ORIGINAL RESEARCH

Bacterial profile, antibiotic resistance pattern and associated factors among cancer patients at University of Gondar Hospital, Northwest Ethiopia

Alelign Fentie[1]
Yitayih Wondimeneh[1]
Abera Balcha[2]
Anteneh Amsalu[1]
Birhanemeskel Tegene
Adankie[1]

[1]Department of Medical Microbiology, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia; [2]School of Medicine, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia

Introduction: Cancer is alarmingly increased in developing countries like Ethiopia, where multidrug resistant bacterial infection is rampant. The aim of this study was to determine the bacterial profile, antimicrobial resistance pattern, and associated factors among cancer patients attending University of Gondar Hospital.

Methods: A consecutive 216 cancer patients were recruited from February to April, 2017. Socio-demographic and clinical data were collected using a structured questionnaire. Culture and antibiotic resistance were done following standard microbiological procedures.

Result: The overall prevalence of bacterial infection was 19.4%. The predominant bacterial isolates were *Staphylococcus aureus* (28.6%), followed by coagulase negative staphylococci (26.2%) and *Escherichia coli* (21.4%). Multidrug resistance was detected in 46.5% bacterial isolates. Methicillin resistance was detected in 25% of *S. aureus* and in 45.5% of coagulase negative staphylococci. Fluoroquinolone resistance was detected in 33.3% of *E. coli* isolates. Cancer patients with solid tumor, started cancer therapy, and being symptomatic had higher odds of culture positivity.

Conclusion: The overall burden of bacterial infection among cancer patients is considerably high. The findings of this study inform baseline information for policymakers and call for additional studies with large isolates in different cancer treatment centers in the region and in the country to better understand the bacterial isolate and resistance pattern.

Keywords: cancer patient, bacterial profile, antibiotic resistance, Ethiopia

Introduction

Major advances in the care of cancer patients over the past several decades have led to significant improvement in patient survival. Despite these advances, cancer patients are prone to serious infection complications with substantial morbidity and mortality. In this patient population, infection risk results from a complex interplay between the host's underlying immunodeficiency and the nature of treatment practices they experience (like surgery, radiation therapy, chemotherapy), prophylaxis use, and application of invasive procedures (central venous catheter and urinary catheter).[1] The symptoms of infection in cancer patients could be masked by the cancer treatment modalities,[2] that is an indicator for considering asymptomatic infections.

Previous studies on bacterial infection and drug resistance pattern among cancer patients were mainly focused on bloodstream infection (BSI) with hematologic malignancies.[2] However, cancer patients who have solid tumors might have a tendency to undergo surgery to remove the tumor or sometimes due to other medical reasons. This,

Correspondence: Birhanemeskel Tegene Adankie
Department of Medical Microbiology, University of Gondar, P.O. Box 196, Gondar, Ethiopia
Tel +251 91 191 0816
Email meskelbirehane@gmail.com

thus, increases the potential of acquiring bacterial infection either by endogenously normal flora near the operative sites or exogenously from the hospital environments, such as in the air, hospital staff, inanimate objects, and medical equipment, as a result of their prolonged and frequent contact.[4,5]

Therefore, patients with both type of cancer are highly susceptible to almost any type of bacterial infection.[6] Among Gram positive bacteria (GPB) genus Staphylococcus and from Gram negative bacteria (GNB): *Escherichia coli, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* are frequently associated.[7] Moreover, frequent prescription of broad-spectrum antibiotics as prophylaxis among cancer patients may potentially alter the composition of endogenous flora and select multidrug resistant pathogens such as methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), and Gram-negative bacilli (eg, fluoroquinolone-resistant Escherichia coli [FREC]).[8–10] As a result, empirical antibiotic treatments of cancer patients are continually challenged by (1) the change in frequency of Gram-positive and Gram-negative bacteria and (2) the emergence of new antimicrobial resistant pathogens. The pattern and prevalence of resistance may vary with respect to geographical location and difference in infection prevention and control strategies between health care facilities.

In Ethiopia, the cancer care services were first started in an organized manner in 1998 at Tikur Anbesa Specialized Hospital,[11] and have been subsequently scaled up into eight cancer centers including the University of Gondar Hospital in 2015. The treatment of bacterial infections in patients with cancer should often rely on the use of established guidelines, along with consideration of the local epidemiology and antibiotic susceptibility patterns of the potential etiologic agents. However, in Ethiopia identification and drug susceptibility testing are not routinely performed, so patient management is based on empirical treatment. The actual burden and antimicrobial resistance pattern of bacterial isolates are not known. Thus, the present study provides baseline information on the spectrum of bacterial isolates, antimicrobial resistance patterns, and associated risk factors in cancer patients attending the University of Gondar Hospital, Northwest Ethiopia.

