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Supportive Care and Others

Bacteriological Profile and Antibiotic Sensitivity Pattern of Clinical Isolates in a Tertiary Cancer Care Center in the Northeast India

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Abstract

Background This study was performed to determine the bacteriological profile and antibiotic sensitivity pattern of culture samples of patients with cancer at our institute. The study was undertaken to formulate an antibiotic policy for the treatment of infection in these patients.

Materials and Methods The study was performed in the Department of Microbiology of a regional cancer center during the period from January 2017 to December 2017. Samples were collected under all aseptic precaution, and they were processed as per the Clinical and Laboratory Standard Institute Guideline 2017.

Results A total of 464 clinical samples (urine, blood, sputum, pus, etc.) were collected and processed for culture, of which 198 (42.67%) samples showed culture positive that were identified as per standard recommended procedures and antibiotic susceptibility testing was performed on isolates as per the Clinical Laboratory Standard Institute guidelines 2017. *Escherichia coli* (48), *Staphylococcus aureus,* (45) *Klebsiella pneumoniae* (52), Coagulase-negative *Staphylococcus* (17), and *Pseudomonas aeruginosa* (15) were most commonly encountered. Of the 132 Gram-negative isolates, 101 (76.5%) were extended-spectrum β-lactamase producers. Among the 45 staphylococcal isolates, 18 (40%) were methicillin-resistant *S. aureus.*

Conclusion The present study reveals microbiological profile in patients attending our cancer institute.

Keywords
- extended-spectrum β-lactamase
- immunocompromised
- methicillin-resistant *Staphylococcus aureus*
- multidrug resistance

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Introduction

Cancer increases a patient's risk of getting a serious infection. In spite of the recent advances made by medical science in cancer treatment, infections still remain a major cause of morbidity and mortality in patients diagnosed with cancer.[1,2] Cancer patients are often immunocompromised because of the disease process itself and also due to various interventions such as chemotherapy. In addition, there are usually other associated risk factors for acquiring infection such as long-term catheterization, mucositis due to cytotoxic agents, neutropenia, and stem-cell transplantation.[3] Infectious complications are a serious cause of morbidity and mortality in patients with underlying hematological malignancies. Moreover, in solid tumors, although there is no prolonged neutropenia, the presence of multiple other risk factors is responsible for an immunocompromised state, like there is obstruction caused by the tumor, disruption of normal anatomical barriers, therapeutic procedures, chemotherapy, radiation, and use of medical devices such as catheter, stent, and prosthesis.[4,5] The common sites of infection seen in cancer patients undergoing treatment are bloodstream, respiratory, gastrointestinal tract, skin soft tissue, and urinary tract infections. In the present-day context, there is the emergence of multidrug-resistant organisms in certain infections. Antimicrobial resistance poses a major threat to patient's treatment, as it leads to severe morbidity and high-mortality rates, increased hospital stay, and severe economic burden to the patient and healthcare system.[4]

Empirical therapy with broad-spectrum antibiotic and subsequently de-escalating to a narrower-spectrum drug after culture sensitivity results are available is the current approach for the treatment of cancer patients with infection. This study aimed to document the most common bacterial profile and the antimicrobial susceptibility patterns in clinical samples of cancer patients undergoing treatment at our center.

Materials and Methods

Two hundred and fifty patients with various malignancies were included in this study. The present study was conducted for 1 year in a Regional Cancer Center in the Northeast India. This was a retrospective and observational hospital-based study performed at the Department of Microbiology of the institute. The Institutional Ethical Committee's clearance was obtained prior to conducting the study. This study was conducted on all clinical isolates from samples of patients received from different oncology units from January 2017 to December 2017. All relevant samples were collected as per hospital sample collection protocol from various clinical areas; these included urine, skin and soft tissue, blood, and respiratory samples. The clinical data were obtained from the requisition forms and from the respective units and wards of the patient. All samples were processed as per standard microbiology laboratory standard operating procedures.[6,7] The isolates were identified by their colonial morphology, Gram-staining, and different biochemical reactions using standard techniques. Criteria for antimicrobial sensitivity testing were performed as per the Clinical Laboratory Standard Institute (CLSI, United States) guidelines.[8] Antimicrobial sensitivity testing was done on Mueller-Hinton agar by Kirby-Bauer's disc diffusion method. Commercially available discs (HiMedia) were used. Zones of inhibition were measured the next day and were correlated with CLSI interpretive breakpoints to characterize them as sensitive, intermediate, and resistant. For drugs for which CLSI breakpoints were not available, interpretative breakpoints were provided by the manufacturer. *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853 were used for quality control.

