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Risk factors and outcomes of fetal macrosomia in Iringa municipality hospitals: A case-control study

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Abstract
Background: Factors associated with fetal macrosomia include genetics, duration of gestation, and diabetes mellitus. This condition may lead to complications for both the mother and the neonate. Thus this study aims to determine risk factors and outcomes of fetal macrosomia in comparison to those in normal-weight neonates.
Methods: A hospital-based case-control study involving 61 cases of neonates who weighed ≥ 4000g at birth and 122 controls who were neonates delivered on term with normal weight. A questionnaire was used to collect data. Data analysis was done using SPSS version 23. Bivariate and multivariate logistic regression analyses were done to identify risk factors associated with fetal macrosomia.
Results: The incidence of macrosomia was 3.26% in the Iringa municipality. Gestation age of ≥40 weeks (AOR 3.56, 95% CI= 1.65-7.69), and weight ≥80kgs post-delivery (AOR 10.22, 95% CI=2.74-38.12) were associated with delivery of macrosomia. Women with macrosomia had higher chances of prolonged labour, 2nd-degree perineal tear, and postpartum hemorrhage while their babies had hypoglycemia (AOR=8.65, 95%CI=3.23 – 23.17) compared to controls.
Conclusions: Risk factors for fetal macrosomia included a gestation age of ≥ 40 weeks, and mother weighing ≥ 80kgs post-delivery Macrosomia is an important cause of maternal and neonatal complications.
Keywords: Fetal macrosomia, risk factors, complications, neonates

Introduction

The term macrosomia is defined as birth weight above the 90th percentile of weight for that gestation. (Choukem *et al.*, 2016) Based on the variation in cut-points, it is proposed that macrosomia can be subdivided into Class I (birthweight 4000–4499g), Class II (4500–4999g), and Class III (≥5000g). Attempts at perinatal diagnosis of macrosomia have proven difficult and are often inaccurate. (Living, 2012) Diagnosis of fetal macrosomia is made by measuring birth weight after delivery; therefore, the condition is confirmed retrospectively, after delivery of the neonate.

The prevalence of macrosomia ranges from 8 to 21 %. (Rockhill *et al.*, 2015) In the USA the incidence of macrosomia is 10%, whereas, in Nigeria, the incidence of 2.5 to 5.5% has been reported. (Adesina and Olayemi, 2003; Choukem *et al.*, 2016; Olokor *et al.*, 2015) Previous studies that were carried out in a

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tertiary hospital in Tanzania reported the prevalence of macrosomia to be 2.3 % and 3.9% respectively. (Living, 2012; Said and Manji, 2016).

Factors associated with fetal macrosomia include genetics, duration of gestation, and diabetes mellitus (and/or gestational diabetes). Genetic, racial, and ethnic factors influence birth weight and the risk of macrosomia. (Gaudet *et al.*, 2014) Genetic factors, such as parental height and weight, may play a role in determining the birth weight of the neonate. Maternal age of more than 35 years, parity of more than four, with a previous history of delivering macrosomia and having gained 13-15 kgs throughout the index pregnancy. Male neonates typically weigh more than female neonates and thus comprise a greater proportion of neonates with birth weights exceeding 4000 g at any gestational age. (Frederick *et al.*, 2008; Fuchs *et al.*, 2013; Onyiriuka, 2006; Said and Manji, 2016; Wang *et al.*, 2017).

The pathophysiology of macrosomia can be explained based on Pedersen's hypothesis of maternal hyperglycemia leading to fetal hyperinsulinemia and increased utilization of glucose. (Kc *et al.*, 2015) Hence, increased fetal adipose tissue because the glucose can cross the placenta. However, the maternal-derived or exogenously administered insulin does not cross the placenta. As a result, in the second trimester, the fetal pancreas, which is now capable of secreting insulin, starts to respond to hyperglycemia and autonomously secrete insulin regardless of glucose stimulation. (Premalatha *et al.*, 2013) This combination of hyperinsulinemia and hyperglycemia leads to an increase in the fat and protein stores of the fetus, resulting in macrosomia. (Premalatha *et al.*, 2013) Hyperglycemia in the fetus results in the stimulation of insulin, insulin-like growth factors, growth hormone, and other growth factors, which in turn, stimulate fetal growth and deposition of fat and glycogen. (Rao *et al.*, 2013).

Advanced gestational age results in macrosomia by allowing the growth process to continue in utero. Advanced maternal age contributes as well, as the basal metabolic rate and metabolic body demand decrease with the advancement of age therefore increasing the risk of macrosomia. (Frederick *et al.*, 2008; Fuchs *et al.*, 2013; Wang *et al.*, 2017).

Fetal macrosomia may cause several maternal complications such as increased risks of prolonged labor, emergency cesarean section, obstetrical trauma, traumatic deliveries and postpartum hemorrhage, and maternal death. (Vercellini *et al.*, 2015; Zamorski.MA, 2001) Uterine rupture/dehiscence is independently associated with fetal macrosomia as reported in one study. (Diaz *et al.*, 2002).

On the other hand, Fetal complications include fetal distress, and neonatal hypoglycemia, compared with those appropriate for gestation age. (Weissmann-Brenner *et al.*, 2012) Other reported fetal complications include shoulder dystocia secondary to trauma to the brachial plexus during birth, facial nerve injuries, birth asphyxia, lower Apgar score (<7 at 5 min), and fracture of the humerus or clavicle. (Nassar *et al.*, 2003; Vinturache *et al.*, 2015).

Few reports provide detailed comparable information regarding the risk factors and outcome of fetal macrosomia in Tanzania, especially in regional hospitals. Considering the paucity of studies on fetal macrosomia in the Iringa municipality, the present study was undertaken to determine risk factors and outcomes of fetal macrosomia in comparison to those in normal-weight neonates in the Iringa Municipality.

Material and methods

Study design and population

This was a hospital-based case-control study, involving neonates with birth weight equal to or more than 4000gms as cases and normal birth weight neonates as controls. The study took place at Iringa Municipality, Tanzania from September to December 2017. It was carried out in two health facilities, the Iringa Regional Referral Hospital (IRRH) and Frelimo Hospital. Administratively, Iringa Municipality

has one Division, 18 wards, 40,545 households and 192 streets. These 2 health facilities offer expert obstetrics services for Iringa's urban and suburban populations.

Inclusion and exclusion criteria

All neonates delivered at IRRH and Frelimo maternity wards in the Iringa municipality from 18th September to 27th December 2017 were eligible for the study. Cases were all neonates delivered with a birth weight of 4000g or greater and their mothers, while controls were the next two neonates of the same sex as that of cases delivered with normal birth weight and their mothers. Multiple pregnancies and preterm babies were excluded from the study.

Sample size and sampling procedure

The sample size was calculated by using the following formula.

$$n = (\frac{r+1}{r})\frac{(\bar{p})(1-\bar{p})(Z_{\beta}+Z_{\alpha/2})^2}{(p_1-p_2)^2}$$

Z_{β}= 0.84 for power (1-β) of study is 80%
Z_{α}=desired level of statistical significance, for 0.05 significance level= 1.96

Ratio of controls to cases =2:1. Thus controls = 61 X 2=122
Thus,
n = cases =61, controls =122 making a total sample size (N) of 183.
A consecutive sampling technique was employed in selecting cases of macrosomic neonates. Controls were selected by picking the next two neonates of similar sex as that of the macrosomic neonate with normal weight after the selected case.

Data collection

The mother and the neonate of the selected cases and controls were followed to their admission wards or observation rooms for face-to-face interviews once they were clinically stable following delivery. The purpose and procedure of the study were explained and those who gave consent and agreed to participate in the study were enrolled in the study consecutively until the sample size was achieved.

Data collection was completed using a structured questionnaire. A validated questionnaire that has been used in similar studies (Said and Manji, 2016) was adapted to suit the study. It consisted of three parts. The first part included socio-demographic characteristics of the women namely age, occupation, marital status level of education, and residency. The second part of the questionnaire comprised maternal factors such as parity, past obstetric history (history of previous macrosomic delivery, diabetes, or gestational diabetes), excessive weight gain in index pregnancy, and post-delivery weight. The last part contained questions about fetal gender as a factor. Data was supplemented with information from the antenatal card, clinical notes, partograph, and precise measures of neonatal weight and maternal height.

At recruitment, a blood sample was drawn by a nurse from neonates' heel prick for random blood sugar estimation at the second, fourth, and sixth 6 hours after delivery. The machines were checked weekly with laboratory standards and quality control samples for quality assurance. Neonates with hypoglycemia were managed based on the standard treatment guidelines of the unit.

Data analysis

The data obtained from this study were coded and analyzed using Statistical Package for Social Sciences software (SPSS) for Windows (Version 23, Armonk, New York: IBM Corp). The independent variables were defined as follows: Diabetes mellitus included those who were diagnosed with having

raised plasma glucose prior or during pregnancy, postdate gestation age above 40 weeks, previous macrosomia, weight > 80kgs after delivery, and parity.
Gestation age was estimated from the first day of the last normal menstrual period using Naegele's formula, for those not sure of their dates, extrapolations from gestation age on booking recorded in the antenatal care card (ANC) were used. The date of quickening and use of first-trimester ultrasonography was used to estimate the gestation age if it was available.

Birth asphyxia was defined as a one-minute APGAR score of <5 and a fifth-minute score of <7. Neonatal respiratory distress syndrome was diagnosed by the presence of evidence of respiratory compromise (retractions and/or nasal flaring and tachypnea) shortly after delivery and a persistent oxygen requirement for more than 24 hours. Shoulder dystocia if prolonged delivery of head with a turtling sign with the use of obstetrics manoeuvers.
Statistical analysis involves calculations of percentages, ratios, means, and confidence intervals. The Z-test, the t-test, and the Chi-square test were used in ascertaining the level of significance of differences, *p*-value < 0.05 was considered significant.

Ethical approval
The study was approved by the Institution Review Board of the Muhimbili University of Health and Allied Sciences (MUHAS) and permission to collect data was granted by the office of the District Medical Officer (DMO) of Iringa and the Medical Officer in Charge of the Hospitals. Only those participants who freely gave consent to participate were included in the study. All information was handled confidentially and access to data was only granted to the co-authors.

Results
During the data collection period, a total of 1871 deliveries were done in the study area, of which 61 (3.26%) were macrosomic neonates with birth weight ≥ 4000 grams. There were more (41, 67.2%) male than female neonates (20, 32.8%). The overall cesarean section (C/S) rate was 45.9% and C/S for the delivery of macrosomic neonates accounted for 18.5% of the total cesarean section rate.

Risk factors for fetal macrosomia
On univariate analysis, the risk factors significantly associated with fetal macrosomia were the gestational age, previous history of delivering a macrosomic child, maternal weight at delivery, mother's height, mother's age, and mother's employment status. However, upon performing an adjusted multivariate analysis, a significant association between delivering a macrosomic neonate and maternal factors like gestational age and weight at delivery was found. Women who delivered at the gestation age of ≥40 weeks were almost four times more likely to deliver macrosomic babies (AOR= 3.56, 95% CI =1.65-7.69). Women who weighed ≥80 kg at delivery had 10 times higher odds of delivering a macrosomic neonate [Table 1].

Table 1: Bivariate and multivariate logistic regression analysis of maternal risk factors associated with the delivery of macrosomia

Risk factors associated with Fetal Macrosomia	Cases	Control	COR [95% CI]	AOR [95% CI]
Gestational age				
37-39	23	83	Ref (1)	Ref (1)
40-42	38	39	3.52 [1.85-6.69]	3.56[1.65-7.69]
Previous macrosomia				
No	47	111	Ref (1)	Ref (1)
Yes	14	11	2.73[1.18-6.35]	1.67[0.56-5.05]
Diabetes mellitus				
No	53	118	Ref (1)	Ref (1)
Pre-gestational	04	01	8.91 [0.97-81.60]	0.31[0.00-1.07]
Gestational	04	03	2.97 [0.64-13.73]	0.95[0.01-1.05]
Weight at delivery(kg)				
<80	46	117	Ref (1)	Ref (1)
≥80	15	05	7.63 [2.62-22.20]	10.2[2.74-38.12]
Height(cm)				
≤160	16	53	Ref (1)	Ref (1)
>160	45	69	2.16 [1.10-4.237]	1.05[0.48-2.28]
Age				
< 30	30	83	Ref (1)	Ref (1)
≥30	31	39	2.2 [1.18-4.23]	1.31[0.61-2.82]
Marital status				
Single	6	30	Ref (1)	Ref (1)
Married	55	92	2.99[1.17-7.64]	2.45[0.71-8.53]
Occupation				
Not employed	24	75	Ref (1)	Ref (1)
Self-employed	15	21	2.23[1.00-5.00]	1.36[0.48-3.86]
Employed	22	26	2.64[1.27-5.50]	1.26[0.38-4.16]

Level of education				
No formal education	2	4	Ref (1)	Ref (1)
Primary	27	83	0.65[0.11-3.75]	0.37[0.05-2.73]
Secondary	28	30	1.87[0.32-11.00]	0.74[0.08-6.61]
College	4	5	1.60[0.19-13.70]	1.12[0.09-14.27]

Maternal complications and fetal macrosomia

Maternal complications that were significantly associated with delivering a macrosomic neonate included prolonged labor, 2nd degree perineal tear, and postpartum hemorrhage (PPH). The odds of prolonged labor in mothers with macrosomic children were 3 times higher than in mothers with normal birth-weight children. Mothers with macrosomic children were 9 times more likely to experience 2nd degree perineal tears compared to their counterparts, and the risk of PPH was 5-fold higher among cases [Table 2]..

Table 2: Maternal complication associated with fetal macrosomia

Maternal Complication	Cases N (%)	Control N (%)	COR [95%CI]	AOR [95%CI]
Prolonged labour				
Yes	20 (32.8)	17 (13.9)	2.33[1.04-5.25]	3.01 [1.44-6.32]
No	41 (67.2)	105 (86.1)	Ref (1)	Ref (1)
Shoulder dystocia				
Yes	03 (4.9)	01 (0.8)	1.92[0.16-22.46]	6.26 [0.64-61.48]
No	58 (95.1)	121 (99.2)	Ref (1)	Ref (1)
Perineal tear				
No	43 (70.5)	109 (89.3)	Ref (1)	Ref (1)
1st degree tear	04 (6.6)	09 (7.4)	0.51[0.04-0.52]	1.13 [0.33-3.85]
2nd degree tear	14 (22.9)	04 (3.3)	0.19[0.04-1.05]	8.87 [2.76-28.47]
Post Partum Hemorrhage				
Yes	05 (8.2)	02 (1.6)	1.60[0.25-10.09]	5.36 [1.00-28.46]
No	56 (91.8)	120 (98.4)	Ref (1)	Ref (1)

Neonate complications and fetal macrosomia

There was no significant difference in the occurrence of neonatal complications between macrosomic neonates and normal-weight neonates except for the hypoglycemic state. The macrosomic neonates were nine times more likely to suffer from hypoglycemia as compared to normal-weight neonates (COR=8.65, 95%CI=3.23 – 23.17) [Table 3].

Table 3: Immediate neonatal complication associated with fetal macrosomia

Neonatal Complication	Case N (%)	Control N (%)	COR [95%CI]
Meconium aspiration			
Yes	03 (4.9)	02 (1.7)	3.10 [0.51-19.09]
No	58 (95.1)	120 (98.3)	Ref (1)
Respiratory distress			
Yes	03 (4.9)	02 (1.7)	3.10 [0.51-19.09]
No	58 (95.1)	120 (98.3)	Ref (1)
Hypoglycemia			
Yes	19 (31.1)	06 (4.9)	8.65 [3.23-23.17]
No	41 (67.2)	112 (91.8)	Ref (1)
Low APGAR score			
Yes	03 (4.9)	02 (1.7)	3.10 [0.51-19.09]
No	58 (95.1)	120 (98.3)	Ref (1)
Stillbirth fresh			
Yes	01 (1.6)	04 (3.3)	0.49 [0.05-4.50]
No	60 (98.4)	118 (96.7)	Ref (1)

Discussion

The incidence of fetal macrosomia in the current study was less than reports from elsewhere (Fuchs *et al.*, 2013; Najafian and Cheraghi, 2012; Wang *et al.*, 2017) but higher than previous results from Tanzania. The differences in the proportions between various reports can be attributed to differences in genetics, socio-cultural and socio-economic status of the population studied. Poor socioeconomic status, and lower pre-pregnancy weight in our setting contribute to lower incidence of fetal macrosomia. (Said and Manji, 2016).

The current study depicted that gestational age of above 40 weeks and maternal weight over 80 kgs post-delivery were risk factors for fetal macrosomia in the index pregnancy. Gestational age at delivery was found to be one of the factors strongly associated with the delivery of fetal macrosomia. The current study pointed out that about two-thirds of women with a gestation age of 40 weeks and above delivered macrosomic neonates, and the odds were four-fold higher compared to those with a gestation age of less than 40 weeks. This is supported by other studies (Alberico *et al.*, 2014; Najafian and Cheraghi, 2012; Said and Manji, 2016; Toweel, 2009) which revealed similar findings, however, a study done in Cameroon did not show an association between gestation age and macrosomia. (Choukem *et al.*, 2016) This observation in the current and other parallel studies is due to continuous in-utero fetal growth in the absence of risks of intrauterine fetal growth restrictions.

Compared to the control group, the chances of delivering a macrosomic neonate were 10-fold high in women who weighed more than 80 kgs post-delivery and 16-fold high in those who were diabetics. Similar findings were noted by Said et al. (Said and Manji, 2016) Obesity and diabetes are associated with an increasing rate of macrosomia hence diet counseling and management of diabetes with insulin would lower the risk of macrosomia. (Koyanagi *et al.*, 2013).

Studies have found an association between the previous delivery of a macrosomic baby with a subsequent similar event in the index pregnancy, (Najafian and Cheraghi, 2012; Onyiriuka, 2006; Said and Manji, 2016) however, this was contrary to the findings of this study. It has been postulated that women with recurrent delivery of macrosomia have deranged glucose metabolism and thus suffer from post-gestation diabetes. An increase in circulating blood glucose levels in these mothers consequently influences the fetal epigenome, thereby influencing the expression of genes that direct the accumulation of body fat or related metabolism. (Herring and Oken, 2011).

Similar to documented complications of fetal macrosomia in the literature. (Beta *et al.*, 2019; Lao and Cheng, 2014; Vercellini *et al.*, 2015; Zamorski.MA, 2001) Prolonged labor, postpartum hemorrhage, and second-degree perineal lacerations were significant maternal complications in the macrosomia group. Prolonged labor during delivery of macrosomia was three times more than in normal-weight neonates. Similar findings were reported in a previous study from Tanzania and China. (Lao and Cheng, 2014; Said and Manji, 2016) A phenomenon of prolonged labor in macrosomia is still prevalent in poor resource areas where an intrauterine diagnosis of macrosomia and eventual assisted or operative delivery is still not common like in our setting as opposed to a study from China and Brazil. (Sá *et al.*, 2003; Wang *et al.*, 2017).

Perineal tear and postpartum hemorrhage in some occasions are an event-event consequential phenomenon, and in this study, it was found that a 2nd-degree perineal tear was 9 times more likely to occur during delivery of macrosomic infant than a non-macrosomic one. The odds of postpartum hemorrhage were 5 times more in the macrosomic group compared to the non-macrosomic group. Similar findings were reported elsewhere, (Alsammani and Ahmed, 2012; Elie, 2014) the trend of perineal tear and postpartum hemorrhage in the macrosomic group goes parallel indicating that birth trauma during delivery of macrosomia contributes to the incidence of postpartum hemorrhage. Uterine atony and perineal tear after the birth of a macrosomic neonate may explain the prevalent occurrence of postpartum hemorrhage in the macrosomic group.

Regarding neonatal complications, in the current study fetal hypoglycemia was 5 times more likely to occur in macrosomic newborns as compared to those delivered with normal birth weight. This is in agreement with studies done elsewhere. (Choukem *et al.*, 2016; Rezaiee *et al.*, 2013; Said and Manji, 2016; Wang *et al.*, 2017) This can be explained by persistent hyperinsulinemia during fetal life by pancreatic beta-cells leading to hypoglycemia.

This study has a limitation of recall bias just as in any other case-control study since most participants tend not to recall correctly their experience. We could not study the association between

pre-pregnancy body mass index and risk of macrosomia because most women did not know their weights before conceiving. Moreover, there may be some errors in ascertaining the gestation age based on the menstrual cycle pattern. Another limitation of the study is a small sample size, which was ascertained by a wide confidence interval for some factors, thus, this led to a limited statistical power to adequately account for the differences in the occurrence of complications between the two groups. However, despite these limitations, this study lays a foundation for further studies involving large samples and of multicentric nature.

Conclusion

The incidence of macrosomia in the Iringa municipality was 3.26% and it was associated with a gestation age of ≥40 weeks, and a weight ≥ 80kgs post-delivery. Delivery of macrosomia was also found to be associated with maternal complications, which included prolonged labor, second-degree perineal tear and postpartum hemorrhage. The neonatal complication was newborns hypoglycemia as the only immediate neonatal complication of macrosomia. Having discovered the risks and anticipated outcomes of macrosomia in patients, early interventions and preparedness for anticipated outcomes of macrosomia in both maternal and fetal. This can give better outcomes with timely and appropriate management of complications related to macrosomia.

Declaration of conflicting interests

The authors declare no conflicts of interest.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Risk Factors and the Evolution of Tuberculosis Cases in the Laayoune and Tarfaya Provinces of Morocco

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Abstract
Background: Tuberculosis remains a major public health concern in Morocco. The main objective of this study was to evaluate its prevalence and analyze how risk factors influence the development of the disease and treatment failure rates in the Laayoune and Tarfaya provinces of Morocco.
Methods: This research took the form of a retrospective study of 1,333 tuberculosis cases, with all forms being combined, that were reported to the Center for the Diagnosis and Treatment of Respiratory Diseases in Laayoune between 2006 and 2012. We utilised the chi-square/Fisher's test for categorical analysis. Following this, a multivariate logistic analysis was undertaken to discern factors linked to Pulmonary/ extrapulmonary tuberculosis, presenting findings through odds ratios (OR) accompanied by 95% confidence intervals (CIs). Post-estimation analyses using the 'Lincom' command were executed to compute adjusted ORs and 95% CIs, amalgamating effects from preceding logistic models.
Results: This study found that 61.2% of patients were diagnosed with a form of pulmonary tuberculosis, while 38.8% presented extrapulmonary tuberculosis, including 12.2% lymph node cases and 15.9% pleural cases. In terms of treatment outcomes, 36.5% managed to complete their treatment, while 24.8% of pulmonary tuberculosis patients were cured. Nevertheless, 21.1% of patients needed to be transferred to other cities, 14.3% were lost to follow-up, and 3.2% died during treatment. 38.7% of patients had unfavourable outcomes, while 61.3% had favorable outcomes. A multivariate logistic analysis identified the risk factors associated with pulmonary and extrapulmonary tuberculosis and any adverse outcomes. Patients in some age groups had a significantly higher risk of pulmonary tuberculosis, when adjusted for diabetes (aOR=13.16, 95% CI[4.54-38.12]), more so once smoking was also taken into account (aOR=31.49, 95% CI [9.55-103.8]). Additionally, this study highlights how the high prevalence of pulmonary tuberculosis can be linked to smoking and a rural origin, with it underscoring a greater vulnerability among younger (aOR =7,16, 95% CI[2,34-21,83]) and elderly adults (aOR= 7,78 95% CI [2,24-27,00]), particularly those with diabetes.
The study identifies challenges in terms of diagnostic delays and providing access to healthcare in rural areas. The study's findings help improve our understanding of tuberculosis and will inform the development of more effective preventive strategies.
Keywords: pulmonary tuberculosis, extrapulmonary tuberculosis, risk factors and treatment results.

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Introduction

Tuberculosis (TB) is a major public health challenge around the world. Before the COVID-19 pandemic, it ranked ninth among the leading causes of death globally (Ben Ayed et al., 2018). According to a 2021 report on global tuberculosis by the World Health Organization (WHO), TB remains the leading cause of mortality among various infectious diseases (Chakaya et al., 2022) so it remains a serious threat to global public health and constitutes a major public health problem. Nevertheless, unlike the common concerns about pulmonary tuberculosis (PTB), extrapulmonary tuberculosis (EPTB) has received less attention. EPTB involves mycobacterium tuberculosis (MTB) infecting organs and sites outside the respiratory system. Indeed, it can affect various organs, leading to unusual symptoms and imaging findings. Diagnosing and managing EPTB is problematic because of the difficulty in obtaining samples and the low etiological positivity (Rodriguez-Takeuchi et al., 2019) Compared to PTB, however, there has been a significant increase in EPTB. The Global TB Report 2020 revealed that in 2019, 16% of all TB patients had EPTB (OMS, 2020, p. 202) In the United States and Europe, the share of EPTB cases has been found to vary from 20% to 53% (Rowińska-Zakrzewska et al., 2013, pp. 1974–2010)

The prevalence of tuberculosis and the deaths attributed to it remain particularly high in low- and middle-income countries (Harling et al., 2008; Költringer et al., 2023, pp. 2005–2015) Several factors can influence the risk of developing tuberculosis, such as sociodemographic factors like age, sex, and occupation; environmental factors like indoor air pollution; practices and conditions that hinder the body's immune system (e.g., smoking, malnutrition, alcohol consumption, HIV, diabetes); and therapeutic challenges associated with the emergence of drug-resistant tuberculosis (Gelaw et al., 2019; Lönnroth et al., 2009). Morocco has not been spared the burden of tuberculosis. In 2019, the WHO estimated around 35,000 new cases and 2,900 deaths were linked to this disease, which is equivalent to a mortality rate of 8.1 per 100,000 inhabitants. In 2020, the total number of recorded cases was 29,018 once all forms were combined. In the same year, 240 cases of tuberculosis–HIV co-infection were identified (MSM, 2020) Faced with this alarming situation, we urgently need to increase the awareness of tuberculosis and improve measures to combat it. In Morocco, studies investigating TB and its associated factors are still limited.

Our study acknowledges the global context of TB while emphasizing the specific relevance to Laayoune and Tarfaya. According to the statistical report published by the Moroccan Ministry of Health in 2021, the issue of tuberculosis persists in the provinces of Laayoune and Tarfaya (MSPM, 2021). Furthermore, the study conducted in Laayoune, Morocco, revealed a higher prevalence of tuberculosis in males, predominantly in its pulmonary form (70.90%), while EPTB was more common in females (61%). The highest morbidity burden was observed in individuals aged ≥15 years (92.40%). Key risk factors influencing the defence against tuberculosis included HIV infection and smoking (Eddabra & Neffa, 2020).

This research therefore seeks to deepen our understanding of tuberculosis as a persistent global public health problem. We analyze the prevalence of the disease in detail together with the risk factors (e.g., age, diabetes, smoking, family history) and assess their impact on the risk of developing the disease. In addition, we examine how these same factors influence the risk of TB treatment failing. These obtained findings should contribute to developing better prevention and treatment strategies for combatting this persistent disease in the Laayoune and Tarfaya provinces of Morocco.

Sample and Methods

Research Design and Study Population

This study focused on two provinces in the Laayoune-Sakia El Hamra region, namely Laayoune and Tarfaya, which are located on the Atlantic coastline. In 2012, these two provinces had a total population of 260.000 inhabitants. In terms of their exact geographical locations, Laayoune is

located at a latitude of 27°09'44" North and a longitude of 13°12'11" West, while Tarfaya is located at a latitude of 27°56'22" North and a longitude of 12°55'34" West.

This research is based on a retrospective study of 1,333 cases of tuberculosis of all types that were reported to the Center for Diagnosis and Treatment of Respiratory Diseases (CDTRD) in Laayoune over seven years from January 2006 to December 2012. During this study, all cases were consecutively included over time. Data collection was based on systematically filled medical records. These reported cases originated from various sources in the two provinces, such as a military hospital, various public health centres, public sector pulmonologists, and general practitioners and specialists in the private sector.

All parameters relating to reported cases—including age, sex, affected organs, results of biological and radiological examinations, treatment administered, clinical condition of patients, and so on—were carefully recorded in the medical records. The individual treatment of patients was also recorded in a register kept at the CDTRD. These individual patient records, which were systematically updated, comprised the main source of data for our study. During the study period, we identified 1,333 cases of tuberculosis that were managed and treated at the CDTRD in Laayoune. In this study, the rural-urban classification of participants was determined based on their residential status at the time of enrollment. Urban origin was assigned to participants residing in urban areas, while rural origin was designated for those residing in rural areas. The determination of rural or urban status was made considering established geographic and administrative criteria. This classification provides a basis for assessing the potential impact of residence on tuberculosis outcomes, allowing for a comprehensive analysis of the influence of rural or urban origin on the study parameters.

Case Selection: Inclusion and Exclusion Criteria

To ensure a good representation and minimize any potential sampling bias, we included all TB cases that were diagnosed and reported during the study period.

Operational definitions

- **Classification of tuberculosis**: This encompasses categories of tuberculosis PTB and EPTB —for which the patients were diagnosed and subsequently administered treatment.
  TB relapse was characterized by the appearance of a new episode of TB in a previously treated patient who was considered "cured" upon completing treatment.
- **Cured**: This outcome applies to patients with pulmonary tuberculosis where the infection was bacteriologically confirmed at the start of treatment. To be considered cured, a patient must have negative test results (e.g., a smear examination or culture) in the last month of treatment and at least once before this.
- **Treatment completed**: This category covers TB patients who completed their treatment without any evidence of failure. However, data may be lacking to indicate that the test results for a smear examination or culture were negative during the last month of treatment and at least once before this, either because the tests were simply not carried out or because the results were unavailable.
- **Treatment failure**: This outcome applied to TB patients who continued to have positive test results from a smear examination or culture after five or more months of treatment.
- **Death**: This applies to TB patients who died for various reasons before, or during, treatment.
- **Lost to follow-up**: Patient was considered lost to follow-up if they failed to start treatment or their treatment was interrupted for two or more consecutive months because this indicates irregular follow-up for the recommended treatment.
- **Favorable treatment outcomes** fall into two categories, namely patients who completed their treatment and those who were deemed to be cured.

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- **Adverse treatment outcomes** include cases of death, transfer to other cities, and patients lost to follow-up.

Statistical Analysis

We used Stata version 14 to perform our statistical analysis, with categorical variables being analyzed using the chi-square test and Fisher's exact tests. Variables with a P value less than 0.10 in the univariate analysis were included in a multivariate analysis, which used the multiple logistic regression method to identify independent variables associated with the transition from PTB to EPTB. Variables with a P value < 0.05 were considered independent risk factors, and the results were presented as odds ratios (OR) with a 95% confidence interval (95% CI). We also performed additional post-estimation analyses using the "Lincom" command to calculate the adjusted ORs at 95% CIs for the combined effects of factors from the previous multivariate logistic models.

Ethical Considerations

This work followed the ethical principles outlined in the Declaration of Helsinki for medical research involving human subjects. The necessary authorizations were obtained from the Regional Directorate of the Ministry of Health in Laayoune and the CDTRD in Laayoune to obtain access to the records required to conduct the study for the seven years from January 2006 to December 2012. In addition, the participants provided oral consent before any interviews when appropriate.

Results

Sociodemographic characteristics of patients with tuberculosis and clinical manifestations

This study considered a total of 1,333 cases of TB. It should be highlighted that a clear gender disparity emerged, with 1.73 men being diagnosed for each woman.

Among the studied cases, 817 (61.2%) had PTB, while 517 (38.8%) had EPTB. The latter category included 163 cases (12.2%) of lymph node tuberculosis and 212 cases (15.9%) of pleural tuberculosis. In terms of treatment outcomes, 330 (24.8%) of the PTB patients were cured, while 486 (36.5%) completed their treatment. Among the cases studied, however, 281 (21.1%) were transferred to other cities, 191 (14.3%) were lost to follow-up, and 43 (3.2%) died during treatment. Overall, 515 patients (38.7%) had unfavourable outcomes, while 816 (61.3%) had favorable ones (figure 1, Table 1).

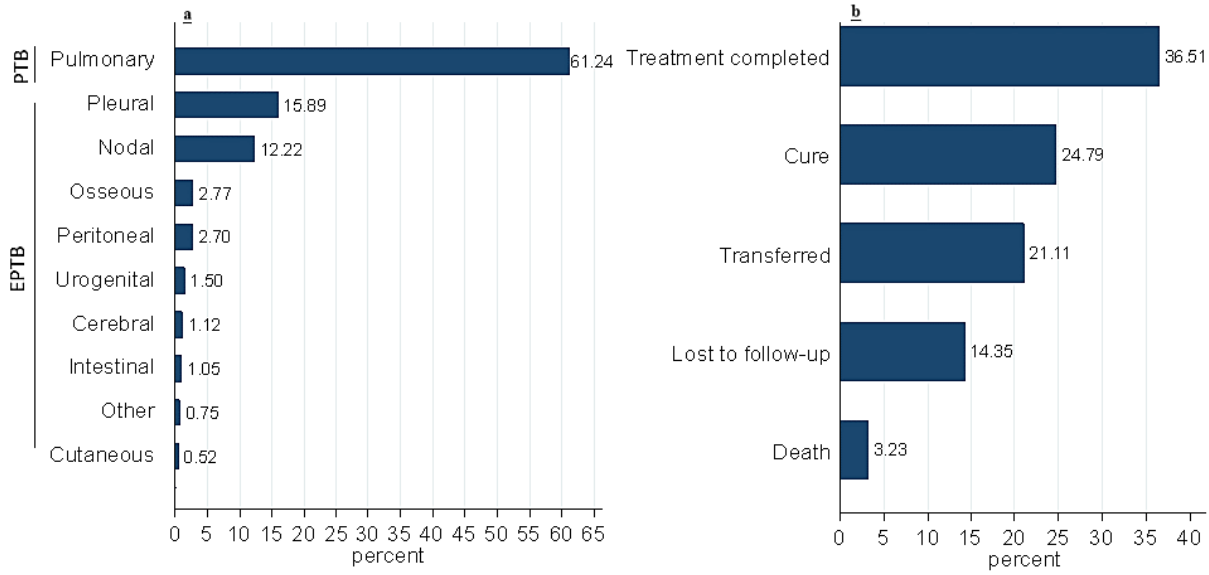

Figure 1: Tuberculosis Epidemiology: PTB vs. EPTB Distribution (a) and Case Progression (b).

Analysis of risk factors associated with PTB and EPTB

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Compared to patients with EPTB aged younger than 15 years, a significantly higher risk was observed in patients with PTB in the age groups of 15–24 years, 25–34 years, 35–44 years, 45–54 years, 55–64 years, and 65 years or older, as shown in **Table 1**. This risk is 13 times higher (95% CI: 4.54 to 38.12) when adjusted for diabetes, and it reaches 31 times higher (95% CI: 9.55 to 103.8) when adjusted for both diabetes and smoking. Similarly, patients with a history of relapse, a male gender, a rural origin, diabetes, a family history, and a smoking habit were significantly and positively associated with a greater risk of developing PTB compared to patients with EPTB.

Multivariate logistic modelling of risk factors associated with adverse outcomes

The results of this analysis revealed that patients from rural areas have a greater risk of unsuccessful treatment outcomes when compared to patients from an urban setting, with the aOR being 2.66 (95% CI: 1.23–5.75). Once this rural origin is combined with smoking, however, it rises to 3.52 (95% CI: 1.45–8.52). Moreover, the association between a rural origin, smoking, and unsuccessful treatment outcomes is particularly strong among younger age groups, particularly among patients aged 25–34 years with an aOR of 7.16 (95% CI: 2.34–21.83) and patients aged over 64 years old with an aOR of 7.78 (95% CI: 2.24–27.00).

Table 1: The results of the univariate analysis and logistic multivariate analysis of risk factors associated with PTB and EPTB (N=1333).

	Location of tuberculosis		p-value	Univariate analysis [c] OR (95% CI) p-value	Multivariate analysis [a] OR (95% CI) p-value
	PTB N (%)	EPTB (%)			
Age (years)					
<15	19 (2.3)	41 (7.9)		Ref	Ref
15-24	178 (21.8)	115 (22.2)		3.34(1.84-6.03) ***	**3.25(1.61-6.56)** **
25-34	255 (31.2)	153 (29.6)		3.59(2.01-6.42) ***	**2.95(1.48-5.91)** **
35-44	151 (18.5)	86 (16.6)	***	3.78(2.06-6.93) ***	**3.50(1.70-7.22)** **
45-54	113 (13.8)	55 (10.6)		4.43(2.35-8.34) ***	**3.55(1.66-7.59)** **
55-64	53 (6.5)	39 (7.5)		2.93(1.48-5.80) **	**2.42(1.06-5.52)** *
≥65	48 (5.9)	28 (5.4)		3.69(1.80-7.57) ***	**5.57(2.27-13.63)** ***
≥65[a]					**13.16(4.54-38.12)** ***
≥ 65[b]					**31.49(9.55-103.8)** ***
Episode of tuberculosis					
New case	744 (91.1)	499 (96.5)		Ref	Ref
Relapse	68 (8.3)	12 (2.3)	***	3.08(2.03-7.09) ***	**3.80(1.81-8.00)** ***
Failure	5 (0.6)	6 (1.2)		0.55(0.16-1.84)	**0.49(0.04-6.02)** NS
Sex					
Male	578 (70.7)	266 (51.7)	***	Ref	Ref
Female	239 (29.3)	249 (48.3)		0.44(0.35-0.55) ***	**0.49(0.37-0.65)** ***
Origin					
Urban	733 (96.6)	475 (98.5)	*	Ref	Ref
Rural	26 (3.4)	7 (1.5)		2.40(1.03-5.58) *	**2.55(1.05-6.18)** *
Diabetes					
No	632 (93.2)	403 (96.4)	*	Ref	Ref
Yes	46 (6.8)	15 (3.6)		1.95(1.07-3.54) *	**2.36(1.24-4.48)** **
Family history					
No	623 (91.9)	393 (94.0)	NS	Ref	Ref
Yes	55 (8.1)	25 (6.0)		1.38(0.85-2.26)	**1.96(1.14-3.37)** *
Smoking					
No	591 (87.0)	399 (95.5)	***	Ref	Ref
Yes	88 (13.0)	19 (4.5)		3.12(1.87-5.21) ***	**2.39(1.40-4.09)** **

 https://dx.doi.org/10.4314/thrb.v25i1.2

a: Combined effect of age ≥ 65 and diabetes; b: Combined effect of age ≥ 65, diabetes and smoking; * p < 0.05, ** p < 0.01, *** p < 0.001.

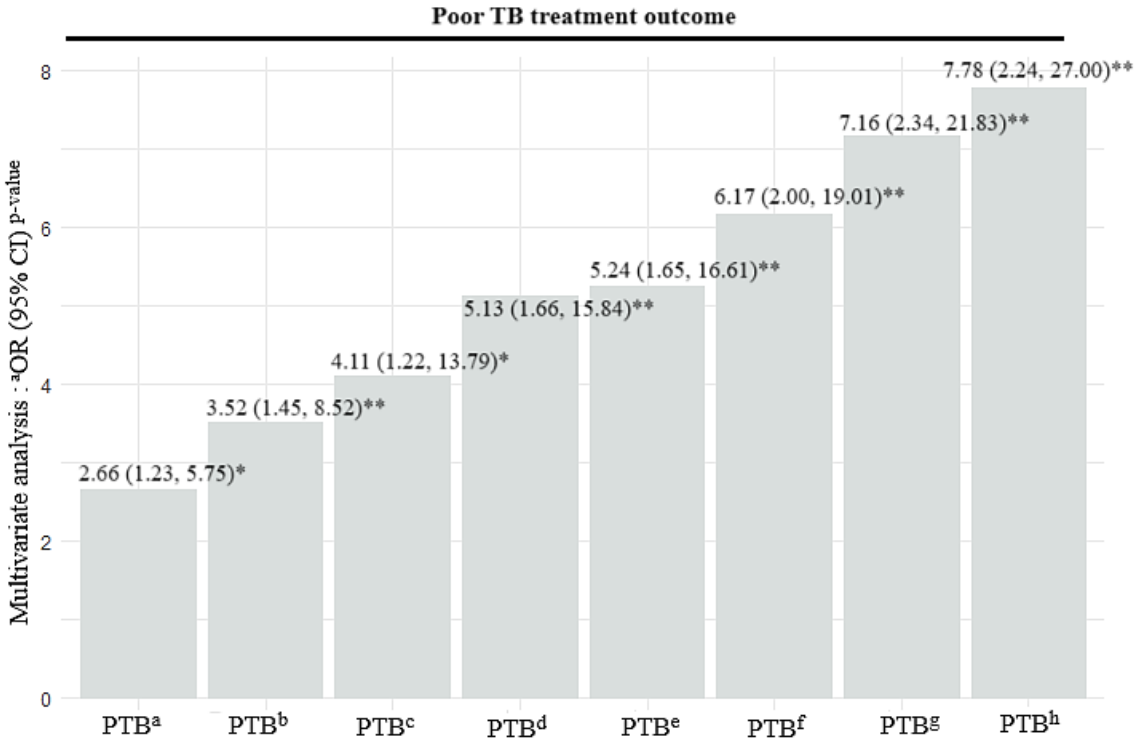

Figure 2: The multivariate model of risk factors associated with poor TB treatment outcomes (PTB: pulmonary tuberculosis).

a: The effect of a rural origin in tuberculosis patients; b: The combined effect of a rural origin and smoking in tuberculosis patients; c: The combined effect of a rural origin and smoking among tuberculosis patients aged 55–64 years; d: The combined effect of a rural origin and smoking among tuberculosis patients aged 35–44 years; e: The combined effect of a rural origin and smoking among tuberculosis patients aged 15–44 years; f: The combined effect of a rural origin and smoking among tuberculosis patients aged 45–54; g: The combined effect of a rural origin and smoking among tuberculosis patients aged 25–34 years; h: The combined effect of a rural origin and smoking among tuberculosis patients aged 65 and over. In addition, a, b, c, d, e, f, g, and h were adjusted according to the episode of tuberculosis, sex, diabetes, and family history. * p < 0.05, ** p < 0.01, *** p < 0.001.

Discussion

Tuberculosis stands as a significant global health concern. In developing countries, major global health organizations view TB as a serious public health challenge, making substantial investments to mitigate TB-related mortality and morbidity (WHO, 2023). In the present study, the prevalence of PTB was found to be 61.4%, which is much higher than that for EPTB at 36.6%. This is consistent with the findings of several previous research efforts (Arnedo-Pena et al., 2019; Chahboune et al., 2022; Chakaya et al., 2022; Eddabra & Neffa, 2020)Indeed, a TB infection usually starts in the respiratory tract, but it can spread to the blood and lymph nodes if the immune response is insufficient for containing the bacteria in the lungs. Nevertheless, the pathogenesis of tuberculosis is not fully understood. Studies have shown that women may be more prone to active EPTB, which would be consistent with our observations (Min et al., 2023; Sbayi et al., 2020; Tahseen et al., 2020).

Age is linked to the risk of PTB. We found that while children younger than 15 years have a lower risk of developing PTB, they are more likely to develop lymph node and pleural tuberculosis, regardless of sex, which is consistent with previous research (Dubois et al., 2022; Ramos et al., 2019). Additionally, another study conducted in Northwest Morocco revealed that younger patients are preferentially affected by lymph node tuberculosis (Sbayi et al., 2020). Similarly, a study carried out in the Casablanca-Settat region found that extreme age groups were more prone to pleural and lymph node tuberculosis (Chahboune et al., 2022). Some pathophysiological and diagnostic factors have been suggested for young patients, but the mechanisms that underlie the varying prevalences of pleural tuberculosis between sexes remain unknown, so this requires further research (Alpert et al., 2020; Carr, 2015; Jmaa et al., 2020). The lower prevalence of PTB among children may be partly due to neonatal BCG vaccination. Nevertheless, among those aged 15–64 years, the risk of PTB increases significantly, with it peaking at 70.4% among those aged 15–44 years, which is consistent with data from the Ministry of Health in Morocco (MSM, 2015).

This increased risk may result from cumulative exposure to MTB, air pollution, smoking, and other age-related risk factors. On the other hand, the increased risk of PTB among younger people could be mainly attributed to the transmission of the disease within the community being facilitated by frequent gatherings in school and other social activities, thus increasing the risk of exposure. Furthermore, our study revealed a significantly higher prevalence of EPTB among women, especially for lymph node and pleural tuberculosis, regardless of age. This observation is consistent with the results of studies conducted in Spain (Rolo et al., 2023) and Pakistan (Tahseen et al., 2020) all also reported a higher prevalence of lymph node tuberculosis in women, although unlike in our results, pleural tuberculosis was found to be more common in men. The underlying reasons for women's increased predisposition to EPTB remain unknown, but biological factors like sex hormones and genetic elements may well be playing a role in influencing the immune system (Gupta et al., 2022(Gupta et al., 2022).

Smoking and diabetes are two factors that were independently associated with the risk of PTB, and this risk increases significantly for people aged over 64 with diabetes (a 2.36 times higher risk) and especially for those with diabetes who smoke simultaneously (5.65 times higher risk). This correlates with the findings of Yorke et al. (2017) in highlighting how smoking and diabetes worsen the severity of TB. This has already been reported by a Moroccan Multicenter National Study, indicating that diabetes and smoking are independent risk factors for tuberculosis (Aachari et al., 2022). Furthermore, numerous studies have reported that 5–30% of tuberculosis patients also have diabetes, especially in developing countries where tuberculosis is more widespread, thus favouring the co-occurrence of tuberculosis and diabetes (Berbudi et al., 2020; Niazi & Kalra, 2012; World Health Organization, 2017). Some interesting research has also found that hyperglycemia is associated with an increased risk of delayed diagnosis for PTB, which can have serious implications for ongoing community TB transmission and disease outcomes at treatment clinics (Wang et al., 2017). Furthermore, the combination of tuberculosis and diabetes may interfere with therapeutic interventions for tuberculosis, as well as diabetes management, and this may influence the course of the disease (Bisht et al., 2023).

Underlying immune mechanisms that could be responsible for the increased susceptibility to tuberculosis in diabetic patients include defects in bacterial recognition, reduced phagocytic activity, slow migration of macrophages and antigen-presenting cells, alterations in chemokine/cytokine secretion, and an impaired T lymphocyte response. Such factors compromise the immune response, thus increasing the burden and disease pathogenicity of MTB in various organs, including the lungs and liver (Alim et al., 2020; Vallerskog et al., 2010). To reduce this risk, diabetic patients need to maintain good metabolic control. The impaired immune mechanisms that result from hyperglycemia highlight the importance of using diabetes management to prevent the complications of tuberculosis. Indeed, a joint effort to manage both diabetes and tuberculosis is needed to improve patient health outcomes and reduce the overall burden of tuberculosis in at-risk populations.

It comes to smoking, significantly increases the risk of MTB infection in several ways: For example, it reduces the activity of the alveolar macrophages, disrupts mucociliary clearance, weakens the immune response of pulmonary lymphocytes, affects the activity of the pulmonary dendritic cells, and decreases the effectiveness of natural killer cells (Underner & Perriot, 2012). Indeed, previous studies have reported higher mycobacterial loads in the sputum of smoking patients (Adegbite et al., 2020). Our results also highlight the important role that smoking plays in the positivity of tuberculosis bacilli in the sputum of patients with PTB. It is therefore imperative to promote smoking cessation to strengthen the immune response, reduce smokers' vulnerability to tuberculosis, and improve the overall health of smokers' lungs.

Our study of reported cases between 2006 and 2012 consisted of 93.2% new cases and 6% relapses. In 2020, Eddabra and Neffa conducted a similar study in the same province and noted a very similar trend, with 93.40% being new cases and 6.60% being retreatments (Eddabra & Neffa, 2020). Taking these two results together, the prevalence of tuberculosis cases in the region over several years shows a certain stability in the epidemiological situation of the disease.

Tuberculosis relapse was identified as a significant factor contributing to the onset of the disease in individuals in this study. Although most patients with tuberculosis can be cured with standard combination therapeutic regimens, there is still a risk of a subsequent episode or recurrence of the disease in some patients after completing their initial treatment (Zong et al.(Zong et al., 2018). Patients with recurrent TB often require longer treatment cycles with the use of more toxic drugs, and overall, it reduces the chance of treatment success, promotes further transmission of mycobacterium tuberculosis (MTB), and increases the TB burden (Liu et al., 2020). TB recurrence can arise from two distinct origins, namely a relapse in the form of an endogenous reactivation of the initial infection or an exogenous reinfection with a new MTB strain (Ruan et al., 2022; Ruan et al., 2022). High relapse rates typically result from insufficient treatment of TB, while high reinfection rates suggest poor case management and the presence of many undetected cases circulating in the community (Du et al., 2021; Du et al., 2021; Folkvardsen et al., 2020)

Our study found that men had a greater tendency to develop PTB than women did with a prevalence of 61.2%. This male predominance for TB cases has been noted in Morocco, where men constitute the majority of adult TB patients (Chahboune et al., 2022; Eddabra & Neffa, 2020). Several reasons have been put forward to explain this gender disparity in tuberculosis prevalence. For example, in many countries, women have limited access to health care, which can lead to greater numbers of undiagnosed TB cases. Furthermore, screening and diagnostic strategies for women that are potentially less sensitive can lead to the prevalence of tuberculosis among females being underestimated.(Citro et al., 2021).

Family history is also considered a risk factor for PTB, with the prevalence of TB among patients with PTB and family history being 8% in our study, which is consistent with the findings of a Moroccan study (Sabri et al., 2019). This figure reflects the findings of another study conducted in sub-Saharan Africa (7.8%) (Shah et al., 2014) but it is somewhat higher than that reported by a study in Nepal (1.6%) (Gyawali et al., 2012). On the other hand, it is far lower than the value reported in a previous study carried out in Peru (34%) (Otero et al., 2016).

These wide variations may be attributed to differences in the study population, living conditions, and population density, which are important risk factors for respiratory diseases like tuberculosis (Citro et al., 2021; Kampala et al., 2013), as well as to each study's diagnostic methods (Federal Ministry of Health, 2012). Additionally, disparities in household contacts, socioeconomic status, lifestyle, and dietary habits could also explain these differences (Chandrasekaran et al., 2017).

The prevalence of active PTB is 2.55 times higher in rural areas than it is in urban areas, suggesting that there are diagnostic delays in rural areas due to several factors, such as limited access to health facilities, a lack of diagnostic services close to villages, long distances to the nearest health centre, and a lack of monitoring among health workers (Citro et al., 2021; Belay et al., 2012).

What is more, rural populations often have limited knowledge of TB's symptoms and frequently underestimate its severity, leading to delays in diagnosis and treatment (Aljassim & Ostini, 2020). Thus, it is imperative to implement specific strategies that are tailored to local circumstances to improve the public health system and better meet the needs of TB patients in rural areas.

Patients from rural areas are also at greater risk of treatment failure than those from urban areas, and this observation is consistent with research that has shown geographic disparities in TB management due to limited access to health care in rural areas (Abubakar et al., 2008; Nidoi et al., 2021). Although TB recurrence is lower in rural than it is in urban areas, adverse outcomes are more common in rural areas, thus increasing the risk of spreading multidrug-resistant tuberculosis. Likewise, most studies identify urban areas as having better outcomes thanks to more efficient patient monitoring systems and easier access to health services (Adatu et al., 2003; Cattamanchi et al., 2015). Thus, barriers to accessing diagnostics and treatment can influence TB treatment outcomes.

The results suggest that the association between a rural origin, smoking, and treatment failure is more marked in patients aged over 64 and younger adults, particularly those aged 25–34. A Moroccan study also found a high risk of treatment failure among smokers aged over 50 years, with the variation in risk being due to confounding factors for which adjustments were made (Tachfouti et al., 2011).

Smoking is associated with lower cure rates, faster progression, and increased severity of TB. Indeed, a clear immunopathological connection has been established between smoking and tuberculosis (Maurya et al., 2002). In this study, when combined with a rural origin and age, smoking lowers the treatment success rate. Previous work has also established a significant association between smoking as a predictor and risk factor for poor adherence, as well as a higher rate of treatment discontinuation, in TB care settings (Chang et al., 2004; Khan et al., 2020). This is particularly significant because untreated patients are at high risk of developing drug-resistant tuberculosis and spreading the disease in the community (Shamaei et al., 2009). Smoking is therefore a modifiable risk factor that can have a major impact on PTB outcomes (El Hamdouni et al., 2019). Indeed, reducing the prevalence of smokers in the general population could reduce the incidence of PTB and poor treatment outcomes like treatment failure (Khan et al., 2020). It therefore seems appropriate to include tobacco interventions when designing tuberculosis-control strategies, such as offering smoking cessation treatment at the time of diagnosis to improve the chances of a successful TB treatment.

Limitations

This study has its limitations, most notably its retrospective nature. To strengthen the validity of the cause-and-effect relationships identified in this study, diverse multicenter studies are required. Furthermore, it is important to recognize that our results may have been influenced by potential confounding factors that were unaccounted for, given that the study is based on medical records, and this limited the analysis to a small number of factors. Future research is therefore needed to search for such factors.

More specifically, some potential confounders like HIV infection, obesity, alcohol/drug abuse, and so on were not documented in the data we used for this study. It is therefore essential to consider these variables in future research to obtain a more complete picture. Finally, some caution should be taken when generalizing our results to a larger population, given that our data is derived from the two provinces of Laayoune and Tarfaya in the south of Morocco.

Conclusion

In conclusion, this in-depth study of tuberculosis analyzed 1333 cases and revealed vital information about the prevalence, risk factors, and distribution of tuberculosis cases according to the origin of the disease. It confirms that PTB is particularly prevalent in men and highlights the role that rural

origin, age, diabetes, smoking, and family history play in determining the risk of developing tuberculosis.

The results highlight that younger adults and elderly people are more vulnerable, particularly smokers with diabetes. This study also reveals the significant role that smoking plays as an independent factor associated with PTB, thus highlighting the importance of taking measures to encourage smoking cessation among the population, especially for high-risk groups.

In addition, this study demonstrates that a rural origin is associated with an increased risk of TB treatment failure, particularly for smoking patients of all ages. Smoking has a major impact on tuberculosis outcomes by weakening the immune system, so smoking interventions, including smoking cessation treatment at the time of diagnosis, are essential for improving TB treatment outcomes and reducing the disease's prevalence, thereby promoting better public health.

There are also challenges related to diagnostic delays in rural areas, so we call for improved access to health care and campaigns to increase awareness of TB symptoms in these regions. Overall, this research provides crucial data to better understand tuberculosis and develop prevention and treatment strategies that will be more effective. It highlights the complexity of the disease's progression in society and the need to address multiple risk factors to reduce its burden on public health.

