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Antimicrobial Drug Utilization and Resistance Trends in Septicemia Patients: A Comprehensive Study at a Tertiary Care Hospital

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Abstract **Original Research Article**

Background: Septicemia is still among the leading causes of morbidity and mortality worldwide, especially among patients in the intensive care unit. The right use of antimicrobial agents is central to the successful management of septicemia, but increasing incidences of antimicrobial resistance are a big challenge. ***Objective:*** This study aimed to quantify the antimicrobial usage, resistant organisms, and clinical performance in septicemia patients in a tertiary healthcare facility in Bangladesh. ***Methods:*** A prospective observational study was done in the Department of Medicine, Community Based Medical College Hospital, over a period of 16 months. One hundred and ten participants with septicemia and admitted to the ICU were recruited. Demographic data, antimicrobial consumption, microbiological results, and clinical outcomes were gathered and examined. ***Results:*** Most of the patients were male (54.5%) and within the age group of 31–40 years. Cephalosporins were the most common first-line antimicrobials (13.3%), while macrolides (12.3%) and carbapenems (11.7%) were at the second and third rank, respectively. There were frequent alterations in antimicrobial therapy; in 28 percent of cases, ceftriaxone was replaced by levofloxacin. Patients with resistant infections had the advantage of a longer hospital and ICU stay of at least 1 week ($p<0.01$). 16% in patients with resistant infections. ***Conclusion:*** The topics discussed in this study include the issues arising from septicemia management due to antimicrobial resistance, the requirement of broad-spectrum empiric therapy, often changing antimicrobial regimens, and overall poor outcomes for such resistant infections. Overall, the present results highlight the need for strict adherence to principles of antimicrobial stewardship, local resistance pattern monitoring, and the creation of novel therapeutic interventions. Additional multi-centered trials to determine strategies against septicemia and AMR in limited resource facilities should be conducted.

Keywords: Septicemia, antimicrobial resistance, Infections, Cephalosporins.

INTRODUCTION

Septicemia continues to be a major source of morbidity and mortality and is most prevalent in intensive care units. This is an illness that usually occurs when a patient develops systemic inflammation due to an infection that, if not well managed, may lead to organ failure and death [1]. Septicemia requires the proper and timely utilization of antimicrobial agents; however, the occurrence of antimicrobial resistance represents a formidable challenge. Over the last few years, concern has been raised with the rising rates of septicemia and the appearance of multidrug-resistant organisms [2]. Previous investigations have estimated that septicemia occurs in between 6% and 30% of ICU patients and is associated with mortality ranging from 10% to 50%. The nature and distribution of septicemia are multifactorial owing to patient-related factors like age and underlying diseases, as well as the microbial population in a given region or community [3]. It is crucial to point out that the prudent utilization of antimicrobial agents is critical in the management of septicemia. Nevertheless, the choice of the appropriate empiric therapy has raised some concerns because of the constant emergence of different levels of antimicrobial resistance [4]. The World Health Organization has agreed that antimicrobial resistance is among the top ten threats that humanity will continue to face for the remaining years. In regard to the case of septicemia, resistance may result in effective treatment being administered only in delayed time and restraining

prolonged hospital stays, increased costs, and adverse patient outcomes [5]. Knowledge of antimicrobial use and resistance patterns in a particular community is crucial for the selection of initial therapy as well as for the development of initiatives to improve antimicrobial use [6]. Various researchers have noted that it is crucial to consider geographic-specific susceptibility patterns when it comes to the use of antimicrobials. However, there is a lack of data coming from many parts of the world, especially developing nations where surveillance may be financially constrained [7].

