Original Article

Utilization Patterns of Antimicrobials at a Tertiary Care Hospital's Intensive Care Unit

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ABSTRACT

Introduction: Antimicrobials are readily prescribed to seriously ill patients, accounting for a large portion of the drugs administered in intensive care units (ICU). **Objective:** Aimed to explore the antibiotic usage patterns in the ICU patients of a tertiary care hospital, Sylhet MAG Osmani Medical College Hospital. **Methods:** A hospital-based retrospective observational study was conducted to explore the pattern of usage of antibiotics in the ICU of Sylhet MAG Osmani Medical College Hospital. The medical records of 530 patients admitted to the ICU from July 2020 to June 2021 were reviewed. **Results:** Antibiotic treatment was given to 94.0% of the ICU patients. A culture sensitivity test was done in 72.1% of patients; blood samples were more frequently cultured (42.0%). 412 (95.2%) of the 433 samples showed a positive culture result. Klebsiella made up 33.3% of the isolated organism. The mean amount of antimicrobials given per patient was 2.5±1.4. Cephalosporin (38.8%), Carbapenem (31.3%), and Penicillin (29.0%) were the most commonly given antimicrobial groups. About half of the patients (50.8%) received multiple antibiotics. The most frequently used drug combinations were Ceftriaxone and Metronidazole, which were given to 48.0% of the patients. **Conclusion:** Cephalosporin and Carbapenem were most frequently utilized as antibacterial agents in this ICU. However, due to the rise of resistance, physicians should be more aware of using these drugs.

***Keywords*:** Antimicrobial agents, Cephalosporins, Carbapenem, ICU patients, Sylhet.

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Introduction

Intensive care units (ICUs), recognized as intensive treatment units or medical crisis units, are specialized places for patients with serious illnesses to get particular and tailored clinical management. Patients with complex infectious illnesses treated in the ICU can become a significant source of transmissible organisms that can spread and cause nosocomial infections. Nosocomial infections are a

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critical public health problem in today's healthcare structure and a significant cause of mortality among hospitalized patients. ICU patients are more prone to nosocomial infections than general ward patients.[1] Nosocomial diseases affect persons in economically developed and developing nations.[2] While staying in the ICU, patients have been prescribed various medications. Antimicrobial drugs treat critical illness and prevent infections in critically sick patients with low immunity, higher sensitivity to pathogenic microorganisms, and various medical procedures (catheterization) or medical device use (ventilator).[3] Antimicrobial medicines are commonly provided to surgical patients admitted to the ICU to treat and prevent postoperative infections.[4]

The total number of antimicrobial agents (AMA) used in ICUs is ten times higher than in regular hospital wards.[5] Because various academics have expressed worry about AMAs' improper and irrational use, evaluating and monitoring the prescription pattern of AMAs is critical. Furthermore, the emergence of medication resistance has been a topic of discussion.[6] By 2050, the estimated 700,000 individuals who expire every year because of drug-resistant diseases will have risen to 10 million.[7] The evolution of resistance is aided by indiscriminate and inappropriate antimicrobial use, a lack of laboratory facilities, and notification.

Despite this, according to the World Health Organization (WHO), about 50% of antimicrobial drugs are misused worldwide.[8] Inappropriate antibiotic usage involves incorrect antimicrobial selection and poor antimicrobial use, such as inadequate doses, short duration, minor intervals, and unsuitable routes.[9] Improving the use of AMA is a critical public health and patient safety problem and a national priority.[10,11] In this context, the current study explored the use of antimicrobial drugs in ICU patients at a tertiary referral hospital in Sylhet, Bangladesh.

Methods

Study design and settings

This hospital-based retrospective observational study aimed to explore the antibiotic usage patterns in the ICU patients of a tertiary care hospital, Sylhet MAG Osmani Medical College Hospital, Bangladesh, from July 2020 to June 2021. The study was conducted by the Department of Pharmacology and Therapeutics, Sylhet Women's Medical College, in collaboration with Sylhet MAG Osmani Medical College Hospital.

