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Research Article

Bacterial Causes of Infections and Their Antimicrobial Sensitivity Pattern in Cancer Patients

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Abstract: ***Background:*** The increased risk of bacterial infections in the cancer patient is further compounded by the rising trends of antibiotic resistance in commonly implicated organisms. In Bangladesh the frequency of infections caused by E. coli, Klebsiella spp. and Proteus Spp. are high. Now a day the increasing resistance among several organisms is also a matter of concern. We have very few data regarding this issue. ***Aim of the study:*** The aim of this study was to document the bacterial causes of infections and describe their antimicrobial sensitivity pattern in cancer patients. ***Methods and Materials:*** This was a descriptive observational study, conducted in Department of Medical Oncology, National Institute of Cancer Research and Hospital, Dhaka, Bangladesh, during the period from January 2018 to December 2019. In total 19 cancer patients with bacterial infection were selected as study population. All cases were diagnosed from blood, urine, skin/soft tissue and respiratory samples i.e. cough swabs of patients. Samples were processed as per standard microbiology laboratory operating procedures. Socio-demographic and clinical data of respondents were collected using a structured questionnaire. Culture and antibiotic resistance were done following standard microbiological procedures. ***Results:*** According to culture reports we observed E. coli, Proteus, Klebsiella spp. and Pseudomonas spp. were associated in isolates formations in 53%, 21%, 16% and 10% cases respectively. In analyzing the antimicrobial susceptibility among all participants we observed, against all causative organisms (E. coli, Proteus, Klebsiella and Pseudomonas) 94.74% susceptibility had been shown by Ertapenem, Imipenem, Tobramycin, Fleroxacin Amikacin, Ceftriaxone, Cefuroxime, Nalidaxic acid, Dihydrofuran and Vancomycin. Then 89.47% susceptibility had been shown by Ceftriaxone, Doxycycline, Tetracycline, Levofloxacin, Ceftriaxone, Peniciline, Cotrimoxazole and Carbenicillin. Besides these, 94.74% susceptibility had been shown by 84.21% susceptibility had been shown by Amikacin, Gentamicin, Ampicillin, Cotrimoxazole and Piperacillin. On the other hand, in this study, more than 20% resistance was found against Ciprofloxacin, Vancomycin, Cefepime, Cefixime, Ceftazidime, Azithromycin, Aztreonam, Cefotaxime, Amoxicillin, Ceftriaxone, Meropenem and Amoxyclav. ***Conclusion:*** Ertapenem, Imipenem, Tobramycin, Fleroxacin, Amikacin, Ceftriaxone, Cefuroxime, Nalidaxic acid, Dihydrofuran and Vancomycin, Ceftriaxone, Doxycycline, Tetracycline, Levofloxacin, Ceftriaxone, Peniciline, Cotrimoxazole and Carbenicillin. Amikacin, Gentamicin, Ampicillin, Cotrimoxazole and Piperacillin may be considered as the best antibiotics against E. coli, Proteus, Klebsiella and Pseudomonas infections in cancer patients.

Keywords: Bacterial causes, cancer patients, infections, antimicrobial sensitivity.

INTRODUCTION

Basically, the increased risk of bacterial infections in the cancer patient is further compounded by the rising trends of antibiotic resistance in commonly implicated organisms. In Bangladesh this is particularly true in case of Gram negative bacilli such as E. coli, Klebsiella spp. and Acinetobacter spp. Now a day the increasing resistance among Gram positive organisms is also a matter of concern. Till now in spite of vast advances made by medical science in cancer treatment, infections remain a major cause of morbidity and mortality in patients diagnosed with cancer. The cancer patient is immunocompromised because of the nature of

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the disease itself and also due to interventions in the form of chemotherapy, immune therapy etc., 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 [1]. This increased risk of bacterial infections is further compounded by the rising trends of antibiotic resistance in commonly implicated organisms all over the world. This is particularly true in the case of members of Enterobacteriaceae group like Escherichia coli and Klebsiella pneumoniae and the nonfermenter group of organisms such as Acinetobacter spp. In the Indian setting. There is already widespread resistance to the cephalosporins as shown by ESBL (extended spectrum β-lactamase) and Ampicillin producers among the Enterobacteriaceae [2]. Rampant use of antibiotics has unfortunately led to increasing resistance to the carbapenems as well, and this is generally due to carbapenemase production by the organisms [3]. Prevalence of Metallo-β-lactamase (MBL) producing organisms including New Delhi MBL-1 (NDM-1) is also on the rise in India [4]. Increasing resistance among Gram-positive organisms is also a matter of concern. High rates of Methicillin-Resistant Staphylococcus aureus (MRSA) in clinical samples have been noted in one study from North East India [5]. Similarly, resistance to the glycopeptide antibiotics such as vancomycin and tiecoplanin among clinical isolates of enterococci is also increasing [6]. The symptoms of infection in cancer patients could be masked by the cancer treatment modalities [7] that are 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 [7]. 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 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 [8]. Therefore, patients with both type of cancer are highly susceptible to almost any type of bacterial infection [9]. Among Gram positive bacteria (GPB) genus Staphylococcus and from Gram negative bacteria (GNB): Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa are frequently associated [10]. 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]) [11]. As a result, empirical antibiotic treatments of cancer patients are continually challenged by the change in frequency of Gram-positive as well as Gram-negative bacteria and 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 as well as control strategies between health care facilities. 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.