Some of the many considerations that predispose an individual to develop septicemia are age, male gender, diseases like diabetes and chronic obstructive pulmonary disease (COPD), and procedures invasive and hospitalization for a longer time. These risk factors are important to recognize to help in implementing early detection and intervention [8]. The selection of empiric antimicrobial agents in septicemia depends on clinical findings regarding the probable source of the infection, the local resistance profile of organisms, and other factors regarding the patient. Empirical regimens frequently employ a first-generation or a second-generation cephalosporin as the beta-lactam and aminoglycosides or fluoroquinolones [9]. Yet, the best empiric therapy may differ from center to center and region to region. Surveillance of antimicrobial use is important in evaluating the magnitude and extent of prescribing as well as in identifying potential problems. Research has also indicated that the implementation of published standards on the use of antimicrobials can enhance outcomes as well as mitigate the development of resistance. However, sustainable antimicrobial stewardship programs have been difficult to implement across most healthcare facilities [10]. The effects of concern resulting from AMR are far-reaching on patient experiences with septicemia. Non-susceptible infections have been linked with high death risks, prolonged hospitalization, and higher health charges. Second-line or reserve antimicrobials to manage resistant infections also pose questions about the likelihood of exacerbating resistance to such crucial organisms [11] Due to these challenges, surveillance of antimicrobial use and resistance patterns in septicemia should be conducted on a regular basis. This information is crucial for directing empiric therapy, shaping local antibacterial guidelines, and supporting worldwide strategies in fighting antimicrobial resistance [12].

Consequently, the present study intends to meet this necessity by generating more detailed information about the overall consumption of antimicrobial agents, the rates of microbial resistance, and the related clinical efficacy of a large sample of septicemia patients across a troubleshooting tertiary care hospital. Thus, through analyzing these features in a large-scale clinical practice setting, the authors aim at providing additional insights that may help in enhancing the local approach to managing septicemia during the antimicrobial resistance era.

METHODS

The prospective random observational study was performed for 16 months at the Community-Based Medical College Hospital in Bangladesh. The study received ethical consideration from the institutional ethics committee, and informed consent was sought from all the participants or their guardians.

Inclusion Criteria:

- Patients aged 18 years or older
- Admitted to the intensive care unit (ICU) with a diagnosis of septicemia
- Receiving antimicrobial therapy

Exclusion Criteria:

- Patients under 18 years of age
- Pregnant women
- Patients with a known history of drug allergy
- Patients with incomplete medical records

Socio-demographic, clinical, antimicrobial prescribing practices, microbiology, and clinical outcomes were recorded in the data set. The antimicrobial susceptibility testing was done in accordance with the culture laboratory's procedures. Data was analyzed with the help of SPSS statistical software. Demographic and clinical characteristics were summarized using descriptive statistics. Categorical variables were compared using the chi-square test, while the student's t-test was used for continuous variables. 05 was used as the level of significance.

RESULTS

Table 1: Demographic characteristics, (N=110)

Characteristics	Frequency (n)	Percentage (%)
Gender		
Male	60	54.5
Female	50	45.5
Age group (In years)		
18-30	22	22.0
31-40	30	30.0
41-50	25	25.0
51-60	28	28.0
>60	5	5.0

Characteristics	Frequency (n)	Percentage (%)
Occupation as per Kuppuswamy socioeconomic scale		
Skilled	35	35
Semi-skilled	25	25
Unskilled	30	30
Unemployed	20	20
Education level		
Illiterate	45	45.0
Primary school	20	20.0
High school	25	25.0
Graduate	10	10.0
Post graduate	10	10.0
Socioeconomic background		
Lower	40	40.0
Middle	50	50.0
Upper	20	20.0
Living status		
Rural	75	68.0
Urban	35	32.0