Data collection procedures

Data were collected from all adult patients (18 years and above) receiving antimicrobial therapy in the ICU of Sylhet MAG Osmani Medical College Hospital. Pregnant women and lactating mothers were excluded from the study. The patient's hospital admission and treatment files were checked thoroughly. General data of the patients included patient's age, gender, diagnosis, and risk factors for infection due to MDR pathogens; infection-related data included duration of ICU stay, date of diagnosis of infection, no. of the patient received an antibiotic, sources of infection (nosocomial or community-acquired), and microbiological documentation; and data regarding antibiotic used included total amount of drugs used per patient, the total amount of antimicrobials consumed per patient, more than one antibiotic (concurrent or sequential), antibiotic treatment of the current illness (type and duration of antibiotic consumption).

Clinical infection criteria

Nosocomial infection, also referred to as 'Healthcare-Associated Infection' (HAI), was absent during admission but acquired while receiving health care within 48 hours of admission to a hospital. Unless the patients were moved straight from another hospital or discharged within the 30 days before the present admission, infections arising within 2 days of arrival to the hospital were suggested community-acquired. A patient who received two or more antibiotics was said to be using them concurrently. This was known as sequential usage when the first antibiotic was stopped and a second antibiotic started. Clinical microbiology protocols were followed for bacterial identification. The disc diffusion technique was used to identify antibiotic sensitivity and resistance using several antibiotic discs. A zone of inhibition was used to track the sensitivity.

Statistical analysis

Descriptive statistics were expressed as frequency (percentage) and mean (±standard deviation, or SD) for categorical and continuous data. Data was entered, curated, and analyzed using Microsoft Excel Worksheet 2010. It was presented in tables and charts (pie and bar diagrams).

Ethical approval

The participants' confidentiality was maintained throughout the study. All procedures were conducted according to the guidelines of the Declarations of Helsinki. Ethical approval was taken from the Sylhet MAG Osmani Medical College Hospital, Bangladesh. (Reference: OMCHS/Dir. office/2021/3136).

Results

A total of 530 cases and documents from the ICU were analyzed. The mean age of the patients was 53.4±9.6 years and within the range from 19 to 84 years. A maximum of 42.0% of cases were above 60 years, and minimum cases belonged to the age group of 19 to 32 years, i.e., 12.8% of patients. 54.2% of cases were male, and 45.8% were female. Most of the cases (36.2%) were suffering from septicemia. Other disorders included cardiovascular problems (25.7%), difficult acute abdomen (8.3%), and unintentional accidents (6.4%). Other minor health complications were found in the individuals (23.4%). In 40.2% of the patients, risk factors for infections caused by multidrug-resistant organisms were found. The most prevalent risk factors reported in this study were past antibiotic therapy and previous hospitalization (within the last three months) in 73.2% and 68.1% of individuals, respectively. Continued immunosuppressive sickness or therapy (27.7%), home wound care (12.2%), and hemodialysis within one month were other common risk factors (2.8%). (Table 1)

The mean stay in the ICU was 6.0 days (ranging from 0 to 9 days). AMAs were given to 94.0% of the patients. Nosocomial infection was observed in 53.2% of patients; the rest were patients with community-acquired infection. In 72.1% of the patients, an antibiotic culture and sensitivity test were done. Before initiating antibiotic medication, 433 samples for bacterial culture were collected from 359 individuals. Blood samples (42.0%), urine samples (31.4%), respiratory samples (13.4%), stool samples (5.8%), peritoneal samples (2.8%), and samples from other sites were all cultured samples (4.6%). A total of 95.2% of 433 samples yielded a positive culture report. The most common isolates were ESBL-producing Enterobacteriaceae, primarily Klebsiella pneumonia (33.3), E. coli (19.9%), and Pseudomonas (16.0%), followed by Acinetobacter spp. (15.1%), Staphylococcus aureus (12.9%), and miscellaneous species (2.9%). (Table 2)

During the study period, antibiotics were prescribed as empirical therapy, culture-directed therapy, clinically documented therapy, and failure of prior antimicrobial therapy. During the current hospitalization, 51.4% of patients received empirical therapy. Cephalosporins (Ceftriaxone, Ceftazidime, and Cefepime) were used empirically in 57.0% of cases, Carbapenems (Imipenem, and Meropenem) in 28.9% of cases, Vancomycin in 23.8% of cases, Piperacillin- Tazobactam in 23.1% of cases, and Metronidazole in 14.8% of cases. (Table 3)

Cephalosporin was the most commonly prescribed antimicrobial drug (38.8%), followed by Carbapenem (31.3%), Penicillin (28.9%), Aminoglycosides (19.7%), Fluoroquinolone (18.5%), and Antiamoebic drugs (17.1%) during the study period (Figure 1).