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Advanced Maternal Age, Gestational Diabetes, and Parity: A Moderated Mediation Model for Preeclampsia

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Abstract
Background: As the trend of delaying pregnancy continues to grow globally, the prevalence of preeclampsia is expected to increase along with it, placing a significant burden on health systems. This study explores the mediating roles played by gestational diabetes and parity in the relationship between maternal age and preeclampsia.
Methods: This retrospective study considered 700 full-term pregnancies, with preeclampsia being the outcome of interest. Data were gathered from pregnant women at the El Idrissi provincial hospital in Kenitra, Morocco. We used Hayes' PROCESS macro model 7 (version 4.2) to analyze the direct effects and indirect effects in terms of moderated mediation while controlling for any family history of hypertension and hyperglycemia.
Result: The results show that gestational diabetes partially mediates the relationship between maternal age and preeclampsia with an indirect effect of 0.5275 (Boot SE = 0.2833, Boot CI%: 0.0151, 1.1258) for patients of advanced age and 0.8824 (Boot CI %: 0.0266, 1.7895) for those of very advanced age. In addition, parity moderates this relationship (advanced age x parity: β=0.2339, 95% CI: 0.1372, 0.3306; very advanced age x parity: β=0.2446, 95% CI: 0.0343, 0.4549). Finally, the mediating effect of gestational diabetes is also moderated by parity with a moderated mediation index of 0.4964 (Boot CI %: 0.0103, 1.1143) for patients of an advanced age and 0.5192 (Boot SE = 0.3677, Boot CI %: 0.0005, 1.4035) for those of a very advanced age.
Conclusion: A very advanced maternal age is an independent risk factor for preeclampsia. Multiparous women, especially older women, also have an increased risk of gestational diabetes, further increasing the risk of preeclampsia.

Keywords: maternal age; gestational diabetes; preeclampsia; parity; moderated mediation model.

Introduction

According to the International Federation of Gynecology and Obstetrics (FIGO), an advanced maternal age (AMA) is defined as being 35 years or older at the time of the expected delivery (Frick, 2021). This age limit was historically established based on the reduced fertility and increased risk of chromosomal abnormalities and miscarriages that typically occur after this age (Lopian et al., 2023). Currently, the definition of very advanced maternal age (vAMA) is a matter of some debate, although some researchers consider an age of 40 years or more at the time of expected delivery to be a very advanced maternal age (vAMA) (Kahveci et al., 2018).

Delaying pregnancy until an older age carries significant health risks for women and their babies because women aged over 35 years at the time of delivery exhibit increased rates of gestational diabetes (Vounzoulaki et al., 2020), preeclampsia (Vandekerckhove et al., 2021), and

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maternal and neonatal morbidity and mortality (Vounzoulaki et al., 2020). Moreover, these risks increase further with increasing maternal age.

As the trend of delaying pregnancy continues to grow globally, the prevalence of preeclampsia is expected to increase along with it, placing a significant burden on health systems. Nevertheless, many of the complications associated with preeclampsia are preventable, highlighting the importance of closely monitoring pregnant women and making timely interventions to optimize maternal and neonatal outcomes.

International research has recently indicated that the proportion of AMA and vAMA pregnant women is increasing year by year (J. Cao et al., 2022). In addition, with the spread of assisted reproduction techniques, the proportion of AMA mothers is expected to increase over the years to come (Shan et al., 2018). According to a survey conducted by the World Health Organization (WHO) among 308,149 mothers and newborns in 29 countries in Africa, Asia, Latin America and the Middle East, the proportion of AMA mothers reached 12.3% (Laopaiboon et al., 2014).

Recent studies have also shown that advanced maternal age and gestational diabetes are significant predictors of preeclampsia (Dai et al., 2023; J. Li et al., 2023; Sun et al., 2023). Additionally, a large-scale meta-analysis of 120 million participants revealed a near-universal trend, namely that the risk of gestational diabetes (GDM) increases linearly with age (Y. Li et al., 2020). Preeclampsia has also been significantly associated with gestational diabetes (J. Li et al., 2023). Nevertheless, the exact biological mechanisms linking maternal age, GDM, and preeclampsia are only partially understood, although many pregnancy-related conditions involve changes in oxidative stress and inflammation (Al-Gubory et al., 2010; Mullins et al., 2013; Myatt & Cui, 2004).

These alterations have also been observed with ageing, so they could affect placental function in older women (Barja, 2014; de Steenwinkel et al., 2013; Girard et al., 2014; Myatt, 2010; Schetter et al., 2010). Indeed, studies have identified placental dysfunctions in older women, such as reduced amino acid transport, abnormalities in cell turnover, and reduced placental efficiency (Lean et al., 2017). The precise association between maternal age and GDM remains unclear, although elevated insulin resistance, increased levels of circulating adipokines and inflammatory markers, and oxidative stress may at least partially explain this phenomenon (Fontana et al., 2007; Shin & Song, 2015).

He et al. also proposed the hypothesis that there is a reduced concentration of fatty acids in the placenta of women aged 35 and older, with this being accompanied by elevated inflammatory markers like IL-1β and TNF- α in the context of GDM (He et al., 2022). However, the specific signalling pathway that could explain the connection between lipid metabolism and glucose homeostasis in the context of GDM remains unclear.

Nevertheless, gestational diabetes contributes to preeclampsia through hyperglycemia, inflammation, neutrophil hyperactivation, and oxidative stress, because these factors impair placental vascularization, thus triggering preeclampsia, and obesity only amplifies these mechanisms (Yang & Wu, 2022).

Given the significant associations among an advanced maternal age, preeclampsia, and gestational diabetes, as well as the association between gestational diabetes and preeclampsia, it is plausible that gestational diabetes plays a mediating role in the relationship between an advanced maternal age and preeclampsia. Nevertheless, few studies have examined how advanced maternal age and gestational diabetes interact to worsen preeclampsia outcomes.

The interaction between parity and age on the risk of gestational diabetes also modifies the effect of age on this risk during pregnancy. According to Dai et al. advanced age and parity increase the risks of both gestational diabetes and preeclampsia, with their interaction intensifying the risks (Dai et al., 2023). Thus, multiparity (i.e., the second or further pregnancy) together with advanced maternal age may exacerbate the negative effect of gestational diabetes in causing preeclampsia. Our study examines and tests these links through a moderated mediation model.

The proposed conceptual model is presented in Figure 1. Based on a literature review, we formulated the following hypotheses:

Hypothesis 1. Gestational diabetes mediates the relationship between maternal age and preeclampsia.

Hypothesis 2. Parity moderates the relationship between maternal age and gestational diabetes.

Hypothesis 3. Parity moderates the mediating effect of gestational diabetes on the relationship between maternal age and preeclampsia.

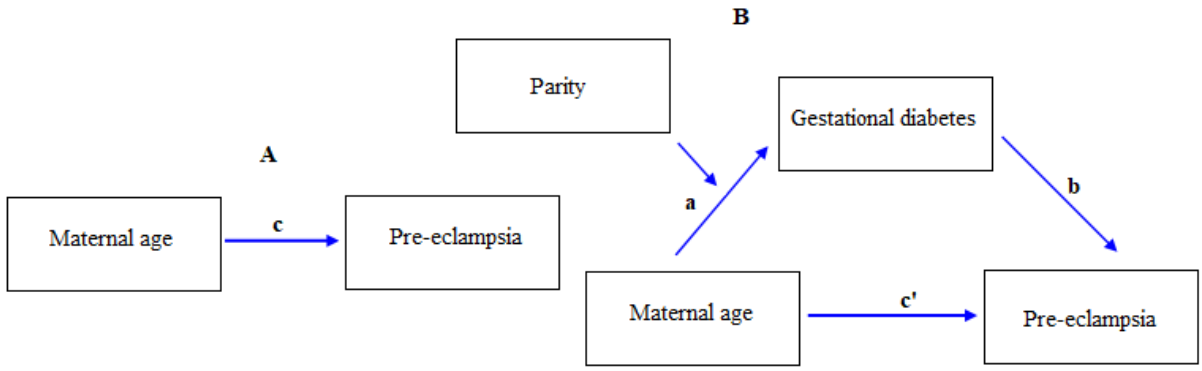

Figure 1: The hypothesized mediating effect of gestational diabetes on the association between advanced maternal age and preeclampsia and the proposed moderating effect of parity. (**A**) depicts the direct effect of maternal age on pre-eclampsia, while (**B**) depicts how the effect of maternal age on pre-eclampsia is mediated by gestational diabetes. Interaction index *a* refers to the direct effect of the predictor on the mediator, *b* refers to the direct effect of the mediator on the outcome variable, *c* refers to the direct effect of the predictor on the outcome, and *c'* refers to the direct effect of a predictor after controlling for the indirect effect of the predictor through the mediator on the outcome.

Materials and Methods

The Study Population and Research Design

This study was conducted in Kénitra Province in the Rabat-Salé-Kénitra region in the northwest of Morocco. This province had approximately 1,061,435 inhabitants in 2015, and it is divided between urban areas (606,993 inhabitants) and rural areas (454,442 inhabitants). There are approximately 214,640 households, including 139,687 in urban areas and 74,953 in rural areas (HCP, 2015).

This retrospective study was conducted at the maternity ward of El Idrissi Provincial Hospital in Kenitra, Morocco between April and October 2021. It collected information by reviewing patient records at this tertiary hospital for 700 pregnant women who attended prenatal consultations in primary health centres and gave birth at this maternity ward.

During this empirical study, we took into account three types of bias to guarantee reliable results. Selection bias was reduced through representative random sampling (Infante-Rivard & Cusson, 2018). For classification bias (Greenland, 1980), we checked the classification of subjects to avoid errors linked to exposure and the risks being studied (i.e., gestational diabetes and preeclampsia). In addition, multivariate logistic modelling was used to account for potential confounding factors (Jean et al., 2009).

Exposure

According to the International Federation of Gynecology and Obstetrics (FIGO), an advanced maternal age (AMA) is defined as being 35 years or older at the time of expected delivery (Frick, 2021). This age limit was determined in the past based on the reduced fertility and increased risks of chromosomal abnormalities and miscarriages that typically occur after this age (Lopian et al.,

2023). For this study, the term "very advanced maternal age" (vAMA) refers to women expected to give birth at the age of 40 or older (Lean et al., 2017).

Outcome

Preeclampsia is associated with significant proteinuria (greater than 0.3 g per 24 hours) and pregnancy-related hypertension (i.e., systolic blood pressure greater than or equal to 140 mmHg and/or diastolic blood pressure greater than 90 mmHg) manifesting after the 20th week of amenorrhea (Fox et al., 2019).

The Mediating Role of Gestational Diabetes

This study considered gestational diabetes as a mediator of interest in the relationship between maternal age and the risk of preeclampsia. This variable was selected based on previous studies that have demonstrated its association with maternal age (Schummers et al., 2018) and preeclampsia (J. Li et al., 2023).

A fasting capillary blood glucose test was performed at the first prenatal visit (fasting positive ≥0.92 and ≤1.25g/l). The women were invited again at a gestational age between 24 and 28 weeks to fast for an induced hyperglycemia test (OGTT) with 75g of glucose (positive fasting ≥0.92 g/l or after 1 hour ≥1.8g/l or after 2h ≥ 1.53g/l) (Utz & Assarag, 2016).

The Moderating Effect of Parity

Parity, which can be divided into primiparous and multiparous, can play a significant role in increasing the risk of gestational diabetes in older women (Dai et al., 2023; Orazulike et al., 2015). Women with an older maternal age and multiparity have an increased risk of gestational diabetes (Wagan et al., 2021). These findings suggest that parity may act as a buffer against the negative consequences of an advanced maternal age. In particular, if gestational diabetes mediates the relationship between maternal age and preeclampsia, and parity modifies the relationship between maternal age and gestational diabetes, then the mediating effect of gestational diabetes should also be influenced by parity.

Covariates

Confounding factors connected to maternal age, preeclampsia, and gestational diabetes were considered as potential covariates (Endeshaw et al., 2016; Lamminpää et al., 2012; Lewandowska, 2021; Sun et al., 2023). A family history of hypertension (yes or no) and a family history of hyperglycemia (yes or no) were considered to be potential confounders in this study.

Ethical Considerations

This investigation followed the ethical principles of the Declaration of Helsinki for medical research involving human subjects. The necessary authorizations were obtained from the Regional Directorate of the Ministry of Health in Rabat and from the Directorate of the El Idrissi provincial hospital to gain access to maternity services that were needed to conduct the study. The participants also gave oral consent before any interviews where applicable.

Data Analysis

All analyses were performed using SPSS and Stata, version 18. The continuous variables are expressed as mean ± standard deviation. Student's *t-test* was adopted to compare two groups of variables. However, the parametric ANOVA test and multiple comparisons of means by Bonferroni's test were used to estimate the significance of differences between the parameters examined.

Following the procedure of Baron and Kenny, we examined the mediating effect of gestational diabetes on the relationship between maternal age and preeclampsia (Baron & Kenny, 1986) (Figure 1).

A logistic regression model assessed the impact of maternal age on preeclampsia without considering gestational diabetes (path c), while another model evaluated the relationship between maternal age and gestational diabetes (path a). The association between gestational diabetes and preeclampsia was also analyzed (path b). If gestational diabetes was found to completely mediate the relationship between maternal age and preeclampsia (path c'), it would indicate that the relationship was fully mediated, otherwise, it was partially mediated.

The prevalences of gestational diabetes and preeclampsia, adjusted by maternal age, were estimated using the "margins" command (Williams, 2012). A moderated mediation analysis was performed using the PROCESS macro version 4.2 for SPSS (Hayes, 2017), thus using the bootstrap method (5000 samples) to estimate the indirect effects and the moderated mediation index at a confidence interval of 95%. Significant results were regarded as those whose confidence interval excluded zero.

Results

The average age of participants in our sample was 27.15 ± 7.08 years, with the youngest age being 15 years and the oldest age being 47 years. The results of the Bonferroni multiple comparison indicated that patients aged 40 years and older had significantly higher blood glucose levels than their younger counterparts, including those aged younger than 35 years. Similarly, patients aged 35 to 39 years had significantly higher blood glucose levels than those aged less than 35 years. What is more, patients with preeclampsia experienced significantly higher blood sugar levels than patients without preeclampsia. Using the Student's t-test, we also discovered that patients with a family history of hypertension and hyperglycemia experienced significantly higher blood glucose levels, as shown in Table 1.

Table 1: Comparison of characteristic values for the sociodemographic and clinical data of patients based on the Student/ANOVA test

Parameter	Gestational diabetes
Age	
Age less than 35 years	0.5323±0.21[a]
advanced maternal age	0.7816±0.27[b]
very advanced maternal age	0.9636±0.20[c]
Preeclampsia	
Yes	0.77±0.36[a]
No	0.56±0.23[b]
Family history of hypertension	
Yes	0.70±0.24[a]
No	0.57±0.30[b]
Family history of hyperglycemia	
Yes	0.67±0.27[a]
No	0.57±0.24[b]

Mean that do not share a letter are significantly different.

Binary Logistics Regression

The ORs (odds ratios) and 95% CIs for gestational diabetes and preeclampsia are presented in Figure 2. AMA [p-value < 0.01] and vAMA [p-value < 0.001] were associated with a significantly higher risk of preeclampsia in the unadjusted model (Figure 2a). Following adjustment (Figure 2b), vAMA [p-value < 0.01] and gestational diabetes [p-value < 0.001] were positively related to preeclampsia. In the other model (Figure 2c), parity [p-value < 0.01], AMA [p-value < 0.001], and vAMA [p-value < 0.01] were positively associated with gestational diabetes.

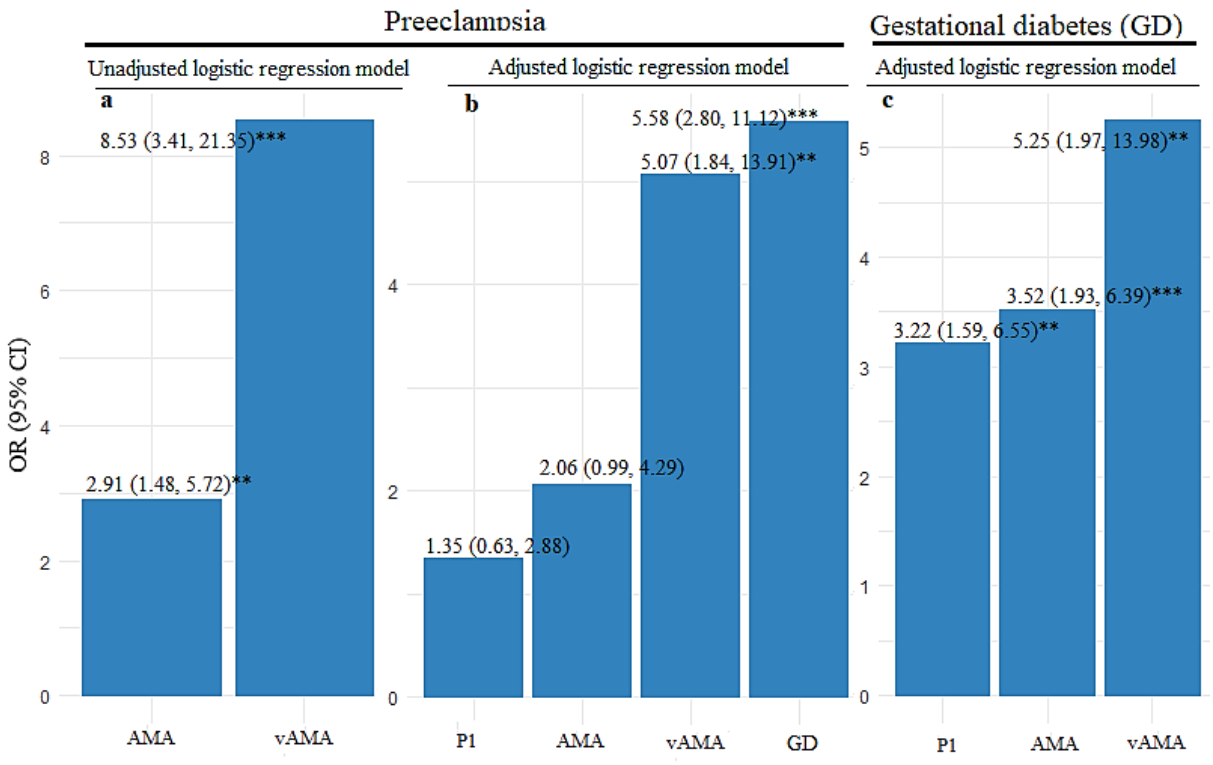

Figure 2: Univariate analysis of the association between maternal age and preeclampsia (a), as well as adjusted analysis between risk factors for preeclampsia and gestational diabetes (b & c). P1: multiparous; A: Age less than 35 years (reference category); AMA: advanced maternal age; vAMA: very advanced maternal age; GD: gestational diabetes. The last two models were adjusted for any family history of hypertension or hyperglycemia. ** $p < 0.01$, *** $p < 0.001$.

Prevalence of Gestational Diabetes and Preeclampsia

On analyzing the data from 700 full-term pregnancies, we observed that 12% of patients had gestational diabetes and 8% had preeclampsia. Once we investigated the prevalence of preeclampsia according to maternal age and gestational diabetes, some significant results emerged. After adjusting for any family history of hypertension and hyperglycemia, the prevalence of preeclampsia was significantly higher in patients with gestational diabetes [24.04%; $p < 0.001$], as well as in those of advanced or very advanced age [10.36%; $p < 0.001$; 20.38%; $p < 0.01$, respectively], as shown in Figures 3a and 3b.

On analyzing the prevalence of gestational diabetes according to maternal age and parity, some significant results were again observed. After adjusting for any family history of hypertension and hyperglycemia, the prevalence of gestational diabetes was significantly higher in women of advanced or very advanced age [21.85%; $p < 0.001$; 28.42%; $p < 0.01$, respectively], as well as in multiparous women [14.40%; 95% CI: 11.48, 17.33; $p < 0.001$]. The interaction between maternal age and parity revealed that among women of advanced and very advanced age, the risk of gestational diabetes increased almost sevenfold [26.89%; $p < 0.001$] when compared to patients younger than 35 years who were not multiparous [3.88%; $p < 0.01$]. In vAMA and multiparous patients, the risk increased almost ninefold (Figure 4a, 4b). Since the associations in the logistic models and predicted probabilities were found to be significant, a moderated mediation analysis could be considered later (Figure 1).

Testing for a Mediation Effect and Moderated Mediation Effect

Mediation analysis confirmed Hypothesis 1. As shown in Table 2, the regression coefficients reveal a relationship between maternal age and gestational diabetes [AMA: $\beta = 0.2485$; $p < 0.001$; vAMA:

β =0.4157; p < 0.001], as well as another one between gestational diabetes and preeclampsia [β =2.1225; p < 0.05], and these were significant after adjustment for any family history of hypertension and hyperglycemia. The bootstrapped indirect effect was 0.5275 [Boot CI %: 0.0151, 1.1258] in patients of an advanced age and 0.8824 [Boot CI %: 0.0266, 1.7895] in patients of a very advanced age. This confirms that an advanced or very advanced age is linked to gestational diabetes, which further increases the risk of preeclampsia, thus confirming Hypothesis 1.

To test Hypotheses 2 and 3, a moderated mediation analysis was performed. As expected, parity was found to moderate the relationship between maternal age and gestational diabetes (Table 3). The interaction between maternal age and parity had a significant effect on gestational diabetes (AMA x parity: β =0.2339; p<0.001 and vAMA x parity: β =0.2446; p<0.05]. This indicates that the effect of an advanced or very advanced maternal age on gestational diabetes differed in patients according to the number of previous deliveries. Figure 5 shows the interaction patterns. The positive relationship between maternal age and gestational diabetes was stronger in patients with an advanced or very advanced age compared to those younger than 35, thus confirming Hypothesis 2.

Table 2: Results of mediation analysis (N =700).

	Dependent Variable : GD (R^2=0.2365, p < 0.001)		Dependent Variable : Preeclampsia (R^2C&S= 0.062; R^2MCF= 0.12, p < 0.001)	
Direct relationship	β	95% CI	β	95% CI
Predictors				
Advanced maternal age vs. A	0.248***	(0.202, 0.294)	0.5075	(-0.2674, 1.2824)
Very advanced maternal age vs. A	0.415***	(0.328, 0.502)	1.1983	(0.1303, 2.2663)
Family history of hyperglycemia	0.054	(-0.000, 0.110)	0.2254	(-0.6160, 1.0669)
Family history of hypertension	0.083**	(0.021, 0.146)	0.9708	(0.1278, 1.8138)
Gestational diabetes (GD)			2.1225**	(0.8054, 3.4396)
Constant	0.083	(0.499, 0.536)	-4.3181	(-5.2247, -3.4114)
Relative conditional indirect effects of X on Y: Maternal age → Gestational diabetes → Preeclampsia				
Indirect relationship	Indirect effect	Boot SE	BootLLCI	BootULCI
Advanced maternal age vs. A	0.5275	0.2833	0.0151	1.1258
Very advanced maternal age vs. A	0.8824	0.4496	0.0266	1.7895

A: Age less than 35 years old; * p < 0.05, ** p < 0.01, *** p < 0.001.

Table 3: Results of moderated mediation analysis (N =700).

	Dependent Variable: GD (R^2=0.2770, p < 0.001)		Dependent Variable: Preeclampsia (R^2C&S= 0.0621; R^2MCF= 0.1211, p < 0.001)	
Direct relationship	β	95% CI	β	95% CI
Predictors				
Advanced maternal age vs. A	0.0863*	(0.0061, 0.166)	0.507	(-0.2674, 1.282)
Very advanced maternal age vs. A	0.2194*	(0.0320, 0.406)	1.198	(0.1303, 2.266)
Parity	0.0214	(-0.0153, 0.058)		
Advanced maternal age vs. A	0.2339***	(0.1372, 0.330)		
Very advanced maternal age vs. A	0.2446*	(0.0343, 0.454)		
Gestational diabetes (GD)			2.122	(0.8054, 3.439)
Family history of hyperglycemia	0.0557*	(0.0018, 0.109)	0.225	(-0,6160, 1.066)
Family history of hypertension	0.0629*	(0.0015, 0.124)	0.970	(0.1278, 1.813)

Constant		0.5055	(0.4750, 536)	-4.318	(-5.2247, -3.411)
Relative conditional indirect effects of X on Y: Maternal age → Gestational diabetes → Preeclampsia					
Indirect relationship		Indirect effect	Boot SE	BootLLCI	BootULCI
Maternal age	Parity				
AMA	Primiparity	0.1831	0.1560	-0.0338	0.5645
AMA	Multiparity	0.6795	0.3592	0.0201	1.4302
Index of Moderated Mediation		0.4964	0.2876	0.0103	1.1143
vAMA	Primiparity	0.4656	0.3251	-0.0725	1.1839
vAMA	Multiparity	0.9848	0.4977	0.0289	1.9925
Index of Moderated Mediation		0.5192	0.3677	0.0005	1.4035

A: Age less than 35 years old; AMA: Advanced maternal age; vAMA: Very advanced maternal age ; * p < 0.05, ** p < 0.01, *** p < 0.001.

The results also confirmed the conditional indirect effect of parity. The moderated mediation index was 0.4964 [Boot CI %: 0.0103, 1.1143] for patients of an advanced age and 0.5192 [Boot CI: 0.0005, 1.4035] for patients of a very advanced age, indicating that the mediating effect of gestational diabetes on the relationship between maternal age and preeclampsia varies by parity. Among multiparous women, gestational diabetes mediated the relationship between advanced maternal age and preeclampsia [indirect effect = 0.6795, Boot CI %: 0.0201, 1.4302]. Furthermore, in women of very advanced age, the mediating effect of gestational diabetes was also significant (indirect effect = 0.9848, Boot CI %: 0.0289, 1.9925). Thus, Hypothesis 3 was confirmed. The final model is shown in Figure 5.

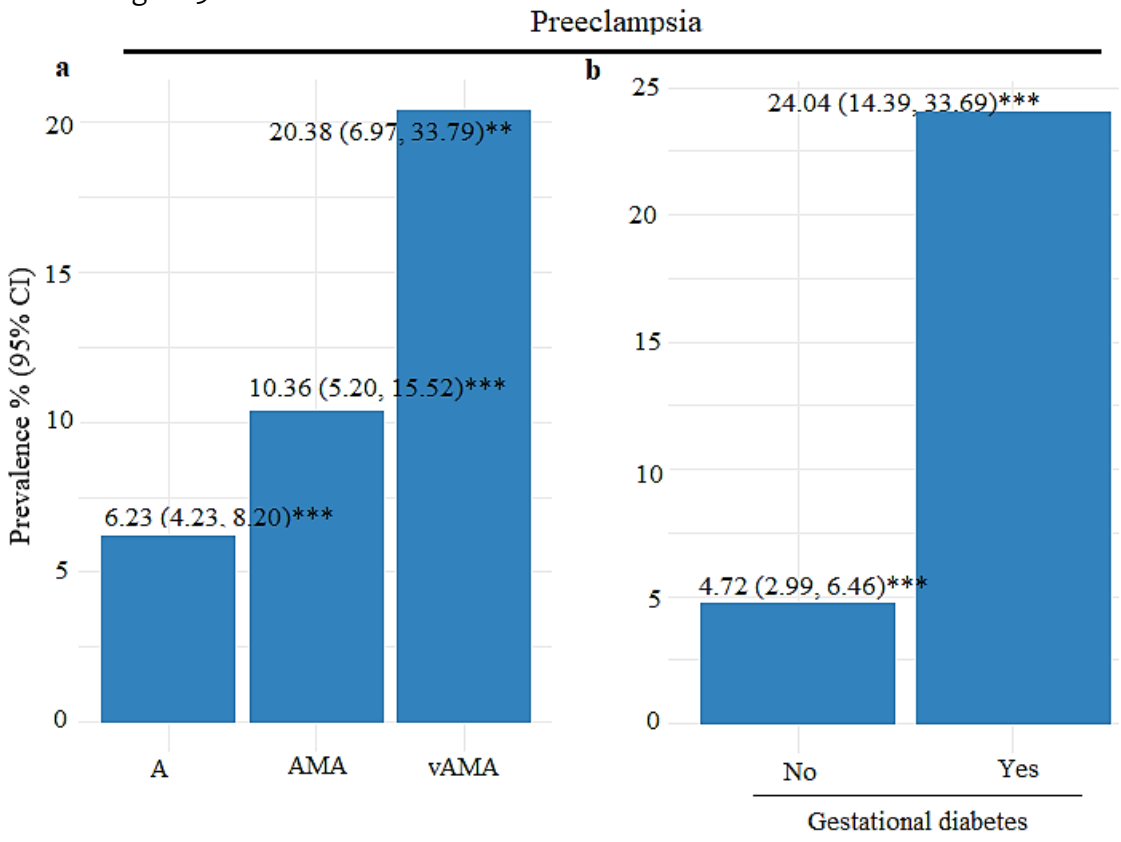

Figure 3: The adjusted prevalence (%) [95% CI] of preeclampsia in female patients.
A: Age less than 35 years old; AMA: advanced age; vAMA: very advanced age. The models were adjusted for any family history of hypertension and hyperglycemia.

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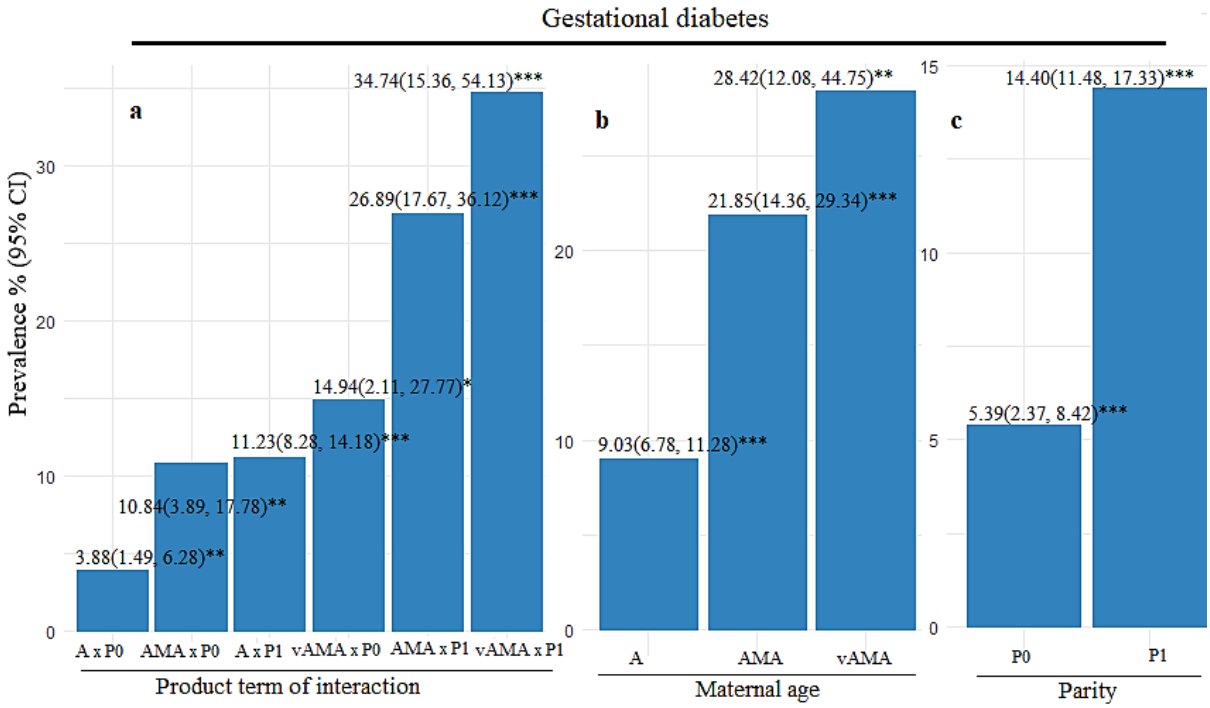

Figure 4: The adjusted prevalence (%) [95% CI] of gestational diabetes in patients.
A x P0: Age less than 35 years x primiparous; AMA x P0: advanced age x primiparous; A x P1: Age less than 35 years x multiparous; vAMA x P0: very advanced age x primiparous; AMA x P1: advanced age x multiparous; vAMA x p1: very advanced age x multiparous. The models were adjusted for any family history of hypertension and hyperglycemia.

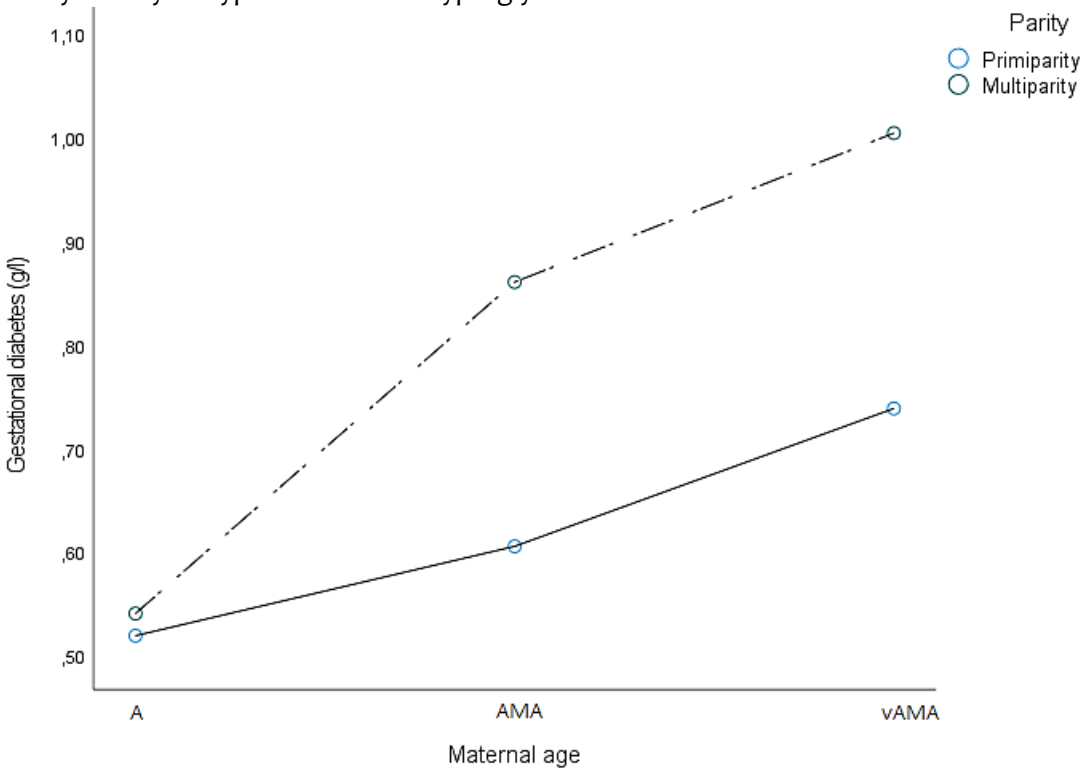

Figure 5: Influence of parity and gestational diabetes on preeclampsia.

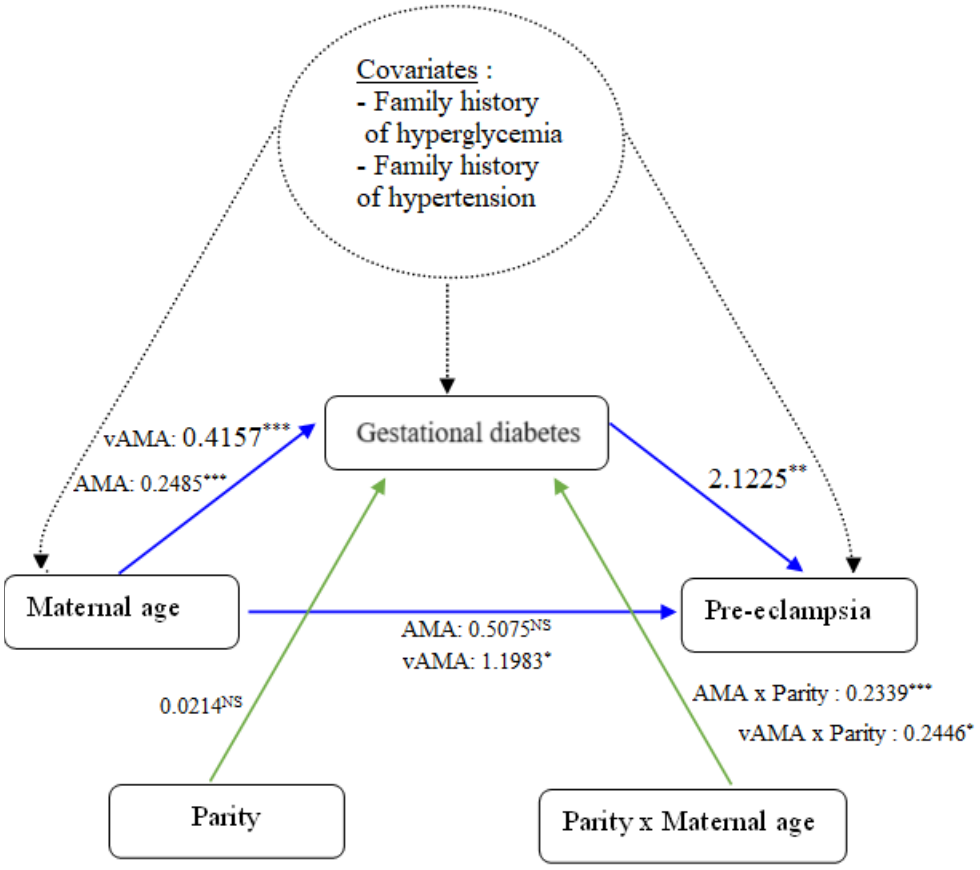

Figure 6: The final moderated mediation model.

Discussion

The Mediating Effect of Gestational Diabetes

Our study confirms a significant link between a very advanced maternal age and the risk of preeclampsia with there being a prevalence of 20.38% in women aged 40 and over, compared to 10.36% in women of an advanced age and 6.23% in women under 35 years old. These results are consistent with previous studies, although some research has reported conflicting findings. For example, Bartsch et al reported a 60% increase in the risk of preeclampsia in women over 40 years old (Bartsch et al., 2016), while Khalil et al and Claremont et al did not find any significant differences when compared to younger women (Claramonte Nieto et al., 2019; Khalil et al., 2013). The epidemiological inconsistencies in these results may be due to the use of relatively small samples in some of these studies, and multivariate analysis did not confirm these results ((Vincent-Rohfritsch et al., 2012).

There is also strong evidence for an increased risk of preeclampsia in women of advanced maternal age. For example, Poon et al observed an increased risk of preeclampsia from the age of 32, with this increasing by approximately 4% for each additional year (Poon et al., 2010). Khalil et al also noted a significant relationship between maternal age and the risk of preeclampsia, with there being an 8% higher risk among women aged 35 to 39 and a 50% higher risk among those aged 40 and older, even after adjusting for confounding variables (Khalil et al., 2013).

Meta-analyses that bring together data from millions of births have further confirmed these findings, with one showing a relative risk of 1.2 for women over 35 years old, 2.4 for those over 40 years old, and 3.6 for those over 45 years old (Lisonkova et al., 2017). Specific studies have reinforced these findings, such as that of Smithson et al, who observed a doubling of the risk in women over 45 compared to those aged 40 to 45 (Smithson et al., 2022). Recent surveys have also shown a doubling in the risk for women over 50 compared to those aged 40 to 49 (Schwartz et al., 2020).

In our study, women aged 35 to 39 were not significantly associated with a risk of preeclampsia, but this risk became 5.07 for women aged 40 and above.

However, other evidence shows that maternal ageing can lead to an inflammatory profile and elevated oxidative stress, which are linked to pregnancy complications, particularly placental dysfunction (Burton & Jauniaux, 2018). Older women without complications generally show a decline in anti-inflammatory cytokines, including IL-10 and IL-RA, which are associated with increased antioxidant capacity. Low IL-10 levels in elderly mothers correlate with placental dysfunction, as had been confirmed for IL-10-deficient mice through an increased sensitivity to inflammatory stimuli(Chatterjee et al., 2011). It is therefore essential to further explore the relationship between ageing, reductions in anti-inflammatory cytokines, and the vulnerability of older women to adverse effects on placental function (Da Silva et al., 2012).

In older mothers with complications, the oxidative stress is elevated despite the increased antioxidant capacity (Lean et al., 2021). This suggests that significant oxidative damage is linked to inadequate antioxidant responses, leading to altered placental function after pregnancy complications (Myatt & Cui, 2004). Future studies are therefore needed to confirm the role that oxidative damage plays in placental dysfunction for older mothers.

Older women who developed complications show reduced levels of placental hormones (hPL, sFlt, PlGF), thus confirming placental dysfunction (Lean et al., 2021). There is evidence to suggest that these biomarkers are linked to placental dysfunction, particularly with preeclampsia (Kenny et al., 2014).

In brief, the studies' results support our conclusion that very advanced maternal age has a direct impact on the risk of pre-eclampsia, as shown in our final moderated mediation model illustrated in Figure 6.

Despite having a high antioxidant capacity, older mothers with complications experience strong oxidative stress, potentially damaging the placenta, and this is linked to inadequate antioxidant responses and placental alterations (Myatt & Cui, 2004), but future studies are needed to confirm these links.

PlGF represents a promising biomarker for predicting complications in older mothers (Heazell et al., 2019), but large-scale studies will be needed to develop an integrated prediction model, improve personalized care, and reduce complications without any unnecessary interventions.

The results of our study confirm that a very advanced maternal age is a significant predictor of preeclampsia, with gestational diabetes playing a mediating role. Indeed, maternal age directly influences preeclampsia, but it also has an indirect effect via gestational diabetes. Thus, this study highlights how gestational diabetes strengthens the link between an advanced or very advanced maternal age and preeclampsia.

Our results also provide further empirical evidence to support the notion that a very advanced maternal age plays a key role in predicting preeclampsia. Furthermore, it is important to highlight how gestational diabetes plays a mediating role in the link between maternal age and preeclampsia. Indeed, while maternal age has a direct impact on preeclampsia, it also has an indirect effect on gestational diabetes, indicating the mechanism by which gestational diabetes bridges the link between an advanced or very advanced maternal age and preeclampsia. More importantly, if an expectant mother's advanced maternal age is not addressed from the start, it may ultimately lead to her developing gestational diabetes, which if continued to be left unaddressed, could increase the risk of preeclampsia.

When assessing the prevalence and mediating effects of gestational diabetes, we found that 28.42% of vAMA women and 21.85% of AMA women developed gestational diabetes during their pregnancy, compared to just 9.03% of women aged less than 35 years. A previous study also found that the risk of gestational diabetes increased significantly with age, from 2% in women aged 20 to 21% in those aged 40 (Al Rowaily & Abolfotouh, 2010). This is consistent with our results and further confirms that the risk of gestational diabetes increases with maternal age. Furthermore,

our results suggest that gestational diabetes could potentially play a mediating role. The mediated proportion, which indicates the extent to which the total effect of the association with preeclampsia can be explained by gestational diabetes, was highest in pregnant women of advanced and very advanced maternal ages, reaching up to 50.96% and 42.41%, respectively.

Additionally, ages 35 and above were significantly associated with gestational diabetes. According to Schummers et al, there is a linear increase in the risk of gestational diabetes along with the age of the mother. Compared with women aged 20 to 24 years, the adjusted relative risks (RR) for women aged ≥ 35 years, ≥ 40 years, and ≥ 45 years are 3.2, 4.2, and 4.4 (Schummers et al., 2018), which reflects our conclusions. In contrast, a study in China reported a peak adjusted prevalence of gestational diabetes in women aged 30–34 years, followed by a decrease after age 35 (Zhang et al., 2011). This finding raises concerns by suggesting that gestational diabetes may be affecting more and more relatively young women.

Nevertheless, it should be noted that this study had a limited number of participants in the older group, so further research would be needed to confirm this trend. For their part, Carolan et al. examined the combined effect of increasing maternal age and ethnicity on rates of gestational diabetes, with their results revealing differences in gestational diabetes rates between women born in Asia and those born in other regions, namely Australia, Europe, Oceania, the United Kingdom, Africa, and the Middle East (Carolan et al., 2012).

Our results indicate that pregnant women of all ages should be screened for gestational diabetes, particularly in resource-limited settings. An optimal threshold for selective screening, however, could be set at 25 years.

Ageing is generally associated with systemic insulin resistance and gestational diabetes in women of childbearing age (Y. Li et al., 2020). With increasing age, lean muscle mass can decrease, while visceral fat increases. In turn, this decreased muscle mass can result in reduced glucose elimination in the body, leading to glucose intolerance (Barbieri et al., 2001).

In women with GDM, insufficient insulin secretion to counteract systemic insulin resistance is notable (Chiefari et al., 2017). What is more, ageing reduces the ability of pancreatic β cells to proliferate during pregnancy, potentially promoting GDM in pregnant women (Rieck & Kaestner, 2010). As mentioned above, the increase in systemic insulin resistance is mainly due to age-related changes related to skeletal muscle mass and visceral fat mass (Barbieri et al., 2001; Gautier et al., 1998). Nevertheless, the exact mechanisms causing this resistance remain to be identified, although hypoxia could be playing a role (Arcidiacono et al., 2021). Furthermore, a recent study confirmed that a high preconception BMI, which is indicative of visceral adiposity and insulin resistance, plays a key role in developing GDM, suggesting that it could be targeted through public health policies (Mirabelli et al., 2023).

Another Chinese study of a population of women with gestational diabetes aged 35 to 40 years opened up another avenue of research by suggesting that the underlying mechanism could potentially involve dysfunctions in amino acid and fatty acid metabolism, thus worsening insulin resistance. This study also found that the combination of several long-chain fatty acids and amino acids could be used to predict gestational diabetes in older women as early as the first trimester, but future research will of course need to confirm these metabolic markers. Furthermore, metabolic profiling provides valuable guidance for clinical obstetricians to provide specific advice about appropriate nutrition for women over 35 years of age with gestational diabetes (He et al., 2022).

Furthermore, women with gestational diabetes in our study appeared to be at a higher risk of developing preeclampsia. Even after controlling for confounding factors, gestational diabetes remained an important clinical determinant of preeclampsia. A previous study also showed that gestational diabetes increased the occurrence of preeclampsia, which is consistent with our study (J. Li et al., 2023). An international HAPO study of more than 23,000 pregnant women from nine countries revealed that hyperglycemia is positively linked to preeclampsia, even after adjusting for many factors (e.g., clinical centre, age, BMI, height, smoking, alcohol consumption, family history

of diabetes, etc.) (HAPO Study Cooperative Research Group, 2009). Nevertheless, some studies indicate that there is no independent link between gestational diabetes and preeclampsia after taking into account pre-pregnancy weight and other factors (Cheung et al., 2018; Košir Pogačnik et al., 2020).

In contrast, other studies have suggested that advanced age is not independently associated with the occurrence of preeclampsia in women with gestational diabetes (Osuagwu et al., 2020). Only one retrospective study has posited that an advanced age is an independent risk factor for preeclampsia in women with gestational diabetes (Yogev et al., 2004). Although gestational diabetes is associated with preeclampsia, the precise mechanism remains unclear. Indeed,

The underlying relationship between GDM and the occurrence of preeclampsia can be explained through various factors. Hyperglycemia triggers inflammation and the autophagy of trophoblasts, thus hindering their migration and invasion. GDM also leads to the hyperactivation of neutrophils that release excess neutrophil extracellular traps (NETs), thus reducing villous blood flow and causing preeclampsia-related placental ischemia. Furthermore, GDM increases oxidative stress, leading to a reduction in circulating nitric oxide (NO) and vasodilation dysfunction. Advanced glycation end-products (AGEs) also increase with GDM, thus promoting preeclampsia through oxidative stress and inflammation. Pro-inflammatory cytokines such as TNF-α and IL-6 are also elevated in women with GDM, and this contributes to endothelial dysfunction and preeclampsia (Yang & Wu, 2022).

Some research has indicated that TNF-α, IL-6, and C-reactive protein (CRP) are independent risk factors for preeclampsia in women with gestational diabetes (Barden et al., 2004; Žák & Souček, 2019). Others have suggested that in addition to elevated CRP levels, an imbalance between interleukin 17 and interleukin 35 may play a role in the development of preeclampsia in women with gestational diabetes (W. Cao et al., 2018).

Obesity is the main risk factor for preeclampsia in women with GDM, because this has been associated with oxidative stress, inflammation, and fatty acid imbalance (Lopez-Jaramillo et al., 2018). Furthermore, pre-pregnancy hyperinsulinemia and insulin resistance contribute to problems with cytotrophoblast migration and uterine spiral artery remodelling, thus increasing the risk of placental ischemia (Lopez-Jaramillo et al., 2018).

While some studies question the direct link between gestational diabetes and preeclampsia, particularly when taking pre-pregnancy weight into account, obesity has also been identified as a major risk factor for preeclampsia, because it exacerbates oxidative stress, inflammation, and disturbances in fat metabolism, with this being mainly due to pre-existing hyperinsulinemia and insulin resistance. Understanding this mechanism will be essential for identifying markers and developing preventive measures, so it warrants further research.

The Moderating Effect of Parity

As hypothesized, parity exhibited a positive moderating effect on the relationship between maternal age and gestational diabetes. In particular, when the maternal age was advanced (≥35 years) and very advanced (≥40 years), the risk of gestational diabetes was significantly higher in multiparous patients than in primiparous patients, highlighting how multiparity plays an important role in worsening the risk of gestational diabetes in older patients, as confirmed by other studies (Dai et al., 2023; Wagan et al., 2021).

Nevertheless, it should be noted that our findings differ from those of some previous work that has suggested that primiparity is a risk factor associated with gestational diabetes (Ben-David et al., 2016; Laine et al., 2018). It is important to note, however, that these contrasting results could be attributed to the fact that first-time women with a history of gestational diabetes have a 50% risk of recurrence in their subsequent pregnancies (Kruse et al., 2015). Although we did not take into account any history of gestational diabetes in this analysis, this parameter could potentially have explained the persistence of gestational diabetes in certain multiparous patients.

Furthermore, the effect of parity on the risk of gestational diabetes has also been associated with advanced age in patients, as a higher number of pregnancies tends to be observed in women of advanced maternal age (Dode & Santos, 2009). Additionally, several previous studies have revealed associations between advanced maternal age, pre-pregnancy adiposity, and the prevalence of gestational diabetes (Collier et al., 2017; Shin & Song, 2015). Furthermore, the results from a study that took into account the body mass index (BMI) showed that obese primiparous women had a five times higher risk of gestational diabetes than primiparous women with a normal BMI (Laine et al., 2018). Not taking into account the BMI in our study could partly explain the inconsistency in these results.

A possible explanation for the association between multiparity in older women and gestational diabetes could lie in how episodes of insulin resistance may contribute to the decline in β cell function because each pregnancy is characterized by an episode of insulin resistance (Yong et al., 2021). Similarly, Wang et al supplied additional evidence to show that multiparous women with gestational diabetes were more likely to have poor glycemic control (Wang et al., 2022). Given the negative impact of parity on the risk of gestational diabetes, multiparous women who develop gestational diabetes are advised to engage in greater physical activity to achieve optimal glycemic control (Wang et al., 2022). Indeed, the 2019 Canadian guidelines for physical activity during pregnancy recommend at least 150 minutes of moderate-intensity physical exercise per week for pregnant women. Nevertheless, we suggest that at least 60 minutes of moderate physical activity per week is sufficient for first-time mothers with gestational diabetes, while we recommend exercising at least 90 minutes per week for multiparous women(Obstetricians, 2015).

The Moderated Mediation Effect of Parity

Parity plays a central role in pregnancy complications, including gestational diabetes and preeclampsia. It also moderates the mediating effect of gestational diabetes in the relationship between maternal age and preeclampsia, although this effect is only significant in multiparous pregnant women. Increasing parity may lead to increased insulin requirements due to the intense demand on pancreatic β cells during pregnancy. These increased insulin requirements are influenced by various factors, such as maternal age, a high body mass index (BMI), and changes in placental hormonal secretion (Skajaa et al., 2018).

In summation, parity is a crucial element in determining how an advanced maternal age affects the risk of gestational diabetes, which in turn may aggravate the risk of preeclampsia. Understanding these complex interactions between maternal age, parity, gestational diabetes, and preeclampsia is essential for obstetric risk management. Health professionals must consider these relationships to ensure optimal maternal care and prevent complications during pregnancy.

Implications and Limitations

The results highlight the increased risks for women of advanced maternal age (AMA or vAMA) depending on their parity, with these having major implications for maternal healthcare and the prevention of obstetric complications. This study has limitations, however, such as its retrospective nature and the use of a sample from a single hospital. Diverse multicenter studies are therefore needed to establish more robust cause-and-effect relationships. Our results could also have been influenced by unmeasured factors that warrant further research.

In addition, the sample size is limited, which could affect the robustness of the results. Overall, it is essential to explore potential confounding factors—such as the pre-pregnancy BMI, multiple pregnancies, education level, and other variables—to gain a complete understanding of the links between maternal age, gestational diabetes, and preeclampsia. Finally, any generalization of the results to a larger population must be performed with caution given that the data originated from a single hospital.

Conclusion

In summary, this study confirms the significant impact of advanced maternal age on preeclampsia, particularly in women aged 40 and over. In addition, an advanced maternal age was linked to an increased risk of gestational diabetes, which appears to also mediate the relationship between an advanced maternal age and preeclampsia. Parity, meanwhile, acts as a moderator, with multiparous women at even greater risk of gestational diabetes and consequently preeclampsia. Overall, this study revealed a complex nexus between maternal age, parity, gestational diabetes, and preeclampsia, thus highlighting the need for tailored prevention and management strategies for optimal obstetric outcomes.

Nevertheless, it is important to emphasize that further research is imperative. For example, further exploration of the mechanisms that underlie these complex associations, particularly at the molecular and cellular level, is needed to improve our understanding of how maternal age, gestational diabetes, and preeclampsia interact.

It would also be beneficial to conduct randomized clinical trials aimed at evaluating the effectiveness of preventive interventions—such as through lifestyle modifications, dietary changes, and drug treatments—aimed at reducing the risk of developing gestational diabetes and, by extension, preeclampsia in older pregnant women.

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Pregnancy Complications in Women with Uterine Fibroids and the Role of Stem Cells

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Abstract

Introduction: Uterine fibroids are a prevalent and benign tumor in the uterine wall that commonly affects women of reproductive age. These growths can lead to adverse pregnancy outcomes. This study aims to investigate the crucial role of myometrial stem cells in the development of fibroids and their impact on pregnancy complications.

Methods: The following terms were used in the PubMed, Embase, Scopus, ScienceDirect and MEDLINE databases to search for articles in English: Uterine Fibroids, Myometrial stem cells, Pregnancy complications, and Hormones. The articles selected were systematic reviews, meta-analyses, randomized controlled trials, and reviews. These data were searched from 2016 to May 2023.