Materials and methods
Ethical consideration
The proposal was reviewed and approved by the School of Biomedical and Laboratory Science ethical committee. Permission was obtained from the University of Gondar Hospital administration. The purpose of the study was explained to each study participant. In addition to informed written consent, obtained from each adult participant, assent was obtained from a parent or legal guardian of patients under the age of 18 years. Patient information was anonymized and deidentified prior to analysis. The laboratory result was given to the attending physician and treated accordingly.

Study design, area, and period
A hospital-based cross-sectional study was conducted at the University of Gondar Hospital, cancer treatment center from February to April, 2017. The hospital is located in Gondar town, which is 182 km from Bahir Dar, the capital city of Amhara regional state, and 747 km from Addis Ababa, the capital city of Ethiopia. Apart from other services, the established cancer treatment center provides services for 2,300 cancer cases. The cancer treatment center has outpatient and inpatient departments with 20 beds. The most common treatment available for cancer patients in the center are surgery and chemotherapy.

Study population
All cancer confirmed patients who visited the University of Gondar Hospital cancer treatment center during the study period.

Operational definition
Multiple drug resistant (MDR) was defined as a bacterial isolate, which is resistant to one or more antibiotics in three or more classes of antimicrobials agents.[31]

MRSA and methicillin-resistant coagulase negative staphylococci (MRCoNS) were defined as *Staphylococcus aureus* and CoNS resistance for cefoxitin disk (≥21 mm).[12]

BSI was defined as isolation from blood of one (monomicrobial) or more (polymicrobial) clinically significant organisms during a febrile episode.

A febrile patient was defined as a cancer patient having a single auxiliary temperature of >37.5°C sustained over a 1-hour period.

Clinical and laboratory data
Clinical examination and other co-morbidity factors were diagnosed by an oncologist. Socio-demographic and clinical data were collected by using a structured questionnaire by nurses working in the center. According to the patients' clinical status, different types of specimen were collected.

Blood sample collection and processing

Blood samples (5 mL for adults and 1 mL for children each) for cultures were obtained from each patient who developed fever at the time of diagnosis. Blood samples were drawn from two different sites of peripheral vein aseptically (disinfecting with 70% alcohol and 2% tincture of iodine) by experienced nurses prior to any antibiotic use. The collected blood samples were then transferred into culture bottles of sterile tryptic soy broth (Oxoid Ltd., Basingstoke, UK). Bottles were incubated at 37°C for 7 days and observed for signs of bacterial growth (turbidity, hemolysis, clot formation) on a daily bias for up to 7 days. Bottles which showed signs of growth were gram stained and subcultured on blood agar, chocolate agar, MacConkey agar, and mannitol salt agar (Oxoid Ltd.). These plates were than aerobically incubated for 18–24 hours at 37°C. Blood sample containing broths with no bacterial growth after 7 days was subcultured before being reported as a negative result.

Absolute neutrophil count

Samples (2 mL and 1 mL of blood from adults and children, respectively) were collected simultaneously using ethylene diamine tetra acetic acid tubes during blood collection for culture. Absolute neutrophil count was done using a XT-4000i hematology analyzer (Sysmex Europe GmbH, Norderstedt, Germany).

Urine sample collection and processing

Midstream urine was collected with a sterile urine container from both symptomatic and asymptomatic urinary tract infection (UTI) cases. Midstream urine specimens were inoculated on cystine lactose electrolyte deficient (CLED) by using a calibrated loop (0.001/mL). All the media were incubated at 37°C for 18–24 hours. Significant bacteriuria was defined as a colony count $\geq 10^5$ CFU/mL urine.

Wound swab/ear discharge collection and processing

Before antibiotics were started, wound swab and ear discharge samples were collected aseptically based on the clinical manifestations of the cancer patients by using a sterile saline moistened cotton swab. The swabs were streaked on MacConkey agar, chocolate agar, blood agar plates, and mannitol salt agar. These plates were then aerobically incubated for 18–24 hours at 37°C.

