drug resistance mechanismsare included alongside percentage identity match and sequence coverage by default parameters.**

ARO term	SNP	Detection criteria	AMR gene family	Drug class	Resistance mechanism	% ID of matching region	% length of resistance sequence
mtrA		protein homolog model	resistance-nodulation-cell division (RND) antibiotic efflux pump	Macrolide, penam	efflux	96.05	100
arr-1		protein homolog model	rifampin ADP-ribosyltransferase (Arr)	rifamycin	inactivation	84.51	99.3
MtbrpoB mutants conferring resistance to rifampicin	D516G, H526T, L511R	Protein variant model	rifamycin-resistant beta-subunit of RNA polymerase (rpoB)	rifamycin	Target alteration/replacement	100	52.39

Table 5. Myc_UDSM_BC05 antibiotic drug resistance genotypes annotated via the CARD pipelines. Models for detection criteria, antimicrobial resistance gene families, drug class and drug resistance mechanisms are included alongside percentage identity match and sequence coverage by default parameters.

RGI Criteria	ARO Term	SNP	Detection Criteria	AMR Gene Family	Drug Class	Resistance Mechanism	% Identity of Matching Region	% Length of Reference Sequence
Perfect	efpA		protein homolog model	major facilitator superfamily (MFS) antibiotic efflux pump	rifamycin antibiotic, isoniazid	antibiotic efflux	100	100
Strict	qacG		protein homolog model	small multidrug resistance (SMR) antibiotic efflux pump	disinfecting agents and antiseptics	antibiotic efflux	39.81	106.54
Strict	RbpA		protein homolog model	RbpA bacterial RNA polymerase-binding protein	rifamycin antibiotic	antibiotic target protection	93.69	97.37
Strict	mtrA		protein homolog model	resistance-nodulation-cell division (RND) antibiotic efflux pump	macrolide antibiotic, penam	antibiotic efflux	96.05	100
Strict	arr-1		protein homolog model	rifampin ADP-ribosyltransferase (Arr)	rifamycin antibiotic	antibiotic inactivation	84.51	99.3
Strict	Mycobacterium tuberculosis embB mutant conferring resistance to ethambutol	E378A	protein variant model	ethambutol resistant embB	polyamine antibiotic	antibiotic target alteration	99.8	48

Strict	Mycobacterium tuberculosis embA mutant conferring resistance to ethambutol	P913S	protein variant model	ethambutol resistant embA	polyamine antibiotic	antibiotic target alteration	99.73	68.74
Strict	Mycobacterium tuberculosis embC mutant conferring resistance to ethambutol	T270I	protein variant model	ethambutol resistant embC	polyamine antibiotic	antibiotic target alteration	99.71	33
Strict	Mycobacterium tuberculosis intrinsic murA conferring resistance to fosfomycin	C117D	protein variant model	antibiotic-resistant murAtransferase	fosfomycin	antibiotic target alteration	100	34.69
Strict	Mycobacterium tuberculosis rpoB mutants conferring resistance to rifampicin	D516G, H526T, L511R	protein variant model	rifamycin-resistant beta-subunit of RNA polymerase (rpoB)	rifamycin antibiotic	antibiotic target alteration, antibiotic target replacement	99.78	45.14
Strict	Mycobacterium tuberculosis 23S rRNA mutation conferring resistance to capreomycin	A2145G, A2045G	rRNA gene variant model	23s rRNA with mutation conferring resistance to aminoglycoside antibiotics	aminoglycoside antibiotic	antibiotic target alteration	96.28	100

Discussion

From this study it has been observed that the genome size of BC02 is significantly smaller by approximately 3.2 Mb than that of BC05. This could generally account for a small number of CDS, therefore all the protein assignments in Figure 1 correspond with the smaller BC02 genome relative to that of BC05. The genome sizes of NTM strains are becoming known to be relatively larger compared to those of MTBC (Yoon et al. 2020). Thus, the numbers of CDS are considerably larger. This work also supports that observation, with the BC05 having a huge size and proteome.

In this study, phylogenetic analysis was achieved through PATRIC. The initial prediction of the phylogenetic placement of each strain as indicated in Figure 2 shows that each of the strains forms a cluster with *Mycolicibacterium acapulense,* suggesting a close relationship between them.

The results of the initial phylogenetic placement of the two strains (Figure 2) shows that they form cluster with *Mycobacterium acapulense* suggesting their close relationship. However, other members of the genus *Mycolicibacterium* are missing from this automated phylogenetic tree analysis. This suggests that the PATRIC phylogenetic analysis algorithms could not successfully manage to retrieve some of the most relevant reference genomes. It could also imply that the database is yet to be updated to include a wide range of the most recent genomes of the genus *Mycolicibacterium*. To overcome this shortfall, we had to incorporate other phylogenomic approaches with the most recent and up-to-date databases for proper placement.

A detailed search through the NCBI assembly database revealed that *Mycobacterium*/LQIX correlates to the former *Mycobacterium* sp. GA-1199 (GenBank assembly accession no.**GCA_001500045.1**), whose current best match is *Mycolicibacterium novocastrense,* with average nucleotide identity of 95.18%, query coverage of 86.65% and subject coverage of 75.67%. These findings point to the NTM, potentially *M. novocastrense* as the best match for the BC05 genome. Presented in Figure 4, the phylogenetic position of each from GBDP distances calculated from 16S rRNA lies within the genus *Mycolicibacterium*. It then follows that both Myc_BC02 and Myc_BC05 comprise part of the NTM group and are potentially suggestive of co-infection or super-infection with MTBC. Based on the 16S rRNA phylogeny (Figure 3), the two strains are closer to each other than to the reference strain. However, the two strains also form potentially separate clades, indicating a possible difference between them, basally rooted from *Mycolicibacterium vaccae*. Their possible difference is suggestive of further genomic differences and potential virulence and antibiotic resistance features.

The pan-genome comparative analysis provides the highest throughput and the most reliable results in genomics. In the case of phylogenetics, whole-genome-based comparison has demonstrated the potential to discriminate intraspecific differences based on multiple markers to establish various positions and lineages within and between groups (Coscolla et al. 2021; Vázquez-Chacón et al. 2021; Stephen Kanyerezi and Patricia Nabisubi 2020). The TYGS database can retrieve the most closely and distant related strains based on several computations integrating ANI and genome-genome distance calculation (GGDC). We observed that the two study strains formed a separate

clade from MTBC such as *M. tuberculosis* H37Rv, *M. africanum* ATTC 25420, and *M. caprae* ATTCC BAA-824 or *M. microti* ATTCC 19422, which are well-established strains of the MTBC.

The results of the phylogenies reconstructed from both the 16S rRNA gene (Figure 3) and genome-wise comparison (Figure 4) reiterate the prior observation from Figure 2 that the two strains BC02 and BC05 are potential members of the NTM group. A previous study based on 16S rRNA and hsp56 gene sequences from Muheza Designated District Hospital, Tanzania revealed the presence of *M. kumamotonense, M. scrofulaceum/M. avium, M. acapulcensis/flavescens, M. avium,* and *M. flavescens/novocastrense,* among others (Hoza et al. 2016). Also, another case study from Dar es Salaam exposed the presence of *M. yongonense* (Mnyambwa et al. 2018). This work confirms through genomics that *M. novacastrense/flavescens* is among the most common clinical NTM species in Tanzania, especially from Nothern regions of Tanzania. However, the insufficiency of genomic data in Tanzania and East Africa hampers pan-genomic comparison within the region to establish appropriate possible linkages for tracing the potential transboundary distribution of the NTM strains.

Observations from ANI values results showed that the two strains appear closer to each other than between each and the reference strains. This is strong evidence that the strains belong to closely related taxonomic groups. The accepted species delimitation for most bacterial samples ranges from 95 – 96% (Jain et al. 2018). From the above results (Table 1) the strains BC02 and BC05 meet the criteria, i.e., ANI = 99.8%, genomic distance of 0.01 and the probability that the two are in the same species is 96.41%. In addition,

the strains match with *M. novocastrense* by 95.5% ANI and about 64% with *M. flavescens.*

Analysis of the mutation associated with antimicrobial resistance genotypes in BC02 and BC05 strains was performed on anti-TB drugs. The evolution of multidrug-resistant MTBC strains is vastly growing to integrate virtually all the established mechanisms of resistance against anti-TB drugs (Senghore *et al.,* 2020). According to literature the most established beta-lactamase gene in *Mycobacterium* spp (particularly *M. tuberculosis* strain ATCC 25177 / H37Ra) is the class C beta-lactamase (BLaC) (Bhattacharya *et al.,* 2021), which in the UniProt database (https://www.uniprot.org/uniprot/A5U493), is described as a representative of extended beta-lactamase antibiotic resistance and is known to portray extensive penicillinase, cephalosporinase, as well as carbapenamase activities. However, the BlaA gene is elusive as a beta-lactamase, considerably characterized in *Mtb var bovis, Mtb var canettii, Mtb var orygis*, and *Mycobacterium lactis* (Bhattacharya *et al.,* 2021).

Therefore *in vitro* and *in vivo* studies are instrumental in the characterization of the antibiotic resistance mechanism for the BC02 strain. With different coverages and percentage identities ranging from 36 – 98%, the BC02 strain possesses the potential to resist a wide of other drugs including fosfomycin, macrolides, vancomycin, tetracycline, and gentamycin/tobramycin, among others. These forms of resistance are also common among the notorious MTBC strains from various parts (Kidenya *et al.,* 2018; Joean *et al.,* 2020; Katale *et al.,* 2020). This concurrence in the genotypic multidrug resistance is a strong indication for the co-existence of

coinfections and co-pathogenesis between the less explored NTM strains and the commonly known MTBC strains such as the *Mtb* H37Rv and *Mtb var africanum, among* others reported from recent studies (Ishiekwene *et al.,* 2017; Stepanyan *et al.,* 2019).

Observation from this study attracts huge attention to the role of NTM co-pathogens as auxiliary agents in the drug resistance process. Here we demonstrate that these resistance genotypes of BC02 and BC05 isolates are comparative to those of MTBC strains (Parthasarathy *et al.,* 2016; Katale *et al.,* 2020). In terms of drug resistance, the BC02 strain presents a narrow resistome spectrum, while BC05 demonstrates a potentially broad spectrum resistome, encompassing rifamycin, isoniazid, macrolides, polyamines, as well as fosfomycin, which correlates with resistance patterns among members of the MTBC such as *M. tuberculosis* H37Rv, *M. tuberculosis africanum, M. tuberculosis var mungi, M. tuberculosis var bovis,* and *M. tuberculosis var kansasii* (Vázquez-Chacón *et al.,* 2021; Al-Mutairi *et al.,* 2019; Parthasarathy *et al.,* 2016). Until 2018, the first macrolide-binding protein was yet to be elucidated (Zhang *et al.,* 2018). The current findings underscore the possible coexistence of MTB and NTM strains with the potential for macrolide resistance.

In addition, rifamycin resistance is profoundly demonstrated in both BC02 and BC05 by mechanisms involving both adenosine diphosphate (ADP)-ribosyltransferase activity as well as single nucleotide polymorphism (SNP), leading to rifamycin-resistant beta-subunit of RNA polymerase (rpoB). These mechanisms are evident even in the extensively drug-resistant MTB *M. tuberculosis* H37Rv (Joean *et al.,* 2020). Our findings therefore suggest that molecular diagnostic techniques integrating the principle of DNA hybridization such as those in the GeneXpert or GenoType MTBDRplus (Dorman *et al.,* 2012) kits are not specific to MTBC strains, rather they could potentially detect the BC02 and BC05 strains in the TB samples as the inherent assays focus on the presence of SNPs associated with rifampicin and/or isoniazid, among other drug resistances.

Although WGS provides rapid and comprehensive diagnosis of Mycobacterium organisms and their resistance mechanisms and WHO has acknowledged its potential in determining resistance TB there are challenges that has to be addressed before its implementation in low-income countries. Those challenges include high costs of equipment, training of technical staff, and expertise guidance in clinical interpretations of WGS results. The major limitation to this study was lack of funds which could enable inclusion of large number of samples for WGS but also unavailability of databanks of African origin for Mycobacteria strains.

Conclusion

Long-read sequencing supports the recovery of nearly full genomes of strains. Comparative genomic analysis shows that the BC02 and BC05 strains in this study are NTM and belong to *Mycolicibacterium*. Since the samples were obtained from symptomatic relapse TB patients, this study concludes that the strains have the potential to cause pulmonary tuberculosis and probably resistant TB. While the two strains are closest to each other, they conform to *Mycolicibacterium novocastrense* as the closest relative.

With the current screening for antibiotic resistance repertoire, this study infers the existence of multidrug-resistant NTM strains whose resistance encompasses a wide range of drug classes including beta-lactam,

macrolides, polyamines, aminoglycosides, and rifamycins. Precisely, the BC02 strain is genetically resistant to penicillins and carbapenems as well as rifamycin drugs, while the BC05 strain is genetically resistant to most first-line anti-TB drugs including rifamycin, isoniazid, and ethambutol, among others. Phenotypic studies coupling standard antimicrobial assays with transcriptomics, proteomics, or other *omics*-based methods would further our understanding of the exact mechanisms of drug resistance portrayed by each strain towards effective management of pulmonary tuberculosis in Tanzania and the sub-Saharan Region in general.

Competing interests

The authors declare that they have no competing interest related to this article.

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COVID-19 vaccine hesitancy and associated factors among medical students in Tanzania: Evidence from the Catholic University of Health and Allied Science, Mwanza region

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Abstract

Background: Since the outbreak of COVID-19, the government of Tanzania has made efforts and initiatives to protect its citizens. These efforts and control measures are aligned with WHO guidelines and the National Response Plan for Controlling the COVID-19 Outbreak. Unlike other control measures, the Vaccine remained a promised solution to end the COVID-19 pandemic. Therefore, this study aims to determine the COVID-19 hesitancy level and associated factors among medical students. Furthermore, it aims to provide valuable insights and information that can be applied in future immunization campaigns/strategies to improve vaccination rates among this particular group of future medical professionals during the pandemic.

Methods: This is an analytical cross-sectional survey conducted to assess the COVID-19 vaccine hesitancy and associated factors among 580 undergraduate medical students at the Catholic University of Health and Allied Science (CUHAS) in Mwanza region, Tanzania. Data was collected through a structured questionnaire and analyzed using STATA version 18.0 to extract descriptive and inferential statistics to determine the factors influencing COVID-19 vaccine hesitancy in this particular group of future medical professionals. All the statistics were obtained at a 5% significant level.

Results: The vaccine hesitancy was 75.6% (95% CI, 71.9%-79.2%). Thus, more than half (54.3%) of the medical students do not trust the efficacy of the COVID-19 vaccine with an AOR of 2.96 (95% CI, 1.80-4.86, p-value<0.001); likewise, the safety of Vaccine AOR 0.1.89 (95% CI, 1.11-3.21, p-value=0.019). Further, students who do not prefer free riding (i.e., letting others get the vaccine and believing to get the beneficial effect of herd immunity without being vaccinated) were less likely to deny the Vaccine than those who prefer free riding AOR 0.31 (95% CI, 0.31, 0.13-0.75, p-value=0.009). Despite insignificant odds, too much politics behind the COVID-19 vaccine influences vaccine hesitancy with AOR 1.14 (95% CI, 0.61-2.15, p-value=0.676).

Conclusion: The study concludes that despite the efforts to communicate public health information to encourage people to overcome vaccine hesitancy and receive Vaccines, the reluctance to get vaccinated against COVID-19 remains higher than the acceptance rate among medical students.

Keywords: COVID-19, Hesitancy, Medical students, Vaccine

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Introduction

The Coronavirus disease of 2019, popularly known as COVID-19 or UVIKO-19 in the Swahili language, is still a global pandemic threat with little known about the impact of the disease and Vaccines on the human race. The pandemic has also impacted African nations, including Tanzania, with severe costs to lives, economies, and community social functioning (Konje et al. 2022; Pritchard et al. 2021). Unlike other control measures, the Vaccine is a promised solution to end the COVID-19 pandemic (Konje et al., 2022; Pritchard et al. 2021).

From that regard, to prevent an increase in COVID-19-related morbidity and death that is exacerbated by the nation's inability to handle severe and critical cases and the advent of novel virus strains, also, in line with the global response, like other least developing countries in Africa, Tanzania accepts and introduces vaccines as an essential measure to maintain community and population well-being. The Ministry of Health (MoH) has developed a guideline for COVID-19 vaccination to ensure immunization services align with the National Immunization Strategy (NIS) of Tanzania from 2021 to 2025 (Haonga 2022; MoH 2021). While there are several COVID-19 vaccines under development and use, the country will only use COVID-19 vaccines approved and registered by the Tanzania Medicines and Medical Devices Authority (TMDA).

In phase one, the vaccination strategy program targeted vulnerable groups, including people with high comorbidities, health workers (HWs), Community health workers (CHWs), business people who frequently travel, and medical students (Jain et al. 2021a; Kumar 2021). Phase two ideally focuses on the public health spectrum, that everyone is vulnerable to risks when it comes to COVID-19. Hence, vaccination programs must be provided to all eligible people at less cost if not fully subsidized by the government and other health entities internationally.

Until February 2023, however, the total number of eligible Tanzanians fully vaccinated against COVID-19 was slightly over 32,093,594, translating to about 45% of the total population and 87% of the target population above 18 years (MoH 2022; WHO 2022). In justifying why medical students are essential in the vaccination program/interventions, stakeholders in public health argue that it is crucial to increase vaccination rates among medical students since they are more likely to encounter COVID-19 in their practice, also, as the upcoming generation of clinicians and doctors must counsel reluctant individual who takes less precaution measure about the disease infection to at least accept and take the Vaccine (Lucia, Kelekar, and Afonso 2020; Ulbrichtova and Svihrova 2022).