Ceftriaxone was the most commonly given antimicrobial medicine, with 186 (37.3%) patients receiving it. Meropenem was given to 138 patients (27.7%). In 98 (19.7%) and 46 (9.2%) patients, a combination of Amoxicillin plus Clavulanic acid and Piperacillin plus Tazobactum was utilized, respectively. Antibiotics such as Amikacin, Moxifloxacin, and Metronidazole were being used in 98 (19.7%), 86 (17.3%), and 85 (17.1%) patients, respectively. Other antibiotics included Ciprofloxacin and several Cephalosporin generations, such as Cefuroxime (with or without Clavulanic acid), Ceftazidime, and Cefepime, which were given to 18 (4.8%) patients. (Figure 2)

Antimicrobial medicines were prescribed on average 2.5±1.4 times per patient. Antibiotics were not given to 32 of the patients. The remaining 498 patients received two or more antibiotics simultaneously or sequentially, with 49.2% receiving one antibiotic and 50.8% receiving two or more antibiotics simultaneously or sequentially. One hundred fifty-three patients (30.7%) received two antibiotics, 12.7% received three antibiotics, 4.4% received four medications, and 3.0% received five antibiotics. The most common combination was Ceftriaxone and Metronidazole, given to 48.0% of the individuals.

In figure3, the mean duration of staying in the ICU was6.0±2.0 days. The minimal range of antibiotic therapy was 1 day, and the maximum was 14 days. 15.0% of patients received antibiotic therapy for up to 3 days. Maximum patients (58.0%) received antibiotics from 4 to 10 days, and 27.0% received antibiotics for more than 10 days.

Table 1: Risk factors for infection due to MDR organisms (n=530)

Risk factors	Frequency (n)	Percent (%)
Antimicrobial therapy in the preceding three months	156	73.2
Hospitalization for ≥48 hours in the preceding three months	145	68.1
Ongoing immunosuppressive illness or therapy	59	27.7
Home wound care	26	12.2
Haemodialysis within one month	6	02.8
Intravenous antibiotic therapy or chemotherapy at home	4	01.9

Multiples responses

Table 2: Infection profile of the patient (n=530)

Parameters	Frequency (n)	Percent (%)
Number of patients received antibiotics (n=530)	498	94.0
Origin of infections (n = 498)		
• Nosocomial / Hospital-acquired infection	265	53.2
• Community-acquired infection	233	46.8
Culture and sensitivity preformed (n=498)	359	72.1
Total samples for culture taken (n, n/patient)	433, 1.21	
Culture sites (n=433)		
• Blood sample	182	42.0
• Urine sample	136	31.4
• Respiratory sample	58	13.4
• Stool sample	25	05.8
• Peritoneal sample	12	02.8
• Others	20	04.6
Total positive culture report (n=433)	412	95.2
Clinical isolates for positive reports (n=412)	137	33.3
• Klebsiella pneumoniae	82	19.9
• E. coli	66	16.0
• Pseudomonas	62	15.1
• Acinobacter spp.	53	12.9
• Staphylococcus aureus	12	02.9
• Others		

Table 3: Antimicrobial utilization state of the patients (n=498)

Parameters	Frequency (n)	Percent %)
Types of indication:		
• Empirical therapy	256	51.4
• Culture directed treatment	139	27.9
• Clinically documented infection	87	17.5
• Failure with prior antibiotic treatment	16	03.2