Results: The study found that myometrial stem cells differentiated into smooth muscle cells, contributing to fibroid development. These fibroid stem cells had distinct hormone receptor characteristics. Hormonal imbalances and genetic predisposition led to the uncontrolled growth of myocytes, which played a central role in the formation of fibroids. Estrogen and progesterone, which support
uterine tissue growth, were identified as key factors in this process. In addition, ECM remodeling, angiogenesis, inflammation, and dysregulated signaling pathways were shown to be implicated in fibroid development.

Conclusion: Uterine fibroids have a significant impact on pregnancy outcomes, leading to various complications such as preterm birth, cesarean delivery, placental abnormalities, and heavy bleeding. The severity of these complications depends on factors like fibroid size, location, and individual factors. Therefore, understanding the complex interplay of factors, including the involvement of myometrial stem cells, hormonal influence, inflammation, and ECM changes, is crucial for improving patient care.

The knowledge gained from this study has the potential to inform targeted therapies and interventions for women with fibroids during pregnancy, ultimately improving the health of both mother and baby. However, further research is needed to elucidate precise mechanisms and develop more effective treatments for managing pregnancies complicated by fibroids.

Keywords: Uterine fibroids, Pathophysiology, stem cells, hormones, genetics

Introduction

Uterine fibroids, or leiomyomas or myomas, are the most common benign tumors of the female reproductive tract, affecting a substantial proportion of women during their reproductive years (Stewart et al. 2016). While most of these growths are asymptomatic and often go unnoticed, uterine fibroids can present various clinical challenges, particularly concerning pregnancy. The association between uterine fibroids and adverse pregnancy outcomes has been the focus of

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extensive research and clinical inquiry in recent years. Increasing community awareness and education on uterine fibroids can lead to a better understanding of the risk factors linked with this illness. It is important to note that there is a lack of data from research on uterine fibroids within underrepresented groups (Marsh et al. 2018). This review article offers a complete assessment of the existing research, focusing on the complicated relationship between uterine fibroids and pregnancy problems.

Uterine fibroids, characterized by the abnormal growth of smooth muscle cells within the uterine wall, can manifest in various sizes and locations within the uterine cavity. These non-malignant growths often give rise to bothersome symptoms, comprising heavy menstrual bleeding, pelvic pain, and reproductive issues (Stewart et al. 2017). Beyond their impact on gynaecological health, uterine fibroids have emerged as a significant concern in pregnancy, with growing evidence suggesting their association with adverse maternal and fetal outcomes (Jayes et al. 2019).

Given the occurrence of uterine fibroids among women of reproductive age and the potential implications for maternal and fetal health, careful consideration of the impact of uterine fibroids on pregnancy complications is of paramount importance (Ezzedine and Norwitz 2016). The most frequent mode of delivery was cesarean section (61.82%). Threatened preterm labor was a significant issue in 21.82% of pregnancies, and blood transfusion was necessary in 20.00% of cases. Postpartum hemorrhage (PPH) was experienced in 9.09% of pregnancies, while 47 patients (42.72%) remained symptom-free throughout their pregnancies (Choudhary, Inamdar and Sharma 2023). While some investigations have reported an amplified risk of undesirable results such as preterm birth, cesarean delivery, and placental abnormalities in pregnant women with uterine fibroids, the exact mechanisms underlying these associations remain a subject of ongoing investigation (Dasgupta et al. 2017).

This review aims to synthesize the current body of knowledge, shedding light on the intricate relationships between uterine fibroids and pregnancy complications. In pursuit of this goal, we will systematically examine the available literature, explore potential pathophysiological mechanisms, and critically assess the clinical implications of these findings. By consolidating the existing evidence, we hope to provide clinicians, researchers, and healthcare providers with a comprehensive resource for informed decision-making and improved patient care from the perspective of pregnancy complicated by uterine fibroids.

The origin of uterine fibroids is believed to stem from the unchecked growth of smooth muscle cells within the uterine wall. Mesenchymal stem cells (MSCs) are thought by some researchers to have a part in the formation of uterine fibroids. These MSCs can differentiate into numerous cell types, such as smooth muscle cells, and may be involved in developing fibroid tumors (Shen et al. 2013). Due to their regenerative potential, stem cells could potentially be involved in the formation and sustenance of uterine fibroids. A possible explanation for the growth of fibroids is that stem cells found in the uterine tissue may develop into smooth muscle cells (Mas et al. 2020). Scientists are exploring potential therapies for uterine fibroids using stem cells. Mesenchymal stem cells (MSCs) could be used to target the development of fibroids and alleviate the symptoms associated with them. These treatments aim to control the disease using stem cells' regenerative and anti-inflammatory properties (Nishino et al. 2019).

Nonetheless, it's crucial to underscore that further research is required to comprehensively grasp the precise function of stem cells in uterine fibroids and to formulate efficient stem cell-driven treatments. Despite these ideas and potential therapeutic approaches, precise references may be scarce. Therefore, it is recommended to refer to recent scientific publications or ongoing clinical trials (Donnez and Dolmans 2016). It is estimated that 0.1% to 3.9% of women experience this condition during pregnancy, but it affects approximately 20% to 40% of women (Cavaliere et al. 2021). In specific research findings, the documented occurrence of uterine fibroids during pregnancy ranges from 1.6% to 16.7%, with variations noted from trimester to trimester (Tîrnovanu et al. 2022).

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Methods

To find relevant papers for our literature review, we conducted a thorough search of several electronic databases, including PubMed, MEDLINE, Scopus, EMBASE, and ScienceDirect, from January 2016 to May 2023. We used the following text words as search terms: "uterine leiomyomas," "hormonal imbalance," "pregnancy complications," and "uterine fibroids." We only considered papers written in English and did not apply any geographic restrictions. Additionally, we examined the reference lists of all identified articles to find studies not captured by electronic searches. Two authors (JM and RV) independently assessed the electronic search and the eligibility of the studies. The final inclusion of the studies was decided after a detailed examination, and we included all randomized clinical trials, retrospective studies, literature reviews, case reports, and series that dealt with patients having evidence of uterine leiomyomas. Nearly 89 studies were reviewed and only 57 have passed the inclusion criteria of the current study. Any differences were discussed, and a consensus was reached.

Stem cells in the uterus and fibroid development

Recent research has shed light on the connection between uterine fibroid development and the association of stem cells in the uterine tissue. One key aspect of this relationship is the role of myometrial stem cells, which are indispensable for the typical growth of the myometrium and the expansion of the uterus during pregnancy (El Sabeh et al. 2021). These myometrial stem cells undergo division, ultimately generating progenitor cells that undergo differentiation into smooth muscle cells, constituting the primary structural component of the myometrium (Ono et al. 2015). Uterine fibroids develop from the myometrial cells, which are the smooth muscle cells of the uterus.

The growth of these fibroids is predominantly influenced by the concentrations of estrogen circulating in the bloodstream (Longo and Bulun 2013). Figure 1 illustrates the proliferation of smooth muscles in the uterine fibroid. A solitary mutation in a stem cell can potentially initiate the formation of fibroid tumors (Moravek and Bulun 2015). Stem cells within fibroids, capable of self-renewing and differentiating, play a pivotal role in maintaining the equilibrium of myometrial tissue. These specialized cells are essential for preserving the regular functioning and structure of the myometrium (Ono et al. 2012). Maintaining myometrial tissue homeostasis is contingent upon the crucial attributes of self-renewal and differentiation found in fibroid stem cells (Salas et al. 2022). Fibroid stem cells exhibit minimal expression of estrogen and progesterone receptors, specifically ERα and PGR, respectively (Serna et al. 2018).

Researchers isolated normal myometrial and fibroid cells, demonstrating essential stem/progenitor cell characteristics using distinct surface markers to enrich a subset of myometrial or fibroid cells. These samples were obtained from women undergoing surgery for symptomatic uterine fibroids, including hysterectomy or myomectomy (Mas et al. 2015). Estrogen and progesterone, hormones that prepare the uterine lining for pregnancy each menstrual cycle, seem to encourage fibroid growth. Fibroids possess more estrogen and progesterone receptors than regular uterine muscle cells (Kim, Kurita and Bulun 2013).

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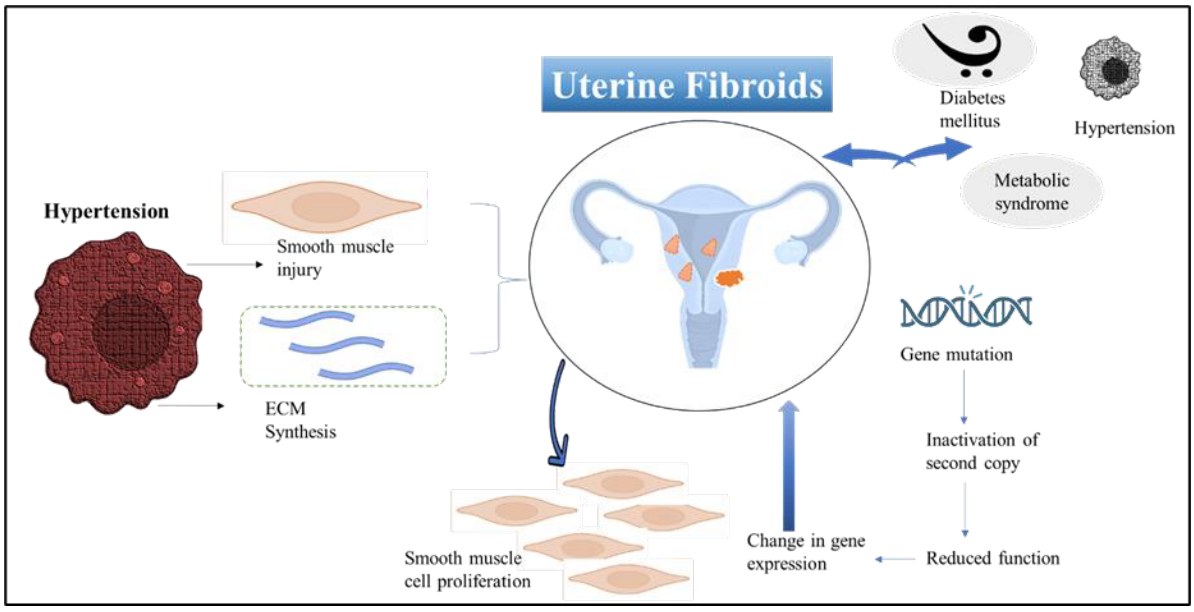

Figure 1. Smooth muscle proliferation in uterine fibroids

Impact of uterine fibroids during pregnancy

Among some women with uterine fibroids, they experience pain, heavy bleeding, and concerns about being able to get pregnant. Women's experience of uterine fibroids during pregnancy can vary considerably based on several factors, such as the size and location of the fibroids and their overall health (Coutinho et al. 2022). Compared to women who do not have fibroids, women with fibroids face an increased relative risk of experiencing pregnancy loss regardless of the fibroid's location. In such cases, a pre-conception saline infusion sonogram is extremely helpful for identifying submucosal fibroids (Guo and Segars 2012). If fibroids cause incomplete cervical dilation, the birth canal may be blocked, requiring a cesarean. As a result of fibroids, there is a possibility of placenta previa (implantation of the placenta over the cervix) and placental abruption, which may cause heavy bleeding and negatively affect the oxygen supply to the baby (Kwas et al. 2021). Fibroids can interfere with fertility by blocking the fallopian tubes or preventing embryo implantation in the uterus (McWilliams and Chennathukuzhi 2017). There is a possibility that fibroids may grow during pregnancy due to increased levels of hormones and blood flow. As a result of this growth, the patient may experience increased discomfort and complications (Wong et al. 2016). It is essential to highlight that not all women with uterine fibroids may have these pregnancy difficulties, and many have normal, healthy pregnancies. The effect of fibroids on pregnancy varies greatly depending on the person (Grube et al. 2019).

Stem cell research and uterine fibroids

Stem cell research has been conducted to gain a deeper understanding of how stem cells contribute to the formation of uterine fibroids and to pioneer innovative treatment strategies for addressing these fibroids (Carneiro 2016). Researchers created organoids from human myometrial and uterine fibroid stem cells to explore uterine fibroids' pathophysiology and uncover new treatment targets (Santamaria et al. 2018) Figure 2. Based on current research findings, uterine stem cells have been observed to transform stem cells that initiate tumors in the context of leiomyomas, endometriosis, and adenomyosis (Wilczynski et al. 2022). Research has used stem cell-derived organoids to study uterine fibroids' pathophysiology and develop new therapies (Elkafas et al. 2020). Other studies have focused on identifying uterine fibroids' risk factors, developmental origins, and pathogenetic pathways to create novel targeted therapeutics (Yang et al. 2022).

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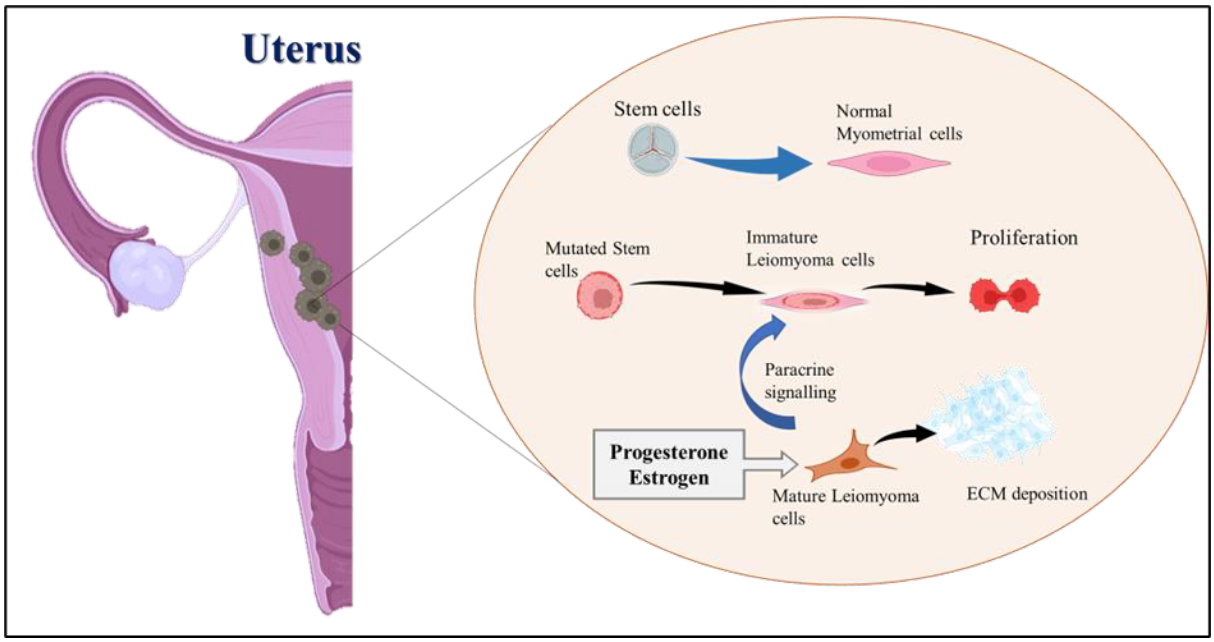

Figure 2. Proliferation of stem cells in Uterine fibroids

Pathophysiology

The precise mechanisms and pathophysiology of stem cells linked to uterine fibroids in pregnant women remain incompletely understood. However, recent research has begun to provide some insights into this area. In contrast, the myometrium usually remains moderately quiescent throughout the reproductive cycle; it undergoes substantial expansion during pregnancy and then regresses after childbirth (El Sabeh et al. 2021). Uterine stem cells have been associated with various gynecological conditions, including endometrial cancer, fibroids, endometriosis, and pregnancy loss. Researchers have isolated myometrial and fibroid stem cells using specific surface markers, enriching a subset of these cells that display essential progenitor and stem cell features. Fibroid stem cells possess self-renewal and differentiation capabilities and are crucial in maintaining myometrial tissue balance (Banerjee et al. 2022).

Biomechanical forces play a role in determining the transformation of fibroid stem cells and the receptivity status of the endometrium. Most myometrial cells are expanded during pregnancy from stem cells in the human myometrium (Celik et al. 2022). Models of OCT4-GFP transgenic mice have been used to study myometrial stem cell ontogeny (Brakta, Mas, and Al-Hendy 2018). Nevertheless, further research is required to understand the mechanisms and pathophysiology of stem cells associated with uterine fibroids in pregnant women, as illustrated in Figure 3.

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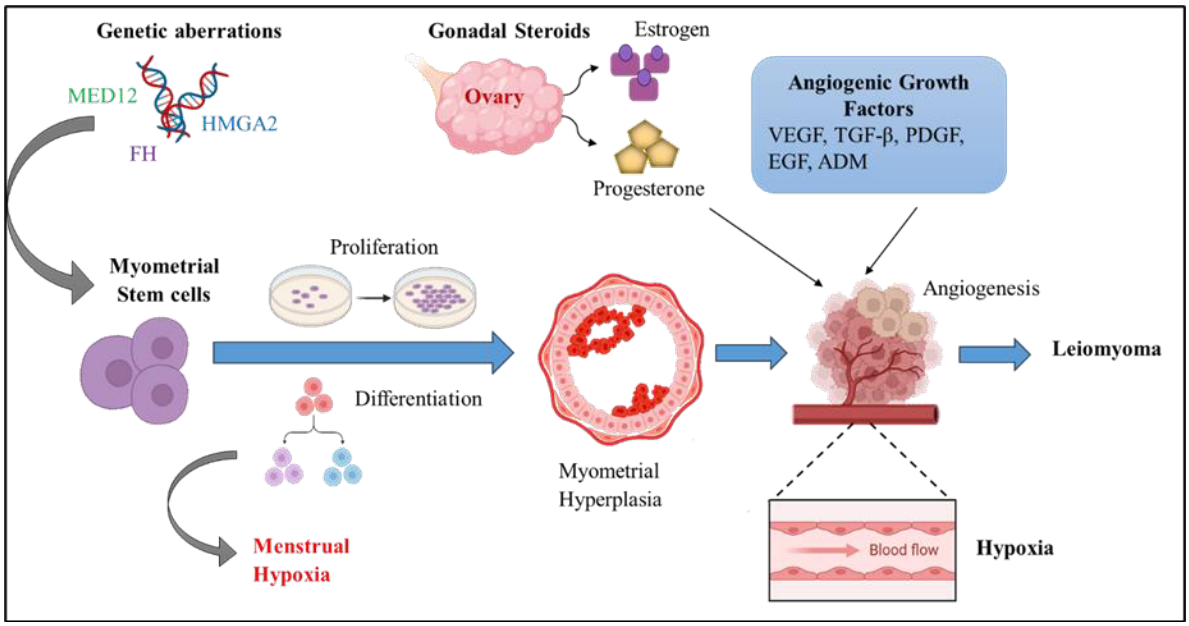

Figure 3. Pathophysiology of uterine fibroid stem cells

Predisposition

There is an aspect to the development of fibroids. Women with a family history of fibroids are more likely to develop them. Fibroids may develop when specific gene mutations involve cell growth and extracellular matrix regulation (ECM) (Girigoswami et al. 2021). Stem cell mutations have been allied with the formation of uterine fibroids. Most fibroid tumors have alterations in the MED12 gene, and mutations in HMGA2 expression in myometrial cells also result in abnormal proliferation (Gallagher and Morton 2016). A biallelic germline mutation in the fumarate hydratase gene (FH) has been associated with fumarate hydratase deficiency, resulting in uterine fibroids (Prusinski, Al-Hendy, and Yang 2019). These mutations may cause abnormal stem cell growth, leading to fibroids forming in the uterus (Giuliani, As-Sanie, and Marsh 2020).

While the exact cause of leiomyomas remains unclear, genetic factors have been identified as playing a part in the development of uterine fibroids. Here are several genes that have been linked to the development of these growths. RAD51L1 gene partners with HMGIC in translocations, causing structural disruptions in genes and contributing to the onset of uterine fibroids (Mediakare et al. 2011); Mutations in the Fumarate hydratase (FH) gene have been correlated with the progress of uterine fibroids (Kubinova et al. 2012); TERT, TERC, OBFC1 genes are involved in regulating telomere length, which is linked to genetic susceptibility to uterine leiomyoma (Valimaki et al. 2018).

ATM and TP53 genes play a role in safeguarding genome stability and are also associated with a genetic predisposition to uterine leiomyoma (Guleria and Chandna 2016). Recent research has revealed that the transcription factor protein known as AP-1 is inhibited in leiomyomas, potentially influencing gene transcription and contributing to the formation of uterine fibroids. While additional molecular investigations are needed to comprehend the origins and development of uterine fibroids fully, genetic studies have offered valuable insights into the genetic underpinnings of this condition (Edwards et al. 2019).

Hormonal Influences

Estrogen and progesterone, two hormones for females, play a part in the growth of fibroids. These hormones support the growth and maintenance of the lining of the uterus (endometrium) during the cycle. Fibroids often have levels of receptors for estrogen and progesterone, making them responsive to changes (Chakrabarti 2023). Estrogen plays a role in the growth of fibroids during the reproductive years. It stimulates cell proliferation and activates blood vessel growth

within fibroids (Borahay et al. 2017). Similarly, progesterone contributes to fibroid growth by supporting the maintenance of the lining. Fibroid cells contain receptors for progesterone (Ilicic, Zakar, and Paul 2017).

Other influences

Fibroids are muscle cells (myocytes) in the wall that grow abnormally due to factors like imbalances or genetic influences. The development of a cluster of cells eventually leads to the formation of a fibroid (Islam et al. 2018).

Restructuring of Extracellular Matrix (ECM)

A build-up of ECM components, including collagen and fibronectin, characterizes fibroids. This restructuring of the ECM supports the fibroid and aids in its enlargement (Leppert, Jayes, and Segars 2014).

Formation of New Blood Vessels

A blood supply is necessary for fibroids to continue to grow. They can stimulate the formation of blood vessels, known as angiogenesis, ensuring an oxygen and nutrient supply (Tal and Segars 2014). As fibroids increase, their oxygen requirements may surpass the available supply, resulting in localized hypoxia or low oxygen levels. In this manner, further stimulation of angiogenesis and factors that promote fibroid growth can be achieved (Kirschen et al. 2021).

Inflammation

Persistent uterine inflammation can cause fibroid proliferation. Cytokines and inflammatory signals released during chronic inflammation can increase cell proliferation, gene expression alterations, angiogenesis, and ECM formation, promoting fibroid growth. The effects of this can have a significant impact on an individual's health and quality of life (Van den Bosch et al. 2015). Cellular signaling pathways involving growth factors like TGF-beta, IGF, VEGF, and cytokines may become dysregulated in fibroid tissue. These signaling molecules can influence cell proliferation, the deposition of ECM components, and inflammation (Borahay et al. 2015). Angiogenic factors involved in Figure 4 illustrate uterine fibroids. Enlarging fibroids can exert physical pressure on adjacent organs and structures, causing pelvic pain, increased urination frequency, and constipation (Rezk, Kahn, and Singh 2023). The condition affects primarily middle-aged women with painful lesions on their extremities (Subbrayan et al. 2021).

The interplay of these factors collectively contributes to uterine fibroids' initiation, enlargement, and persistence. The pathophysiology of fibroids can differ among individuals, and not all fibroids follow the same course. Moreover, the specific triggers for fibroid development may vary from person to person, making it a complex and multifactorial condition. Ongoing research aims to uncover more insights into the underlying mechanisms of fibroid pathophysiology, which could lead to improved diagnostic and treatment approaches in the future.

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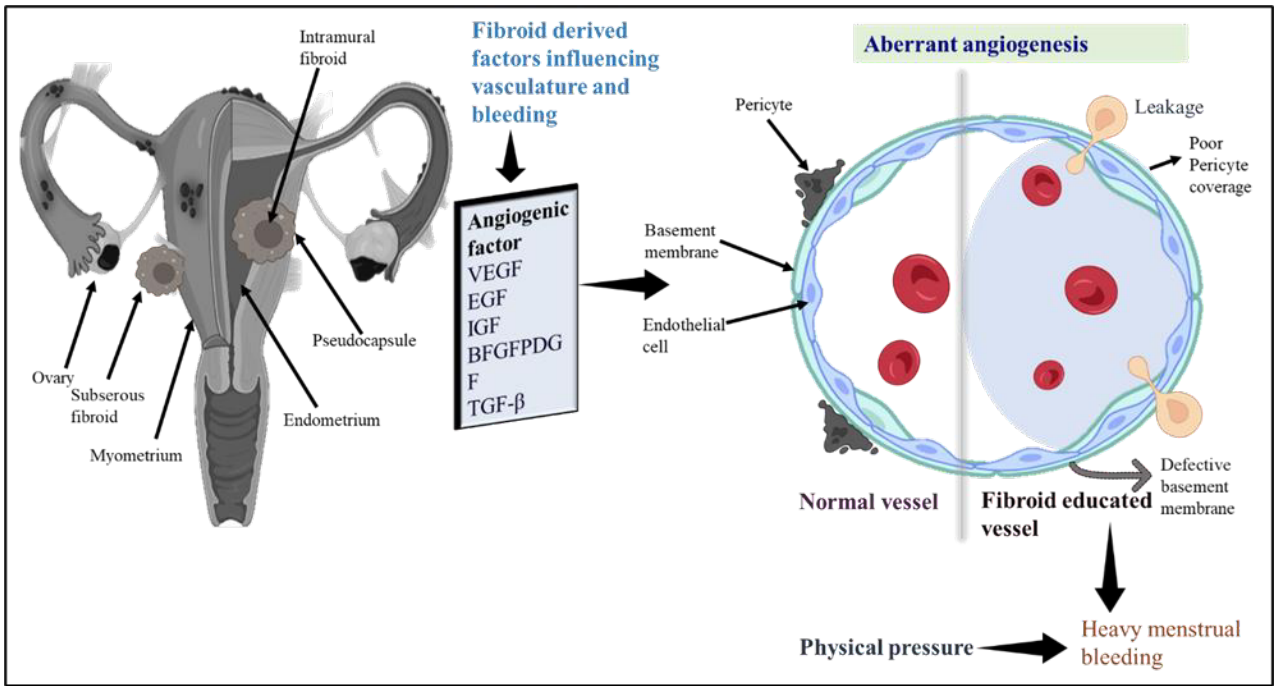

Figure 4. Development of angiogenic factor in uterine fibroids

Results and Discussion

The purpose of this review is to explore the complex mechanisms that contribute to fibroids development. During pregnancy, myometrial stem cells are essential for the growth of the uterus. These stem cells differentiate into smooth muscle cells, which are the primary structural component of the uterus. However, a single mutation in a stem cell can trigger fibroid formation. Stem cells within fibroids maintain myometrial tissue balance through self-renewal and differentiation.

Fibroids can cause complications during pregnancy, leading to pregnancy loss, cesarean sections, placenta-related issues, and fertility problems. Although not all women experience these issues, the impact of fibroids varies among individuals. Stem cell research offers valuable insights into fibroid pathophysiology. Organoids created from myometrial and uterine fibroid stem cells help with understanding and potential treatments. Uterine stem cells can transform into tumor-initiating stem cells in various gynecological conditions.

Ongoing research into the pathophysiology of stem cells in uterine fibroids during pregnancy focuses on biomechanical forces and myometrial cell expansion during pregnancy. Family history and gene mutations play a role in fibroid development, with specific gene mutations linked to abnormal stem cell growth and fibroid formation. Estrogen and progesterone promote fibroid growth by stimulating cell proliferation, blood vessel growth, and uterine lining maintenance.

Fibroid development is influenced by genetic imbalances, extracellular matrix restructuring, angiogenesis, and inflammation. Uterine fibroids are a complex condition influenced by stem cells, genetic factors, hormonal influences, and other contributors. Understanding these interactions can lead to improved diagnostic and treatment approaches in the future, benefiting women's health and well-being.

Conclusions and future perspectives

Uterine fibroids, the most common benign tumors affecting women, have garnered increasing attention for their potential adverse impact on pregnancy outcomes. These growths, characterized by the abnormal proliferation of smooth muscle cells within the uterine wall, can

manifest with various symptoms, including pelvic pain and heavy menstrual bleeding. However, their association with pregnancy complications, such as preterm birth and cesarean delivery, has raised concerns and sparked extensive research.

Understanding the intricate relationship between uterine fibroids and pregnancy complications is paramount due to their prevalence among women of reproductive age. While some studies have reported increased risks associated with uterine fibroids during pregnancy, including placental abnormalities and heavy bleeding, the precise mechanisms underlying these associations remain subject to ongoing investigation.

Recent research has shed light on the potential involvement of stem cells, and uterine fibroids are often caused by myometrial stem cells. Moreover, hormonal influences, genetic predisposition, extracellular matrix restructuring, angiogenesis, and inflammation have all been implicated in the pathophysiology of fibroids. Despite the complexity of uterine fibroids and their impact on pregnancy, it is crucial to emphasize that not all women with fibroids experience pregnancy complications, and many have normal, healthy pregnancies.

Therefore, personalized care and understanding the unique factors influencing each individual's experience are essential. Stem cell research offers promising avenues for comprehending the underlying mechanisms of uterine fibroids and developing novel treatment approaches. Mesenchymal stem cells, with their regenerative and anti-inflammatory properties, have emerged as potential targets for therapeutic interventions.

In conclusion, uterine fibroids represent a multifaceted condition with diverse implications for pregnancy. While research has made significant strides in unravelling their pathophysiology and potential treatments, ongoing investigations are necessary to provide more precise insights and improve diagnostic and therapeutic options. This comprehensive understanding will empower healthcare providers to deliver informed care and support women facing pregnancy complicated by uterine fibroids, ultimately enhancing maternal and fetal health.

Competing interests: The authors declare no conflict of interest to report

Authors' contributions

JM wrote the contents, edited the figures and tables of this manuscript

RV designed the study, edited the contents of this manuscript, and approved the manuscript for submission. “All authors read and approved the final manuscript”

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Knowledge, Attitudes, and Practice of abortion among Adolescent female students in selected Secondary Schools in Moshi Municipality, Kilimanjaro region.

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Abstract
Background: Induced abortion is an intentional termination of intrauterine pregnancy by medical or surgical means. Unsafe abortion is a serious public health problem most significant for adolescent females and one of the leading causes of maternal mortality globally. In Africa, unsafe abortion accounts for more than a quarter of causes of maternal mortality. Tanzania, where abortion is illegal, has the highest incidence of unsafe abortion. This study aimed to determine the knowledge, attitude, and practices towards induced abortion among adolescent female students in four selected secondary schools in Moshi municipality, Kilimanjaro region, Northern Tanzania.
Methods: A descriptive cross-sectional study was conducted among 342 secondary school girls aged 15-19 years from April to June 2019. A multistage sampling technique selected eligible participants. Semi-structured, self-administered questionnaires were used for data collection. Data were entered and analyzed using SPSS software.
Results: The mean age of respondents was 16.7(SD 3.7), and 50.6% (n= 173/342; mean knowledge score =38.9 ±1.4) had inadequate knowledge of induced abortion. More than half, 55.8% (n= 191/342; mean attitude score = 18.9 ± 1.9) had unfavourable attitudes towards induced abortion. Nineteen respondents had induced abortion from unplanned pregnancies. The two main reasons for induced abortion were to finish school (26.3%), and fear of parents' reactions (26.3%).
Conclusion: There was no significant difference in the level of knowledge on induced abortion among study participants. However, the unfavourable attitude towards induced abortion observed is mostly influenced by cultural and religious factors. Two main reasons for induced abortion were fear of termination from school and fear of parents' reactions. Comprehensive sexuality education, contraception counselling and provision, access to post-abortion care services, and parent-daughter communication interventions may be beneficial to prevent unplanned pregnancies may be beneficial to adolescent students attending secondary schools in this setting.

Keywords: adolescent, attitude, knowledge, induced abortion, practice, Tanzania.

Introduction

According to the World Health Organization (WHO) definition induced abortion is the intentional termination of a pregnancy before the foetus can live independently (WHO, 2007, 2011). Induced abortion

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may be voluntarily based on the woman's personal choice or medically indicated to preserve the health or save the life of a pregnant woman. However, existing evidence suggests that most induced abortions are conducted in unsafe conditions. By definition, unsafe abortion is the termination of unintended pregnancy conducted by an untrained personnel, or a trained personnel, in an environment that does not meet the medical safety standards (WHO, 2007, 2011).

Annually, it is estimated that out of 19 million pregnancies that end with unsafe abortion globally, 5.7 million occurred in Low and middle-income countries (LMICs) between 2010 and 2014 (Ganatra et al., 2017). In Africa, 59 % of all unsafe abortions occur in women aged less than 25 years, and 90% live in countries with restrictive abortion laws (WHO, 2007, 2011). Abortion is not permitted under any circumstances in 12 out of 54 African countries. Only four countries, namely Cape Verde, Mozambique, South Africa, and Tunisia have relatively liberal abortion laws (WHO, 2007, 2011). Tanzania is among African countries with high unsafe abortion rates approximated at 36 per 1000 women under 25 years old. The highest rates are reported in Lake Zone (51 per 1000) and the lowest rates in Zanzibar (11 per 1000) among women aged 15 - 44 years (Keogh et al., 2015; Norris, Harrington, Grossman, Hemed, & Hindin, 2016).

The most at-risk group for induced abortion in LMICs are adolescent girls aged 15-19 years who are less likely than adult women to obtain safe abortion. Compared with older women, adolescents are more likely to experience unsafe abortion from untrained personnel, have a self-induced abortion, delay seeking post-abortion care, and terminate pregnancy in the first three months (Ganatra et al., 2017). As a result of unsafe abortion adolescents experience life-threatening complications such as severe haemorrhage, and sepsis from childbirth. Other disabilities include reproductive tract infections (RTI), pelvic inflammatory diseases, and infertility (Keogh et al., 2015; Norris et al., 2016).

Abortion is illegal in Tanzania and carries a heavy jail sentence unless the termination of pregnancy is under a medical emergency (Keogh et al., 2015; Nkata, Barros, & Nyamhanga, 2017; Norris et al., 2016). Although the penal code explicitly states that termination of pregnancy is legally permitted if it is to save a woman's life, the law does not specify what level of healthcare provider may perform a legal termination. The Tanzanian government however has not incorporated this provision into its national laws, despite the ratification (Woog & Pembe, 2013).

In Tanzania, adolescent girls with unplanned pregnancies face social consequences, such as being expelled from the education system (Keogh et al., 2015; Nkata et al., 2017; Norris et al., 2016). Two main reasons most adolescent girls undergo unsafe abortion are because of the existing restrictive abortion law (Johnson, Mishra, Francheska, Khoslaa, & Ganatraa, 2017; Keogh et al., 2015; Norris et al., 2016; Sorensen et al., 2010), and fear of being curtailed from education (Nkata et al., 2017).

Given the above-cited punitive restrictions most induced abortions are conducted under unsafe, covert situations, putting adolescent girls at high risk of maternal mortality caused by severe bleeding, and sepsis (Abiola, Oke, Balogun, Olatona, & Adegbesan-Omilabu, 2016; Atakro et al., 2019; Espinoza, Samandari, & Andersen, 2020; Lin et al., 2018; Sorensen et al., 2010).

The secondary education system in Tanzania is categorized into public or private and includes two tiers. The first tier is four years for the ordinary level and the second tier is two years for the advanced level. In Tanzania, the education policy permits children enrolment at the age of seven for primary education thus starting ordinary level secondary education at 15. Sexuality education in Tanzania is guided by the national guidelines for implementing HIV/AIDS and life-skills education programmes in schools. It is not a standalone subject but is mainstreamed in other subjects namely Biology and Civics for O-level and General Studies and Biology for A-level (United Republic of Tanzania, 2017a).

This study aimed at determining the knowledge, attitude, and practice towards induced abortion among adolescent female students aged 15 to 19 years in four selected secondary schools in Moshi municipality, Kilimanjaro region, Northern Tanzania. The study findings would add information to the existing evidence on knowledge, attitude, and practice towards induced abortion and recommendations for appropriate interventions that will ensure universal access to legal, safe and comprehensive sexual and reproductive healthcare services among adolescent female students in secondary schools in this study setting.

Material and methods

Study design

This was a descriptive cross-sectional study conducted between April to June 2019 to assess the knowledge, attitude, and practice of adolescent female students towards induced abortion in Moshi municipality, Kilimanjaro region, Northern Tanzania.

Study area

This study was conducted in the Moshi Urban district, which is one of the seven districts of the Kilimanjaro region of Tanzania. Moshi Urban District is bordered to the North, South, and East by the Moshi Rural District and to the West by the Hai District. According to the 2012 Tanzania national census, the population of the Moshi urban district was 184,292 with Chaga and Pare as predominant tribes. Moshi Urban district has 23 secondary schools with 2538 female students. These include 14 public and 9 private schools where one is a boy only and the remaining 22 are mixed-sex schools.

Study population

The study population was adolescent female students aged 15-19 years old from four selected secondary schools in Moshi municipality.

Eligibility criteria

The study include all eligible female students aged 15-19 years old while excluding those either not consenting or absent from school during data collection day.

Sample size determination

The following assumptions were used to arrive at the required minimum sample size, using Epi-info statistical software to calculate the sample size. To determine the sample size with a 95% level of confidence, a 5 % margin of error, and a proportion of 50.0% (for unknown prevalence), we used the formula for a descriptive cross-sectional study where the target is less than 10,000. The estimated minimum sample size including the 10% of the estimated size to adjust for non-response rate was 422 respondents.

Sampling technique

The multistage sampling technique was used to recruit 422 study respondents from 4 mixed-sex secondary schools. In stage one, four out of 22 secondary schools, were selected using a simple random sampling method by lottery procedure. In stage two students were stratified by their classes (i.e., forms 1 to 6) to make different stratum in each school. The primary sample frame was a list of all female students from forms 1 to 6 forming the sampling units. Every year level in a school formed a secondary sampling frame.

In stage three, the required numbers of students were selected from each stratum proportional to their size using a systematic random sampling technique.

To decide on the sampling interval 10% of the total female population in a school was calculated. The number of the year levels in the school was divided by the result to determine the sample size per class. The sampling interval (*n*th) was then calculated by dividing the number of female students in a class (N) by the class sample size (n). The female students were arranged alphabetically and the first participant was selected blindly using a table of random numbers after which the remaining participants were selected at regular intervals (*n*th) from the secondary sampling frames. The process was repeated until the required school sample size was achieved.

Study variables

The dependent variables in this study were knowledge of induced abortion, attitude towards induced abortion, and practice of induced abortion. Independent variables include socio-demographic characteristics and the sexual behaviour of respondents.

Measurements

Knowledge scores: The level of knowledge of induced abortion was measured using 10 questions (e.g., induced abortion is abortion done by oneself). The expected response 6-point Likert scale ranged from 1= "Strongly disagree", to 6 = "Strongly agree". Responses in each domain were added to create an overall knowledge score, which ranged from a minimum of 10 to a maximum of 60. The mean score of 30 or above was categorized into adequate knowledge (> mean score), and the mean score of below 30 was categorized into inadequate knowledge (< /= mean score). The reliability scale was Cronbach's alpha = .61.

Attitude scores: Attitude towards induced abortion was measured using 6 questions (e.g. It is a sin to induce abortion). The expected response 6-point Likert scale ranged from 1= "Strongly disagree", to 6 = "Strongly agree". Responses in each domain were added to create an overall attitude score, which ranged from a minimum of 6 to a maximum of 36. The mean score of 18 or above was categorized into favourable attitude (> mean score), and the mean score of below 18 was categorized into unfavourable attitude (< /= mean score). The reliability scale was Cronbach's alpha = .62.

Practice: Asking the respondents if they had ever had an abortion in their lifetime assessed the practice of induced abortion. The expected response was 1= Yes, and 2= No.

Data collection

Primary data were collected using a pre-tested self-administered, semi-structured questionnaire adopted from Ethiopia (Yaecob, Abera, & Meleko, 2018), and adapted to fit the study objectives, to assess knowledge, attitude, and practice towards induced abortion from study respondents. The self-administered questionnaire was conducted in English, which is the language used as the medium of teaching in secondary schools in Tanzania. No secondary data was used in this study.

Data analysis

The filled questionnaires were cross-checked daily for accuracy, completeness, and uniformity, and then double-entered in a database. Data were analyzed using Statistical Package for Social Science (SPSS) for Windows Version 20.0 statistical software (Chicago, IL, USA). Descriptive analysis was estimated as

frequency and proportions. A Chi-square test was used to compare proportions between categorical variables. A p-value of .05 or less was considered to be significant.

Ethical considerations

Research and ethical clearance were obtained from the Kilimanjaro Christian Medical University College Ethics Committee (CRERC Number 884). Permission to conduct the study was sought from the local education officer and headmasters of the four selected schools. Written consent was obtained after potential respondents were informed of the study objectives, and their participation was voluntary and free to withdraw from the study. All parents / or guardians of respondents below 18 years received a parental consent form. Written assent to participate in the study was sought from respondents below 18 years old. Adolescents below 18 years who refused to participate in the study were not forced to do so, even if their parents/or guardians consent.

Results

Out of the 422 respondents recruited in this study, 342 (80.7 % response rate) participated in this study. Forty-six respondents refused to participate in this study, 4 participants did not return their questionnaires, and 30 questionnaires were discarded because of incompleteness and inconsistency of data (n=80).

Characteristics of the participants

The age range and the mean age (standard deviation) of the study respondents were 15 to 19 years and 16.7± 3.7 respectively. More than two-thirds, 66.1% of respondents were aged 15 to 17 years, Christians (81.0%), forms 1 to 4 (70.2%), forms 5 to 6 (29.8%), living at home (61.4%), and Chagga tribe (52.3%) [Table 1].

Table 1: Socio-demographic characteristics among adolescent female students in four selected secondary schools in Moshi municipality (N =342).

Variables	Frequency (%)
Age group (years)	
15 – 17	226(66.1)
18-19	116(33.9)
Mean age	16.7±3.7
Religion	
Christian	277(81)
Muslim	65(19)
Class	
Forms 1 to 4	240(70.2)
Forms 5 to 6	102(29.8)
Ethnicity	
Chaga tribe	179(52.3)
Other tribes	163(47.7)
Living arrangement	
At hostel	132(38.6)

At home	210(61.4)

Knowledge of induced abortion

There was no significant difference in the level of knowledge of induced abortion among study participants. Almost half, 50.6% (173/342) had inadequate knowledge compared to 49.4 % who had adequate knowledge of induced abortion. The mean knowledge score was 38.9 ± 1.4. The majority (94. 7%) of the respondents knew that induced abortion can lead to death, while more than a quarter (25.1 %) of respondents were unaware that induced abortion can be done alone by an individual [Table 2].

Table 2: Adolescent female students' knowledge of induced abortion (N=342).

Statements on knowledge of induced abortion	Agreeing response [Frequency (%)]
Induced abortion is an abortion done by myself.	86(25.1)
Induced abortion is an abortion done in the hospital by an untrained person.	124(36.3)
Induced abortion is an abortion done by taking local herbs.	190(55.5)
Induced abortion is an abortion done by a trained doctor in his house.	125(36.5)
Induced abortion is an abortion done by an elderly woman in the community.	135(39.5)
Induced abortion can lead to infection.	288(84.2)
Induced abortion can lead to excessive bleeding.	315(92.1)
Induced abortion can lead to death.	322(94.2)
Induced abortion can be performed through surgical instruments/modern medicines.	299(87.4)
Taking local herbs can induce abortion.	237(69.3)

In bivariate analysis, there was a statistically significant association between the living arrangements of the respondents and their level of knowledge of induced abortion. Respondents staying at the hostel were more likely to be knowledgeable compared to those who were staying at home [Table 3].

Table 3: Association between socio-demographics and knowledge of induced **abortion among adolescent female students in four selected secondary schools in Moshi municipality (n=342).**

Socio-demographic characteristics	Knowledge of induced abortion [Frequency (%)]			P-value
	Adequate	Inadequate	Total	
Age group (years)				
15 – 17	105(46.5)	121(53.5)	226(100)	0.13
18-19	64(55.2)	52(44.8)	116(100)	
Religion				
Christian	143(51.6)	134(48.4)	277(100)	0.43
Muslim	35(53.8)	30(46.2)	65(100)	
Class				
Forms 1 to 4	112(46.7)	128(53.3)	240(100)	0.12
Forms 5 to 6	57(55.9)	45(44.1)	102(100)	
Living arrangement				
At hostel	77(58.3)	55(41.7)	132(100)	< 0.009*
At home	92(43.8)	118(56.2)	210(100)	

*p < 0.01.

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Attitude towards induced abortion

More than half, 55.8 %, (191/342) of the respondents had an unfavourable attitude towards induced abortion compared to 44.2 % who had a favourable attitude. The mean attitude score was 18.9 ± 1.9. The majority, 307/342 (89.8%) of respondents agreed that using family planning methods can prevent unwanted pregnancy, and 12% agreed that they would abort if pregnant, or encourage a friend to abort [Table 4].

Table 4. Adolescent female students' attitude towards induced abortion (N=342).

Statements of attitude towards induced abortion	Agreeing response [Frequency (%)]
It's a sin to perform an abortion.	303(88.6)
Induced abortion can kill because of its complications.	305(89.2)
Using family planning methods can prevent unplanned pregnancies.	307(89.8)
Unplanned pregnancy should be aborted.	56(16.4)
I would undergo an abortion if pregnant.	41(12)
I would encourage my friend to abort if pregnant.	41(12)

The practice of induced abortion

Table 5 below presents the respondents' practice of induced abortion. Out of 342 respondents 19 (5.6%), reported having an abortion. Five respondents had an abortion at 15 years or below, and the remaining 14 had an abortion at age 16 years or above. Ten respondents had one previous abortion, compared with nine who had 2 or more. Sixteen respondents reported their abortions were done in a private health facility, two at home, and one in a public health facility. Seventeen respondents reported their abortions were performed by a health professional, and two by traditional healers. Nine respondents reported their abortion was carried out using the surgical method, while eight used medical aborting drugs, and two used local herbs to induce their abortion. Five of the respondents induced abortion to finish school, five because of fear of parents' reactions, four because of lack of money to support the child, three because of rejection by partner and family, and two because of the shame in society. Thirteen respondents, experienced complications, compared with six who did not. Of thirteen respondents who experienced complications post-abortion, eight reported excessive bleeding, four had abdominal pains, and one had nausea/vomiting.

Table 5. Adolescent female students' practice of induced abortion (n=19).

Variables	Frequency (%)
Age at first abortion	
15 years or below	5(26.3)
16 years or above	14(73.7)
Number of previous abortion(s)	
1	10(52.6)
2 or more	9(47.4)

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A place where abortion was done	
Public health facility	1(5.3)
Private health facility	16(84.2)
Home	2(10.5)
A person who performed an abortion	
Health professional	17(89.5)
Traditional healer	2(10.5)
Material used to induce abortion	
Surgical methods of abortion	9(47.4)
Medical abortion drugs	8(42.1)
Local herbs	2(10.5)
Reasons for inducing abortion	
To finish school	5(26.3)
Fear of parents	5(26.3)
Lack of money to support the child	4(21.1)
Rejection by partner and family	3(15.8)
Shame in society	2(10.5)
Experienced any complications	
Yes	13(68.4)
No	6(31.6)
Type of complications (n=13)	
Excessive bleeding	8(61.5)
Abdominal pains	4(30.8)
Nausea /vomiting	1(7.7)

Discussion

This study aimed to determine the knowledge, attitude, and practice towards induced abortion among adolescent female students in 4 selected secondary schools in Moshi municipality. The study established that there was no significant difference among respondents related to their knowledge of induced abortion. This is contrary to studies done in Nigeria (Abiola et al., 2016), and Goma (Paluku, Kalisoke, Wandabwa, & Kiondo, 2013b), in which 88.3 % and 61.3% respectively of respondents were knowledgeable on induced abortion. On the other hand, inadequate knowledge of induced abortion was observed in a study among female students in different settings in Ethiopia (Gelaye, Nigussie, & Mekonen, 2014; Yaecob et al., 2018). The observed non-differential in the level of knowledge on induced abortion could be a result of ineffective sexuality education programs delivered in secondary schools in Tanzania Although this study

did not assess sexuality education or any form of life skills taught in the respective schools, existing literature suggests that sexuality education taught in Tanzania is inadequate (Mkumbo, 2010). An alternative explanation could be the difference in the sources of information about induced abortion in different study settings (Abiola et al., 2016; Paluku et al., 2013b; Yaecob et al., 2018).

In the current study, respondents who were living in hostels were more likely to be knowledgeable of induced abortion compared to those who stayed at home. This is in line with findings from a study done by Abiola et al (2016) in Nigeria where most respondents first heard about abortion from their friends, with whom they interact frequently (Abiola et al., 2016).

More than half of the respondents in this study had an unfavourable attitude towards induced abortion, which could be influenced by religious beliefs. Most respondents in this study were either Christians or Muslims-both doctrines did not advocate abortion and agreed that abortion was a sin against God. This is in line with the proposals suggested by several studies, which claim that religious abhorrence of abortion, impedes health-seeking behaviour for PAC services in SSA (Abiola et al., 2016; Paluku et al., 2013b; Yaecob et al., 2018). Also, based on religious belief, becoming pregnant before marriage, or inducing abortion is seen as an abomination, and may promote the stigma related to abortion (Abiola et al., 2016). It is important to increase awareness of the benefits of PAC services in this setting regardless of the social, cultural and religious stigmatisation towards abortion, to reduce the mortality and morbidity associated with induced abortion (Atakro et al., 2019).

Countries such as Tanzania, with restrictive abortion law (Johnson et al., 2017; Keogh et al., 2015; Nkata et al., 2017; Sorensen et al., 2010), need to introduce a curriculum-based comprehensive sexuality education (CSE) to young adolescents during the primary school education level (7-14-year-olds) to address multiple sexual psychosocial risk and protective behaviours, including knowledge, perceived risk, values attitudes, perceived norms and self-efficacy (WHO., 2018). Currently, sex education in Tanzania focuses on increasing knowledge alone and is limited in addressing skills, relationships, attitudes, and values, which are essential components of CSE (Mkumbo 2010). For example, one important sub-topic covered in sex education for secondary schools is family planning. However, the content only covers the meaning and importance of family planning. Such deficits are inconsistent with the Government's efforts to address the problem of increasing rates of teenage pregnancy among school girls (Mkumbo 2010). Existing evidence suggests that CSE has a positive effect on increasing adolescents' knowledge and refining their attitudes towards sexual and reproductive health, by delaying risky sexual behaviours and increasing contraception use (WHO., 2018).

Most respondents reported their first abortion at a young age (16 years or above), although most had aborted only once. This study revealed that health professionals working in private for-profit health facilities did most of the abortions. Very few respondents attended a traditional healer to induce abortion. The Tanzanian health system is categorized as public (government-owned), private (not-for-profit owned/or private for-profit owned). Government-owned health facilities are supervised directly by the Ministry of Health, Community Development, Gender, Elderly and Children (MoHCDGEC), and follow government regulations, including the restrictive abortion law, making it difficult for adolescent girls with unplanned pregnancy to access PAC services (United Republic of Tanzania, 2017b). Hence, the only option for adolescent girls to undergo an abortion is the private-for-profit health facilities (Keogh et al., 2015; Nkata et al., 2017; Norris et al., 2016). Further, this study showed that most respondents who underwent an abortion used surgical methods of abortion or medical abortion drugs. Similar findings were reported

from a study conducted in Zanzibar, where adolescent girls, used a blend of herbs, and medical abortion drugs to ensure that the abortion does not fail (Norris et al., 2016).

The most common complications mentioned by respondents who induced abortion were excessive bleeding and abdominal pains. Surprisingly, in this study, most respondents experienced complications post-abortion even though health professionals working in private-for-profit facilities did most of the abortions. The most probable explanation for this observation could be that most health professionals working in private-for-profit facilities are not well-trained and competent to perform safe abortions (Norris et al., 2016). Further, existing literature on induced abortion suggests that excessive bleeding is the main cause of both morbidity and mortality, which impact the health of adolescent girls with unplanned pregnancies worldwide (Espinoza et al., 2020; Johnson et al., 2017; WHO, 2007, 2011). The Tanzania Ministry of Health must make efforts to train health professionals working in private-for-profit health facilities on PAC services to reduce the risk of severe complications post-abortion among adolescent girls (Espinoza et al., 2020; Johnson et al., 2017; WHO, 2007, 2011).

In this study, the two main reasons mentioned by most respondents who induced abortion were to finish their education and fear of parents' reaction. These results concur with findings from studies conducted in Ethiopia (Cadmus & Owoaje, 2011; Yaecob et al., 2018), Tanzania (Keogh et al., 2015; Nkata et al., 2017; Norris et al., 2016), and Ghana (Atakro et al., 2019). The restrictive abortion law existing currently in Tanzania may be perceived as a barrier; therefore to avoid having their educational aspirations terminated most female students opt for an abortion (Cadmus & Owoaje, 2011; Keogh et al., 2015; Nkata et al., 2017; Paluku, Kalisoke, Wandabwa, & Kiondo, 2013a). Recently the Government of Tanzania, through the Ministry of Education, Science and Technology have announced that pregnant schoolgirls will be allowed to continue with formal education after delivery. However, female students will be banned from attending school while pregnant (Guardian, 26th Nov 2021).

Fear of parents' reactions arises from the fact that in most African societies, culturally abortion is a taboo, and seen as an embarrassing and shameful act associated with stigma, and a sign of disrespect to discuss premarital sex and pregnancies with parents. Atakro et al. in Ghana also reported that fear of parental/ guardian disappointment and resentment was one of the contributing factors to induced abortion practices (Atakro et al., 2019). The solution to this challenge is to increase parent-daughter communication about sexuality issues, by training parents in the requisite knowledge and communication skills to impart to their adolescent girls on how to deal with sexual challenges confronting them (Babalola, Vondrasek, & Brown, 2001).

Further qualitative research to explore the views and perceptions of parents, religious leaders, and health care providers of contributing factors to induced abortion practices among female secondary school students in this study setting is warranted.

Study limitations

This study is not exempted from limitations. First, this is a cross-sectional study design; hence it is unable to demonstrate the causal-effect relationships reported in this study. Second, the study enrolled only female students from selected secondary schools and the findings can only be generalizable to the study population and setting. Third, the study respondents were asked very sensitive issues such as their practices of abortion, which is illegal in Tanzania hence the possibility of recall bias and social desirability bias cannot be excluded and may influence the respondent's responses regarding their practices. Finally, the validity of the study findings may be affected by the below-normal acceptable range of Cronbach's

alpha internal reliability scales used to assess the level of knowledge (α = .61) and attitude (α = .62) toward induced abortion.

Conclusion

In conclusion, there was no significant difference in the level of knowledge on induced abortion among study participants. However, the unfavourable attitude towards induced abortion observed is mostly influenced by cultural and religious factors. Two main reasons for induced abortion were fear of termination from school and fear of parents' reactions. Comprehensive sexuality education (CSE), contraception counselling and provision, access to post-abortion care (PAC) services, and parent-daughter communication interventions may be beneficial to prevent unplanned pregnancies in adolescent students attending secondary schools in this setting.