Focusing on medical students, studies argue that medical students represent a significant part of the healthcare community and are active members of the COVID-19 response (Gala et al. 2022; Jain et al. 2021a; Lucia, Kelekar, and Afonso 2020; Ulbrichtova and Svihrova 2022). However, 61.9% of medical students in the USA are not vaccinated (Gala et al. 2022). In Uganda, a study revealed low levels of acceptance of 37.3% towards the COVID-19 vaccine among medical students, low self-perceived risks of COVID-19, and many had relied on social media that provided them with negative information (Kanyike et al. 2021). Hence, vaccine acceptability remains low among this group of future health professionals.

In Tanzania, little evidence is known on the determinants of COVID-19 vaccine hesitancy. Therefore, this study aims to determine the COVID-19 hesitancy level and associated factors among medical students. Furthermore, it aims to provide valuable insights and information that can be applied in future immunization campaigns/strategies to improve the vaccination rate among this particular group of future medical professionals during the pandemic.

Methods

Study design and setting.

This analytical cross-sectional survey was conducted to assess the COVID-19 vaccine hesitancy among medical students enrolled in different schools of Catholic University of Health and Allied Science (CUHAS) in Mwanza.

Study subjects and sampling methodology.
The study population comprised all undergraduate students enrolled in the Doctor of Medicine (DoM), Pharmacy, Radiology, Medical Lab, and Nursing programs at CUHAS in the Mwanza Region of Tanzania. These programs were selected because, during the second and third year of study, students in all five programs must complete clinical rotations and are, therefore, likely to have greater exposure to COVID-19 infection. The study sample size consisted of 593 respondents, and this estimation was done used Cochran's (1977) formula as well as including other details from previous report status of COVID-19 in Tanzania, whereby the prevalence of COVID-19 was 6.7 percent (MoH 2022), marginal error of 2.25 percent, and adjusted by 20 percent non-response rate. Furthermore, a simple random sampling technique was used to select students to participate in this study.

Data collection tools and procedures
Students were interviewed using a prepared structured questionnaire, and data on demographic patterns and information about their previous experiences were obtained. The questionnaire consisted of close-ended questions with three (3) sections. Section one consisted of questions about the demographic characteristics of respondents; section two, questions about vaccine hesitancy; section three consisted of questions about the acceptability of the COVID-19 vaccine. From that regard, the researcher developed a tool for data collection (a questionnaire) based on other similar studies (Hanna et al. 2022; Id et al. 2022; Islam et al. 2021; Kaur et al. 2022; Unicef, USAID, and CADRES 2021), such as the standard tools by the Centre of Disease Control (CDC) on assessing the acceptability of the COVID-19 vaccine (CDC, 2021) and WHO guide on communicating with the community about COVID-19 vaccine of 2021). Before going to the field, the tool was pre-tested among forty-one (41) medical students of the Muhimbili University of Health and Allied Science (MUHAS) to test the validity of the research instrument, including the consent form and questionnaire.

Data Analysis
Variables and measures
The study variables were grouped into major categories named dependent and independent variables. The dependent variable was the acceptability of Vaccines, whereby data on vaccination, willingness/intention to take, and recommend vaccines to others were collected. All the items of the dependent variable were self-reported and measured using a nominal scale. The independent variable was vaccine hesitancy, which was grouped into five (5) domains: convenience, politics of COVID-19 vaccination, perceived risk of infections, safety concerns, free riding, and vaccine deniers. All the independent variable items were self-reported and measured using a nominal and Likert scale.

Statistical analyses
Data collected were entered and managed using an open data kit (ODK collect) Android version 2022.2.2 under a confidential management procedure to maximize data quality. Thereafter, data from ODK was exported to Stata version 18.0 (Stata Corp, College Station, TX, USA) statistical software for analysis. Descriptive statistics were employed to describe the study background of participants. However, mean/median was used to summarize the age and scaled questions, while proportions and frequency tables were deployed to summarise categorical variables. Since the outcome variable was measured using the dichotomous scale, therefore, logistic regression analysis in this case bivariable (COR), and multivariable (AOR) analysis was carried out to identify variables in hesitancy factors having a significant association with vaccination status, the p-value of less than 0.05 (significant level) was considered statistically significant.

Ethical Consideration

Every participant, in this case, a medical student, was fully informed about the study and asked to participate voluntarily. The data collected was used only for this study and kept confidential. Participants' identities were replaced by codes and kept secure to ensure confidentiality. Participants were assured that refusing to participate or withdraw from the study was and will not result in any penalties or affect a student's rights while at the university. The study proposal secured ethical clearance from the Research and Publication Ethical Committee at MUHAS (Reference number: BU/03/5026/Vol.III/1196). Additionally, permission to conduct the data collection activity was obtained from the Catholic University of Health and Allied Sciences (CUHAS) before the study began. All ethical considerations were considered to ensure that the study was conducted ethically and that the rights and welfare of the participants were protected throughout the study.

Results

Demographic Profile of the Students

In total, 580 medical students were enrolled in the study; the median age was 24, interquartile range [IQR, 23-25 years]. More than half of the students (52.4%, n=301) were male compared to 47.6% (n=274) female. 92.0% (n=526) of all surveyed students reported being single/unmarried, 6.8% (n=39) reported having a chronic disease, and 15.8% (n=90) reported ever being involved in any COVID-19 response team during the management of the pandemic. Regarding the main source of information about the COVID-19 pandemic, 70% (n=406) of all medical students reported using television/media websites, followed by 56.4% (n=327) relayed on Friends/family members/lectures, while 53.5% (n=310) used Social Platforms (Facebook, WhatsApp, and Twitter., etc.) (Table 1).

Table 1: Demographics Characteristics (N=580)

Variable	Frequency	Percentage
Age (median, [IQR])	24, [23-25]	
Sex (n=574)		
Male	301	52.4
Female	273	47.6
Marital status (n=572)		
Not married	526	92.0
Married	46	8.0
Programme (BSc)		
Medicine	346	59.7
Pharmacy	62	10.7
Nursing	85	14.7
Laboratory	62	10.7
Radiology	25	4.3
Any chronic diseases (n=573)		
No	534	93.2
Yes	39	6.8
Ever been part of any COVID-19 response team/program (n=570)		
No	480	84.2
Yes	90	15.8
The main source of information †		

Variable	Frequency	Percentage
Ministry of Health website	259	44.7
World Health Organization (WHO)	282	48.6
Primary care physician	84	14.8
Scientists/Scientific releases	118	20.3
Pharmacists	53	9.1
Social Platform (Facebook, WhatsApp, Twitter., etc.)	310	53.5
Friends/family members/lectures	327	56.4
Television/media website	406	70.0

† = multiple responses

Acceptability of COVID-19 Vaccine among Medical Students

The study assesses the acceptability status of the COVID-19 vaccine among medical students (Table 2). Results indicate that about one-quarter of medical students had received any COVID-19 vaccine 24.4% (n=135, 95% CI, 20.9%-28.2%). Further, only 24.6% (n=130) intend to take the COVID-19 vaccine in the future, in this case, in the next three (3) months. Half of the medical students reported having close family/friend/relative already vaccinated against COVID-19, While more than three-quarters of medical students are likely to recommend the Vaccine to other close relatives and friends (i.e., 54.5% somewhat likely and 27.9% extremely likely).

Moreover, the study used the percentage scale measurement of 1-10 to measure the level of trust and hesitancy about the COVID-19 vaccine among medical students. The purpose was to establish the proportion of medical students' trust and hesitation to get COVID-19 vaccines. Slightly more than half of the students reported trusting the COVID-19 vaccine, with a mean of 5.81 (SD=2.765). Similarly, to the hesitancy level, slightly half of the students reported having moderate hesitancy of the COVID-19 vaccine with a mean of 5.83 (SD=2.823) (Table 2).

Table 2: Acceptance of COVID-19 Vaccine among Medical Students

Variable	Frequency	Percentage
Ever received any dose of the COVID-19 vaccine (n=553)		
No	418	75.6
Yes	135	24.4
Trust of COVID-19 vaccine (Mean, SD)	5.81, 2.765	
Intention to the Vaccine in the next three (3) months		
No	399	75.4
Yes	130	24.6
The hesitancy of the COVID-19 vaccine (Mean, SD)	5.83, 2.823	
Close family/friend/relative already vaccinated (n=578)		
No	90	15.6
Not sure	199	34.4
Yes	289	50.0
Recommend Vaccine to others (n=578)		
Not at all likely	102	17.6
Somewhat likely	315	54.5
Extremely likely	161	27.9

Hesitancy of COVID-19 Vaccine Among Medical Students

The study was to identify persistent hesitancy factors that hinder medical students from getting the COVID-19 vaccine even after implementing public health campaign intervention. The purpose was to highlight the key issues that stakeholders in health sectors can focus on to impact public health behavior among medical students.

The hesitancy factors were grouped into six (6) domains: convenience, political issues, perceived risk of infections, safety concerns, free riding, and vaccine denials (Table 3). On the convenience spectrum, slightly more than half of the medical students (54.3%, n=315) do not trust the efficacy of the COVID-19 vaccine, followed by 37.4% (n=217) do not trust the safety of COVID-19 vaccine, and 28.8% (n=167) do not trust the safety of any vaccine. Further, more than half of the medical students affirm that there is too much politics behind the COVID-19 vaccine in Tanzania (i.e., 40.7% agreed and 28.5% strongly agreed). Likewise, 54.4% (n=314) of all medical students affirmed that they did not trust the government health officials in promoting the COVID-19 vaccine (i.e., 39.5% Agreed and 14.9% Strongly agreed).

Regarding the perceived risk of infections, 30.7% (n=178) of students are little concerned about getting COVID-19 infections. While on the Vaccine's safety, 42.7% (n=247) affirm the Vaccine to be moderately safe. Also, 48.5% (n=281) are somewhat likely to take the COVID-19 vaccine if it helps to protect themselves and others. Nevertheless, one quarter (25.1%, n=140) of all students affirm that they are not eligible to get a COVID-19 vaccine, and 26.2% (n=152) relayed the benefits from the protection and overall vaccination efforts of others already vaccinated. Lastly, 18.6% (n=215) affirmed never taking the COVID-19 vaccine even if it is made mandatory by the university (Table 3).

Table 3: Hesitancy Factors Persist Even After Public Health Campaign Intervention among Medical Students (n=580)

Variable	N (%)
Convenience†	
Do not trust the safety of ANY vaccine	167(28.8)
Do not trust the safety of COVID-19 vaccines	217(37.4)
Do not trust the efficacy of COVID-19 vaccines	315(54.3)
Not afford to pay for COVID-19 vaccines	87(15.0)
Not afford to pay for transport to get to a COVID-19 vaccination location	66(11.4)
Politics of COVID-19 vaccination	
There is too much politics behind the COVID-19 vaccine in Tanzania.	
Strongly disagree	57(9.8)
Disagree	122(21.0)
Agree	236(40.7)
Strongly agree	165(28.5)
Don't trust government health officials to promote the COVID-19 vaccine.	
Strongly disagree	73(12.6)
Disagree	191(33.0)
Agree	228(39.5)
Strongly agree	86(14.9)
Perceived risk of infections	
Concerned about getting COVID-19	
Not at all concerned	78(13.5)
A little concerned	178(30.7)
Moderately concerned	166(28.6)
Very concerned	158(27.2)

Variable	N (%)
Safety concerns	
Concerned about the Safety of COVID-19 vaccine	
Not at all safe	74(12.8)
A little safe	152(26.3)
Moderately safe	247(42.7)
Very safe	105(18.2)
Likelihood of taking COVID-19 vaccine if it helps protect others	
Not at all likely	87(15.0)
Somewhat likely	281(48.5)
Extremely likely	211(36.4)
Freeriding	
If eligible to get a COVID-19 vaccine	
No	140(25.1)
Yes	417(74.9)
Benefit from the protection and overall vaccination efforts of others who are already vaccinated	
Strongly disagree	79(13.6)
Disagree	99(17.1)
Neutral	249(43.0)
Agree	116(20.0)
Strongly agree	36(6.2)
Vaccine deniers	
Take the COVID-19 vaccine if mandated by the heads of your institution.	
No	107(18.6)
Not sure	252(43.9)
Yes	215(37.5)

† = *multiple responses*

Furthermore, the researcher used logistic regression to identify factors in hesitancy domains associated with not receiving the COVID-19 vaccine (i.e., 1=No and 0=Yes) (Table 4).

The bivariate results revealed that being part of any COVID-19 response team/program reduces the chance of vaccine denial compared to being involved with COR 0.26 (95% CI, 0.16-0.42, p-value<0.001). The odds remain unchanged even during multivariate analysis AOR 0.29 (95% CI, 0.16-0.54, p-value<0.001). Medical students who do not trust the safety of the COVID-19 vaccine are more likely not to be vaccinated compared to those who trust the safety with COR 1.79 (95% CI, 1.17-2.75, p-value=0.007). The odds remain unchanged even during multivariate analysis AOR 0.1.89 (95% CI, 1.11-3.21, p-value=0.019). Also, students who do not trust the efficacy of the COVID-19 vaccine are more likely not to be vaccinated compared to those who trust the efficacy with COR 2.47 (95% CI, 1.65-3.68, p-value<0.001) and AOR 2.96 (95% CI, 1.80-4.86, p-value<0.001) during bivariate and multivariate analysis respectively. Medical students who are very concerned about getting COVID-19 infectious are less likely to deny the Vaccine compared to those who are not all concerned with COR 0.17 (95% CI, 0.08-0.36, p-value<0.001) and AOR 0.40 (95% CI, 0.16-0.98, p-value=0.045). On free riding, medical students who affirm to be eligible to get a COVID-19 vaccine were less likely to denial the Vaccine compared to those who affirm not being eligible with COR 0.15 (95% CI, 0.07-0.31, p-value<0.01) and AOR 0.31 (95% CI, 0.31, 0.13-0.75, p-value=0.009) respectively.

However, some of the factors were only significant during bivariate or multivariate analysis. This includes the fact medical students who are extremely likely to take the COVID-19 vaccine if it helps protect others were less likely to deny the Vaccine compared to those who are not at all likely with COR 0.12 (95% CI, 0.05-0.27, p-value<0.001)

while during multivariate analysis AOR 0.47, (95% CI, 0.17-1.32, p-value=0.152). Lastly, the medical students who intend to accept the COVID-19 vaccine if it is made mandatory by the head of the institution (university) were less likely to deny the Vaccine compared to those who did not at all accept with COR 0.20 (95% CI, 0.10-0.38, p-value<0.001) while AOR 0.48 (95% CI, 0.22-1.03, p-value=0.060).

Table 4: Hesitancy factors associated with COVID-19 vaccine acceptability among medical students even after public health campaign intervention.

Variables	Ever received COVID-19 Vaccine		COR, 95% CI	p-value	AOR, 95% CI	p-value
	Yes N (%)	No N (%)				
Ever been part of any COVID-19 response team/program.						
No	91(19.9)	366(80.1)	1		1	
Yes	43(48.9)	45(51.1)	0.26, 0.16-0.42	**<0.001**	0.29, 0.16-0.54	**<0.001**
Do not trust the safety of COVID-19 vaccines.						
No	98(28.2)	249(71.6)	1		1	
Yes	37(18.0)	169(82.0)	1.79, 1.17-2.75	**0.007**	1.89, 1.11-3.21	**0.019**
Do not trust the efficacy of COVID-19 vaccines.						
No	83(33.6)	164(66.4)	1		1	
Yes	52(17.0)	254(83.0)	2.47, 1.65-3.68	**<0.001**	2.96, 1.80-4.86	**<0.001**
There is too much politics behind the COVID-19 vaccine in Tanzania.						
Disagree	45(26.0)	128(74.0)	1		1	
Agree	90(23.7)	290(76.3)	1.13, 0.75-1.71	0.555	1.14, 0.61-2.15	0.676
Don't trust government health officials to promote the COVID-19 vaccine.						
Disagree	64(25.0)	192(75.0)	1		1	
Agree	71(24.1)	224(75.9)	1.05, 0.71-1.55	0.800	0.72, 0.39-1.32	0.287
Concerned about getting COVID-19						
Not at all concerned	10(13.2)	66(86.8)	1		1	
Moderately concerned	52(16.3)	268(83.8)	0.78, 0.37-1.62	0.506	1.04, 0.44-2.48	0.921
Very concerned	73(46.5)	84(53.5)	0.17, 0.08-0.36	**<0.001**	0.40, 0.16-0.98	**0.045**
Likelihood of taking COVID-19 if it helps protect others						
Not at all likely	7(8.2)	78(91.8)	1		1	
Somewhat likely	40(15.3)	221(84.7)	0.50, 0.21-1.15	0.103	0.81, 0.29-2.28	0.688
Extremely likely	88(42.7)	118(57.3)	0.12, 0.05-0.27	**<0.001**	0.47, 0.17-1.32	0.152
If eligible to get a COVID-19 vaccine						
No	8(6.1)	123(93.9)	1		1	
Yes	124(30.9)	278(69.2)	0.15, 0.07-0.31	**<0.001**	0.31, 0.13-0.75	**0.009**

Variables	Ever received COVID-19 Vaccine		COR, 95% CI	p-value	AOR, 95% CI	p-value
	Yes N (%)	No N (%)				
Benefit from the protection and overall vaccination efforts of others who are already vaccinated						
Disagree	49(28.5)	123(71.5)	1		1	
Neutral	49(20.9)	186(79.2)	1.51, 0.96-2.39	0.076	1.28, 0.71-2.30	0.405
Agree	36(24.8)	109(75.2)	1.21, 0.73-1.99	0.464	1.29, 0.67-2.51	0.438
Take the COVID-19 vaccine if mandated by the heads of your institution.						
No	14(13.3)	91(86.7)	1		1	
Not sure	30(12.6)	208(87.4)	1.07, 0.54-2.11	0.853	1.23, 0.56-2.69	0.607
Yes	88(43.1)	116(56.9)	0.20, 0.10-0.38	**<0.001**	0.48, 0.22-1.03	0.060

Discussion

This study about acceptability focuses on vaccination status against COVID-19 among medical students and establishes the hesitancy level. While only a quarter of them reported vaccinating against COVID-19, more than half of medical students hesitate or are reluctant to receive the Vaccine (Kanyike et al. 2021; Mohammed et al. 2022). The high level of vaccine hesitancy among medical students is concerning, given their role as future healthcare professionals. It is crucial for medical students to not only have access to accurate and reliable information about the Vaccine but also to have a strong belief in its safety and effectiveness (Gala et al. 2022; Lucia, Kelekar, and Afonso 2020; Ulbrichtova and Svihrova 2022). Their acceptance and endorsement of the Vaccine can significantly influence public perceptions and attitudes toward vaccination. It is evident that hesitance is due to concerns about the Vaccine's safety, efficacy, and long-term effects Addressing these concerns and providing clear, evidence-based information is essential to build trust and increase vaccine acceptance among medical students (Gala et al. 2022; Habib et al. 2022; Jain et al. 2021b; Kanyike et al. 2021; Mohammed et al. 2022).