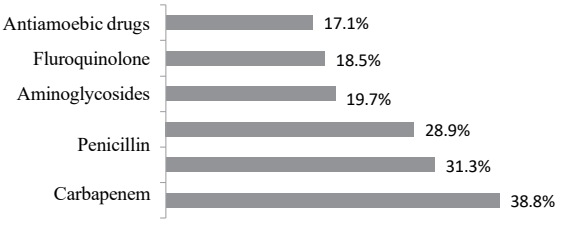

Fig 1: Most commonly used antimicrobial drug groups in ICU

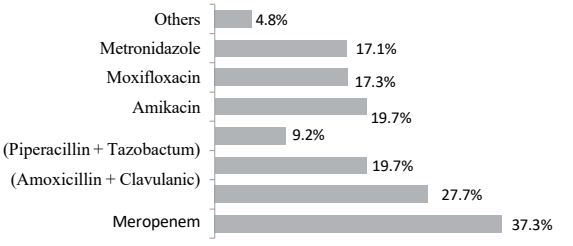

Fig 2: Commonly prescribed antimicrobial drugs used in ICU

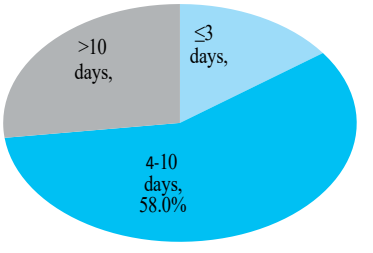

Fig 3: Duration of antimicrobial therapy in days

Discussion

In the present study, the ratio between males and females was 1.18:1; the male was 54.2%, and the female was 45.8%, similar to males' 61.0% and female39.0% in other studies.[12,13] In the ICU, the maximum number of cases was above 60 years, i.e., elderly patients. This could be because cardiovascular disease and other co-morbid conditions like diabetes, hypertension, etc., are

common in such populations. Pandiamunian et al. and Williams et al. also found older adults in their studies.[14,15] Average age of patients was about 53 years. Studies done previously in India and Nepal have observed that the average age of patients is approximately 50 years.[16,17]

A more significant number of the cases were admitted because of septicemia (36.2%), cardiovascular emergencies (25.7%), and complicated acute abdomen (8.3%), whereas in other studies most common indication was postoperative complications followed by sepsis.[3,13] Prior antibiotic therapy was a predisposing factor for the development of MDR-bacteria. This study observed that 40.2% of patients had a minimum of one predisposing factor for infection caused by multidrug-resistant pathogens, especially hospitalization for ≥48 hours in the preceding three months and antimicrobial therapy in the initial three months, similar to another published report.[18] A study observed that the possibility of developing hospital-acquired infection was 9.1 times greater among patients admitted to the ICU than those admitted to general wards.[19] In a study conducted by Crucio in Latin America, the frequency of hospital-acquired infection in the ICU was 46.5%, whereas in our study, the rate was 53.2%.[20]

Antibiotic therapy was based on susceptibility testing of microorganisms isolated from urine blood or infected tissues. Pathogen-directed treatment could be a means to decrease antibiotic use and improve patients' outcomes. In this study, antibiotic susceptibility testing was performed in 72.1% of patients, where the positive rate is 95.2%; nevertheless, 27.9% of the patients received a culture-directed treatment. The most frequent sample processed was the blood sample (42.0%), followed by the urinary sample (31.4%). These findings are correlated with Curcio's results.[20] The most commonly isolated microorganism was *Klebsiella pneumoniae* (33.3%), whereas in another study, *Pseudomonas aeroginosa* was the most commonly isolated microorganism.[21,22]

The mean duration of staying in the ICU was 6.0±2.0 days. In several studies conducted in ICUs in India, Nepal, and the USA, the average length of stay in ICU was 6.2, 4.0, and 5.2 days, respectively.[23,24] Prevalence of antimicrobial consumption in ICUs has been reported elsewhere. In South Africa and Ghana, 75.0% and 71.0% of ICU patients were prescribed antibiotics, respectively.[3] In this study, 94.0% of the patients consumed antibiotics during their ICU stay, consistent with John et al.,[18] and Mahendra et al.[25] But, the prevalence of AMA utilization was not consistent with some previous studies conducted in Turkey and Nepal, where they notified that 57.5% and 30.0% of the ICU patients were prescribed antibiotics, respectively.[17,26] These dissimilarities may be because of different study topographic regions and various population groups. Since ICU patients are at high risk for developing infections, different steps are generally taken to control the transmission of infection.[27] Initiating empirical therapy in ICU patients was related to reducing the frequency of nosocomial infections.[28] Hence, several authors suggest using broad-spectrum AMAs for the empirical therapy for these severe infections.