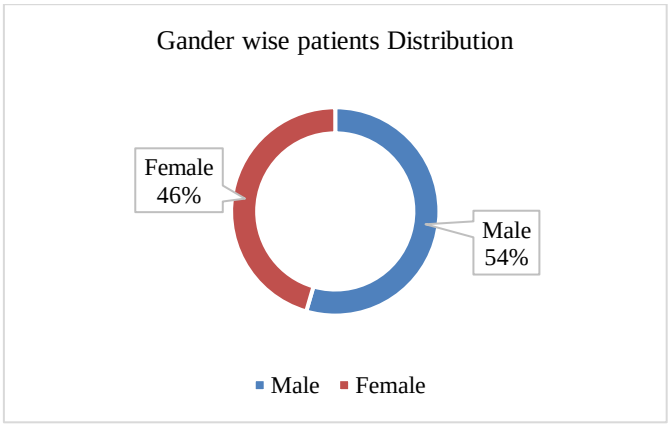

Figure I: Pie chart showed distribution of the patients by Gander (N=110)

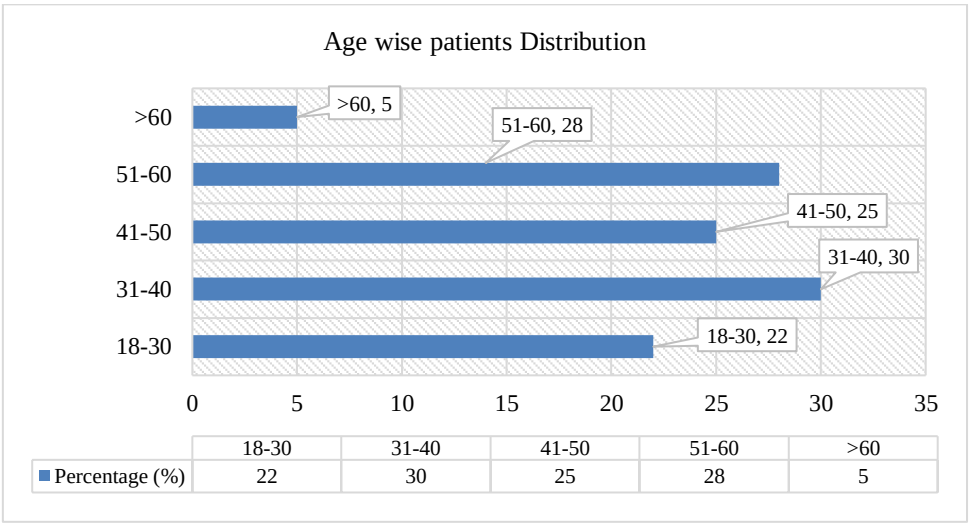

Figure II: Bar chart showed distribution of the patients by age (N=110)

A total of 110 patients meeting the inclusion criteria were enrolled in the study. The demographic characteristics of the study population are presented in Table 1. The majority of patients were male (54.5%), and the most common age group was 31-40 years (30%). A significant portion of the patients (45%) were illiterate and half of the patients (50%) came from a middle socioeconomic background. A majority of the patients

(68%) resided in rural areas, whereas 32% lived in urban settings.

