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Microbiological profile and antibiotic vulnerability of bacterial isolates from cancer patients

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Abstract: The development of multiple types of infections in patients admitted to the oncology ward is quite obvious. The infection accompanying mortality in cancer patients is attributed majorly to bacteria and then to fungi. Infections can be successful if an appropriate antibiotic is used based on the knowledge of their sensitivity pattern as well as commonly occurring bacteria. A retrospective study was designed to assess numerous bacteria isolated from infections in cancer patients reported to oncology centers of tertiary care hospitals in the Makkah region, Saudi Arabia. Total, 678 cancer patients were enrolled during this study. The clinical isolates were obtained from urine, blood, respiratory samples, soft tissues and skin areas. The processing of the samples was done in accordance with the "Standard Microbiology Laboratory Operating Procedures". The identification of the isolated was done to their species and vulnerability tests were done as per the guidelines of "Clinical Laboratory Standards Institute". During this study, 300 samples were acquired from both medical and surgical oncology wards and were cultured during the study period. *Klebsiella pneumonia, Staphylococcus aureus, Acinetobacter species, Escherichia coli* and *Pseudomonas aeruginosa* were the microbes that were encountered mostly. The resistance against various antibiotics was found to be encountered by Acinetobacter species whereas resistance against fluoroquinolones, cephalosporin and carbapenems was >50%, found to be encountered by *K. pneumonia*. There was 43.80% resistance was found against methicillin by the *Staph. aureus* species. This study concludes that an enhanced antibiotic resistance was found by gram-negative bacilli specifically, *E. coli, K. pneumonia and Acinetobacter* species. The resistance pattern was not found remarkably in gram-positive strains although, MRSA frequency is found to be upsurged.

Key words: Cancer; Antibiotics; Bacterial isolates; Malignancy.

Introduction

The research in the field of cancer has increased in past few years. Despite newer approaches to treat cancer, an important source of "morbidity and mortality" is considered to be the onset of numerous infection types in cancer patients. The development of multiple types of infections in patients admitted to the oncology ward is quite obvious. The major reason behind this statement is the chemotherapy and cancer that makes the immunity of these admitted patients compromised (1). The immunity in the cancer patient remains compromised due to the particular nature of the disease as well as an interruption by the chemotherapy. Many other factors also contribute significantly towards the onset of bacterial infections in cancer patients The infections that are emerged in cancer patients cause a disorder of the treatment pattern, hospital stay, an increase in treatment cost as well as a reduced survival rate in patients. The infection accompanying mortality in cancer patients is attributed majorly to bacteria and then to fungi (2).

Successful treatment of infection is possible only if antibiotic therapy was selected appropriately using the great knowledge of their sensitivity pattern as well as commonly occurring bacteria. This is the reason for a decline of bacterial infections caused by gram-negative (-ve) pathogens over the past two decades (3). The identification, treatment and prevention of infections need a striking knowledge of the ever-altering spectrum of infections. In most cases, infection management is a main deal among the patients since infections are considered as one of the main causes of patient illness which could to mortality if not handled properly (4). The bacterial infections epidemiology among cancer patients has changed significantly with the passage of time in recent decades and has shifted from gram -ve to gram +ve pathogens. In numerous countries of the world, gram -ve pathogens have dominated the scene as a principal cause of infections among cancer patients (5,6). Not only the mortality rate among the patients has reduced with the appropriate use of antibiotics but the danger of multidrug resistance has also been diminished (7). The incidence of multidrug-resistant bacteria is directly associated with the patients having compromised immunity. The members of the *Enterobacteriaceae* group are the culprit of such a handful of infections. In many Asian countries including India, Pakistan, Bangladesh, etc., the pattern of resistance in already remarkable against cephalosporin (8). The resistance against carbapenems is due to extensive use of this antibiotic against infections in which, the microbes produce carbapenems (9). In India, the incidence of metallo-β-lactamase producing microbes is on the go (10).

Another matter of great concern is the rising resistance against antibiotics in gram-positive strains. An important result is published in a study from Northern India in which a higher incidence of MRSA (methicillin resistance Staph. aureus) in clinical samples has been

found (11). In the same way, the resistance among enterococci isolates is also been increasing for glycopeptide antibiotics (12). The broad-spectrum antibiotics are randomly tried to treat infections in cancer patients till the receipt of culture tests reports. Clinicians need to get to know about the pattern of antibacterial susceptibility that might differ from one geographical zone to another. The study was designed to investigate numerous bacteria isolated from the infections in cancer patients reported to tertiary care cancer hospital at the Medical City, Makkah Saudi Arabia.

