# Determine the Antimicrobial Susceptibility Pattern of Different Antimicrobials Used for Treating Infections in Cancer Patients: An Institutional Based Study 

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#### Abstract

Background: Malignancy is a leading cause of death worldwide, and accounted for 7.6 million deaths (around $13 \%$ of all deaths) in 2008. Broad spectrum antibiotics are commonly used as empirical therapy in febrile cancer patients. Hence; the present study was undertaken for determining antimicrobial susceptibility pattern of different antimicrobials used for treating infections in cancer patients. Materials \& Methods: From the suspected cases of blood stream infection from cancer patients, a total of 344 blood samples were collected for culture. Blood samples were collected before starting the antimicrobial therapy. The antibiotic susceptibility testing of the isolates were done by Kirby- Bauer disk diffusion method on Mueller Hinton agar. Isolates were grown in peptone water by incubating at $37^{\circ} \mathrm{C}$ and turbidity was matched with 0.5 MacFarland standards. Then lawn culture was done on Mueller Hinton agar plate and commercial antibiotic disks were placed. The plates were incubated at $37^{\circ} \mathrm{C}$ overnight and on the next day the zones of inhibition were measured and susceptibility/ resistance interpreted. Results: Out of total 30 CONS cases, sensitivity was found in Vancomycin (100\%), Linezolid (93.3\%), Amoxy-clav (80\%), Cefoxitin ( $80 \%$ ), Amikacin ( $73.3 \%$ ), Ceftriaxone ( $73.3 \%$ ), Ciprofloxacin (53.3\%), Cotrimaxazole (33.3\%), Erythromycin (26.7\%), and Tetracycline (20\%). Out of total 12 COPS cases,


sensitivity was found in Vancomycin (100\%), Linezolid (91.7\%), Amoxy-clav (83.3\%), Ceftriaxone (83.3\%), Amikacin (66.7\%) Ciprofloxacin (41.7\%), Erythromycin (41.7\%), Tetracycline ( $41.7 \%$ ), Cotrimaxazole ( $25 \%$ ) and Cefoxitin ( $25 \%$ ). Out of total 12 isolates of Staph aureus (COPS) 3(25\%) cases were found to be MRSA. Above table shows sensitivity pattern of gram negative bacilli enterobactericae (E coli and klebsiella).
Conclusion: The clinicians should have thorough knowledge for appreciating empirical therapy as well switch over to the best regime based on antibiotic susceptibility pattern to improve the overall outcome of the patient's health.

Key words: Antimicrobial, Cancer, Susceptibility.

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## INTRODUCTION

Malignancy is a leading cause of death worldwide, and accounted for 7.6 million deaths (around $13 \%$ of all deaths) in 2008. Deaths from cancer are projected to continue to rise to over 11 million in 2030, and lung cancer is the leading cause of cancer death worldwide. The potential for anti-microbial resistance is an important concern for clinicians treating patients with confirmed or suspected bacterial infection 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. ${ }^{1-3}$

Broad spectrum antibiotics are commonly used as empirical therapy in febrile cancer patients. The use of "early empirical" therapy has reduced the mortality in patients with leukemia and bacteremia from $85 \%$ to $20-36 \%$ over the last five decades. However, the widespread use of antimicrobials has resulted in the emergence of multidrug-resistant bacteria. It is essential therefore to monitor trends of antimicrobial resistance and develop appropriate antibiotic policy. ${ }^{4,5}$ Hence; under the light of above mentioned data, the present study was undertaken for determining antimicrobial susceptibility pattern of different antimicrobials used for treating infections in cancer patients

## MATERIALS AND METHODS

The present study was undertaken for assessing and determining antimicrobial susceptibility pattern of different antimicrobials used for treating infections in cancer patients. From the suspected cases of blood stream infection from cancer patients, a total of 344 blood samples were collected for culture. Blood samples were collected before starting the antimicrobial therapy. The inoculated blood culture bottles were incubated overnight at $37^{\circ} \mathrm{C}$ aerobically and sub-cultured on day 2 , day 3 , day 4 and finally on day 7 . Subcultures were done on Blood agar, Chocolate agar and MacConkey agar. The antibiotic susceptibility testing of the isolates were done by Kirby- Bauer disk diffusion method on

Mueller Hinton agar. Isolates were grown in peptone water by incubating at $37^{\circ} \mathrm{C}$ and turbidity was matched with 0.5 MacFarland standards. Then lawn culture was done on Mueller Hinton agar plate and commercial antibiotic disks were placed. The plates were incubated at $37^{\circ} \mathrm{C}$ overnight and on the next day the zones of inhibition were measured and susceptibilityl resistance interpreted according to CLSI guidelines. All the results were summarized in Microsoft excel sheet and were analysed by SPSS software. Chi- square test and independent t test were used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