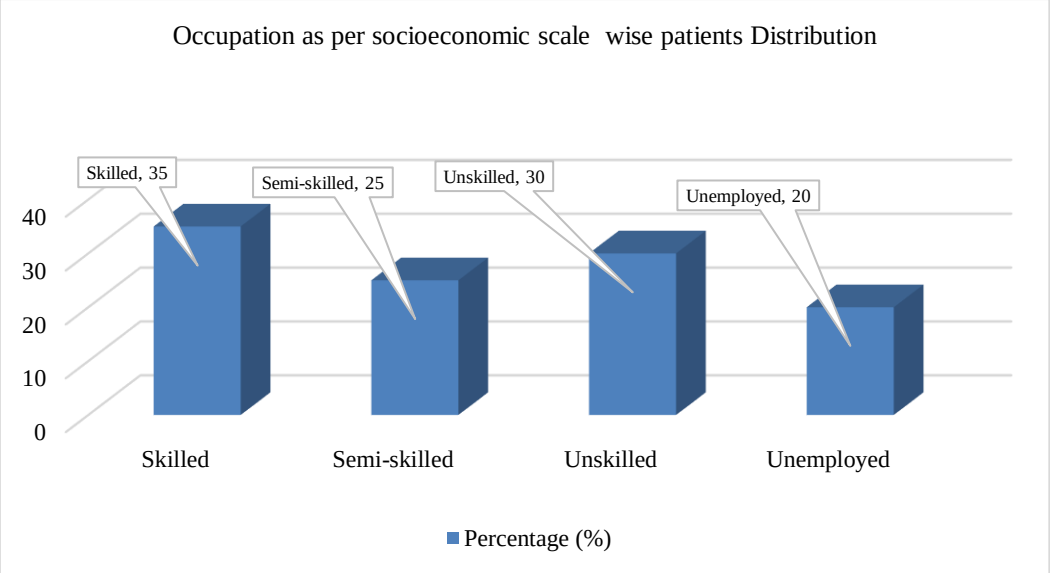

Figure III: Column chart showed distribution of the patients by Occupation as per socioeconomic scale (N=110)

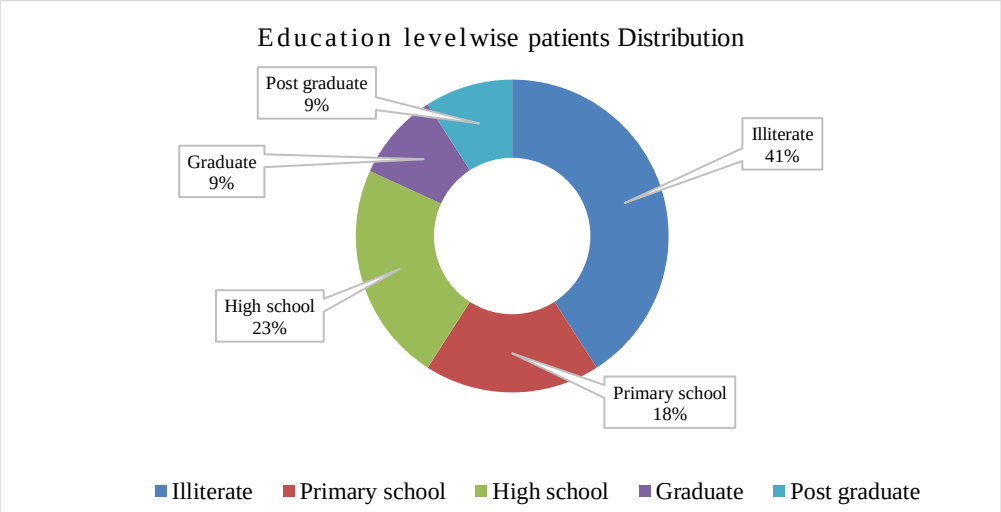

Figure IV: Pie chart showed distribution of the patients by Education level (N=110)

Table 2 outlines the risk factors for septicemia identified in the study population. The most prevalent risk factors were male gender (65%) and age over 60 years (5%). Other notable but less frequent risk factors included coma, acute respiratory distress syndrome (ARDS), reintubation, neurosurgery, and chronic obstructive pulmonary disease (COPD), each present in 2-3% of patients.

Table 2: Risk factors for septicemia

Risk factor	Frequency (n)	Percentage (%)
Age > 60 years	5	5.0
Male gender	65	65.0
Coma	3	3.0
ARDS	3	3.0
Reintubation	3	3.0
Neurosurgery	3	3.0
COPD	2	2.0