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Competing interests

No competing interests.

Authors' contributions

BN is the guarantor. All authors contributed to the conception and design of this manuscript as follows. FAK, JSN and ALM conceived the study and wrote the manuscript under the supervision of BN.
All authors read the final draft of the manuscript and provided feedback. All authors read and approved the final manuscript.

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Obstetric factors associated with the uptake of Postnatal Care among mothers who gave birth in the last six months in Dodoma Region, Tanzania

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Abstract
Background: The World Health Organization defines postnatal care when it is given to the mother and her newborn baby immediately after the birth of the placenta and for the first six weeks of life. The majority of maternal and neonatal deaths occur during childbirth and the postpartum period which can be prevented through adequate utilization of antenatal and postnatal care services.
Objective: To assess obstetric factors associated with the uptake of postnatal care services among mothers who gave birth in the last six months in Dodoma region, Tanzania
Method: This community-based cross-sectional study was conducted among 420 study participants from January to March 2021. Logistic regression analysis was carried out to measure obstetric factors associated with the uptake of postnatal care. An adjusted odds ratio with a 95% confidence interval and p-value less than 0.05 was applied.
Results: The uptake of the recommended four postnatal care visits was 136 (32%). Mothers who received counselling during ANC were almost 4 times more likely to utilize adequate PNC services than their counterparts (AOR=3.737; 95%CI =1.176-31.882; P=0.025). Those who delivered by C/Section were almost 12 times more likely to utilize PNC services adequately (AOR=11.913; 95%CI =3.0901- 45.933; P=0.000). Awareness of the PNC schedule was 18 times more likely to use the PNC services adequately compared with their counterparts (AOR=18.092; 95%CI =8.239- 39.726; P=0.000). Awareness of maternal danger signs was almost 5 times more likely to utilize PNC service adequately than their counterparts (AOR=4.691; 95%CI =2.168- 10.153; P=0.000).
Conclusion: The overall uptake of adequate postnatal care in the study area was low. Obstetric factors were found as strong predictors of adequate PNC service uptake among study participants. There is a need to strengthen routine health education during the antenatal and postpartum periods to enhance adequate PNC services uptake among women.

Keywords: PNC; Uptake; Obstetric; Factors

Background

Postnatal care (PNC) is the care provided to a mother and her newborn baby in the first six weeks after birth. The postnatal period (PNP) is the time beginning immediately following the delivery of the placenta and extending through the six weeks (42 days) of birth. This period signifies a critical

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phase in determining the mother's and her newborn's health and survival (WHO, 2015). The goal of care during the early postnatal period is to promote the physical well-being of both mother and baby and support the developing relationship between the baby and his or her parents and family (WHO, 2015). Lack of care in the postnatal period from skilled providers may result in death or disability as well as missed opportunities to promote healthy behaviors affecting women, newborns, and children.

Studies in Africa showed that, every year approximately 125,000 women die in the first-week post-delivery, 50% of these deaths occur in the first week after the delivery while others happen within 24 hours following delivery (Mahmood et al., 2010). In Tanzania, the maternal mortality ratio was 556 per 100,000 live births (MoHSW, MoH, NBS, OCGS, 2016) and the neonatal mortality rate of 24/1000 live births in 2022 (MoHSW, MoH, NBS, OCGS, 2023). This indicates that Tanzania is still far from meeting the Sustainable Development Goal (SDG) targets of reducing the maternal mortality ratio to 70 per 100,000 live births and neonatal mortality to 12/ 1000 births by 2030 (SDG Targets 3.1 and 3.2, respectively (United Nations, 2016). Therefore, postnatal care services target to reduce preventable maternal and neonatal deaths which mostly occur within the first 24 hours and/or 3 days following delivery.

The postnatal care package insists on coverage of four PNC visits, and the first must be within the first 24 hours, at least three additional PNC are recommended for all mothers and newborns, on day 3 (48–72 hours), between days 7–14, and 6 weeks (WHO, 2015). PNC is meant to offer the mothers the opportunity to access check-ups for bleeding and vital signs (Temperature, Pulse, Respiration, and BP), support breastfeeding, check the breasts to prevent mastitis, manage anemia, promote nutrition and insecticide-treated bed nets, receive vitamin A supplementation, and be able to obtain counseling about danger signs and options for contraceptive services (Warren et al., 2010). The care given in the postpartum period helps the healthcare providers detect and manage complications that may occur following delivery (Wudineh et al., 2018). PNC if appropriately done within the recommended time prevents the great majority of maternal deaths (World Health Organization, 2010).

Previous studies have shown that proper management of life-threatening conditions soon after delivery has been shown to prevent maternal and prenatal morbidity and mortality (Bhutta et al., 2014; Singh et al., 2014). Although there is a high rate of death among postnatal mothers and neonates, especially in the first two days post-delivery post-natal services are inadequately utilized. A study done in 2016 that involved six developing countries, reported that only 36% of mothers utilized PNC adequately within 42 days post-delivery (Adhikari & Kumar, 2016). In Tanzania only 50.2% of mothers who had a live birth in the two years before the survey received a postnatal check during the first two days post-delivery. In the Dodoma region, 55.3% of mothers received a postnatal check during the first two days of delivery indicating low utilization of services (MoHSW, MoH, NBS, OCGS, 2023).

Different scholars indicated that PNC services utilization is affected by several factors including maternal age, educational level of a mother, place of delivery, mode of delivery, number of pregnancies, awareness about obstetric-related danger signs, and awareness about PNC services (Berhe et al., 2019; Limenih et al., 2016; Workineh & Hailu, 2014). Other factors found in the literature include the number of antenatal care (ANC) visits, urban residence, and women's autonomy (Berhe et al., 2019; Workineh & Hailu, 2014).

However, the factors of the utilization of PNC services are not the same across different cultures and socioeconomic statuses within a society. For example, Tanzania, is a country, that has an increased health facility network where PNC services are exempted for all postnatal mothers.

Reproductive health services are extensively expanded, including the deployment of skilled healthcare providers and an increase in the budget for health which is meant to ascertain all postnatal mothers and others get quality health services from the public health facilities (MoHCDGEC, 2015). The country has also emphasized private and non-governmental partnerships in the health sector, whereby private health facilities are available for mothers free of choice; yet, the uptake of PNC is still low, especially in Dodoma Region. There was a need to determine the uptake of postnatal care services and the influence of obstetric factors on postnatal care services utilization in the Dodoma region. Therefore, the objective of this study was to assess the obstetric factors associated with postnatal care services utilization among mothers who gave birth in the last six months in Dodoma region, Tanzania.

Methods

Study design and setting

The study employed a community-based cross-sectional study design using a quantitative approach conducted from 1st January to 28th March 2021. The study was conducted in Dodoma region, the capital city of Tanzania. Dodoma region is composed of seven districts: Chamwino, Bahi, Kondoa, Mpwapwa, Kongwa, Chemba, and Dodoma Municipal. Three districts, namely Chamwino, Mpwapwa, and Dodoma municipal were involved in this study. The selected districts have a total of 235 health facilities (11 hospitals, 21 health centers, and 203 dispensaries). Reproductive and child health services including PNC are provided daily in all health facilities except in some remote areas which have no health facilities where the outreach programs are carried out once a month. Data obtained from respective District Reproductive and Child Health Coordinators (DRCHcos) for each selected district shows that there were a total of 97,710 women of childbearing age (WCBA) from Chamwino district, 93,080 from Mpwapwa district, 146, 862 from Dodoma Municipality.

Study population, inclusion and exclusion criteria

Mothers who were 7th to 12 weeks post-delivery who were ready to participate and those with good health conditions were included in the study. However, those mothers who were sick and who lived less than six months in the study area at the time of the interview were excluded from the study.

Sample size and sampling technique

The required sample size was calculated using the following formula ($n = z2\ p\ (1-p)/e2$) whereby; n = sample size, z =1.96, e = 5%, and p = 46% (proportion of women using postnatal care services in Dodoma region (National Bureau of Statistics, 2016). An attrition rate of 10% was employed and the required minimum sample size of 420 participants. The sample size was distributed into selected districts by proportional allocation of sample size as shown in *Table 1.*

Table 1: **Sample Size Distribution of Study Population In Selected Districts**

District	Target population	Population proportion	Sample size
Dodoma Municipality	146,862	0.43495	183
Chamwino	97,710	0.28938	121
Mpwapwa	93,080	0.27567	116
Total	337,652	1	420

The current study employed a multistage sampling technique to obtain study representative sample from the region. In the first stage, the list of all districts in the Dodoma Region was obtained and Dodoma Municipality was selected purposively as it is only an urban district with people of different backgrounds. Two other districts (Chamwino, and Mpwapwa) were selected by a simple random method using a lottery method with a replacement approach. In the second stage, simple random sampling was used for two wards from each of the selected districts by using a table of random numbers and obtained six wards. In the third stage, a similar sampling technique was applied to select three villages/streets from each selected ward and obtained a total of 18 villages/streets. From each of the selected villages/streets, all households with mothers who delivered within seven to twelve weeks during the study period were eligible for the study. At the household level, participants were selected randomly and within the households, only one participant was selected.

Data Collection Tools and Procedures

Data was collected through a structured and semi-structured questionnaire using the face-to-face interview method. The data collection tool was prepared in English and translated to Kiswahili. The tools were pre-tested to ensure consistency of the variables included in the study and a village used for pretesting was excluded during actual data collection. Two research assistants (nurses) were used to collect data after training on data collection for one day.

Statistical Analysis

The data were entered, cleaned, and transformed (recoded) using SPSS software version 26. Univariate analysis was computed for each independent variable to assess their proportion. A Chi-square test was done to examine the preliminary relationship between the dependent variable (PNC services utilization) and independent variables (obstetric factor). All variables with $P<0.05$ were retained for reduced and full model analysis. Bivariate analysis was done using a logistic regression model to examine the crude association of predictors on PNC service utilization. Adjusted Odds ratio and 95% CI were used to measure the statistical association value 0.05 was used to determine the statistical significance of the tests.

Ethical Approval and consent to participate

Ethical clearance and permission were sought from the University of Dodoma Research and Ethical Conduct Committee with Ref. NO.MA. 84/261/02/214, and permission for research conduct was sought from Regional Administrative Secretary (RAS) for Dodoma region with Re.122/467/01F/175. Verbal consent to participate in the research was obtained from each participant and was assured the right to withdraw from the study at any time of the study. They were also assured of confidentiality and only identification numbers were used to identify participants.

Results

Socio-demographic characteristics of study participants

This study involved 420 participants. The majority of the participants 54.3% were aged between 20 to 29 years, 86.4% were currently married, 68.6% had primary education level, 91.4%, were not employed and 346 incurred no cost to reach a health facility *(Table 2)*.

Table 2: Sociodemographic Characteristics of Participants (N=420)

Variables	N	%

Age (years)		
18- 19	23	5.5
20 to 29	228	54.3
≥30	169	40.2
Marital status		
Never married	45	10.7
Married	363	86.4
Separated/Divorced	12	2.9
Place of residence		
Rural	237	56.4
Urban	183	43.6
Education level		
Informal	28	6.7
Primary	288	68.6
Secondary or higher	104	24.7
The employment status of the mother		
Employed	36	8.6
Self-employed	101	24.0
Peasants	283	67.4
Employment status of husband		
Not married/ Separated/Divorced	57	13.6
Employed	45	10.7
Self-employed	168	40
Peasants	150	35.7
Estimated time to reach a health facility		
>30 min	149	35.5
30 min to 1 hour	241	57.4
≥2 hour	30	7.1
Cost to reach the health facility		
No cost	346	82.4
500 to 2000 TZS	71	16.9
>2000 TZS	3	0.7

Obstetric Information of the Participants

Of 420 study participants studied, the majority 400 (95.2%) started ANC visits late (≥12 weeks GA) 253 (60.2%) had 4 or more ANC visits, 359 (87.1%) were not counselled about PNC services during ANC, and 386 (91.9%) delivered at the health facility for the current baby. *(Table 3).*

Table 3: Distribution Of Obstetric Information Of Participants (N = 420)

Variables	N	%
ANC visits		
<4	167	39.8
≥4	253	60.2
Gestational age at the first ANC visit (weeks)		
<12	20	4.8
≥12	400	95.2
The health provider attended the mother during the first ANC visit		

Skilled Personnel	247	58.8
Un skilled personnel	173	41.2
Counselled on PNC during ANC		
Yes	49	11.7
No	371	88.3
Parity		
1 to 2	210	50.0
3 to 5	146	34.8
>5	64	15.2
The mother received support from the husband		
Yes	231	55.0
No	189	45.0
Type of support from husband		
Accompaniment	170	40.4
Financial	67	16.0
None	183	43.6
Place of delivery for current baby		
Health facility	386	91.9
Home	34	8.1
Mode of delivery		
SVD	373	88.8
C/Section	47	11.2
Awareness of PNC schedule		
No	273	65.0
Yes	147	35.0
Awareness of maternal danger signs		
No	294	70.0
Yes	126	30.0

Uptake of Postnatal Care Services Among Study Participants

Results from this study showed that the majority 95.6% of participants attended PNC visits at least once while 4.5% did not attend PNC visits during their postnatal period. Results also showed that only 32.2% of participants completed the recommended four PNC visits (adequate PNC utilization). Regarding the number of PNC attended, the majority (67.8%) of study participants attended PNC less than four visits and 78.6% received PNC services within the first 24 hours as shown in *Table 4*.

Table 4: Uptake of Postnatal Care Services (N = 420)

Variables	N	%
Attended PNC at least once		
YES	401	95.6%
NO	19	4.5%
Number of PNC attended		
Four or more visits	136	32.2%
Less than four visits	284	67.8%
Timing of receiving the first PNC visits		
Within the first 24 hours	330	78.6%
Between 48 to 72 hours	64	15.2%
Between 7 - 14 days	7	1.7%

At six weeks	0	0%

Types of Postnatal Care Services Received

Participants were asked about PNC services received during their attendance at the PNC clinic. According to them, within the first 24 hours post-delivery, 124 (29.5%) participants said they were assessed for the color of per vaginal discharge (lochia), 193 (46%) got their newborn babies immunized against polio and Tuberculosis (Polio and BCG), 10 (2.4%) counseled on timely and Exclusive Breastfeeding. About 93 (22.1%) did not attend during these visits. Regarding PNC services provided between 48 to 72 hours, 41 (9.8%) received wound assessment for those who underwent C/S, 40 (9.5%) counseled on EBF, 128 (30.5%) received vaccination services for their newborn babies, while the majority 211 (50.2%) did not attend during this visit. Between 7 to 14 days, 43 (10.2%) got their stitches removed (for those who underwent C/S, 93 (22.1%) were reminded of EBF, and 18 (4.3%) received vaccination services for their babies. However, the majority 267 (63.3%) did not attend the clinic for PNC services. During 6th week post-delivery, 313 (74.5%) reported their babies received pentavalent and Rotarix vaccine, 4 (1%) received health education on EBF, and 103 (24.5%) did not attend during this visit. *(Figure 1).*

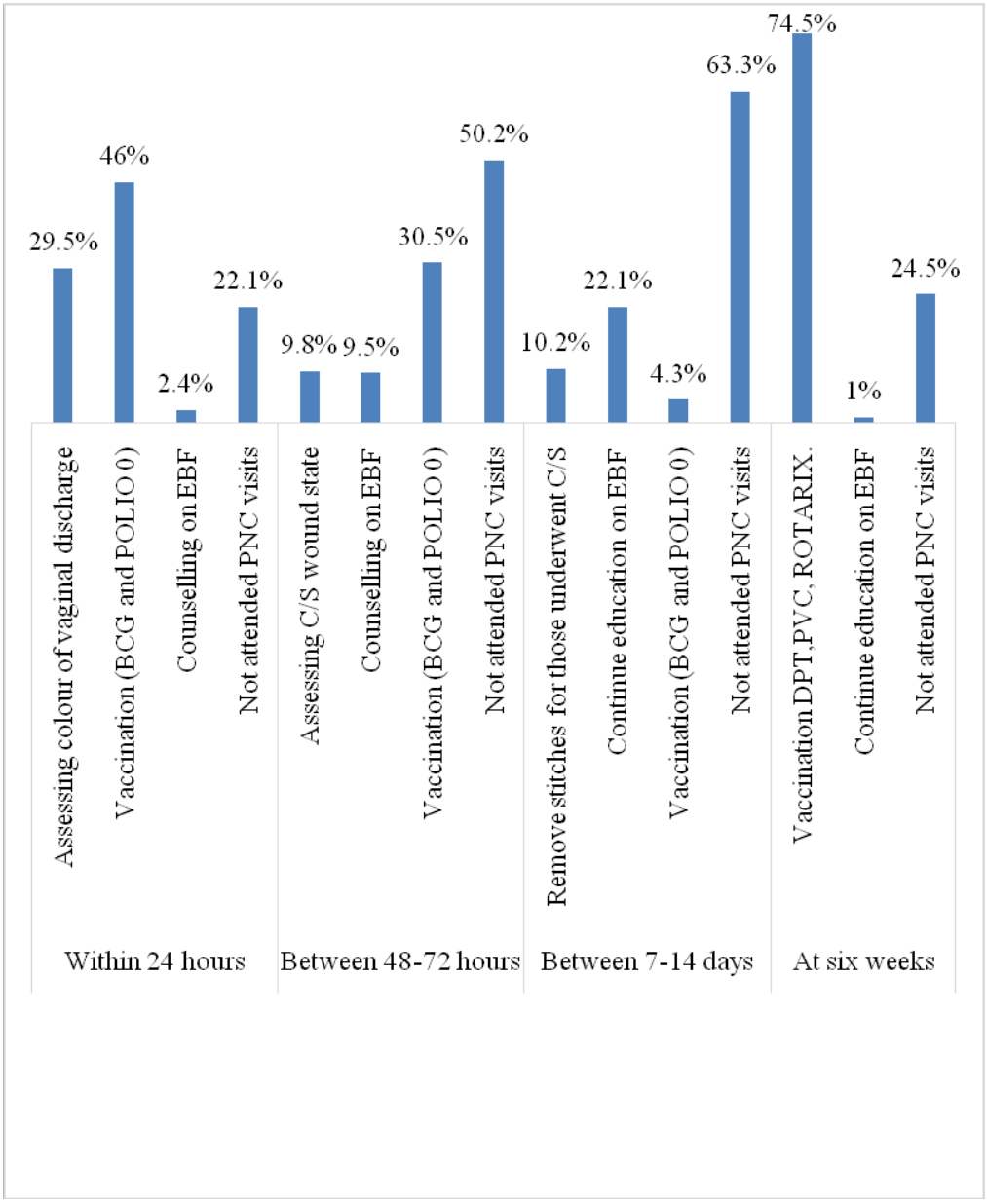

Figure1: Postnatal care services received at different visits

Obstetric factors associated with the Postnatal Care services Uptake

Bivariate and multivariate logistic regression analyses were done to determine the association of Obstetric factors on the uptake of postnatal care services. Results from the bivariate logistic regression analysis showed that C/Section delivery, Place of delivery, parity (> 5), counselled on PNC during ANC, and those who were aware of maternal danger signs and PNC schedule were significantly associated with adequate uptake of PNC services during the postnatal period compared with their respective reference category (P <0.05).

After adjusting for potential confounders in multiple logistic regression model results showed that variables such as counselled on PNC during ANC, Deliver by C/Section, awareness of

PNC schedule, and awareness of maternal danger signs remained the strong predictors of adequate PNC service uptake among study participants. Regarding if mothers received counselling services results showed that, mothers who were counselled on PNC during ANC was almost 4 times more likely to utilize adequate PNC services compared to their counterpart (AOR=3.737; 95%CI =1.176-31.882; P=0.025). Concerning mode of delivery, mothers who delivered by C/Section was almost 12 times more likely to utilize the PNC services adequately compared with those who delivered by normal vaginal delivery (AOR=11.913; 95%CI =3.0901- 45.933; P=0.000). Mothers who were aware of the PNC schedule were 18 times more likely to use the PNC services adequately compared with their counterparts (AOR=18.092; 95%CI =8.239- 39.726; P=0.000). Again those mothers who were aware of maternal danger signs were almost 5 times more likely to utilize PNC service adequately than their counterparts (AOR=4.691; 95%CI =2.168- 10.153; P=0.000) (*(Table 5)*.

Table 5: Obstetric factors associated with Postnatal Care services Utilization (N = 420)

Variables	Univariate OR at 95%CI	P-value	Multivariate aOR at 95%CI	P-value
ANC Visits				
< 4 (Ref)				
≥ 4	1.15(0.76, 1.75)	0.512	0.71(0.33, 1.54)	0.391
Gestational Age				
< 12	1.42(0.57, 3.55)	0.458	0.78(0.16, 3.89)	0.762
≥ 12 (Ref)				
Health provider attended the mother during the first ANC visit				
Skilled personnel	1.07(0.70, 1.64)	0.744	1.114(0.53, 2.35)	0.778
Unskilled personnel (Ref)				
Received counselling on PNC during ANC				
Yes	21.42(8.83, 51.95)	**0.000**	3.73(1.18, 31.88)	**0.025**
No (Ref)				
Parity				
1 to 2 (Ref)				
3 to 5	1.06(0.68, 1.65)	0.795	1.37(0.46, 4.08)	0.571
> 5	0.44(0.22, 0.88)	**0.020**	1.49(0.49, 4.54)	0.479
Support from Husband				
Yes	1.696(1.12, 2.58)	**0.013**	1.04(0.04, 28.62)	0.980
No (Ref)				
Type of support				
Accompaniment	1.53(0.97, 2.41)	**0.067**	1.11(0.04, 32.37)	0.954
Financial	1.92(1.07, 3.46)	**0.030**	1.11(0.04, 30.16)	0.950
None (Ref)				
Place of Delivery				
H/Facility	2.98(1.13, 7.89)	**0.028**	2.26(0.45, 11.6)	0.329
Home (Ref)				
Mode of delivery				
Normal (Ref)				
C/Section	24.93(9.58, 64.87)	**0.000**	11.91(3.09, 45.93)	**0.000**

Awareness on PNC schedule				
Yes	57.64(30.78, 107.94)	**0.000**	18.09(8.24, 39.73)	**0.000**
No (Ref)				
Awareness of maternal danger signs				
Yes	21.87(12.82, 37.32)	**0.000**	4.69(2.17, 10.15)	**0.000**
No (Ref)				

Discussion

This was a community-based study conducted to assess the influence of obstetric factors on the uptake of postnatal care services among study participants. The finding from this study showed that less than half (32.4%) of participants received recommended four PNC services (adequate utilization) during their postnatal period. This finding is almost similar to the finding of a study conducted in Ethiopia with a prevalence of 34.8% and Morocco at 30.1% (Ayana Hordofa, 2015; Elkhoudri et al., 2015). However, the uptake of adequate PNC services in the current study is lower than the results of a study done in Uganda,50%, and Kenya, 47% (Akunga et al., 2014; Wudineh et al., 2018).

Again, the uptake of postnatal care services in the present study was higher than the finding of studies conducted in Tigray, Northern, Ethiopia, 8% (Workineh & Hailu, 2014), Gambia 22.4% (Barrow & Jobe, 2020), India, 29% (Kaur & Kaur, 2017) and Morogoro, Tanzania 25% (Mohan et al., 2015). The observed discrepancy from these studies could be due to time differences as there was some improvement in the availability and accessibility of maternal health services over time. Another reason could be due to contextual and socio-demographic differences among study participants.

The current study revealed that the uptake of adequate PNC services has been significantly influenced by the mode of delivery, whereby postnatal mothers who gave birth by C/ section were more likely to utilize PNC services adequately compared to those who delivered by spontaneous vaginal delivery. A similar finding was observed in previous studies conducted in 33 sub-Saharan African countries, Ethiopia and Tanzania (Benova et al., 2019; Limenih et al., 2016; Mohan et al., 2015). This can be explained that mothers who delivered by caesarean section utilized adequate PNC services as a part of follow-up care for their complications and then had better opportunities to receive health education on postnatal care services. Again, this might be due to fear of complication and therefore utilized PNC services to prevent further complications hence increased healthcare-seeking behaviour.

Concerning the influence of knowledge of postnatal care services, the present study revealed that those women who know about PNC services were more likely to use the service than those who lack knowledge of PNC services. This was similar to the results of a study conducted in northwest Ethiopia and Urban Northern Ethiopia which revealed that postnatal women who were knowledgeable about postnatal care services and maternal complications during the postpartum period were more likely to utilize postnatal care services compared with those who did not know (Gebrehiwot et al., 2018; Limenih et al., 2016).

Mothers who were aware of the PNC schedule were more likely to use adequate PNC services compared with their counterparts. This was similar to the results of a study conducted in Ethiopia which revealed that postnatal women who were aware of the postnatal care service and

maternal complications during the postpartum period were more likely to utilize postnatal care services adequately compared with their counterparts (Beyene et al., 2022; Zeleke et al., 2021). Again, a similar study conducted in northern Ethiopia noted that those women who lacked knowledge of postnatal care services were less likely to utilize the service (Gebrehiwot et al., 2018). Awareness of obstetric danger signs was also found to be a strong predictor of adequate PNC utilization. Mothers who were knowledgeable about obstetric danger signs were more likely to utilize PNC service as compared to those who did not mention any obstetric danger signs.

This result is similar to the study conducted in Kenya (Mayieka, 2019), and Uganda (Sacks et al., 2017). This can be explained by the fact that awareness of obstetric danger signs is an important factor in motivating mothers and their families to utilize health care services adequately with intention of receiving preventive interventions and management of obstetric danger signs. Previous studies have also supported the role of counselling in increasing awareness among postnatal mothers during antenatal and post-delivery and prior discharge home (Berhe et al., 2019; Limenih et al., 2016; Tessema et al., 2020; Wudineh et al., 2018).

Strengths and limitations of a study

The study has presented evidence on obstetric factors associated with adequate uptake of postnatal care services among women in the Dodoma region which could be used as input to strengthen interventions on reproductive health locally and in other similar areas. However, there could be recall bias in the study since the women were asked for retrospective information within the past six weeks after delivery.

Conclusion and recommendation

Although the majority of participants attended PNC services at least once, the overall utilization of adequate postnatal care among women in the study area was low. Obstetric factors associated with adequate PNC service uptake were mothers being counselled during ANC, delivery by cesarean section, awareness of the PNC schedule, and awareness of maternal danger signs. Therefore, to enhance adequate PNC services utilization, healthcare providers and other health stakeholders need to strengthen routine health education during the antenatal and postpartum periods.

Abbreviation

ANC**:** Antenatal care**;** TDHS: Tanzania Demographic and Health Survey; TDHS-MIS Tanzania Demographic and Health Survey-Malaria Indicator Survey; PNC; Postnatal Care; RMNCAH: Reproductive, maternal, newborn, child, and adolescent health; SDGs: Sustainable Development Goal; WHO: World Health Organization

Competing interests

No conflict of interest.

Authors' contributions

AFN, NM contributed to the design of the study, data collection, data analysis and drafting of the manuscript. NG and SN contributed to data analysis and critical review of the manuscript. All authors read, commented on, and approved the final draft of the of the manuscript

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Barriers to early postnatal care attendance among women in Ubungo Municipality in Tanzania: A qualitative study

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Abstract

Introduction: Adequate utilization of postnatal care services is associated with improved maternal and neonatal health outcomes. The World Health Organization recommends postnatal women attend postnatal care as early as seven days after delivery because most maternal deaths occur within 7 days of the postnatal period. However, many postnatal women attend postnatal care very late during the 42 days and mainly for child immunization purposes. Little information is known on barriers to postnatal women who delay initiating postnatal care clinics for seven days post-delivery. This study explored barriers to attending early postnatal care among women attending early postnatal care services in Ubungo municipality, Dar es Salaam.

Methods: A cross-sectional study design using a qualitative approach was used to explore factors associated with early postnatal care attendance among postnatal women in Ubungo Municipal, Dar es Salaam, Tanzania. Study participants were purposively selected. In-depth interviews were used to collect data. Audio-recorded interviews were transcribed verbatim and translated into English. Thematic analysis approach was used to excerpt barriers to delaying seeking early postnatal care services in Ubungo Municipality.

Findings: The finding revealed a lack of awareness of the appropriate time to start early postnatal care visits and the recommended number of postnatal visits, the perception of postnatal women that the postnatal period is a normal condition that does not require health personnel's attention, thus the perception that no need to initiate early postnatal care clinics if they were not sick. Similarly, long waiting times, transport costs, and healthcare providers' attitudes were major reasons reported by postnatal women to contribute to late postnatal care attendance. Thus, healthcare providers should continue providing education to pregnant women on when and the importance of attending early postnatal care.

Keywords: *Barriers, early postnatal, Dar es Salaam, Tanzania*

Introduction

Worldwide, more than half of maternal deaths occur after childbirth (Ronsmans and Graham, 2006). Postpartum haemorrhage and sepsis are the leading causes of maternal deaths (Khan et al., 2006). The postnatal period begins immediately after the birth of the baby and extends up to 42 days. It is described as an instant postpartum period which covers 24 hours from birth, followed by early postpartum periods from day 2 to day 7; and from day 8 through 42 days is known as a late postpartum period. The postnatal period is a critical time for both mothers and babies who need a close follow-up since about 60% of maternal deaths occur during the early postpartum period (first week postpartum) (WHO, 2010). Moreover, early postnatal care (PNC) visits potentially capture early detection of

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postnatal danger signs which are necessary for protecting maternal health and prevention of maternal deaths. Additionally, early PNC offers an opportunity for a woman to discuss with healthcare providers the effective use of family planning methods, exclusive breastfeeding, screening of HIV/AIDS and nutrition status (WHO, UNICEF, UNFPA, 2019, Lwelamira et al., 2015). In 2017, it was estimated that 295,000 maternal deaths occurred during pregnancy, delivery, and postnatal with 94% reported from low and middle-income countries (LMICs) (WHO et al., 2019). The majority of maternal and neonatal deaths are caused by preventable conditions such as haemorrhage, sepsis, hypertensive disorders, or neonatal sepsis, birth asphyxia and prematurity, respectively (WHO, et al., 2019, WHO, 2013, Ronsmans and Graham, 2006).

Low PNC coverage, few postnatal visits, and late attendance of postnatal women are common problems throughout Sub-Saharan Africa posing difficulty in accomplishment of the WHO recommendation of a postnatal schedule of at least three times. PNC is an opportunity to provide preventive care and management of existing potential causes of maternal morbidity and mortality (Hokororo et al., 2015). Tanzania still ranks the highest in maternal cases with about 556 deaths per 100,000 live births caused by low coverage of postnatal attendance of 46% (TDHS, 2015-16). Most maternal deaths occur during the first week of life and certainly, the first two days after birth are the most crucial period for postnatal care.

Several factors have been reported to be the cause of late initiation of early postnatal care (PNC) among postnatal women, which may vary between rural and urban areas (Ndugga et al., 2020). Some studies show that the timing of initiation of the postnatal care visit is of paramount importance for ensuring a continuum of care and health outcomes for women and children. There are many factors affecting early postnatal care attendance in developing countries such as availability of services, accessibility and quality of health services including demographic characteristics of the women's socio-economic status, knowledge of the importance of early postnatal care services, previous pregnancy experience and cultural beliefs (Konje et al., 2021). For example, a study conducted in Dodoma Tanzania at the time of initiating care reported that only 41.7% of the postnatal mothers initiated care within 7 days (Lwelamira, et al., 2015).

Even though women have heard of PNC very few access the services. This is, mostly, because women do not recognize the importance of seeking PNC. Some women think that since they have delivered the baby successfully they do not need the PNC. Some women are not able to obtain PNC services because they are not delivered in the health facility and yet others stay far from the clinics and fear the cost of obtaining PNC services (UNDP, 1998).

The scarcity of vehicles, especially in remote areas, and poor road conditions can make it extremely difficult for women to reach even relatively nearby facilities. Walking is the primary mode of transportation, even for women in labour (Williams et al., 1985). In rural Tanzania, for example, 84 per cent of women who gave birth at home intended to deliver at a health facility but did not due to distance and lack of transportation (Bicego et al., 1997). Fees reduce women's use of maternal health services and keep millions of women from having hospital-based deliveries or from seeking care even when complications arise. Even when formal fees are low or non-existent, there may be informal fees or other costs that pose significant barriers to women's use of services. These may include costs of transportation, drugs, food, or lodging for the woman or for family members who help care for her in the hospital (Gertler and van der Gaag, 1988; Gertler et al., 1988).

According to Mit (1999) in her study looking at the knowledge and attitude of mothers towards PNC in Lusaka, she found that the older women, covering 60% of the women with positive attitudes, did not utilize PNC services. It was also revealed that the majority of those with poor knowledge (54%) had no source of information on PNC meaning the IEC was not adequately given in the health institutions. IEC on the importance of PNC seems to be inadequate in the health centres, so

it needs to be intensified and strengthened. While another study conducted in Algeria by United Nations Population Fund, (2002) on factors associated with maternal mortality revealed that maternal mortality was high estimated at 117 per 100,000 live births. Factors related to such high rates of maternal mortality include insufficient attention given to the mothers and underutilization of PNC. The study also revealed that low utilization of these services was higher in poor areas where infrastructure, human resources and access to care were particularly deficient (UNFP, 2002).

In some cases traditional beliefs and practices are associated with low utilization of PNC services, e.g. most mothers are kept in seclusion after delivery for about one week because it is believed that during this time they are considered to be impure (Mwelwa, 1997). Several socio-demographic characteristics of the individual affect the underlying tendency to seek care (Addai, 2000). In this regard, good examples are maternal age and parity, which have been examined as determinants of healthcare use repeatedly (Adekunle et al., 1990; Celik and Hotchkiss, 2000; Leslie and Gupta, 1989).

The greater confidence and experience of the older and higher parity women, together with greater responsibilities within the household and for child care, have been suggested as explanatory factors for their tendency to use services less frequently (Kwast and Liff, 1988). Maternal education has also been shown repeatedly to be positively associated with the utilization of maternity care services (Addai, 2000; Addai, 1998; Beker et al., 1993; Celik and Hotchkiss, 2000). Although, in general, women in higher socioeconomic groups tend to exhibit patterns of more frequent use of maternal health services than women in the lower socioeconomic groups, factors such as education appear to be important mediators (Addai, 2000; Leslie and Gupta, 1989).

Another important factor affecting the utilization of maternity care services, especially in Africa, is the cultural background of the woman (Leslie and Gupta, 1989). The cultural perspective on the use of maternal health services suggests that medical need is determined not only by the presence of physical disease but also by cultural perception of illness. In most African rural communities, maternal health services coexist with indigenous health care services; therefore, women must choose between the options. The use of modern health services in such a context is often influenced by individual perceptions of the efficacy of modern health services and the religious beliefs of individuals (Addai, 2000).

Women in rural Southern Tanzanian though generally positive about antenatal care (ANC) and postnatal care (PNC), also perceived PNC as a service for children of all ages, lasting well beyond 42 days after delivery, discovered, in their study of rural southern Tanzanian women (Mrisho, et al., 2009, and Dhakal et al. (2007) also reported that (47%), of women and their families lacked awareness or did not perceive a need for postnatal care.

Nankwanga (2004) revealed that out of 330 participants in the study in Uganda, 139 (42.1%) did not attend post-natal care services at all. Of these, over half (53%) were unaware of PNC services. Fourteen per cent (14%) were attending to other family matters and 7.9% thought it was not necessary. The majority 93 (66.7%) of those who attended did so for immunization of their babies. Similarly, Mohamed (2012) in his study in Zanzibar, Tanzania, revealed that lack of knowledge emerged strongly as the reason for the delays in the decision to seek care and identify the place of care, which contributed to underutilization of health facilities during labour, delivery and postpartum period. Mrisho, et al. (2009) also stated that the majority of women who gave birth at home delayed in seeking PNC services mainly to allow the mother and baby to regain energy lost during childbirth, waiting for the baby's cord stump to fall off, lack of money and distance to the health facility.

Tao et al. (2009) revealed that only 4.2% and 4.5% of women received one or more postnatal visits at home in County A and County B. Perceived reasons given for this low rate of provision and utilization of postnatal care, include limited value placed on postnatal care by women and providers,

inadequate funding for maternal health care, limited human resources and lack of transport in township hospitals. Nevertheless, according to Dhaher et al. (2008), the most frequent reason for not obtaining PNC was that women did not feel sick and therefore did not need postnatal care (85%). Use of PNC was higher among women who had experienced problems during their delivery, had a caesarean section, or had an instrumental vaginal delivery than among women who had a spontaneous vaginal delivery. Interestingly, the same study revealed that the majority of the women deemed PNC necessary.

A study by Warren et al. (2006) revealed that there are feasible, sustainable and cost-effective measures that could be adapted to reach mothers and their newborns, especially for the 18 million African women who deliver at home. For example, about fifteen per cent (15%) of women in Madagascar receive a postnatal visit by a health professional at home. The same study also reported that one pilot study done in rural Kenya also had retired midwives facilitating childbirth at home and visiting the mother and baby two or three times in the first week.

Tanzania as a country adopted the United Nation's Sustainable Development Goals (SDGs), with the third Goal targeting on the reduction of global maternal mortality to less than 70 maternal deaths per 100,000 live births by 2030. The Emergency Obstetric and Neonatal Care (EmONC) assessment survey conducted in 2015 identified the most common causes of maternal deaths. The leading cause of maternal death is haemorrhage which accounts for 39% of maternal deaths is followed by hypertensive disorders in pregnancy (13%), abortion complications (11%) and anaemia (11%) with most of these deaths occurring in early postpartum period (Hokororo et al., 2015, Ndugga et al., 2020).

In Tanzania, the percentage of births taking place in health facilities is 63% while the postnatal care visits are 46% of those only 34% were reported to have a timely check-up that is, within the first 2 days after birth, and 22% reported they were checked within 4 hours after giving birth (TDHS 2015/2016). Maternal mortality continues to be high in Tanzania despite the implementation of interventions such as safe motherhood, emergency obstetric care, and basic emergency obstetric care. In Tanzania, the maternal mortality rate is 524 per 100,000 live births and the neonatal mortality rate at 25 per 1,000 live births (WHO et al., 2019). In Low and Middle-income countries including Tanzania, most maternal deaths occur within the first 24 hours after delivery and it is reported that up to 75% of neonatal deaths occur within the first week of life (WHO et al., 2019).

Ubungo Municipal Council has 62 health facilities that provide postnatal care services. Nevertheless, in the year 2021, only 15.4% of postnatal women attended early postnatal care (Https://dhis.moh.go.tz). Despite the availability of health services for postnatal women, utilization of postnatal services, especially in Ubungo Municipal Council is still low (Https://dhis.moh.go.tz). To my knowledge, no study has been done in Tanzania to explore barriers to early PNC attendance. This study, therefore, sought to assess barriers to early PNC attendance in Ubungo, Dar es Salaam, Tanzania. The findings of the present study are expected to contribute insights into the potential interventions that could be designed to further promote the use of early PNC.

Materials and Methods

Study design and setting

This was a Phenomenological qualitative study. An in-depth interview (IDI) guide was used to explore barriers to attending early postnatal care among postnatal women in Ubungo Municipal Council in Tanzania. The study was conducted at Sinza Hospital and Kimara Health Centre, located in the Ubungo Municipal Council, Dar-es-Salaam region in Tanzania. Ubungo Municipal Council is an urban area with a population of approximately 1,068,623 people (https: //dhis.moh.go.tz.). The Council has 14 administrative wards and 90 streets. The Council covers a total surface area of 210 km2, located in the Northern part of the region. The council has a total of 147 functioning health facilities, 21 of which are

public-owned. Out of 147 facilities, 61 health facilities provide reproductive and child health (RCH) services of which 21 health facilities are publicly owned (https: //dhis.moh.go.tz.).

Sinza Hospital and Kimara health centres were selected to participate in this study due to the high number of women who deliver at the health facilities which contribute to 87% of Ubungo Municipal deliveries with low early postnatal attendance of 15% (Https://dhis.moh.go.tz). Furthermore, Ubungo was selected because it is a highly populated Municipality in Dar-es-Salaam and, therefore, has the potential to serve a huge number of postnatal women with a diversity of characteristics attending postnatal care. In addition, the District Health Information System shows that Sinza Hospital and Kimara Health Centre reported maternal deaths of 9 (2018), 11 (2019) and 6 (2020); and 75% of those maternal deaths occurred in Sinza Hospital and Kimara Health centre (https: //dhis.moh.go.tz.). Besides, 50% of these deaths occurred during the postnatal period mostly caused by postpartum haemorrhage (https: //dhis.moh.go.tz.). Data were collected from April 2022 to May 2022.

Recruitment of study participants

Study participants were recruited purposively by selecting postnatal women who bring children for their first immunization (42 days post-delivery). The study participants were recruited purposively to get rich case participants who would facilitate a rich description, experience and understanding of the phenomena under investigation based on the study topic (Palinkas et al., 2015). To get the intended participants, the meetings between the researcher and the nurse in charge of Sinza Hospital and Kimara Health Center were held before data collection. In the meeting, we discussed the aims of the study and the kind of study participants needed to participate in the study. Participants who participated in this study were postnatal women attending first-child immunization at Sinza Hospital and Kimara Health Centre in Ubungo Municipal Council. A total of sixteen study participants were recruited to participate in this study. This number of study participants was selected based on the principle of data saturation where the responses do not give any new information and the interview stopped (Palinkas et al., 2015, Boddy, 2016).

Data Collection tool

An interview guide was used to collect information from participants through in-depth face-to-face interviews. The interview guide was developed by reviewing different literature (Kelly and, Bourgeault, 2010). The interview guide covered demographic characteristics, perceived susceptibility and barriers that contribute to not attending early postnatal service among postnatal women. The guide also collected valid and insightful findings on postnatal women's perception of early postnatal attendance (Kallio, et al., 2016, Showkat and Parveen, 2017). The interview guide was translated from English into Kiswahili. Translation of the information provided rich information on data and ensured enough information was collected from all participants systematically and comprehensively (Showkat and Parveen, 2017). The PI conducted in-depth interviews in Kiswahili, a language in which all the informants were competent. A conducive room was secured to provide privacy and free conversation between the PI and the informants. The interviews were audio-recorded. Each interview took an average of sixty minutes.

Data Analysis

Data were transcribed verbatim. Data was analyzed by using a thematic analysis approach by applying five stages according to Braun and Clarke to establish meaningful patterns: familiarization with the data, generating initial codes, searching for themes among codes, reviewing themes and presenting the results (Braun and Clarke 2013, Braun, et al., 2019). Nvivo 12 version computer software was used

to aid data analysis process data. The presented findings capture the essence of the data with quotes directly from participants (Kallio, et al, 2016, Braun and Clark, 2006).

Ethical Considerations

Permission to conduct the study was obtained from the Institutional Review Board of the Muhimbili University of Health and Allied Sciences (Ref No DA.282/298/01.C). Further permission was sought from the Municipal director and District Medical Officer of Ubungo Municipality. Further permission was sought from the In-charge of health facilities where the study was conducted before data collection. Similarly, informed written consent was obtained from all study participants to confirm their willingness to participate in this study after they received an explanation of the objectives of the study. Participants' privacy and confidentiality were ensured, and anonymity was maintained (no names were recorded during the interviews). Participants' voluntary participation and their right to withdraw from the study at any time were emphasized. Consent to record the interviews was sought from the study participants.

Results

Demographic characteristics of study participants

A total of 16 postnatal women were interviewed. Their mean age was 27 years. Three postnatal women were aged 25 and below, and 13 participants were above 25 years. Nine postnatal women were standard seven leavers while 6 of them had secondary education levels, and one had a degree. Eleven participants reported attending late postnatal care visits; four attended an early postnatal clinic within seven days. Regarding marital status fourteen were married, two participants were single mothers; ten were para 1-3 and five of them were para four and five.

Perceived risk related to late initiation of PNC attendance

Most of the study participants reported delaying attending early PNC because they were not aware of when to start early postnatal care services at clinics. They further narrated that they do not know the recommended number of PNC visits. One participant had this to say:

> *"When I gave birth, I was not told when I should come back for PNC, but I have heard on the street that when the baby is one month, I should go to the clinic for the baby's immunization. I was not told when to return to the clinic for PNC; I was not informed to return to the clinic early for PNC services"* (IDI, 25 years, a late PNC attendant, 2022).

Many of the study participants believed that the postnatal period was a normal period that didn't need the healthcare provider's attention. They further recounted that they believe the postnatal period is a normal life event rather than a condition requiring health personnel's attention. Most of the study participants further narrated that they waited forty-two days for the child's first immunization unless they felt unwell. One participant had this to state:

> *"I do not see the need to come early to the clinic; I will only go to the clinic for the child immunization after 42 days, mmmh! Maybe if you have a problem during childbirth… For example when you have a cesarean section, but if you give birth normally there is no need to come [to the clinic]"* (IDI, 25 years, a late PNC attendant, 2022).

Many study participants reported that they were not aware of when to initiate postnatal care early. The study participants revealed that mothers who attend late postnatal visits are not clear on when to attend early postnatal clinics. One postnatal mother said that:

"*We are not informed when to come for postnatal care attendance, there is no timetable on when to attend postnatal clinic earlier, this is the reason I didn't come early for postnatal care*" (IDI, 31 years a late PNC attendant, 2022).

Barriers to early PNC Attendance

Some of the study participants mentioned the shortage of nurses and a high number of clients as the reason for the long waiting time in the health facility. The study participants further reported perceiving long waiting times during the consultation at the PNC as a significant barrier contributing to early postnatal care attendance. They further narrated that they can wait up to three hours without receiving the PNC service, thus discouraging women from attending the PNC. For example, one participant commented:

> "*At the health facility, you stay for a long time without being served for two to three hours, this affects clinical attendance*" (IDI, 22 years old, a late PNC attendant, 2022).

One study participant had this to add:

> "Long *waiting hours for PNC service is a challenge because sometimes you find yourself in a queue among many other clients waiting for one nurse who is busy providing care, at least there would be as many as three nurses, one will be doing this [examining children, for instance], and another one doing that [weighing the children], in that way maybe we could spend less than an hour at the PNC clinic. Otherwise, that is a challenge"* (IDI 33 years, a late PNC attendant, 2022).

Financial difficulties as a barrier to early PNC attendance

Some study participants reported that the social socioeconomic status of the women is significantly associated with non-utilization of the early postnatal care services among postnatal mothers. Study participants reported that transportation cost to and from the clinic is a barrier that makes postnatal women delay initiating early postnatal care services. They affirmed that there are some costs involved in going to and from the health facility for PNC. The study participants recounted that transport cost depends on the distance from the health care facility. They said that those who live far from the health facility paid more cost than those who live near the health facility. One participant had this to share:

One of the participants said:

> *"The cost to attend PNC services is too high for me to come to the health facility … I am using almost 20,000 Shillings for fare and other uses per one visit at the health facility ... Where I come from, there are no major hospitals [health care centre] that provide PNC services, I think my low economic status contributes to not attending early postnatal care within seven days [post-delivery]"* (IDI, 22 years, a late PNC attendant, 2022).

Another study participant had this to share on transport costs:

> *"The cost of travel is a major obstacle among some women to attend PNC services. The fare to go to a health facility by Bajaj [a tricycle] is 5,000 Tanzanian shillings and to return is 5,000 thousand Tanzanian shillings, a total of 10,000 thousand is too much for us with low economic status and who live far from the health facility"* (IDI, 38 years a late PNC attendant, 2022).

Quality of service provided as a barrier to attending early PNC

Quality of the service is another barrier mentioned by study participants. Some study participants narrated that they did not see the importance of attending PNC within seven days after giving birth because of the quality of services given during postnatal care attendance. One participant opined:

> "*I do not see any importance of attending early PNC service, because even if you come early there is nothing important health care providers will do to you [mother and the baby], they will just ask you some questions then you go home*" (IDI, 28 years, a late PNC attendant, 2022).

Many of the study participants perceived early PNC attendance as for those mothers who faced some problems like over-bleeding during delivery if the baby fell sick after delivery or failing to breastfeed.

But if you deliver safely without any problem for the mother or the baby you continue with your life as usual. One participant commented that:

> "*Early postnatal attendance is important if you have a problem like continued heavy bleeding, maybe the baby has a fever, unable to suck [breastfeed] then you must come back very early if you are well life goes on you just wait for child immunization*" (IDI 28 years, a late PNC attendant, 2022).

Most of the study participants reported being unaware of postpartum complications and the role of medical services during the postnatal period. They narrated that mothers who delivered normally and with no problem don't see the importance of attending PNC which is why most postnatal mothers do not attend early postnatal services. One participant commented that:

> "*In my opinion, once the mother has given birth and the baby is doing well, it is important to focus on the baby`s immunization schedule and the development of the baby. Mmmh! If you had a problem during childbirth, for example, you may have had an earlier operation, but if you have a normal birth, I do not see the need to come early to PNC services*" (IDI, 25 years, a late PNC attendant, 2022).

Furthermore, many of the study participants reported not recognizing the benefits of early PNC visits for their health rather than the progress of their newborns. One participant said that:

> "*Mmmmh! I think postpartum clinic attendance is for the baby to get immunization and to monitor baby's health and his development or if the baby has any problem*" (IDI, 25 years a late PNC attendant, 2022).
>
> Another study participant had this to share:
>
> "*All I know is that postpartum attendance is to check the development of the baby, also it is for the baby to get immunization and is not for examining the mother's health as far as she had normal vaginal delivery that means the mother had given birth without any complications*" (IDI, 31 years a late PNC attendant, 2022).

Providers' attitudes as a barrier to early PNC attendance

Some study participants reported those healthcare providers' attitudes as one of the barriers contributing to the late initiation of postnatal care attendance.

Some study participants recounted that healthcare providers are using abusive language and disrespecting them, something which might contribute to the late initiation of PNC**.** One study participant had this to narrate:

> "*You find they [nurses] encouraging us to come early in the morning, but when you reach there they are busy talking, charting on phones and if you ask them they become very angry … They bring their home anger at work … For example, one day I came here [at the clinic] when my child was sick, I did not know the procedure … When I arrive at the clinic, I put my clinic card waiting to be called… All the people [mothers] at the clinic are gone, when I asked the health care providers why I was not called for the service, they became angry and said why did you put the card without asking … I was so embarrassed about that day … I am of the view that such behaviours make the mother not to come for checkup early during postnatal period … They wait for child immunization unless she [the baby] had a [health] problem*"(IDI, 31 years a late PNC attendant, 2022).

Most of the postnatal women in this study recognized good care given by the health care providers; study participants who attended late PNC also recognized the advantages of early PNC attendance and had this to say:

> "It *is important to attend early postnatal care because it helps to know the condition of the child, the child is medically examined properly, you grow up in peace, the challenge is like time spent at the facility, there is a queue in RCH clinics*" (IDI, 38 years, late PNC attendant).

Negligence of postnatal period

Most of the study participants narrated that negligence is a reason for some women not attending postnatal care early. They narrated that healthcare providers insist on attending early PNC within seven days after delivery. Despite being insisted to attend early PNC majority of mothers don't adhere to what they are told by the health care providers. One study participant had this to say:

> "*From my experience, other women are not taking things seriously … When they are discharged they get advice from their mothers that they just stay home as they are feeling well, and they can go back during child immunization at 42 days. As they have no complications life goes on. They don't care for early PNC attendance at all*" (IDI, 23 years an early PNC attendant, 2022).

Cultural beliefs as barrier contributing to early PNC attendance

Few study participants reported that cultural beliefs and practices such as the belief that postnatal mothers are not allowed to go outside until 42 days elapse after delivery; a postnatal mother has to stay indoors for 42 days without going outside. The study participants recounted that such cultural beliefs can act as barriers to not attending early postnatal care visits. One study participant said;

> "*Like us Muslims, our religion states that we must go out 42 days after delivery that is when a Muslim mother who has delivered is allowed to be free to continue with life as usual. Is that right? Then you are allowed to attend the clinic, and at that time the baby will be a little bit healthier, yes! At least the weight of the baby would have increased*" (IDI, 31 years, a late PNC attendant, 2022).

The majority of study participants appreciated the spouse support during PNC attendance. They recounted that engagement of the family members especially husbands in early PNC service is of paramount importance as men are the key decision-makers who permit women to attend PNC services. One participant has this to say:

> "*My husband is the one advising me to attend early postnatal care visit, paying for transport, After coming back the first thing he looks at is the card, and asks me what the doctor said, he wants to know how the baby is progressing as well as me*" (IDI, 26 years old, an early PNC attendant, 2022).

Discussion

This study aimed to explore barriers to attending early postnatal care among women attending early postnatal care services in Ubungo municipality, Dar es Salaam.

The findings revealed a lack of knowledge and information on the importance of early postnatal care services and when to start early postnatal care. There is a perception that the postnatal period is a normal life event rather condition that requires the attention of health care personnel. This is in line with the study conducted in Northern Ethiopia which reported that women without any prior postnatal-related complications did not see the importance of early postnatal attendance. Therefore, the postnatal women waited until they fell sick or their children were sick that is the time they initiated early postnatal care visits (Gebrehiwot et al., 2018).

They further revealed that postnatal women did not attend early postnatal care because they did not receive all the recommended components of postnatal care. When women go for PNC they report receiving counseling or are asked few questions therefore they see that there is no importance

of attending early PNC. This finding shows that attending health facilities for maternal and child health services did not guarantee that women and their newborns received all of the recommended components of postnatal care services. Furthermore, Amsalu et al., 2022 revealed that 78% of participants reported being not appointed to PNC as a reason for non-utilization of the service. They further revealed that poor counselling was mentioned as one of the reasons for not utilizing the PNC services. Poor counseling was attributed to a lack of training in healthcare providers and a shortage of human power in the setting (Amsalu et al., 2022, Berhe et al., 2017).

Also, the findings revealed that postnatal women attending antenatal care (ANC) clinics several times, and delivered in the health facilities, did not attend early postnatal care services, this is contrary to the study findings from Bahi, Dodoma Tanzania and Ethiopia that showed those women who attended ANC services and delivered in health facilities utilize early postnatal care services (Hokororo et al., 2015, Ayele et al., 2019). The differences in these studies might be due to different study contexts.

Long waiting time was the most mentioned barrier in this study that negatively affected the decision to start attending PNC services early. This study's finding corresponds with findings from a study conducted in rural Tanzania, which reported long waiting times as a problem that discourages postnatal women from accessing the service (Mahiti et al., 2015). A high number of clients and a shortage of nurses are mentioned as the reasons for the long queues in the PNC clinics that make postnatal women not utilize PNC services early. Furthermore, a lack of healthcare personnel is often a barrier to the provision of effective early PNC services.