Bacterial identification

The bacterial pathogens were identified after appearance of growth on subcultured/cultured plates of blood/wound swab/discharge samples and significant growth on CLED by standard microbiological and biochemical procedures.[13] CoNS were only considered as causative pathogens if similar pathogens were isolated on two blood samples drawn on separate occasions.

Antimicrobial susceptibility testing

Antibiotic susceptibility testing of bacterial isolates was done by Kirby Bauer disc diffusion method using Muller Hinton agar (MHA) plate (Oxoid Ltd.).[14] Three-to-five pure colonies from a fresh non-selective agar plate were selected and transferred to 5 mL sterile nutrient broth (Oxoid Ltd.) and thoroughly mixed to make the suspension homogenous. The mixture was transferred into sterile normal saline by sterile pipette and turbidity was adjusted visually with sterile normal saline to match with a 0.5 McFarland standard. The suspension was then inoculated uniformly over the entire surface of a MHA plate using a sterile swab. The inoculated plates were left at room temperature to dry for 3–5 minutes. Using sterile forceps, the antibiotic discs were placed on MHA by considering 24 mm distance between each disk and 15 mm from the border. The tested antibiotic discs include: ciprofloxacin (5 µg), gentamicin (10 µg), norfloxacin (10 µg), and nitrofurantoin (300 µg), for both Gram positive and Gram negative bacterial isolates; cot-trimoxazole (25 µg), penicillin (10 µg), vancomycin (30 µg), cefoxitin (30 µg), and tetracycline (30 µg) for GPB. Amikacine (30 µg), ceftriaxone (30 µg), cefepime (30 µg), cefixime (5 µg), ampicillin (10 µg), amoxicillin/clavulanic acid (20/10 µg), and nalidixic acid (30 µg) were used for GNB. After 18–24 hours incubation at 37°C, the zone of inhibition was measured and reported as susceptible (S), intermediate (I), or resistance (R), according to the clinical and laboratory standard institute (CLSI) guideline.[12]

Quality control

The reliability of the study findings was guaranteed by implementing quality control measures that include sterility and performance checks throughout the whole process of the laboratory work. *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, and *S. aureus* ATCC 25923 control strains were used. Moreover, the validity and completeness of the questionnaire were checked daily by the principal investigator.

Data analysis

Data were entered, coded, and analyzed using SPSS software version 20. Variables that showed a significant association in a bivariate analysis were selected for further analysis using

multivariable logistic regression analysis. A *P*-value <0.05 was considered as statistically significant. The strength of the association was interpreted using an adjusted odds ratio in a 95% confidence interval.

Ethics approval and consent to participate

This study was approved by the institutional review board (IRB) of University, College of Medicine and Health Sciences. Informed written consent and/assent was obtained from study participants. Patient information was anonymized and deidentified prior to analysis.

Results

Sociodemographic characteristics

A total of 216 cancer patients were included in the study. Out of these, 136 (63.0%) were females and 80 (37.0%) were males, with a male-to-female ratio of a 1:1.7. The mean age±SD of study participants was 41.5±17.77 years, range 1–73 years. The majority (134, 62.0%) of study subjects had no formal education, and 83 (38.4%) had housewife as their occupation. Among the study population, 111 (51.4%)

were rural in residence and 138 (63.9%) were recruited in the outpatients department (Table 1).

Clinical characteristics of study populations at the time of diagnosis

Out of 216 cancer patients, 167 (77.3%) had a solid tumor. Among the total, breast cancer (41, 19.0%) was the highest, followed by lymphoma (34, 15.7%) and ovarian tumor (26, 12.0%). Thirty-six (16.7%) cancer patients were stage IV, and 155 (71.8%) had started cancer therapy. Of these, the most frequently used were chemotherapy (114, 73.5%), either alone or in combination with surgery or radiotherapy. The majority of the patients (145, 67.1%) had a history of catheterization and had at least one sign and symptoms (116,

Table 1 Socio-demographic characteristics of cancer patients at the University of Gondar Hospital, Northwest Ethiopia, 2017

Characteristics (n=216)	Frequency	Percentage
Age (years)		
<25	32	14.8
25–44	74	34.3
45–64	87	40.3
>65	23	10.6
Sex		
Male	80	37.0
Female	136	63.0
Educational level		
No formal education	134	62.0
Primary	45	20.8
Secondary	10	4.6
Tertiary	27	12.5
Occupational status		
Civil servant	28	13.0
Farmer	59	27.3
Merchant	20	9.3
Housewife	83	38.4
Others	26	12.0
Residence		
Rural	111	51.4
Urban	105	48.6
Patient setting		
Inpatient	78	36.1
Outpatient	138	63.9