Moreover, interventions and educational programs should be developed to specifically target medical students and address their unique concerns. These programs should focus on providing accurate information about the COVID-19 vaccine, addressing any misconceptions, and emphasizing the importance of vaccination in protecting public health. Additionally, fostering open and respectful dialogue about vaccine hesitancy among medical students can help address their concerns and provide a platform for discussion and clarification.

In addition, the concept of freeriding, as measured by the perception of eligibility for the Vaccine, is an important factor to consider in

understanding vaccine hesitancy among medical students. Freeriding refers to individuals who may feel they are not directly impacted by a particular issue or believe that others will take responsibility for addressing the issue, leading to a lack of personal motivation to take action. In the context of COVID-19 vaccination, the low odds of hesitancy among medical students who perceive themselves as eligible for the Vaccine can be attributed to several factors. First, eligibility criteria are often based on established guidelines prioritizing high-risk individuals or those in specific occupations, such as healthcare workers and people with chronic or long-term diseases (Abila et al. 2020).

Therefore, medical students, being part of the healthcare profession and response team, may perceive themselves as eligible due to their role in patient care and exposure to infectious diseases. This perception of eligibility may contribute to a stronger sense of responsibility and a greater understanding of the importance of vaccination. Secondly, medical students are likely to have a higher level of knowledge and understanding of vaccine efficacy and safety due to their education and training in healthcare. They are more likely to be familiar with the scientific evidence supporting the COVID-19 vaccine and may have greater trust in the regulatory processes and guidelines governing its use. This increased knowledge and trust can reduce hesitancy and increase their willingness to accept the Vaccine.

While the lack of statistical significance may indicate that the relationship between political concerns, distrust in government health officials, and vaccine hesitancy among medical students is not strongly supported by the data, it is still important to acknowledge the potential influence of these factors (Bonell et al. 2020; Tatar and Wilson 2021).

The perception of politics influencing the Vaccine can contribute to hesitancy by fostering skepticism and doubts about the safety and efficacy of the Vaccine. Similarly, lacking trust in government health officials may undermine confidence in their recommendations and communication efforts (Randolph and Viswanath 2004). Therefore, addressing these concerns and building trust is crucial in promoting vaccine acceptance among medical students. It is essential to provide transparent and reliable information about the Vaccine's development, regulatory processes, and the scientific evidence supporting its safety and effectiveness. Open dialogue, clear communication channels, and engagement with medical students can help address their specific concerns and provide reassurance. Collaborative efforts between healthcare institutions, government bodies, and educational institutions can play a vital role in building trust and countering vaccine hesitancy.

Conclusion

The study concludes that despite the efforts communicated public health information to encourage people to overcome vaccine hesitancy and receive Vaccine, the reluctance to get vaccinated against COVID-19 remains higher than the acceptance rate among medical students.

Recommendation

The ministry of health (MoH) and other stakeholders in Health sectors should implement targeted communication and educational in this case campaigns specifically designed for medical students. These campaigns should focus on providing accurate, evidence-based information about the COVID-19 vaccine, addressing concerns related to politics, and building trust in government health officials. Moreover, utilize various channels, such as workshops, seminars, online platforms, and peer-to-peer discussions, to effectively reach and engage medical students.

Limitation of the study

This study was conducted only among medical students in the Mwanza region, the results from this study may be difficult to project to all medical schools in Tanzania. Likewise, this study prioritizes understanding the core factors behind student vaccine hesitancy, such as misinformation exposure, while acknowledging the potential role of communication channels. Finally, the questionnaire was self-administered, suggesting the possibility of information bias. Therefore, to enhance generalizability, the researcher ensured the study sample was large enough to include all medical students from all Five (5) programs. This helped to ensure that the findings represent a wider range of medical

students' perspectives. However, the findings of this study can be applied with caution and within the context of medical students so as to impact the public health behaviour among this targeted group across the Tanzania context.

Finally, a pre-test of the questionnaire and revising for clarity and content were done before releasing the final form. This helped minimize the risk of participants misunderstanding the questions and ensures clarity as well address information bias associated with self-administered questionnaires.

Data availability
The data that supports the findings of this study cannot be shared publicly but will be available upon request of a researcher.

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Synergy and Antagonism in Antimalarial Crude Extract Combinations

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Abstract

Background

Malaria accounts for around 4.8% of all recorded fatalities in Tanzania. Medicinal plants such as *Caesalpinia bonducella, Azadirachta indica,* and *Annickia kummeriae* have demonstrated promise in treating many diseases, including malaria. However, their combined activity against malaria has not been documented. Combination therapy using some medicinal plants with antimalarial activities may enhance safety and efficacy and reduce the evolution of parasite resistance.

Objectives

This study aimed to investigate antiplasmodium activities of different combinations of crude extracts from selected medicinal plants. *Azadirachta indica leaves, Annickia kummeriae* and *Caesalpinia bonducella* were extracted using dichloromethane (DCM).

Methods

An in vivo acute toxicity study of both individual and combined crude extracts was carried out according to Chinedu *et al.,* 2015. The *in vivo* antiplasmodial activity of individual and combined crude extracts was performed in mice inoculated with *Plasmodium berghei* (ANKA strain) using Peters's 4-day suppressive test.

Results

Individually, *Caesalpinia bonducella* crude extracts exhibited the highest *in vivo* antiplasmodial efficacy (91% parasite suppression) than *A. kummeriae* (73% parasite suppression) and *A. indica* (60% parasite suppression) at 800 mg/kg/day. The *A. indica* and *A. summarize combinations and A. indica* and *C. bonducella* demonstrated higher antiplasmodial activity (synergism-combination index 0.29 and 0.97, respectively) than their constituents. However, combining *A. kummeriae* and *C. bonducella* produced the lowest antiplasmodial activity (antagonism- combination index 40.67) than its extracts. The high antiplasmodial potencies (ED_{50}) demonstrated by AiAk and AiCb are significant and critical results for traditional, complementary and alternative medicine.

Conclusion

Therefore, these preliminary findings suggest that AiAk and AiCb are potential antiplasmodium herbal therapies. Further research should be undertaken to investigate the antiplasmodium effect of AiAk and AiCb in humans.

Keywords: Complementary and Alternative Medicine, Synergist- anti-plasmodium activities *Caesalpinia bonducella, Azadirachta indica, Annickia kummeriae*

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Introduction

Malaria is the most critical health problem in Tanzania, where it causes 3.1% of all malaria cases and deaths and 4.1% of all deaths worldwide in 2021 (WHO, 2021). This means that preventing and controlling malaria should be a top priority. According to recent data, about 90% of the population in mainland Tanzania live in malaria-transmission areas. Strategies used for malaria control include malaria case management, malaria vector control using ITN, and malaria intermittent treatment in pregnant mothers (WHO, 2017). Malaria control in Tanzania through treatment faces challenges due to widespread antimalarial drug resistance (Schönfeld, 2007; Kumar *et al.,* 2015).

Drug resistance to antimalarial drugs has become a significant hurdle in the successful treatment of the *P. falciparum* infection and has contributed significantly to global malaria-related mortality (WHO, 2017). *Plasmodium falciparum* has resisted nearly all current antimalarial drugs, which hinders malaria control strategies (Arrow *et al.,* 2004). Therefore, developing new effective and affordable anti-malarial drugs to combat this disease is essential.

The development of new antimalarials from highly active natural products is crucial in order to overcome the increasing resistance of *Plasmodium* to malarial drugs (Bero, 2009; Akin-Osanaiye *et al.,* 2013; Moustapha *et al.,* 2018). Historically, medicinal plants have served as sources of new pharmaceutical products like quinine and artemisinin (Newman *et al.,* 2000; Koehn, 2005) and inexpensive starting materials for synthesising many known drugs. Lemma *et al.,* 2017 identified 977 plant species with potential antiplasmodial activities.

Accordingly, about 70 to 80% of people in developing countries rely on using herbal remedies for malaria treatment worldwide (WHO, 2015). *In vivo, antiplasmodial activity of some individual medicinal plants has* indicated relatively low parasitaemia suppression. Studies that assess the interaction between crude extracts from medicinal plants with antiplasmodial activity are scarce. Evidence suggests that the interaction of different crude extracts may be vital in enhancing therapeutic efficacy, optimizing dosage, increasing the level of target inhibition, reducing or delaying the development of drug resistance and simultaneous reduction of toxic effects (Williamson, 2001; Bero, 2009; Ginsburg & Deharo, 2011).

Several studies on antiplasmodial activity of *Azadirachta indica, Annickia kummeriae* and *Caesalpinia bonducella* indicated antiplasmodial activity ranging from 30% to 70% (Moshi *et al.,* 2009; Nondo *et al.,* 2016; Akin-Osanaiye *et al.,* 2013; Malebo *et al.,* 2015). However, the nature of the interaction between the combinations of different crude extracts from these plants on plasmodium infection has not been studied. Therefore, this study intended to use a mice model to assess the in vivo antiplasmodial activity of individual crude extracts of selected medicinal plants and evaluate their interactional antiplasmodial effects. Specifically, we determined the antiplasmodial activity of A. indica, A. kummeriae, and C. bonducella in mice infected with Plasmodium berghei. We evaluated the interaction between combined crude extracts from *A. indica, A. kummeriae,* and *C. bonducella* in mice infected with *Plasmodium berghei.*

It was postulated that the combined utilization of crude extracts would yield greater efficacy than their application in animal models. The findings of this study will be helpful in the quest for more effective herbal remedies for malaria and the development of novel anti-malarial medications based on complementary, alternative, and traditional medicine.

Materials and methods
Collection and Authentication of Plant Materials

Three medicinal plants were harvested from different areas in Tanzania. *Azadirachta indica* leaves and *Caesalpinia bonducella* roots were collected from Makuburi and Pugu, respectively, in Dar es Salaam, whereas the *Annickia kummeriae* roots were collected from Kisiwani Kisarawe, Pwani. The collected medicinal plants were identified in the Department of Botany, University of Dar es Salaam. The voucher specimens were deposited for future use.

Preparation and Extraction of Plant Materials
The harvested plant materials were air-dried for three weeks at room temperature and then pulverized into coarse granules ready for extraction. About 150 g of each of the selected plant materials (*A. indica, A. kummeriae* and *C. bonducella*) was extracted using the cold maceration method by soaking in 1 litre of Dichloromethane at room temperature for 24 hours and filtered through Whatman filter paper number 1 to remove debris. The procedure was repeated twice to ensure exhaustive extraction of plant materials. The extracts obtained were pooled together. The filtrates obtained were then concentrated in a rotary evaporator to remove solvent at 45°C under reduced pressure to prevent the thermal decomposition of labile compounds. The extracts were dried on air and kept in a freezer at -20°C until the day of use.

Phytochemical Analysis of Crude Extracts
The crude extracts were subjected to qualitative phytochemical analysis (based on chemical reactions) of secondary metabolites, including alkaloids, flavonoids, tannins, steroids, phenolics, saponins, cardiac glycosides and terpenoids (Mamta & Jyoti, 2012; Trease & Evans, 2002).

***In vivo* Antiplasmodial Activity Assay and Study Design**
In vivo, antiplasmodial activity of individual and combined extracts was determined using the 4-day suppressive test described by Peters W 1975. An experimental study design was employed whereby 150 albino mice were used (Figure 1). The age and size of the animal were considered when making the choice. Individual crude extracts were tested at three nontoxic doses (200 mg/kg, 400 mg/kg, and 800 mg/kg) (Figure 1). The same procedure was followed when crude extract was used in combination.
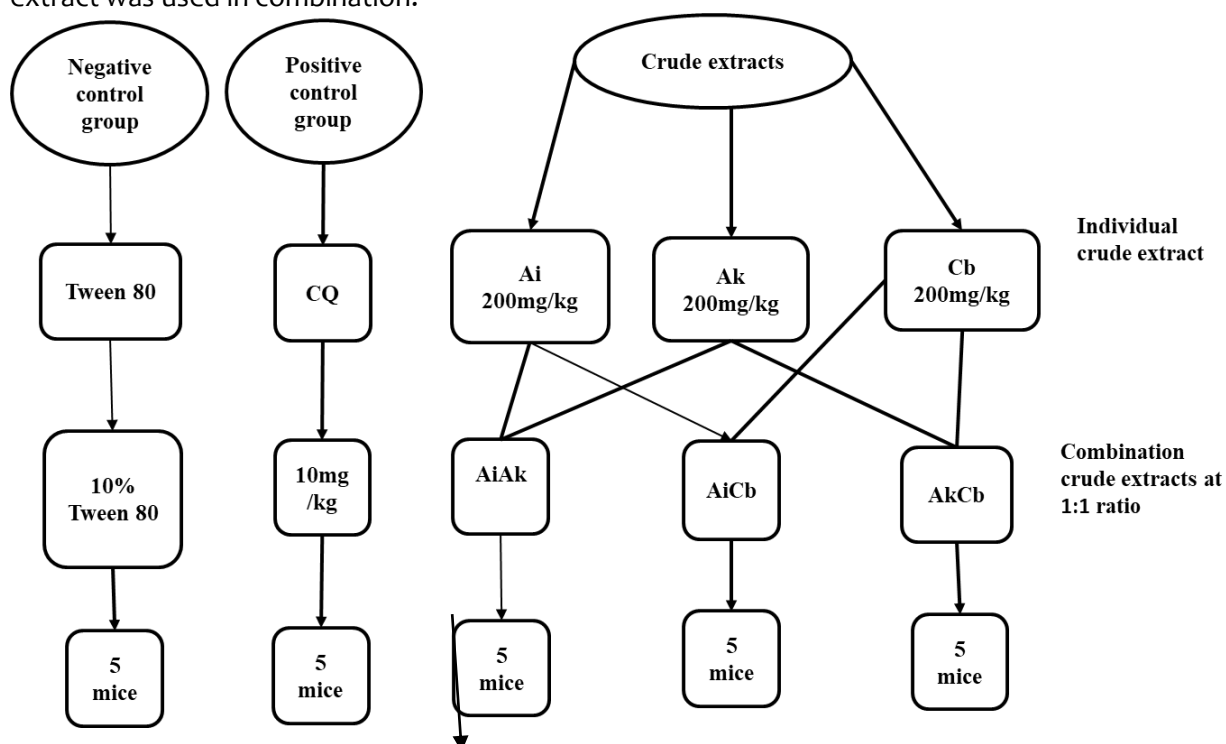

Figure 1: Study design to assess antiplasmodial activity for individual and combined crude extracts for all selected dosages.

Study Animals

Swiss albino mice weighing 20–30 g of either sex, raised at the University of Dar es Salaam, Department of Zoology and Wildlife Conservation were used in this study. Animals were acclimatized to the laboratory conditions and supplied with food and water *ad libitum* for two weeks before being used for the test. The animals were handled according to the National and International Guidelines for Handling of Laboratory Animals as well as per the Organization for Economic Cooperation Development (OECD) Guideline no. 425 and the study received ethical clearance from the University of Dar es Salaam and the National Institute for Medical Research (NIMR) in Tanzania.

Malaria Parasites and Preparation of Infected Red Blood Cells Suspension

Blood stage *P. berghei* ANKA parasites used in the study were kindly donated by Dr. Lindsay Stewart of the Department of Pathogen Molecular Biology, London School of Hygiene and Tropical Medicine, United Kingdom to Muhimbili University.

Donor mice with high parasitaemia were anesthetized by diethyl ether; blood was collected through the sinus vein and diluted with sterile normal saline (0.9% w/v sodium chloride) to make a suspension of 1×10^8 infected red blood cells (iRBCs) per mL, which was used to infect test mice. Each mouse was inoculated with 2×10^7 iRBCs with *P. berghei* in 0.2 mL via tail vein and left for three hours before crude extracts administration.

Dosage Preparation and Administration of Extracts to *P. berghei* Infected Mice

Each crude extract was dissolved in 10% Tween 80 to make individual dosages of 200 mg/kg, 400 mg/kg and 800 mg/kg (Nondo *et al.,* 2016). Then dosages at 1:1 ratios for each combination were prepared. Before dose administration, the body weight of each infected mouse was assessed, and the dose administered crudely was calculated according to the body weight.

Administration of the Extracts to *P. berghei* Infected Mice

After three hours post-infection, the mice were randomly allocated into groups of 5 mice each: The negative control group received 10% Tween 80 (5 ml/kg/day), the positive control group received chloroquine (10 mg/kg/day), and treatment groups received different doses of extracts (200, 400, or 800 mg/kg/day). Dose administration was done orally, once daily, starting on the day of infection and continued for four doses while parasitaemia was determined on day 5.

Malaria Parasitaemia Determination

On the fifth-day post P. berghei infection, thin blood smears were prepared from a drop of blood taken from the tail snip of each mouse. The smears were fixed with methanol and stained with 10% Giemsa solution. Malaria parasitaemia was determined under a microscope (×100 magnification). The number of parasitized erythrocytes was examined under three different fields on each slide and averaged to give the parasitaemia of individual animals. The percentage parasitaemia and suppression were calculated for all the doses of plant extracts using formulas.