Materials and Methods

Ethical approval

The study was conducted at the Laboratory Medicine Department, Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah, Saudi Arabia, in accordance with the declaration of Helsinki and its amendments. The studies involving human participants were reviewed and approved by the Internal Review Board of the local Human Research Ethics Committee of Security Forces Hospital Makkah (SFHM) (Reference No. 0430-140621). The samples were taken from the patients only for this current investigation and for no other study. Written informed consent was obtained from all the study patients after the elucidation of the purpose and objective of the study to them. All obtained information was kept confidential by giving a unique code and evaluated only by the PI of this study. The lab results were communicated to doctors and nurses for better patient management.

Study design, area, and duration

This was a retrospective study that was conducted at the Laboratory Medicine Department, Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah, Saudi Arabia for a duration of one year from June 2020 to May 2021.

Demographic data of the patients

Sociodemographic variables including patient's age, education, profession, residence, marital status, and other relevant clinical data were collected using a predesigned questionnaire. Each sample was obtained for bacteriological lab analysis by a trained health care professional.

Sample size and sampling technique

During this study, 678 patients enrolled at the early stage of this study. Amongst the enrolled, 300 of them were available for microbiology workup and samples were obtained. All surgical (solid tumors) and medical oncology (hemato-lymphoid malignancies) patients were enrolled in the study. The clinical isolates were obtained from urine, blood, respiratory samples, soft tissues and skin areas. The processing of the samples was done in accordance with the "Standard Microbiology Laboratory Operating Procedures". The identification of the isolated was done to their species and vulnerability tests were done as per the guidelines of "Clinical Laboratory Standards Institute" (13,14).

Microbiological studies

The clinical samples were collected from alleged cases of infections. Samples were stained using gram staining following inoculation onto chocolate agar, blood agar and MacConkey agar (HiMedia). Prepared samples were incubated in the presence of air at a temperature of 35°C for 15 hours. Blood culturing was performed by BacT/ALERT system (BioMerieux, USA). The acquired positive cultures were further subjected to sub-culturing onto the chocolate agar, blood agar, and MacConkey agar (HiMedia) and then incubated at a temperature of 35°C for 15 hours in the presence of air. The proof of identity of the pathogenic growth and antimicrobial vulnerability assay of the acquired isolates were confirmed using the VITEK 2 system (BioMerieux, France), and minimum inhibitory concentration values were taken as sensitive or resistant using the CLSI guidelines (Clinical and Laboratory Standards Institute).

Antibiotics used for gram-positive pathogens

The following antibiotics were chosen for gram-positive organisms: Cefoxitin (30 µg), Penicillin (10 units), Gentamicin (10µg), Ampicillin (10 µg), Clindamycin (2 µg), Co-amoxicillin-clavulanate (20/10 µg), Vancomycin (30 µg/MIC), Trimoxazole (1.25/23.75 µg), and Linezolid (30µg).

Antibiotics used for gram-negative pathogens

The following antibiotics were chosen for gram-negative organisms: Ciprofloxacin (5µg), Levofloxacin (5µg), Cefuroxime (30µg), Amikacin (30µg), Ceftazidime (30µg), Cefepime (30µg), and Cefoperazone-sulbactam (75/25µg).

Statistical analysis

Descriptive statistical methods were used for the analysis of the data which was entered into Microsoft Excel 2010. Chi-square test and odds ratio was used to establish the connotation. The results are characterized in the form of frequency tables and graphs.

Results

A total of 678 patients were admitted to both medical and surgical oncology wards during the study period. Out of all these patients, 442 were diagnosed with a bacterial infection. Figure 1 below displays the age of all the admitted patients.

Patients having solid organ tumors possessed an ave-

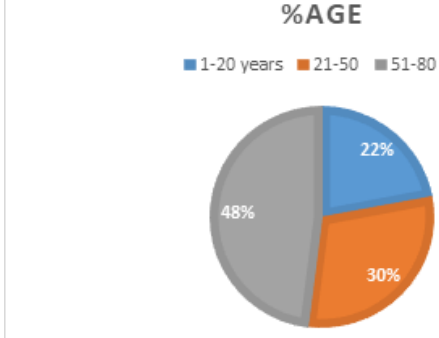

Figure 1. Distribution of patients according to age in years.

