Original Research Paper

Volume - 14 | Issue - 09 | September - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Medical Microbiology

A STUDY ON BLOODSTREAM INFECTIONS IN CANCER PATIENTS FROM A ONCOLOGY INSTITUTE AND REGIONAL CANCER CENTRE,TELANGANA SOUTH INDIA

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ABSTRACT **Introduction:** Bloodstream infections (BSI) remain a major cause of morbidity and mortality in patients undergoing treatment for cancer. Aim is to access the use of new potent antibiotics against bloodstream infection in cancer patients and to determine the cross resistance of bacterial strains. **Materials and Methods:** This retrospective study is a single-center's experience including both pediatric and adult patients with malignancy, who were receiving care at our hospital which is a Regional Cancer Centre, of over a 6 months period, between January 2022 and June 2022. Blood cultures were done using BacT/ALERT 3D system. We studied the bacterial spectrum & antimicrobial susceptibility pattern of bacterial strains in cancer patients. Susceptibility of microbial isolates to antibiotics was performed with a VITEK 2 compact automated system (Biomerieux Inc., France) according to the Clinical and Laboratory Standards Institute recommendation in 2015. **Results:** A total of 243 blood cultures were examined. The patient's age ranged from 1 to 72 years. The majority of patients 139 (57.2%) had hematologic malignancies as opposed to solid and other tumours or malignancies 104 (42.7%). Out of 243 blood samples which came for culture in our Institute, 6 were Central line-associated bloodstream infections ,(CLABSI) cases. Total positives ere 63 (25.9%) and,total negatives were 180 (74.1%) .Among the total positives, Gram-negative bacilli were the predominant causative agents of BSI constituting 61.9% (n = 39/63) of isolated organisms, 33.33% (n = 21/63) of infections were caused by Gram-positive cocci while polymicrobial infections accounted for 4.76% (n = 3/73) of these cases. **Conclusion:** High resistance observed in this study warrants the needs of surveillance of resistant pattern of antimicrobial agents. Due to increased level of drug resistance, following Culture and Sensitivity patterns as Investigation of choice would be a prudent choice in high- risk cases especially in Blood stream infections in Cancer patients.

KEYWORDS : Bloodstream infections(BSI), hematologic malignancies , Central line-associated bloodstream infections (CLABSI), Gram-negative bacteria, Culture and Sensitivity

INTRODUCTION

Infection is a continuous and significant problem in patients with cancer. Cancer causes both direct and indirect effect on a patientís immune system. Many factors increase the susceptibility of immunosuppressed cancer patients to infection. These include neutropenia during aggressive therapy, altered gut flora because of frequent antibiotic administration, disruption of skin and damage of epithelial surfaces by cytotoxic agents. Bloodstream infection (BSI) is a leading infectious complication among cancer patients and has a negative impact on patients outcome. These infections are being reported as a leading cause of morbidity and mortality worldwide. Moreover, BSI represents about 15% of all nosocomial infections.[1]

Mostly Gram-negative bacilli (GNB) have been implicated to be the aetiological agents of BSI. However, few studies report Gram-positive cocci (GPC) as the culprits.[2,3,4]. Furthermore, the empiric coverage should be based on local antimicrobial susceptibility data and the severity of disease. It is crucial for institutions to identify local patterns of microorganisms and their susceptibilities in order to appropriately inform choice of empiric antibiotics for these infections and to promote antibiotic stewardship.

To the best of our knowledge, studies on bacteriological profile of BSI in cancer patients and the antibiograms of the isolates are comparatively less than the same from intensive care unit studies that do not emphasize on cancer patients.[5] Accordingly, we planned to conduct this study to determine the microbiological profile of the cancer patients developing BSI and the antibiotic susceptibility pattern of the organism isolated. Having these data available will help in understanding the actual burden and deriving the preventive measures for such infections, as well as provide insight for correct use of antibiotics according to their antibiogram in our health-care settings.

MATERIALS AND METHODS

This retrospective study is a single-center's experience including both paediatric and adult patients with malignancy, who were receiving care at medical/surgical oncology department of our hospital over a period between January 2022 and June 2022. All hospitalized cancer patients undergoing anti-cancer therapy, with suspected blood stream infection, were studied. No discrimination was made on the basis of age or gender. Patients already undergoing anti-microbial therapy and those having fever due to non-infectious causes such as blood transfusion and drug infusion etc., were excluded from the study. Only one isolate per patient was studied at a time and total blood samples were taken for analysis. All data included were obtained from patients records.