The percentage of parasitaemia was then calculated using the formula:

$$\% \text{ Parasitaemia} = \frac{Number\ of\ infected\ RBCs}{Total\ number\ of\ RBCs} \times 100\%$$

The extract activities were also determined by calculating the percentage of parasitaemia suppression by using the formula:

$$\% \text{ Suppression} = \frac{Parasitemia\ of\ negative\ control - Parasitemia\ of\ test}{Parasitemia\ of\ negative\ contol} \times 100\%$$

Data Analysis
Determination of Antiplasmodial Activity of Individual Extracts in *P. berghei* Infected Mice
Data from all experimental animals were tested for conformity to normality (Kolmogorov–Smirnov's test) and variance homogeneity. The results were expressed as mean ± standard error of the mean (SEM). One-way ANOVA was used to establish differences between mean parasitaemia suppression between groups. Also, Tukey's comparison test was used to compare the antiplasmodial ability of crude extracts in lowering the number of parasitaemia in the control group. Significant differences were considered when P<0.05.

Determination of Interaction Effects between DCM Crude Extracts in *P. berghei* Infected Mice
A dose-response curve was generated for both individual and combination extracts to analyse the interaction effect between different extract combinations. The logarithm of their dose was plotted against the activity to obtain a nonlinear regression curve-fitting (Bell, 2005). The ED_{50}, a dose or amount of drug that produces a healing response or desired effect in 50% of the subjects taking it, was then determined from their nonlinear regression equations to determine the type of interaction. Synergy was considered when the effect of the combination was more significant (lower ED_{50}) than the one expressed from individual plant extract doses. At the same time, antagonism was considered when the combination effect was lower (higher ED_{50}) than individual plant extracts (Williamson EM, 2001). Furthermore, according to Gathirwa *et al.,* 2007 and Tarkang *et al.,* 2014 the interaction effects were evaluated by calculating the combination index (CI), a quantitative measure of drug combination effects and the obtained values were compared to the standards; whereby synergistic reaction was considered when CI < 1, additive 1 < CI < 2 and antagonistic when CI > 2.
The formula calculated the combination index:

$$\text{Combination index} = \frac{ED50 \text{ Extract A in combination}}{ED50 \text{ Extract A alone}} + \frac{ED50 \text{ Extract B in combination}}{ED50 \text{ Extract B alone}}$$

Results
Phytochemical Analysis
Phytochemical analyses of crude extracts from all plant species collected showed *Caesalpinia bonducella* (roots) with more phytometabolites than *A. indica* (leaves) and *A. kummeriae* (roots) (**Table 1**)

Table 1:   **Phytochemical analysis of *Azadirachta indica, Annickia kummeriae* and *Caesalpinia bonducella* DCM crude extracts**

SN	Phytochemical Test	Medicinal Plant		
		A. Indica	*A. Kummeriae*	*C. bonducella*
1.	Alkaloids	+	+	+
2.	Flavonoids	-	-	+
3.	Tannins	-	-	-
4.	Steroids	-	-	-
5.	Phenolics	-	-	-
6.	Saponins	-	-	-
7.	Cardiac glycosides	-	-	+
8.	Terpenoids	-	-	+

+ = present; **-** = absent

Antiplasmodial Activity of *A. indica*, *A. kummeriae* and *C. bonducella* DCM crude extracts

Parasitaemia suppression in *P. berghei*-infected mice with *A. indica, A. kummeriae* DCM *C. bonducella* extract increased significantly in a dose-dependent manner, with a high dosage of 800 mg/kg exhibiting a percentage of parasite suppression approaching that of the positive control (**Table 2**). Of the three DCM crude extracts, *C. bonducella* had the highest antiplasmodial activity, followed by *A. kummeriae* and *A. indica*, which showed the lowest antiplasmodial activity.

Table 2: The summary of antiplasmodial activity of dichloromethane extract of *A. indica, A. kummeriae* and *C. bonducella* DCM crude extracts at different doses against *P. berghei* ANKA

Treatment Group	Mean percentage parasitaemia at day 5±SEM (n=5)			Mean percentage suppression of parasitaemia at day 5		
	A. indica	*A. kummeriae*	*C. bonducella*	*A. indica*	*A. kummeriae*	*C. bonducella*
Negative Control (10% Tween 80)	52.09 ± 2.04	50.55 ± 0.00	53.73 ± 2.41	0	0	0
200 mg/kg	40.15 ± 2.08	33.66 ± 1.01***	22.23 ± 1.43***	22.93	33.41	58.61
400 mg/kg	31.32 ± 2.39**	27.74 ± 4.10***	10.42 ± 5.44***	39.88	45.12	80.60
800 mg/kg	20.72± 6.32***	13.51 ± 1.82***	4.98 ± 7.54**	60.24	73.26	90.72
Positive Control (CQ 10 mg/kg)	2.01 ± 0.83***	2.01 ± 0.83***	2.01 ± 0.83***	96.63	96.63	96.63

Note: * means, the mean percentage parasitaemia of the extracts were extremely significantly different from that of negative control**

Antiplasmodial Activity of Combined DCM Crude Extracts

On day five post-infection, the percentage parasitaemia was measured in *P. berghei*-infected mice receiving combinations of *A. indica* and *C. bonducella* (AiCb) and *A. indica* and *A. kummeriae* (AiAk) at three different doses (200, 400, and 800 mg/kg). Additionally, the percentage parasitaemia suppression was computed and recorded. The *in vivo* antiplasmodial activity of combined crude extracts also exhibited a dose-dependent suppression of parasite growth. The AiCb combination had higher antiplasmodial activity compared to *A. indica* and *C. bonducella* extracts when used individually. The same trend was observed in AiAk combination that also demonstrated higher antiplasmodial activity compared to its constituent extracts when used individually (Figure 2, 3 and 4). On the other hand, the combined crude extract of AkCb showed a lower percentage of parasitaemia suppression than the individual crude extracts, indicating antagonistic actions.
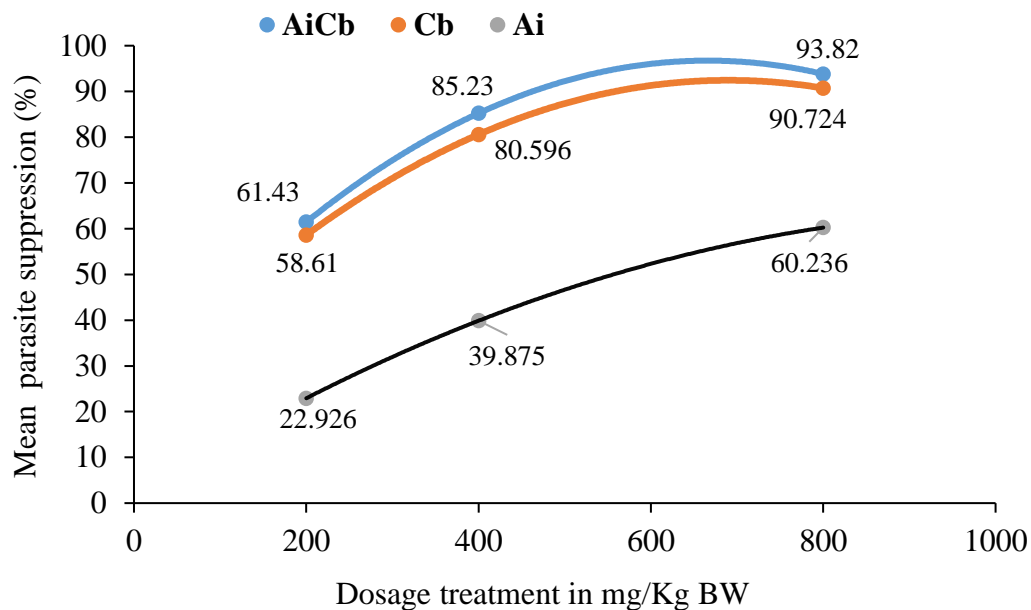
Figure 2: Percent parasitaemia suppression by AiCb combination in comparison
to individual crude extracts in experimentally *P. berghei-infected* mice

Dose-Response Curves of AiAk, AiCb and AkCb crude extracts Combinations

The potency of separate and combined crude extracts was measured by determining the ED_{50}, the dose or amount of medication that generates a healing response or desire effect in 50% of participants. The ED_{50} for individual and combined crude extracts was determined on day 5 post infection (Figure 6, 7 and 8). Individually, the ED_{50} values were low in *C. bonducella* (126.63), moderate in *A. kummeriae* and higher in *A. indica* as shown in Table 3 and Figure 4. AiCb and AiAk combinations had lower ED_{50} values compared to individual extracts. However, the ED_{50} for the AkCb combination was much higher compared to its constituents, demonstrating antagonistic interaction (Figure 5, Table 3). Among the formed combinations, the effective dose (ED_{50}) value was lower in AiAk, followed by AiCb and higher in AkCb combination (Figure 5 and - Table 3).
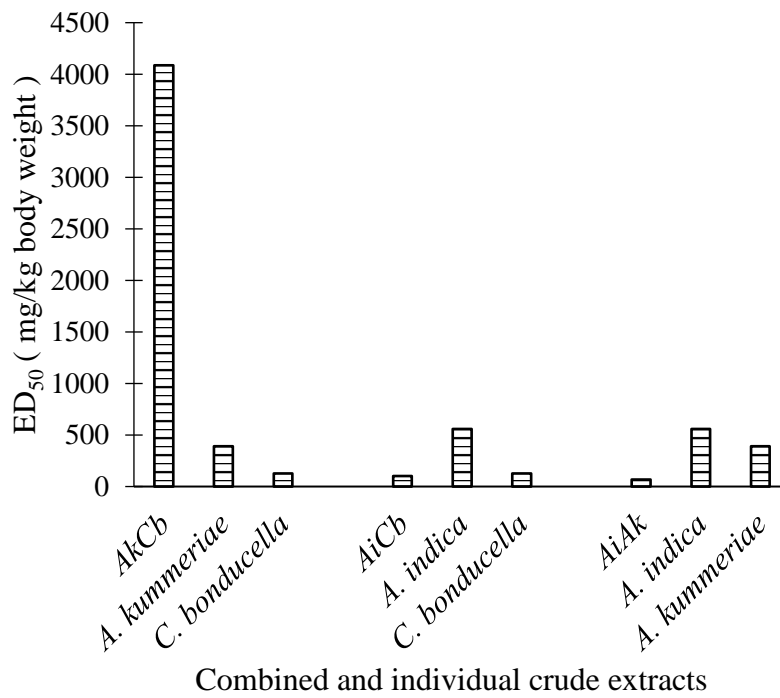
Figure 5: The ED_{50} for individual and combined DCM crude extracts of *A. indica, A. kummeriae* and *C. bonducella* in *P. berghei* infected mice
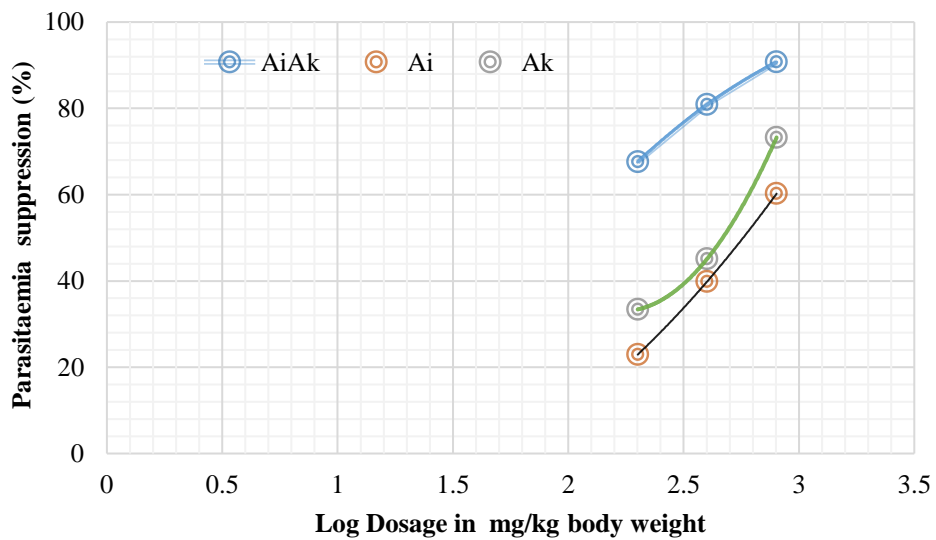

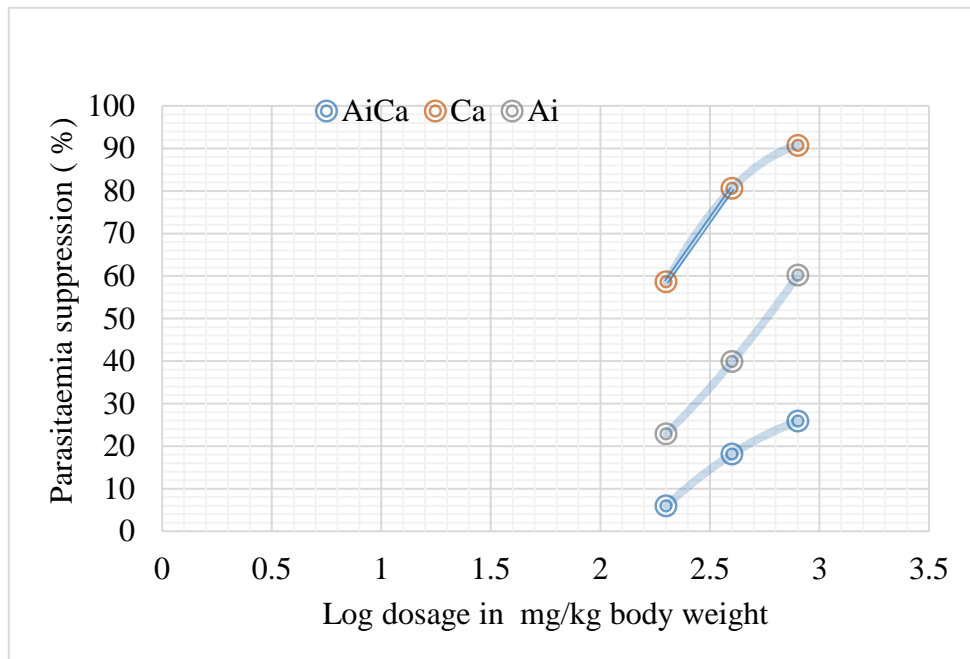**Figure 6:** A dose response curves of AiAk DCM crude extracts combination

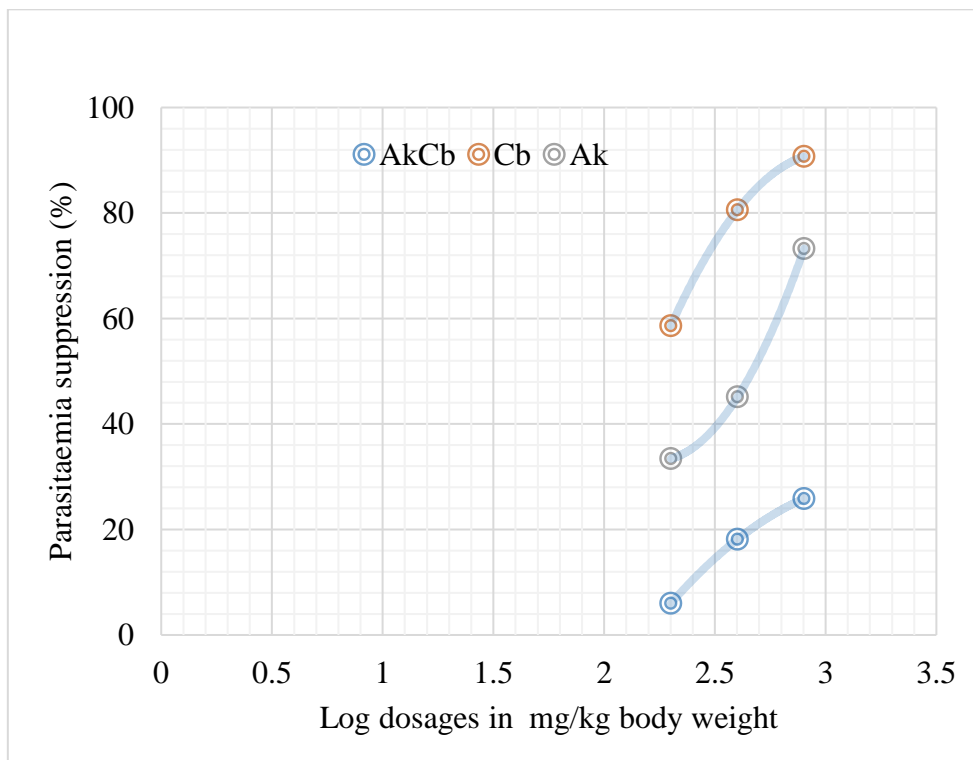**Figure 7:** A dose response curves of AiCb DCM crude extracts combination

Figure 8: A dose response curves of AkCb DCM crude extracts combination

To investigate the nature of interaction, the combination index (CI), a quantitative measure of drug combination effects was calculated. AiAk and AiCb combinations had the combination index (CI) of 0.293 and 0.979, respectively, indicating synergism. However, AkCb combination had the CI of 40.67 indicating a strong antagonism (Table 4).