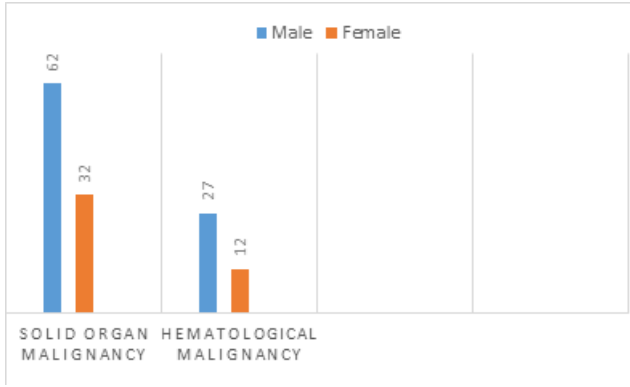

Figure 2. Gender wise cancer patient's distribution.

rage age of 50 years. The majority of the patients were in an age group of 55-60. The maximum age patient was recorded at 72 years whereas; minimum age was recorded in a patient as 4 years. The patients having hematological malignancy were in an age group of 32 years. The results are shown in Figure 2.

A sum of 300 samples were collected from both medical (n=150) and surgical (n=150) oncology wards and were cultured during the study period. The details are displayed in Table 1.

The microbial profile for both medical and surgical cancer patients is given in Table 2 below.

The susceptibility pattern of numerous microbes against antibiotics is shown in Figures 3-5 below.

The resistance against various antibiotics was found to be encountered by Acinetobacter species whereas resistance against fluoroquinolones, cephalosporin and carbapenems was >50%, found to be encountered by *K. pneumonia*. There was 43.80% resistance was found against methicillin by the *Staph. aureus* species.

Discussion

Epidemiology of infections associated with cancer patients has shifted from gram-negative to gram-positive and this is the observation of researchers around the globe. Bacteremia and pneumoniae infections are the ones that are seen mostly in cancerous patients (15). The results of our study showed relatively more patients with skin and soft tissues infections in comparison to those with UTIs (Table-1). In our investigation, an extended number of both gram+ and gram- organisms were isolated as shown in Table 2. The results displayed a higher resistance of E. coli and *K. pneumoniae* against third-generation cephalosporins including cefotaxime and ceftazidime as well as beta lactamase inhibitors. The results are in consistent with the study that was conducted in Karnataka (16) and Bhopal (17). More or less fifty percent of the strains of both E. coli and K. pneumoniae were found to be extended-spectrum beta-lactamase producers. The susceptibility to aminoglycosides including gentamycin and *amikacin* was retained by 50% of the *P. aeruginosa* and *E.coli* isolates. Though >50% of *Acinetobacter and K. pneumoniae* isolates were resilient to antibiotic gentamicin.

A Chinese study showed a total resistance of 6.6% with less than half of which were producing the carbapenemases KPC-2, IMP-4, and NDM-1 (18). Another Indian study indicated NDM-1 from numerous sites,

Table 1. Detail of samples microbial sensitivity and culture.

Sample collection site	Medical oncology ward (n=)	Surgical oncology ward (n=)
Blood	60 (40.00%)	21 (14.00%)
Respiratory source	28 (18.66%)	18 (12.00%)
Urine	42 (28.00%)	101 (67.33%)
Skin source	20 (13.33%)	10 (6.66%)
Total	**150**	**150**

Table 2. Microbial profile for surgical and medical cancer patients.

Microbes	Medical oncology	Surgical oncology	Total
Gram-positive organisms			
Staph. aureus	18	16	34
Enterococcus species	6	5	11
Other streptococci	9	4	13
Coagulase negative staphylococcus	7	14	22
Gram-negative organisms			
K. pneumoniae	30	32	62
Shewanella putrefaciens	2	1	3
Acinetobacter spp	8	3	11
Pseudomonas aeruginosa	10	48	58
K. ozonae	0	0	0
K. oxytoca	2	2	4
Proteus vulgaris	3	4	7
Proteus mirabilis	4	7	11
Citrobacter species	0	1	1
Serratia mercescens	1	1	2

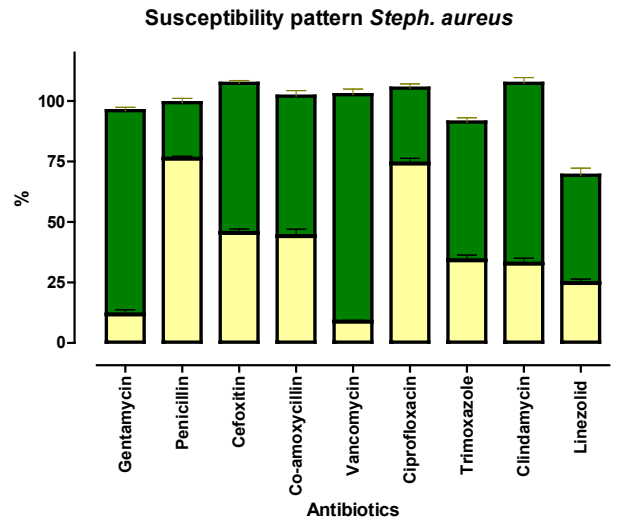

Figure 3. Antibiotic susceptibility pattern of *Steph. aereus*.