Table 1: Showing resistance and sensitivity pattern of gram positive cocci (CONS \& COPS)

|  | CONS ( $\mathbf{n}=\mathbf{3 0}$ ) |  | COPS (n=12) |  |
| :--- | :---: | :---: | :---: | :---: |
|  | No. of Sensitive Isolates | $\%$ | No. of Sensitive Isolates | $\%$ |
| E | 8 | 26.7 | 5 | 41.7 |
| AMC | 24 | 80.0 | 10 | 83.3 |
| COT | 10 | 33.3 | 3 | 25.0 |
| Tetra | 6 | 20.0 | 5 | 41.7 |
| CTR | 22 | 73.3 | 8 | 66.7 |
| Cefox | 24 | 80.0 | 9 | 75.0 |
| Cipro | 16 | 53.3 | 7 | 58.3 |
| LZ | 28 | 93.3 | 11 | 91.7 |
| VA | 30 | 100 | 12 | 100 |
| AK | 22 | 73.3 | 8 | 66.7 |

Table 2: MRSA isolates among staph aureus from BSI

|  | No. of cases | $\%$ |
| :--- | :---: | :---: |
| Staph Aureus Isolates (Total Number) | 12 | 100 |
| MRSA | 3 | 25.0 |

Table 3: Sensitivity pattern of gram negative bacilli enterobactericae (E-coli and Klebsiella)

|  | E-Coli $(\mathbf{n}=10)$ |  | $\%$ | Klebsiella $(\mathbf{n}=13)$ |  |
| :--- | :---: | :---: | :---: | :---: | :---: |
|  | No. | $\%$ | No. | 4.4 |  |
| AMP | 3 | 30.0 | 4 | 53.8 |  |
| AMC | 6 | 60.0 | 7 | 30.8 |  |
| COT | 4 | 40.0 | 4 | 40.0 |  |
| Tetra | 5 | 50.0 | 4 | 38.5 |  |
| CTR | 4 | 40.0 | 5 | 55.6 |  |
| Cipro | 5 | 50.0 | 5 | 55.6 |  |
| AK | 5 | 50.0 | 5 | 84.6 |  |
| IPM | 9 | 90.0 | 11 | 92.3 |  |
| MRP | 9 | 90.0 | 12 | 61.5 |  |
| CAZ | 6 | 60.0 | 8 | 30.8 |  |
| DO | 5 | 40.0 | 5 | 55.6 |  |
| Genta | 4 | 40.0 | 5 |  |  |

Table 4: Distribution of ESBL Producing E. Coli and Klebsiella Pneumoniae

| S.N. | Organism | Total Number | ESBL Producers | Percentage (\%) |
| :--- | :--- | :---: | :---: | :---: |
| $\mathbf{1}$ | Escherichia coli | 10 | 3 | $30.0 \%$ |
| $\mathbf{2}$ | Klebsiella pneumoniae | 13 | 4 | $30.8 \%$ |
|  | Total | 23 | 7 | $30.43 \%$ |

## RESULTS

The inhibition zone diameter was measured in mm with the help of a special measuring scale and results recorded for each isolate separately as Sensitive, resistant, intermediate ( $\mathrm{S}, \mathrm{R}, \mathrm{I}$ ) according to the given standard zone size, The discs used were ready-made disc obtained from Hi-media Pvt. Ltd. In present study, out of total 30 CONS cases, sensitivity was found in Vancomycin (100\%), Linezolid (93.3\%), Amoxy-clav (80\%), Cefoxitin (80\%), Amikacin (73.3\%), Ceftriaxone (73.3\%), Ciprofloxacin (53.3\%), Cotrimaxazole (33.3\%), Erythromycin (26.7\%), and Tetracycline $(20 \%)$,. Out of total 12 COPS cases, sensitivity was found in Vancomycin (100\%), Linezolid (91.7\%), Amoxy-clav (83.3\%), Ceftriaxone (83.3\%), Amikacin (66.7\%) Ciprofloxacin (41.7\%), Erythromycin (41.7\%), Tetracycline (41.7\%), Cotrimaxazole (25\%) and Cefoxitin $(25 \%)$. Out of total 12 isolates of Staph aureus (COPS) $3(25 \%)$ cases were found to be MRSA. Above table shows sensitivity pattern of gram negative bacilli enterobactericae (E coli and klebsiella). E. coli shows sensitivity $30 \%, 60 \%, 40 \%$, $50 \%, 40 \%, 50 \%, 50 \%, 90 \%, 90 \%, 60 \%, 50 \%, 60 \%$ and $40 \%$ in Meropenum ( $90 \%$ ), Imipenum ( $90 \%$ ), Amoxy-clav ( $60 \%$ ), Ceftazidine (60\%), Tetracycline (50\%), Ciprofloxacin (50\%), Amikacin (50\%), Doxycycline (50\%) Cotrimoxazole (40\%), Ceftriaxone (40\%), Gentamycin (40\%) and Ampicillin (30\%).
Out of total 13 klebsiella cases, in Meropenum (92.3\%), Imipenum (84.6\%), Ceftazidine (61.5\%), Ciprofloxacin (55.6\%), Amikacin ( $55.6 \%$ ), Gentamycin ( $55.6 \%$ ), Amoxy-clav ( $53.8 \%$ ), Ampicilline (44.4\%), Tetracycline (40\%), Ceftriaxone (38.5\%), Cotrimoxazole ( $30.8 \%$ ) and Doxycycline ( $30.8 \%$ ). Out of total 23 isolates of Escherichia coli and Klebsiella pneumoniae, $7(30.43 \%$ ) were found ESBLs producers. Out of 10 Escherichia coli isolates $3(30 \%)$ were found ESBLs producers and of the 13 Klebsiella pneumoniae isolates $4(30.8 \%)$ were found ESBLs producers.