Table 2 Clinical characteristics of cancer patients at the University of Gondar Hospital, Northwest Ethiopia, 2017

Clinical profiles	Frequency	Percentage
Type of cancer		
Hematological	49	22.7
Solid	167	77.3
Specific type of cancer		
Breast cancer	41	19.0
Lymphoma	34	15.7
Ovarian cyst	26	12.0
Leukemia	19	8.8
Cervical cancer	15	6.9
Colon cancer	11	5.1
Lung cancer	9	4.2
Retinoblastoma	9	4.2
Colorectal cancer	7	3.2
Others	45	20.8
Stage of cancer		
Stage I	12	5.6
Stage II	19	8.8
Stage III	31	14.4
Stage IV	36	16.7
Unknown stage	118	54.6
Started cancer therapy		
Yes	155	71.8
No	61	28.2
Types of cancer therapy		
Chemotherapy	114	73.5
Surgery	84	54.2
Radiotherapy	3	1.9
History of catheter use		
Yes	145	67.1
No	71	32.9
Febrile		
Yes	23	10.6
No	193	89.4
Clinical status		
Symptomatic cases	116	53.7
Asymptomatic cases	100	46.3

53.7%) for different clinical features. Of these, 23 (10.6%) were febrile at the time of diagnosis (Table 2).

Bacterial profiles and site of isolation

Bacterial cultures were positive in 42 patients (19.4%, 95% CI=14.4–25.0) with 43 isolates. Polymicrobial growth was recovered only in one specimen. Among the 42 culture positive cases, 6% (6/100) were from the urine of asymptomatic patients. The majority of the isolates were from urine (n=32) and wound swab (n=7), with a low frequency of the isolates from blood (n=3) and ear discharge (n=1) samples. GPB species (25, 58.1%) were higher than GNB species (18, 41.9%). GPB accounted for 41.9% (18/43) of the UTI, 9.3% (4/43) of wound infections, and 7% (3/43) of blood stream infections while GNB attributed to 32.6% (14/43) of UTI and 7% (3/43) of wound infections. The overall predominant bacterial isolates were *S. aureus* (12, 28.6%), followed by CoNS (11, 26.2%) and *E. coli* (9, 21.4%). The most common

isolates identified in UTI were *E. coli* and CoNS (9, 28.1%) each (Table 3).

Antimicrobial resistance pattern

As to the antimicrobial resistant pattern for GPB, high resistance rates were observed, among total GPB, to penicillin (18, 72.0%) and cot-trimoxazole (10, 43.5%). On the other hand, a low resistance rate was detected for nitrofurantoin (1, 5.6%). Among the predominant isolates, MRSA and MRCoNS were detected in three (25%) and five (45.5%), respectively. VRE was also detected in one isolate (Table 4).

Similarly, high resistance rates to ampicillin (15, 88.2%), amoxicillin/clavulonic acid (14, 82.4%), and nalidixic acid (8, 57.1%) were observed in GNB. On the other hand, all GNB were sensitive to nitrofurantoin and had shown low resistance to amikacine (1, 5.6%). Among the most common isolated GNB, *E. coli* showed a higher rate of resistance to amoxicillin/clavulonic acid (8, 88.9%), ampicillin (7, 77.8%),

Table 3 Distribution of bacterial isolates from different clinical specimens among cancer patients at the University of Gondar Hospital, Northwest Ethiopia, 2017

Bacterial isolates	Clinical features				
	Blood (n=23)	Urine (n=191)[a]	Wound swab (n=12)	Ear discharge (n=2)	Total (%) (n=228)
Staphylococcus aureus	2	7 (21.9)	3	0	12 (28.6%)
CoNS	1	9 (28.1)	1	0	11 (26.2%)
Enterococci spp.	0	2	0	0	2 (4.8%)
Subtotal of Gram positive	3	18	4	0	25 (58.1%)
Escherichia coli	0	9 (28.1)	0	0	9 (21.4%)
Klebsiella pneumoniae	0	1	1	0	2 (4.8%)
Proteus spp.	0	2	0	1	3 (7.1%)
Citrobacter spp.	0	1	1	0	2 (4.8%)
Enterobacter spp.	0	1	0	0	1 (2.4%)
Pseudomonas aeruginosa	0	0	1	0	1 (2.4%)
Subtotal of Gram negative	0	14	3	1	18 (41.9%)
Grand total	3 (2.4%)	32 (16.8%)	7 (58.3%)	1 (50%)	43 (19.9%)

Note: [a]Including 100 urine sample from asymptomatic cases.
Abbreviation: CoNS, coagulase negative staphylococci.