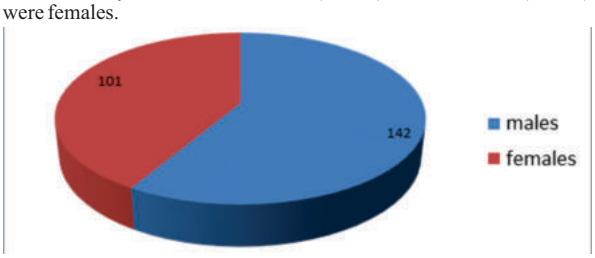
Blood cultures were done using BacT/ALERT 3D system. We studied the bacterial spectrum & antimicrobial susceptibility pattern of bacterial strains in cancer patients. Susceptibility of microbial isolates to antibiotics was performed with a VITEK 2 compact automated system (Biomerieux Inc., France) according to the Clinical and Laboratory Standards Institute recommendation in 2015. Cancer diagnosis was classified as either hematologic malignancy or solid tumor. Demographic data and clinical variables including age, sex, type of malignancy and clinical characteristics of infections and microbiology data, for each patient, were collected.

Data Analysis

The data was analyzed and evaluated on the basis of averages and percentage values. The results were presented in the form of tables, figures and graphs.

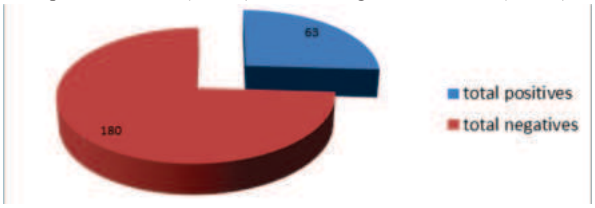
RESULTS

A total of 243 blood cultures were examined. The patient's age ranged from 1 to 72 years. There were 142 (58.4%) males and 101 (41.5%) were females.



Graph 1 : Males 142(58.4%), and Females-101(41.5%) distribution of cases among total of 243

The majority of patients 139 (57.2%) had hematologic malignancies as opposed to solid and other tumours or malignancies 104 (42.7%). Out of 243 blood samples which came for culture in our Institute, 6 were Central line-associated bloodstream infections ,(CLABSI) cases. Total positives are 63 (25.9%) and, total negatives were 180 (74.1%) .



Graph 2 : Positive 63 (25.9%), and Negative 180 (74.1%) distribution of cases among total of 243

Among total number of males and females, pediatric and adult distribution of cases and the percentage of positivity is mentioned in the Graph 3. Percentage of positivity is more among adults [total-106 (positives-42) –positivity -39.6 %] when compared to pediatric patients [total-137 (positives-21) –positivity -15.3 %].

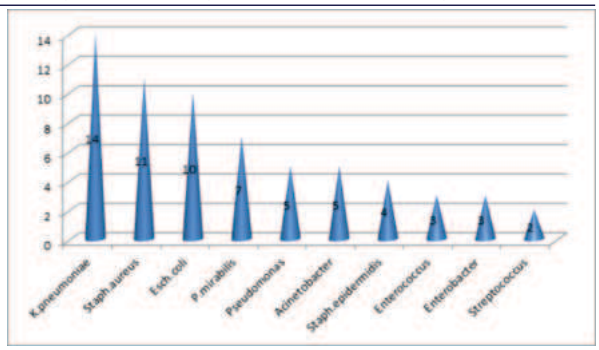
Graph 3 : Male: Female & Pediatric: Adult distribution of cases

Among the total positives, Gram-negative bacilli were the predominant causative agents of BSI constituting 61.9% (n = 39/63) of isolated organisms, 33.33% (n = 21/63) of infections were caused by Gram-positive cocci while polymicrobial infections accounted for 4.76% (n = 3/73) of these cases. Klebsiella pneumoniae (n=14), Staphylococcus aureus(n=11), Acinetobacter baumannii(n=10), constitute the major cause of Blood stream infections while Esch.coli, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus epidermidis etc. and others follow, as mentioned in the table 1.