OBJECTIVES

General Objective

- To document the bacterial causes of infections and describe their antimicrobial sensitivity pattern in cancer patients.

Specific Objective

- To collect information regarding the socio-demographic characteristics of cancer patients.
- To collect information regarding the clinical characteristics of cancer patients.
- To collect information regarding the antimicrobial sensitivity on several causative organisms in cancer patients.

METHODOLOGY & MATERIALS

This was a descriptive observational study and it was conducted in Department of Medical Oncology, National Institute of Cancer Research and Hospital, Dhaka, Bangladesh, during the period from January 2018 to December 2019. In total 19 cancer patients with several bacterial infections attended the mentioned hospital with proper documentation were selected as study population. The age range of the participants was 18-60 years. All cases as well as isolates were diagnosed from blood, urine, skin/soft tissue and respiratory samples i.e. cough swabs of patients. Samples were processed as per standard microbiology laboratory operating procedures. Socio-demographic and clinical data of respondents were collected using a structured questionnaire. Culture and antibiotic resistance were done following standard microbiological procedures. The study was reviewed and approved by the ethical committee of the mentioned hospital. Proper writtenconsents were taken from all the participants before starting data collection. 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. The blood samples were collected, processed and 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 basis for up to7 days. Bottles which showed

signs of growth were gram stained and sub cultured on blood agar, chocolate agar, Mac Conkey agar, and mannitol salt agar. 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 sub-cultured before being reported as a negative result. Absolute neutrophil count was done using a XT-4000i hematology analyzer (Sysmex Europe GmbH, Norderstedt, Germany). Midstream urine of the participants 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 colony count $\geq 10^5$ CFU/mL urine. The swabs/ear discharges of the patients were streaked on Mac-Conkey agar, chocolate agar, blood agar plates, and mannitol salt agar. These plates were then aerobically incubated for 18-24 hours at 37°C. The bacterial pathogens among patients were identified after appearance of growth on sub-cultured/cultured plates of blood/wound swab/discharge samples and significant growth on CLED by standard microbiological and biochemical procedures [12]. Antibiotic susceptibility testing of bacterial isolates was done by Kirby Bauer disc diffusion method using Muller Hinton agar (MHA) plate (Oxoid Ltd.) [13]. All the necessary data were collected, coded, analyzed and disseminated by using MS Office and SPSS software version 20.

RESULTS

In this study, a total of 19 cancer patients were included in the study. Out of these, 11(57.59%) were male and 8 (42.11%) were female, with a male-female ratio of a 1.38:1. The mean age (±SD) of study participants was 42.21±15.9 years, range 18-71 years. In this study, the highest number of patients was found from 41-60 years' age group which was 47.37%. Then 36.84% and 15.79% patients were found from 10-40 and >60 years' age groups respectively. On the other hand, in diagnosis procedure Ca Lt. Breast (Recurrence Local) and adenoma were found in 15.79% patients separately. Then in 10.53% patients Ca Rectum, Ewing's Sarcoma, Ca Lung (Rt) and Liver metastasis were found separately. Moreover, in 5.26% patients Ca Buccal mucosa, Ca Cervix, Ca Left lung, Ca Rt middle ear, Fibrosarcoma, Osteosarcoma, Ca Rt. Breast and Ca Lung (Lt) were involved separately. Besides these, fever, including surgical, wounds and ports, change in cough or new cough and unusual vaginal discharge or irritation were found as present complaints in 10.53%, another 10.53%, 5.26% and in another 5.26% respectively. Besides these complaints, some other complaints were associated in 21% participants. In this study among all the participants only 26.32% participant gave history of taking antibiotics was found. In this study among all the participants the mean (±SD) Hb%, RBC, WBC and Platelet counts were 10.84±1.67, 3.49±0.00,7713.79±5868.75 and 144807.25±129325.25 respectively. Besides these, in analyzing the differential count we found, the mean (±SD) Neutrophil, Lymphocyte, Basophil and Monocyte were 58.17±23.50, 22.71±18.36, 1.71±3.05 and 2.64±1.79 respectively. In this study according to culture reports we observed E. coli, Proteus, Klebsiella spp. and Pseudomonas spp. were associated in isolates formations in 53%, 21%, 16% and 10% cases respectively. In analyzing the antimicrobial susceptibility among all participants we observed, against all causative organisms (E. coli, Proteus, Klebsiella and Pseudomonas) 94.74% susceptibility had been shown by Ertapenem, Imipenem, Tobramycin, Fleroxacin Amikacin, Ceftriaxone, Cefuroxime, Nalidaxic acid, Dihydrofuran and Vancomycin. Then 89.47% susceptibility had been shown by Ceftriaxone, Doxycycline, Tetracycline, Levofloxacin, Ceftriaxone, Peniciline, Cotrimoxazole and Carbenicillin. Besides these, 84.21% susceptibility had been shown by Amikacin, Gentamicin, Ampicillin, Cotrimoxazole and Piperacillin. On the other hand, in this study, more than 20% resistance was found against Ciprofloxacin, Vancomycin, Cefepime, Cefixime, Ceftazidime, Azithromycin, Aztreonam, Cefotaxime, Amoxicillin, Ceftriaxone, Meropenem and Amoxyclav.

