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Prescribing Pattern of Antimicrobial Agents in Medicine Intensive Care Unit of Tertiary Care Teaching Hospital of Central India

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ABSTRACT

Our aim was to evaluate the prescribing pattern of antimicrobial agents in the Medical intensive care unit. The study of prescribing pattern is a part of medical audit which will monitor, evaluate and suggest modifications in prescribing practices of medical practitioners so as to make medical care rational and cost effective. This was a prospective observational study in 16 bedded medicine intensive care unit and data was collected from March 2018 to November 2018, followed by data compilation and statistical analysis. The sample size was calculated to be 238 using open Epi software. The study revealed doctor's prescribing habits in a Medicine ICU, with 77.6% of patients receiving antimicrobial agents, accounting for 8.2% of total drugs. Most patients were middle-aged, predominantly male. Polypharmacy was common, with an average of 9.6 drugs per patient. Cardiovascular emergencies were the main reason for admission, followed by respiratory and central nervous system diseases. Broad-spectrum antibiotics like ceftriaxone were preferred. Respiratory diseases received the highest antimicrobial prescriptions (31.02%). Variability in prescription was noted, possibly due to different prescribers and lack of guidelines. Improvements could involve implementing an antibiotic policy and routine culture sensitivity testing for common infections. It is extremely necessary to evaluate and monitor the prescribing pattern of antimicrobial from time to time for enabling suitable modifications in prescribing patterns, to increase the therapeutic benefits and also to decrease the adverse effects for optimizing the health care services.

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Key Words
Antimicrobial agents, medicine intensive care unit

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INTRODUCTION

The study of prescribing pattern is a part of medical audit which will monitor, evaluate and suggest modifications in prescribing practices of medical practitioners so as to make medical care rational and cost effective[1]. In critical care unit infections are high and of serious hospital problems. Infections acquired during the hospital stay are generally called nosocomial infections, initially known as infections arising after 48 hour of hospital admission and after 3 days of hospital discharge[2,3]. These infections are opportunistic and microorganisms of low virulence can also cause disease in hospital patients whose immune mechanisms are impaired. Hence, antimicrobial resistance increases in such cases making increase in morbidity and mortality[4].

The most common nosocomial infections contracted in critical care are ventilator-associated pneumonia, central line-associated blood stream infection and urinary catheter-related urinary tract infection. Continual surveillance, audit and hand hygiene are therefore vital[5]. ICU patients are particularly at risk of developing infections with multidrug-resistant (MDR) organisms, which are more prevalent in this environment. More recently, pan antibiotic resistant coliforms, including carbapenems, have emerged[6]. Term “pan resistance” refer to pathogens that are specifically resistant to 7 antimicrobial agents (cefepime, ceftazidime, imipenem, meropenem, piperacillin-tazobactam, ciprofloxacin and levofloxacin)[7]. Appropriate and adequate antibiotic coverage is essential in the treatment of these patients.

Indiscriminate use of antimicrobials increases the risk of bacterial drug resistance[8,9]. High incidences of infectious disease, too much usage of antibiotics and bacterial resistance are reported from developing countries like India[10-13]. Resistant bacteria spread rapidly in these countries due to setting specific factors, such as overcrowding, poor sanitation and a warm-humid climate. Rising rates of bacterial resistance is increasingly seen as a global problem[14-17].

The medically inappropriate, ineffective and economically inefficient use of antimicrobials is commonly observed in the health care system throughout the world, especially in developing countries. Although 50% or more of drug expenditures may be wasted through irrational prescribing, this often remains unnoticed by those who are involved in the health sector decision making or the delivery of health services[18]. Choosing between delaying necessary antimicrobial therapy and exposing the patient to unnecessary therapy requires that two contrasting risks be balanced that of untreated infection versus late antimicrobial complications. The prescribing of antibiotics in the ICU is usually empirical. Appropriate antibiotic utilization in this setting is crucial, not only in ensuring an optimal outcome, but in curtailing the emergence of resistance and containing costs[19].

The World Health Organization has established antibiotic use as a priority in its campaign for the rational use of medications[20]. It is extremely necessary to evaluate and monitor the prescribing pattern of antimicrobials from time to time for enabling suitable modifications in prescribing patterns; to increase the therapeutic benefits and also to decrease the adverse effects for optimizing the health care services. Therefore, we planned an audit to study the reasons for starting antibiotic therapy, the duration of antibiotic treatment and the agreement between clinical suspicion and microbiological results in intensive care practice. The aim of the study is to evaluate the prescribing pattern of antimicrobial agents in the Medical Intensive Care Unit of Netaji Subhash Chandra Bose Medical college, Jabalpur, Madhya Pradesh, India.