These findings correspond with the findings from a study conducted in northwest Tanzania that reported workload due to healthcare providers' shortage and multitasking among healthcare providers as barriers to PNC services utilization (Konje, et al., 2021). These similarities might be due to several factors such as geographical location, methodology used, inadequate staffing level and the overwhelming workload experienced by healthcare providers which encouraged women not to initiate PNC until six weeks after delivery. Therefore, the findings of this study suggest increasing the number of healthcare personnel, especially nurses; will help to reduce the long waiting time at the health facility.

Financial constraints such as transportation costs perpetuate late PNC initiation. It was indicated by women in this study that lack of fare for transport to and from the health facilities is a barrier for them to attend early in PNC services. The transport costs to and from the health care facility prevented women from going for early PNC visits and even when fares were at a low rate, women who lived in extreme poverty could not afford to pay. These findings are similar to studies conducted in Bahi, Tanzania, Kenya and Nigeria which showed that transport to reach healthcare facilities is the biggest challenge for postnatal women to utilize early PNC services. (Gebrehiwot et al., 2018, Mahiti et al., 2015, Ochieng and Odhiambo, 2019, Somefun and Ibisomi, 2016, Amsalu et al, 2022).

Religious beliefs and other cultural practices are among the barriers mentioned by the participants as barriers to utilizing early PNC services. For example, Muslim women have to remain indoors until 42 days after delivery limiting them from initiating PNC clinic visits. Likewise, another belief is that postnatal women do not recognize the benefits of early postnatal care visits for their health rather than the progress of their newborns and not for women`s health. These findings correspond with findings from other studies elsewhere (Bishanga et al., 2019, Iyanda, 2016).

Furthermore, the study findings revealed that postnatal women perceived that early PNC attendance is not urgent if there is no complication during pregnancy, or delivery and immediately after delivery they attend only when they had complications like heavy vaginal bleeding, or fever without any problems for the mother or the baby they come for child immunization. These findings are congruent with studies conducted in Kenya and Indonesia that show that a woman who just

delivered a baby attends early postnatal care if they are sick, if they are not sick, then there is no need to seek PNC care. They wait until they are sick that is the time they attend PNC. This might be due to complications encountered during delivery that drive postnatal women to attend PNC service early (Ochieng and Odhiambo, 2019, Somefun and Ibisomi, 2016, Mon et al., 2018).

The study findings revealed that some healthcare providers' attitudes and abusive language were the reason for not initiating early PNC. Also, the study findings revealed that poor relationships between healthcare providers and postnatal women can act as a barrier to attending early PNC. Our study findings are similar to findings from other studies which were conducted elsewhere (Bishanga et al., 2019, Mon et al., 2018, Berhe et al, 2017, Simona et al., 2022) revealed that miscommunication and disrespectful behaviour from healthcare providers are influencers of the non-utilization of PNC services. Furthermore, workload and poor working conditions are among the factors contributing to healthcare providers' misbehaviors (Mahiti et al., 2015, Ochieng and Odhiambo, 2019, Iyanda, 2016).

Additionally, the findings from this study showed limited knowledge of postpartum complications among postnatal women and postnatal women not being scheduled for PNC and other suboptimal quality of PNC care as barriers to health health-seeking behaviour during the postpartum period. These results are consistent with the study findings conducted in Ethiopia, Northwest Tanzania, South Indonesia and Uganda that reported most mothers lack awareness of danger signs during the postpartum period which is why most of the women do not attend early PNC services; it has been noted that presence of birth-related complications increases immediately seeking PNC (Gebrehiwot et al., 2018, Bishanga et al., 2019, Mon et al., 2018, Ndugga et al., 2020). This implies that postnatal women visit health facilities only when they face complications or when they or their children are ill.

Strengths and Limitations and mitigations of the study

This study was conducted at two public health facilities that are accessible by the majority of the Ubungo and other Dar es Salaam residents, so other health facilities were excluded from this study. However, in-depth interviews with a small number of study participants of postnatal women can be considered a strength by exploring barriers to early PNC attendance. Since this study was facility-based there was a possibility of missing the experience of other women who did not attend the health facilities where the study was conducted. However, this study emphasized selecting a variety of study participants. Limitations aside, these study findings shed some light on barriers to early PNC attendance among postnatal women in Ubungo Municipality.

Conclusion

Delay in seeking early PNC services remains a big problem in Tanzania. The study findings revealed that the long waiting time, lack of information on the availability of early postnatal services, proper timing to initiate early postnatal clinic, transport costs, distance from the health facility, economic status, and providers' attitude were the major reasons reported to contribute to late initiation of early PNC service. We recommend that the Ministry of Health should continue to remind healthcare providers to continue providing education to pregnant women and the delivered mothers before discharge on the importance of PNC attendance starting from antenatal clinics, antenatal wards, postnatal wards, and postnatal clinics. Regarding long waiting times, the government of Tanzania should employ more healthcare workers so that they serve pregnant and PNC women without delay. Further, after delivery, healthcare providers should remind and schedule dates for early PNC visits before women are discharged.

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Coping with Challenges and Aftermath of COVID-19 among Street Food Catering Operators in Dodoma City: Lessons and Policy Implications

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Abstract

Introduction: Street food catering forms an important part of the food system in urban areas of Tanzania, and other parts of Africa, particularly by providing nutrition for poor consumers and means of livelihood for those who operate them. However, governments have for a long time excluded them from the traditional safety-net measures enjoyed by other traders whenever there is a major economic crisis in the society such as the effects of COVID-19 pandemic. With the devastating effect of COVID-19, it is important to evaluate how the sector reacted and coped during and after the pandemic crisis. This understanding is important if we need to formulate effective recovery policies and strategies. This paper examined the street food catering in Dodoma city in Tanzania. Specifically, the paper sought to determine the characteristics of people who operate such businesses to identify challenges imposed by COVID-19 analyze the adopted coping strategies and attempt to recommend appropriate recovery policies and strategies.

Methods: The study was conducted in Dodoma City. The study area was purposively selected because of its nature of being fast-growing and of its recent status as the national capital of the United Republic of Tanzania. A cross-sectional research design was used to collect data from 113 operators or owners of street food catering places, who were randomly selected. A questionnaire was used to collect data. Descriptive statistics was used to analyze data.

Results: Results indicated that the majority of the operators were in age between 25 and 44 years. The most common short-term and long-term challenges of COVID-19 on street food catering included a reduction in the number of customers and deterioration of trade, respectively. The most common coping strategies included shortening the supply chain, use of cash on delivery and digitalized marketing systems.

Conclusion: Contactless mobile payments have proved to have a clear advantage during the pandemic. more importantly, lowering the money transfer charges. Both the challenges and the resulting coping strategies tend to comply with what has been happening globally concerning the impact of the COVID-19 pandemic, and therefore much of what has been recommended elsewhere internationally may likely apply to the case of street food catering in Dodoma city and Tanzania.

Keywords: Street food catering, COVID-19 challenges, coping strategies

Introduction

Street food catering plays an important role in cities and towns in many developing countries to meet the food demands of city dwellers (Bouafou *et al*., 2021). The expansion of such services in Africa is explained by rapid urbanization and the multiple constraints associated with urban life

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such as distance between workplaces and home, poverty, change in women's activities and the emergence of new food styles (Joyce *et al*., 2020). Additional reasons include lack of adequate means of transport, lack of time for preparing meals at home, and lack of canteens in workplaces (Canet, 1997). For years, the sale and consumption of food from street catering has been researched and given several names including "street food", "popular catering", or "eating out" (Akindes, 1991; FAO, 2009; Steyn *et al*., 2014; Staatz & Hollinger, 2016; Sousa et al., 2019; Te Lintelo, 2017). Workers, employees, students, schoolchildren, and travellers are known to be the major consumers of such services (Canet, 1997; Te Lintelo, 2017; Sousa *et al*., 2019; Adjalo *et al*., 2020; Bouafou *et al*., 2021). Apart from ensuring food security for low-income urban populations, selling street food has proven to be a viable socio-economic activity providing gainful employment for populations with limited education and skills in Africa (Mousavi *et al*., 2016; Staatz and Hollinger, 2016; Sousa *et al*., 2019; Joyce *et al*., 2020).

On the other hand, the onset of the COVID-19 pandemic in 2019 is known to have placed unprecedented stresses on food supply chains worldwide (Chowdhury *et al*., 2020; WHO, 2020) with bottlenecks in farm labour, processing, transport and logistics, as well as significant shifts in demand (Hobbs, 2020; Bakalis *et al*., 2020). Most of these disruptions were a result of policies adopted to contain the spread of the virus (OECD, 2020). Hobbs (2020) and Bakalis *et al*. (2020) reported that COVID–19 had effects of demand side shocks on food supply chains including consumer panic buying behaviours or hoarding behaviours by consumers with respect to key items, and the sudden change in consumption patterns away from the food service sector to meals prepared and consumed at home.

Tanzania announced the first case of COVID-19 on 16 March 2020 (Mumbu and Hugo 2020). Tanzania introduced control measures for COVID-19 local transmission which included closure of schools' levels and ban of all public or social gatherings while the subsequent date the order was extended to colleges and higher education for indefinite close (Mumbu and Hugo 2020). Most African governments, including Tanzania, had considered food supply chains to be "essential" and therefore exempted them from 'lockdown' policies (Thurlow, 2020), however, the food systems in those countries have not remained immune to the effects of the pandemic. Severe effects on small-scale commercial food catering businesses in Tanzania have been reported (Mdoe *et al*, 2020; Kissoly, 2021; Kissoly *et al*., 2021). Generally, it was observed that most impacts on food systems were indirect, and mainly caused by declining consumer incomes and demand for food, even when farmers, food processors, and traders were exempted from lockdowns (Thurlow, 2020).

As hinted above, the street food catering forms an important part of the food system in urban areas of Tanzania, and other parts Africa, particularly by providing nutrition for poor consumers and means of livelihood for those who operate them. However, governments have for a long time excluded them from the traditional safety-net measures enjoyed by other traders whenever there is a major economic crisis in the society such as the effects of COVID-19 pandemic. Instead, such traders have usually relied on their own informal and traditional means including rotating credit groups and neighborhood associations to offer support in the event of economic shocks and crises (Resnick, 2020). However, with a systemic shock like COVID-19, such ad-hoc social coping mechanisms are likely to be strained. Thus, it is important to look back and evaluate how the sector reacted and coped during and after the pandemic's crisis and therefore recommend ways in which the government and other stakeholders can intervene to support this important sector of the informal economy.

It has recently been shown that different types of businesses in the informal economy sector are disproportionately impacted by the measures to prevent the spread of COVID-19 and the associated economic downturn (WIEGO, 2022). Therefore, if we have to design and implement effective recovery policies and strategies, it is important to have a good understanding of the experiences of various types of informal economy businesses that are

commonly operating, and which are touching the lives of many people in our society. This paper is an attempt of such a venture where it seeks to examine the street food catering in Dodoma city in Tanzania. Specifically, the study intends to determine the characteristics of people who operate such businesses identify challenges imposed by COVID-19 within the business sector analyze the adopted coping strategies and attempt to recommend appropriate recovery policies and strategies.

Methodology

Description of the study area

The study was conducted in Dodoma City, which is the newly crowned capital of the United Republic of Tanzania. The city is among the most rapidly growing cities in the country since it is now a focal point for government activities. Dodoma is a small city located in the middle of Tanzania with a population of 765,179 based on 2022 national population census (URT, 2022). The city was announced as the capital of the United Republic of Tanzania in 1973 during the era of President Julius K. Nyerere. Prior to this decision, Dar es Salaam on the east coast of Tanzania was the capital city. Dodoma was chosen so the capital is located centrally within the country, and to diversify social and economic development. However, most government functions remained in Dar es Salaam until the official move in 2016. Since that time, Dodoma has experienced a rapid influx of people, not only of civil servants relocated from Dar es Salaam, but also from other parts of Tanzania in search of emerging economic opportunities. The city was purposively selected for the study because of this characteristic of rapid growing.

Selection of respondents

A cross-sectional research design was used in this study, and the sampling unit was the individual street food catering operator. Dodoma City was selected purposively since it is rapidly urbanizing following the shift of government activities from Dar es Salaam to Dodoma in 2016. Four categories of street food catering operators were distinguished, namely Street Restaurants, Roadside food vending, Marketplace food vending, and Bus Stand food vending. A short description of each category is given in Box 1, while Table 1 shows the sampled individuals. Through observation, sixteen localities were identified to have a high concentration of street food catering places in the city of Dodoma, and therefore were purposively selected to be the focal points of the study. Within each selected locality, operators of street food catering places (mostly owners or managers) were proportionately selected randomly from a sampling frame which was constructed by listing all the operators within the locality. A total of 113 respondents were sampled and interviewed for the study (Table 1).

Box 1: Description of the different categories of surveyed street food catering places

- *Street Restaurants*: these are small eating places selling mostly breakfast consisting of tea with bread, fried buns or chapatis, and famous beef, goat, or chicken soups. They also include lunch meals of staple dishes such as famous maize ugali, rice or cooked bananas served together with sauce relish of meat, beans, and vegetables. Fried potato chips with eggs and/or roasted meat has also become popular. Soft drinks such as industrial sodas and bottled water are also available. Street restaurants provide facilities for sitting usually fabricated wooden or plastic benches with makeshift tables. Apart from being located along busy streets, they are also found in some specialized places such as near offices, schools, and construction sites.
- *Roadside food vending*: Unlike the Street Restaurants, these do not provide sitting places, and therefore much of the food or dishes served are for take-aways. Some of them are mobile whereby the commodities are sold from push carts or carried in special containers. Soft drinks such as sodas and bottled water are also common.
- *Marketplace food vending*: These are like the Street Restaurants except that these are specialized in crowded open marketplaces. Most of the customers here are the traders in those marketplaces who spend long hours in their businesses – and therefore tend to have permanent clients.

- *Bus Stand food vending*: These have characteristics resembling those of both Roadside as well as those of Marketplace food vending. While they sell take-away foods to the passing-by Bus passengers, they also serve quite a big number of individuals who earn their living by doing various businesses at the Bus stations ranging from taxis (including 'boda boda' and 'bajaj'), shoe shining, and other vendors such newspaper boys, ticket clerks, etc.

Table 1: Categories of the surveyed operators of street food catering services in Dodoma City

Category of street food catering service	Male	Female	ToTAL (%)
- Street Restaurants	8	3	11 (9.74%)
- Roadside food vending	15	15	30 (26.55%)
- Marketplace food vending	14	22	36 (31.86%)
- Bus Stand food vending	14	22	36 (31.86%)
TOTAL	**51**	**62**	**113 (100%)**

Data collection, processing, and analysis

Primary data were collected using questionnaires which were administered through face-to-face interviews to the sampled owners of the street food catering places. Quantitative data were analysed using the computer software IBM SPSS Statistics Version 23 whereby descriptive statistical analysis was conducted.

Results

Characteristics of the surveyed street food catering operators

The mean age of the surveyed operators of street food catering was 33.7 years (with a maximum and minimum of 57 and 19 years, respectively, and a standard deviation of 8.4). The majority (76%) of the operators were of the age between 25 and 44 years old. Sex distribution between males (46.9%) and females (53.1%) was even. The mean household size was 3.6 (maximum of 13 and minimum of 1, with a standard deviation of 2.3). The mean number of employees for each business owner was 7.3 (maximum of 25 and minimum of 1, and standard deviation of 5.1). The majority (77%) of street food catering operators had secondary school education or above. Table 2 summarizes the characteristics of the surveyed business owners.

Table 2: Characteristics of the surveyed operators of street food catering places

Characteristic	Frequency	Per cent
Age in years		
Teenagers (less than 20)	1	0.9
20 – 24	13	11.5
25 – 29	30	26.5
30 – 34	20	17.7
35 – 39	19	16.8
40 and above	30	26.5
Total	*113*	*100.0*
Sex		
Male	53	46.9
Female	60	53.1
Marital status		
Still single	31	27.4
Married	80	70.8
Divorced or widowed	2	1.8
Total	*113*	*100*
Highest level of education attained		
No formal education	2	1.8
Primary school	31	21.2
Secondary school	52	46.0
Non-university college	12	10.6
University	16	20.4

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Total	*113*	*100*

Short-term challenges of COVID-19 on street food catering

Operators of street food catering were asked to report various short-term challenges of COVID-19 in their businesses (Table 3). The results show that almost all of them (99.1%) complained of a reduction in number of customers. Other reported major concerns included a reduction in profit, limited operations of distributors, decreased sales and a shortage of working capital.

Table 3: Reported short-term challenges of COVID-19 on street food catering

Challenge	Frequency	Per cent
Reduction in the number of customers	111	99.1
Reduction in profit	110	98.2
Limited operation of distributors	110	98.2
Decreased sales	108	96.4
Shortage of working capital	108	96.4
Absent of employees	86	76.8
Product expiry	52	46.4

NB: Percentages do not add to 100 because of multiple responses/answers

Long-term challenges of COVID-19 on street food catering

Again, the owners of the street food catering places were asked to report the most common long-term challenges they were facing with respect to COVID-19 in their businesses. Results in Table 4 show that almost all of them (99.1% and 97.3%, respectively) were concerned about the reduction in trade relationships and supply chain destruction. Other reported challenges include job cuts and prolonged debts.

Table 4: Reported long-term challenges of COVID-19 on street food catering

Challenge	Frequency	Per cent
Reduction in the trade relationship	111	99.1
Supply chain destruction	109	97.3
Job cuts	78	69.6
Prolonged debts	77	68.8

NB: Percentages do not add to 100 because of multiple responses/answers

Coping strategies with COVID-19 in street food catering

Results in Table 5 show that most of the interviewed operators of street food catering reported shortening of the supply chain (97.2%) and employing cash on demand (94.7%) to be the most used coping strategies against COVID-19. Other reported coping strategies include the use of digitalized marketing through mobile phone applications and receipt payment via bank. More than forty per cent of the interviewed operators of street food catering (Table 5) reported to have turned much focus on using digitalized marketing through mobile phone applications.

Table 5: Reported coping with COVID-19 among operators of street food catering

Coping strategy	Frequency (N = 113)	Per cent
Shortening of supply chain	110	97.3
Employ cash on demand	107	94.7
Use of digitalized marketing through mobile phone application	47	41.6
Receipt payment via bank	39	34.5

NB: Percentages do not add to 100 because of multiple responses/answers

Discussion

Characteristics of the surveyed street food catering operators

Results in Table 2 show that the majority were in the age group known to be most economically productive in Tanzania (Assenga *et al.*, 2013). Sex distribution between males and females was even, implying that, unlike other kinds of informal businesses, street food catering is not gender biased, that women can also have good access.

Short-term challenges of COVID 19 on street food catering

The reduction in the number of customers (Table 3) implies that either customer hesitated to eat in those places to avoid crowding as required by 'social distancing' measures to prevent COVID-19 pandemic spread, or customers had less money to spend. Globally, there has also been a clear change in consumer behaviour or purchasing habits due to COVID-19 whereby the number of visits to hotels, restaurants, and other eating-out places decreased significantly (Bakalis *et al.* 2020; Hobbs, 2020; Nan, 2020; and Saini *et al.*; 2020). The decreasing number of customers might also be a result of more people preparing meals at home for themselves and their families (Hobbs, 2020; Bakalis et al., 2020).

As governments around the world took up social distancing policies, many consumers engaged themselves in stockpiling behaviours in anticipation of movement restrictions and fear of disruptions to food distribution systems (Hobbs, 2020). The results in Table 3 agree with the rapid socio-economic impact assessment of COVID-19 in Tanzania that was conducted by a team of researchers from ESRF. Accordingly, the government's decision to close schools for 30 days did cut off the essential market of a specific group of traders, including small restaurants that earn most of their income from sales made to school children and students (ESRF, 2020).

Long-term challenges of COVID-19 on street food catering

Reduction in trade relationship and supply chain destruction in Table 4 have been reported by ESRF (2020) who reported the sale of agricultural crops in Tanzania to various domestic and foreign markets was disrupted affecting both small- and large-scale farmers. Job cuts and prolonged debts imply that although Tanzania did not lock down hotels, restaurants, pubs, or other hospitality services, still many employees lost their jobs during the COVID-19 pandemic. The findings in Table 4 are also in agreement with those reported globally.

Saini et al. (2020) reported that dairy farmers in America had to dump 3.7 million gallons of milk every single day because of disrupted supply routes due to the coronavirus. Similarly, Vavra (2020) and Nicola *et al.* (2020) reported that social distancing, self-isolation, and travel restrictions have led to a reduced workforce across all economic sectors and caused many jobs to be lost worldwide.

Coping strategies with COVID-19 in street food catering

Shortening the supply chain (Table 5) can be described as reducing the processing time required for supply chain activities (logistics, information, cash flow and design process), something that gives the trader higher profit margins. The interviewed respondents reported to have resorted to buying many of the materials they use in their businesses such as firewood, charcoal and raw food commodities (maize and wheat flours, sugar, rice, banana, cooking oil, vegetables, and fruits, etc) directly from the producers rather

than going through some agents or middlemen. On the other hand, the use of cash on demand, which is also known as "collect on delivery", "cash on delivery," or simply COD, is a payment method in which customers don't pay for mailed goods until they have received them. This system tends to enhance consumer confidence, especially for companies that have not yet earned strong brand recognition. Most of the interviewed respondents were adopting home delivery to avoid crowding, and therefore maintain the required social distancing. As one interviewed respondent in one of the sampled Street Restaurants remarked: "*A client would call me through my mobile phone to order his/her meal of fried potato chips with roasted beefsteak or fried eggs, I then wrap it nicely with an aluminium foil and put it in a shopping bag. With a little fee, the parcel is given to a waiting motorcycle delivery boy*". Digitalized marketing through mobile phone applications (Table 5) was among the coping strategies used by street food operators.

Tanzania Mainland has five companies that provide mobile phone services, and each of them also provides electronic money transfer services. The mobile phone companies together (with their money transfer services) include Vodacom (MPesa), Tigo (TigoPesa) Halotel (HaloPesa), Airtel (AirtelPesa) and the Tanzania Telecommucation Company Limited (TTCL) with TTCL-Pesa. Respondents reported using the electronic money transfer services in doing their business by making payments to their suppliers of goods they require, and in receiving payments from their customers.

The findings agree with the international experience that effective implementation of short food supply chains coupled with cash-on-delivery could offer an additional mechanism to cope with the issue of food resilience during the resulting COVID-19 lockdowns (Bakalis et al., 2020). Globally, it is reported that consumer practices have changed because of physical distancing (commonly referred to as social distancing) and e-shopping; and there has been an overall increase in the use of online platforms to order food, which have served as an alternative to closed restaurants (Bakalis *et al*., 2020).

Conclusion and recommended appropriate recovery policies and strategies

As highlighted earlier, the street food catering business in urban areas of Tanzania, and the rest of Africa, is critically important for two reasons. First, it is part of the food system in urban areas where it provides nutrition and food security for many poor individual consumers, and secondly, it is a means of economic and livelihood support for those who operate them. Therefore, the government of Tanzania and its development partners should ensure that the sector is well supported against any emerging economic crisis such as the COVID-19 pandemic.

In a compiled compendium by IFPRI researchers titled "COVID-19 and Global Food Security", the use of social safety nets is strongly recommended in coping with the challenges of the pandemic (Gilligan, 2020). Accordingly, evidence from past research on the design, implementation, and effectiveness of social assistance programs during economic crises are used to provide guidance whereby several points are emphasized as follows: *To strengthen and expand targeting* where safety nets often exclude a high proportion of the poorest portion of the population should expand coverage and make efforts to reach those who face substantial livelihood risks and have limited social support; t*o invest more in mobile via* subsidizing mobile phone ownership and lowering the money transfer charges.

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Oral Hygiene Status and Experience of Orthodontic Appliance Breakage Among Adolescents and Young People Treated at Smiles Dental Clinic, Dar es Salaam, Tanzania

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Abstract
Introduction: Treatment of malocclusion with fixed orthodontic appliances can create some stagnations that harbour plaque with concomitant obstruction to conventional oral hygiene procedures.
Objectives: The purpose of the present study was to assess oral hygiene status, and determine its effect on treatment duration and orthodontic appliance failure among adolescent and young orthodontic clients treated at Smile Dental Clinic.
Methods: A retrospective study covering the period between 2019 and 2022 was conducted at Smile Dental Clinic. A total of 176 dental records of adolescent and young orthodontic clients aged 10 to 24 years were accessed to collect information on oral hygiene status, number of dental visits, missed scheduled appointments, socio-demographics and status of brackets and molar tube breakages.
Results: A high proportion of female (71.4%) and young orthodontic clients aged 20 – 24 years (50.6%) had good oral hygiene. A significantly high proportion of clients in boarding schools (67.8%) and those who frequently missed scheduled appointments (91.9%) had poor oral hygiene status. Treatment duration was longer for clients with poor oral hygiene (30.5 months versus 26.8 months) but those with good oral hygiene made significantly fewer numbers of dental visits (8 versus 10). Clients with poor oral hygiene were 9 and 14 times more likely to experience broken molar tubes and broken brackets respectively.
Conclusion: Oral hygiene of adolescent and young orthodontic clients treated is sub-optimal and affects the rate of orthodontic appliance failure and duration of fixed orthodontic treatment duration. Increased exposure to oral hygiene messages through frequent dental visits may help to motivate clients to maintain good oral hygiene.

Keywords: Oral hygiene, bracket failure, molar tube, orthodontic treatment, Smiles dental clinic, Tanzania.

Introduction

Malocclusion can negatively affect patients' oral health-related quality of life, especially the psychological aspects (Masood et al 2013, Mtaya et al, 2008). To address the consequences of malocclusion, orthodontic treatment is provided to enhance individuals' dental function and aesthetics as well as their social well-being and quality of life (Buthelezi &Madiba, 2021). However, treatment of malocclusion with fixed orthodontic appliances can create some stagnations that harbour plaque which is a harmful layer of bacteria on the teeth that cause permanent damage to

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dental tissues ranging from white spot lesions to dental caries (Kawasar et al, 2017; Attasi & Awartani, 2010; Zachrisson et al, 1971).

treated with multi-bracket appliances (MB) show increased plaque accumulation and increased gingivitis (Klukowska et al, 2011; Heintze et al, 1999; Liu et al 2011). The physiological cleaning mechanism of oral muscles and saliva is restricted by the irregular surface of the MB (Kafle et al, 2020). In addition, studies have shown altered microbial flora in patients with MB (Liu et al, 2011; Freitas et al, 2014; Turkkahraman et al, 2005; Yanez-Vico et al 2015; Naranjo et al, 2006).

Apart from enhancing plaque accumulation, fixed orthodontic appliances components such as brackets, elastic ligature and archwires impede conventional oral hygiene procedures (Arici et al, 2007), therefore placing orthodontic patients with poor oral hygiene control at increased risk of poor treatment outcomes such as bracket failure, and developing gingivitis and periodontitis (Thornberg et al, 2009; Zachrisson et al, 1972).

Adherence to proper oral hygiene practices during orthodontic treatment is critical to maintaining good oral health and achieving successful treatment results. To maintain good oral and periodontal health, orthodontic patients are required to practice optimal oral hygiene measures such as brushing their teeth at least twice a day and using additional tools including interdental aids and mouthwash (Aljohani & Alsaggaf, 2020).

Therefore, maintaining an adequate level of oral hygiene during orthodontic treatment requires commitment from the patient to practice good oral hygiene measures and to develop skills that demand time, effort, and motivation. Whereas some studies reported rapidly declining of clients' adherence to the recommended frequency of tooth brushing after the initial bonding in one study (Jihad, 2018; Lara-Carrillo et al, 2010; Sawai et al, 2019; Pandey et al, 2019; Shah et al, 2018; Eid et al, 2014), others have demonstrated that patients' oral health-related behaviour improved during and after orthodontic treatment (Aljohani & Alsaggaf, 2020; Al-harbi et al 2018; Baheti & Toshniwal, 2015; Alhaija et al 2018; Atassi &Awartan, 2010; Martignon et al, 2010).

In Tanzania, there is a scarcity of studies which have explored the effect of oral hygiene on orthodontic treatment duration and outcomes. Therefore, the present study assessed oral hygiene status and explored its association with orthodontic treatment duration and appliance breakage among clients at Smile Dental Clinic.

Materials and methods

A retrospective study was conducted to explore the association between oral hygiene and orthodontic treatment duration and outcomes. Information on oral hygiene, appliance breakages, missed dental appointments and sociodemographic was extracted from patients' files. The sample size comprised of all 176 individuals aged 10 – 24 years with malocclusion and treated with fixed orthodontic appliances at Smile Dental Clinic. The oral hygiene of all patients seen at the clinic is assessed by a dental assistant before sending them to either the general dentist or orthodontist. Thus, a practical, easy-to-use Visible Plaque Index (VPI) was used to assess the quality of oral hygiene through clinical observation of the presence of biofilm on dental surfaces using simple categorical definitions of the presence and absence of plaque (Ainamo & Bay, 1975).

During each dental visit, oral hygiene was assessed by examining six teeth in the dentition (16, 21, 24, 36, 41 and 44). If one of these teeth was missing, an adjacent distal tooth or if non-existence, a mesial tooth was examined. Teeth were divided into four areas mesial, lingual, distal and buccal. Using a periodontal probe, each quarter of the tooth was swept approximately 1mm into the sulcus to detect plaque. If visible plaque was apparent on the probe, it was counted as positive. The maximum positive plaque was 24 per examined individual. The individual index value was calculated by dividing the sum of the positive plaque findings by the sum of the assessed surfaces times 100. A score of 25% to 39%

was considered good oral hygiene and a score of 40% to 100% was rated as poor oral hygiene. To get an average score for all the dental visits made, the sum of oral hygiene per cent scores for each individual's visits was divided by the total number of individual visits.
Collected data was analysed using SPSS version 23.0 (IBM Corp, Armonk, NY, 2015). The chi-square test was used to measure the association between oral hygiene status and independent variables such as age, sex, health insurance status and school type. T-test was used to compare mean treatment duration, frequency of orthodontic appliance breakages, and mean number of dental visits between clients with poor and good oral hygiene status. The level of significance was set at $P<.05$.

Results

From January 2019 to December 2022 a total of 11,912 teeth surfaces of 176 adolescents and young orthodontic clients were examined to assess oral hygiene status. On average a client made 10 dental visits throughout treatment with those with good oral hygiene having made fewer dental visits (8 versus 10). Less than half (48.3%) of the studied orthodontic patients had health insurance and more than half were in boarding school (57.4%) and had poor oral hygiene (56.2%). Poor oral hygiene varied with sex, age, school type and adherence to scheduled dental appointments. A high proportion of female orthodontic clients (71.4%) and those aged 20 – 24 years (50.6%) had good oral hygiene compared to their counterparts. Those in boarding schools (67.8%) and who missed dental appointments (91.9%) had poor oral hygiene compared to their counterparts. A significantly high proportion of those who experienced breakage of orthodontic appliances (broken bracket 89.9% and broken molar tube 91.9%) had poor oral hygiene (Table 1).

Table 1. Profile of Orthodontic Patients (N = 176)

	Poor oral health % (n)	**Good oral health % (n)**	**P value**
Sex			
Males	42 (42.4)	22 (28.6)	0.041
Females	57 (57.6)	55 (71.4)	
Age			
10 – 14 years	34 (34.3)	19 (24.8)	0.023
15 – 19 years	35 (35.4)	19 (24.8)	
20 – 24 years	30 (30.3)	39 (50.6)	
Health insurance			
Insured	50 (50.5)	35 (45.4)	0.506
Not insured	49 (49.5)	42 (54.6)	
School type			
Boarding	67 (67.8)	34 (44.2)	0.002
Day	32 (32.3)	43 (55.8)	
Broken brackets			
Yes	89 (89.9)	42 (54.5)	0.000
No	10 (10.1)	35 (45.5)	
Broken molar tube			
Yes	95 (96.0)	34 (44.2)	0.000
No	4 (4.0)	43 (55.8)	
Missed appointments			
Yes	91 (91.9)	58 (75.3)	0.000
No	8 (8.1)	19 (24.7)	

Table 2. Mean Treatment Duration, Number of Dental Visits and Frequency of Broken Orthodontic Appliances

	Poor oral hygiene (n = 99)	Good oral hygiene (n = 77)	All N = 176
The mean number of broken brackets	2.4 (1.4)**	0.7 (0.5)	1.6 (1.4)
Mean number of broken molar tubes	1.3 (0.5)**	0.5 (0.4)	0.9 (0.8)
The mean number of dental visits	10	8**	10
Mean treatment duration (months)	30.5**	26.8	28.8

**P>0.0001; *P>0.005

Orthodontic patients with poor oral hygiene frequently experienced broken orthodontic appliances, had longer treatment duration (30.5 months versus 26.8 months) and made more dental visits (10 versus 8) compared to their counterparts with good oral hygiene (Table 2).

Table 3. Association of Oral Hygiene with Dental Visits, Broken Orthodontic Appliances and Treatment Duration (Adjusted for Insurance, Dental Visits, Sex and Age).

	Adjusted Odd Ratio	95% Confidence Interval
Girls	0.6	0.3 – 1.3
10 – 14 years	**1**	
15 – 19 years	0.4	0.2 – 1.3
20+ years	**0.3**	**0.1 – 0.9**
Day scholars	0.7	0.3 – 1.8
Health insured patients	1.4	0.1 – 3.1
Broken molar tube	**9.1**	**3.5 – 23.5**
Broken bracket	**13.5**	**3.9 – 47.1**
Dental visits	1.5	0.6 – 3.4

Orthodontic patients with broken brackets and broken molar tubes were more likely to have poor oral hygiene. However, those aged 20 – 24 years were less likely to have poor oral hygiene (Table 3).

Discussion

Good oral hygiene during orthodontic treatment is essential for achieving optimum results in a short duration of treatment (Kafle et al, 2020). Results of this study showed that more than 50% of patients had poor oral hygiene which varied with the sociodemographic characteristics of the studied clients. In line with other studies (Jakavice et al, 2023; Jihad, 2018; Aikins & Ututu, 2017; Mtaya et al, 2009) we demonstrated that female and young orthodontic clients have optimal oral hygiene compared to male and adolescent orthodontic clients. However, our findings are in disagreement with a study which did not find differences in the oral hygiene status of male and female, and adolescent and young orthodontic clients (Buthelezi, 2021)

Orthodontic clients studying in boarding schools demonstrated poor oral hygiene, this may be due to limited exposure to oral hygiene messages because of less contact with orthodontists stemming from few dental visits and frequently missed dental appointments. Other studies indicated

that adherence to orthodontic treatment follow-up visits strongly correlates with improved oral hygiene status of patients Yan et al, 2022; Hussein & Ismail, 2023; Atassi & Awartan, 2010). Results of our study point to a similar direction, that is high proportion of orthodontic patients with poor oral hygiene had missed more dental appointments and made very few dental visits.

The orthodontic treatment duration of the studied adolescents and young people was longer than the required less than 2 years to complete comprehensive orthodontic treatment (Tsichlaki et al, 2016). In the current study, more than half of the clients had poor oral hygiene which substantially contributed to orthodontic appliance failure (clients with poor oral hygiene were more likely to experience broken molar tubes and brackets). Several other studies have also shown that poor oral hygiene is significantly associated with broken orthodontic appliances (Jakavice et al, 2023; Li et al, 2022; Buthelezi, 2021; Kafle et al, 2020; Al-Duliamy, 2018; Jihad, 2018).

The Visible Plaque Index was proposed by Ainamo and Bay (1975) and was used to assess the quality of oral hygiene through clinical observation of the presence of biofilm on dental surfaces using simple categorical definitions (presence or absence of plaque). The index is very simple and practical but prone to subjectivity. Nevertheless, the use of one dentist who assessed and recorded the oral hygiene status of all adolescent and young orthodontic clients to inform clinical decisions may have minimized the subjectivity. Nevertheless, the results should be interpreted with caution as some of the clinical information concerning the plaque values might have been lost in the process of quantifying the index.

Conclusion

Oral hygiene of adolescent and young orthodontic clients treated is sub-optimal to the extent it increases the rate of orthodontic appliance failure and affects the duration of fixed orthodontic treatment duration. Increased exposure to oral hygiene messages through frequent dental visits may help to motivate clients to maintain good oral hygiene.

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Complementary Feeding Practices and Psychosocial Care Level of Nursing Mothers of Under-five Children in Ogun State.

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Abstract
Introduction: Psychosocial care is the 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. 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 was used to collect information on socio-economic status; psychosocial care during complementary feeding practices and 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 ages 20 to 29 years, 88.1% were married, and others were either 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 served food. There was an insignificant relationship between maternal psychosocial care and complementary feeding practices (χ^2; 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 under-nutrition, hence, enabling normal 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 normal growth and development of infants and young children require care that adequately meets their basic physical needs such as nutrition, health, and clothing well as their 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.

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 the weaning-aged children.

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 have an impact on feeding during the complementary feeding period; this period necessitates 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; it is also about how psychosocial treatment is delivered. 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).

Mother's 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 and by 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, the purpose of this study was 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. IfoLocal Government Area has its headquarters in Ifo town with an area of 521 km^2 (201 sq.m) and a population of 698,837 at the 2006 census (National Bureau of Statistics (NBS, 2006).

Study design, sample size determination

The study was a cross-sectional design, and data were collected using multistage sampling techniques.A purposive sampling method was initiated since the study was on nursing mothers specifically. Eleven Basic Health Centers (BHCs) were also purposively selected for the study. Thereafter, a simple random sampling method was used to select the nursing mothers from each of the BHCs. This study was carried out within four months between the months of March and June 2022. A pilot study according to Wilkerson (2021) was done in the month of March among 39 mothers to improve the study protocol. The sample size was statistically calculated and comprised 385 nursing mothers and infants.

Ethical approval

Written informed consent was obtained from the respondents to ensure privacy. The questionnaires were self-administered and data were collected anonymously. The author

institution's Health Research Ethics Committee approved the study protocol, with the following assigned number: IPH/OAU/12/1793.

Selection of Participants

A structured and self-administered questionnaire was used to collect information on socioeconomic status and psychosocial care during complementary feeding practices of the nursing mothers. Healthy mothers with healthy children ages six (6) to (23) months were selected using a simple random technique. The mothers were selected during the postnatal visitation to Basic Health Centres for routine immunization of their children at Ifo Local Government Area in Ogun State, South West Nigeria.

The self-administered questionnaire, comprising three sections was used to collect information on complementary feeding practices and psychosocial care of the nursing mothers. These sections include Section A: Socio-demographic and economic characteristics such as occupation, income and educational level (Gokhale et al., 2022). Section B: Psychosocial care practices of nursing mothers during complementary feeding such as interacting with the child during feeding, encouraging the child to eat and serving colorful foods oncolorful plates (WHO, 2021; Brown, 2021).

In determining the psychosocial care practices of the mothers, a 4- 4-point Likert Scale, according to the definition of McLeod (2019) was used. For the positive statement, Never was scored 1, Seldom 2, Often 3 and Always 4. For the negative statement, Never was scored 4, Seldom 3, Often 2 and Always 1. In all, 16 questions were asked which was upgraded to 100%. This means each score was allotted 6.25 marks. The psychosocial care practice was therefore graded as follows: Bad (<50% of the total score); Average: (50-75% of the total score); Good (>75% of the total score) using Rappaport (2011) grading system. Session C of the questionnaire was to explicit the complementary feeding of the children. Measurement of variables (Minimum dietary diversity (MDD), Minimum meal frequency (MMF) and Minimum acceptable diet (MAD) were carried out according to UNICEF (2022) infant feeding indicators.

Data analysis

Data was analyzed by using SPSS Statistics for Windows, Version 23.0 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). The socio-demographic indices of the respondents were expressed in frequencies and percentages. The descriptive values were expressed in mean (±SD) and percentages of the study population. The regression model was used to establish the relationship between complementary feeding and psychosocial care of the nursing mothers.

Results

The socio-demographic characteristics of the respondents as indicated in Table 1 showed that the highest proportion (50.9%) of the respondents 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.

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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

The psychosocial care practice of nursing mothers during complementary feeding of infants is presented in Table 2 and Figure 1.Table 2shows how mothers were concerned about the amount of food their children ate from the meals served. According to this study, mothers experimented witha variety of foods, when their children refused to eat. This was done in order to determine which of the foods would be the most acceptable by the children and encourage the children to eat more. The present study established that the majority of the nursing mothers did not make their children's meals more colorful or serve them on colorful plates that were attractive to children, and besides, quite a number of them force-feed their children instead of encouraging them to complete their meals. The study also established that a large proportion of the study population (68%) had average, while 30.9% had good knowledge and practised psychosocial care, while the remaining 1.1% exhibited bad psychosocial care during child feeding practices (Figure 1).

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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 colorful	158 (41.0)	58 (15.1)	56 (14.5)	113 (29.4)

Relationship between Practices of Psychosocial care and Complementary Feeding

The relationship between maternal psychosocial care and complementary feeding practices is shown in Table 3. The result establishes that there was 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 (≥4 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. This study established that nursing Mothers introduced complementary food earlier, that is, between the age of 6 and 8 months to their infants. However, there was no significant ($p>0.05$) relationship between the psychosocial care and the period of initiating the complementary feeding. Besides, there was no significant relationshipbetween 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 hadan impact on the psychosocial care provided to the children during complementary feeding.

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

Parameters	Psycho-Social Care Practices Classifications						*P* values
	Bad		Average		Good		
	'n'	%	'n'	%	'n'	%	
Commencement of Complementary Feeding							
<6 months	12	3.12	12	3.12	0	0	
6-11 months	66	17.14	219	56.88	16	4.16	0.214

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12-17 months	12	3.12	17	4.42	11	2.86	
18-23 months	0	0	9	2.34	11	2.86	
Minimum Dietary Diversity (MDD)							
Not met	57	14.81	203	52.72	13	3.38	0.487
Met	21	5.45	78	20.26	13	3.38	
Minimum Feeding Frequency(MFF)							
Not met	14	3.64	66	17.14	23	5.97	0.332
Met	54	14.02	216	56.10	12	3.12	
Minimum Acceptable Diet (MAD)							
Not met	58	15.06	214	55.58	22	5.71	0.525
Met	19	4.93	58	3.89	14	3.63	
Timely Introduction of Complementary Feeding							
Timely introduced	51	13.25	205	53.24	24	6.23	0.553
Not timely introduced	26	6.75	67	17.40	12	3.12	
Appropriate Complementary Feeding Practices							
Inappropriate	52	13.50	215	55.84	15	3.89	0.913
Appropriate	23	5.97	69	17.92	11	2.86	

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

	Psychosocial Care Practices						
Parameters	**Bad**		**Average**		**Good**		***p*-value**
	N	**%**	**N**	**%**	**N**	**%**	
Age group							
<20	0	0	4	1.04	2	0.52	
20-29	52	13.51	142	36.88	2	0.52	0.043**
30-39	6	1.56	72	18.70	76	19.74	
40-49	1	0.26	8	2.08	20	5.19	
Marital Status							
Single	13	3.38	27	7.01	0	0	
Married	54	14.02	224	58.18	44	11.43	
Divorced	7	1.81	2	0.52	4	1.04	0.960
Separated	7	1.81	3	0.78	0	0	
Widow	0	0	0	0	0	0	
Educational Level							
Primary	30	7.79	85	22.08	2	0.52	
Secondary	19	4.94	121	31.43	13	3.38	0.163
Tertiary	8	2.08	72	18.7	5	1.3	

None	6	1.56	21	5.45	3	0.78	
Religion							
Christianity	12	3.12	179	46.5	33	8.57	
Islam	18	4.68	111	28.83	12	3.12	0.031**
Traditional	1	0.26	11	2.86	0	0	
Others	5	1.3	3	0.78	0	0	
Ethnicity							
Hausa	10	2.6	29	7.53	1	0.26	
Ibo	16	4.16	49	12.72	5	1.3	0.187
Yoruba	50	13.0	199	51.69	16	4.16	
Others	2	0.52	7	1.82	1	0.26	

*** means significance at p<0.05**

Discussion

The socio-demographic characteristics of the respondents as indicated in this present study showed that highest proportion (50.9%) of the respondents was within the age ranged 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 aged 20 to 29 years. The marital status of respondents shows that large proportion of the nursing mothers were living together with their husband, while the remaining were either separated or single parents. The educational background of the nursing mothers indicates that three-quarter 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 ofinfants showed that mothers were concerned about the amount of food their children ate from the meal served (Table 2). According to this study, mothers experimented withvariety of foods, when their children refused to eat. This was done to determine which of the foods would be the most acceptable by the children and encourage the children to eat more.The present study established that majority of the nursing mothers did not make their children's meal more colorful or serve it on colorful plates that were attractive to children. Meanwhile, feeding the children colored foods had the dual objectives of providing nutrition and promoting good taste (Brown, 2021).

The majority of 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 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 between the ages of 20-29 years to had bad psychosocial practices during complementary feeding. This same age group had 72.4% of average practices of complementary feeding. Meanwhile, mothers between ages of 30-39 years had just 3.9% of bad complementary feeding practices and mothers of ages between 40-49 years had only 1% bad practices according to Table 4. This shows that maternal age has to do with psychosocial care practices during complementary feeding. Shagaro et al., (2021) reported that maternal experience on previous children influence complementary feeding practices in Ethiopia. Psychosocial care during complementary feeding could enhance the food intake by infants during complementary feeding. It is well established that psychosocial care exhibited by nursing mothers

or caregivers encourages adequate child's food and nutrient-dense intakes; hence, facilitate growth and development in children (Ogunba, 2010).

The mothers' psychosocial care practices is important 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 thequantity and quality 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 guidelines of complementary feeding.

The relationship between maternal psychosocial care and complementary feeding practices is shown in Table 3. The result establishes that there was 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 lower percentage of MAD achieved. However, fewer children received the Minimum Dietary Diversity (≥4 food groups) which accounts 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. Thisfinding is similar to the report of Samuel & Ibidapo (2020) in Southwestern Nigeria, Asmare *et al*., (2020) in the Northeast Ethiopia, and Ben*et al*. (2021) in Russia.It is worth to note that if mothers could provide their infants at least four different food groups each day, MDD might be achieved (WHO, 2020). The nursing Mothers in thispresent study were observed to introduce complementary food early between the age of 6 and 8 months to their infants. However, there was no significant (p>0.05) relationship between the psychosocial care and the start of complementary feeding. Besides, there was no significant relationship 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 hadimpact on 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 that further research should be conducted on the influence of nutrition education of psychosocial care during complementary feeding. This may improves psychosocial care awareness and practices among nursing mothers and caregivers.

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

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Authors' contributions
Ogunba BO, the principal investigator, conceptualized and designed the study; Akinrinmade Remilekun prepared the draft of the manuscript and reviewed the manuscript; Dagunro OR and Amanam EM jointly conducted the study, data analysis and interpretation

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Antimicrobial Susceptibility Pattern of Bacterial Isolates and Associated Factors for Bacteriuria among Cancer Patients Attending Ocean Road Cancer Institute, Tanzania

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Abstract
Background: Cancer patients are among people at high risk of infection with antibiotic-resistant bacteria causing bacteriuria as a consequence of cancer-induced immunosuppression and complex cancer treatments.
Methodology: A hospital-based cross-sectional study involving the quantitative method of data collection was carried out to determine the prevalence of bacteriuria, antibacterial susceptibility pattern of the causative isolates and associated risk factors among cancer patients attending Ocean Road Cancer Institute. A convenient sampling technique was used to obtain 422 cancer patients. A urine sample was collected to establish the prevalence of bacteriuria and the antibacterial susceptibility pattern of the isolates. Interviews were carried out with study participants using a questionnaire to collect social-demographic data. A clinical record collection form was used to collect clinical data of each participant. Data analysis was performed using descriptive statistics (mean, frequencies and proportions) and binary logistic regression by using SPSS software version 20.
Results: The prevalence of bacteriuria among asymptomatic and symptomatic cancer patients was 3.6% and 14.0%, respectively. *Escherichia coli* accounted for a large proportion of all Gram-negative bacteria isolates (53%). The other Gram-negative bacteria were *Pseudomonas species* (16%), *Acinetobacter species* (15%), *Klebsiella species* (10%), *Enterobacter species* (3%), *Proteus mirabilis* (1.5%), and *Aeromonas species* (1.5%). *Enterococcus species* contributed roughly two-thirds of all Gram-positive bacteria isolates (67%). Multidrug resistance (MDR) was found in 27 (75%) of *Escherichia coli* isolates. The factors associated with bacteriuria in cancer patients were sex, patients' settings, history of antibiotic use and occupation.
Conclusion: Bacteriuria, particularly that caused by MDR *Escherichia coli*, is common among cancer patients at Ocean Road Cancer Institute and is associated with sex, patients' settings and occupation.

Keywords: Bacteriuria, cancer patients, Ocean Road Cancer Institute

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Introduction

Advances in treatment options for cancer diseases have led to increased survival rate of cancer patients (Sime *et al.,* 2020). However, these treatment strategies cause immunosuppression leading to an increased risk of opportunistic infections (Fazeli *et al.,* 2018) that contribute to significant morbidity and mortality among patients (Sime *et al.,* 2020, Tancheva *et al.,* 2010). Most studies have been conducted on blood stream infections and hematologic malignancies (Tancheva *et al.,* 2010, Fazeli *et al.,* 2018, Fentie *et al.,* 2018, Sime *et al.,* 2020). However, cancer patients are at high risk of infection with antibiotic-resistant bacteria causing bacteriuria as a consequence of cancer-induced immunosuppression, complex cancer treatments and catheterization (Shrestha *et al.,* 2021).

Although there is lack of published data on clinical significance or treatment of asymptomatic bacteriuria (ASB) in cancer patients and because of the serious morbidity that could result, it is important that consideration should be given to its eradication (Zhanel *et al.,* 1990). According to studies conducted in various countries, the prevalence of urinary tract infection (UTI) in cancer patients ranges from 5% to 36%. (Alrwa 2008, Tigabu *et al.,* 2020). Despite global variation in the prevalence of UTI among different cancer patients, majority of studies have focused on single cancer populations, such as cancer of the uterine cervix (Cybulski *et al.,* 2005). Few have studied the epidemiology of UTI among different cancer groups and types. Moreover, there is an increase in resistance to commonly used antibiotics among bacterial species and strains that cause UTI due to the prolonged or repeated use of these drugs as prophylaxis in cancer patients and prolonged hospital stays (Shrestha *et al.,* 2021).

In many countries, treatment of bacteriuria among cancer patients relies on empirical therapy (based on clinical symptoms and signs) rather than treatment guided by laboratory findings, resulting in the probable irrational use of antibiotics. This is attributed to a lack of manpower, training and unavailability of quality laboratory services (Fentie *et al.,* 2018, Saleem *et al.,* 2019). Treatment of UTI in cancer patients based on empirical therapy is very challenging especially in advanced stage of this disease (Datta *et al.,* 2019). This is because, in cancer patients, clinical diagnosis of UTI is very tricky as it is complicated by cancer induced immunosuppression, nature of cancer treatment practices (like surgery, radiation therapy, chemotherapy) and non-specific clinical features (White *et al.,* 2003, Reinbolt *et al.,* 2005, Sandoval et *al.,* 2012). Additionally, prophylactic and empirical therapy of UTI in cancer patients is compromised by the emergence of new antimicrobial resistant pathogens and change in the frequency of causative bacterial species (Fentie *et al.,* 2018, Bhat *et al.,* 2021).

In Tanzania, bacteriuria (ASB and UTI) has been frequently reported among febrile children, HIV patients and women. The reported prevalence of bacteriuria among these groups ranges from 11.4 % to 63.47% (Sekharan *et al.,* 2017, Gidabayda *et al.,* 2018). In previous studies *Escherichia coli* was the most frequently isolated species. Other species include *Klebsiella pneumoniae, Proteus spp Pseudomonas aeruginosa, Staphylococcus saprophyticus, Staphylococcus aureus, Citrobacter spp* and *Enterococcus spp*, (Mwambete & Msigwa 2017, Gidabayda *et al.,* 2018, Ngowi *et al.,* 2021). Despite high prevalence of bacteriuria in Tanzania, there is paucity of information about this disease in other at-risk groups such as cancer patients. Moreover, there is lack of information on the factors associated with bacteriuria among cancer patients. This study was conducted to determine the prevalence of bacteriuria, antibacterial susceptibility pattern of the causative isolates and associated factors among cancer patients attending Ocean Road Cancer Institute (ORCI).

Materials and Methods

Study area

This study was conducted at ORCI in Dar es Salaam, a tertiary cancer hospital in Tanzania (https://www.orci.or.tz). ORCI is the only specialized institute for cancer treatment in Tanzania. The institute works in partnership with the Ministry of Health to create and maintain an integrated, accessible, affordable, and high-quality cancer healthcare system in the country. ORCI offers numerous patient services including laboratory services, diagnostic imaging, chemotherapy, radiotherapy, palliative care services, cervical cancer screening, and an HIV/AIDS care and treatment clinic. Outpatient and inpatient departments see an average of 3000 and 350 patients per month, respectively. Each month, approximately 150 cases of UTI were recorded (Source: ORCI (Registry) (Union for International Cancer Control 2021).

Study design and population

A hospital based cross-sectional study involving quantitative method of data collection was carried out at ORCI between March and May 2022 to investigate the prevalence, antimicrobial susceptibility pattern of bacterial isolates and associated factors for bacteriuria among cancer patients. Study participants were cancer confirmed patients attending inpatient or outpatient clinics at the hospital during the study period.

Sample size estimation and sampling procedure

The sample size for this study was calculated from a formula by Daniel *et al.*, 1995. The study used the expected prevalence of 50% (This prevalence was used since no previous relevant studies in Tanzania were found), tolerated margin of error of 5% and standard deviation of 95% CI (1.96). The estimated sample size for this study was 422 adults after adjusting for non-response rate of 10%. Convenient sampling technique was used whereby study participants were recruited based on their availability. An average of 30 patients was seen per day, with an average of 10 agreeing to participate and meeting the study's criteria. The participants were recruited serially until the sample size was met.

Eligibility criteria

Patients attending cancer clinics at ORCI with confirmed cancer disease, who provided written informed consent and were able to provide urine samples were included. Study participants who were unable to give socio-demographic information, on antibiotic treatment and/or had a recent history of antibiotic treatment for the last three weeks at the time of data collection were excluded.

Data collection techniques and procedures

Interview using structured questionnaires

Interviews were conducted to collect socio-demographic information from cancer patients. A simple questionnaire was used to collect information such as sex, age, marital status, education, occupation and residency.

Clinical records data collection

A special clinical record data collection form was used to collect information on type of malignancy, time when the patient was diagnosed with cancer, time of hospital stay, catheter use, anti-cancer therapy, antibiotics therapy and patient settings (inpatient or outpatient) from the patient's general medical practitioners' records.

Urine sample collection

Patients were instructed to carefully collect their midstream urine (Cheesbrough 2009) using a provided sterile screw cap wide-neck and leak proof disposable plastic urine container (Hi Media laboratories Pvt. Limited, Mumbai, India). For those who were in catheter, catheter specimen urine collection was done by an experienced nurse. Samples were immediately transported to the Muhimbili University of Health and Allied Sciences (MUHAS) microbiology laboratory and processed within two hours of collection.