In our study, 51.4% of the patients underwent empirical therapy during current treatment, where broad-spectrum Cephalosporins were prescribed to 57.0%. These findings were closely related to previous studies.[12,17,25] Regarding antibiotic prescription during the study period, the more commonly prescribed groups were the Cephalosporin group (38.8%) followed by the Carbapenem group (31.3%). The penicillin group was given to (28.9%) of patients, and the Aminoglycoside group to (19.7%). Reviewing related studies found that Penicillin, 1st generation Cephalosporins, and Quinolones were more frequently prescribed AMAs in Pakistan. Consequently, a study conducted in Brazil, where Cephalosporins, Aminoglycosides, and Fluroquinolones were the most frequently prescribed antimicrobial in ICU.[29,30]The most frequently prescribed antimicrobial drug was Ceftriaxone (37.3%), followed by Meropenem 138 (27.7%) and Amoxicillin+ Clavulanic acid (19.7%), which was contrary to a study in India, which shows the antimicrobial agent with maximum consumption was Metronidazole (24.0%), followed by Ceftriaxone (17.2%) and Amoxicillin + Clavulanic acid (11.2%).[3]

Although Cephalosporins and Carbapenems were commonly considered drugs for treating severe infections due to Gram-negative organisms, there is evidence of the development of Cephalosporins and Carbapenem-resistant pathogens worldwide.[20] Several studies from Dhaka City reported a variation in resistance pattern against Cephalosporins at different times. In 2015, Yasmeen et al. reported 68.0% resistance against Cefixime and 30.0% against Ceftriaxone. Research conducted in

the Northern part of Bangladesh showed that Cephalosporin resistance had risen by more than 70.0%.[31] A study by Stewardson et al. illustrated that Carbapenem-resistant Enterobacteriaceae (CRE) infections raised the mortality rate in low-economic and middle-economic countries.[32] Duin et al. demonstrated that Carbapenem-resistance by Klebsiella Pneumoniae Carbapenemase (KPC) is very frequent in South-Asian countries, including Bangladesh.[33]In our study, 50.8% of patients took more than one AMA. A South India study revealed that 57.8% of patients were given more than one antimicrobial agent.18 On average, each patient has prescribed 2.5±1.4 AMAs, related to some studies where the average number of prescribed antimicrobial drugs was 3.0 and 3.4, respectively.[3,11]

Conclusion

It was observed that a wide use of more than one antibiotic simultaneously. Most of these can be considered rational, such as the most common combination of Ceftriaxone and Metronidazole because of their different spectrum of action, and this combination was a sensible choice for diseases like abdominal sepsis. The study provides an important conclusion about using antimicrobials in SOMCH's ICU. Antimicrobial drugs like ceftriaxone and Carbapenem were regularly used. For various reasons, the prescribing practices discovered in our study appear to be justified: (i) Nearly half of the infections were nosocomial, meaning MDR microorganisms caused them. (ii) Besides Ceftriaxone and Carbapenem, almost 70.0% of the patients had prior antibiotic medication during their hospitalization. ICU doctors believed extending the antibacterial spectrum of previously given medicines was a good idea. (iii) Our patients had a high prevalence of ESBL-producing *Entero bacteriaceae*. Carbapenem was the medication of choice against ESBL-producing *Entero bacteriaceae* because it was resistant to their hydrolyzing action. (iv) To reduce the mortality of critically ill patients, a novel method is to start broad-spectrum antibiotic medication as soon as feasible after acquiring essential microbiologic samples, ideally within the first hour.

Limitation

It was unable to assess the reasonableness of prescriptions because of the retroactive nature of the study. We anticipate our current study will spark interest in further studies with more artistic figures to confirm or refute our findings.

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