Table 3: Effective dose of individual and combined DCM crude extracts in mice infected
        Plasmodium berghei at 200, 400 and 800 mg/kg

Plants name or combination	Effective dose ED_{50} (mg/kg/day)	Retention factor (R^2)	95% confidence interval (mg/kg)	Regression equation
A. indica	558.45	0.9972	226.28 – 1378.25	y= 61.977x - 120.55
A. kummeriae	391.73	0.9464	203.44 – 754.27	y= 66.194x - 121.64
C. bonducella	126.63	0.9565	44.33 – 361.70	y= 53.346x - 62.162
AiAk	67.47	0.9925	15.73 – 289.37	y=38.455x - 20.338
AiCb	101.02	0.9520	15.73 – 648.74	y= 52.143x -54.516
AkCb	4085.95	0.9837	749.99 – 22260.26	y= 33.03x - 69.281

Table 4: Interaction between *Azadirachta indica, Annickia kummeriae* and *Caesalpiniabonducella* DCM crude extracts against *Plasmodium berghei* at different combinations

	Ratios of extracts in mg/kg		Mean $FED_{50} \pm$ SEM		
Combinations	Extract A	Extract B	FED_{50} of Extract A	FED_{50} of Extract B	Combination Index (CI)/ Mean FED_{50}
AiAk	1	1	0.1208 (Ai)	0.1722 (Ak)	0.293 SYN
AiCb	1	1	0.3634 (Ai)	1.603 (Cb)	0.979 SYN
AkCb	1	1	10.42 (Ak)	32.25 (Cb)	40.67 MKD-ANT

Discussion

This investigation validates the antiplasmodium properties of crude extracts of *A. indica, A. kummeriae,* and *C. bonducella* that were obtained from locations other than Dar es Salaam (Malebo *et al.,* 2013; Akin-Osanaiye *et al.* 2013; Nondo *et al.* 2016). In the current study *C. bonducella* exhibited the highest *in vivo* antiplasmodial efficacy compared to that of *A. kummeriae* and *A. indica* at 800 mg/kg/day. *Caesalpinia bonducella* suppression rate was nearly to that of the standard antimalarial drug, CQ. The detected highest antiplasmodial efficacy of *C. bonducella* might be due to the presence of more than one class of phytochemicals, namely, alkaloids, terpenoids, flavonoids and cardiac glycosides. Evidence suggests that complex mixtures of phytochemicals tend to interact, either in potentiating the antimicrobial effect or interfering with each other activity (Lila & Raskin, 2005; Credo et al., 2018).

        The interaction between phytochemicals in *C. bonducella* extract may have potentiated the antiplasmodium activity observed in this study. In addition, *C. bonducella* had the lowest ED_{50} compared to *A. indica* and *A. kummeriae.* The lowest ED_{50} in *C. bonducella* further suggests highest potency against malaria parasite. This was more apparent from a dose-response curve, where the ED50 values of the extract in combination were lower than that of individual extracts (A. indica and A. summarize), suggesting higher potency.

The current study demonstrates the first-time nature of the interaction between *A. indica, A. kummeriae* and *C. bonducella* crude extracts in *P. berghei-infected* mice. The AiAk and *AiCb* combination revealed a synergistic effect. This was more apparent from a dose-response curve, where the ED50 values of the extract in combination were found to be lower than that of individual extracts (A. indica, A. summarize and C. bonducella), suggesting higher efficacy. Moreover, by comparing the combination index (CI) to the standards, the CI of AiAk and AiCb combination also suggest a strong synergism between the extracts against plasmodium infection.

The current study is consistent with previous research that found synergistic interactions between many plant extracts, such as those which protect against *P. berghei* and include cryptolepine and artemisinins (Forkuo et al., 2016), artemisinin and triclosan (Mishra *et al.,* 2007), and *Uvaria acuminata* and *Premna chrysoclada* (Gathirwa *et al.,* 2010). It follows that given the current reliance on herbal therapy in traditional, complementary and alternative medicine (TCAM) in Sub-Saharan Africa (James et al., 2018), the high antiplasmodial potencies demonstrated by AiAk and AiCb are significant and key results for TCAM. Therefore, these findings, while preliminary, suggests that AiAk and AiCb are potential antiplasmodium therapies. Further research should be carried out to investigate safety of AiAk and AiCb in *P. falciparum* infection in human.

In contrast to AiAk and AiCb combinations, the ED50 and CI values of the AkCb exhibited characteristics consistent with an antagonistic reaction. The formed combination had the lowest antiplasmodial activity compared to that of *A. kummeriae* and *C. bonducella* when used individually. These findings suggest A. *kummeriae* and *C. bonducella* work best when used individually rather than in combination. Gathirwa *et al.* (2010) reported an antagonistic antiplasmodium reaction between *Grewia plagiophylla* and *Combretum illairii* crude extracts. However, it is beyond the scope of this study to examine the mechanism involved the antagonist activities observed from the A. *kummeriae* and *C. bonducella* combination against Plasmodium infection. Nevertheless, the parasitemia suppression rate that *A. kummeriae* demonstrated in this study, means that it can still be regarded as a potential antimalarial in line with earlier findings by Malebo et al. (2013), who discovered that compounds isolated from methanolic plant extracts showed high activities against multi-drug resistant *Plasmodium falciparum* K1 strain using *in vitro* model.

Overall, this study reports for the first time the existence of synergistic activity between A. indica and A. kummeriae as well as between A. indica and C. bonducella against P. berghei infection, suggesting that AiAk and AiCb can be considered as potential plant extracts-antimalarial combinations. This study also provides an exciting opportunity to advance our knowledge on exploring compounds responsible for the increased antiplasmodium efficacy in AiAk and AiCb formed extracts. Further studies need to be carried out in order to determine the optimal and safer dosing of these herbal extracts in human subjects and the biochemical mechanisms behind their antiplasmodial interactions.

Conclusions

The DCM crude extracts of *A. indica, A. kummeriae* and *C. bonducella* demonstrated a dose dependent antiplasmodial activity in *P. berghei* infected mice. The AiAk and AiCb combination exhibited synergistic anti-plasmodium activity. A. indica, A. summarize, and *C. bonducella* work best in AiAk and AiCb DCM combination rather than individually. The high antiplasmodial potencies demonstrated by AiAk and AiCb are significant and key results for TCAM.

Conflict of Interest
All authors declare that they have no conflicts of interest that could potentially influence the integrity, objectivity, or credibility of the research findings presented in this paper. All authors are committed to upholding the highest standards of ethical conduct in academic and scientific research.

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Headache to a Patient with the Coexistence of Chiari I Malformations and Primary Empty Sella Syndrome: A Case Report

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Abstract

Background: Chiari I malformations (CM-I) and Primary Empty Sella syndrome (PESS) are rare disorders of structural defects within a skull. Headache is the most common presenting symptom in both conditions. However, CM-I and ESS comorbidity in patients with severe headaches is yet to be reported.

Case description: The patient was a 38-year-old woman with a one-year history of headaches at various localisations (occipital and bilateral frontal) preceded by mood agitation. Physical examination was significant for obesity. Magnetic resonance imaging (MRI) revealed a 6.4 mm cerebellar tonsil descent through the foramen magnum and hypointense (CSF-filled) flattened sella. The lipid panel showed elevated cholesterols (total) and low-density lipoprotein (LDL) levels. She was medically managed, with no report of symptoms relapses at one-month and two-month follow-ups.

Conclusion: This is the first report on comorbid CM-I and PESS in adults presenting with cephalalgia. PESS and CM-I co-occurrence may present with mixed headache localisation; careful history-taking and imaging are mandatory for diagnosis confirmation. Future extensive studies are warranted to analyse the pathophysiological interplay between these two rare disorders.

Keywords: Adult, Case report, Chiari I malformations, Empty sella syndrome

Introduction

Chiari malformations are a spectrum of hindbrain pathologies affecting the cervical cord, cerebellum, base of the skull, and brainstem; Chiari malformations type 1 (CM-I) is the most common (McClugage & Oakes, 2019). With the advent of neuroimaging techniques, CM-I is increasingly identified in the population.

CM-I is defined as the caudal displacement of one or both cerebella tonsils by > 5 mm and 3–5 mm below the foramen magnum (McClugage & Oakes, 2019). Headaches (Chiari headache) are the most typical presenting symptoms in CM-I and vary based on the patient's age (McClugage & Oakes, 2019; Olesen, 2018). However, typical adult presentations include occipital headaches and neck pain worsened by the Valsalva manoeuvre, coughing, or sneezing (Olesen, 2018). Furthermore, epidemiological studies on CM-I have shown female

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preponderance, with a prevalence rate of 0.1% to 0.5% (McClugage & Oakes, 2019).

The term empty sella syndrome (ESS) refers to a rare condition in which the subarachnoid space herniation into the sella turcica results in compression and flattening of the pituitary gland and pituitary stalk stretching through an incompetent seller diaphragm (Chiloiro et al., 2017; Miljic et al., 2000). ESS incidence varies in autopsy cases and is estimated to be 5.5 -12%, while in patients undergoing neuroimaging, it is estimated to be 12% and up to 35% in clinical practice (Chiloiro et al., 2017).

Based on pathophysiology and aetiology, ESS is subdivided into two categories: primary ESS (PESS), known for lacking a specific identifiable cause, and secondary ESS, resulting from surgery, radiation, haemorrhage, or infarction of the pituitary gland (Miljic et al., 2000). Headaches are the most frequently reported symptoms of PESS (Catarci et al., 1994).

However, despite headache being the most common presenting feature among these two rare disorders. Comorbidity is yet to be reported in scientific literature. We present the first case report on the coexistence of CM-I with PESS, confirmed by magnetic resonance imaging (MRI); we further report a marked symptom improvement during the follow-up period.

Case report

The patient was a 38-year-old female who presented to the neurology department with a history of recurrent headaches that persisted for over a year. She elaborated that the headache episodes were severe and associated with dizziness and neck pain. She also reported left-sided facial and lower limb numbness. The nature of the headaches was pulsating and brief (approximately <5 minutes), localised bilaterally at the frontal region and occipital area with neck movement restriction. Headaches were aggravated by noise but not change in position, smell, or menstruation. No accompanying photophobia, vomiting, or nausea were reported. She had no history of radiation, pituitary gland surgery, or trauma. Before each headache attack, she experienced an agitated mood. There were no symptoms suggestive of hypopituitarism. She reported prior multiple consultations at different hospitals without significant headache relief. She was obese, with intact blood pressure (121 / 94 mmHg). Neurological examination was unremarkable.

Laboratory testing identified elevated cholesterol levels with total cholesterol of 6.10 (0-5.2), LDL 4.53 (2.59-3.34), and HDL 1.1 (1-2.2) mmol/l. Initially, we ordered a spine MRI (Fig. 1B), which revealed a 6.4mm caudal descent of the cerebellar tonsil through the foramen magnum, suggesting CM-I. Nevertheless, this could not fully explain our patient's frontal localisation of headache and preceded mood disturbances. We then ordered a brain MRI (Fig. 1A), which showed CSF-filled (hypodense) sella turcica and tonsillar herniation, suggesting co-occurrence of CM-I and PESS.

The patient was started with a 75 mg pregabalin and atorvastatin 20 mg oral dose daily and instructed on a dietary approach to reduce weight along with physiotherapy. Monthly evaluation with a neurologist was set, with scheduled repeated ophthalmologic examinations and pituitary function tests. At the one-month follow-up, she reported improved symptoms of headache, dizziness, facial numbness, and lower limb numbness. However, no adverse effects of the medications were reported.
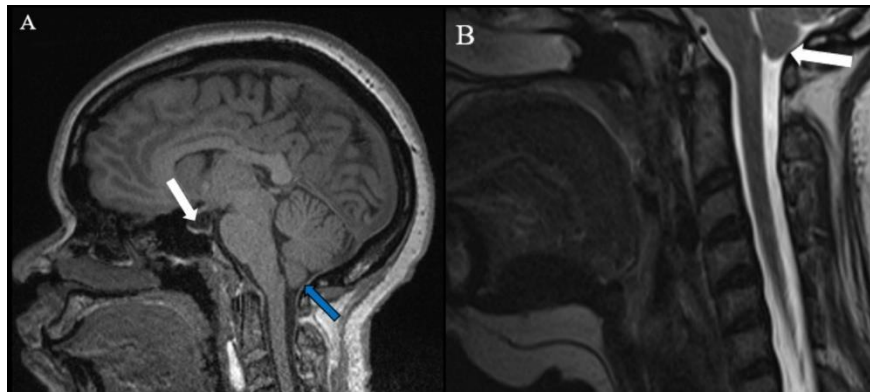
Figure 1 (A) T1-weighted brain MRI, sagittal view. The white arrow shows CSF-filled sella and flattened contents. The blue arrow indicates the descent of the cerebellar tonsil through the foramen magnum. (B) T2-weighted, spine MRI, sagittal view. The white arrow shows the descent of the cerebellar tonsil through the foramen magnum caudally.

Discussion

We presented a case report of the co-occurrence of PESS and CM-I in a patient with recurrent and severe headaches. To our knowledge, no prior reports have been published demonstrating comorbid ESS and CM 1 in adults presenting with headaches.

CM-I was diagnosed based on the fulfilment of the third edition of the International Classification of Headache Disorders (Olesen, 2018), which included demonstrated CM-I on spine MRI, a history of short-lasting headache presentation, occipital localisation, neck pain, and associated symptoms of cranial nerve involvement. However, our patient had multiple headache localisation, including bilateral frontal region, accompanied by mood changes and elevated cholesterol levels, which CM-I could not fully explain. Hence, we had to explore brain MRI further.

Several hypotheses on the pathophysiology of the CM-I-related headache have been developed; Oldfield's and William's theories are the most common. While Oldfield's view depicted a caudal pulsatile pressure effect with mechanical influence on the spinal cord, William's theory explains the role of expanding the intraabdominal pressure and its consequence in higher craniocaudal pressure on trigeminal afferents of the meninges, resulting in a headache (McClugage & Oakes, 2019).

PESS was confirmed by the MRI (brain) and other supportive features, including frontal headache presentation and obesity (Catarci et al., 1994; Chiloiro et al., 2017). Most PESS patients are asymptomatic; however, an increased likelihood of PESS has been proposed in middle-aged, overweight women presenting with recurrent headaches (Catarci et al., 1994). Despite headache being the most frequent complaint in ESS, it has been reported to be nonspecific; however, our patient headache localisation is similar to (Catarci et al., 1994), who reported up to 82% of the patients presenting with anteriorly localised headaches and with daily occurrence. Furthermore, like a previous study (Catarci et al., 1994), our patient did not present with ophthalmological findings. The agitated mood in our patient preceded headaches; indeed, psychiatric disturbances have previously been reported in PESS, with mechanisms remaining largely unknown (Kuzman et al., 2008). Our case lacked CSF dynamics evaluation and pituitary levels due to our hospital's limited setting. However, other reports on PESS patients reported that pituitary functioning was within the normal range (Sutar, 2020). Furthermore, the

dyslipidemia observed in patients may be linked to obesity, as the etiological relationship between headache and hyperlipidemia has been previously suggested in the literature (Olesen, 1977).

Several mechanisms have been proposed to explain the occurrence of ESS; these include chronic intracranial hypertension (IH), incompetence/absence of the diaphragm sellae, and temporary expansion followed by regression of the pituitary gland, allowing the CSF accumulation into the sella turcica, and hence its enlargement and remodelling (Chiloiro et al., 2017). Likewise, the interplay between intraabdominal, intrathoracic, and intracranial pressure due to obesity proposes the aetiology of headaches in our patients (Chiloiro et al., 2017). On the other hand, headaches have been postulated to arise secondary to traction on pain-sensitive vascular-meningeal structures in the sella cavity (Miljic et al., 2000). Indeed, this makes idiopathic IH a crucial differential diagnosis in our patients.

Comprehending the natural history is essential in CM-I therapeutic decision-making. A definitive presentation of cephalalgia and imaging findings is critical for deciding a CM-I treatment option (McClugage & Oakes, 2019). However, our patient lacked features of Valsalva-induced headaches or an associated syrinx, which could necessitate surgery options (McClugage & Oakes, 2019). Similarly, ESS treatment aims to reassure the patient and keep the patient symptom-free; weight loss and medication to target headaches have proven efficient in obese and overweight ESS patients (Catarci et al., 1994). On that basis, we managed our patient medically and weight loss instructions and kept the patient on monthly follow-ups, and the patient reported a successful outcome.

Conclusion

Headaches are multifactorial. PESS and CM 1 can co-occur with multiple headache presentations (localisation). Despite Tanzania's limited resources and busy outpatient settings, detailed patient history and confirmatory imaging are mandatory to establish the precise aetiology of headaches. Extensive studies are warranted to examine the interaction between CM 1 and ESS.

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Factors Associated with Anthropometric Status of Primary School Children in Dodoma, Tanzania

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Abstract

Background: Malnutrition in school-age children significantly affects their health, cognitive development, and educational attainment. This study aimed to assess the nutritional status of school-age children and the influence of socioeconomic, demographic, and environmental factors on their nutritional well-being. This study focused on primary focus was on primary school children in Dodoma. sought to identify children who could be at risk of malnutrition. The study intended to establish baseline data regarding the nutritional status of school children that could contribute to a comprehensive understanding of the nutritional landscape among primary school children in the region. This information could subsequently inform nutritionists and policymakers to plan interventions to improve these children's nutritional status.

Methods: A cross-sectional study involving 248 pupils was conducted in eight primary schools in Dodoma. Four schools were selected from Chamwino and Dodoma urban districts, respectively, whereby two government schools and two private schools were selected from each district. The other four schools were situated in the urban district of Dodoma, comprising two government and two private schools. The study assessed the prevalence of stunting, wasting/thinness, underweight, and overweight/obesity among primary school children. Stunting was characterized by impaired growth and development with low height for age, while underweight was defined as low weight relative to age. Wasting/thinness refers to insufficient flesh, with body weight falling below skeletal and physical standards. Overweight/obese indicates excessive fat tissue accumulation that could impact health. Data were analyzed using the WHO AnthroPlus v1.0.4 software and SPSS v26 software for Windows.

Results: Prevalence rates among the surveyed pupils were as follows: stunting (10.5%), underweight (3.6%), thinness (2.8%), and overweight/obesity (10.1%). Stunting was more prevalent in boys (13.2%) than in girls (8.2%), and it exhibited an upward trend with increasing age. The prevalence of underweight was higher in public schools (8.2%) compared to private schools (3.2%). Thinness was more common in public schools (85.7%) compared to private schools (14.3%) and was more prevalent in rural areas (57.1%) and among younger children (57.1%). Overweight/obesity was more prevalent among girls (91.0%) compared to boys (88.6%). Schools in urban areas showed a higher prevalence of overweight/obesity (90.3%) than those in rural areas (89.5%). Private schools (95.2%) had a higher prevalence of overweight/obese pupils compared to public schools (84.7%). Pupils residing in urban areas were more likely to become overweight/obese compared to their counterparts living in rural settings.