Table 4 Antimicrobial resistance of GPB isolated from cancer patients at the University of Gondar Hospital, Northwest Ethiopia, 2017

Antimicrobial tested	GPB isolates, N (%)			
	Staphylococcus aureus (n=12)	CoNS (n=11)	Enterococci spp. (n=2)	Total
Ciprofloxacin	1 (8.3)	5 (45.5)	1 (50.0)	7 (28.0)
Gentamycin	1 (8.3)	4 (36.4)	–	5 (21.7)
Nitrofurantoin	0	0	1 (50)	1 (5.6)
Norfloxacin	0	2 (22.2)	1 (50)	3 (16.7)
Cot-trimoxazole	5 (41.7)	5 (45.5)	–	10 (43.5)
Penicillin	7 (58.3)	10 (90.9)	1 (50)	18 (72.0)
Vancomycin	–	–	1 (50)	1 (50)
Cefoxitin	3 (25.0)	5 (45.5)	–	8 (34.8)
Tetracycline	3 (60)	1 (50)	1 (50)	5 (20.0)

Abbreviations: GPB, gram-positive bacterial; CoNS, coagulase negative staphylococci.

and nalidixic acid (6, 66.7%). Moreover, fluoroquinolone (ciprofloxacin and/or norfloxacin) resistance was observed in 33.3% of *E. coli* (FREC) (Table 5).

MDR

In this study, the prevalence of MDR was 20 (46.5%), while five (11.6%) bacterial isolates were sensitive to all antibiotics tested, and none of the isolated pathogens were resistant to all antibiotic classes tested. On the other hand, the result of drug resistance patterns compared within species specific showed that two (100%) of the *K. pneumoniae* and six (66.7%) *E. coli* were MDR isolates (Table 6).

Factors associated with culture positivity rate

In a bivariate logistic regression analysis, cancer patients with solid tumor were 3.3 times more likely to be culture

positive (COR=3.31; 95% CI=1.120–9.805; P=0.03) as compared to patients with hematological cancer. Moreover, the culture positivity rate among cancer patients started cancer therapy (COR=2.77; 95% CI=1.104–6.969; P=0.015), being catheterized (COR=2.91; 95% CI=1.221–6.930; P=0.016) and being symptomatic during diagnosis (COR=7.85; 95% CI=2.826–17.589; P=0.00) were significantly higher as compared to their counterparts. None of the socio-demographic factors, patient setting, specific type of cancer, stage of cancer, or hospital admission had statistically significant association with culture positivity.

In multivariate logistic analysis, cancer patients who started cancer therapy were 3.38 times more likely culture positive (aOR=3.38; 95% CI=1.286–8.882: P=0.014) as compared to patients who had not yet started therapy, and cancer patients with solid tumor had 3.9 times higher odds of culture positivity (aOR=3.91; 95% CI=1.026–9.882: P=0.045) as

Table 5 Antimicrobial resistance pattern of GNB isolated from cancer patients at the University of Gondar Hospital, Northwest Ethiopia, 2017

Antimicrobial tested	GNB isolates, N (%)						
	Escherichia coli	*Proteus* spp.	*Klebsiella pneumoniae*	*Citrobacter* spp.	*Pseudomonas aeruginosa*	*Enterobacter* spp.	Total
Ampicillin	7 (77.8)	3 (100)	2 (100.0)	2 (100.0)	—	1 (100)	15 (88.2)
Amikacine	1 (11.8)	0	0	0	0	0	1 (5.6)
AMC	8 (88.9)	2 (66.7)	2	2	—	0	14 (82.4)
Ceftriaxone	3 (33.3)	0	1	0	—	0	4 (35.5)
Ciprofloxacin	3 (33.3)	0	1	1	0	0	5 (27.8)
Gentamycin	2 (22.2)	0	2	0	1	0	5 (27.8)
Nalidixic acid	6 (66.7)	0	1	1	—	0	8 (57.1)
Nitrofurantoin	0	0	0	0	—	0	0
Norfloxacin	3 (33.3)	0	1	1	—	0	5 (35.7)
Cefepime	3 (33.3)	0	1	1	0	0	5 (27.8)
Cefixime	3 (33.3)	1 (33.3)	1	1	—	0	6 (35.3)

Abbreviations: AMC, amoxicillin/clavulonic acid; GNB, gram-negative bacterial.