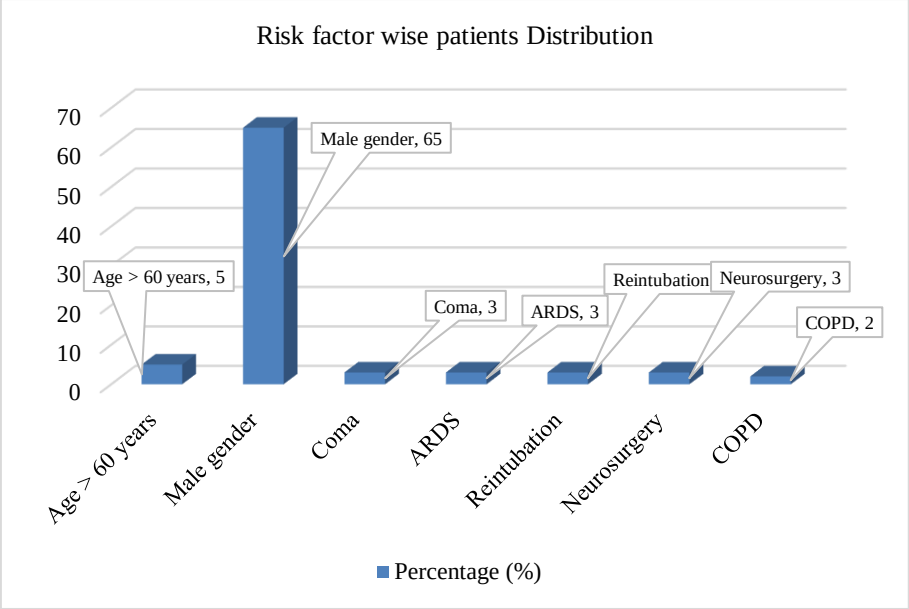

Figure V: Column chart showed distribution of the patients by Risk factor (N=110)

The antimicrobial agents used at the time of ICU admission are detailed in Table 3. Cephalosporins were the most frequently prescribed class (13.3%), followed by macrolides (12.3%) and carbapenems (11.7%).

Table 3: Antimicrobials used at the time of ICU shift of patients

Antimicrobials used	Frequency (n)	Percentage (%)
Cephalosporins	43	13.3%
Macrolide	40	12.3%
Carbapenem	38	11.7%
Piperacillin + Tazobactam	36	11.1%
Linezolid	34	10.5%
Vancomycin	32	9.9%
Levofloxacin	30	9.3%
Clindamycin	28	8.6%
Amikacin	25	7.7%
Gentamicin	18	5.6%