Microscopy examination of urine

On a clean dry slide 1-2 drops of urine sample were placed and covered with cover glass. The slide was examined by light microscope using high power field. The presence of pus cells, red blood cells, epithelial cells, and bacteria was recorded (Cheesbrough 2009).

Bacteria isolation and identification

Isolation of causative agent of UTI was done using pre-prepared Cystine-Lactose-Electrolyte-Deficient Agar (CLED) medium (Oxoid Ltd, Basingstoke, Hampshire, UK) (Muñoz *et al.,* 1992). Using sterile calibrated loop of 0.001ml (Biologix plastic (Changzhou) Co., Ltd., China), urine specimens were inoculated into a plates of culture media. The plates were incubated at 37° C for 18-24 hours. After 18-24 hours of incubation, the plates were examined for the presence of significant growth of colonies. A bacterial count of 10^5/ml or (100 colonies or more in medium) indicated bacteriuria (Alrwa 2008).

Bacterial identification was performed through a series of morphological and biochemical procedures. First bacteria colonies with significant growth were examined morphologically for size, consistency, shape and ability to ferment lactose. Then the colonies were used to prepare smear for Gram staining using reagent kit (Micromaster Laboratories Pvt. Ltd., Maharashtra, India). The smear was examined microscopically using oil immersion objective (Alrwa 2008).

Further identification was done using biochemical tests for both Gram positive and negative bacteria. For Gram positive bacteria the following biochemical tests were performed; catalase test, coagulase test, mannitol fermentation test and aesculin test. Gram negative bacteria were tested using the following biochemical tests; kligler iron agar, citrate test, oxidase test, urease test and sulfide - indole - motility test. Gram negative bacteria that were not identified using the mentioned identification procedures were transported to the National Public Health Laboratory where further identification test was performed by using VITEK MS (Biomerieux Inc. France) which uses the Matrix Assisted Laser Desorption /Ionization Time of Flight (MALDI-TOF) technique.

Antimicrobial susceptibility test, MDR determination and ESBL detection

Antimicrobial susceptibility test was performed using the Kirby-Bauer disc diffusion susceptibility testing method. Control organisms for susceptibility testing were obtained from MUHAS Microbiology laboratory. They included *Escherichia coli* (ATCC 25922) to control gram-negative bacilli, *Staphylococcus aureus* (ATCC 25923) to control gram-positive cocci and *Pseudomonas aeruginosa* (ATCC 27853). The number of *Escherichia coli* with MDR was calculated by taking the number of *Escherichia coli* with MDR divided by the total number of *Escherichia coli* isolates and multiplied by 100 to get the percentage. The percent resistance was only calculated when at least 30 isolates of the same species had been tested (Center for Disease Control 2018). A double disk synergy test was used to detect ESBL producing bacteria. Amoxyclav was placed between third generation cephalosporins (ceftazidime and ceftriaxone) at a distance of 20 mm from each other. A bacterium was considered to be ESBL producer when there was any distortion or increase in the zone of inhibition towards amoxyclav (Rawat & Nair 2010).

Data processing and analysis

Data collected was cleaned prior to coding, entered, and then analyzed using statistical package for the social sciences (SPSS) version 20 (IBM Corporation 2011). The collected data were double entered to minimize errors during data entry and to ensure that no information was left out. The prevalence of bacteriuria, ASB and symptomatic bacteriuria (UTI) among cancer patients was measured as proportion of positive cases. Bacteriuria was defined as having urine culture results with $\geq 10^5$ cfu per ml, maximum growth of two organisms (one must be bacterium). ASB was defined as bacteriuria without any accompanying clinical symptoms. The prevalence of ASB among cancer patients was measured as proportion of positive ASB cases. Symptomatic bacteriuria (UTI) was defined as having urine culture results with $\geq 10^5$ cfu per ml, maximum growth of two organisms (one must be bacterium) and accompanied with at least one of the following symptoms; fever (>38°C), supra-pubic tenderness, costovertebral angle pain or tenderness, urinary urgency, urinary frequency and/or dysuria.

The prevalence of UTI among cancer patients was measured as proportion of positive bacteriuria (ASB and UTI) cases. Percentage resistance of each organism per drug was calculated by taking the number of resistant isolates per total number of tested isolates and reported as a proportion (percentage). Univariate logistic regression was carried out to assess the association between the prevalence of UTIs with socio-demographic and other investigated factors. Factors with p-values < 0.2 were subjected to multivariate logistic regression analysis to obtain adjusted odds ratios. The level of significance was set at 5% (0.05) two-tailed at 95% confidence interval. The strength of associations was judged by the odds ratio.

Ethical statement

Ethical approval was sought from the MUHAS Senate Research and Publications Committee **(MUHAS-REC-02-2022-955)**. Permission to conduct the study was obtained from the Director of ORCI. At the beginning of the study patients were given information about the study and details of the procedures that were performed, potential risks and benefits involved. Their willingness to voluntarily participate in the study was sought and written informed consent was requested and documented. Each patient was given study identification number and confidentiality was

maintained. No patient names or any personal information were recorded. The results of patients with significant bacterial growth and antimicrobial susceptibility testing were sent to the attending clinicians to guide management.

Results

Demographic characteristics of the study participants

A total of 422 participants consented to participate in this study. The mean age (SD) was 51.5 (12.88) years, ranging from 18 to 87 years old. The demographic characteristics of the study participants are summarized in Table 1. Out of 422 participants, 351 (83.2%, 95% CI: 79.6-86.5) were female, 302 (71.6%, 95% CI: 67.3-75.6) were married and 157 (41.5%, 95% CI: 36.7-46.4) were peasants. Half of the participants had attained primary level of education. Most of participants in the study, 169 (40.0%, 95% CI: 35.3-44.8), came from the eastern zone, which included Dar es Salaam, Morogoro, and Pwani regions. The zone with the fewest participants was Zanzibar 10 (2.4 %, 95% CI: 1.2-4.0).

Table 1. Demographic characteristics of the study participants (N=422).

Variable	Categories	n (%)	95% CI
Sex	Male	71 (16.8)	13.5-20.4
	Female	351 (83.2)	79.6-86.5
Age in years	Mean	51.5	50.3-52.8
Age group	Young adults (< 36 years)	39 (9.2)	6.6-12.1
	Middle aged adults (36-55 years)	228 (54.0)	49.3-59
	Older adults (> 55 years)	155 (36.7)	31.8-41.0
Marital status	Married	302 (71.6)	67.3-75.6
	Single	39 (9.2)	6.6-12.1
	Divorced	26 (6.2)	3.3-7.8
	Widow	55 (13.0)	10.0-16.4
Occupation	Peasant	175 (41.5)	36.7-46.4
	Self-employment	114 (27.0)	23.0-31.3
	House wife	87 (20.6)	16.8-24.4
	Employed	46 (10.9)	8.1-14.0
Level of education	No formal education	102 (24.2)	20.1-28.2
	Primary	211 (50.0)	45.0-54.5
	Secondary and above	109 (25.8)	21.8-30.1
Residence (Tanzanian Geographical Zones)	Northern	65 (15.4)	12.1-19.0
	Eastern	169 (40.0)	35.3-44.8
	Central	49 (11.6)	8.8-14.9
	Southern	20 (4.7)	2.8-6.9
	Southern highlands	39 (9.2)	6.6-11.8
	Lake zone	12 (2.8)	1.4-4.5
	Western	17 (4.0)	2.4-6.2
	South west highlands	41 (9.7)	6.9-12.8
	Zanzibar	10 (2.4)	1.2-4.0

Clinical characteristics of the study participants

Table 2 provides a summary of the clinical records of the study participants. Outpatients outnumbered inpatients by 248 (58.8%, 95% CI: 53.8-63.5) to 174 (41.2%, 95% CI: 36.5-46.2). Based on histological classification of cancer, the majority of the study participants had carcinoma 391 (92.9%, 95% CI: 90.3-95.0). The least number of participants were those having lymphoma 3 (0.7%, 95% CI: 0.0-1.7). Based on common affected sites classification, cancer of the female reproductive organs (cervix, vulva, and uterus) was the most common, accounting for 219 (51.9%, 95% CI: 46.9-56.4) cases, while cancers of the blood and lymphatic systems were the least common, accounting for 7 (1.7%, 95% CI: 0.5-3.1) cases. The cancer stage of many participants was not known. For the participants with a known stage of cancer, many participants had cancer stage II, 127 (30.1%, 95% CI: 25.8-34.6). The majority (77.0%, 95% CI: 73.0-81.0) of the study participants had localized cancer while most (32.9%, 95% CI: 28.4-37.4) of the participants were receiving chemoradiotherapy treatment. A low percentage of the participants had indwelling urinary catheters (0.9%, 95% CI: 0.2-1.9) and 36% of participants had clinical symptoms of UTI. The majority of the study participants had no comorbidities. However, participants with comorbidities were marked with a high number of seropositivity for HIV, 86 (20.4%, 95% CI: 16.6-24.2).

Table 2. Clinical characteristics of the participants (N=422).

Variable	Categories	n (%)	95% CI
Patient setting	Inpatients	174 (41.2)	36.5-46.2
	Outpatients	248 (58.8)	53.8-63.5
Cancer types based on histological classification	Carcinoma	391 (92.9)	90.3-95.0
	Sarcoma	23 (5.5)	3.3-7.6
	Leukemia	4 (0.9)	0.2-1.9
	Lymphoma	3 (0.7)	0.0-1.7
Cancer types based on common affected sites classification	Skin	16 (3.8)	2.1-5.7
	Breasts	66 (15.6)	12.3-19.4
	Prostate	14 (3.3)	1.7-5.2
	Digestive system	54 (12.8)	9.5-15.9
	Cervix, Vulva and Uterus	219 (51.9)	46.9-56.4
	Blood and lymphatic systems	7 (1.7)	0.5-3.1
	Others	46 (10.9)	8.3-14.2
Cancer stage	Stage I	33 (7.8)	5.5-10.4
	Stage II	127 (30.1)	25.8-34.6
	Stage III	49 (11.6)	8.5-14.7
	Stage IV	59 (14.0)	10.9-17.3
	Unknown	154 (36.5)	31.8-41.0
Cancer progression	Localized	325 (77.0)	73.0-81.0
	Disseminated	97 (23.0)	19.0-27.0
Type of treatment	Radiotherapy	97 (23.0)	19.2-27.3
	Chemotherapy	84 (19.9)	16.4-23.9
	Chemoradiotherapy	139 (32.9)	28.4-37.4
	None	102 (24.2)	20.1-28.2
Treatment status	In progress	190 (45.0)	40.3-50.0
	Completed	130 (30.8)	26.3-35.5
	Not started	102 (24.2)	20.1-28.2
Catheterization	Yes	4 (0.9)	0.2-1.9

	No	418 (99.1)	98.1-99.8
Clinical symptoms of UTI	Yes*	152 (36.0)	31.3-40.8
	No	270 (64.0)	59.2-68.7)
Other underlying diseases	HIV	86 (20.4)	16.6-24.2
	Diabetes Mellitus	12 (2.8)	1.2-4.5
	Hypertension	20 (4.7)	2.8-6.9
	Asthma	2 (0.5)	0.0-1.2
	None	302 (71.6)	67.1-75.8
History of antibiotic use	Yes	5 (1.2)	0.2-2.1
	No	417 (98.8)	97.9-99.8

***** The symptoms include fever (>38°C), supra-pubic tenderness, costovertebral angle pain or tenderness, urinary urgency, urinary frequency and dysuria

Prevalence of bacteriuria by microscopy and culture methods

Out of 422 participants, 74 (17.5%, 95% CI: 14.0–21.1) had significant urinary bacterial culture growth results (bacteriuria) and 101 (23.9 %, 95% CI: 19.9-28) had microscopy (pyuria) positive results. The results of bacteria determination differ significantly between culture and microscopy methods and culture and dipstick methods ($p < 0.001$).

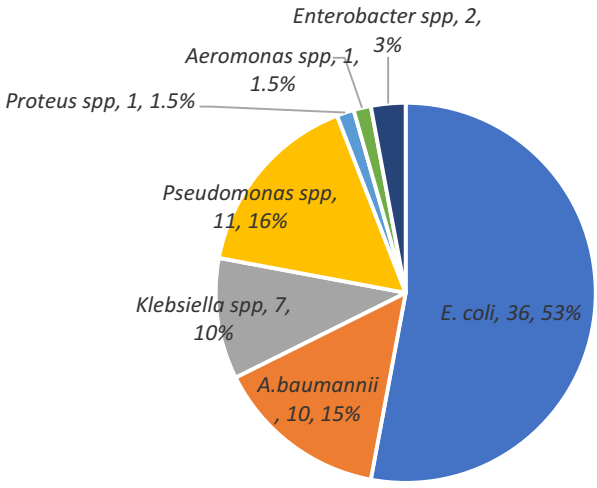
Prevalence of asymptomatic bacteriuria and symptomatic bacteriuria

Fifteen (20.3%) of the 74 patients with significant urinary bacterial culture growth results (bacteriuria) had no symptoms of UTI (asymptomatic bacteriuria) and 59 (79.7%) had at least one symptom of UTI (symptomatic bacteriuria). Hence, out of the 422 study participants the proportion of patients with ASB was 3.6% (95% CI: 1.9-5.4), and symptomatic bacteriuria was 14% (95% CI: 10.7-17.3). Females had a significantly higher proportion of bacteriuria (19.7%) than males (7.0%, p=0.011). Furthermore, the proportion of participants with bacteriuria was higher in the elderly (15.5%), widows (27.3%), employed (23.9%), those with no formal education (21.6%), and Zanzibar residents (30%). The differences, however, were not statistically significant ($p > 0.05$). Females (15.7%, $p = 0.026$) and widows (27.3%, $p = 0.024$) had the highest proportion of symptomatic bacteriuria participants.

Inpatients (24.1%), catheterized patients (100%), participants with history of antibiotic use (80%) and participants with clinical symptoms of symptomatic bacteriuria had a significantly higher proportion of bacteriuria ($p < 0.05$). Furthermore, the proportion of participants with bacteriuria was higher in the participants with carcinoma (18.4%), cancer of reproductive organs (22.4%), cancer stage I (24.2%), localized cancer (18.8%), not started treatment (19.6%), progressing with treatment (17.4%), catheterized (100%) and with hypertension (20.0%). The differences, however, were not statistically significant ($p > 0.05$). Inpatients (19.5%, $p = 0.06$), participants with prostate cancer (21.4%, $p = 0.043$), catheterized (75.0%, $p = 0.009$) and history of antibiotic use (80%, $p = 0.002$) had significantly higher proportion of symptomatic bacteriuria. Furthermore, the proportion of participants with symptomatic bacteriuria was higher in the participants with carcinoma (15.1%), cancer stage III (18.4%), localized cancer (15.4%), in radiotherapy treatment (16.5%), not started treatment (15.7%) and with diabetes mellitus (16.3%). The differences, however, were not statistically significant ($p > 0.05$).

Identified bacterial species, resistance pattern and multidrug resistance

Figure 1 depicts the type of bacteria species and the percentage of bacterial isolates in each bacteria species. From 74 culture positive samples, 80 bacterial isolates were obtained. Six patients were co-infected with two bacteria species. The vast majority of the isolates (85%) were Gram-negative bacteria. *Escherichia coli* accounted for a large proportion of all Gram-negative bacteria isolates (53%) and all bacteria isolate (45%). The other Gram-negative bacteria were *Pseudomonas species* (16%), *Acinetobacter species* (15%), *Klebsiella species* (10%), *Enterobacter species* (3%), *Proteus mirabilis* (1.5%), and *Aeromonas species* (1.5%). *Enterococcus species* contributed roughly two-thirds of all Gram-positive bacteria isolates (67%) and was the third (10%) frequently isolated among all bacteria. *Staphylococcus aureus* and coagulase-negative *Staphylococcus* each contributed an equal number (16.5%). Unexpectedly, one isolated *Escherichia coli* strain was found to be a sulfide reducer, and 13 strains were non lactose fermenters. The other isolated urinary tract pathogen was *Candida spp*. (0.5%).



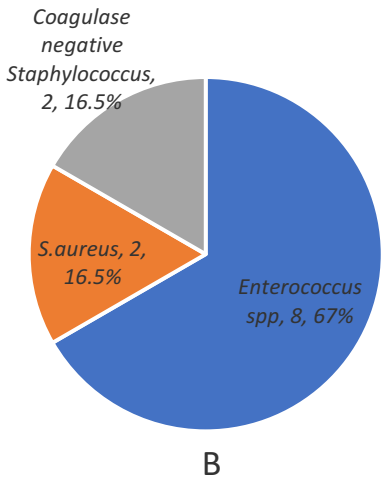


Figure 1: The proportion of each isolated Gram negative bacteria species (A) and Gram positive bacteria species (B).

Table 3 shows the antimicrobial resistance data for Gram-negative bacterial isolates. Of the 12 antibiotics tested, *Escherichia coli* was found to be more resistant to Trimethoprim-Sulfamethoxazole and least resistant to Meropenem. For the other gram-negative bacteria isolates, the lowest percentage of resistance reported was against Gentamicin (9.4%), while the highest percentage of resistance reported was against Nitrofurantoin (66.7%). The number of ESBL producing *Escherichia coli* was found to be 12 (33.3%) isolates while for the other gram-negative bacterial isolates it was found to be 1 (8.3%).The number of MDR *Escherichia coli* isolates were 27 (75.0%) recovered from the urine of 27 (6.4%) cancer patients.

Table 3. Antimicrobial resistance pattern and multidrug resistance of Gram-negative bacteria

Class	Antibiotics	Percentage of resistant isolates					
		Escherichia coli (N=36)		Other gram-negative bacteria (N=32)		Total isolates	Overall resistant (%)
		Isolates tested (%)	Resistant (%)	Isolates tested (%)	Resistant (%)		
Aminoglycosides	AK	36 (100.0)	14 (38.9)	32 (100.0)	7 (21.9)	68 (100.0)	21 (30.9)
	GM	36 (100.0)	15 (41.7)	32 (100.0)	3 (9.4)	68(100.0)	18 (26.5)
Beta-lactams	AMC	36 (100.0)	15 (41.7)	12 (37.5)	2 (14.0)	48 (70.6)	17 (35.4)
	TZP	36 (100.0)	24 (66.7)	32 (100.0)	13 (40.6)	68 (100.0)	37 (54.4)
Carbapenems	MEM	36 (100.0)	4 (11.1)	32 (100.0)	10 (31.3)	68 (100.0)	14 (20.6)
Cephalosporins	FOX	36 (100.0)	6 (16.7)	13 (40.6)	2 (15.4)	49 (72.1)	8 (16.3)
	CRO	36 (100.0)	20 (55.6)	21 (65.6)	7 (33.3)	57 (83.8)	28 (49.1)
	CAZ	36 (100.0)	18 (50.0)	32 (100.0)	10 (31.3)	68 (100.0)	28 (41.2)
Nitrofurans	F	36 (100.0)	7 (19.4)	12 (37.5)	8 (66.7)	48 (70.6)	15 (31.3)
Fluoroquinolones	CIP	36 (100.0)	20 (55.6)	32 (100.0)	15 (46.9)	68 (100.0)	35 (51.5)
Folate Pathway Inhibitors	SXT	36 (100.0)	32 (88.9)	21 (65.6)	12 (57.1)	57 (83.8)	44 (77.2)
Tetracycline	DO	36 (100.0)	23 (63.9)	20 (62.5)	8 (40.0)	56 (82.4)	31 (55.4)
ESBL		36 (100.0)	12 (33.3)	12 (37.5)	1 (8.3)	48 (70.6)	13 (27.1)
MDR		36 (100.0)	27 (75.0)	NA	NA	NA	NA

Abbreviations: AK-Amikacin, GM-Gentamicin, AMC- Amoxiclav, TZP- Piperacillin-Tazobactam, DO-Doxycycline, FOX-Cefoxitin, CRO- Ceftriaxone, CAZ- Ceftazidime, MEM- Meropenem, CIP- Ciprofloxacin, F-Nitrofurantoin, SXT- Trimethoprim-Sulfamethoxazole, NA-Not Applicable, ESBL-Extended Spectrum Beta Lactamase, MDR-Multiple Drug Resistance. Gram-positive bacteria isolates were highly resistant to erythromycin, penicillin, and ciprofloxacin (66.7 %). Resistance to nitrofurantoin, gentamicin, clindamycin, and cefoxitin was lower in these bacteria isolates (25.0 %).

Factors associated with bacteriuria among cancer patients

Table 4 shows the factors associated with bacteriuria in the cancer patients studied. The results of binary logistic regressions revealed a statistically significant relationship of bacteriuria and the sex, marital status, occupation, residence patients' settings and history of antibiotic use. However, after adjusting for the confounders using multivariate logistic regression, only participants' sex, setting, history of antibiotic use and occupation were found to be significantly associated with bacteriuria. When compared to female participants, male participants had a lower risk of developing a bacteriuria (AOR = 0.2, 95% CI: 0.1-0.6). Furthermore, the risk of bacteriuria was found to be lower in peasants (AOR = 0.3, 95% CI: 0.1-0.7) and housewife (AOR = 0.2, 95% CI: 0.1-0.6) when compared to employed. Based on patients' setting the risk of bacteriuria was higher in inpatients (AOR = 2.0, 95% CI: 1.2-3.5) when compared to inpatients. Participants who had history of antibiotic use were more likely to have bacteriuria (AOR = 13.6, 95% CI: 1.3-137.8).

Table 4. Factors associated with bacteriuria among cancer patients

Variable	Categories	COR (95% CI)	p-value	AOR (95% CI)	p-value
Sex	Female	1		1	
	Male	0.3 (0.1-0.8)	0.015	0.2 (0.1-0.6)	0.003
Age group	Older (> 55 yrs)	1			
	Middle aged (36-55 yrs)	0.9 (0.5-1.5)	0.869		
	Young (< 36 yrs)	1.0 (0.4-2.4)	0.950		
Marital status	Widow	1		1	
	Married	0.5 (0.3-1.0)	0.052	0.5 (0.2-1.1)	0.081
	Single	0.5 (0.2-1.3)	0.178	0.4 (0.1-1.2)	0.095
	Divorced	0.5 (0.1-1.6)	0.245	0.5 (0.1-1.8)	0.279
Occupation	Employed	1		1	
	Peasant	0.5 (0.3-1.2)	0.147	0.3 (0.1-0.7)	0.006
	Self-employment	0.8 (0.4-1.9)	0.692	0.5 (0.2-1.1)	0.093
	House wife	0.5 (0.2-1.4)	0.204	0.2 (0.1-0.6)	0.004
Level of education	No formal education	1			
	Primary	1.2 (0.6-2.3)	0.678		
	Secondary and above	0.7 (0.4-1.3)	0.294		
Residence (Tanzanian Geographical Zones)	Zanzibar	1		1	
	Northern	1.3 (0.3-6.1)	0.716	1.4 (0.2-9.7)	0.588
	Eastern	0.3 (0.0-2.5)	0.252	0.4 (0.1-1.6)	0.199
	Central	0.4 (0.1-1.1)	0.288	0.7 (0.3-1.9)	0.481
	Southern	0.3 (0.0-1.7)	0.080	0.3 (0.1-1.2)	0.100
	Southern highlands	0.4 (0.1-1.4)	0.199	0.5 (0.1-2.9)	0.434
	Lake zone	4.7 (0.4-54.8)	0.191	1.7 (0.3-8.3)	0.335
	Western	0.9 (0.4-2.3)	0.877	0.7 (0.2-2.3)	0.595
	South west highlands	1.0 (0.3-3.6)	0.954	0.3 (0.0-3.3)	0.529
Patient setting	Outpatients	1		1	
	Inpatients	2.1 (1.3-3.5)	0.004	2.0 (1.2-3.5)	0.013
Cancer types based on common sites classification	Prostate	1			
	Skin	0.000	0.998		
	Breasts	0.4 (0.1-1.2)	0.276		
	Digestive system	0.6 (0.1-2.4)	0.552		
	Cervix, Vulva and Uterus	0.8 (0.2-3.1)	0.934		
	Blood and lymphatic	0.000	0.999		
	Others	0.7 (0.1-2.9)	0.578		
Cancer stage	Stage I	1			
	Stage II	1.4 (0.6-3.5)	0.425		
	Stage III	0.7 (0.4-1.3)	0.277		
	Stage IV	1.2 (0.5-2.6)	0.728		
	Unknown	1.3 (0.5-2.2)	0.938		
Cancer progression	Localized	1			
	Disseminated	1.4 (0.8-2.8)	0.225		
Type of treatment	Radiotherapy	1			
	Chemotherapy	0.9 (0.5-1.9)	0.850		
	Chemoradiotherapy	0.7 (0.3-1.5)	0.340		
	None	0.8 (0.4-2.0)	0.642		
Treatment status	Not started	1			

	In progress	1.1 (0.5-1.9)	0.775		
	Completed	1.3 (0.6-2.5)	0.494		
Other underlying diseases	Diabetes Mellitus	1			
	None	0.7 (0.1-3.3)	0.664		
	HIV	0.8 (0.2-4.1)	0.792		
	Hypertension	0.8 (0.1-5.6)	0.818		
	Asthma	0.000	1.000		
History of antibiotic use	No	1		1	
	Yes	19.8 (2.2-180.1)	0.008	13.6 (1.3-137.8)	0.027

Discussion

Cancer is one of the leading causes of death worldwide. Around 10 million people died from cancer diseases worldwide in 2020 alone (WHO 2022). Infection is one of the leading causes of deaths among cancer patients (Sime *et al.,* 2020) and bacterial infections are fairly common in cancer patients (Datta *et al.,* 2019, Shrestha *et al.,* 2021). However, the health consequences of some bacterial infections among cancer patients, such as UTI, have not been adequately investigated. The purpose of this study was to determine the prevalence, antimicrobial susceptibility pattern of bacterial isolates, and associated factors for bacteriuria (ASB and/or UTI) among cancer patients attending ORCI in Dar es Salaam, Tanzania, in order to broaden knowledge and improve cancer patient management.

As expected, the prevalence of bacteriuria in cancer patients in Tanzania is high. Out of 422 participants, the prevalence of general bacteriuria, ASB and UTI found in this study were 17.5%, 3.6% and 14% respectively. The proportion of bacteriuria and UTI recorded in this study was lower than that reported in other countries such as Sudan, India, and Kuwait, but higher than that reported in Sweden, Japan, Kenya, and Ethiopia (Alrwa 2008, Tigabu *et al.,* 2020). According to Sime *et al*., differences in the prevalence of bacteriuria and UTI among cancer patients across countries can be attributed to differences in geographical location, study population, sample size, and infection sources (Sime *et al*., 2020). When compared to other studies conducted in other populations such as febrile children, HIV patients, and pregnant women in Tanzania, the prevalence of bacteriuria and UTI in cancer patients falls within the range of prevalence obtained in other studied populations (11.1% to 63.47%) (Sekharan *et al.,* 2017, Gidabayda *et al.,* 2018).

Escherichia coli was the most frequently isolated species. In the vast majority of uncomplicated UTI cases like our study participants (Wagenlehner *et al.,* 2020), *Escherichia coli* was the most common isolated bacteria. Some strains, however, were non-lactose fermenting *Escherichia coli*, which is a rare finding reported in few studies (Shatalov 2019). One strain was also a sulfide reducer. This was also reported in a study conducted in the United States of America (Maker & Washington 1974). The frequency of *Escherichia coli* isolates in this study is higher than that reported in a study conducted in a cancer specialized hospital in Ethiopia, Egypt and India (Ashour & El-Sharif 2009, Parikh & Bhat 2015, Sime *et al.,* 2020). Like in many cases, *Escherichia coli* was followed by other Gram-negative bacteria, including *Pseudomonas species*, *Acinetobacter species, Klebsiella species,* and *Enterobacter species*. These bacteria were frequently associated with cancer patients (Bhat *et al.,* 2021).

Gram-positive bacteria were also isolated but less frequently than Gram-negative bacteria, as in many other studies. *Enterococcus* species accounted for approximately 10% of all isolates and were the most frequently isolated Gram-positive bacteria, accounting for roughly two-thirds of all

Gram-positive bacteria isolates. The proportion of *Enterococcus* species isolated in our study is similar to that found in Nepal by Shrestha *et al*., 2021. The bacteria were among the most commonly isolated bacteria from cancer patients (Bhat *et al.,* 2021). In the case of other Gram-positive bacteria, our study recovered fewer isolates than in some other reported studies, with the exception of one study conducted in Ethiopia, which found no Gram-positive bacteria (Sime *et al.,* 2020).The finding of few Gram-positive isolates in this study could possibly be due to fact that most uropathogens are Gram-negative.

The proportion of antimicrobial resistance varied from 11.1% to 88.9% detected on Meropenem and Trimethoprim-sulphamethoxazole respectively when tested against *Escherichia coli* isolates. When compared to other studies conducted in Ethiopia, Egypt, and India, the level of multidrug resistance demonstrated by *Escherichia coli* isolates is extremely high (Ashour & El-Sharif 2009, Parikh & Bhat 2015, Fentie *et al.,* 2018, Sime *et al.,* 2020). Resistance to Trimethoprim-Sulfamethoxazole was higher in the isolates. Recent studies in children attending Bagamoyo and catheterized patients at Bugando hospital in Mwanza, Tanzania, found a comparable proportion of uropathogenic *Escherichia coli* resistance (Sangeda *et al.,* 2022, Ndomba *et al.,* 2022). Like the findings reported in Ethiopia, *Escherichia coli* was highly susceptible to Meropenem (Sime *et al.,* 2020).

The proportion of *Escherichia coli* and other Gram-negative bacteria isolates producing Extended Spectrum beta-lactamase was lower than that reported in Mwanza among isolates recovered from catheterized patients' urine (Ndomba *et al.,* 2022). Except for a few drugs like Amoxyclav, Gram-negative bacteria isolates in our study showed a similar pattern of antimicrobial resistance as reported in other studies (Fentie *et al.,* 2018, Sime *et al.,* 2020). Despite the small number of isolates recovered in this study, Gram-positive bacteria have demonstrated high resistance to some antibiotics tested. A large number of Gram-positive bacteria isolates were penicillin resistant. This finding is consistent with Tigabu *et al* 2020 findings in Ethiopia. Moreover, ciprofloxacin and nitrofurantoin are the two recommended first-line antibiotics for empirical treatment of UTIs in Tanzania (Kambi *et al.,* 2002). Most commonly isolated bacteria have shown resistance to both of these drugs. However, many isolates were resistant to ciprofloxacin than to nitrofurantoin. This could be attributed to its more widespread use than nitrofurantoin**.**

Bacteriuria has been associated with the following factors; sex, patients' setting and occupation. The results of multivariate logistic regression showed that male cancer patients had a lower risk of developing bacteriuria than female cancer patients. Furthermore, the risk of bacteriuria was found to be lower in unemployed and housewives versus employed and in outpatients versus inpatients. Females are more prone to bacteriuria than males for anatomical and hormonal reasons, according to general knowledge (Sime *et al.,* 2020, Shrestha *et al.,* 2021). Working cancer patients have a higher risk of developing bacteriuria than non-working patients. Similar results have been discovered in other populations, such as employed versus unemployed women. The high risk of bacteriuria in the employed population may be related to chronic infrequent urination in this population (Wang *et al.,* 2002, Markland *et al.,* 2018).

Chronic infrequent urination in the working population is thought to be the result of behavioral risk factors learned over time as a result of environmental influences. Infrequent urination may also occur in the workplace due to restrictions on toilet access and availability, the autonomy to use the restroom when necessary, and adaptive behaviors to avoid urine production, such as fluid restriction. These differences may also be caused by occupational activities that

affect urinary-holding behaviors, such as stressful job demands, working in hot or cold environments, and having to wear specific clothing that may limit the ability to use the restroom when needed (Markland *et al.,* 2018). When compared to outpatients, inpatients had a higher risk of bacteriuria, an observation that suggests a high rate of nosocomial infections. This suggestion is supported by the finding that the majority of the bacteria isolated were those commonly associated with hospital acquired infections (Fazeli *et al.,* 2018). Also it has been shown that cancer patients are more susceptible to health facility acquired infection due to their prolonged hospital stay as a result of cancer treatment (Shrestha *et al.,* 2021, Fainsinger *et al.,* 1992).

Conclusion

Bacteriuria, particularly that caused by MDR *Escherichia coli*, is common among cancer patients at ORCI and is associated with sex, patients' settings and occupation**.**

Limitations

The study only included a population from a single site. As a result, the study's findings may not reflect the situation in other cancer treatment facilities in the country.

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Authors' contribution

MA and EL conceived the study. MA and IM collected data and performed laboratory investigations. MA performed analysis and data interpretation. MA drafted the manuscript. EJ and IM revised the manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Availability of data and material

All data generated or analysed during this study are included in this published article.

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Prevalence and Risk factors associated with Sexually Transmitted Infections among Women of reproductive age attending reproductive and child health clinics in Dodoma and Dar es Salaam Tanzania

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Abstract
Introduction: Sexually transmitted infections (STIs) continue to cause reproductive morbidity worldwide. Socio-demographics and behaviour influence the likelihood of contracting reproductive tract infections and significantly predict STI acquisition. Determining prevalence and analysing the population's socio-demographic and sexual behaviour can assist in determining its risk profile and prevention strategies. This study aimed to determine the prevalence and risk factors of curable STIs, bacterial vaginosis and vaginal candidiasis among women of reproductive age attending reproductive and maternal health clinics in Dar es Salaam and Dodoma.
Method: This was a cross-sectional study where high vaginal and endocervical swabs from 400 women were collected and tested for the presence of reproductive tract infections using culture, wet mount preparation, and Gram stain. Women were interviewed on sociodemographic factors, sexual behaviours and clinical symptoms using a pretested questionnaire. A chi-square test was conducted to determine the factors associated with curable STIs. Logistic regression was done to determine independent predictors for STIs using SPSS version 23.
Results: Prevalence of *Neisseria gonorrhoea*, *Trichomonas vaginalis*, vaginal candidiasis and bacterial vaginosis was 2.5%,9.8%,13.5%, and 23.3% respectively. High education level was associated with a reduction in the likelihood of having STIs (AOR=0.41, 95%CI: 0.17-0.97). Likewise, consistent condom use was associated with a reduction in the likelihood of having STIs (AOR=0.16, 95% CI: (0.073-0.34). Participants with the recent history of STI were more likely to have STIs (AOR=2.4, 95%CI:1.05-5.27).
Conclusion: High prevalence of *Trichomonas vaginalis,* bacterial vaginosis and vaginal candidiasis in studied women calls for an intervention to prevent infection complications. We recommend health education and screening interventions to all reproductive-age women to reduce transmission of curable STIs and bacterial vaginosis.

Keywords: STIs, prevalence, reproductive age women, Tanzania

Introduction

Sexually transmitted infections (STIs) continue to cause reproductive morbidity worldwide. Approximately 374 million people aged 15 to 49 years were infected with one of the four curable STIs (chlamydia, syphilis, gonorrhoea, and trichomoniasis) worldwide in 2020 (World Health Organisation, 2023). The highest incidence (96 million cases) occurred in African region (World Health Organisation, 2021). Additionally, high prevalence of bacterial vaginosis was reported in Sub-Saharan African women (Torrone *et al*., 2018).

Women are disproportionally infected by STIs and bacterial vaginosis leading to morbidity, and irreversible complications (van Gerwen *et al.,* 2022). *Neisseria gonorrhoea* leads to pelvic inflammatory diseases (PID), ectopic pregnancy, infertility in women and ophthalmia neonatorum in newborns (Unemo *et al.*, 2019; Reekie *et al.,* 2018). Additionally, gonorrhoea, trichomoniasis or bacterial vaginosis infections

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lead to preterm birth, low birth weight, and premature rupture of membrane in pregnant women (Gao *et al.*, 2021;van Gerwen *et al.*, 2021; Ravel *et al.*, 2021). Furthermore, vaginal candidiasis has been linked to preterm birth (Roberts *et al.,* 2015).

Factors that have been identified to predispose to STIs acquisition includes early marriage, sexual debut at young age, multiple sexual partners, low education level, history of STIs, and inconsistence condom use (Kakaire *et al.*, 2015; Ginindza *et al.*, 2017; Birhane *et al.,* 2021; Masatu *et al.*, 2022). However, these factors, cannot be generalised to other groups or settings as they are often particular to the population group for which they have been identified and verified (World Health Organisation, 2021). Understanding the factors associated with curable STIs in women of reproductive age is necessary to design an intervention for prevention.

Studies conducted in Tanzania have reported different STI prevalence among women in different settings ranging from 0.5%-34.2% for *N. gonorrhoea*, 5% - 32.9% for *Trichomonas vaginalis*, 23.9-26.7% for bacterial vaginosis and 10.4%-14.0% for vaginal candidiasis (Msuya *et al.*, 2009; Buhalata *et al.,* 2013; Francis *et al.*, 2014; Hokororo *et al.*, 2015; Majigo *et al.,* 2015;Juliana *et al.*, 2020; Msemwa *et al.*, 2022; Aboud *et al.,* 2023). However, most of these studies addressed STIs prevalence among high-risk women attending STI clinics (Aboud *et al.*, 2023; Buhalata *et al.*, 2013), women working in bars, hotels, food vendors and other recreation areas (Francis *et al.*, 2014), asymptomatic women opting for Intrauterine Devices (IUDs) (Masatu *et al.*, 2022) and special categories such as pregnant women, and HIV positive women (Chiduo *et al.*, 2012; Hokororo *et al.*, 2015; Juliana *et al.*, 2020; Shaffi *et al.*, 2021).

There is a paucity on epidemiological data on curable STIs (*N. gonorrhoea* and *T. vaginalis*), bacterial vaginosis and vaginal candidiasis among women of reproductive age attending reproductive and child health clinics in Tanzania. This study aimed to determine the prevalence and risk factors associated with curable STIs (*N. gonorrhoea* and *T. vaginalis),* bacterial vaginosis and vaginal candidiasis among women of reproductive age attending reproductive and child health clinics in Dar es salaam and Dodoma region.

Material and methods

Study design

This was cross-sectional analytical study conducted from May 2022 to November 2022 among women of reproductive age attending reproductive and child health clinics in district hospitals in Dodoma and Dar es salaam, Tanzania.

Study population

The study population composed of women attending reproductive and child health clinic in District hospitals in Dodoma and Dar es salaam**.** Inclusion criteria were: - sexually active women aged 18 to 45 years and willing to provide samples for the diagnosis of genital tract infections. Exclusive criteria were: -women who were on antibiotics for the past two weeks, pregnant women and women on menses.

Sample size

The sample size was estimated using the Cochran formula (Glen, 2020), at 95 % confidence interval, using previous prevalence of STI in reproductive age women of 36.21% (Ramadhani *et al.,* 2017) and a 5 % margin of error. The minimum sample size was 389 women, however, a total of 400 women were enrolled.

Sampling

This was a two-stage sampling where two districts from each region were randomly selected and the district hospitals from the selected districts were used for the study. Eligible women attending reproductive and child health clinics in the district hospitals were consecutively enrolled to the study after signing a written consent form.

Data collection

Women were interviewed individually in a private room using pretested structured questionnaire in Swahili language to collect sociodemographic and sexual behaviour data. Socio demographic data were age, employment status, education level, and marital status. Sexual behaviour data included number of lifetime partners, age at sexual debut, condom use, recent history of STI infection, alcohol and drug use, and new sexual partner in the past three months. Symptoms and signs suggestive of reproductive tract infection such as abnormal vaginal discharge, dysuria, vaginal itch, post coitus bleeding and lower abdominal pain were recorded. High vaginal and endocervical swabs were collected using Dacron swabs for the diagnosis of reproductive tract infections. To ensure confidentiality the Dacron swabs and questionnaires were labelled using numbers instead of names.

Laboratory methods

Endocervical swabs were inoculated onto Modified Thayer Martin Agar (Oxoid, Unipath Limited, Basingstoke, UK) for the isolation of *N. gonorrhoea*. Plates were placed in anaerobic candle jar with 5% CO_2. The plates were incubated at 37°C for 48 hours. Presumptive gonococci colonies were identified based on their morphological appearance, gram stains and biochemical tests. Intracellular diplococci bacteria that were Gram negative and showed catalase and oxidase positive properties were identified as *N. gonorrhoea.*

T. vaginalis was diagnosed by a wet preparation from the vaginal posterior fornix swabs using normal saline and examined microscopically (x40) within an hour after collection of the swab. The presence of motile trichomonads with characteristic jerky movement, undulating membrane and presence of four flagella confirmed presence of *T. vaginalis* (Stoner *et al.,* 2013).

Vaginal smears for bacterial vaginosis diagnosis were obtained by swabbing lateral vaginal wall and were smeared on a sterile glass slide. The slides were Gram stained and observed microscopically under oil immersion (1000x magnification). Three bacteria morphotypes were quantified and scored following Nugent criteria (Nugent *et al*., 1991). These were large Gram-positive rods (lactobacillus morphotypes) Small Gram variable rods (*Gardenerella vaginalis*), curved Gram variable rods (*Mobiluncus* species morphotypes) and gram-negative rods *Bacteroides* species morphotypes). A score of zero to three was interpreted as normal, a score of four to six was identified as intermediate, and a score of seven to ten was interpreted as bacterial vaginosis infection (Nugent *et al.*, 1991). Ten percent of the positive and negative slides for *T. vaginalis* and bacterial vaginosis were re-examined by another medical laboratory technician for quality assurance.

Vaginal candidiasis was isolated by culture using Sabouraud dextrose agar (SDA). Plates were incubated for 72 hours at 35°C. Candida was identified as smooth, soft, shiny creamy rapid-growing colonies of yeast (Cheesbrough, 2006). Cells of *Candida* species were identified by picking a small portion of the colonies using wire loop and added to the slide containing a drop of 20% KOH. Microscopically *Candida* species was identified as distinctive or budding yeast cells (Namkinga *et al.,* 2013). Germ-tube tests was performed to confirm *C. albicans* (Namkinga *et al.,* 2013). Infected women were treated according to the national guidelines.

Data analysis

Data analysis was performed using Statistical Package for Social Science (SPSS) version 23. Descriptive analyses were performed for sociodemographic, behavioural factors and symptoms. Categorical variables were denoted as percentages and continuous variables were summarized as means with standard deviations. The prevalence of curable STIs was calculated as proportions of participants with positive test for *T. vaginalis* and *N. gonorrhoea*. Chi square test was performed to determine associations of sociodemographic, sexual behavioural, symptoms, bacterial vaginosis, and vaginal candidiasis infection with curable STIs. Logistic regression model was used to determine independent factors for curable STIs. Variables with p-value less or equal to 0.05 in bivariable analysis were analysed in the multivariable model for independent associations. Adjusted odds ratio and 95% confidence interval were calculated and a p-value <0.05 was considered statistically significant.

Ethical approval

Study protocol was approved by the National Health Research Ethics Committee (NatHREC) Dar es salaam, Tanzania with an approval number of NIMR/ HQ/R.8a/Vol. IX 3720. Permission to conduct study was obtained from the Reginal medical officer, District medical officer and the doctor in charge of the hospital. Written informed consent was obtained from the women before enrolment. Data were stored by the principal investigator in a password protected computer.

Results

Characteristics of the study population

Four hundred women of childbearing age were enrolled in this study. The mean age of the participants was 28±6.8 years. Fifty one percent (51%) of the participants were recruited from Dar es salaam. Majority (43.8%), of women were between 18-25 years, (41.0%) were married, (51.7%) had secondary school education and above, and (66.8%) were employed. The mean age of sexual debut was 17.5 ±1.85 years. Thirty percent of the participants had more than two sexual life partners, while (21.3%) had new partner in the past three months. Twenty five percent of women reported condom use with new partner, 26.5% were alcohol users, and 1.3% were drug users. Twenty eight percent (28%) of the participants reported a recent history of STIs infection (Table 1).

The most reported symptoms were dysuria (28.8%) followed by abnormal vaginal discharge 29.7% and vaginal itch 22.8%. Other reported clinical signs or symptoms were post-coital bleeding 19.8% and lower abdominal pain 10% (Table 1).

Prevalence of curable STIs and other genital tract infections

Overall prevalence of curable STIs was 12.0% (48/400) (which included *N. gonorrhoea* and *T. vaginalis*). Additionally, 35.8% (143/400) of the women had non STIs specifically vaginal candidiasis and bacterial vaginosis. The prevalence of *N. gonorrhoeae* among the participants was 2.5% (95% CI: 1.8-2.7) while prevalence of *T. vaginalis* was 9.8% (95% CI: 8.9-10.7). Among the women, 13.5% (95% CI: 12.2-14.8) had vaginal candidiasis and 22.3% (95% CI: 20.2-24.4) had bacterial vaginosis. Furthermore, 14 % (56/400) of the examined women had mixed infections (Data not shown)

Sociodemographic factors associated with curable STIs.

The prevalence curable STIs was higher in women residing in Dar es salaam compared to prevalence in women residing in Dodoma, however, the difference was not statistically significant. Similarly, there was no statistically significant difference in prevalence of curable STIs between age groups. Women with no education and primary school education had significantly higher prevalence of curable STI compared to women who had secondary and post-secondary school education (p=0.001). Women who were employed had higher prevalence of curable STIs compared to non-employed women, however, the difference was not significant. Regarding marital status, married women had lower prevalence of curable STIs compared to cohabiting and single women. The difference was statistically significant p=0.013 (Table 1).

Sexual behaviour factors associated with curable STIs.

Women who reported to have their sexual debut at age below 18 years had significantly higher prevalence of curable STI compared to women who had sexual debut at the age of 18 years and above (p=0.001). Moreover, women who reported having more than two sexual life partners had significantly higher prevalence of curable STI compared to women who reported to have one lifetime partners (p=0.008). Similarly, women who had new sexual partner in the last three months had significantly higher prevalence of curable STI compared to women who did not have new partners in the previous three months (p=0.001). Additionally, women who reported condom use with new partner had low prevalence of curable STI compared to non-users and this difference was statistically significant (p=0.001). Alcohol users had higher prevalence of curable STIs compared to non-users. The difference was statistically significant p=0.02.

However, there was no statistically significant difference in curable STIs between women who use drugs against non-users (Table 1).

Symptoms associated with curable STIs.

Women with vagina discharge, dysuria and vagina itch symptoms had higher prevalence of curable STI compared to women without these symptoms; the difference was statistically significant (p=0.001). Moreover, there was statistically significant difference in prevalence of curable STI between women who reported lower abdominal pain and women who did not have lower abdominal pain (p=0.004). However, the difference in prevalence between women who reported post coitus bleeding and those who did not have post coitus bleeding was not statistically significant. Furthermore, the prevalence of vaginal candidiasis and bacterial vaginosis was significantly higher in women who were positive for curable STI compared to women who were negative (p=0.001) (Table1).

Predictors of STIs

Independent predictors that were associated with curable STIs in multivariable analysis included education level, condom use, and a recent history of STI. Increasing education level was associated with a reduction in the likelihood of having STIs (AOR=0.41, 95%CI: 0.17-0.97). Similarly, condom use was associated with reduction in the likelihood of having STIs infection (AOR=0.16, 95% CI: (0.073-0.34). However, women who had STIs infection in the past were two times more likely to have STIs infection compared to women with no history of STIs (AOR=2.4, 95%CI:1.05-5.27) (Table 1).

Table 1: Sociodemographic, sexual behavioural factors, and symptoms of women with curable sexually transmitted infections attending reproductive and child health clinics in Dodoma and Dar es salaam.

Variables	N=400	Positive for Curable STIs	Bivariate analysis	P- value	Multivariate analysis	P-value
		N (%)	COR 95%CI		AOR 95%CI	
Residence						
Dodoma	196	18(9.2)	1			
Dar es salaam	204	24(11.7)	0.95(0.52-1.74)	0.088		
Age group (Years)						
18-25	175	15(8.6)	1			
26-35	160	23(14.4)	1.79 (0.89-3.57)	0.09		
36-45	55	10(15.4)	1.94(0.82-4.57)	0.13		
Education level						
Primary level and below	193	37(19.2)	1			
Secondary level and above	207	11(5.3)	0.24(0.12-0.48)	0.001	0.41(0.17-0.97)	0.042
Employment status						
Non-employed	133	12(9.0)	1			
Employed	267	36(13.5)	1.57(0.8-3.1)	0.253		
Marital status						
Single divorced widowed	158	22(13.9)	1			
Married	164	9(5.5)	0.34(0.16-0.81)	0.013		
Cohabiting	78	17(21.8)	1.72(0.84-3.47)	0.128		
Age at sexual debut						
Less than18 years	168	36(21.4)	1			
18 years and above	232	12(5.2)	0.25(0.10-0.39)	0.001		
Lifetime partners						
One	109	8(7.3)	1			
Two	170	16(9.4)	1.31(0.54-3.17)	0.548	-	
More than two	121	24(19.8	3.12(1.34 -7.29)	0.008		
New partner past three months						
No	237	9(3.8)	1			
Yes	163	39(23.9)	7.96(3.7-16.9)	0.001		
Condom use with new sexual partner						
No	298	31(30.4))	1			
Yes	102	17(5.7)	0.12(0.073-0.026)	0.001	0.16(0.07-0.34)	0.001

Alcohol use						
No	254	23(9.1)	1			
Yes	146	25(17.1)	2.1(1.13-3.81)	0.017	-	
Drug/substance abuse						
No	395	46(11.6)	1			
Yes	5	2(40.0)	5.0(0.82-31.07)	0.053	-	
History of STIs						
No	290	23(7.9)	1			
Yes	110	25(22.7)	3.4(1.84-6.33)	0.001	2.4(1.05-5.27)	0.038
Vaginal discharge						
No	281	19(6.8)	1			
Yes	119	29(24.4)	4.44(2.39-8.31)	0.001	-	
Lower abdominal pain						
No	360	37(10.3)	1			
Yes	40	11(27.5)	3.3(1.53-7.17)	0.004	-	
Post-coital bleeding						
No	321	38 (11.8)	1			
Yes	79	10 (12.7)	1.08(0.51-2.27)	0.084	-	
Dysuria						
No	286	23(8.0)	1			
Yes	114	25(21.9)	3.2(1.74-5.94)	0.001	-	
Vaginal itch						
No	309	23(7.4)	1			
Yes	91	25 (27.5)	4.71(2.52-8.81).	0.001		
Vaginal candidiasis						
Negative	346	32(21.4)	1			
Positive	54	16(29.2)	4.13(2.1-8.2)	0.001	-	
Bacterial vaginosis						
Negative	311	25(8.0)	1			
Positive	89	23(25.8)	3.98(2.13-7.46)	0.001		

COR - Crude Odds ratio, AOR - Adjusted Odds ratio, CI - Confidence Interval
*Curable STIs denote infection with any of the following sexually transmitted pathogens; *Trichomonas vaginalis* or *Neisseria gonorrhoea*

Discussion

The study focused on assessing the prevalence of curable STIs (*T. vaginalis* and *N. gonorrhoea)*, bacterial vaginosis, and vaginal candidiasis infection among women of childbearing age attending reproductive and child health clinics in Dodoma and Dar es salaam region. The results revealed a high prevalence of genital tract infection, with bacterial vaginosis having the highest prevalence at 22.3% followed by vaginal candidiasis13.5% and *T. vaginalis* 9.8%; the lowest prevalence was *N. gonorrhoea* 2.5%.

The prevalence of *T. vaginalis* in the current study was 9.8 % which was consistence with previous reported prevalence of 8.7% and 8.0 %among women in Mwanza and in Dar es salaam (Buhalata *et al.*, 2013; Majigo *et al.*, 2015). However, it was lower than the prevalence of 19.0% reported in women working in bars and other recreation areas near large mines in Northwest Tanzania (Francis *et al*., 2014) and prevalence reported among women presented with vaginal infection in Dar es salaam 13.3% (Majigo *et al.,* 2021). Additionally, the prevalence of *T. vaginalis* in our study was in line with the rates reported in other countries, such as Swaziland 8.4% (Ginindza *et al.,* 2017), South Africa 10% (Abbai & Ramjee 2013) and India 8.5% (Madhivanan *et al*., 2009). In contrast *T. vaginalis* prevalence in this study was higher than prevalence reported in Ethiopia 2.1% (Mulu et al. 2015), but lower than the prevalence reported in Brazil 16% (von Glehn *et al*., 2017) and New Papua Guinea 22.4% (Vallely *et al.,* 2016). These variations in prevalence could be attributed to different diagnostic tests used and socio-behaviour factors of the population studied.

Prevalence of bacterial vaginosis in this study was high at 23.3%, which is similar with the reported rates in Mwanza 25.6% (Buhalata *et al*., 2013) and Dar es salaam 26.7% (Shaffi *et al.,* 2021). However, it was lower than prevalence of 41.2% reported in women with vaginal discharge in clinics in Dar es salaam (Majigo, *et al.*, 2015). Similar studies from Brazil and Ethiopia have reported higher prevalence rates at 30.1% and 48.6% respectively (Marconi *et al.*, 2015:Bitew *et al.*, 2017). The difference in prevalence could be attributed to hygiene practices and socio behavioural factors among populations studied. The high prevalence of bacterial vaginosis is concerning as it signifies a disruption of the vaginal normal flora, leading to the domination of pathogenic organisms. Vagina douching and other intravaginal practices have been associated with increased prevalence of bacterial vaginosis (Majigo *et al.,* 2021). Bacterial vaginosis infection should be treated promptly to prevent sequalae associated with the infection such as risk of acquiring STIs, endometriosis, and pelvic inflammatory disease, all of which may lead to infertility (Ravel *et al*., 2021).

Regarding vaginal candidiasis, prevalence in the current study (13.5%) was comparable to the prevalence reported in Mwanza (14.0%) (Buhalata *et al*., 2013), but, lower than the prevalence of 19.4% and 44.3% reported in Dar es salaam (Majigo *et al.*, 2015; Majigo *et al.*, 2021). Likewise, it was consistence with prevalence reported in Rwanda 10.6% (Ndorycyimpaye *et al*. 2020), but lower than prevalence reported in Iran 32.7% (Rasti *et al.* 2014), United Arab Emirates 31.6% (Salvi, 2019) and in Vietnam 51.3% (Anh *et al.* 2021). The distribution of vaginal candidiasis varies among countries and population studied, this could be influenced by specie responsible for vaginal candidiasis and predisposing factors such as contraceptive use, spermicide and condom use, antibiotic use, personal hygiene, clothing, and sexual habits (Gonçalves *et al*., 2016).

The prevalence of *N. gonorrhoea* in the current study was consistence with prevalence of 3.5% reported in women presented with discharge in Dar es salaam (Majigo *et al*., 2015) and prevalence of 4.0% reported in Northwest of Tanzania (Francis *et al.*, 2014). However, it was lower than the prevalence of *N. gonorrhoea* reported previously 8.4% by Buhalata *et al.* (2013). Nevertheless, the prevalence in this study was in line with pooled prevalence of *N. gonorrhoea* in women of reproductive age reported in Sub Saharan Africa

(Kassa *et al.,* 2020). The difference in prevalence could be attributed to different populations studied and the diagnostic methods that were used.