Conclusion: Significant rates of stunting, thinness, underweight, and overweight/obesity were observed among primary schoolchildren in Dodoma, Tanzania. These findings underlined the necessity to enhance nutrition interventions to improve the nutritional status of both public and private primary school pupils in Tanzania.

Keywords: Anthropometric status, Primary school children, Nutritional status, Socioeconomic factors, and Dodoma, Tanzania

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Introduction

Malnutrition encompasses insufficient or excessive nutrient intake and imbalances or impaired utilization of essential nutrients. The double burden of malnutrition encompasses both undernutrition (i.e., stunting, underweight and wasting) and overnutrition (i.e., overweight and obesity) (WHO, 2021). Malnutrition is a prevalent public health issue across the globe that is rapidly increasing in low and middle-income countries. In 2020, an estimated 149.2 million children under the age of five years suffered from stunting, while 45.4 million children experienced wasting(Khanam *et al.,* 2017). The World Health Organization reported that, in 2019, more than 38 million children under the age of five years were either obese or overweight, and it is anticipated that this number will increase to 50 million by 2025(*WHO, 2019*). In Africa, despite high levels of undernutrition, overweight and obesity rates in children are increasing. The prevalence of overweight and obesity among school-aged children (SAC) is more than 10% in many countries, such as South et al., Kenya, and Tanzania(Mekonnen *et al.,* 2018). In Tanzania, the 2019 School Malaria and Nutrition survey reported that the prevalence of stunting, thinness, overweight and obesity were 25%, 11% and 5%, respectively(John *et al.,* 2019).

Children are the backbone of society, and their health status serves as a foundation for the health of the entire society. Research has demonstrated that growth delays among school-aged children can impede their learning, cognitive development, and academic progress(Mohammadi *et al.,* 2022). Undernutrition remains a major contributor to disease susceptibility, morbidity, and mortality among school-aged children, especially in resource-constrained countries. This issue is responsible for about half of all deaths in this population globally(Assemie *et al.,* 2020). Like under-five children, school-aged children are considered one of the most susceptible groups to undernutrition in Sub-Saharan Africa (Appleby *et al.,* 2019).

Urban children are highly susceptible to growth and nutritional deficiencies due to various factors, such as overcrowding, inadequate sanitation, unclean drinking water supply in residential areas, and other conditions that are often associated with lower socioeconomic status(Amare *et al.,* 2020; Mohammadi *et al.*, 2022). Parental education is a crucial proxy indicator of socioeconomic status, with a lack of proper hygiene and poor food habits being other reasons for nutritional deficiencies directly linked to parental education (Alderman & Haeday, 2017). In urban areas, poor eating habits, lack of dietary diversity, and excessive consumption of energy-dense, nutrient-poor junk foods and sweetened beverages contribute to overnutrition among children(Bhattacharyya *et al.,* 2021).

The malnutrition problem of school-age children is of foremost importance to all nations as this group forms future generations (Yeasmin & Islam, 2016). The existence of a triple burden of malnutrition among school-aged children and adolescents in Tanzania poses a growing health challenge. The prevalence of undernutrition in different studies conducted in India was 49% underweight and 51% stunted. In Kenya, it was 47.1%; in Ghana, 33%; and in Ethiopia, 48.5%. According to previous studies, undernutrition is a common problem among school-aged children, especially those in public schools who are more vulnerable to undernutrition due to socioeconomic-related variations(Agbozo *et al.,* 2016; Ali *et al.,* 2022; Endris *et al.,* 2017). However, there is an increasing body of evidence that childhood obesity often persists throughout adulthood and higher possibility of lifestyle modification in children as opposed to adults, interventions aiming at modifying risk factors to prevent childhood obesity should be a top priority(Hlaing *et al.,* 2012).

This paper focuses on undernutrition and overnutrition in line with the Tanzania National Multisectoral Nutrition Action Plan which provides an important opportunity to improve the nutrition and health status among this demographic (NMNAP 2021/22-2025/26). The present study was conducted to find out the nutritional status of school children and explore socioeconomic,

demographic, and environmental factors associated with nutritional status among primary school children so that a basis for planning strategic intervention program can be undertaken from the result of this study, which will improve their health, physical growth and development, school academic performance and progress in whole life.

Methodology
Description of Study area
This research was carried out in Dodoma and Chamwino district in Dodoma region, Tanzania. Dodoma is one of the regions with higher prevalence of undernutrition among children less than five years(*TDHS, 2022*). Dodoma is a fast-growing city with rapidly changing lifestyles, modernization and socio-economic transition with population of approximately 3,085,625 (*NBS,2022*). The two

Sampling techniques
A stratified sampling technique was used to acquire a total of 248 children. The main sampling unit was registered primary schools. The schools were stratified into districts based on location and were sampled separately. Through this probability sampling technique, the population of school children in each school was divided into strata based on school ownership and area of residence. A total of eight primary schools, that is four government and four private schools located in urban and rural areas, were randomly selected. Average of 31 children were selected from each of selected government and private primary schools. Approximately six to seven students were selected from each class.

Sample size.
The sample size was calculated based on (Kothari, 2004) formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

Where n = sample size, z = 1.96 for a confidence limit of 95%, p = expected prevalence of overweight and obesity (18.6%), d = degree of desired precision (in this study was 0.05) and q = 1 – p.
n = (1.96²). 0.186. (1- 0. 186)/ (0.05²)

districts namely Dodoma Urban district and Chamwino Rural districts were selected purposely to allow comparison in the anthropometric status of primary schools in the two districts Chamwino districts was in rural setting while Dodoma Urban district was in urban setting.

Study design.
A cross-sectional study design was employed for this research.

Sampling Frame and eligibility criteria
The study included all children aged between 6 to 13 years studying in primary schools in the selected districts. Exclusion criteria were children with physical or mental impairments, chronic illnesses, and those enrolled in boarding schools or participating in special school programs.

By using the formula and assuming an expected prevalence rate of 18.6% for overweight and obesity based on a previous study by(Mosha & Fungo, 2010), and a desired degree of precision of 0.05, the sample size of 248 pupils was selected. To obtain the sample, a random sampling technique using a table of random numbers was employed, and 31 children were randomly selected from each of the 8 schools.

Data collection
Construction of a Questionnaire
A questionnaire was formulated to solicit information from the participants. The questionnaire was divided into three sections. Section A established rapport with the participants, section B solicited information about socioeconomics such as the child's age and sex, school type, child's place of residence, grade level, parents' occupations, birth order, occurrences of parental death, and the number of people living in the household. Section C solicited information related to weight, height, and other health details, including instances of illness in the past four weeks, treatment for the illness, using mosquito nets while

sleeping at night, and the frequency of handwashing before meals and after visiting restrooms.

Pre-testing the questionnaire

The questionnaire was pre-tested outside the study area. Pre-testing was carried out in one of the governments and private schools located in Morogoro region after the completion of formal training of research assistants. Subsequent to pre-testing the questionnaire, necessary adjustments were made based on the feedback and insights gathered from the respondents.

Administration of the Questionnaire

Before administration of the questionnaire the enumerators were trained to acquaint themselves with the questionnaire proper procedure to ask the questions and proper recording of the responses. The pre-tested questionnaire was then administered to the study subjects through face-to-face interviews. These interviews were conducted within the school premises during the mid-morning or lunch break hours of the day.

Measurements taken.

Anthropometric measurements involving weight, height, and age were taken according to standardized protocols outlined by the World Health Organization (WHO, 2007). Age of children was recorded from the administration form of children with the help from academic teacher. Weight and height were measured using standard procedures. Weight was measured using a standard weighting scale (digital electronic SECA scale; (Model 8811021659, German) that was kept on a firm horizontal surface. The subject was weighted without shoes and with light clothing by ensuring the removal of heavy-worn clothing such as sweaters and the weight was recorded to the nearest 0.1kg. Height was measured using stadiometer 9model no PE-AIM-101-USA) and recorded to the nearest 0.1cm. Subjects were requested to stand upright without shoes on their back kept against the wall and heels put together in a V-shape while looking forward. Each measurement was measured twice to find an average.

Data analysis

Data were compiled, coded, cleaned and analyzed using SPSS software version 26.0 for Windows and the WHO AnthroPlus tool. Data collected were entered into the WHO Anthro-Plus software (version 1.0.4), which facilitated computation of Z-score indices in line with the WHO's 2006 growth references for children aged 5-19 years(De Onis et al., 2007). The indices used were height-for-age (HAZ), weight-for-age (WAZ), and body mass index-for-age Z-scores (BMIZ). The categorization of HAZ, WAZ, and BMI for age Z-score were as follows: <-3SD severe underweight or stunting or wasting, ≥-2SD to <-2.9SD moderate underweight or stunting or wasting, -1SD to -1.9SD mild underweight or stunting or wasting, ≥-1SD to ≤+1.9SD normal, +2SD to +3SD overweight or tall, and >+3SD obese or over tall slender. Within the SPSS software, demographic characteristics of primary school children were succinctly summarized and presented as frequencies and percentages. Nutritional status of primary school children was condensed into frequencies and percentages, depicting the number of children falling into each nutritional status category (underweight, normal, overweight, and obese). The correlations between various factors (treated as independent variables) and the nutritional status of children were analysed using the Chi-square (X^2) test. Fisher's exact test was employed when at least one expected value was below 5. Subsequently, all variables that exhibited p-values < 0.05 from the Chi-square test were incorporated into a multivariable logistic regression analysis. This multivariable model helped to account for confounding variables and elucidated the associations between these factors and the nutritional status of children. The dependent variable in this analysis was a binary variable denoting whether children were overweight/obese.

Ethical Consideration

Ethical approval for the execution of this study was obtained from the Tanzania

National Institute for Medical Research (NIMR) reference NIMR/HQ/R.8a/Vol.IX/4250. Written consent was obtained from the parents of all school children who participated in the study, indicating their willingness to allow their children to participate. Written consent was also obtained from school officials, while pupils aged 6 to 13 years provided both verbal and written consent. To ensure confidentiality, each pupil was assigned an identification number.

Results

Characteristics of the primary school children
Most of the participants (67.3%, n=81) were aged between 6 and 9 years. There was a relatively equal distribution of male and female children (46.0% and 54.0%, respectively). Half of the children were in private schools, while the other half were in public schools. In terms of grade/class level, 58.1%, (n=144) of the children were in grades 1 to 3, and 41.9%, (n=104) were in grades 5 to 6. Employment was the most common occupation among fathers (35.9%, n=89), while among mothers, majority were businesswomen (37.5%, n=93). In terms of family structure, most children were from households with 1 to 3 adults (71.4%, n=177) while 61.7%, (n=153) came from families with 1 to 3 children. The birth order distribution showed that, majority of children were from families with 1 to 3, (48.8%, n=121). Majority of children (91.9%, n=228) had not experienced death of either parent as shown in (Table 1).

Table 1: Socio-economic and demographic characteristics of the primary school children (N=248)

Characteristic	No. of Respondents	%
Age		
6 – 9	167	67.3
10 – 13	81	32.7
Sex		
Male	114	46.0
Female	134	54.0
School type		
Private	124	50
Public	124	50
School location		
Rural	124	50
Urban	124	50
Grade/Class Level		
1 – 3	144	58.1
5 – 6	104	41.9
Fathers occupation		
Employed	89	35.9
Farmer	41	16.5
Businessman	76	30.6
Studying	40	16.1
I don't know	2	0.8
Mothers occupation		
Employed	57	23.0
Farmer	30	12.1
Businesswoman	93	37.5
Housewife	47	19.0
I don't know	21	8.5
Birth order		
1 – 3	79	28.2
4 – 6	121	48.8
> 6	57	23.0
Death of either parent		

Yes	20	8.1
No	228	91.9
Number of adults		
1 – 3	177	71.4
4 – 6	63	25.4
> 6	8	3.2
Number of children		
1 – 3	153	61.7
4 – 6	95	38.3
> 6		

Environmental and other health risk factors affecting the health of primary school children

Among the selected participants, 17.7%, (n=44) preferred to drink boiled water, while majority, (82.3%, n=204), consumed unboiled water. The sanitation facilities used by children indicated that, 71%, (n=176) had access to flush toilets, whereas 29%, (n=72) utilized pit latrines. Regarding waste disposal methods, 73.4%, (n=182) used pit systems, 8.9%, (n=22) resorted to burning, 2.8%, (n=7) used in open dumping, while 14.9%, (n=37) relied on dustbin trucks. Four weeks preceding the survey, 58.9% of the participants experienced sickness, while 41.1% did not get sick. In terms of seeking treatment, majority of children (21%, n=52) sought medical assistance from government health facilities, while 9.7% of the children sought medical assistance from religious/missionary health facilities. Additionally, 14.9% of the children visited local pharmacies to purchase some drugs/pills, 2.4% consulted local or traditional healers, while the remaining (47.6%) did not seek any treatment. Sleeping under mosquito nets was practiced by a significant proportion of the children, with 89.9%, (n=223) using mosquito nets for protection against mosquitoes, while 10.1% did not use mosquito nets. Hand hygiene practices indicated that, 81.5% of the respondents washed their hands before taking meals and after visiting toilets while 73% washed their hands using water only as presented in (Table 2).

Table 2: Environmental and other health risk factors associated with Primary school children(n=248)

Characteristics	No. of Respondents	%
Drinking water		
Boiled	44	17.7
Not boiled	204	82.3
Kind of toilet facility		
Flush toilet	176	71
Pit latrine	72	29
Place to waste disposal		
Pit	182	73.4
Burning	22	8.9
Open dumping	7	2.8
Dust bin track	37	14.9
Sick in the past 4 weeks		
Yes	146	58.9
No	102	41.1
Seeking treatment		
Government	52	21.0
Religious/missionary	24	9.7
Pharmacy/drugstore	37	14.9
Local shop	11	4.4
Local herbs/traditional healer	6	2.4

None	118	47.6
Sleep under mosquito net		
Yes	223	89.9
No	25	10.1
Hands washing before meal		
Frequently	202	81.5
Infrequently	46	18.5
Hands washing after visiting a toilet		
Frequently	181	73
Infrequently	67	27
Materials used for handwashing		
Water only	238	96
Water and soap	10	4
Wearing shoes		
Sometimes	35	14.1
Always	213	85.9

Factors associated with nutritional status of the primary school children
Stunting

The chi-square test conducted for comparative analysis revealed significant associations between children's stunting rate and factors such as age, school type, birth order, parental death, and the number of children within the household as shown in (Table 3). This suggested that, children aged 10-13 years, those attending public schools, those born as fourth or later siblings, those who have experienced the death of either mother or father, and those living in households with more than four siblings were more likely to be stunted. Conversely, sex, school location, source of drinking water, and seeking treatment did not exhibit a significant association with stunting (p>0.05).

There was a relatively stronger tendency for male children, those attending schools located in rural settings, those who did not consume boiled water, and those who did not seek any treatment when sick to be stunted. Although these tendencies were not statistically significant, they indicated a higher likelihood of stunting among these groups of children as shown in table 3.

Table 3: Association between children's stunting (Height for Age Z-score) and socio-economic, environmental and health characteristics (N=248)

Characteristics		Stunted (n, %)	Normal (n, %)	P-Value
Age				0.000*
	6 – 9	7(4.2)	16(95.8)	
	10 – 13	19(23.5)	62(76.5)	
Sex				0.219
	Male	15(13.2)	99(86.8)	
	Female	11(8.2)	123(91.8)	
School type				0.021*
	Public	19(15.3)	105(84.7)	
	Private	7(5.6)	117(94.4)	
School location				0.060
	Rural	18(14.5)	106(85.5)	
	Urban	8(6.5)	116(93.5)	
Birth order				0.036*
	1 – 3	4(5.7)	66(94.3)	
	4 – 6	11(9.1)	110(90.9)	
>6		11(19.3)	46(80.7)	
Death of either parent				0.031*

Father	1(16.7)	5(83.3)	
Mother	4(36.4)	7(63.6)	
Both	0(0.0)	3(100)	
None	21(9.2)	207(90.8)	
Number of children			0.001*
1 – 3	8(5.2)	145(94.8)	
4 – 6	18(18.9)	77(81.1)	
Source of drinking water			0.587
Boiled	3(6.8)	41(93.2)	
Not boiled	23(11.3)	181(88.7)	
Seeking treatment			0.156
Government	9(34.6)	43(19.4)	
Religious/missionary	2(7.7)	22(9.9)	
Pharmacy/drugstore	0(0.0)	37(16.7)	
Local shop	1(3.8)	10(4.5)	
Local Herbs/traditional healer	0(0.0)	6(2.7)	
None	14(53.8)	104(46.8)	

*p-Value: Chi square test, *p<0.05; Fisher's Exact Test, **p<0.05*

Underweight

The chi-square test conducted for comparative analysis revealed that, there were no significant associations between children's underweight rate and their age, sex, school type, school location, birth order, death of either parent, number of children living in the household, type of drinking water, and the location where they seek treatment when they were sick. These factors did not show a significant association with underweight, (p>0.05) as shown in (Table 4).

There was a relatively higher tendency for children who were aged 6-9 years, male children, children in public schools, those studying in urban settings, children without both parents, children born as fourth or later siblings, those living in households with more than four children, children who consumed unboiled water, and children who did not seek any treatment or seek treatment from government health facilities to be underweight. Although these tendencies were not statistically significant, they increased the likelihood of underweight among these groups of children as shown in table 4 below.

Table 4: Association between children's Weight for Age Z-score and socio-economic, environmental and health characteristics (N=167).