For Gram-positive organisms, the antibiotics to be tested and reported were chosen from the following (depending on the organism isolated): Penicillin, erythromycin, clindamycin, gentamicin, and high level, amoxicillin-clavulanate, cefoxitin, levofloxacin, vancomycin linezolid, and cotrimoxazole.

For Gram-negative, the antibiotics for respective organisms were chosen from the following: amoxicillin–clavulanate, ciprofloxacin, levofloxacin, gentamicin, amikacin, netilmicin, cefuroxime, cefotaxime, ceftazidime, cefepime, cefoperazone-sulbactam, cefepime-tazobactam, imipenem, and meropenem. Colistin susceptibility was performed using minimum inhibitory concentration method, with E-test strips. In the present study, vancomycin susceptibility test could not be done by microbroth dilution method as recommended, due to nonavailability of this facility in the institute where this study was conducted.

Results

A total of 464 samples of 250 patients were received and processed from different departments of the institute as shown in ►**Table 1**. Of the 250 patients, 108 were <40 years of age and 142 were above 40 years of age. The male-to-female ratio

Table 1 Samples received and processed from different departments of the institute

Specimen	Specimen received for bacterial culture			
	Medical oncology	Surgical oncology	Gynecologic oncology	Head and neck
Urine	30	34	19	3
Blood	240	6	0	0
Respiratory	15	9	4	28
Skin and soft tissue	10	28	14	24
Total	295	77	37	55

Table 2 Patient profiles of the present study

Patient profile	*n*
Total number of patients	250
Age (y)	
<40	108
>40	142
Male	166
Female	84
Type of malignancies	
Hematological malignancies	104
Gastrointestinal malignancies	69
Gynecological malignancies	31
Head-and-neck malignancies	46
Patients with neutropenia	130
Patients without neutropenia	120

Table 3 Total number of culture positive of each specimen

Specimen	Total	Culture positive (%)
Urine	86	64 (74)
Respiratory	56	40 (71)
Skin and soft	76	32 (42)
Blood	246	62 (25)

was 2.1. Type of malignancies detected in the present study were hematological malignancies in 104 (41.6%), gastrointestinal malignancies in 69 (27.6%), gynecological malignancies in 31 (12.4%), and head-and-neck malignancies in 46 (18.4%) patients. One hundred and thirty (52%) patients were neutropenic and 120 (48%) patients were nonneutropenic (►**Table 2**). The highest number of neutropenic patients was cases with hematological malignancies followed by gastrointestinal malignancies and gynecological malignancies. Neutropenic patients were mainly in the age group of <40 years. Of 130 neutropenic patients, blood culture was positive in 46 patients.

One-hundred and ninety-eight (42.67%) organisms were isolated. The total number of organisms isolated from various clinical samples is shown in ►**Table 3**.

Of the 132 Gram-negative isolates, 101 (76.51%) were extended-spectrum β-lactamase (ESBL) producers as shown in ►**Table 3**. Carbapenem resistance in *E. coli* and *Klebsiella pneumoniae* was 18% and 19%, respectively. Of the 45 staphylococcal isolates, 18 (40%) were methicillin-resistant *S. aureus* (MRSA) (►**Table 4**).

All the *S. aureus* isolates were sensitive to vancomycin (100%), linezolid (100%), and teicoplanin (100) (►**Fig. 1A**).

In the present study, sensitivity pattern of *E. coli* was to colistin (100%), imipenem (82%), meropenem (88%), ertapenem (80%), piperacillin–tazobactam (68%), amikacin (84%), netilmicin (89%), gentamicin (92%), and cefepime (46%) (►**Fig. 1B**).

In the present study, sensitivity pattern of the *K. pneumoniae* was to colistin (100%), imipenem (81%), meropenem (82%), ertapenem (80%), piperacillin–tazobactam (67%), amikacin (89%), netilmicin (92%), gentamicin (68%) and cefepime (32%) (►**Fig. 1C**).

In the present study, sensitivity pattern of the *P. aeruginosa* was to colistin (100%), imipenem (84%), meropenem (86%), piperacillin–tazobactam (76%), amikacin (82%), netilmicin (94%), gentamicin (85%), and cefepime (57%) (►**Fig. 1D**).