MATERIALS AND METHODS

The study was carried out after obtaining approval from the institutional ethics committee, Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India. The data was collected from March 2018 to November 2018, followed by data compilation and statistical analysis. This was a prospective observational study in 16 bedded medicine intensive care unit. To evaluate the drug prescribing pattern a data collection proforma sheet was prepared. The demographic and clinical treatment data of patients was collected in proforma containing following details: Age and sex of patients, diagnosis of patient, total number of drugs prescribed Number and type of antimicrobial prescribed, dose and route of administration, number of fixed dose combination, duration of stay in ICU, percentage of drug which were from the list of essential drugs, relevant investigation results. All the data were collected from patient record sheet. Diagnoses of the patient were also not revealed.

Sample Size: On the basis of result of pilot study, the power of study was 80%, confidence interval as 95% and allowable error as 5%, the sample size was calculated to be 238 using open Epi software. Hence, total 250 patient record sheets were evaluated during study period.

Inclusion Criteria: Patient who are equal or more than 14 years of age of either gender admitted in medicine intensive care unit for >24 hours, N.S.C.B Medical College, Jabalpur.

Exclusion Criteria: Patients who were getting transferred to other specialty intensive care units or other wards or discharged within 24 hours of admission get excluded from the study.

Antibiotic drug utilization was expressed in two ways- the total number of DDDs/ 100 patient-days and percentage of patients receiving any particular antibiotics. It can be calculated as:

$$\text{DDD/100 patient-days} = \frac{[\text{total dose during study period (gm.)} \times 100]}{[\text{DDD (gm)} \times \text{study period (days)} \times \text{bed strength} \times \text{average occupancy}}$$

$$\text{Occupancy index} = \frac{[\text{total in} - \text{patients service days for a period} \times 100]}{\text{total in patients bed count} \times \text{number of day in periods}}$$

Drug consumption was calculated as sum of amount (gm.) of that antibiotic used in each patient during the study period[21]. For calculating the duration of stay in ICU, the day of admission was included but the day of discharge/shift to ward was excluded. Whereas DDD of specific drug was obtained from WHO website[22] which is multiply by total number of days of study period which is of 9 month (275 days), bed strength of medicine ICU is 16 and average occupancy (index) in medicine intensive care unit in this study was 0.36.

Data Analysis: Data was further analysed for the following:

- Age and sex distribution of patients admitted in medicine ICU. Patients in each group were further segregated as males and females
- Total number of drug prescribed per patient
- Total number of antimicrobial prescribed
- Presenting complain and antimicrobial agents prescribed
- Frequency of prescription of antimicrobial agents
- Antibiotic use density in DDD/ patient-days of five frequently used antimicrobial agents according to DDD/100 patient-days along with ATC
- Frequently prescribed fixed dose combinations
- Duration of stay of patients in MICU
- Frequently used combination of drugs in MICU
- Antimicrobial agents are checked weather they are present in essential drug list (EDL) by WHO and essential drug list (EDL) by Madhya Pradesh

Statistical Analysis: The data were entered in computer software MS Excel. The data were expressed as mean (± SD). The magnitude of antimicrobial agent used in the hospital were presented in proportions. The association between the number of antimicrobial used and age, sex, presenting complain and duration of stay were determined using the chi-square test. A $p<0.05$ was considered significant.

RESULTS AND DISCUSSIONS

The table depicts patient demographics in a Medicine ICU. Among 250 patients, the highest number (75, 30%) fell in the 45-60 age group, followed by 58 (23.2%) aged 18-30. Both 31-45 and >60 age groups had 57 patients each (22.8%), while <18 age group had only 3 patients (1.2%). The mean age ± SD of admitted patients was 42±18 years. Additionally, the table shows gender distribution, with 153 males (61.2%) and 97 females (38.8%), yielding a male/female ratio of 1.6:1 (Table 1).

The table demonstrates that most patients, 144 (57.6%), were prescribed 6-10 drugs, followed by 81 patients (32.4%) receiving 11-15 drugs. Only 16 patients (6.4%) were prescribed up to five drugs, while nine patients received more than fifteen drugs. In total, 2367 drugs were prescribed to 250 patients during their stay in the MICU. The mean±SD number of prescribed drugs was 9.6±2.9.