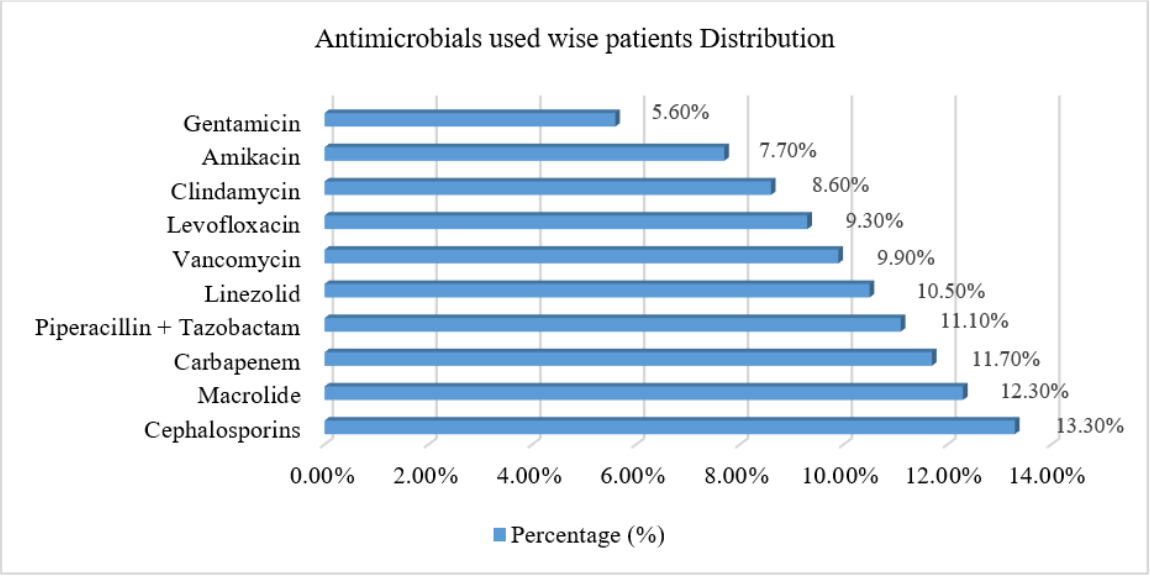

Figure VI: Bar chart showed distribution of the patients by Antimicrobials used (N=110)

Concomitant drug therapy is presented in Table 4, with calcium channel blockers being the most common (35.2%), followed by beta-blockers (29.5%).

Table 4: Concomitant drug therapy

Concomitant drug therapy	Frequency (n)	Percentage (%)
Beta blockers	36	29.5%
Calcium channel blockers	43	35.2%
Magnesium sulphate	34	27.9%
Diuretics	14	11.5%
Levetricetam	15	12.3%
Phenytoin	10	8.2%
Rosuvastatin	8	6.6%
Insulin	6	4.9%
Enoxaparin	6	4.9%

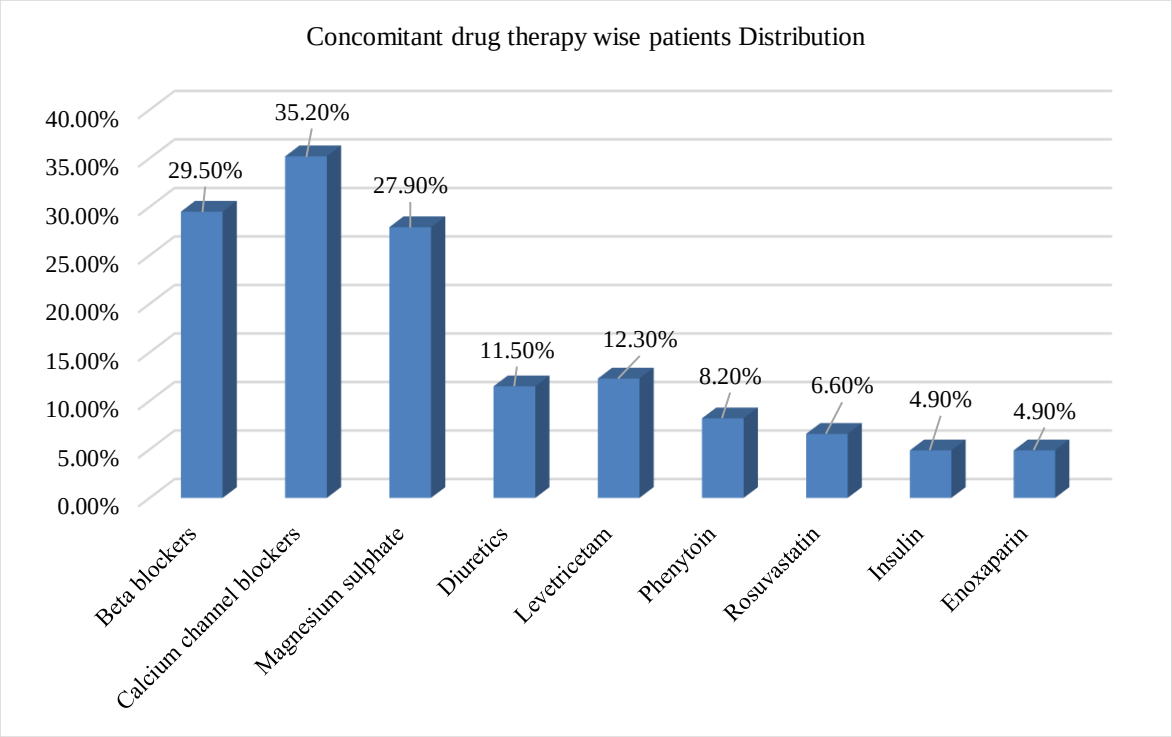

Figure VII: Column chart showed distribution of the patients by Concomitant drug therapy (N=110)

Changes in antimicrobial therapy during the course of treatment are shown in Table 5. The most frequent change was from ceftriaxone to levofloxacin (28% of changes).