Table 6 Multiple drug resistance patterns of bacteria isolated from cancer patients at the University of Gondar Hospital, Northwest Ethiopia, 2017

Bacterial isolates	Antibiogram pattern, N (%)						
	R0	R1	R2	R3	R5	R6	MDR
Staphylococcus aureus	3 (25.0)	4 (33.3)	1 (8.3)	3 (25.0)	1 (8.3)	0	4 (33.3)
CoNS	0	5 (45.5)	1 (9.1)	1 (9.1)	3 (27.3)	1 (9.1)	5 (45.5)
Escherichia coli	1 (11.1)	1 (11.1)	1 (11.1)	3 (33.3)	1 (11.1)	2 (22.2)	6 (66.7)
Proteus spp.	0	1 (33.3)	1	1	0	0	1 (33.3)
Klebsiella pneumoniae	0	0	0	1	0	1	2 (100.0)
Enterococci spp.	1	0	0	0	0	1	1 (50.0)
Citrobacter spp.	0	0	1	0	1	0	1 (50.0)
Enterobacter spp.	0	1	0	0	0	0	0
Pseudomonas aeruginosa	0	1	0	0	0	0	0
Total	5 (11.6)	13 (30.2)	5 (11.6)	9 (20.9)	6 (14.0)	5 (11.6)	20 (46.5)

Note: R0: sensitive for all classes of antibiotics; R1: resistance for one class of antibiotics; R2: resistance for two classes of antibiotics; R3: resistance for three classes of antibiotics; R5: resistance for five classes; R6: resistance for six classes of antibiotics.
Abbreviations: MDR, multiple drug resistance; CoNS, coagulase negative staphylococci.

Table 7 Factors associated with culture positivity rates of cancer patients at the University of Gondar Hospital, Northwest Ethiopia, 2017

Variables		Culture result		COR (95% CI)	AOR (95% CI)	*P*-value
		Neg, n (%)	Pos, n (%)			
Sex	Male	68 (85)	12 (15.0)	1		
	Female	106 (77.9)	30 (22.1)	1.60 (0.769–3.346)		
Age (years)	<25	27 (84.4)	5 (15.6)	1		
	25–44	56 (75.7)	18 (24.3)	1.74 (0.582–5.173)		
	45–64	72 (82.8)	15 (17.2)	1.13 (0.373–3.395)		
	≥65	19 (82.6)	4 (17.4)	1.14 (0.269–4.797)		
Education	No formal education	104 (77.6)	30 (22.4)	1.27 (0.443–3.636)		
	Primary	40 (88.9)	5 (11.1)	0.55 (0.143–2.110)		
	Secondary	8 (80.0)	2 (20.0)	1.10 (0.177–6.848)		
	Tertiary	22 (81.5)	5 (18.5)	1		
Occupation	Civil servant	22 (78.6)	6 (21.4)	1		
	Farmer	48 (81.4)	11 (18.6)	0.84 (0.275–2.563)		
	Merchant	19 (90.0)	1 (5.0)	0.19 (0.021–1.749)		
	Housewife	64 (77.1)	19 (22.9)	1.09 (0.386–3.073)		
	Others	22 (84.6)	4 (15.4)	0.87 (0.231–3.297)		
Residence	Rural	87 (78.4)	21 (24.6)	1.33 (0.676–2.631)		
	Urban	87 (82.9)	18 (17.1)	1		
Patient setting	Inpatient	59 (75.6)	19 (24.4)	1.61 (0.813–3.191)	1.52 (0.710–3.266)	0.280
	Outpatient	115 (83.3)	23 (16.7)	1	1	
Type of cancer	Hematological	45 (91.8)	4 (8.2)	1	1	
	Solid	129 (77.2)	38 (22.8)	3.31 (1.120–9.805)[a]	3.19 (1.026–9.882)[b]	0.045
Stage of cancer	I	10 (83.3)	2 (16.7)	1		
	II	16 (84.2)	3 (15.8)	0.94 (0.133–6.628)		
	III	26 (83.9)	5 (16.1)	0.96 (0.160–5.786)		
	IV	26 (72.2)	10 (27.8)	1.92 (0.357–10.363)		
	Unknown stage	96 (81.4)	22 (18.6)	1.15 (0.234–5.604)		
Hospital admission	No	23 (92.0)	2 (8.0)	1	1	
	Yes	151 (79.1)	40 (20.9)	3.05 (0.689–13.468)	1.24 (0.221–6.915)	0.810
Cancer treatment	Yes	119 (76.3)	36 (23.2)	2.77 (1.104–6.969)[a]	3.38 (1.286–8.882)[b]	0.014
	No	55 (90.2)	6 (9.8)	1	1	
Catheter use	Yes	110 (75.9)	35 (24.1)	2.91 (1.221–6.930)[a]	2.04 (0.747–5.580)	0.164
	No	64 (90.1)	7 (9.9)	1	1	
Symptomatic for infection	No	94 (94.0)	6 (6.0)	1	1	
	Yes	80 (69.0)	36 (31.0)	7.05 (2.826–17.589)[a]	7.85 (3.086–19.980)[b]	0.001
Neutrophil count (cells/µL)	<4,000	84 (84.0)	16 (16.0)	1.71 (0.203–14.484)		
	4,000–11,000	81 (76.4)	25 (23.6)	2.78 (0.335–23.006)		
	>11,000	9 (90.0)	1 (10.0)	1		