Table-I: Demographic characteristics of participants (N=19)

Characteristics	n	%
Age (years)		
18-40 Years	9	47.37
41-60 Years	7	36.84
>60 Years	3	15.79
Sex		
Male	11	57.89
Female	8	42.11

Table-II: Clinical and histopathological characteristics of participants (N=19)

Characteristics	n	%
Diagnosis		
Ca Lt. Breast (Recurrence Local)	3	15.79
Adenoma of parotid gland	3	15.79
Ca Rectum	2	10.53
Ewing's Sarcoma	2	10.53
Ca Right Lung	2	10.53
Liver metastasis	2	10.53
Ca Buccal mucosa	1	5.26
Ca Cervix	1	5.26
Ca Left Lung	1	5.26
Ca Rt middle ear	1	5.26
Fibrosarcoma	1	5.26
Osteosarcoma	1	5.26
Ca Rt. Breast	1	5.26
Present complaints		
Fever	2	10.53
Including surgical wounds and ports	2	10.53
Change in cough or new cough	1	5.26
Unusual vaginal discharge or irritation	1	5.26
Others	4	21.05
History of taking antibiotics		
Present	5	26.32
Absent	14	73.68
Sample		
Pus	7	36.84
Urine	5	26.32
Discharge from any sites	4	21.05
Sputum	2	10.53
Others	1	5.26
Complete blood count (Mean ±SD)		
Mean Hb%		10.84±1.67
Mean RBC		3.49±0.00
Mean WBC		7713.79±5868.75
Mean Platelet		144807.25±129325.25
Differential Count (Mean ±SD)		
Mean Neutrophil		58.17±23.50
Mean Lymphocyte		22.71±18.36
Mean Basophil		1.71±3.05
Mean Monocyte		2.64±1.79

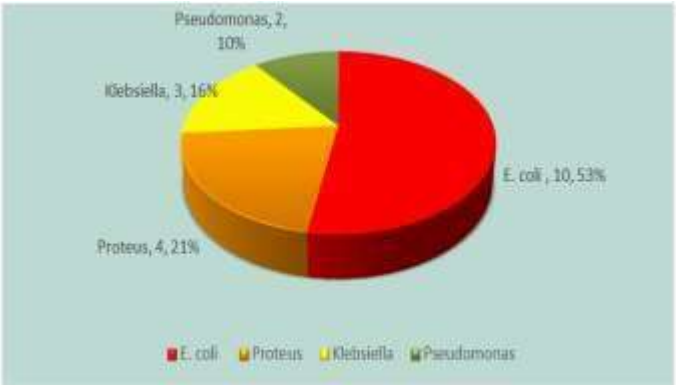

Fig-I: Antimicrobial susceptibility among all participants (N=19)

Table-III: Antimicrobial susceptibility among all participants (N=19)

