Tanzania Journal of Health Research
Volume 25, Number 1, January 2024
https://dx.doi.org/10.4314/thrb.v25i1.11

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[1], 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%).

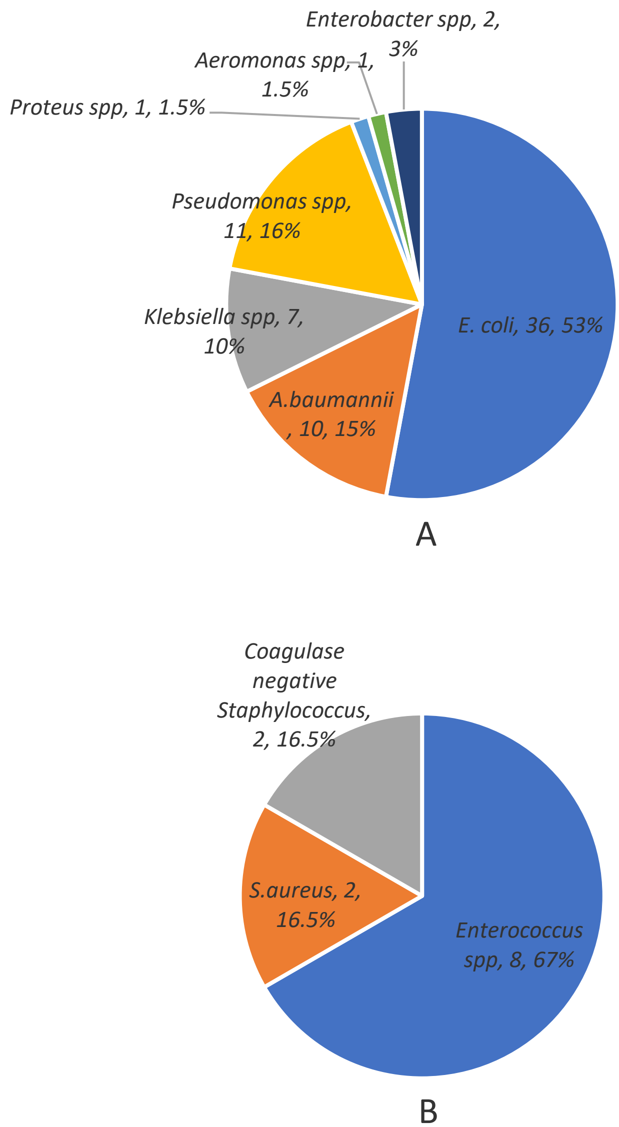

Figure 1: The proportion of each isolated Gram negative bacteria species (A) and Gram positive bacteria species (B).

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.

Acknowledgement

We would like to thank the staff and management of ORCI, National Public Health Laboratory and MUHAS for their support towards this work.

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.

Funding

No specific funding was received for conducting this study.

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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