The (Fig. 1) displays the antimicrobial agent prescription patterns among patients. The highest proportion, 88 patients (35.20%), received one antimicrobial agent. A total of 56 patients (22.40%) did not receive any antimicrobial, while 45 patients (11.20%) were prescribed two antimicrobials. Additionally, 28 patients each were prescribed three and four antimicrobials and five patients (2%) were on 5-7 antimicrobials. Out of 250 patients admitted to the MICU during the study period, antimicrobials were prescribed to 194 patients (77.6%), constituting 8.2% of the total drugs prescribed. The average number of antimicrobial agents prescribed per patient was 2.1 ± (1.3 SD). Notably, 24.4% of patients received more than two antimicrobial agents. There was no statistically significant ($p>0.05$) difference between different age groups of patients in proportion of patients in groups for number of antimicrobial prescribed. There was no statistically significant ($p>0.05$) difference between males and females in proportion of patients for number of drugs used in a patient.

The table outlines the primary indications for admission, with cardiovascular emergencies being the most common, accounting for 74 patients (29.6%), followed by respiratory diseases in 40 patients (16%), central nervous system disorders in 36 patients (14.4%) and multiple system involvement in 22 patients (8.8%). Gastrointestinal and renal diseases accounted for smaller proportions, with 14 patients (5.6%) and 6 patients (2.4%) respectively. Other indications were reported in 58 patients (23%).

Antimicrobial prescriptions varied among different conditions, with respiratory diseases patients receiving the highest proportion at 31.02%, followed by central nervous system diseases at 15.88% and cardiovascular

diseases at 11.41%. Among these, respiratory disease patients had the highest percentage of patients prescribed antimicrobials, with 16% of patients receiving 31.02% of the drugs. Conversely, cardiovascular disease patients had the lowest proportion, with 29.6% of patients receiving only 11.41% of the antimicrobial agents.

There was statistically significant ($p<0.001$) difference between groups of patients according to affected system, in the proportion of patients in groups for number of antimicrobial used in a patient. Respiratory system had higher number of patients with multiple antimicrobial prescriptions than other groups.

The most frequently prescribed antimicrobial agents in the MICU during the study period were ceftriaxone, administered to 101 patients (25.06%), followed by clindamycin in 54 patients (13.4%), metronidazole in 38 patients (9.43%) and amoxicillin + clavulanic acid in 37 patients (9.18%). Piperacillin + tazobactam was prescribed to 29 patients (7.2%), meropenem to 28 patients (6.95%) and azithromycin to 25 patients (6.2%). Less frequently prescribed antimicrobial agents included artesunate in 17 patients (4.22%), levofloxacin in 10 patients (2.48%) and oseltamivir in 9 patients (2.23%). Vancomycin was prescribed to 8 patients (1.99%), ciprofloxacin to 7 patients (1.74%) and acyclovir to 6 patients (1.49%). The least prescribed antimicrobial agents were cefixime, clarithromycin, albendazole and linezolid, each in 4 patients (0.99%), fluconazole in 3 patients (0.74%) and gentamicin and amikacin in 2 patients (0.5%) each. Cefuroxime, ceftazidime, cefoperazone + sulbactam, imipenem + cilastatin, ofloxacin and moxifloxacin were each prescribed to one patient (0.25%) during the study period. The majority of antimicrobial agents were administered intravenously to 331 patients (82.13%), while 72 patients (17.86%) received them orally (Table 7, Fig. 2).

In patients with respiratory diseases, the most frequently prescribed drugs were clindamycin, followed by azithromycin and then the fixed-dose combination of piperacillin + tazobactam. These medications were often used in combination. Among patients with central nervous system diseases, ceftriaxone was the most commonly prescribed drug, followed by clindamycin and metronidazole.

Many patients with non-infective etiology, such as cerebrovascular accidents (CVA) or myocardial infarctions (MI), either received no antibiotics or were rarely prescribed with only one antibiotic. In patients with cardiovascular diseases, the most commonly prescribed drugs were ceftriaxone, followed by amoxicillin + clavulanic acid and metronidazole. Similarly, many of these patients presented with non-infective diseases like myocardial infarction, resulting in limited antibiotic prescriptions. Table illustrate the DDD/100 patient-days of frequently prescribed drugs are ceftriaxone 25.51, clindamycin 11.57, metronidazole 11.16, amoxicillin + clavulanic acid 8.48 and piperacillin + Tazobactam 10.04.