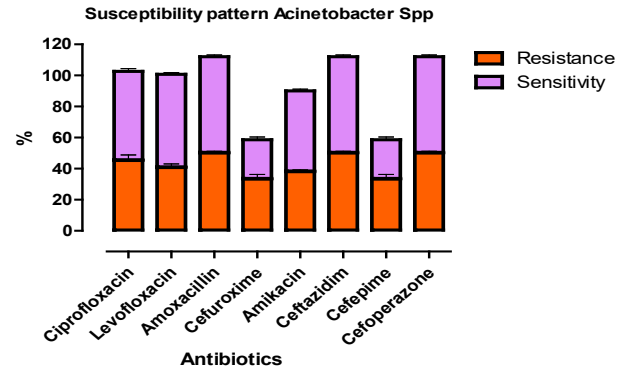

Figure 4. Antibiotic susceptibility pattern of *Acinetobacter spp*.

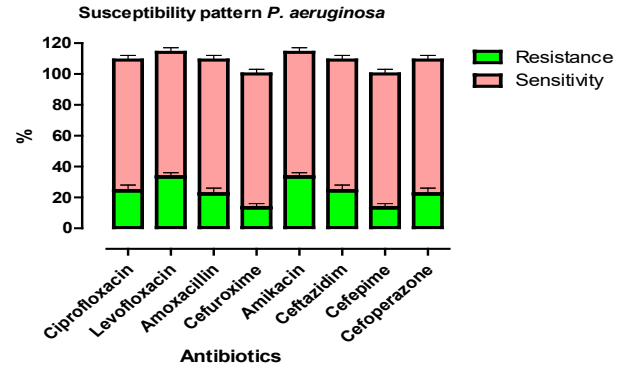

Figure 5. Antibiotic susceptibility pattern of *P. aeuroginosa*.

majorly among *E. coli* and *K. pneumoniae* and they were found highly prevalent and resistant to all antibiotics used in the study with an exception of tigecycline and colistin (19).

In our study, molecular aspects were not done in order to identify carbapenemases and therefore, remained failed to characterize them (20, 21). A study that was done in Odisha, displayed a higher resistance rate of Acinetobacter species to various antibiotics including ceftazidime (9%), meropenem (22%) and gentamycin (76%) (22). In very few isolates of Acinetobacter species were found to be colistin-resistant. It is to be revealed that antibiotic resistance is not significant amongst the gram+ bacteria. During the current study, it was observed that Gram-positive organisms were not that resistant to the antibiotics used in the study. There is a scarcity of reports related to the patient admitted to the oncology department for the treatment of various types of cancer in respect to the antibiotic vulnerability of different bacteria and other microorganisms to the antibiotics used during the treatment of infections. With the increase in the number of cancer patients, it is of very high demand that more information should be made available to understand and explore the vulnerability of the infection-causing bacteria to the antibiotics used in their treatment. This information will not only reduce the duration of healing and thus reduce the suffering of cancer patients but will save the therapy cast as well if the right antibiotic is used for the treatment of a specific infection. There is a lot of data available to express how a microorganism develops resistance to antibiotics and is a matter of great concern to physicians around the world especially in countries with a poor economy. Some of the key factors that are considered responsible for developing antibiotic resistance include antibiotic misuse and the use of antibiotics in the different sources of food like meat, poultry and dairy product. It has been established through many studies that antibiotics are used in the production process of these food sources (23-26). Health regulatory authorities and WHO itself is in a struggle to make policies about how and when to use antibiotics on the national and international levels. One such effort is the "Chennai declaration" which is an initiative that provides advice and recommendations on this issue (27-29). Hopefully, with the information presented in this manuscript, the problem of antibiotic resistance will be solved since using this information a patient can be effectively treated using the right sort of antibiotics.

This study revealed that an enhanced antibiotic resistance was found by gram-negative bacilli specifically, *E. coli, K. pneumonia and Acinetobacter* species. The resistance pattern was not found remarkably in gram-positive strains although, MRSA frequency is found to upsurge.

Conflict of interest

The authors declare no conflict of interest.

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