Table 5: Change of antimicrobial agents

Previously Used Antimicrobials	Changed Antimicrobials	Frequency (N)	Percentage (%)
Ceftriaxone	Levofloxacin	7	28%
Piperacillin + tazobactam	Colistin, meropenem	6	24%
Cephalosporins	Polymyxin B	4	16%
Macrolide	Meropenem	4	16%
Carbapenem	Meropenem	2	8%
Vancomycin	Meropenem	1	4%
Levofloxacin	Colistin	1	4%

Table 6 compares the mean duration of hospital and ICU stay between all patients and those with resistant infections. Patients with resistant infections had significantly longer stays in both the hospital and ICU ($p<0.01$).

Table 6: Comparison of mean period of stay in ICU and total hospital stay

Parameters	Duration of hospital stay, days, mean ± SD	Duration of ICU stay days, mean ± SD	P value
All patients included	13.22±0.45	4.34±0.45	<0.01
Resistance cases	19.22±0.45	8.18±0.45	<0.01

Clinical outcomes are presented in Table 7. Overall mortality was 18.18%, but this increased to 63.16% in patients with resistant infections.

Table 7: Clinical outcome in admitted patients

Clinical Outcome	Total Cases (n)	Total Cases (%)	Resistant Cases (n)	Resistant Cases (%)
Recovered	90	81.82%	14	36.84%
Death	20	18.18%	24	63.16%
Total	110	100%	38	100%

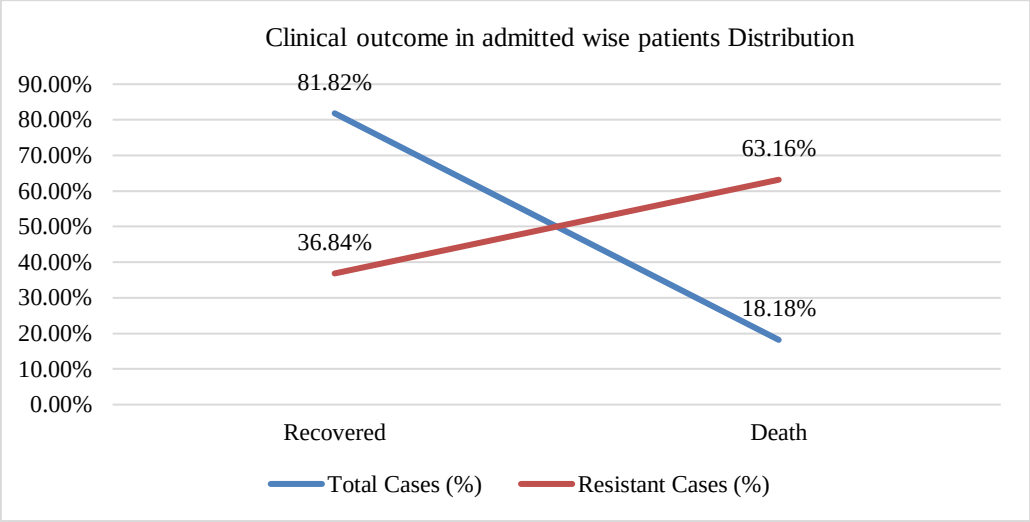

Figure VIII: Line chart showed distribution of the patients by Clinical outcome in admitted (N=110)