Characteristics	Underweight (n, %)	Not underweight (n, %)	P-Value
Age			.ᵃ
6 – 9	9(5.4)	158(94.6)	
10 – 13			
Sex			0.733
Male	5(6.7)	88(95.7)	
Female	4(4.3)	70(93.3)	
School type			0.181
Public	6(8.2)	67(91.8)	
Private	3(3.2)	91(96.8)	
School location			1.000
Rural	4(5.1)	75(94.9)	
Urban	5(5.7)	83(94.3)	
Birth order			0.250
1 – 3	1(1.9)	53(98.1)	
4 – 6	5(6.0)	79(94.0)	

>6	3(10.3)	26(89.7)	
Death of either parent			0.174
Father	0(0.0)	4(100)	
Mother	1(33.3)	2(66.7)	
Both	0(0.0)	2(100)	
None	8(5.1)	150(94.9)	
Number of children			0.119
1 – 3	4(3.3)	116(96.7)	
4 – 6	5(10.6)	42(89.4)	
Drinking water			0.625
Boiled	2(8.0)	23(92.0)	
Not boiled	7(4.9)	135(95.1)	
Seeking treatment			0.367
Government	4(12.5)	28(87.5)	
Religious/missionary	0(0.0)	18(100)	
Pharmacy/drugstore	1(2.9)	33(97.1)	
Local shop	0(0.0)	8(100)	
Local herbs/traditional healer	0(0.0)	6(100)	
None	4(5.8)	65(94.2)	

p-Value: Chi square test, *p<0.05; Fisher's Exact Test, **p<0.05, *^{a} It is important to note that weight-for-age reference data were not provided beyond the age of 10 years. This was due to the fact, that this indicator does not differentiate between height and body mass during the age period when many children undergo pubertal growth spurt. Consequently, some children could appear to have excess weight based on weight-for-age, while in reality they were simply experiencing increased height.

Wasting

The chi-square test conducted for comparative analysis revealed that, there were no significant associations between children's wasting rate and factors such as age, sex, school type, school location, birth order, parental death, number of children living in the household, type of drinking water used, and being sick in the past four weeks. These factors did not demonstrate any significant association with wasting(p>0.05) as shown in (Table 5).

There was a relatively stronger tendency for the following childrengroups to experience wasting, children aged 6-9 years, female children, children attending public schools, children studying in rural settings, children without both parents, children who were born as fourth or later siblings, children living in households with more than four children, children who consumed unboiled water and children who had been sick in the past four weeks. Although these associations were not statistically significant, they indicated a higher likelihood of wasting among these groups of children as presented in table 5.

Table 5: Association between children Weight for Height Z-score and socio-economic, environmental and health characteristics.

Characteristics	Wasted (n, %)	Normal (n, %)	P-Value
Age			0.686
6 – 9	4(57.1)	163(67.6)	
10 – 13	3(42.9)	78(32.4)	
Sex			0.457
Male	2(28.6)	112(46.5)	
Female	5(71.4)	129(53.5)	
School type			0.120
Public	6(85.7)	118(49.0)	
Private	1(14.3)	123(51.0)	
School location			1.000

Rural	4(57.1)	120(49.8)	
Urban	3(42.9)	121(50.2)	
Birth order			0.928
1 – 3	2(28.6)	68(28.2)	
4 – 6	3(42.9)	118(49.0)	
>6	2(28.6)	55(22.8)	
Death of either parent			0.103
Father	1(14.3)	5(2.1)	
Mother	1(14.3)	10(4.1)	
Both	0(0.0)	3(1.2)	
None	5(71.4)	223(92.5)	
Number of children			0.110
1 – 3	2(28.6)	151(62.7)	
4 – 6	5(71.4)	90(37.3)	
Source of drinking water			0.611
Boiled	2(28.6)	199(82.6)	
Not boiled	5(71.4)	42(17.4)	
Sick in past 4 weeks			0.703
Yes	5(71.4)	100(41.5)	
No	2(28.6)	141(58.5)	

*p-Value: Chi square test, *p<0.05; Fisher's Exact Test **p<0.05*

Overweight/Obese

The chi-square test conducted for comparative analysis yielded significant associations between children being overweight/obese at both school type (private or public) and the number of children in the household as presented in (Table 6). This suggested that children attending private schools and those residing in their households with 1-3 children were more likely to be overweight/obese.

On the other hand, factors such as age, sex, school location (rural or urban), birth order, parental death, source of drinking water and seeking for treatment did not indicate a significant association with being overweight/obese (p>0.05). There was a relatively stronger inclination for children aged 10-13 years, female children, those attending urban schools, those in private schools, those living in households with more than four siblings, and children with both parents present to be overweight/obese as presented in table 6.

Table 6: Association between children Weight for Height Z-score and socio-economic, environmental and health characteristics.

Characteristics	Normal (n, %)	Overweight/obese (n, %)	P-Value
Age			0.822
6 – 9	16(9.6)	72(88.9)	
10 – 13	9(11.1)	151(90.4)	
Sex			0.534
Male	13(11.4)	101(88.6)	
Female	12(9.0)	122(91.0)	
School type			0.010*
Public	19(15.3)	105(84.7)	
Private	6(4.8)	118(95.2)	
School location			1.000
Rural	13(10.5)	111(89.5)	
Urban	12(9.7)	112(90.3)	

Birth order			0.284
1 – 3	4(5.7)	66(94.3)	
4 – 6	13(10.7)	108(89.3)	
>6	8(14.0)	49(86.0)	
Death of either parent			0.221
Father	1(16.7)	5(83.3)	
Mother	3(27.3)	8(72.7)	
Both	0(0.0)	3(100)	
None	21(9.2)	207(90.8)	
Number of children			0.008*
1 – 3	9(5.9)	144(94.1)	
4 – 6	16(16.8)	79(83.2)	
Source of drinking water			0.408
Boiled	6(13.6)	38(86.4)	
Not boiled	19(9.3)	185(90.7)	
Seeking treatment			0.148
Government	3(5.8)	49(94.2)	
Religious/missionary	2(8.3)	22(91.7)	
Pharmacy/drugstore	1(2.7)	36(97.3)	
Local shop	3(27.3)	8(72.7)	
Local herbs/traditional healer	1(16.7)	5(83.3)	
None	15(12.7)	103(87.3)	

p-Value: Chi square test, *p<0.05; Fisher's Exact Test, **p<0.05

Discussion

Prevalence of undernutrition and overnutrition among primary school children

The primary objective of this study was to assess the anthropometric status of primary school-aged children in both Dodoma urban and Chamwino districts, located in Dodoma. About 67.3%, (n=167) of the participants fell within the age range of 6 to 9 years, which was termed "the young strata." This age range was consistent with the Tanzanian national guidelines for admitting students to Standard I, in which children are required to be six years of age or older and possess the ability to read and write. According to the findings of this study, age was found to have a significant impact on the nutritional status of the children. This was consistent with a study conducted in Ethiopia(Berhanu *et al.,* 2023), which indicated that the risk of malnutrition tends to decrease as a child grows older.

Prevalence of stunting was found to be 15.3%, (n=19) in public schools and 5.6%, (n=7) in private schools within the study population. Stunting prevalence was observed to be higher among boys than in girls, and it also exhibited an upward trend with increasing age. Stunting prevalence was observed to be higher among boys than in girls, since boys have a higher likelihood of experiencing stunting compared to their girl counterparts this may be due to family size, gender bias, parents' attention to boys and parental preferences for male children in some areas (Adedeji *et al.,* 2017). This pattern could be explained by the understanding that, stunting is a form of chronic malnutrition that becomes more evident during later childhood stages. As the child's age surpasses the critical window of growth, the ability to reverse the stunting condition diminishes(Bliznashka *et al.,* 2021).

This observation aligns with findings from studies conducted in Tanzania and other African countries. These studies have consistently shown that, boys have a higher likelihood of experiencing stunting compared to their girl counterparts. The likelihood of a child to be stunted increases with age (Mohamed *et al.,* 2022).

Prevalence of underweight differed between public and private schools, with rates of 8.6%, (n=6) observed in public

schools and 3.2%, (n=3) in private schools for children aged below 10 years. These differences can be attributed to various factors such as lifestyle variations, feeding habits, parental education and differences in socioeconomic status. There appeared to be a significant impact of rural and urban backgrounds on underweight prevalence. Children from rural areas tended to be more underweight compared to their urban counterparts. This trend of rural-urban variations has been reported in similar studies, even among children below five years of age (TNNS, 2018).

In this study, prevalence of thinness among school-aged children aged 6-13 years was approximately 2.8%, (n=7). The observed magnitude of thinness was lower when compared to findings from other studies conducted in various regions. For instance, studies conducted in Tanzania (11.2%), Ghana (19.5%), Forega, Ethiopia (21.4%), Southern Ethiopia (13.6%), Northern Ethiopia (26.1%), Nigeria (18.9%), and West Bengal, India (28%) reported higher prevalence rates of thinness among children aged 6-13 years (Mohamed *et al.,* 2022).

Prevalence of thinness differed significantly between public and private schools, with rates of 76.0% in public schools and 24.0% in private schools. This discrepancy could be attributed to the absence of school feeding programs in public schools, which may have led to extended periods of hunger or reliance on snacks that are purchased during break times. These factors could contribute to the higher prevalence of thinness among children in public schools (Mwaikambo *et al.,* 2015).

Students attending private schools usually come from families with higher socio-economic status. Wealthier families can afford school fees and might enrol their children in schools that offer school lunch programs. These families might provide transportation to or from school to home by private cars or school buses, ensuring easier access to nutritious meals. This context could explain the lower prevalence of thinness among children attending private schools.

These observations are in line with a study conducted by Mwaikambo *et al.* (2015).

Underweights and thinness were higher among children in public schools than in private schools. Similarly, several studies indicated that underweights in public schools was more prevalent than in private schools (Mohammed *et al.,* 2022). This difference may be due to various factors such as lifestyle variations, feeding habits, parental education, difference socioeconomic status, this aligns with (Mwaikambo *et al.,* 2015). Residence in urban or rural areas is another contributing factor to underweight and thinness among schoolchildren. The current review revealed a higher prevalence of underweights and thinness in rural areas than in urban areas. Other findings of the present study included the high rate of slimness and underweights, in rural areas compared to urban areas. Possibly due to failure of access to food, safe water and sanitation where similar results have been reported in other studies in other parts of the world (Mohammed et al., 2022).

This study also revealed a lower prevalence of overweight/obesity among school aged children compared to similar studies conducted in Tanzania. For instance, a previous study conducted in Tanzania by Vincent et al. (2012) reported a 15% prevalence of overweight/obesity among school children aged 9-11 years. Another study involving primary school children aged 7-17 years in Arusha Urban, Tanzania, reported an overweight and obesity prevalence of approximately 18% (Chomba *et al.,* 2019). In the selected study sample, the prevalence of overweight/obesity among primary school children was 16.4% in public schools and 83.6% in private schools.

Urban schools exhibited a higher prevalence of overweight/obese pupils compared to the rural schools. This trend could be attributed to shifts in lifestyles and dietary behaviors across various population groups within the region. Environmental factors such as the increased availability of fast-food outlets in urban areas may have contributed to these trends. This phenomenon agreed with

findings from a study conducted in Morogoro, Tanzania (Muhomba *et al.,* 2023).

Determinant factors of Stunting and Overweight/Obesity among primary school children

In the bivariate logistic regression analysis, several factors including the child's age, school type, birth order, parental death, and the number of children in the household were identified as independent predictors of stunting, with p< 0.05. Consequently, all these variables were included in a multivariable logistic regression model and upon adjustment, only age and the number of children living in the household maintained their significant associations (p<0.05) with stunting.

The study findings revealed that children aged 10-13 years had a lower likelihood of being stunted (Adjusted Odds Ratio, AOR = 0.26; 95% Confidence Interval: 0.09, 0.73) compared to siblings aged 6-9 years. Conversely, children living in households with more than four children were strongly associated with stunting (AOR = 2.718; 95% Confidence Interval: 1.076, 6.864) in comparison with children living in households with fewer than four children.

Both age and the number of children living in the household were identified as significant (p<0.05) predictors of stunting. Stunting demonstrated a noteworthy increasing trend with advancing age, with older age emerging as an independent predictor of stunting. This study highlights an inverse association, indicating that a decrease in age leads to 19% increase in the stunting rate of children aged 10-13 compared to children aged 6 to 9 years.

This observation was in line with previous reports showcasing the progression of height deficit with increasing age in sub-Saharan Africa(Mushtaq *et al.,* 2011). Having several siblings in the household greater than four was also a significant predictor of stunting among children. This observation might be attributed to a lower level of childcare and reduced dietary intake due to the larger number of children in the household. Similar findings have also been observed in other parts of the world(Yeasmin *et al.,* 2016).

Both bivariate logistic regression and multivariate logistic regression models revealed significant associations (p<0.05) between school type, the number of children living in a household and being overweight/obese. Results of this study indicated that children attending public schools were 0.041 times (Adjusted Odds Ratio, AOR = 0.357; 95% Confidence Interval: 0.133, 0.957) less likely to be overweight or obese compared to children in private schools. Moreover, children residing in families with more than four children were 0.042 times (AOR = 2.526; 95% Confidence Interval: 0.162, 0.905) more likely to be overweight or obese.

School type and the number of children living in the household were identified as significant (p<0.05) predictors of overweight/obesity. It was observed that 80% of pupils attending private schools were more likely to become overweight or obese compared to their counterparts in public schools. This phenomenon could be attributed to the fact that a considerable number of pupils in public schools skipped meals, which could lead to lower weights and undernutrition.

Increase in obesogenic environments was noted for children whose movements were restricted by their parents or guardians. This trend was noticed in children who had limited opportunities to engage in spontaneous physical activities. These findings are in line with those reported by(Pangani *et al.,* 2016). Children living in households with fewer than four children exhibited a positive association with being overweight or obese, unlike their counterparts in larger households. This situation arisen from the availability of sufficient and excess food for children in families with fewer members. This correlation was also reported by(Pangani *et al.,* 2016). It is crucial for the public to recognize these patterns as indicators of an increasing double burden: Children with ample food resources are more susceptible to overweight and obesity, while those facing

food scarcity are at high risk of becoming underweight.

Conclusions and recommendations

This study provided significant insights into the prevalence of stunting, thinness, underweight, and overweight/obesity among pupils aged 6 to 13 years in both public and private schools in Dodoma. The prevalence of undernutrition was higher in boys than in girls, more common in public schools than in private schools, and more prevalent among pupils residing in rural areas. The prevalence of overnutrition was higher in private schools, more common among girls than boys, and prevalent among pupils residing in urban areas. The study also established a correlation between stunting and overweight/obesity. We hence recommend monitoring children's nutrition status in school and efforts should be directed towards providing school feeding programs in order to mitigate the consequences of undernutrition resulting from children experiencing hunger at school.

Strength and Limitation

The major limitation of this study was its failure to address the nutritional status of overfed children. A longitudinal study could have enabled the subjects to be profiled over time. Additionally, respondents' ability to accurately remember and answer certain questions was a limitation. Reporting of hygiene could have been inflated, as is often the case with self-reported hygiene behaviors. The education level of the children's parents could also introduce a source of bias.

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Seroprevalence of Syphilis among Pregnant Women Attending Antenatal Care in Yaqshiid District, Mogadishu, Somalia

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Abstract

Background: The prevalence of syphilis among pregnant women in Somalia has been poorly studied, despite its significant impact on maternal and fetal health. In Somalia, the last syphilis study was conducted approximately 30 years ago, leaving a critical knowledge gap regarding the current epidemic of syphilis among pregnant women.

Materials and methods: From January 2023 to April 2023, a hospital-based cross-sectional study was conducted on maternal and child health. A total of 300 pregnant women were included in the study, and the seroprevalence of syphilis was determined using the Venereal Disease Research Laboratory. This one-step quick diagnostic test cassette was used as the preliminary screening tool, and Positive results were confirmed using the full chemiluminescence immunoassay (CLIA) analyzer MAGLUMI. A structured questionnaire was used to collect demographic characteristics and knowledge regarding syphilis transmission and mother-to-child transmission. SPSS Version 27.0 was used to analyze the gathered data. Statistical significance was set at *p* < 0.05.

Results: Overall, 5.3% (16/300) of pregnant women had syphilis seroprevalence. Seroprevalence rates were higher in women aged 24-34 (50.0%). There were significant relationships between syphilis infection and education (p < 0.000), occupation (p < 0.000), and residence (p = 0.002). Furthermore, a significant majority of pregnant women (78%) were unaware of syphilis transmission routes and its correlation to HIV risk (81.7%). Stillbirths constituted 23.3% of pregnancy-related problems, whereas 17% of pregnant women had a prior record of blood transfusions.

Conclusions: The study found an alarming syphilis seroprevalence in pregnant women, especially in certain demographic groups. The lack of knowledge of syphilis transmission and its effects highlights the necessity for targeted education. Improved prenatal care, health awareness, and effective prevention should lessen the effects of syphilis on mother and newborn health.

Keywords: syphilis, pregnant women, seroprevalence, demographic characteristics, knowledge gap.

Introduction

Syphilis is still the most common congenital infection in the world, and if left untreated, it can have serious effects on both the mother and her growing fetus (Rac et al., 2017). Congenital syphilis, a disorder in which a fetus becomes infected during pregnancy, can result in stillbirth, miscarriage, premature birth, birth abnormalities, and long-lasting physical or neurological alterations. ("Syphilis in Pregnancy," 2022). The spirochete Treponema palladium causes the widespread sexually transmitted illness known as syphilis (Lendado et al., 2022). Although this illness is typically thought to be sexually

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transmitted, it can also infrequently spread through blood transfusions, non-sexual contact, and even in utero (Wubete et al., 2019).

The World Health Organization (WHO) reported approximately 200,000 stillbirths and infant deaths due to congenital syphilis in 2019, making it the second leading cause of preventable stillbirths worldwide (Hoque et al., 2021). According to the WHO, 10–12 million new cases of syphilis are reported annually. Infection rates vary greatly among nations in the same area as well as among different groups investigated for syphilis. In developed countries, the seroprevalence during pregnancy is typically low, ranging from 0.02% in Europe to 4.5% in parts of the United States. In contrast, the prevalence of congenital syphilis has increased dramatically in the rural areas of Eastern Europe and Central Asia. In Africa, high rates of syphilis seropositivity (3-18%) have frequently been recorded in prenatal clinics

Approximately 2.7% (ranging from 0.1% to 10.3%) of pregnant women in Sub-Saharan Africa (SSA) are affected with syphilis, which amounts to over 900,000 pregnancies that are at risk annually. Research conducted in East African nations revealed an adjusted mean prevalence rate of syphilis at 4.6%, which is the second highest prevalence rate after Southern Africa (Befekadu et al., 2022a). In Somalia, the prevalence of syphilis among women receiving prenatal care in Somalia was reported to be 4.07% in 2019, according to data provided by the World Bank from officially recognized sources (*Somalia - Prevalence Of Syphilis (% Of Women Attending Antenatal Care) - 2024 Data 2025 Forecast 2010-2019 Historical*, n.d.). Another study conducted Jama reported prevalence of syphilis among pregnant women that is 3% in Mogadishu, Somalia (Jama et al., 1987a).