Discussion

The type of malignancy, the status of the malignancy (i.e., active or remission), and the intensity of the treatment directed against it are all important factors in determining infection risk.[9] In cancer patients, there is increased risk of skin and soft-tissue infection and bacteremia.[9] In this study, patient specimen showed a higher number of urinary tract infection followed by skin and soft tissue, respiratory, and blood. However, some of these isolates from urinary and respiratory trace could be colonizers and this study was not powered to differentiate between the two.

Among the Gram-negative isolates, there were high rates of resistance to the third-generation cephalosporins (cefotaxime/ceftazidime) and also to the β-lactam-β-lactamase inhibitor combinations such as cefoperazone-sulbactam and piperacillin–tazobactam. Among the 62 Gram-positive Staphylococcal isolates, 18 (29%) were MRSA. Among the *S. aureus* isolates, all were sensitive to vancomycin, linezolid, and teicoplanin.

Enterococcus faecalis was isolated from four urine samples of gynecology oncology. Gynecological malignancy disrupts barriers in the female genitourinary tract predisposing to infection with *Enterococci*, enteric aerobes, and anerobic bacteria.[9]

In our study, out of 246 blood cultures, 62 were positive. Patients with neoplasms presenting with *Enterobacteriaceae* bacteremia were more likely to have infection with *K. pneumoniae* and *E. coli.* This association may be explained by host and pathogen factors.[10] The culture isolates were *K. pneumoniae* (26), *E. coli* (22), and *S. aureus* (14). All *Enterobacteriaceae* isolates were ESBL producer. Moreover, this is a real matter of great concern.

Out of the total 132 Gram-negative isolates from all clinical specimen, 101 (76.51%) were ESBL producers. Carbapenem resistance in *E. coli* and *K. pneumoniae* was 18% and 19%, respectively. Similar finding with rates of multidrug resistance organisms has been noted in a study from Mumbai.[1,2] However, fortunately, the antimicrobial profile of carbapenems (imipenem, meropenem, ertapenem) and aminoglycosides (gentamicin, amikacin, netilmicin) showed >50% sensitivity. Although a susceptibility of 50% is not enough for empirical treatment, for nonneutropenic patients, carbapenems can be an empirical choice of treatment. Aminoglycosides are to be preserved for use in the urinary tract as they achieve good concentration there.

Moreover, all Gram-negative isolated were sensitive to colistin. Similar results were seen in a study conducted in a tertiary care cancer center in Delhi.[1] Carbapenems-resistant

Table 4 Organisms isolated from different departments

Organisms isolated	Medical oncology	Surgical oncology	Gynecology oncology	Head and neck oncology	Total	MRSA	ESBL
Escherichia coli	34	6	8	0	48		40
Klebsiella pneumoniae	30	10	2	10	52		43
Staphylococcus aureus	17	17	7	4	45	12	
Coagulase negative staphylococcus	5	6	4	2	17	6	
Pseudomonas aeruginosa	3	4	3	5	15		7
Serratia odorifera	0	0	1	0	1		1
Citrobacter spp.	0	1	2	0	3		2
Proteus vulgaris	2	3	2	0	7		4
Proteus mirabilis	3	1	0	0	4		3
Morganella morganii	1	0		0	1		1
Serratia marcescens	0	1	0	0	1		0
Enterococcus faecalis			4		4		

Abbreviations: ESBL, extended spectrum β lactamase; MRSA, methicillin-resistant *Staphylococcus aureus*.