Table 1: Isolates of bloodstream infections (n=63)

Pathogen		n(%)
1.	Klebsiella pneumoniae	14 (22.2%)
2.	Staphylococcus aureus	11 (17.46%)
3.	Acinetobacter baumannii	10 (15.8%)
4.	Escherichia coli	7 (11.11%)
5.	Proteus mirabilis	5 (7.93%)
6.	Pseudomonas aeruginosa	5 (7.93%)
7.	Staphylococcus epidermidis	4 (6.34%)
8.	Enterococcus faecalis	3 (4.76%)
9.	Enterobacter aerogenes	3 (4.76%)
10.	Streptococcus pneumonia	2 (3.17%)

Among the Gram-positive bacilli, among 11 of Staph. Aureus, 6 were with methicillin-resistant and 5 with methicillin-sensitive strains were isolated,while 2 cases involved vancomycin-resistant E. faecalis strain among a total of 3 positive isolates.



Graph 4 : Graph showing pathogens isolated from bloodstream infections

Most of the GPC showed complete susceptibility to vancomycin and Teicoplanin. Higher rate of resistance was seen among coagulase-negative staphylococci isolates as compared to S. aureus among various groups of antibiotics tested [Table 2]. Lowest resistance is seen with Tigecycline among all Gram positive cocci isolated.

Table 2 : Antibiotic Resistance pattern of Gram positive cocci

Antibiotic	Staph.aureus (n=11)(%)	Staphylococcus epidermidis (n=4)(%)	Enterococcus faecalis (n=3)(%)	Streptococcus pneumonia (n=2)(%)
Oxacillin	6(54.5)	2(50)	3(100)	1(50)
Gentamicin	8(72.7)	4(100)	2(66.6)	2(100)
Ciprofloxacin	9(81.8)	3(75)	3(100)	2(100)
Levofloxacin	6(54.5)	3(75)	1(33.3)	1(50)
Erythromycin	10(90.9)	4(100)	2(66.6)	1(50)
Clindamycin	7(63.6)	2(50)	2(66.6)	0
Lineolid	4(36.3)	1(25)	0	0
Daptomycin	3(27.2)	2(50)	1(33.3)	1(50)
Teicoplanin	3(27.2)	2(50)	0	0
Vancomycin	9(81.8)	1(25)	2(66.6)	1(50)
Tigecycline	6(54.5)	0	1(33.3)	1(50)
Trimethoprim/ sulfamethoxazole	9(81.8)	3(75)	3(100)	1(50)

Among the Gram negative bacilli isolated from the samples, Enterobacter aerogenes were completely resistant to Amikacin, Ceftriaxone and Gentamicin. Imipenem, Tigecycline, Meropenem and Ertapenem were more sensitive to most of the organisms when compared to other antibiotics. The Antibiotic Resistance pattern of all Gram negative Bacilli were shown in Table 3.

Table 3 : Antibiotic Resistance pattern of Gram negative Bacilli

Antibiotic	K. pneumoniae (n=14) (%)	Acinetobacter baumannii (n=10) (%)	Escherichia coli (n=7) (%)	Proteus mirabilis (n=5) (%)	Pseudomonas aeruginosa (n=5) (%)	Enterobacter aerogenes (n=3) (%)
Amikacin	7(50)	6(60)	6(85.7)	4(80)	3(60)	3(100)
Amoxicillin/ Clavulanic acid	9(64.2)	5(50)	4(57.1)	4(80)	2(40)	2(66.6)
Colistin	6(42.8)	6(60)	4(57.1)	3(60)	3(60)	1(33.3)
Cefuroxime	7(50)	6(60)	6(85.7)	4(80)	4(80)	2(66.6)
Cefuroxime Axetil	5(35.7)	7(70)	5(71.4)	3(60)	4(80)	2(66.6)
Ceftriaxone	8(57.1)	8(80)	5(71.4)	4(80)	3(60)	3(100)
Cefoperazone/ Sulbactum	6(42.8)	5(50)	4(57.1)	2(40)	2(40)	1(33.3)
Cefepime	10(71.4)	7(70)	6(85.7)	3(60)	3(60)	2(66.6)
Ertapenem	5(35.7)	4(40)	4(57.1)	2(40)	2(40)	0
Gentamicin	10(71.4)	8(80)	7(100)	4(80)	4(80)	3(100)
Imipenem	8(57.1)	5(50)	3(42.8)	3(60)	3(60)	1(33.3)
Meropenem	9(64.2)	6(60)	4(57.1)	2(40)	2(40)	1(33.3)
Nalidixic Acid	8(57.1)	9(90)	6(85.7)	5(100)	5(100)	2(66.6)
Piperacillin/ Tazobactum	4(28.5)	7(70)	5(71.4)	2(40)	3(60)	1(33.3)