DISCUSSION

The findings of this study will be relevant in understanding the specific trends of antimicrobial usage and resistance in septicemia patients at a tertiary health care facility in Bangladesh. The distribution of the sex and age of the patients in our study cohort, as well as the higher number of male patients and highest incidence in the 31-40 age group, is also in line with other studies prevalent in this region. Similarly, Anitha *et al.*, [13]. conducted a similar study in a similar context, and they found proportionate age and gender distribution. We endorse the findings of our study regarding septicemia risk factors, inclusive but not limited to male gender and increased age. However, the proportion of some comorbidities like COPD (2%) in our subjects is low as compared to the Western studies. It is also quite possible that the fundamental differences in the composition of the population studied and the approach to diagnosis might be the reason for this. Indeed, our data on the current and appropriate antimicrobial utilization show that the first-line antimicrobials of choice are the broad-spectrum agents, cephalosporin and macrolides. It is generally in conformity with the guidelines for empiric treatment of septicemia as practiced in other countries. Nonetheless, carbapenems were slightly more often used (11.7% of first-line therapy), which warrants further discussion on the reasons for it and may indicate local resistance or irrational use of the drugs crucial for combating multi-resistant organisms. A study conducted by Westhölter *et al.*, [14]. described a slightly lower carbapenem utilization rate of 7.5% in septicemia patients, indicating differences across healthcare facilities. The fact that antimicrobial therapy is often changed, for example, from ceftriaxone to levofloxacin or from initially used agents to colistin or meropenem, points to a high level of resistance to initial compounds. This finding is rather shocking but is in line with the world over due to the growing instances of antimicrobial resistance. A cross-sectional study with a multicenter conducted in India by Gandra *et al.*, [15]. also showed similar trends towards escalated use of reserve antibiotics in septicemia cases. The effect of antimicrobial resistance on the sides of the patient is demonstrated in the picture associated with length of stay to death. Other studies also supported this claim on hospital and ICU stays because patients with resistant infections usually take longer time to recover than patients with non-resistant infections. The excess length of stay or antibiotic use observed in our study is in the range of those found in other studies, such as the large European study conducted by Lambert [16] and

associates, where it was discovered that resistant infections in ICU patients were linked to an extra length of stay of 5–13 days.

The case fatality rate observed in our study (18. 18% overall, 63. 16% in the resistant cases) is comparable with the septicemia mortality reported in the literature in low- and middle-income countries. Nevertheless, the high mortality in resistant cases shows the role of effective initial therapy and the necessity of strict antimicrobial stewardship. Several strengths of this study include its prospective design, extensive data collection, and addressing a significant healthcare concern in a resource-limited country. However, it has its drawbacks, as well: The single-center study design may thus reduce generalizability, and the relatively small patient cohort does not allow for further sub analysis. Also, we did not describe the initial choice of empiric therapy, and knowing this information could help explain the rates and reasons for therapy variations and their consequences. These studies have implications for clinical practice as well as policy. The marked rate of first-line antimicrobial resistance indicates that there should be an ongoing process of reassessment and possibly modification of the empiric therapy protocols applicable in a given locale. This is specifically worrying in light of the frequent use of carbapenems and other broad-spectrum agents as initial therapy, a trade that may have been necessary given the local resistance patterns but which exacerbates the problem and underlines the importance of new antimicrobial development and the efficiency of conservationist measures.

CONCLUSION

Hence, the study offers a synthesis of the profile of antimicrobial utilization and resistance in septicemia patients admitted to a tertiary-care hospital in Bangladesh. Coping with irreversibility in clinical antimicrobial use: antimicrobial resistance is confirmed, different empiric therapy is required, antimicrobial regimens change often, and multifocal resistant infections have unfavorable outcomes. These findings highlight the essential need for the implementation of antimicrobial stewardship, monitoring of local resistance profiles, and research into newer agents. Future prospective multi-center studies involving larger samples are required to expand on these observations and elicit the best practice approach to mitigating septicemia and the challenge of AMR within resource-constrained environments.

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