Risk factors for syphilis transmission during pregnancy include young age, African-American and Hispanic ethnicity, low socioeconomic level, less education, inadequate prenatal care, prostitution, and substance misuse. (Tsimis & Sheffield, 2017). Obstetric consequences associated with syphilis encompass spontaneous miscarriage, non-immune hydrops, stillbirth, preterm labor, low birth weight, heightened neonatal mortality, and congenital syphilis in newborns. (Uku et al., 2021). A study conducted in Sub-Saharan Africa revealed that untreated maternal syphilis resulted in an estimated 205,901 poor pregnancy outcomes, including spontaneous abortion, stillbirth, low birth weight, neonatal death, and congenital syphilis (Befekadu et al., 2022a). Syphilis continue to be a significant contributor to reproductive morbidity and adverse pregnancy outcomes in underdeveloped nations (Geremew & Geremew, 2021).

Although the proper medical care for pregnant women usually prevents these issues, the main obstacle has been the inability to detect the infected women and ensure that they receive treatment. Utilizing non-treponemal tests like rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) test, along with confirming positive results using treponemal tests like the fluorescent treponemal antibody absorption (FTA-ABS) assay, is a cost-effective approach for screening in the first trimester. it remains a substantial cause of avoidable child mortality in developing countries, notably in Sub-Saharan Africa, (Genç & Ledger, 2000), (Hamid, n.d.) and (Befekadu et al., 2022a).

Programs that involve syphilis testing combined with adequate, rapid penicillin therapy for pregnant women who test positive for Treponema pallidum infection have been found to be effective in lowering unfavorable pregnancy outcomes. (Gomez et al., 2013). Patients who are allergic to penicillin should be desensitized before treatment. (Genç & Ledger, 2000). The actual risk factors for treatment failure, which affect both the expectant mother and her fetus, are complex and include severe congenital syphilis as shown by sonographic fetal anomalies, delayed or insufficient treatment (less than 30 days before delivery), and delayed diagnosis. (Stafford et al., 2019).

Despite the severe impact of syphilis on the health of mothers and babies, there is a lack of research on the prevalence of syphilis among pregnant women in Somalia. This leaves a serious knowledge gap regarding the country's current syphilis infection rate in pregnant women. Consequently, this study aimed to determine the prevalence of syphilis in pregnant women and the association between syphilis and demographics and knowledge gaps using primary screening tests.

Materials and methods
Study subjects, papulation and criteria
This study employed a cross-sectional methodology to determine the prevalence of syphilis among pregnant women residing in Yaqshid District, Mogadishu, Somalia.

Sample size calculation
The sampling technique was a non-probability sampling technique, and the sample size was calculated using Slovin's formula ($n = N/(1 + Ne^2)$) with a confidence interval (CI) of95% and an e of5% marginal error.

$n = 1200/(1 + 1200 \times 0.05^2) = 300$ participants

Inclusion
This study included all pregnant women attending antenatal care (ANC) at Yaqshiid Maternal and child health Center who agreed to participate.

Exclusion criteria
Pregnant women who were incapacitated to provide consent, those who showed documented hypersensitivity, and those who had received a previous diagnosis and treatment for syphilis were excluded from the study.

Data Collection
Trained nurses collected relevant data including demographic information, medical history, risk factors associated with syphilis, and blood samples from each participant. There was strict confidentiality regarding the information provided in the questionnaires, and the data were double-checked daily to ensure accuracy. The Venereal Disease Research Laboratory (VDRL), a one-step quick diagnostic test cassette, was originally used to analyze blood samples (serum).

Laboratory investigations
The VDRL rapid test can be employed with either blood, serum, or plasma samples. However, serum samples were used in the present study. The VDRL rapid test kit comprises an instructional manual, buffer solution bottle, and single-use cassette test. Showing in **Figure 1.** (*Monlab - Material Para Laboratorio de Diagnóstico Clínico - Syphilis*, n.d.)
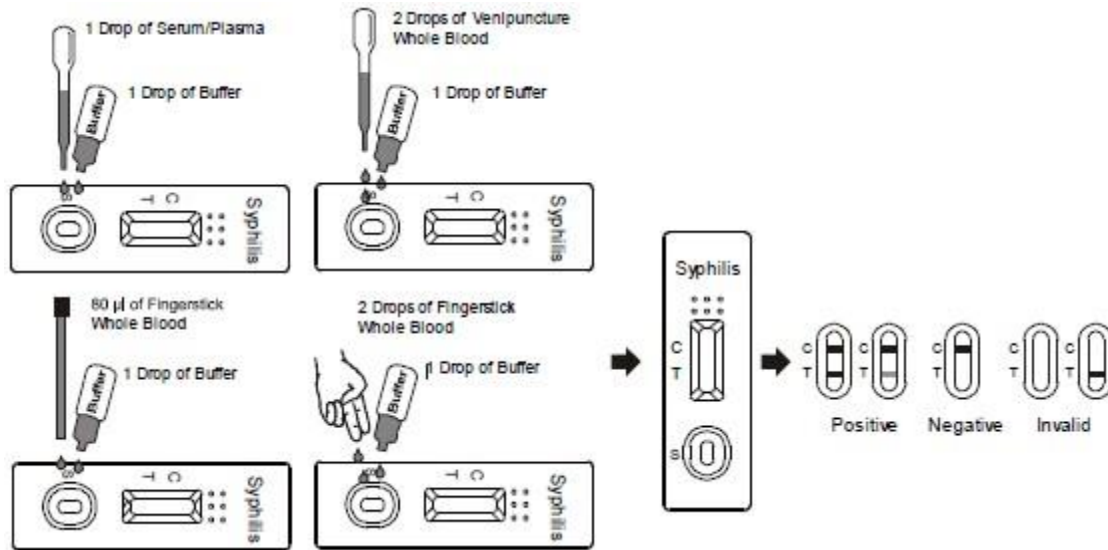
Figure 1: Rapid test cassette for syphilis test (VDRL)

Interpretation of results
The test results show the presence of two separate lines, one in the control line region, referred to as C, and the other in the test line zone, marked as T. A positive result was indicated by the presence of any color in the test line region (T), which was dependent on the concentration of TP antibodies present in the samples. A negative single-colored line is observed in the control line region (C). The absence of a line in the test line region (T) was indicative of a negative result.

MAGLUMI® Syphilis (CLIA) Enzyme-Linked Immunosorbent Assay (ELISA)
SPECIMEN COLLECTION AND PREPARATION
Serum samples were collected using standard sampling tubes and centrifuged at ≥ 10,000 RCF (Relative Centrifugal Force) for 15 minutes. Collected blood aseptically following the universal precautions for venipuncture.
TEST PROCEDURE
Preparation of the Reagent
Resuspension of the magnetic microbeads took place automatically when the kit is loaded successfully, ensuring the magnetic microbeads are totally resuspended homogenously prior to use.
Calculation of Results
The analyzer automatically calculated the concentration in each sample by means of a calibration curve which is generated by a 2-point calibration master curve procedure. The results are expressed in mIU/mL (*Snibe Co., Ltd.*, n.d.).
Interpretation of Results
Results obtained with the Syphilis assay can be interpreted as follows:
• Non-reactive: A result less than 1.0 mIU/mL (<1.0 mIU/mL) is negative.
• Reactive: A result greater than or equal to 1.0 mIU/mL (≥1.0 mIU/mL) is positive.

Data Analysis
Data analysis was performed using SPSS Version 27.0. Descriptive analyses were conducted in this study. A statistically significant result was defined as having a *p*- value of less than 0.05.

Results

This study included 300 pregnant women, and the overall seroprevalence of syphilis among the pregnant women was 16/300 (5.3%).

Demographic characteristics of the pregnant women who underwent screening. With regard to age, the highest seroprevalence of syphilis was reported in women aged 24-34 (50.0%). Of the total pregnant women, 97.7% (n = 293) were married and 69% (n = 207) were unemployed. Of the pregnant women who underwent syphilis screening, 192 (64%) resided in urban areas. The educational attainment of the pregnant women in question was notably insufficient, with 219 pregnant women, or 73% of the total number of pregnant women, lacking any formal education. The prevalence of syphilis infection was significantly associated with education (p <0.000), occupation (p <0.000), and residence (p = 0.002). **Table 1** is provided.

Table 1: The social demographics and characteristics factors associated with the prevalence of syphilis among pregnant women

Characteristics	Number (300) z	Percent	Syphilis Positive No (%)	Negative No (%)	Chi square Value	* P-value
Age category						
15-24	108	36.0	5 (31.3)	103 (36.3)	0.723	0.697
25-34	120	40.0	8 (50.0)	112 (39.4)		
35-44	72	24.0	3 (18.8)	69 (24.3)		
Marital status						
Married	293	97.7	16 (75.0)	277 (97.5)	0.404	1.000
Divorced	5	1.7	0 (0.0)	5 (1.8)		
Widowed	2	0.7	0 (0.0)	2 (0.7)		
Education						
Formal Education	81	27.0	12 (75.0)	69 (24.3)	19.757	0.000
No Formal Education	219	73.0	4 (25.0)	215 (75.7)		
Occupation						
Employed	93	31.0	12 (75.0)	81 (28.5)	15.297	0.000
Unemployed	207	69.0	4 (25.0)	203 (71.5)		
Residence						
Urban	192	64.0	16 (100.0)	176 (62.0)	9.507	0.002
Rural	108	36.0	0 (0.0)	108 (38.0)		

Additionally, our study reported an association between medical conditions related to pregnancy, obstetric history, and knowledge of syphilis. A total of 264 pregnant women, representing 88% of this study, were identified as being in the multigravida, and a significant proportion of the group, specifically 234 pregnant women, or 78%, demonstrated a lack of awareness regarding syphilis, which is mainly transmitted through sexual contact. Moreover, a significant proportion of pregnant women, specifically 245 (81.7%), lacked awareness regarding syphilis infection, which can increase the risk of HIV transmission or acquisition. Approximately 79.3% of the surveyed pregnant women lacked knowledge regarding the potential transmission of syphilis from infected women to their newborns. Among the various categories of pregnancy-related complications, 70 (23.3%) were identified as stillbirths. Pregnant women who had previously received blood transfusions accounted for 17% of patients. **Table 2.**

Table 2: Medical conditions related to pregnancy, obstetric history, and knowledge of syphilis among pregnant women

Characteristics	Number (300)	Percent	Syphilis		Chi square Value	* P-value
			Positive No (%)	Negative No (%)		
Do you know Syphilis is mainly transmitted through sexual contact						
Yes	66	22.0	12 (75.0)	54 (19.0)	27.667	0.000
No	234	78.0	4 (25.0)	230 (81.0)		
Do you know A man or woman who looks healthy may have syphilis						
Yes	60	20.0	8 (50.0)	52 (18.3)	9.507	0.002
No	240	80.0	8 (50.0)	232 (81.7)		
Do you know Syphilis infection can increase the risk of HIV transmission or acquisition						
Yes	55	18.3	11 (68.8)	44 (15.5)	28.694	0.000
No	245	81.7	5 (31.3)	240 (84.5)		
Do you know Syphilis-infected woman can transmit the infection to their newborn						
Yes	62	20.7	12 (75.0)	50 (17.6)	30.432	0.000
No	238	79.3	4 (25.0)	234 (82.4)		
Have you had a history of blood transfusion						
Yes	51	17.0	12 (75.0)	39 (13.7)	40.295	0.000
No	249	83.0	4 (25.0)	245 (86.3)		
How many times do you get pregnant						
Primigravida	36	12.0	8 (50.0)	28 (9.9)	23.111	0.000
Multigravida	264	88.0	8 (50.0)	256 (90.1)		
Do you have pregnancy-related problems						
Yes	180	60.0	10 (62.5)	170 (59.9)	0.044	0.834
No	120	40.0	6 (37.5)	114 (40.1)		
What Types of pregnancy-related problems						
Abortion	60	20/0	2 (12.5)	58 (20.4)		
Stillbirth	70	23.3	6 (37.5)	64 (22.5)		
Caesarean section	50	16.7	3 (18.8)	47 (16.5)	2.297	0.522
No	120	40.0	5 (31.3)	115 (40.5)		

Discussion

Our findings shed light on the seroprevalence of syphilis in pregnant women, as well as the complex relationships between socio-demographic characteristics, obstetric history, and awareness levels. The overall seroprevalence of syphilis in our study was 5.3%, which is comparable to studies in Somalia (3%) ((Jama et al., 1987b), Ethiopia (1.9%, 2.9%, and 0.44%) (Yitbarek & Ayele, 2019) (Kebede & Chamiso, 2000) and (Tridapalli et al., 2007), South Sudan (22.1%) (Emmanuel et al., 2010), Zambia (12.5%) (Ratnam et al., 1982) and Sub-Saharan Africa (2.9%) (Hussen & Tadesse, 2019). This study's syphilis seroprevalence is similarly comparable to previous studies conducted in Italy (0.49%) (Marangoni et al., 2008), Mexico (0.27%) (Noyola et al., 2006), Bulgaria (0.56%) (Tsankova et al., 2016), and Brazil (1.02%) (Domingues et al., 2014). Possible explanations for the discrepancies include geographical and temporal variations, socioeconomic and cultural variables, and variations in the availability of syphilis diagnosis and treatment.

The correlation between the prevalence of syphilis and socio-demographic parameters exhibited noteworthy patterns. The seroprevalence was highest among women aged 24-34, highlighting the importance of targeting this age group in preventive measures. A recent study conducted in Ethiopia

reported a high prevalence of syphilis in young individuals, with an adjusted odds ratio (AOR=4.3, 95% CI: 2.2 to 7.9, p=0.045) (Befekadu et al., 2022b).

This could be attributed to the higher prevalence of sexual activity within this age group, which increases the likelihood of encountering a spouse with syphilis. The educational level of the pregnant women in the present was noticeably low, with 73% of them lacking any formal education. The increased risk among people with low education demonstrates the importance of health literacy on preventative practices. Our findings are consistent with those of (Befekadu et al., 2022b) who observed that a woman's lack of knowledge of syphilis (AOR=3.3, 95% CI: 1.04 to 10.4, p=0.042) was substantially linked with syphilis. A similar study conducted in Tanzania found no statistically significant link between education and syphilis (Manyahi et al., 2015).

Disparities between urban and rural areas were noticeable, with rural residents being more likely to contract syphilis. In contrast, Ethiopia reported a 3.2% prevalence of syphilis in urban and 2.2% in rural pregnant women (Assefa, 2014). Our result is consistent with another study conducted in Ethiopia, which found a higher frequency of syphilis in rural areas compared to urban areas (COR = 3.48, p = 0.079), (Tareke et al., 2019). The increased prevalence of syphilis among rural inhabitants can be defined to inadequate healthcare access, lower education levels, socioeconomic constraints, cultural norms affecting sexual habits, and a paucity of sexual health education resources in these places.

The significant deficiency (81.7%) in knowledge about syphilis and its correlation with heightened HIV transmission risk underscores the pressing requirement for comprehensive sexual health education initiatives. A study conducted in southern China found that the awareness of syphilis knowledge ranged from 51.7% to 81.1%, (Wu et al., 2016). The discovered deficiency in knowledge on mother-to-child transmission (79.3%) highlights the significance of antenatal education to decrease the risk of vertical transmission. Study done in Uganda reported poor knowledge of syphilis mode of transmission 52.4% (Hakizimana et al., 2023). The high prevalence of stillbirths (23.3%) necessitates additional research into the possible impact of syphilis on negative pregnancy outcomes and emphasizes the need for timely identification and care. This result is consistent with a study conducted in China, which revealed 21.3% stillbirth or fetal death among pregnant women (Qin et al., 2014).

Lack of knowledge on the correlation between syphilis and HIV, as well as limited comprehension of mother-to-child transmission, is sometimes attributed to inadequate sexual health education. Insufficient access to reliable information can make individuals more susceptible to these illnesses. Implementing comprehensive educational programs is essential in order to close this knowledge gap, enabling individuals to acquire the necessary skills to successfully prevent and manage these health risks.

A limitation of our study is cross-sectional study design, small sample size collected because of the relatively short duration of the data collection. The generalizability of the findings may be limited due to the geographical restriction of the sample to Mogadishu and its surrounding rural areas, which may not fully represent the entire pregnant population in Somalia. Future study should use longitudinal studies to investigate the causal links between sociodemographic characteristics, knowledge levels, and syphilis prevalence. Furthermore, interventions addressing identified knowledge gaps should be developed and evaluated to inform public health initiatives.

In conclusion, our findings highlight the multifaceted nature of syphilis prevalence among pregnant women and emphasize the urgency of tailored interventions targeting sociodemographic disparities and knowledge deficits to enhance maternal and neonatal health outcomes.

Ethics Approval and Informed Consent

The Research Ethics Committee of the University of SIMAD School of Medicine and Health Sciences approved this study, and all participants were enrolled voluntarily after receiving the necessary information. The authors followed the EQUATOR Network (https://www.equator-network.org/) guidelines during this study.

Abbreviations

VDRL: Venereal Disease Research Laboratory, HIV: Human Immunodeficiency Virus, WHO: World Health Organization. CLIA: chemiluminescence immunoassay.

Competing interests

The authors have no conflicts of interest to disclose.

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None

Data Availability

The data are available from the authors upon request.

Consent for publication

Not applicable.

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