Tigecycline	4(28.5)	3(30)	4(57.1)	1(20)	2(40)	1(33.3)
Trimethoprim/ Sulfame-thoxazole	8(57.1)	6(60)	3(42.8)	3(60)	4(80)	2(66.6)

DISCUSSION

The potential for anti-microbial resistance is an important concern for clinicians treating patients with confirmed or suspected bacterial infections as they are often resistant to a broad range of antimicrobial agents. Detection of micro-organism in blood culture is considered an indicator of disseminated infection and has been shown to be a valid marker for surveillance of bloodstream infections among critically ill patients. [1]

In our study, both Gram-negative bacteria and Gram positive cocci were found associated with bloodstream infections in cancer patients. Among Gram negative bacilli , Klebsiella pneumonia 14 (22.2%) was the most frequently isolated bacterial strain followed by Acinetobacter baumannii 10 (15.8%), Escherichia coli 7 (11.11%), Proteus mirabilis 5 (7.93%) and Pseudomonas aeruginosa, a common hospital and opportunistic pathogen . [2] 5 (7.93%). In our study, Imipenem [8] , along with Tigecycline, Meropenem and Ertapenem were more sensitive to most of the organisms when compared to other antibiotics. Reports by SENTRY for laboratories in the United Stated, Canada, Latin America and Europe showed E. coli, Klebsiella sp. and P.aeruginosa as the most frequent resistant bacilli to be isolated from bloodstream infections.[6,7] The In vitro activity of different anti-microbial agents in Gram-negative bacteria causing BSI evaluated in our study, showed high resistance rates against cephalosporins in both P. aeruginosa and Enterobacteriaceae.[12]

Among the Gram-positive bacilli, Staphylococcus aureus 11 (17.46%) was the most frequently isolated bacterial strain followed by Staphylococcus epidermidis 4 (6.34%), Enterococcus faecalis 3 (4.76%) and Streptococcus pneumonia 2 (3.17%).Interestingly, in the present study GNB outnumbered GPC in causation of BSI which is in consistent with the previous study from All India Institute of Medical Sciences, New Delhi, India.[9] Our results are consistent with prior research among pediatric oncology patients receiving care in hospital settings.[10,11]

The current study has some limitations. There are inherent limitations of retrospective design of study like, increased risk of bias, cannot control exposure or outcome assessment, and instead relied on accurate recordkeeping. Nonetheless, our study provides important descriptions of this relatively less understood population and provides a platform for future prospective studies.

CONCLUSION

In our conclusion, high resistance observed in this study warrants the need for surveillance of resistant pattern of antimicrobial agents administered to patients undergoing treatment for better patients management. A careful monitoring of anti-microbial use, in hospital, is required to identify the situation in which prescription patterns are contributing to the development of resistance. The lack of any new compounds in the near future indicates that there is need for constant monitoring at national, regional level as these surveillance efforts are essential to provide clinicians with information for choosing empirical treatment regiments and implement strict antibiotic prescribing policies and hospital infection control guidelines. Screening for ESBL production as a routine procedure in clinical laboratories gives valuable information to the clinician in appropriate selection of antibiotics. Moreover, bacterial strains resistant to most classes of antibiotics will continue to arise unless the inappropriate use of these drugs is curtailed. High resistance observed in this study warrants the needs of surveillance of resistant pattern of antimicrobial agents. Due to increased level of drug resistance, following Culture and Sensitivity patterns as Investigation of choice would be a prudent choice in high-risk cases especially in Blood stream infections in Cancer patients.

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