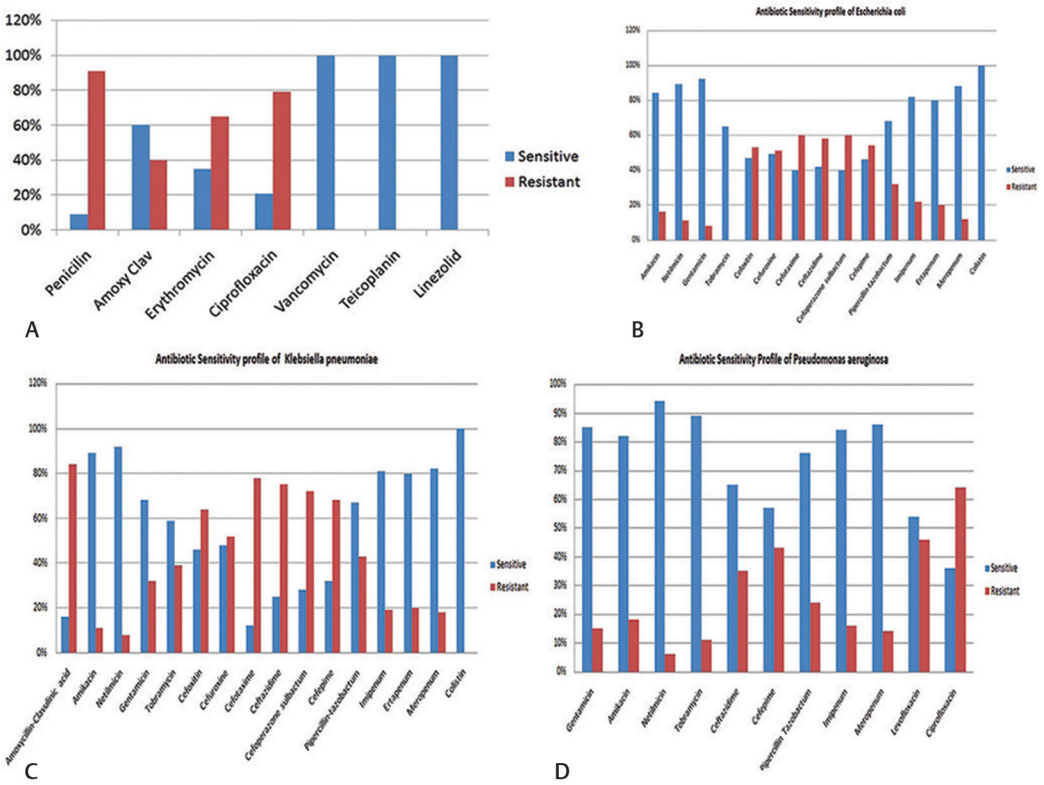

Fig. 1 The sensitivity profile of (**A**) *Staphylococcus aureus*. (**B**) *Escherichia coli*, (**C**) *Klebsiella pneumoniae*, and (**D**) *Pseudomonas*.

Enterobacteriaceae group of organisms, particularly *E. coli* and *K. pneumoniae*, is a worrying factor.

Antibiotic resistance is now emerging among the Gram-positive isolates. High rates of methicillin resistance ranging from 54 to 72.3% and the emergence of vancomycin-intermediate strains of *S. aureus* have been reported from India.[11,12] We did not encounter any vancomycin resistance among staphylococci, and MRSA rates have been approximately 34.28% in another study,[12] and in the present study, MRSA was 40%.

This study showed that the most common organism present in our clinical samples was Gram-negative aerobes. *S. aureus* was the single most common predominant organism isolated from various specimens. The presence of multidrug-resistant organisms was alarmingly high, especially from blood culture isolates. These observations are important, especially for the management and development of empirical antibiotic guidelines. In the present healthcare scenario, it is very important for every healthcare setting to formulate antibiotic policies based on local antibiotic susceptibility patterns so that arbitrary use of antibiotics is avoided and resistance is kept to a minimum.

Neutropenia is a known factor influencing mortality and morbidity.[13] This may be because only cases with severe infections were sent for blood culture. Bacteremia was present in 46 out of 130 samples, but the association of multidrug-resistant strains from these isolates was an important factor. Neutropenic patients were mainly in the <40 years age group. In our study, bacteremia was seen in 35% of the patients compared with 38% as observed by Hurtado et al.[14]

Limitations of the Study

There are several limitations to the study. Mainly, we used manual (Kirby-Bauer's) disc diffusion method for sensitivity analysis. Furthermore, the present study did not examine for anaerobic isolates and fungal isolates in cancer patients undergoing treatment. Furthermore, the present study was not powered to differentiate colonizers from pathogens. Colistin and vancomycin susceptibility could not be done by broth microdilution method.

Conclusion

We emphasize the regular evaluation of local isolates and sensitivity pattern in cancer patients undergoing treatment. In our experience, in cancer patients undergoing a various form of treatment, carbapenem along with aminoglycosides such as netilmicin and tobramycin are standard options for Gram-negative coverage, and linezolid, teicoplanin, and vancomycin can be used for treating Gram-positive infection in cancer patients. It was seen that isolates from bloodstream infections in neutropenic patients were predominantly multidrug resistance organism. It is recommended that every institution should regularly revise their antimicrobial policy based on microbiological data.

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Nil.

Conflict of Interest
There are no conflicts of interest.

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