Notes: [a]Associated factors in bivariate logistic regression analysis. [b]Associated factors in multivariate logistic regression analysis.
Abbreviations: Neg, negative; Pos, positive.

compared to hematological malignancy. Moreover, being symptomatic during diagnosis had 7.9 times higher odds of culture positivity (aOR=7.85; 95% CI=3.086–19.980: *P*=0.001) as compared to asymptomatic cases. However, in the multivariate regression model, we observed that being catheterized is no more an independent predictor (Table 7).

Discussion

The overall prevalence of bacterial infections among cancer patients in this study was 19.4%. This finding was comparable with the studies conducted in Romania (14.92%)[15] and Iran (24.6%) among cancer patients with BSI.[16] However, this

finding was lower as compared to other studies conducted in Sudan (48.1%)[5] and Iraq (mean of 44.2%).[17] The variation in prevalence might be explained by the fact that differences in geographical location and the use of a sensitive blood culture system (BD Phoenix automated microbiology system, Waldorf, Germany) that might increase culture positivity rate.[16,17] Besides the difference in the study population, in Iraq the study population were children with febrile neutropenia, while in Sudan the study was on cancer patients with nosocomial infection, that might have a high culture positivity rate as compared to our study populations, in which almost half of the study population were asymptomatic cancer patients.

The epidemiology of bacterial infections among cancer patients showing a shift in the prevalence from Gram-positive to Gram-negative bacteria and vice versa remains controversial. In this study, GPB were the predominant cause of bacterial infection, as compared to GNB. This finding is in line with studies conducted elsewhere in cancer patients with BSI, febrile neutropenia, or hematological neoplasia.[16,18,19] The possible reasons for the preponderance of GPB in this study might be the increased use of indwelling catheters. Moreover, chemotherapy-induced mucositis and use of both prophylactic and empiric antibiotic regimens targeting GNB diminishes recovery of Gram-negative pathogens, while selecting for GPB were reported.[9,10] In contrary, a study from other African countries reported that GNB were significantly more predominant isolates from cancer patients,[5,7] and current data from other studies indicates the re-emergence of GNB among febrile neutropenic cancer patients.[8,20] This might be due to minimal use or the discontinuation of fluoroquinolones prophylaxis.[21,22] These findings strengthen the need for frequent surveillance for understanding the local epidemiology of bacterial infection among cancer patients.

S. aureus, CoNS, and *E. coli* were the most common bacterial pathogens isolated in cancer patients in this study. More or less similar patterns have been reported in cancer patients in different countries, although the proportion of the bacterial agents varied.[7,17] The GPB *S. aureus* and CoNS are ubiquitous in nature, which are frequently found on the skin and are the main cause of various infections, mainly in patients with solid tumors following indwelling devices, invasive surgical procedures, and contamination from hospital environments.[5,23] Likewise, *E. coli* is a normal member of gastro-intestinal flora and a common cause of both community and hospital acquired UTI. Particularly immunocompromised cancer patients are easily colonized by the bacteria, due to the fact that infection of cancer patients by this bacterium is inevitable.