## 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. 6,7
Out of the 344 samples that were received with clinically suspected BSI, 86 cases were positive for aerobic bacterial growth. The culture positivity rate in the present study was $25.00 \%$. The culture positivity rates shown by other authors vary considerably in the studies conducted in the past literature. ${ }^{7-9}$ The variations in culture positivity rates may be due to prior treatment with antibiotics. In the present study efforts were made to collect samples prior to antibiotic administration in majority of the cases and thus good culture positivity rates were obtained. ${ }^{10}$
In the present study, out of the total 344 blood culture samples that were received, 170 ( $49.4 \%$ ) were from the age group 20-49 years which was followed by > 50 years group accounting for $27.3 \%$ ( $94 / 344$ ) of the blood culture samples, and $80(23.3 \%)$ from age group 12-19 years.
Among the 86 positive blood culture samples, $25 / 86$ (26.6\%) BSI were obtained from the elderly age group of $>50$ years, $21 / 80$ ( $26.2 \%$ ) BSI were from the $12-19$ years age group and among the adult population, $40 / 170(23.5 \%)$ were from the $20-49$ years
age group. The average age of presentation among the adult population was 38.73 years. Also there is clear evidence that immune dysregulation contributes to enhanced susceptibility of elderly patients to sepsis. The clinically suspected as well as culture positive BSIs were seen more commonly among the extremes of age group.
In present study, sensitivity pattern of gram positive cocci (CONS \& COPS). ${ }^{11}$ Out of total 12 COPS cases, high sensitivity was found in Vancomycin (100\%), Linezolid (91.7\%), Amoxy-clav (83.3\%), Ceftriaxone (83.3\%), Amikacin (66.7\%) Ciprofloxacin (41.7\%), Erythromycin (41.7\%), Tetracycline (41.7\%), Cotrimoxazole ( $25 \%$ ) and Cefoxitin ( $25 \%$ ). In present study, out of total 30 CONS cases, we found in Vancomycin (100\%), Linezolid (93.3\%), Amoxy-clav (80\%), Cefoxitin (80\%), Amikacin (73.3\%), Ceftriaxone ( $73.3 \%$ ), Ciprofloxacin ( $53.3 \%$ ), Cotrimoxazole (33.3\%), Erythromycin (26.7\%), and Tetracycline (20\%) sensitive isolates. Garg VK et al described the antimicrobial sensitivity pattern of common organisms in isolates of clinical samples of patients admitted in ICU at our tertiary care cancer center. All clinical samples were collected and processed for culture and antibiotic susceptibility testing were carried out on isolates as per Clinical Laboratory Standard Institute guidelines. A total of 644 specimens were collected. Escherichia coli, Acinetobacter spp., Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus and Enterococcus spp. were most commonly encountered. In positive bacterial cultures, majority were Gram-negative isolates ( $84.14 \%$ ). Klebsiella was the most common gram-negative isolate ( $34.78 \%$ ) and Enterococcus spp. were the most common Gram-positive isolates ( $61.53 \%$ ). A high level of resistance to various antibiotics was noted among Gramnegative bacteria compared to Gram-positive isolates. Majority of the Gram-negative isolates were sensitive to Imipenem, Meropenem, and Colistin sensitivity among Gram-negative isolates was $100 \%$. Linezolid, Teicoplanin and Vancomycin were most sensitive antimicrobials against the Gram-positive bacteria. Regular monitoring of the pattern of resistance of bacteriological isolates in cancer patients is critical to develop antibiotic policy to combat these infections and reduce morbidity and mortality. ${ }^{12}$
Fentie $A$ et al determined the bacterial profile, antimicrobial resistance pattern, and associated factors among cancer patients attending University of Gondar Hospital. A consecutive 216 cancer patients were recruited from February to April, 2017. Cancer patients with solid tumor, started cancer therapy, and being symptomatic had higher odds of culture positivity. The overall burden of bacterial infection among cancer patients is considerably high. ${ }^{13}$
Tohamy ST et al, in their study reported that new empirical antibiotics should be administered including the use of colistin or meropenem alone or both against the MDR GNB in neutropenic cancer patients. ${ }^{14}$

## CONCLUSION

Although regular epidemiological studies of BSIs with respect to the pathogens and their antibiotic susceptibility patterns are thus necessary to guide the clinicians to choose appreciate empirical therapy as well switch over to the best regime based on antibiotic susceptibility pattern to improve the overall outcome of the patient's health.

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