Risk factors for Curable STIs

In our study, we investigated risk factors associated with curable sexually transmitted infections (STIs) among women. One significant finding was that women with secondary and higher education levels had a reduced likelihood of having curable STIs infection (AOR = 0.41, 95%CI: 0.17-0.97). This finding aligns with similar studies conducted in Swaziland, South Africa and Uganda, which also showed that higher education was associated with lower risk of having STIs (Abbai *et al*., 2013; Kakaire *et al*., 2015; Ginindza *et al.*, 2017). Women with high education level are likely to practice safe sex compared to less educated women (Tenkorang, 2012), possibly due to better access to sexual health information and improved negotiation skills with sexual partners. On the other hand, less educated women may face limited options and turn to high-risk behaviours like exchanging sex for cash and other resources from a sexual partner (Ranganathan *et al.,* 2017).

Interestingly, employment was not found to be a significant predictor for curable STIs in our study. However, the type of employment was not explored, which could have explained the substantial risk of STIs among employed women. Earlier studies have revealed that women working in bars and recreational facilities are at high risk of STIs infection (Francis *et al.*, 2014).

Another crucial finding was that condom use was associated with the reduced likelihood of having curable STIs infection. Consistence use of condoms with new partner has been shown to be protective against STIs in various studies(Gita & Brodie, 2013). However, it is important to note that some studies have reported a contrast to our study that, use of condoms was inversely related to STIs (Ginindza *et al*., 2017). Plausible explanation for this discrepancy could be that women who acknowledge not to use condoms with new partners had one faithful partner or they were cured prior to data collection. Nevertheless, promoting condom use remains a crucial strategy for STI prevention.

Women with recent history of STI infection were found to be two times more likely to have STI infection compared to women with no history of STI infection. This align with findings from a study in South Africa where repeated STI diagnosis increased women's susceptibility to HIV infection (Wand & Ramjee, 2015). Having a recent history of STI infection such as gonorrhoea and chlamydia has also been identified as a risk factor for STI infection (Hosenfeld *et al*., 2009). Repeated STI infection can be attributed to factors such as unsafe sex practices, incomplete treatment, untreated partner or continue to engage in risk sexual behaviour after STIs treatment (Bautista *et al*., 2017). Therefore, partner notification, health education and retesting after treatment is important to prevent reinfection.

Although alcohol and drug use has been linked to risky sexual behaviours such as unprotected sex (forgetting or refusing to use protection) and multiple partners which lead to acquisition of STIs (Ghebremichael *et al.*, 2009). In the current study however, alcohol and drug use were not independently associated with curable STI infection. This could be explained by the fact that alcohol use is not equally spread across various demographic groups in the population. Despite recent demographic studies showing that the gender difference in alcohol consumption is decreasing (Strandberg *et al*., 2019), women tend to consume less alcohol compared to men and younger individuals may engage in riskier behaviour compared to old people (White, 2020).The prevalence of drug use in this study was minimal, with only five participants in the interviews reporting a drugs history. Nevertheless, sexual education intervention emphasizing the danger of alcohol use, drug abuse and multiple sexual partners are still necessary to promote safer sexual practices.

Limitation of the study

Despite the limitations of our study, we have been able to shed light on the population at risk of acquiring sexually transmitted infections (STIs) and the associated risk factors among women of reproductive age in Dar es Salaam and Dodoma. However, it is essential to acknowledge potential sources of bias in our findings. First, because sexual activity is a sensitive topic, it is probable that during interviews, social desirability bias could have influenced the interview responses, resulting in underreporting of certain behaviours. Secondly, sociodemographic and behaviour factors were self-reported, participants had to recall past events, therefore, they could have introduced recall bias. Additionally, lack of resources prevented us from using molecular tests for our investigation.

Despite the limitations, our study holds significant value. It has provided valuable insights into the population group who are at risk of acquiring STIs particularly women of reproductive age in Dar es salaam and Dodoma. This information contributes to the STIs epidemiological surveillance data for women of childbearing age in Tanzania. By understanding these risk factors, we can develop targeted interventions to prevent STI acquisition.

Conclusion

In conclusion, our study reported high prevalence of curable STIs, bacterial vaginosis and vaginal candidiasis and identified several risk factors for curable STIs among women. Education level, condom use, and history of STI infection were significant predictors of STI risk. Although alcohol and drug use were not independently associated with STIs in our study, addressing substance abuse and promoting sexual health education remain important aspects of STI prevention strategies. Understanding and addressing these risk factors can help in the development of effective and targeted interventions to reduce the burden of curable STIs in the population.

Based on our findings, we recommend reproductive and child health clinics introduce health education program to create awareness of risk factors that predisposes to the acquisition of STIs and implement aetiologic screening for curable STIs and bacterial vaginosis in women of reproductive age to prevent sequalae associated with STI and bacterial vaginosis infections.

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Acute Toxicity, Immunomodulation Activities, and Phytochemical Profiles of Sapium ellipticum Stem Bark Aqueous Extract

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Abstract

Background: The stem bark of *Sapium ellipticum* is a medicinal plant frequently utilized in traditional medicine for treating a range of ailments. Despite its widespread use, there is limited data regarding the safety and immunomodulatory potential of its extract.

Objective: This investigation was conducted to assess the phytochemical profile, acute toxicity, and immunomodulatory activity of the aqueous extract of *S. ellipticum* stem bark.

Methods: Acute toxicity was assessed using the Organization for Economic Cooperation and Development (OECD) guidelines at doses of 123, 300, and 2000 mg/kg. Immunomodulatory activity was evaluated using real-time quantitative polymerase chain reaction (RT-qPCR) to measure the expression levels of IL-10, IL-6, IL-1Ra, and IL-1β. Phytochemical profiling was carried out using liquid chromatography-tandem mass spectrometry (LC-MS/MS).

Results: The aqueous extract of *S. ellipticum* stem bark did not produce any hematological or biochemical signs of toxicity, indicating that the lethal dose was greater than 2000 mg/kg. The extract showed potential as an immunomodulator, with downregulation of IL-6 and IL-10 and upregulation of IL-1Ra and IL-1β. Phytochemical analysis revealed the presence of anti-inflammatory compounds, such as Fraxetin and L-carnitine. However, the extract also showed upregulation of the pro-inflammatory cytokine IL-1β, with no inflammatory compounds identified.

Conclusion: Findings from the present study suggest aqueous extract of *S. ellipticum* stem bark is safe up to a dose of 2000 mg/kg, and shows immunomodulatory potential through the presence of anti-inflammatory compounds. Furthermore, provides a foundation for future research on the potential medicinal uses of this extract.

Keywords: *Sapium ellipticum*, toxicity, stem bark, immunomodulation, cytokines

Introduction

Medicinal plants have been advocated as alternative drugs for immunomodulation activities. *Sapium ellipticum* (Hochst.) Pax is a plant species in the family Euphorbiaceae (Ighodaro & Akinloye, 2017). This plant species is distributed in different areas of the world such as America, China, Vietnam, India, Malaysia and Western, Central and East Africa (Ighodaro & Akinloye, 2017). *Sapium ellipticum* length ranges from 10 to 15 meters high, is edible and has medicinal use in the treatment of bacterial infections (Ighodaro & Akinloye, 2017). However, it is worth noting that the medicinal properties and uses of this plant may vary depending on the region and culture.

In Africa, *S. ellipticum* has been utilized for a variety of therapeutic purposes. For instance, in Nigeria, it has been used to manage fever, inflammation, and skin infections (Al Muqarrabun et

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al., 2014). In Cameroon, it has been employed as an antidiarrheal agent (Wansi et al., 2014; Merveille et al., 2017; Njouendou et al., 2018). In Kenya, the root decoction of *S. ellipticum* has been used for treating coughs (Ochwang'i et al., 2014), while in Burundi and Zambia, the stem bark decoctions have been used to treat fever, anaemia, elephantiasis, rheumatic problems, and guinea worms (Al Muqarrabun et al., 2014). Similarly, in Ethiopia, the leaves of the plant have been used to manage mumps (Bekele-Tesemma et al., 1993). In Tanzania, the powder of the stem has been applied to wounds, swellings, head and chest to reduce pain (Kisangau et al., 2009; Mpinda et al., 2018; Masalu et al., 2020). Moreover, the leaves of *S. ellipticum* have been used to alleviate abdominal swelling and treat eye diseases (Kisangau et al., 2009). Some communities in Tanzania even use the root decoction of this plant species to treat malaria (Wilfred et al., 2006; Moshi et al., 2010).

Numerous *in vitro* and *in vivo* studies have confirmed the traditional belief in the medicinal benefits of *S. ellipticum* (Evans et al., 2015; Mpinda et al., 2018; Njouendou et al., 2018; Masalu et al., 2020;). The plant's stem bark and leaf extracts have been reported to exhibit antimicrobial properties to a range of species causing bacterial and fungal infections (Ighodaro & Akinloye, 2017; Mpinda et al., 2018; Masalu et al., 2020). These have confirmed the traditional use of the plant in the management of opportunistic infections in Uganda and Tanzania (Kisangau et al., 2009; Ighodaro & Akinloye, 2017; Masalu et al., 2020).

On the other hand, *S. ellipticum* crude extracts have been reported to possess antioxidant activities, thus consumption of extracts from this plant could prevent cancer development, slow ageing and free the body from oxidative stress (Adesegun et al., 2008; Nana et al., 2013; Ochwang'i et al., 2014; Evans et al., 2015). Moreover, *S. ellipticum* has been found to have hypoglycemic effects, thus, showing potential in managing diabetes (Ighodaro & Akinloye, 2017). Methanolic crude extracts of *S. ellipticum* stem bark have been reported to exhibit a hepatoprotective effect against liver damage induced by carbon tetrachloride (CCl_4) in rats (Njouendou et al., 2018). Therefore, *S. ellipticum* is a plant species with a rich history and diverse medicinal uses, warranting the need for ongoing research to enhance scientific understanding, uncover new benefits, and ensure the safety of the communities utilizing its different products for medical purposes.

Evidence has shown that conventional immunomodulating drugs present significant challenges (Crane et al., 2005; Bascones-Martinez et al., 2014), prompting the exploration of alternative options such as plant-based products (Jantan et al., 2015; Nair et al., 2019). *S. ellipticum*, with its rich traditional history and promising *in vitro* evidence, holds the potential as a valuable candidate in this regard. However, there remain substantial scientific gaps, particularly regarding its in vivo toxicity and immunomodulatory activities.

Recently there has been a growing interest in investigating the immunomodulatory potential of medicinal plants (Gupta et al., 2016; Yin et al., 2019; Jeon et al., 2022). This interest has been promoted by studies demonstrating the capacity of plant-based polysaccharides to effectively modulate the immune system through various mechanisms (Yin et al., 2019; Jeon et al., 2022). Plant-based polysaccharides have been associated with the ability to activate immune cells, complements, and cytokines, presenting a unique mechanism for immune system control (Gupta et al., 2016; Yin et al., 2019; Jeon et al., 2022). Therefore, understanding the molecular mechanisms through which these phytochemicals activate or inhibit the expression of genes linked to the enhancement or suppression of immune cells, complements, and cytokines is a new and interesting area of study.

Therefore, this study aimed to bridge these knowledge gaps by conducting the *in vivo* evaluations of acute toxicity and immunomodulatory properties using mice model organisms. Furthermore, the study evaluated the phytochemical profiling to find out the compounds associated with the medicinal properties of the plant species. The results from the study provide

additional and new evidence on the medicinal potential of *S. ellipticum*, which may contribute to further research and clinical trials.

Materials and Methods

Sample collection

The stem bark of *S. ellipticum* was collected in October 2018 from the Bukoba rural district in the Kagera region. To ensure the accuracy of the plant identity, taxonomic identification was conducted by a knowledgeable plant taxonomist. The voucher specimen, with the identification number SN03, was then deposited at the Botany Department of the University of Dar es Salaam (UDSM).

Preparation of crude extract

To obtain aqueous crude extracts from the stem bark of *S. ellipticum*, a total of 500 g of ground plant material was weighed and soaked in 1500 mL of distilled water. The mixture was then left to soak for two days with shaking every 12 hours. After the soaking period, the mixture was decanted and filtered using cloth gauze, and then further filtered using Whatman filter paper number 4 with a pore size of 25 µm. This ensured that any solid particles present in the mixture were removed, leaving only the liquid extract. The filtered extracts were then concentrated using a freeze dryer (ScanVac Coolsafe, LaboGene™) at the Institute of Traditional Medicine located at the Muhimbili University of Health and Allied Sciences (MUHAS). The resulting extract was then stored at 4°C until further analysis was conducted.

Test animals

A total of 24 male Swiss albino mice, aged between 90 to 150 days were procured from the Zoology Department at the University of Dar es Salaam. Male Swiss albino mice were chosen over females to minimize random variations attributed to oestrous or menstrual cycles, which can lead to hormonal fluctuations and introduce additional variables that could complicate the study and necessitate a larger number of research animals. The mice were acclimatized to the laboratory conditions for seven days before the commencement of the experiments. During this period, they were housed in clean, well-ventilated cages, with a 12-hour light and dark cycle. They were also provided with standard rodent pellet feed and water. The mice were monitored daily to ensure that they remained healthy and free from any infections or diseases.

Toxicity evaluation

The acute toxicity of *S. ellipticum* stem bark was evaluated by the Organization for Economic Co-operation and Development (OECD) guideline number 425 for acute toxicity (Organisation for Economic Co-operation and Development, 2002). A total of 12 male mice were used for the study, weighing between 20 g to 35 g, and were divided into three groups to test different doses of the extract: 123 mg/kg, 300 mg/kg, and 2000 mg/kg, with the fourth administered distilled water served as a negative control. The chosen concentrations of the extracts were based on the antibacterial minimum inhibitory concentration of the drug (123 mg/kg) and the recommended concentration for acute toxicity by OECD (2002), *Test no. 423* (300, and 2000 mg/kg). Each group was restricted to three animals, and the experimental conditions were carefully refined to minimize suffering, and to advocate the principles of animal welfare, particularly the three R's (Replacement, Reduction, and Refinement).

The mice fasted for three hours but had free access to water before the extract was administered via oral gavage, based on their body weight. The behaviour (writhing, grooming, convulsion, and alertness), body weight, and rectal temperature of the mice were closely monitored. They were starved for one hour after administration and then given food, after which

their behaviour was observed for four hours and continuously monitored for fourteen days. After the completion of the study, the mice were humanely euthanized, and blood samples were collected using cardiac puncture with a sterile needle and a 1 ml insulin syringe. The blood was stored in tubes containing ethylenediaminetetraacetic acid (EDTA) for biochemical analysis, including alanine transaminase (ALT), aspartate transaminase (AST), total and conjugated bilirubin, and haematology tests, such as red blood cell count (RBC), haemoglobin (HB), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean cell hemoglobin concentration (MCHC), platelet count, white blood cell count (WBC), lymphocytes, neutrophils, basophils, and monocytes.

Immunomodulation assay

Nine male mice weighing between 25 g to 40 g were utilized to evaluate the immunomodulation activity. The mice were distributed into three groups, with each group consisting of three mice. To induce inflammation, each mouse in each group was intraperitoneally challenged with LPS of 1 mg/kg. After three hours, the treatment group was administered with 2000 mg/kg of extract, while the positive control group was given 1 mg/kg of ibuprofen. The negative control group, on the other hand, received only LPS and water, without any extract or ibuprofen treatment. The mice were monitored for four hours following the administration of extract or ibuprofen. After 24 hours, the mice were humanely euthanized, and 200µl of whole blood was taken for RNA extraction.

RNA extraction

RNA was extracted from whole blood using Quick-RNA MiniPrep Plus (Catalog Nos. R1057 & R1058) (https://zymoresearch.eu/products/quick-rna-miniprep-plus-kit) by following the manufacturer's instructions. First, 200 µL of 2X concentrated DNA/RNA Shield™ was added to a 200 µL frozen blood sample and thoroughly combined. Then, 400 µL of 8 U/µL Proteinase K was added to the reagent/blood mixture and well incorporated. The mixture was then incubated at 30 °C for 30 minutes. Isopropanol (408 µL) was added to the mixture in an equal proportion and vortexed. Next, the mixture was transferred to a Spin-Away™ Filter in a collection tube and centrifuged to eliminate genomic DNA. The flow-through was discarded, and 1 mL of 95% ethanol was added to the filter and stirred thoroughly. The mixture was then transferred to a Zymo-SpinTM III CG Column in a collection tube and spun at 10000 RCF for 30 seconds using a Hettrich Zentrifugen MIKRO 220 centrifuge machine. The flow-through was discarded, and the column was washed with 400 µL RNA wash buffer, centrifuged, and the flow-through was discarded again.

To remove any residual DNA, a mixture of 5 µL DNase I (1 U/µL) and 75 µL DNA digestion buffer was added directly to the column matrix and the column was incubated at 30 °C for 15 minutes. Then, 400 µL RNA prep buffer was added, the column was centrifuged at 10000 RCF for 30 seconds, and the flow-through was discarded. 700 µL RNA wash buffer was added to the column, followed by centrifugation, and the flow-through was discarded. Another 400 µL RNA wash buffer was added, followed by centrifugation for 2 minutes to ensure complete removal of the wash buffer. The column was then carefully transferred to an RNase-free tube, and 100 µL DNase/RNase-Free Water was added directly to the column matrix and centrifuged. The eluted RNA was immediately stored at -70 °C.

Real-Time Quantitative Polymerase Chain Reaction (RT-qPCR) Assay

To determine cytokine gene expression, the Luna® Universal One-Step RT-qPCR Kit (NEB #E3005S/L/X/E) (https://www.neb-online.de/literatur/pdf/NEB_Luna_qPCR.pdf) was utilized following the manufacturer's protocol with modifications. Specifically, 5 µL of Luna Universal

One-Step Reaction Mix (1X) was mixed with 0.5 µL of Luna WarmStart RT Enzyme Mix (1X), 0.4 µL of each forward and reverse primers at a concentration of 0.4 µM, and 2 µL of 1 µg template RNA (prepared sample). The total volume was adjusted to 10 µL by adding 1.7 µL of nuclease-free water. RT-qPCR was conducted using an Applied Biosystems 7500 Fast Instrument, with operating conditions detailed in Table 1. The primers used for the targeted cytokines are presented in Table 2.

Table 1: RT qPCR reaction condition of the assay

Cycle Step	Temperature	Time	Cycles
Reverse Transcription	55°C	10 minutes	1
Initial Denaturation	95°C	1 minute	1
Denaturation	95°C	10 seconds	40-45 s for extension and denaturation
Extension	60°C	60 seconds	

Table 2: Primer of cytokines, IL – 1β, IL – 6, IL – 1Ra and IL – 10

Cytokine	Primer 5' – 3'	Sequence	Accession number
IL – 1β	Forward	CAC CTC TCA AGC AGA GCA CAG	M98820
	Reverse	GGG TTC CAT GGT GAA GTC AAC	NW_047658
IL – 6	Forward	TCCTACCCCAACTTCCAATGCTC	E02522
	Reverse	TTGGATGGTCTTGGTCCTTAGCC	M26745
IL – 1Ra	Forward	AAGACCTTCTACCTGAGGAACAACC	C M63101
	Reverse	GCCCAAGAACACATTCCGAAAGTC	NW_047651
IL – 10	Forward	CGGGAAGACAATAACTGCACCC	BC120612
	Reverse	CG GTT AGC AGT ATG TTG TCC AGC	BC137844

LC-MS/MS Profiling of Crude Extracts

Liquid chromatography Mass spectrometry analysis was conducted using Thermo Scientific's Hypersil GOLD Q Mass Spectrometer (X. Wang et al., 2014). The samples were separated using the UltiMate 3000 RSLCnano System and injected in a volume of 10 L into a C18 column (LC column 100 2.1 mm) containing 1.9 mm-sized particles. Chromatographic separation was carried out at a flow rate of 0.3 mL/min using a gradient elution program. The program started with 95% eluent A (water with 0.1 per cent formic acid, v/v) and gradually changed to 5% eluent B (100% acetonitrile acidified with 0.1% formic acid (v/v)) and back over 30 minutes. The exact gradient parameters were 95% eluent A/5% B for 2 min, gradually changing to 95 % A and 5 % B over 13 min, 0 % A/100 % B for 10 min, then returning to 95 % eluent A/5 % B over 5 min.

Mass spectrometry measurements were performed using the Q Exactive and Orbitrap (Thermo Fisher). The system operating parameters were; sheath gas flow rate of 48 arbitrary units, auxiliary gas flow rate of 11 arbitrary units, HESI voltage of 4.0 kV, capillary voltage of 3.5 kV, and capillary temperature of 320 °C. Samples were introduced into the MS through electrospray ionization, and the acquired spectra were scanned with a resolution of 140000 spanning a mass/charge number range of 150–2000 m/z. Data processing and acquisition were done using XCalibur (Version 4.1.31.9).

Statistical Analysis

The results were expressed as the mean value ± standard deviation (SD) of three independent measurements. To evaluate the difference between the controls and extract groups, a one-way analysis of variance (ANOVA) was performed. A p-value less than 0.05 was considered statistically significant for determining the significance of the results.

Results

Behavioural and body weight

The behavioural changes including writhing, grooming, convulsion, and alertness were observed in mice after administering different doses of *S. ellipticum* extract, which were 123 mg/kg, 300 mg/kg, and 2000 mg/kg. The results showed that there were no significant alterations in the behaviour of the mice at any of the administered doses. This indicates that the extract did not induce any observable changes in the behaviour of the mice at the tested doses, suggesting that it is safe and well-tolerated.

Hematological Toxicity

To determine the safety of the crude extracts, haematological analysis results obtained from mice fed with the extracts were compared to those obtained from mice fed with water. The results were also compared to reference ranges established by Serfilippi et al., (2003), as presented in Table 3. The findings revealed that mice fed with extracts at doses of 123 mg/kg and 300 mg/kg exhibited low neutrophil counts, which were within acceptable limits at a dose of 2000 mg/kg. MCHC levels were below the reference range, but the difference was not statistically significant ($p = 0.7744$).

Overall, haematological parameters including RBC, haemoglobin, hematocrit, MCV, MCH, platelet count, WCB, lymphocytes, and monocytes were within the normal range. Statistical analysis using One Way ANOVA showed no significant difference between the experimental group and the control group at 123 mg/kg, 300 mg/kg, and 2000 mg/kg ($p = 0.7053$, 0.9466, and 0.9841, respectively).

Table 3: Hematology parameter of Swiss albino at different doses

Plant crude Extract	123 (mg/kg)	300 (mg/kg)	2000 (mg/kg)	Control	Reference (Serfilippi et al., 2003).
RBC(10^{12}/L)	8.54±0.15	9.56±0.08	9.03±0.18	9.53±0.3	6.66-11.18
Haemoglobin (g/dL)	12.95±0.55	13.95±0.25	13.33±0.55	13.97±0.34	11.0-18.3
Hematocrit %	40.5±1.5	47±0	44.33±2.5	44±1.2	33.1–48.8
MCV(fl)	47.5±0.9	49.15±0.45	49.3±1.9	46.83±0.33	41.2-51.4
MCH (pg)	15.15±0.35	14.6±0.4	14.77±0.35	14.67±0.25	14.1-17.8
MCHC (g/dl)	31.9±0.2	29.7±0.5	29.97±0.55	31.3±0.36	32.2-36.8
Platelet Count (K/µL)	859±148	892.5±552	1000.3±60.5	1336.33±163	784–1808
WBC (K/µL)	3.68±0.97	4.74±1.2	10.75±1.4	8.26±3.4	2.69-18.33
Neutrophils (x 10^9/l)	0.17±0.095	0.23±0.06	4.98±0.86	0.83±1.6	0.58-8.80
Lymphocytes (x 10^9/l)	2.66±0.4	3±0.67	4.89±0.23	4.34±2.02	1.83–15.58
Monocytes (x 10^9/l)	0.085±0.04	0.54±0.25	0.70±0.29	0.18±0.1	0–0.82
Eosinophil (x 10^9/l)	0±0	0±0	0.11±0.03	0.23±0.3	0–0.89
Basophils (x 10^9/l)	0.77±0.4	0.97±0.32	0.06±0.03	1.25±0.69	0–0.11

Liver function indices of plant crude extracts

Table 4 displays the liver function indices of mice that were administered with crude extract at doses of 123 mg/kg, 300 mg/kg, and 2000 mg/kg. Upon performing statistical analysis using one-way ANOVA, no statistically significant difference was found between the experimental group and the control group ($p = 0.9977$).

Table 4: Biochemistry parameters of mice at different concentrations

Biochemistry parameters	123 (mg/kg)	300 (mg/kg)	2000 (mg/kg)	Control (H_2O)	Reference (Serfilippi et al. 2003)
Total bilirubin (µmol/L)	10.65±1.25	1±0	30±5	4.5±1.7	3.42-25.65
Conjugated bilirubin (µmol/L)	4.3±1.9	0.55±0.15	12.4±5.1	0	1.7-22.23
Aspartate aminotransferase (1U/L)	180.5±28.5	262.5±0.5	220±40	294±48.4	35–185
Alanine aminotransferase (1U/L)	25.5± 2.5	56.5±6.5	38.5±8.5	66±20.6	19-166

Immunomodulation activity of the crude extracts

Table 5 shows the RT-qPCR cycles of expression of genes for anti-inflammatory cytokines (IL 10 and IL-1RA) for different treatments. The results indicate that treatment with *S. ellipticum* extract led to higher expression levels of both IL-10 (31.02±0.09 cycles) and IL-1RA (36.15±1.95 cycles) compared to the LPS (negative control) and ibuprofen (positive control) treatment. This suggests that *S. ellipticum* extract may have an immunomodulatory effect by increasing the expression of anti-inflammatory cytokines.

Table 5: RT-qPCR cycles of expression of the gene for anti-inflammatory cytokines

Extracts	IL 10	IL-1RA
	RT-PCR cycles	
S. ellipticum	31.02±0.09	36.15±1.95
LPS (-Ve)	30.83±0.64	38.94±1.32
Ibuprofen(+Ve)	30.38±0.51	37.62±1.53

Table 6 shows the RT-qPCR cycles of expression of genes for pro-inflammatory cytokines (IL 6 and IL-1β) for different treatments. The results indicate that treatment with *S. ellipticum* extract resulted in higher expression levels of IL-6 (37.12±3.84) compared to the LPS (-VE) control (34.17±1.44 cycles) and ibuprofen (+VE) treatment (38.55±3.77 cycles). However, the expression of

IL-1β was lower in the *S. ellipticum* extract treatment (23.74±2.61 cycles) compared to the LPS (-VE) control (26.91±2.86 cycles) and ibuprofen (+VE) treatment (27.89±1.61cycles). These results suggest that *S. ellipticum* extract may have a dual effect on the immune system, with both anti-inflammatory and pro-inflammatory effects.

Table 6: RT-qPCR cycles of expression of the gene for pro-inflammatory cytokines

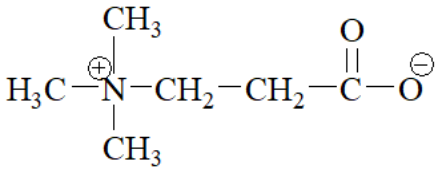
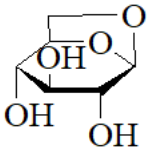
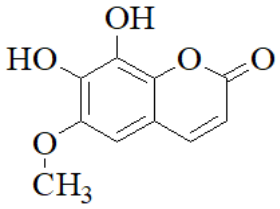
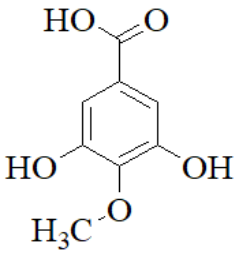
Extracts	**IL 6**	**IL 1β**
	RT-PCR cycles	
S. ellipticum	37.12±3.84	23.74±2.61
LPS (-Ve)	34.17±1.44	26.91±2.86
Ibuprofen(+Ve)	38.55±3.77	27.89±1.61

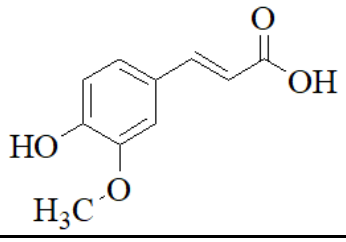
Phytochemical Profile

LC-MS profile of Aqueous Crude Extract

Five (5) phytochemical compounds identified from *S. ellipticum* crude extract are presented in Table 7. The compounds identified are known to have nutritive and medicinal values.

Table 7: LC-MS/MS profile of Aqueous Crude Extract *S. ellipticum*

S/N	Compound name	Retention Time	Chemical structure
1	L-Carnitine	**2.67**	
2	1,6-anhydro-β-D-Glucopyranose	**4.03**	
3	Fratexin	**10.29**	
4	5-Hydroxyisovanillic acid	**18.67**	

5	Trans ferulic acid	**0.68**	

Discussion

Acute Toxicity

Haematology analysis

According to the results, there were variations in the blood parameters of the test and control groups. The low neutrophil counts detected in the experimental groups may be attributed to the effects of the extract at lower doses, which could either suppress cell differentiation processes or act directly on cells, affecting the innate immune response in the mice. Neutrophils play a crucial role in the innate immune system. The findings of the present study were consistent with those of Etame et al., (2017), who used a dose of 200 mg/kg, and observed that neutrophil counts returned to normal upon increasing the extract concentration.

In the current investigation, the mean cell haemoglobin concentrations (MCHC) and basophil levels of all the experimental groups deviated from the reference range. Although the MCHC levels were below the reference range, the low levels could be related to dietary factors such as low iron levels in the mice's food (Ventrella et al., 2016). However, the effects of plant crude extracts on erythropoiesis or polycythemia could only be established if other metrics such as RBC and hematocrit deviated from the reference range.

Basophils are white blood cells that respond to allergens and other antigenic stimuli by producing significant amounts of IL-4 (Rhiouani et al., 2008). Higher basophil counts may indicate the presence of dietary allergens, while low basophil levels suggest the absence of allergens in the diet. In the current study, all the mice used in the experiments had higher basophil levels, suggesting that the food may have contained unidentified allergens (Rhiouani et al., 2008).

The haematological analysis results showed that RBC, haemoglobin, hematocrit, MCV, MCH, platelet count, WCB, lymphocytes, and monocytes were generally within the normal range for the mice fed with crude extract concentrations equivalent to 123, 300, and 2000 mg/kg compared to the control group and reference levels. This indicates that the extracts did not have any toxic effects on the blood parameters, similar to the findings reported by Tom et al., (2018), who observed no changes in blood parameters after toxicity evaluation of *Harungana madagascariensis* at a dose of 600 mg/kg.

Biochemical analysis

When assessing the safety of extracts in animal models such as mice, variations in the liver's biochemical characteristics serve as crucial risk assessment tools (Shittu et al., 2020). Serum aspartate transaminase (AST) and alanine transaminase (ALT) enzymes are clinically significant markers used to identify liver injury, whether inflammation or necrosis. ALT is more concentrated in the liver, and an increase in its serum levels beyond the normal range indicates liver tissue injury. In contrast, aspartate transaminase is less selective than ALT as a biomarker of liver impairment since it is also present in other organs' tissues, such as the kidney, heart, and muscles. However, the higher serum levels of these two enzymes are a sign of liver tissue injury and altered cell membrane permeability (Ramaiah, 2007).

In the current investigation, mice administered with crude extract concentrations equal to 123 mg/kg, 300 mg/kg, and 2000 mg/kg had higher levels of AST than ALT. Mice with elevated serum AST concentrations compared to ALT levels may have had tissue damage in organs other than the liver since ALT levels in the serum are usually higher than AST levels, indicating liver

tissue damage (Ajibade, 2017). This indicates that the liver was not affected by the aqueous stem bark crude extracts of *S. ellipticum* in the current study when doses up to 2000 mg/kg were administered.

According to the results, testing for bilirubin levels in all the mice showed no liver injury. This finding provides more evidence in support of the transaminase test results (ALT and AST). A normal bilirubin level indicates that the liver is functioning correctly by eliminating bilirubin from the body without any hepatic damage (Abou Seif, 2016). Therefore, the current study's results justify the traditional use of *S. ellipticum* stem bark aqueous crude extracts.

Immunomodulation activity of the crude extracts

The anti-inflammatory cytokine IL-10 helps regulate the immune system during infection to minimize harm to the host (Wu et al., 2022). However, downregulation of IL-10 during infection can worsen the condition, as observed in mice treated with an aqueous crude extract of *S. ellipticum,* indicating possible pro-inflammatory activity (Sasaki et al., 2000). On the other hand, interleukin-1 receptor antagonists (IL-1Ra) can prevent prolonged inflammation that may damage the body by antagonizing IL-1α and IL-1β (Yazdi & Ghoreschi, 2016). In the present study, *S. ellipticum* showed relatively strong upregulation of the IL-1Ra gene, which inhibited excessive production of cytokines IL-1α and IL-1β, demonstrating anti-inflammatory properties (T. Wang & He, 2018). Similar results were observed in a study on orange peel extract and *Phleobodium decumanum* (Punzón et al., 2003).

On the other hand, IL-6, a pro-inflammatory cytokine associated with the cytokine storm during infection, has been linked to various inflammatory disorders (Hirano, 2021). In the current study, *S. ellipticum's* aqueous crude extract downregulated cytokine (injected with LPS but no drug provided) when compared to the control group, demonstrating anti-inflammatory properties (de Araújo Moreira et al., 2020). Similar results were reported in studies on ethanolic bark extract of *Terminalia argentea* and *Phleobodium decumanum* (Punzón et al., 2003).

Interleukin-1β (IL-1β) is a key cytokine involved in the stimulation of pro-inflammatory signalling pathways in the brain and peripheral tissues (Goto et al., 2016). The current study demonstrated that *S. ellipticum's* extract had pro-inflammatory activity by upregulating IL-1β when compared to the negative control group (consisting of only LPS-infected cells). Similar results were reported in a study on loquat leaf extract (*Eriobotrya japonica)* by Hoseinifar et al., (2018).

Phytochemical Profile

L-carnitine is an amino acid derivative that plays a critical role in transporting fatty acids into the mitochondria for energy production (Matera et al., 2003). In plants, L-carnitine biosynthesis occurs through the modification of lysine, which is converted into trimethyllysine and then into L-carnitine with the help of enzymes such as trimethyllysine dioxygenase (Jacques et al., 2018; Seline & Johein, 2007). L-carnitine has several potential medicinal uses, such as improving lipid metabolism, reducing inflammation, and boosting protein synthesis (Kraemer et al., 2008). It may also affect erythropoietin (rHuEPO) requirements, decrease pro-inflammatory cytokines, and increase nitrogen balance (Golper et al., 2003). In the context of the present study, the presence of L-carnitine in the stem bark crude extract could be linked to the observed anti-inflammatory properties.

1,6-Anhydro-β-D-Glucopyranose is a rare sugar that was revealed to be present in the stem bark crude extract o*f S. ellipticum* in the present study. It is derived from glucose through the action of enzymes such as 1,6-anhydro-beta-D-glucopyranose synthase. In plants, it is involved in the biosynthesis of cell wall components such as hemicellulose (Liu et al., 2008). The potential medicinal uses of 1,6-anhydro-β-D-Glucopyranose are not well-known, but it has been reported to have some antibacterial properties (Procter et al., 1990). Its presence in the stem bark crude extract of *S. ellipticum* may contribute to its reported antimicrobial activity.

Fraxetin is a flavonoid found in several plant species, including *S. ellipticum*. It is biosynthesized from the precursor molecule naringenin through the action of enzymes such as flavone synthase II (Wang et al., 2014). Fraxetin has several potential medicinal uses, such as antioxidant, antimicrobial, anti-inflammatory, and anti-fibrotic properties (H. Wang et al., 2014). It has also been shown to have the ability to suppress apoptosis triggered by interleukin 1β. In the context of the present study, the presence of fraxetin in the stem bark crude extract can be attributed to its reported antimicrobial activity and anti-inflammatory and immunomodulatory properties.

5-Hydroxyisovanillic acid is a phenolic acid found in the stem bark crude extract of *S. ellipticum*. It is biosynthesized from tyrosine through the action of enzymes such as tyrosine decarboxylase and tyrosine hydroxylase (Khammar & Djeddi, 2012). The potential medicinal uses of 5-Hydroxyisovanillic acid are not well-known, but it has been reported to have some antioxidant properties. Its presence in the stem bark crude extract of *S. ellipticum* could potentially contribute to its reported antioxidant activity.

Trans-ferulic acid is a phenolic acid found in several plant species, including *S. ellipticum*. It is biosynthesized from phenylalanine through the action of enzymes such as phenylalanine ammonia-lyase (Wang et al., 2017). Trans-ferulic acid has several potential medicinal uses, such as anti-inflammatory, antioxidant, and anticancer properties. It has also been shown to have beneficial effects on oxidative stress, inflammation, vascular endothelial damage, fibrosis, apoptosis, and platelet aggregation (Wang et al., 2017). Its presence in the stem bark crude extract of *S. ellipticum* can be attributed to the revealed anti-inflammatory and immunomodulatory properties.

Conclusion

This study evaluated the safety and potential medicinal value of the aqueous extract of *Sapium ellipticum* stem bark. The results demonstrated that the extract was not toxic at doses up to 2000 mg/kg, suggesting a high safety profile. The immunomodulatory activity of the extract was also investigated and showed significant downregulation of the pro-inflammatory cytokines IL-6 and IL-10, as well as upregulation of the anti-inflammatory cytokines IL-1Ra and IL-1β, which may have therapeutic implications in the treatment of inflammatory diseases. Additionally, the phytochemical profiling of the extract using LC-MS/MS revealed the presence of compounds with anti-inflammatory properties, such as Fraxetin and L-carnitine. The upregulation of IL-1β, a pro-inflammatory cytokine, in the extract, suggests that it may have potential as a treatment for certain conditions where increased inflammation is needed. Overall, the results of this study provide important information on the safety and potential therapeutic effects of *S. ellipticum* stem bark extract, and further research is warranted to explore its full potential.

Authors' contributions

The authors of this study contributed equally to the conception, design, writing, review and approval of the manuscript.

Conflict of Interest

No conflict of interest

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Statistical analysis and modelling of the prevalence of malaria in Nyasa district; Tanzania

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Abstract

Background: Demographic, social economic factors influencing the prevalence of Malaria in Nyasa District and the level of knowledge attitude and prevention on malaria disease incurred by the domicile of Nyasa district.

Objective: The demographic conditions affecting the spread of malaria and precautions they take to prevent the disease. Determine the factors affecting the malaria gender-wise.

Methods: A cross-sectional study was conducted using questionnaire on 350 householders selected randomly from two distinguishable wards of Nyasa municipal, Tanzania. Prevalence, incidence, factor analysis to identify knowledge and attitude, binary logistic model on general and gender-wise identifying the significant factors were traced out. Using SPSS 14.5 software model and its adequacy, factors and its validity are verified.

Results: The prevalence rate of malaria in Nyaza is 24.9%, while it is 16.7% in the hills and 36% in sea shores. The ratio of affecting malaria among males and females is 41: 47 and among poor: middle class: Upper class =9.3 :1:.001. The government provide bed nets for 64.1% but 94% are not getting free hospital facilities. About 90% know that malaria is a transmitting killer disease and its symptoms, preventive measures and mosquito breeding timings. Using bed nets (95%), removing stagnant water (71.7%) and cleaning the environment (62%) are the general measures preferred by people. 17% prefer burning coils or repellents and 28% keep meshes to doors and windows. Child malaria was diagnosed by 61.4% families, If the number of family members is more than 3, the chance for affecting malaria is 0.62, There is a need for hospital stay in many malaria patients (Male 38.8% and Female 47.7%). 95% pregnant woman take hospital advice of which 50% go only in the third month and about 60% are going to know the condition of fetus and mother as well as prevent CDs. 75% of malaria-affected people belong to informal or primary education groups, 89% are poor and 10% are middle-class people. Knowledge of prevention and control of malaria depends on 3 factors use, official service, and self-awareness. Similarly, attitude towards prevention and control also depends on 3 factors- seriousness, lack of awareness, and practicability. Binary logistic model on affecting malaria depends on 5 significant variables – altitude of land, sex, age, income, education

Conclusion: The prevalence of malaria is moderately high in Nyasa compared to the national prevalence rate. Women and children are mostly affected by the disease. Most dwellers were aware of the seriousness of the disease and using bed nets as a preventive measure. People are also keen to destroy stagnant water sources and clean the premises to keep away grass and bushes. The important dependent demographic factors for the incidence of malaria were sex, age, depriving conditions of family, lack of sufficient education and the location of areas like seashores or hills.

Keywords: malaria, prevalence, knowledge, prevention, bed net, demographic factors, social and economic factors

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Introduction

Malaria (MOHSW,2008) remains a major cause of morbidity and mortality and more than 600 million cases are reported in each year worldwide with death toll of 2 million cases. Over 90% of these cases occur in sub-Saharan Africa where Falciparum Malaria is pervasive and the major killer of children under 5 years old (Breman J.G. et al, 2007). Malaria is a major public health concern for all Tanzanians especially for children under age 5 years' and pregnant women. The disease is a major cause of morbidity and mortality among outpatient and inpatient admissions. It accounts for up to 40% of all outpatients visit (MoHSW, 2008). Malaria poses many societal and economic burdens in Tanzania, ranging from school absenteeism to low productivity in the workplace. Combinations of interventions such as the use of insecticide-treated nets (ITNs) by all members, maintaining a clean environment around the dwelling (e.g., by removing items that could hold water and inadvertently serve as mosquito bleeding sites), and intermittent preventive treatment (IPTp) for pregnant women, increase the likelihood on malaria prevention and control in the community, (NBS, 2011-12).

The international Roll Back Malaria (RBM) initiative works to reduce the malaria burdens. The primary objective of RBM is to increase access to the most effective and affordable protective measures. The primary objective of IPTp is to prevent malaria-related maternal complications such as maternal anemia and to improve birth outcomes by preventing low birth weight among infants. The strategic plan also includes other vector control measures such as indoor residual spraying (IRS) and epidemic prevention and control. ACT is a response to the emerging resistance of malaria parasites to anti-malarial drugs like Sulphadoxine Pyrimethamine (SP) and Chloroquine, which was used as the first-line antimalarial drugs in Tanzania. But for this time the main medicine which are in use for treatment of malaria are Artemether-Lumefantrine (ALU) which is the first course and if malaria is not solved, then dihydroartesmisinin- piperaquine (DP) are used. (Celine I Mandara, Reginald a Kavishe et al, 2018).

The rationale behind the study was to assess the prevalence of malaria in the demographic, socio economic and environmental conditions leading to malaria infection and the knowledge, attitude and practices of people of Nyasa over the disease. The objective of the study was to assess The demographic conditions affecting the spread of malaria. The feeling of people on affecting malaria and the general precautions they take

The extension of government and health caring system to reduce the prevalence of malaria. In Tanzania, prevalence of malaria has been decreasing from 10% in 2008 to 9.5% in 2012. The study points to one major success in the scheme: health workers reported that the number of malaria patients and the number of severe malaria cases had declined in Ruvuma Region. (Komba A. 2008).

Prevalence of malaria in Tanzania for the last 20 years is decreasing due to the vector control methods adopted by the government of Tanzania with the help of international agencies, still some area in Tanzania shows higher percentage than the prevalence rate of the nation. (NBS 2011-2012). Nyasa is one of the areas where such cases of malaria are found in the colonies. So the study was to concentrate on formulation of statistical model of prevalence of malaria so as to determine the prevalence of malaria in Nyasa District. Demographic factors like sex of respondents, age of respondents, place of residence, level of income, and level of education with malaria cases had influence on prevalence and spread of malaria.

Demographic factors:

Sex: Gender plays a greater role in the prevalence of Malaria in Districts, regionally, nationally and internationally. Female are the one who often experience the impact of Malaria more severely than

male due to a combination of social and economic constraints and pregnant women tend to reduce their immunity to fight against malaria (NBS, 2011-12). In Fako Division, South West of Cameroon, a study was conducted by (Ndamukong-Nyanga J.L. et al (2014)), on socio-demographic and environmental factors influencing asymptomatic malaria and anemia incidence among school children. The result shows that the incidence of asymptotic malaria was 43.4% (CI=38-48.9) and commented that malaria parasite incidence was higher in female.

Age: Children are at highest risk of infection, especially under 5 years, because, their white blood cells are not matured to fight against diseases. Age is an important factor in determining levels of acquired immunity to malaria, (Doolan et al, 2009). Also Amusan O.V, (2017) discovered that immunity is good in 21-30 years (31.8%), 31-40 years (23.8%), and the best in 15-20 years (3.4%). Malaria incidence was significantly highest ($\chi 2=7.1204$, p value=0.03<0.05) in pupils of 6-10 year' age group (49.0%, CI=42.1-59.9) compared with their counterparts.

Place of residence: Among the place of residence, rural areas are at higher risk of being affected by Malaria compared to urban. (Smithson P (2009). However, school surveys in Dar-Es Salaam during a dry spell in 2003 showed that the prevalence of malaria parasites was low: 0.8%, 1.4%, 2.7% and 3.7% in the centre, intermediate, periphery and surrounding rural areas, respectively. Also place of residence can be categorized as low and high land in which malaria occurred high in low land compared to other lands (Mboera et al 2008). A study was conducted in Iringa District, Tanzania among school children within six villages classified into three categories lowland, intermediate and highland and it was established. In a study of Usambara Mountains in north-east Tanzania, a prevalence of malaria in children were observed to decrease by 5% for every 100 m increase in altitude from 82% in the lowlands (at 300m) to 12% in the highlands –(at 1700m) (Bodker. R, 2006). In another study in northern Tanzania (Drakeley CJ, 2005) a 19% to 21% decrease in malaria prevalence has been observed, for every 100m altitude increase. The lower malaria prevalence in the higher altitude is likely to be attributed to the low ambient temperatures (Khaemba B.M,1994). Altitude has been considered as a proxy for temperature on the parasite. However, local variations in seasonality of malaria transmission including vector species composition, topography, host and parasite genetics, and socio-economic factors influence malaria prevalence in any given area (Lindsay. S.W,1996).

Level of education: Most expected thinking is that the educated people prefer more the practices of prevention and control of malaria compared to illiterate. Also children whose mothers have no formal education or who have not completed primary school are more likely to be affected than those whose mothers have completed primary school (NBS, 2011-12). A logistic regression model was used to assess the association between the educational level of patients and malaria infection, the association was significant (Shr-Jie Wang et.al, 2006).The head of the households' level of education had an influence on bed-net retreatment (p=0.0000< 0.001) and acceptability of larval control program (p=0.0000<0.001). In addition, the education level of the household heads played a role on understanding the causes and selection of malaria interventions for the households (Lowassa A, 2012).

Level of income: Among two categories, level of income below 100000Tshs per month are in higher risk of being infected by malaria because they face difficulty to purchase the materials needed for prevention and control of malaria (example bed nets). (Mboera L et al, 2013). The poor people living in a house built with leaves and mud had a higher risk of having malaria compared to those living in a house built with brick and/or concrete (OR = 21.8, 95% CI = 1.29–369.65, p < 0.05). (Shr-Jie Wang et.al,

2006). A significant association was observed between bed-net retreatment, larval control and occupation of the head of the household (Lowassa A. 2012).

There are several studies conducted which focus on the prevention and control of malaria as elaborated below. Sumari *et al*. (2016), conducted a study on knowledge, attitudes and practices on malaria prevention in secondary students Bagamoyo, Tanzania. A sample of 125 children were searched and found that more than half, (63.2%) of school children had knowledge on malaria as a disease and its transmission. A large size -101 children reported that they are going to hospital immediately, when they feel malaria symptoms and avail ALU treatment. Cleaning environment to prevent mosquitoes from breeding, use of bed Nets (LLINs), Indoor Residual Spraying (IRS) and the use of chemotherapies are different practices they undergo to save from this vector. (115 out of 125, 92%).

Mazigo D.H et.al (2013) conducted a study on knowledge, attitudes and practices about malaria prevention and control in the rural area of Geita district, north west of Tanzania. 56% of household heads had knowledge on prevention and control of malaria and most prefer personal protection against mosquitoes by ITNs (77.3%). 86.3% agree with IRS of insecticides, and suggested that education should be provided to the communities. According to Amusan O.V, (2017) a study on knowledge, attitude and practices on malaria prevention and control among private security guards within Kaduna Metropolis, Nigeria was conducted with a sample size of 261 guards. There are 96.94% respondents with a high knowledge about malaria, 78% with a positive attitude,74% with good malaria practices and 96.9% correctly associated mosquito as malaria vector. Wearing long-sleeved shirts, trimming of bushes and use of ITNs are the leading malaria prevention methods practiced by the respondents. Statistically significant association between malaria practice scores and respondent's age (χ^2 =5.2457, p value=0.022<0.05), gender (χ2=9.5495, p value = 0.002<0.05) and level of education (χ^2=7.5503, p value = 0.006<0.05) was reported. Respondent's knowledge about malaria (χ^2=7.0334, p value = 0.008<0.05) and attitude towards malaria (χ^2=5.4118, p = 0.020<0.05) were found significantly influence their practices towards malaria.

Methodology

Population and Sample

A random sample of 350 persons living in Nyasa region were interviewed with a structured questionnaire containing questions regarding the means of protection from malaria, knowledge/awareness about the disease, attitude on treatment and severity of malaria, need of hospital facilities, severely affected groups as well as the social and demographic constraints of the informants. Factor analysis was applied to identify the factors on awareness and attitude. Logistic regression model was adopted to identify the incidence of malaria on social and demographic factors. Odds ratio was used to find the significant variable and model adequacy was confirmed by Hosmer and Lemeshow test. Effectiveness of governmental health activities on people of Nyasa is evaluated using Chi Square test. General binary regression model as well as male and female model were developed with respect to social, geographical and personal factors influencing incidence of malaria.

Statistical Methods

The data was cleaned by fixing outliers and missing information and prevalence of malaria, social and educational background of the house holder and hygienic conditions of house premises were derived by qualitative analysis. Also the knowledge and attitude towards malaria by the residents were formalized by detecting factors. The logistic regression was applied to determine the factors for infecting malaria separately for man and woman. Normal test, Chi square test, Odds ratio, factor

analysis and fitting binary logistic regression models were the statistical tools administered to elicit results.

Factor analysis

Correlation analysis (>0.6), determinant (0.099≠0), KMO test (0.674>0.6), Bartlett's test (χ^2=798.45, p value=0.000) are adopted to restrict the variable for factor analysis. Scree plot with Eigen values >1, PCA method of extraction, Vari-max rotation method, ignoring coefficients with communality < 0.5, total variance explained 72.45% were adopted to get the optimum factors.

Logistic regression model

$$\text{Logit}(Y) = \log_e(\text{odds}) = \ln\left(\frac{\pi}{1-\pi}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_p X_p \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

the probability of occurrence.

$$\pi = \frac{e^{\beta_0+\beta_1 X_1+\ldots+\beta_p X_p}}{1+e^{\beta_0+\beta_1 X_1+\ldots\beta_p X_p}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

β_0 is the Y-intercept, β_0, β_1, $\beta_2 \ldots \beta_p$. are regression coefficients and $X_1, X_2, \ldots X_p$ are explanatory variables. This model could be used to predict prevalence of malaria. In particular

$Logit(\pi_j) = \beta_0 + \beta_1(\text{age}) + \beta_2(\text{sex}) + \beta_3(\text{residence}) + \beta_4(\text{education}) + \beta_5(\text{income})$.

Odds Ratio

The Odds Ratio is greater than one, indicating that the likelihood of the occurrence of success is higher, while an odds ratio is less than one, shows the opposite effect and if the odds ratio is equal to one, it shows the occurrence of two outcomes equally likely.

Results

Prevalence of Malaria

The general prevalence of malaria in Nyasa district was 24.9%. Rrevalence in lower and upper areas of Nyasa significantly differ from Tanzanian rate of infection. There was an occurrence of 20% more cases of malaria in the lowland areas of Nyasa compared to highland areas. (Using Normal test, Z=0.6563 p value=0.5116>0.05). There was significant difference in the rate of incidence of infecting malaria between male and female inhabitants (0.42 in male & 0.4771 in female) (χ2 =10000 p value 0.0000<0.05). But the average number of male and female members infected malaria was equal (Z=0.0002 p-value =0.9998>0.05). Availing information on child incidence of mortality and morbidity due to malaria from the informants, the incidence of malaria under 5 was only 33%. But neonatal mortality was 13.12%, under 5 mortality- 10.5% and it was found that most of this was happened in primary educated or illiterate mother' child of lower strata of economy.

Hospital visit depends on distance of availability of hospital and 2/3rd favor at least a PHC within a distance 1KM. But 35% to 45% are visiting the hospital by travelling more than 1KM from the house. Thus visit to hospital is affected on getting treatment to malaria (χ2=10.517, p value<0.005). 2/3rd agree that the government provide awareness through health professional but only 15% are participating in the awareness programs. Males and females differ on government programs success on malaria

($\chi 2$=4.088, p-value 0.043<0.05). 85% of educated categories avoid the awareness camp. 80% respondents told that hospital service is costly and the average cost for hospitalization is about 10000 Tsh. Free nets are getting among 65% poor, 76% of middle class and 50% of upper middle class. 94% of the poor and 85% of the middle class did not get free medical services in hospital after being affected by malaria. Free service by health department is not provided with respect to the economic condition of the family (χ^2=4.438, p value=0.109>0.05). The cost of treatment on various areas of Nyasa was identical (χ^2=0.009, p value=0.925>0.05).

Knowledge, Prevention and Control

The knowledge about malaria as a transmitting vector was found in more than 95% of inhabitants of Nyasa but the knowledge on prevention is significantly different in males and females. (Z=6.4571, p-value=0.0000<0.05). Feeding time of mosquitoes is known by 87% of participants and identification of malaria symptoms is done by 89%. 7% females and 3% males were not taking any preventive measures to restrict malaria. 79% residing here were taking initiative to drain out stagnant water from living premises while 65 % are constructive to clean the environment.

No significant difference was found among males and females on using mosquito net as a preventive measure (Z=0.6543, p value=0.5128>0.05). Significant difference of opinion was found in males and females on removing dirty water as a prevention (Z =2.8079 p-value =0.0049<0.05). Only 7 respondents in Lipingo region (High altitude) and 10 in Kingerikiti (Occean region) were not taking any preventive measures. There was significant difference by the Lipingo and Kingerikiti people in using mosquito net as a protection. (Z =6.1974 p-value =5.74E-10<0.05). In the low land 96% use bed nets and the use of net was not depending on the education level of the respondent. It is alarming that 15 out of 240 primary educated and 2 of 80 secondary educated respondents do not take any preventive measures.