Antimicrobial agents	n	%
Ertapenem	18	94.74
Imipenem	18	94.74
Tobramycin	18	94.74
Fleroxacin	18	94.74
Amikacin	18	94.74
Ceftriaxone	18	94.74
Cefuroxime	18	94.74
Nalidaxic acid	18	94.74
Dihydrofuran	18	94.74
Vancomycin	18	94.74
Ceftriaxone	17	89.47
Doxycycline	17	89.47
Tetracycline	17	89.47
Levofloxacin	17	89.47
Peniciline	17	89.47
Cotrimoxazole	17	89.47
Carbenicillin	17	89.47
Gentamicin	16	84.21
Ampicillin	16	84.21
Piperacillin	16	84.21
Ciprofloxacin	15	78.95
Cefepime	15	78.95
Cefixime	15	78.95
Ceftazidime	14	73.68
Azithromycin	14	73.68
Aztreonam	14	73.68
Cefotaxime	14	73.68
Amoxicillin	14	73.68
Meropenem	12	63.16
Amoxyclav	11	57.89

Table-IV: Antimicrobial resistance among all participants (N=19)

Antimicrobial agents	n	%
Ertapenem	1	5.26
Imipenem	1	5.26
Tobramycin	1	5.26
Fleroxacin	1	5.26
Amikacin	1	5.26
Ceftriaxone	1	5.26
Cefuroxime	1	5.26
Nalidaxic acid	1	5.26
Dihydrofuran	1	5.26
Vancomycin	1	5.26
Doxycycline	2	10.53
Tetracycline	2	10.53
Levofloxacin	2	10.53
Peniciline	2	10.53
Cotrimoxazole	2	10.53
Gentamicin	3	15.79
Ampicillin	3	15.79
Piperacillin	3	15.79
Ciprofloxacin	4	21.05
Cefepime	4	21.05
Cefixime	4	21.05
Ceftazidime	5	26.32
Azithromycin	5	26.32
Aztreonam	5	26.32
Cefotaxime	5	26.32
Amoxicillin	5	26.32
Meropenem	7	36.84
Amoxyclav	8	42.11

DISCUSSION

The aim of this study was to document the bacterial causes of infections and describe their antimicrobial sensitivity pattern in cancer patients. In our study according to culture reports we observed E. coli, Proteus, Klebsiella spp. and Pseudomonas spp. were associated in isolates formations in 53%, 21%, 16% and 10% cases respectively. In this study association of Gram positive bacteria was not found. But in a study, 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 [14]. In contrary, a study from other African countries reported that GNB were significantly more predominant isolates from cancer patients [10], and current data from other studies indicates the re-emergence of GNB among febrile neutropenic cancer patients [11]. This might be due to minimal use or the discontinuation of fluoroquinolones prophylaxis [15].

These findings strengthen the need for frequent surveillance for understanding the local epidemiology of bacterial infection among cancer patients. *S. aureus*, Coagulase-negative staphylococci(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 [16]. The GPB *S. aureus* and Coagulase-negative staphylococci(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 [17]. 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. In our study, in analyzing the antimicrobial susceptibility among all participants we observed,

against all causative organisms (E. coli, Proteus, Klebsiella and Pseudomonas) 94.74% susceptibility had been shown by Ertapenem, Imipenem, Tobramycin, Flurloxacin, Amikacin, Ceftriaxone, Cefuroxime, Nalidaxic acid, Dihydrofuran and Vancomycin. Then 89.47% susceptibility had been shown by Ceftriaxane, Doxymycin, Tetracycline, Levofloxacin, Ceftriaxone, Peniciline, Cotrimoxazole and Carbenicillin. Besides these, 84.21% susceptibility had been shown by Amikacin, Gentamicin, Ampicillin, Cotrimoxazole and Piperacillin. On the other hand, in this study, more than 20% resistance was found against Ciprofloxacin, Vancomycin, Cefepime, Cefixime, Ceftazidime, Azithromycin, Aztreonam, Cefotaxime, Amoxicillin, Ceftriaxone, Meropenem and Amoxyclav. 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 [17]. In this study, the overall prevalence of MDR was 45% lower than a recent report in the same place from neonatal septicemia (65%) [18]. Among the isolated bacteria, *K. pneumoniae* and *E. coli* were the principal MDR strains concordant with a previous study in the same place [18]. Most studies have shown that cancer patients with hematological malignancy had a higher risk of developing bacterial infection as compared to solid tumor patients [19].

CONCLUSION AND RECOMMENDATIONS

In this study the rate of Gram +ve isolates was found higher than Gram -ve isolates. But most of the antimicrobial agents showed satisfactory susceptibility against GPB isolates. On the other hand, a noticeable number of antimicrobial agents had failed to show satisfactory susceptibility against GNB isolates. So we can conclude GNB isolates are difficult to treat by generally used antimicrobial agents. On the other hand, E. coli had been proved as the most notorious bacteria to treat. This was a single centered study with a small sized sample. So the findings of this study may not reflect the exact scenario of the whole community. So for getting more specific findings we would like to recommend for conducting more studies regarding the same issue.

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