Several studies reported very high rates of methicillin resistance (MR) among *S. aureus* as well as CoNS from cancer patients.[7,16] In this study, 25% of MRSA and 45.5% of MRCoNS were detected. Similarly, consistent findings were also claimed in the same hospital (26.5%),[24] in Ethiopia (pooled prevalence) (32.5%),[25] and in other countries in Saudi Arabia (28.62%)[26] and Libya (35.3%).[7] Although emergence of VRE in cancer patients has been reported, one isolate of VRE was recovered from a urine specimen in this study. This suggests that the utilization of empirical vancomycin in our hospital must be thoroughly scrutinized.

GNB revealed a high resistance rate to ampicillin (88.2%) and for amoxicillin/clavulonic acid (82.4%), similar to the study conducted in Libya.[7,17] Among the predominant GNB isolates, *E. coli* was highly resistant to amoxicillin/clavulonic acid, and ampicillin, which is in agreement with a study conducted in Sudan.[5] In this study, 33.3% of *E. coli* was resistant to fluoroquinolone, which is also comparable with the results reported from Libya.[7] However, it is lower than the report from developed countries where fluoroquinolone is most commonly prescribed as a prophylaxis in cancer patients receiving chemotherapy.[3] When the prevalence of fluoroquinolone resistance in GNB exceeds 20%, it indicates there is widespread use of fluoroquinolone that would encourage multiclass drug resistance.[10]

In this study, nitrofurantoin showed a low level of resistance, which makes this drug a reasonable alternative in the management of UTI in cancer patients. This may have been due to its multiple mechanisms of action and under-usage of this drug in the study area. However, it cannot be used to treat UTI in complicated and febrile infants, because it is excreted in the urine and does not achieve therapeutic concentrations in the bloodstream.[27]

Although the development of MDR is a natural phenomenon, an interestingly extensive raise in the number of immunocompromised conditions, like cancer, increases MDR, thereby contributing to a further spread of MDR isolates, since these patients had frequent follow-up within the hospital.[28] In this study, the overall prevalence of MDR was 46.5% lower than a recent report in the same place from neonatal septicemia (65%).[24] Among the isolated bacteria, *K. pneumoniae* and *E. coli* were the principal MDR strains concordant with a previous study in the same place.[24]

Most studies have shown that cancer patients with hematological malignancy had a higher risk of developing bacterial infection as compared to solid tumor patients.[1,26,29] In this study, cancer patients with a solid tumor were 3.9 times more likely to be culture positive than hematological malignancy, because the majority of patients with solid tumors undergo surgical treatment and catheterization as a result of the development of postoperative or catheter-associated infections is common. Besides, patients who started cancer therapy had higher odds of culture positivity as compared to their counterparts, concordant with the studies conducted in Qatar[29] and Spain.[30] Moreover, cancer patients who were symptomatic during sample collection had ~7.8 times higher odds of culture positivity as compared to asymptomatic cases, indicating that the use of culture and sensitivity test for symptomatic cases are so substantial to underpin

effective treatment and prevention strategies. However, 6% asymptomatic bacteriuria reported in this study should not be undermined in the era of MDR.

Limitations

Despite a number of strengths, our prospective cross-sectional study has some limitations that should be acknowledged. First, it was performed in a single center, which may not reflect the epidemiology of different centers and/or different geographical areas. Second, due to the lack of budget, identification of extended-spectrum β-lactamase and carbapenemase-producing isolates was not done. Third, the duration, type of treatment modality, prior infection histories, and prophylaxis used were not collected.

Conclusion

The overall burden of bacterial infections among cancer patients is considerably higher, particularly in patients with solid tumor, who had started cancer therapy, and those being symptomatic during diagnosis. GPB isolates were higher than GNB. The most common bacterial isolates were *S. aureus,* CoNS, and *E. coli.* Multidrug resistance was detected in 46.5% bacterial isolates. MR was detected in 25% of *S. aureus* and in 45.5% of CoNS isolates. Fluoroquinolone resistance was detected in 33.3% of *E. coli* isolates. The findings of the current study call for a more robust study with a larger isolate number to better understand the resistance pattern of the common bacterial isolates and advise policymakers to develop guideline.

Availability of data and material

All the raw data supporting the findings can be requested from the principal investigator Alelign Fentie.

Author contributions

All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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