More than 60% of respondents irrespective of their educational level were eager to avoid dirty water logging in the premises to avoid spread of malaria. Only 10% of poor are using repellents or coils while 25% opted to close the doors to save from mosquitoes. More than 10 % use gauze wire windows while 3.5% do nothing to prevent mosquito spread. Using coil and gauze wire windows were the strategy mainly considered by upper class. 10% use coils, 25% prefer closing doors, 15% use gauze wire widows. 231/350 (67%) are diagnosing child malaria confidently and handle it well. Only 2 respondents were interested on traditional medicines as treatment for malaria.

Rate of patients taking hospital service after infected malaria in Lipingo area is 0.73 (males) and 0.9 (females) while it is 0.39 (males) and 0.41(females) in Kingerikiti area. Comparing the incidence of malaria on poor category dwellers of Nyasa, males were less affected. (males=134/295=45%, females =147/295=49.8%). Similarly, among the middle class families only 29% males were infected by malaria while it was 46% females.

More than 60% of houses of more than 4 members were affected by malaria. Thus there is a direct proportion of infecting malaria with number of members in a family ($\chi 2$ =5.265, p value 0.072>0.05). 49% affected in families with 1-3 members and it is 60% in families with members >3. Most of the pregnant women (19/20) are visiting hospital in Nyasa during pregnancy. 50% pregnant women are visiting the hospital on third month. 9/20 visits hospitals during pregnancy to get education about ways of life and precautions to be taken at such time. 60 % go to know the growth of fetus and condition of themselves. 11/20 visit to prevent and control disease like malaria. Traditional protection from malaria was realized by 7% in Lipingo and Kingerikiti. 1/17 families of non-formal and 3/13 of higher educated people were using traditional methods to protect from malaria. Incidence of malaria in lowlands and highlands are significantly different (Z=152.23, p value =0.0000<0.05).

Education has significant influence on the practices of prevention and control of malaria. (Z=2.4089, p-value is 0.008 <0.05). Level of income was categorized into three - poor, middle and upper. Families of different income groups differ significantly in Malaria infection (Z=2071.22, p-value 0.000 < 0.05). In the Lipingo ward (Low level), 44% of families were affected badly by infecting malaria while 32% were partly affected and 24% were not affected. It is notable that in the hilly region, 22% of male and 10% of female respondents were infected by this vector. In Kingerikiti (high land) 53% of families were not infected, 28% partly infected and 19% were highly infected. About 15% of males and females were infected in this region. Low land wards were pro malaria infectious compared to high land wards of Nyasa district. More than 50% families in the Kingerikiti highland region is not infected by the disease but it is only 25% in Lipingo low-lying ward.

For the question "Do you know the ways of prevention and control of malaria?", 95.1% of the respondents affirmed yes and ascertained that the participants were using one or other methods to keep away malaria. This is an indicator of seriousness of the vector over the Nyasa District of Tanzania. There is no significant difference in the rate of contracting malaria between males and females who were not taking any precautions against the disease. (Z=1.0943, p value =0.1369>0.05).

All of the young respondents aged between 25—55 year aspired the need that the government and other agencies should act more actively to eradicate the disease. All higher educated respondents are using preventive measures but 15 of 17 primary educated are not using any such methods and it is grave. Barring one, all the non-net-users belong to poor families indicating the need of supplying bed nets or other facilities free of cost to poor by the government and international health organizations. Only 5% of respondents do not use bed net, while 40% were not interested in cleaning environment and 30% were not removing dirty water, creating spread of mosquitoes in the region. So social awareness program is essential to improve the hygienic conditions of Nyasa District. Considering personal healthy practices 94.6% adopt bed nets and 28% close doors and windows and 14% use gauze wire in windows.

About 97% agree that malaria is a life threatening disease. Out of it 60% were much worried about its propagation and health care. About the transmission of malaria from one person to another, 40% agree on it, while 50% disagree and the rest had no idea about it. 90% agree to avoid mosquito bite to protect from malaria. Infection of malaria is unpredictable and it can be infected at any time to anyone. This is the feeling of 88% Nyasa people indicating the fear of contracting malaria in that area. About 30% of respondents are strongly against treating malaria by themselves and require treatment by suitable healthcare units. Another 42% are also not convinced of self-medication.

Pregnant women and children are most suffered by malaria (97%) and the mortality rate is high in this group. As per opinion of 89% respondents, it is certain that malaria requires proper care and medication and if not treated properly on time it will be life threatening. 48% of respondents believe that the work at night in gardens and forests will expose to malaria of which 28% are sure of contracting it. Appropriate medication is essential to recover from malaria according to 93% of Nyasa people showing the need of giving hospital facilities and free medicines. Nyasa people were not keen on buying drugs or taking medicine (72%) indicating the lack of seriousness or the poverty inhibited on them. 91% like to go to health enter or clinics to check the infection of disease immediately after showing symptoms of malaria. The expiry date of medicine is checked by 92% of respondents and it is a good sign about the awareness of medication in proper way. Thus Nyasa people are moderately aware and serious about the danger of contracting malaria. Also they like to get more clinical and health centre care to treat the disease. Most of them oppose self- treatment or lack of treatment, but they are in need of awareness on anti-mosquito bite drive.

Knowledge of prevention and control of malaria

Net use=.398*sleep in net+0.41*members sleep in net + 0.309*repairing net (3)
Official Service =0.614*spray+0.609*visit VHT (4)
Self-awareness=0.769*clean water+0.493* visit HC (5)
Knowledge =average (net use +official service +self-awareness) (6)
Since all values of Cronbach's Alpha are >0.6, the factors show consistency and reliability.

Average response on net use is 1.4 with low SD showing consistent opinion of use of bed net. Official service had a fair average 3.04 indicating that most of respondents are approving the activities of government, but SD is high. Self-awareness has average 1.64 showing need to improve by Nyasa people. Overall knowledge displays an average 2.02 implies that average knowledge level should be improved for prevention of malaria in Nyasa. There is no significant difference in the opinion of net use and government services in different wards, but self-awareness and knowledge on prevention are significantly different in these wards. The official service and self-awareness were significantly different in different economic groups (Z=2.0489, p value=0.008<0.05 and Z=1.8521, p value=0.032 respectively).

Attitude
There are 3 independent factors to identify the attitude and such model contains more than 55% variability of responses of population.
Seriousness= 0.366*dangerous on not completing medicine +0.477* immediate checkup + 0.444* medicine before expiry medicine before expiry. (7)
Lacking awareness=0.626*self-treatment+0.592*drug from un authorized source (8)
Practicability=0.622* life threatening+0.566* save from mosquito bite. (9)
Attitude=average (seriousness+ lack of awareness+ practicability) (10)

Seriousness had a mean response 3.24 with SD=.66 so that on average respondents agree with the need of seriousness. Lacking the awareness had mean 2.57 indicating lack of seriousness by the people of Nyasa. Practicability with mean 2.99 agrees that malaria is life threatening and avoid mosquito bite. Overall attitude takes an average of 2.93 with SD =0.47 implying a fairly agreeing attitude on prevention and control of malaria. Seriousness, practicability and attitude are significantly different in Lipingo and Kigeriketi (Z=1.9953, 2.6520, 2.7477, with respective p values=0.023<0.05, 0.004<0.05, 0.003<0.05). Seriousness and attitude are significantly different in males and females (Z=2.6520, Z=2.09620 with respective p values 0.0004<0.05, 0.018<0.05). Seriousness is different in different age groups (Z=3.0902, p value=0.001<0.05) and lacking awareness also differs on ages (Z=1.8384, p value=0.033<0.05). Attitude is different in various ages (Z=2.8781, p value=0.002<.05) but practicability is identically classified by all ages (Z=0.8632, p value 0.194>.05).

General model-regression output
The model satisfies Lemeshow test = 0.449 > 0.05 and hence goodness of fit. From this model, the odds of being infected by the epidemic in the old ages was 1.373 times higher than younger ages. Regarding sex, the likelihood of being infected by malaria was increased among the females than males in Nyasa District (Odds ratio = 1.590). The odds of being infected by the epidemic was 3.509 times higher for Lowland compared to Highland. The model also showed that the odds of being infected by Malaria in educated group was significantly less compared to illiterates. Odds was 1.693

times higher for illiterates. Also, the odds for the low income group of people to the upper income group is 2.257 showing higher occurrence of malaria among the poor.

In the male and female models there is significant difference in the coefficients of age, ward, education and income. (Z=4.8877, 40.5222. 26.9327, 35.2661 with p values 2.5896 E-06, 0, 1.2266 E-158, 3.4189 E-271 respectively). Also odds ratio predicts high influence of malaria in low lands and it was too much in females. For education, much influence was on lack of education, especially among women. But in the income groups, low income group had more effect, especially in male model.
Thus general model and the gender model emphasize the need of awareness through education and improve poverty conditions to eradicate malaria in Nyasa. The low lands require more attention on malaria prevention projects.

Discussion

Prevalence

Statistics & facts in Tanzania by severe Malaria observatory, USAID report on Presidents Malaria Initiative, UNICEF data on Malaria, WHO report on Malaria prevention, Tanzania and the DHS program for Malaria indicator survey, the following results conclusions and expectations were made on 2017 up to 2022 studies. 16% of all the outpatient visits in mainland Tanzania is due to malaria and 93% are living in malaria transmission areas where this study shows that Ruvuma region is also an area of high risk of malaria. Tanzania is one among 10 countries with highest malaria cases and 3.1% of global death cases and 4.1% of global deaths in 2021. During 2020-2021, incidence rate at risk increases by 2.1% from 123 to 126 per 1000 of the population although the death rate decreased by 1.7 per thousand. 1n 2017, under 5 mortalities was 5%, with incidence of malaria 37% and neonatal mortality was 9%.

Tanzania has recorded a 10 percent decline in malaria prevalence from 18.1 percent in 2008 to 8.1 percent in 2022, according to new statistics from the ministry of Health. The National Malaria Control Programme wants to eradicate malaria by 2030 by reducing the prevalence in children under the age of five to less than 3.5 percent by 2025.The number of people living in areas free from malaria infection increased from four percent (2008) to 41 percent (2022). The number of confirmed malaria cases has declined by 55 percent from 7.7 million in 2015 to 3.5 million in 2022.

Incidence per 1,000 people, has reduced by 64 percent from 162 in 2015 to 58 percent in 2022. Hospital admissions due to malaria cases have decreased by 66 percent from 529,146 in 2015 to 178,549 in 2022, which indicates a decrease in severe cases. The number of malaria deaths recorded in health facilities has decreased by 76 percent, from 6,311 in 2015 to 1,502 in 2022. The new stratification (2022) shows an increase in the number of councils with very low malaria transmission risks from 36 (2020) to 38 (2022) and a decrease in high burden councils from 64 to 57. Data indicates that the central regions of Dodoma, Singida, Manyara, Arusha, Kilimanjaro and Songwe have zero percent prevalence in 2022, Mwanza, Iringa and Dar es Salaam have only one percent. Highest rate was in Tabora (23.4), Mtwara (20), Kagera (18), Shinyanga (16), and Mara (15). Prevalence of malaria is higher in rural areas (10%) than in urban areas (less than 1%).

Prevalence of malaria in children ranges from less than 1 percent in every region in Zanzibar, plus Arusha, Kilimanjaro, Manyara, Dodoma, Singida and Songwe but 20% in Mtwara and 23% in Tabora. In 2017, Under-5 mortality was at 5% while neonatal mortality (under 12 months) was at 9% with incidence of under -5 cases 37%. In the same year, prevalence on mainland varied by region from <1% in the high lands of Arusha to as high as 15% in the southern zone and 24% along the Lake and western

zones. According to DHS, Urban resident's prevalence of malaria is 0.7% while for rural residents it is 10.4%. Also the topography of land influences the prevalence of malaria as southern highlands at 4%, southern lands at 15.7%, south west highlands 3.9% Lake 11.5%.

Prevalence in Nyasa region under this study

The results show that the general prevalence of malaria in Nyasa district was 24.9% which implies that out of 1644 household members there were 409 household members were affected by malaria within the six months (from November,2017 to April 2018).

Prevalence of malaria in Kingerikiti ward located at highland area of Nyasa was 16.7% while in Lipingo ward located at lowland area of Nyasa was 36%. There is 20% more cases of malaria reported in the lowlands of Nyasa compared to highlands. The rates are a little high in this study as sample size was limited to 350 only. This study mention that 76.2% malaria affected cases were from low educated people, 56% domicile in sea land, 89% from poor economic conditions, and out of 350 houses 210 (60%) were affected of which 49% were affected for both male and female in a house, while 31% males and 20% female only were affected in some houses.

Overall, incidence of malaria diagnosed per 1000 person years was 735 among females and 449 among males (IRR = 1.72, 95% CI 1.68–1.77, p < 0.001), with larger differences among those 15–39 years (IRR = 2.46, 95% CI 2.34–2.58, p < 0.001) and over 39 years (IRR = 2.26, 95% CI 2.05–2.50, p < 0.001). Here as in Tanzanian statistics, female occurring malaria is more 0.4771 over male 0.42 in Nyasa with IRR= 1.143. Thus the IRR is less in Nyasa showing less difference in male and female prevalence compared to national level.

1n 2017, under 5 mortalities was 5% with incidence of malaria was 37% and neonatal mortality was 9%. In this study the neonatal mortality is high, 13% and under 5, mortality is 10.5 which may be due to topographical, lack of education and low level of economic conditions but the incidence of malaria under 5 was only 33%,less than national level.

Ownerships of ITNs has steadily increased in Tanzania, reaching a peak of 92% of households with at least one ITN in 2011-2012. But in 2017 it was only 78% and improved in subsequent years to 84%. This study exposes a high rate of using bed net (94.6%) as best prevention measure to curb malaria. Free bed nets were supplied only to 67% of house holder of the survey. 54% children and 51% pregnant women slept under bed nets in 2017. Prevalence of malaria in pregnancy is much higher in girls and women aged 15–19 years and decreases with each subsequent pregnancy.

The disease is also much more prevalent in women living with HIV regardless of the number of times they have been pregnant. In this study, 55% pregnant woman only visit hospital for getting treatment and prevention for malaria and 62% pregnant woman are using bed net. Wealth quintile also affect the infection rate as lowest 14.5%, Second lowest 10.9% and middle income 7.9% are highly affected by malaria while in Nyasa 41% poor and 10% middle class were hit by malaria.

Knowledge, attitude and practices about malaria

In a study by David. Z Munisi et al (2019) in pub med journal, out of a total of 295 samples of symptomatic patients in Tumbi Referral Hospital, 93.9% were aware of malaria and 95.31 % knows that it is transmitted by mosquito. Only 65. 8% were taking proper medication but all are likely to sleep under bed nets. In this study, 97% agree that malaria is a life threatening disease and 60% is of strong opinion. Transmitting malaria from one to other is not having a unique opinion among respondents - 50% are disagreeing while 40% are agreeing and 10% does not know about it. 90% believe that avoiding mosquito bite, malaria can be avoided. Only 94.6% are using bed nets and 2% did not take any

prevention. 95% are aware of malaria infection and prevention measures but 2% men and 3% women are not much aware of this problem.

Another study on knowledge, attitude and practices on malaria infection in Massi and Nanyumbu districts, Tanzania, (Billy Nagasala et al.2023), 1556 household heads were interviewed and all had knowledge of malaria but 47.33% had moderate and 13.83% had high knowledge, 83.87% had bed nets. Knowledge on malaria was influenced by gender (aOR=0.72, p-value 0.03<0.05), level of education (aOR=1.50) and occupation of house holder (aOR=1.90). A study on Tanzanian college students, (Yakobo, Nyahoga 2018), searched the knowledge among students of UDOM, 246 students were taken for opinion. 34 to 40 students from each college, 89.4% prevalence was reported and 98% were confidently told about the vector and 87.8% about prevention. 65.8% identified plasmodium as the intracellular parasite, while 24.6% believed it as bacterium and 8.8% as virus. Only 44.7% used bed net in the campus and 13.4% use anti mosquito sprays or ointments, 76.4 % agreed that ITN is best to prevent malaria. Comparing with this study, our study results that house holders of 60% of male, 51% of female, 95% of age group 25-55 years, 93% of primary or low level education, 94% of poor in the survey are having good knowledge of prevention and control of malaria.

In Lindi urban region, Tanzania, in a knowledge study about malaria control, 89.6% agreed that they knew causes of malaria, but 64.2% only think that mosquitoes were the reason for malaria. 22.5% believe that untreated nets will also leads to mosquito bite and malaria, 41.7 % identify themselves affecting malaria without testing, but only 33% go for test, 7.53% go for traditional treatments, 87.9% seek hospital treatment, 56.7% want to use treated bed nets, 14.6% for household cleanliness and 17.8% clearing bushes to reduce malaria. But in this study 7.4% seek traditional treatment, 71.7% for draining water and 62% for cleaning surroundings to reduce malaria spread.

In Karatu district a study on pregnant women, 80% only identify mosquitos as cause, 81% identify malaria as the most common disease in their area. In the age group of 16-20years pregnant women, 24/30 (80%) has adequate knowledge. In the age of 21-30 years, 47/62 (75.8%) had knowledge, while in more than 30 year pregnant women, 19/22 (86%) had good knowledge on malaria but among the illiterate women, 10 out of 16 (62.5%) were not aware of malaria effect and causes. 26% want immediate treatments on symptoms of malaria, while 42% were going to treatments only after 3 days of onset of symptoms. Another study on rural eastern Tanzania, 243 samples were taken, 53% identify Anopheles mosquitoes was responsible for malaria. They feel that under 5years children, (61%) were most vulnerable, 64% rely on ITNs as prevention for malaria. The mosquitoes were entered through widows (46%) by eave opening (10%) and 4% by wall cuts. 58% attend night time out door gatherings, 77% cooking outdoors, went to bed only after 8 pm.

Comparing with this study, our study exposes 28.9% close the doors window all time and 14.4% use gauze wiring on windows to prevent mosquitoes. Only 67% are capable of diagnosing child malaria by which vulnerability is much higher in Nyasa for children especially under 5. Among the higher education students in eastern Tanzania, in a dissertation 58.8% of respondents had less knowledge about malaria disease, in which female are more (46.5% of female and 35.9% of male) and malaria control practices were taken only by 25 %. But males were affected more in the campus due to their resistance to take preventive measures. Among the students only 31.9% identify the symptoms and 42% only use bed nets, 23% dislike it, not able to buy 20.6%, suffocation 14.6%. Only 38.7% use long clothes in the bed, while 69.3% apply self-treatment and getting complicated. In the wet season in SUA 11072 Anophelene and 3620 Cluecine larva was found in the premises of campus by which the prevalence rate was 34.1% with 2.6% more in wet season.

Thus the prevalence and knowledge attitude on prevention of malaria is moderate in Nyasa people and they are also in need of government healthcare services to improve and save from the disaster due to malaria.

Conclusions

This study enlightened the demographic, social and personal factors influencing malaria like sex, education income. It alerted the prevention by government system and self-hygiene to protect from the disease. Women and children under 5 were expose to contract the disease along with pregnant women. Awareness and attitude towards treatment and precaution should be revamped. Bed nets, closed windows and gauze wires usage should be inspired. Medical care centers with low cost and free of cost should be available within 2Km to help many Nyasa inhabitants. Prevalence of malaria is very high in Nyasa region compared to Tanzania rate of incidence and special care should be given on improving the basic health and poverty in this region.

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Competing Interests

I hereby declare that there is no competing interest by any other authors or researchers or agencies on the results.

Tables and Figures

Table:1 Patient Statistics of malaria in Ruvuma and Nyasa

Place	Age (Years)	No. Malaria Cases	Proportion (%)	Ratio
Ruvuma Region	0-5	171433	40.7	2/5
	>5	250053	59.3	3/5
Nyasa District	0-5	16104	43.9	9/20
	>5	20580	56.1	11/20
Nyasa District Hospital	0-5	1152	36	1/3
	>5	2088	64	2/3
Source: Ruvuma Regional Hospital				

Table 2: Prevalence of malaria at a glance

% Prevalence of malaria			
Tanzania	Nyasa	Lipingo	Kingeriketi
9.2	24.9	36	16.7
p values		0.0000	0.0000

Table:3 The regression output-general

Variable	B	S.E.	Wald	Df	Sig.	Exp(B)
Wards	1.255	0.253	24.67	1	0	3.509

Sex	0.528	0.242	4.751	1	0.029	1.59
Age	0.317	0.111	8.079	1	0.004	1.373
Education	0.527	0.207	6.445	1	0.011	1.693
Income	0.814	0.261	9.743	1	0.002	2.257
Constant	-2.305	0.445	26.829	1	0	0.1

Table 4: Male and Female model-regression output.

Variable	Male B	Sig	Female B	Sig.	Exp(B)	Exp(B)
Age	0.229	0.032	0.258	0.018	1.258	1.294
Wards	0.927	0	1.475	0	2.528	4.373
Education	0.393	0.051	0.691	0.001	1.481	1.997
Income	0.977	0.002	0.485	0.063	2.657	1.624
Constant	-1.234	0.001	2.16	0	0.291	0.115

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Persistent Mullerian Duct Syndrome: A case report

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Abstract
The Müllerian duct is the structure that later develops into the female reproductive tract during embryology. It usually obliterates in males. Persistent Müllerian duct syndrome is a disorder characterized by the presence of female reproductive organs in a male individual. The common presentations in males are undescended testes or inguinal hernias. The uterus and fallopian tubes are noted during surgery. This syndrome is due to deficiency of fetal anti-Müllerian hormone which is caused by mutations of the gene for anti-Müllerian hormone or anti-Müllerian hormone receptor. The testosterone levels are normal that's why the development of external genitalia is normal. Imaging investigations are the key to establishing the diagnosis. The treatment modality is surgical for replacing the gonads into their normal position and probably a hysterectomy. We reported a case of a 30-year-old male presented with painful, tender, firm and mobile supra pubic swelling. On urogenital examination he had a well-developed penis with no urethral meatus, the scrotum divides into two parts forming labia majora-like structure with an opening in between. The testicles were not palpable. Imaging investigations reveal the cystic pelvic mass and bilateral testes were not visualized. On laparotomy, a distended uterus with bilateral fallopian tubes was found. The uterus consisted foul smelling pus and the testicles were found. Drainage of pus and then a hysterectomy was done. The patient did well and was discharged home. Globally a few cases of Persistent Müllerian duct syndrome were reported but with a variation of manifestation. Persistent Müllerian duct syndrome is a rare condition.

Keywords: Persistent mullerian duct syndrome, A case at Dodoma Tanzania, Benjamin Mkapa Hospital

Introduction

The Müllerian duct is the embryonic structure that later on develops into the female reproductive tract which is the oviduct, uterus, cervix and upper vagina. It usually obliterates during early development in males, but it is retained in those with persistent Müllerian duct syndrome.
The presentations in males are undescended testes or inguinal hernias. Occasionally, both testes are undescended (bilateral cryptorchidism). Often one testis has descended into the scrotum normally, and one has not. The uterus and fallopian tubes are noted during surgery. The testes and female reproductive organs can be located in unusual positions.

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Persistent Müllerian duct syndrome is due to an autosomal recessive congenital disorder and is a form of pseudohermaphroditism due to the presence of Müllerian derivatives (Imbeaud S et al 1996).

The condition is due to a deficiency of fetal anti-Müllerian hormone effect caused by mutations of the gene for anti-Müllerian hormone or the anti-Müllerian hormone receptor, also may be due to insensitivity to anti-Müllerian hormone (Renu D, et al 2010).

Genetically, and - Müllerian hormone or Müllerian inhibiting substance is secreted by Sertoli cells during an individual's whole life. Its role is to obliterate the Müllerian ducts. The Sertoli cells in males secrete Anti – Mullerian Hormone, through the presence of a Y chromosome (Josso N et al, 2005)

Persistent Müllerian duct syndrome is very rare globally because up to the year 2017, only 150 cases were documented (Nerune SM, et al; 2010).

Mullerian duct derivatives are present in a male foetus up to the 8th week of gestation, and their regression is mediated by the müllerian inhibitory factor produced by Sertoli cells. Failure of synthesis or release of müllerian inhibitory factor causes the persistence of müllerian structures (Manjunath B G et al: 2010). The Wolffian duct development progresses in a normal direction because the testosterone levels are normal. This leads to normally developed external genitalia.

Investigations are mainly imaging (CT, US and MRI). These can distinguish the Müllerian duct derivatives such as the uterus, fallopian tubes, and the upper part of the vagina. A specific ELISA test can be used to determine Anti Mullerian Hormone levels in the serum and is a useful screening method to guide the molecular diagnosis. In most cases, Persistent Müllerian duct syndrome is usually discovered incidentally during surgery for undescended testes or inguinal hernia in boys with normal external genitalia.

Treatment is surgical and consists of replacement of the gonads within the scrotum, requiring careful dissection of the Müllerian derivatives. Total hysterectomy is not recommended because of the risk to the vas deferens. But otherwise, a hysterectomy can be offered to improve the chances of fertility and to prevent the occurrence of neoplastic tissue formation (Colacurci N, et al: 1997).

Case report

We report a case of a 30-year-old male presented at our surgical clinic with the complaint of progressive mild tender supra pubic swelling (figure 1). He reported the swelling to be of eight months duration, there were neither gastrointestinal nor urinary manifestations associated with the swelling. No history of fever was reported. Neither history of marriage nor childbirth. On examination he was an average-built man with an obvious symmetrical supra pubic swelling, extending above the umbilicus, which was mild- tender and mobile.

On urogenital examination he had a well-developed penis with no urethral meatus, the scrotum divides into two parts forming labia majora-like structure with an opening in between (Figures 2 and 3). Upon catheterization, greenish-yellowish pus was drained. The testicles were not palpable. Ultrasound examination and then a CT scan showed features suggestive of cystic pelvic mass and the impression was a mesenteric cyst.

Bilateral testes were not visualized in the scrotum/inguinal canal/abdomen. On explorative laparotomy under general anaesthesia, a huge, distended uterus was visualized with bilateral fallopian tubes (Figures 4, 5, and 6). When opened, the greenish-yellowish pus with a foul smell of approximately 6 litres was extracted (figure 7). On culture and sensitivity of the pus, the Staphylococcus aureus isolated which was sensitive to vancomycin and cefazolin. No testicles were found. A hysterectomy was done. The patient was kept on intravenous antibiotics and analgesics and was discharged on the fifth day postoperatively after fully recovery.

Figure 1: Displays a patient with abdominal distension prepared and ready for exploratory laparotomy

Figure 2

Figure 3

Both figures 2 and 3 show a penis which has no urethral opening and an opening is shown in between the divided scrotum.

Figure 4

Figure 5

Figure 3, 4 and 5 displays a distended uterus with fallopian tubes on its sides

Figure 6

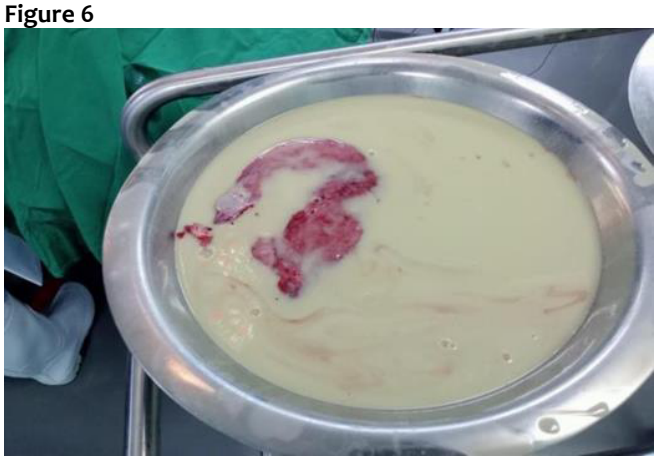

Figure 7: Shows a pus which was drained from the distended uterus

Discussion

Persistent Müllerian duct syndrome is a sexual development disorder characterized by the presence of female reproductive organs in individuals with both normal chromosomes (46, XY) and a normal phenotype of a male. Male sex differentiation is driven by 2 hormones, testosterone and anti-müllerian hormone, responsible for the regression of müllerian ducts in male fetuses.

According to the literature, Persistent Mullerian Duct Syndrome is a rare condition and even in our hospital this condition is not common. A few cases were reported in different articles. Diagnosis is often made incidentally during surgery for an inguinal hernia or during exploration for cryptorchidism. Different cases of Persistent Mullerian Duct Syndrome reported were found to have variations of how they present. In the year 2013, Vijaya Patil et al reported a case of Persistent Mullerian Duct Syndrome in which a patient presented with reduceable painful right-sided groin swelling who had no children and had no sexual dysfunction. Secondary sexual characteristics were well developed and the patient had undescended testes. The scrotum was well developed but semen analysis showed azoospermia (Indian J Surg et al; 2013). In our case, the secondary sexual characteristics were well-developed but the hernia was not present.

In some cases, the reports of histopathological studies of gonads show different variations. For example, in a case reported in 2014 by Vaibhav Nayak et al, a microscopic study of the right gonad showed normal-looking seminiferous tubules with spermatogonia at its various maturation levels for the age of the patient and a normal-looking epididymis. The left gonad showed the structure of the

uterus comprising normal-looking endometrium and myometrium. [8] In our case, the male gonads were not seen radiologically and intraoperatively probably there was testicular agenesis or ectopic testicles.

In patients with intraabdominal testes, both the gonads may be located in a position analogous to the ovaries, with a rudimentary uterus in the centre and the mullerian remnants preventing the mobilization of the testes (Int J Appl Basic Med Res. 2014).

In one case reported in 2021 by Marah Mansour et al, a patient with Persistent Mullerian Duct Syndrome was found to present with abdominal pain and a large cystic mass in the right iliac fossa which after investigations revealed a dermoid cyst in an undescended right-sided testis. Also, a large internal iliac lymph node was found. However, ovaries were not found (Manjunath BG et al; 2010, Mansour, M et al 2021). Our case showed cystic swelling located on the suprapubic region and it was a pus filling the uterus and causing the distension.

Surgical options also depend on the presentation of the condition i.e. no common or single treatment modality. Generally, there should be a removal of mullerian remnants to correct the pathology noted.

Conclusion

Persistent Mullerian Duct Syndrome is a rare condition. Mostly is detected incidentally during surgery for hernia repair, undescended testes or laparotomies for other conditions. Fertility is always unaffected. The pt is phenotypically and genotypically normal.

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Conflict of interest

The Authors have no conflict of interest to declare

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Efficacy of central-shielding external beam radiotherapy for FIGO stage IB2 carcinoma of the cervix: A case report

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Abstract

Introduction: Cervical cancer is now the leading cause of malignancy-related morbidity and mortality in sub-Saharan Africa. Concurrent chemo-radiation using cisplatin alone, or in combination with 5-fluorouracil is considered the main treatment for FIGO stage 1B2 disease or higher for patients who cannot or choose not to have surgery.

Objective: To report the efficacy of central-shielding external beam radiotherapy in the treatment of grade 1, FIGO stage 1B2 carcinoma of the uterine cervix.

Case description: A 55-year-old female reported a history of backache and post-coital pain associated with vaginal bleeding for three months. She was diagnosed with cervical cancer FIGO stage 1B2 and chose not to have surgery.

Method: A computed tomography scan simulation and three-dimensional treatment planning were done, and a total dose of 45Gy of EBRT was administered in fractions for five weeks. Control ultrasonography was then performed to assess the efficacy of CS-EBRT before initiating intracavitary brachytherapy.

Results: Five weeks of CS-EBRT showed significant tumor regression and improvements in health status.

Conclusion: A well-planned central-shielding radiotherapy alone may be curative in selected patients with cervical cancer FIGO stage IB2. Large-scale studies are warranted to compare the efficacy of concurrent chemoradiation with that of radiotherapy in this patient population.

Keywords: Cervical cancer, Human papillomavirus, External beam radiation, Cisplatin.

Introduction

Cancer of the uterine cervix is a major public health concern in sub-Saharan Africa. In 2020, East Africa alone recorded 54,560 new cases of cervical cancer and had unacceptably high age-standardized incidence (40.1) and age-standardized mortality (28.6) rates than anywhere else on earth [GLOBOCAN, 2020]. The HPV (human papillomavirus) oncogenic proteins E5, E6, and E7 crosstalk with PGE_2 (prostaglandin-E2) signaling and COX-2 (cyclooxygenase-2) are known to attack and weaken the immune response, consequently leading to the development of cervical cancer (Zheng & Ding, 2018).

Carcinoma of the uterine cervix stage IB – IIA is confined to the cervix and upper vagina. Tumors of stage IB1 (≤4cm) are normally treated with CCRT (concurrent chemo-radiation therapy), while those of stage 1B2 (≥4cm) are treated with radical hysterectomy and pelvic lymph node

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dissection. However, treatment techniques and modalities must be tailored individually based on clinical, anatomic, and social factors. Accumulating data indicate a notable cure rate with radiotherapy alone for small-stage IB or IIA tumors, whereas the addition of hysterectomy had no survival benefit in this group (Grigsby, 1996). This study, therefore, aimed to investigate the efficacy of central-shielding external beam radiotherapy alone in the treatment of FIGO stage IB2 carcinoma of the uterine cervix.

Case presentation

A 55-year-old female patient presented to the gynaecology department with a three-month history of backache and post-coital pain associated with vaginal bleeding. The patient had five living children and her past obstetric history was insignificant.

Clinical findings

The general condition of the patient was fair, not febrile, and there was no clinical anemia. The patient had a body mass index of 26, blood pressure of 135/90mmHg, and pulse rate of 75 beats per minute.

Diagnostic assessment

Laboratory investigation showed normal urine analysis and normal full blood picture; except for mild anemia (Hb 10g/dl). Speculum examination revealed a hyperaemic cervical lesion about 4-5cm in size, that bled easily when touched. A tissue sample was taken from the lesion and sent for histopathological evaluation. Abdominal-pelvic ultrasonography was then performed and revealed a cervical mass measuring 4.5 x 4.4 x 4.2cm, Fig. 1.

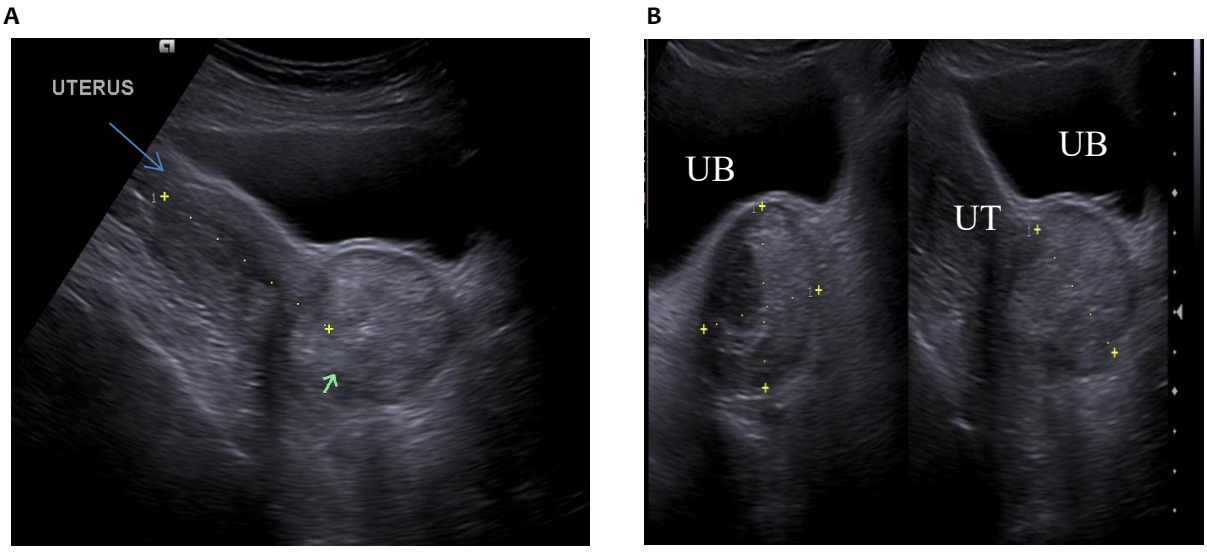

Fig.1 A: An ultrasound image showing a cervical mass (arrow). **B:** Transverse and sagittal images denoting the dimensions of the cervical mass.

There were no signs of hydronephrosis. Biopsy results were positive for a grade 1 invasive squamous cell carcinoma of the uterine cervix. A chest x-ray was ordered to assess for possible lung metastasis but the findings were normal for a chest radiograph. A diagnosis of grade 1, FIGO stage IB2 squamous

cell carcinoma of the uterine cervix was made, and treatment options were explained to the patient and relatives.

Therapeutic intervention

Routine liver and renal function tests were carried out and the patient was simulated on a CT scanner and a three-dimensional conformal RT (3-D CRT) with anteroposterior, and two lateral portals were used for the treatment. The patient received 45Gy of EBRT in 25 fractions of 1.8Gy administered five days a week, for five weeks. The treatment duration was uneventful.

Results

The health status of the patient improved significantly with no backache and without vaginal bleeding. There was a notable regression of the tumor with the size reduced to ≤1cm, Fig. 2.

A **B**

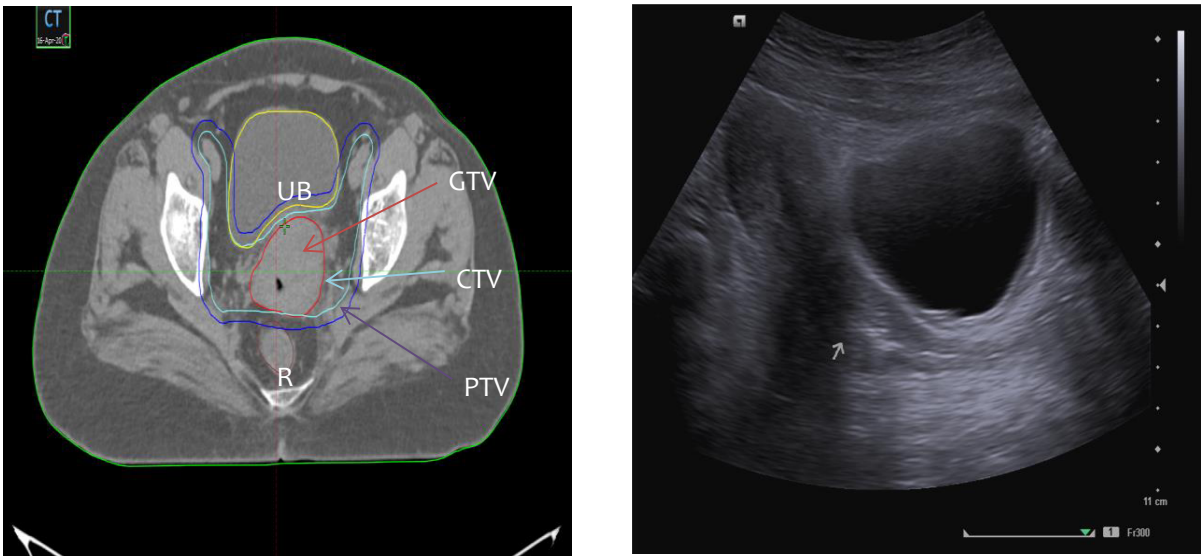

Fig.2. A: Central-shielding EBRT planning. UB- urinary bladder, R- rectum, GTV- gross tumor volume, CTV- clinical tumor volume, PTV- planning tumor volume. **B:** Effect of radiotherapy on the cervical tumor. The arrow shows the place of the original tumor. UT- the uterus.

These findings suggest that the optimal dose of external beam radiotherapy extended to six or seven weeks, plus or minus brachytherapy and without the addition of concurrent weekly cisplatin may be curative for carefully planned patients with carcinoma of cervix stage IB2.

Discussion

Planning of EBRT with 3-D CRT in the treatment of cervical cancer significantly reduces the dose of ionizing radiation delivered to the organs at risk (OARs) notably; the urinary bladder, rectum, and pelvic joints, consequently lowering the risk for radiation-associated complications. Most treatment protocols now include EBRT and ICBT with CCRT as the standard treatment modality for patients with stages I – IVA carcinoma of the uterine cervix. Definitive radiotherapy for cervical cancer consists of whole-pelvic (WP), CS-EBRT, and brachytherapy.

Our understanding of the benefits of CCRT as the standard treatment for advanced loco-regional cervical tumors has been very dynamic because of the conflicting reports from randomized clinical trials. Eifel and colleagues [Eifel *et al*, 2004] reported a survival benefit and improved local tumor control with concurrent chemo-radiation in 403 patients with carcinoma of cervix FIGO stage IB–IIA (tumor size ≥ 5 cm) who received chemo-radiation with three cycles of cisplatin 75mg/m^2 and 5-FU 4g/m^2/96 hour. On the other hand, Pearcey's group (Pearcey *et al*, 2002) observed no benefit of chemotherapy in 259 patients with similar stages of the tumor who received concurrent chemo-radiation with cisplatin 40 mg/m^2/week (up to 6 cycles). This implies that dose and combination factors, as well as patients' characteristics, play a role in the prediction of the outcome in concurrent chemo-radiation therapy. In the case we report here, all such factors were scrutinized and the patient's choice of RT alone was granted, however, with close monitoring.

Treatment recommendations provided by the Group Européen de Curiethérapie–European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) (Haie-Meder *et al*, 2005) provide a clear understanding of the concepts, implications, and terms of the three-dimensional image-guided brachytherapy (3D-IGBT) using computed tomography or Magnetic Resonance Imaging (MRI). These newer technologies make it possible, as in the case presented here, to deliver desired high radiation doses to the tumor while minimizing the doses to adjacent tissues. This addresses not only radiation-associated complications such as fistulas but also increased concerns about chemo-resistance and compliance with chemotherapy.

Conclusions

The findings from this case report suggest a possibility of achieving a curative effect with well-planned radiation therapy alone for a FIGO stage IB2 carcinoma of the uterine cervix. Large-scale studies and clinical trials are warranted to assess its efficacy versus that of the current practice.

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Consent and ethical approval

Permission to publish the case report was obtained from the hospital committee. Written consent was obtained from the patient to report the findings and associated radiological images.

Disclosure

No conflict of interest.

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Annular pancreas as a rare cause of gastric outlet obstruction in a 16-year-old male patient: A case report

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Abstract
Annular pancreas (AP) is a rare cause of congenital gastric outlet obstruction that is usually discovered during the neonatal period. Still, clinical severities can vary over a wide range and definite diagnosis could be delayed until late childhood or adulthood. We report here a case of AP detected in a 16-year-old malnourished male patient who was admitted because of non-bilious vomiting and epigastric fullness after intake of food which was relieved after vomiting. A contrast-enhanced CT scan of the abdomen confirmed the diagnosis of AP. At operation, a complete obstruction of the second part of the duodenum was found, caused by an annular pancreas. No other congenital anomaly of the intra-abdominal organs was noted. He successfully underwent retro-colic gastro-jejunostomy with uneventful postoperative recovery. Though a rare finding, AP should be considered as a differential diagnosis in patients presenting with gastric outlet obstruction after excluding common causes. The rarity of this congenital abnormality and its successful correction by surgical means have prompted us to make the following presentation.

Keywords: *Annular pancreas, duodenal obstruction, surgery*

Introduction

Annular pancreas (AP) is a rare congenital anomaly that causes congenital duodenal obstruction in the neonatal period (Patra *et al.,* 2011).It is characterized by a complete or incomplete ring of pancreatic tissue surrounding the second portion of the duodenum (Patra *et al*., 2011;Alahmadi & Almuhammadi., 2014; Singh *et al*., 2016). Several theories have been proposed but the etiology is still unclear. It is thought to originate from failure of the ventral pancreatic bud to rotate with the duodenum, resulting in encirclement of the duodenum (Leeco., 1910; Baldwin., 1910; Dowsett *et al*., 1989; Shirkhoda., 2000).

AP is usually discovered at the neonatal period.However, the degree of duodenal obstruction and the subsequent obstructive symptoms might be variable, and unrecognized AP has been detected in adolescents or even in adults in some cases (Patra *et al*., 2011; Alahmadi & Almuhammadi., 2014; Singh *et al*., 2016).AP is exceptionally rare in the adult population with incidences varying from 0.005% to 0.015%, and presentation is variable and can mimic a wide range of clinical entities like peptic ulcer, pancreatitisand, more rarely, obstructive jaundice, thereby making the diagnosis difficult (Zyromskiet *al*., 2008; Edman *et al*., 2019; de la Rosa Rodriguez *et al*., 2019; Nur *et al*., 2022).

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Many imaging studies such as X-ray, upper GI series, abdominal ultrasound, abdominal CT scan, ERCP, MRCP, endoscopic ultrasound can be used to diagnose AP. However, in adults x-rays, upper GI series and abdominal ultrasound may be inconclusive. ERCP is effective but invasiveand can precipitate/exacerbate pancreatitis (Singh *et al*., 2016).The diagnosis is currently based on abdominal CT scan and MRCP of the pancreasSingh *et al*., 2016).Surgical bypass leads to fast recovery whenever pancreatic encirclement is associated with duodenal obstruction (Nur *et al*., 2022). In this report, we present a rare case of a 16-year old male patient who presented with obstructive symptoms of duodenal obstruction due to annular pancreas and successfully treated with retro-colic gastro-jejunostomy.

Case report

A 16-year-old male patient presented to our hospital with a recurrent history of non-bilious vomiting since early childhoodworsening in the past 1 year. The vomitus contained food particles that were taken few minutes back. He also complained of epigastric pain and fullness after intake of food which was relieved after vomiting. He reported to have significant weight loss without loss of appetite. He had been treated symptomatically with the clinical diagnosis of chronic gastroenteritis for his recurrent vomiting.

On physical examination, he was found to have the classical signs of malnutrition: Low body weight for age (32kg), prominent bones, depleted fat and muscle, dry and inelastic skin. He was severely wasted, moderately pale but not icteric. His abdomen was soft, scaphoid withmildly palpable distended stomach at the epigastrium. He was found to have positive succession splash.
No masses or hernias were discovered.

Routine biochemical tests revealed hypokalemic hypochloremic metabolic alkalosis, and haematological tests were within normal ranges. Plain abdominal X-Ray and Ultrasound findings were inconclusive for the diagnosis. The arterial phase of an axial multiple detector spiral computed tomography (MDCT) with intravenous and oral contrast only showed a massively dilated stomach full of contrast and a duodenum partially wrapped by the head of the pancreas with the so-called "crocodile jaw" appearance (Figure 1).

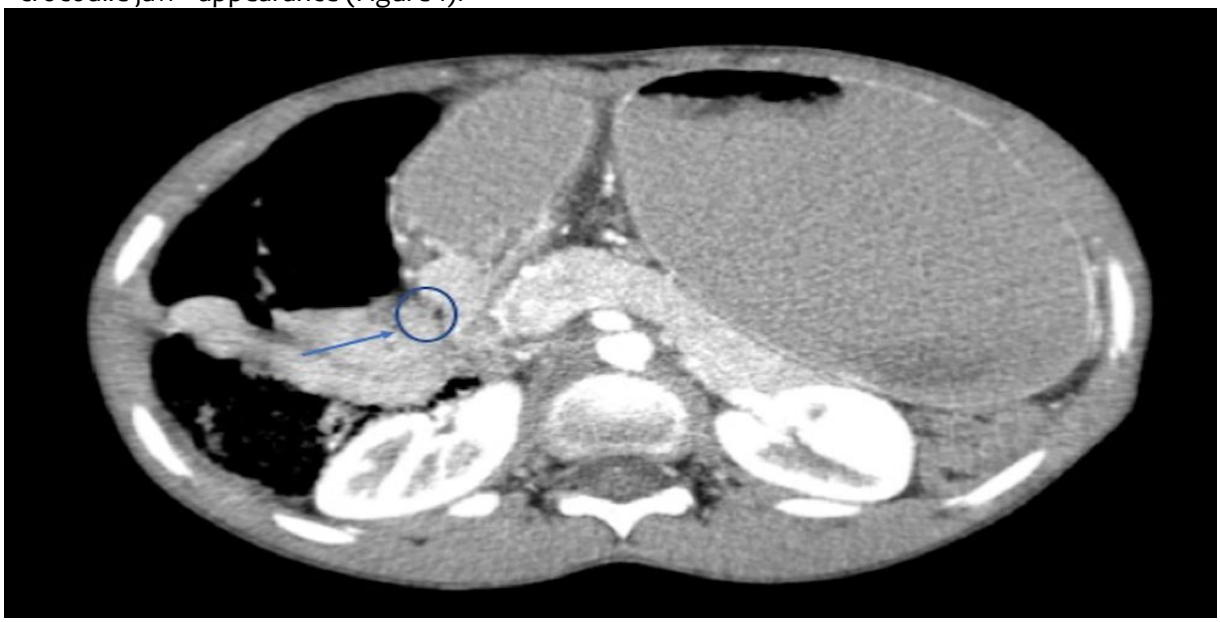

Figure 1: Abdominal computed tomography shows an abrupt narrowing of the duodenal bulb and a massively dilated stomach

A laparotomy with the presumption of an obstructive AP confirmed a thick peri-duodenal band of pancreatic tissue, which required to be bypassed by a retro-colic gastro-jejunostomy. No other congenital anomaly of the intra abdominal organs was noted. Oral feeding started on the fourth postoperative day. The recovery was uneventful, and the symptoms disappeared 2 weeks after the operation. He was dischargedon the 14thpostoperative day after intensive nutritional rehabilitation. At the one-year follow-up, the patient was asymptomatic and his body weight was 45 Kg.

Discussion

Since it was first reported by Tieddmann (1818) and named as annular pancreas by Ecker (1862), only few cases of AP have been reported in literature. AP is a rare congenital abnormalitycharacterized by a complete or incomplete ring ofpancreatic tissue surrounding the second part ofthe duodenum (Patra *et al*., 2011; Alahmadi & Almuhammadi., 2014; Singh *et al*., 2016). Several theories have been proposed to explain the development of annular pancreas. Leeco's and Baldwin's theories are the most acceptable among all. Leeco postulated that the tip of the ventral bud fuses abnormally to the duodenal wall and rotates incorrectly around the duodenum and resulting in a band of fibrous or pancreatic parenchymal tissue around the second part of the duodenum (Leeco., 1910; Baldwin., 1910). Baldwin (1910) reported that this condition arose because of the abnormal movement of the ventral pancreatic bud. The third theory explained by Verga (1972) suggests that the primary abnormality is duodenal with the pancreas "filling the space" around a narrowed duodenum. This results in a complete or incomplete stenosis of the duodenal lumen (Shirkhoda., 2000).

Clinical presentation can vary significantly, from asymptomatic cases to complete duodenal obstruction. The age at presentation depends upon the severity of duodenal obstruction (Patra *et al*., 2011; Alahmadi & Almuhammadi., 2014; Singh *et al*., 2016). It has been estimated that only about 33% of the cases are symptomatic. 50% of patients present in the pediatric age group, 86% of these present in the neonatal period. AP is exceptionally rare inadults and commonly diagnosed during the investigation of symptoms arising due to its complications(Zyromski et al., 2008; Edman *et al*., 2019; de la Rosa Rodriguez *et al*., 2019; Nur *et al*., 2022).In adults, APusually presents between age 20 and 50 and is most commonly associated with abdominal pain and gastric outlet obstruction, secondary to duodenal stenosis (Edman *et al*., 2019).Obstructive symptoms presenting in adults may be due to repeated inflammation, edema leading to fibrosis and scarring (Zyromski et al., 2008; Edman et al., 2019). Sandrasegran *et. al*.(2009) in a study of 40 cases of annular pancreas in adult population revealed that majority of cases were asymptomatic with only 5% cases presenting with gastric outlet obstruction /pancreatitis.

A dual-phase clinical manifestation of AP in the same patient, combining partial duodenal obstruction and abdominal pain and vomiting due to chronic pancreatitis at adult age (Cai *et al*., 2018), as occurred in the patient of the present report, is most unusual. As reported in our patients,vomiting in patients with duodenal obstruction secondary to AP is usually non-bilious in 90% of these cases, mimicking a pyloric obstruction, as the pancreatic encirclement is frequently located proximal to the ampulla of Vater (Patra *et al*., 2011; Singh *et al*., 2016).Delay seeking medical advice contributes to long-lasting unrelieved symptoms in adolescents or adults. It was the case with our patient.Late referral to medical attention was due to cultural, economic and logistic factors common to many rural areas where access to specialist care is still problematic.

The diagnosis of AP can be suggested through imaging tests such as X-ray, upper GI series, abdominal CT scan, ERCP, MRCP, endoscopic ultrasound, but the definitive diagnosis is surgery which is considered diagnostic gold standard (Singh *et al*., 2016).The diagnosis of AP beyond neonatal age requires a high index of suspicion. In adults, ultrasonography, plain abdominal x-ray and upper GI series

may be inconclusive as reflected in our patient. Jadvar and Mindelzun(1999) showed that contrast-enhanced abdominal CT is useful in directly visualizing the completeor partial AP tissue in adults, and Sandrasegaran *et al* (2009) suggested an abdominal CT finding of a crocodile jaw configuration of pancreatic tissue surrounding the second part of the duodenum, which was suggestive of thepresence of AP in adults. This observation is reflected in our patient in whom the definite diagnosis was confirmed by a contrast-enhanced abdominal CT scan.

The treatment of choice in patients with symptomatic AP is surgery. The optimal operationhas been a matter of debate. The goal of surgery is torelieve duodenal or gastric outlet obstruction by abypass surgery of the annulus, which can be achieved viaaduodenoduodenostomy, gastro-jejunostomy, or aduodenojejunostomy (Cai *et al*., 2018).Resection of the annulus is contraindicated since it is associated with serious complicationssuch as pancreatitis, pancreatic fistula formation, andpancreatic insufficiency leading to unacceptablyhigh morbidity(Zyromski*et al*., 2008; Cai *et al*., 2018; Edman *et al*., 2019; de la Rosa Rodriguez *et al*., 2019; Nur *et al*., 2022). The results of previously reported operations are satisfactory, especially the gastrojejunostomy and the duodenoduodenostomy, which are simple operations performed frequently and have the best results (Nur *et al*., 2022). In this study, our patient successfully underwent retrocolic gastrojejunostomy with uneventful postoperative recovery. At one year follow up,the patient had gained weight and was doing well.

Conclusion

In this study, we successfully diagnosed and treated an AP in a 16-yearold male, who suffered from a long standing history of duodenal obstruction without definite diagnosis.The definite diagnosis was confirmed by a contrast-enhanced abdominal CT scan and successfully underwent retrocolic gastrojejunostomy with uneventful postoperative recovery.. An annular pancreas, although rare, should be considered as differential diagnosis in patient with unresolved symptoms of gastric outlet obstruction after excluding common causes.

Ethical considerations

The permission to conduct this case study was obtained from Ikonda Hospital authority (Hospital Management Team) before the commencement of the study. Informed consent was sought from the parents of the patient.

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