(Table 10) shows that amoxicillin + clavulanic acid was the most prescribed fixed dose combination of antimicrobial agent in 36 patients (14.4%) followed by piperacillin+tazobactam in 29 patients (11.6%). Whereas Cefoperazone+sulbactam and imipenem + cilastatin was prescribed only in one patient each (0.4%) during study period

(Table 11) shows maximum 195 patients (78%) stayed for 1-5 days in MICU during study period followed by 39 patients (15.6%) for 6-10 days. Ten patients (4%) admitted for 11-15 days whereas 6 patients (2.4%) stayed for more than fifteen days. Average duration of stay of patients in MICU was 4.14 days. There was statistically significant ($p<0.0001$) difference between groups of patients duration of stay, in the proportion of patients in groups for number of antimicrobial used in a patient. Significantly more numbers of antimicrobial agents were used per patients with increase in duration of stay in MICU (Table 12).

(Table 13) shows that many combination of drug were used during treatment of patients in MICU among which most common are clindamycin + (piperacillin + tazobactam), clindamycin + azithromycin and ceftriaxone + clindamycin followed by ceftriaxone + metronidazole than clindamycin + (piperacillin + tazobactam) +azithromycin.

(Table 14) shows that out of total 27 antimicrobial agents which are used during study period 77.8 % belongs to essential drug list (EDL) by WHO (2013). Whereas 66.7% of AMAs belongs to essential drug list of Madhya Pradesh (2018). The (Table 15) above highlights that piperacillin + tazobactam, ofloxacin and cefoperazone + sulbactam were not included in the WHO Essential Drug List (2013). Despite this, piperacillin + tazobactam was prescribed to 29 patients. Antimicrobial agents not listed in the Essential Drug List of Madhya Pradesh included ceftazidime, imipenem + cilastatin, clarithromycin, vancomycin, linezolid and oseltamivir. Furthermore, antimicrobial agents absent from both lists were cefuroxime, meropenem and moxifloxacin. Interestingly, meropenem was prescribed to 28 patients despite not being included in the aforementioned lists.

The study, conducted in collaboration between the Pharmacology and Medicine departments at Netaji Subhash Chandra Bose Medical College and Hospital in Jabalpur, Madhya Pradesh, focused on the medicine Intensive Care Unit (ICU). A total of 250 patients were

observed prospectively over a nine-month period (March 2018 to November 2018), followed by data compilation and statistical analysis. The study aimed to analyze the antibiotic usage patterns and consumption among patients admitted to the medicine ICU. The average age of admitted patients was 42±(18 SD) years, with a predominant middle-aged demographic (46-60 years), consistent with previous findings. Male patients constituted 61.2% of the total, outnumbering female patients (38.8%), a pattern consistent with prior studies. Across all age groups, male patients outnumbered females, except in the 18-30 age group where genders were equally represented. This observation aligns with previous Indian studies, indicating a male predominance in ICU admissions within the Indian context.

Older individuals are at higher risk of adverse drug events due to comorbidities, polypharmacy and age-related changes in drug pharmacodynamics and pharmacokinetics. In our ICU study, the average number of drugs prescribed was 9.6 (±consistent with Thomas *et al*. (9.9 drugs/patient). However, William *et al*. reported a lower average of 6.23 (±2.73 SD), while the Maharashtra study found 7.82[23]. Conversely, averages were higher in Eastern India (10.5 drugs/patient)[24] and Central India (11.3 drugs/patient)[25]. Extensive polypharmacy, defined as five or more medications, is a significant concern[26].

Efforts should focus on minimizing the average number of drugs to reduce the risks of drug interactions, bacterial resistance and hospital costs. Of the 250 patients in our study, 194 (77.6%) were prescribed antimicrobial agents. The average number of antimicrobial agents per patient was 2.1±(1.3 SD), consistent with findings from William *et al*. and Gedam *et al*. However, lower averages were observed in studies from Puducherry (1.13)[27] and South India (1.73±0.04)[28]. In this study, cardiovascular emergencies, particularly myocardial infarction, were the most common indication for ICU admission, followed by respiratory and central nervous system diseases, consistent with previous reports by Thomas *et al*., Gedam *et al*. and Nibrad *et al*. However, Patel *et al*. noted septicaemia and head injury as common causes, possibly due to the inclusion of patients from medical and surgical ICUs[23,25,29].

Ceftriaxone emerged as the most commonly prescribed antimicrobial agent (AMA) in our study, aligning with previous studies conducted across various regions of India[23-25,27,28,30-33]. Adhikari *et al*., however, reported metronidazole as the most common AMA prescribed. Cephalosporins are favored for their lower toxicity and broad-spectrum activity. Clindamycin followed ceftriaxone as the second most commonly prescribed drug, with metronidazole ranking third. The

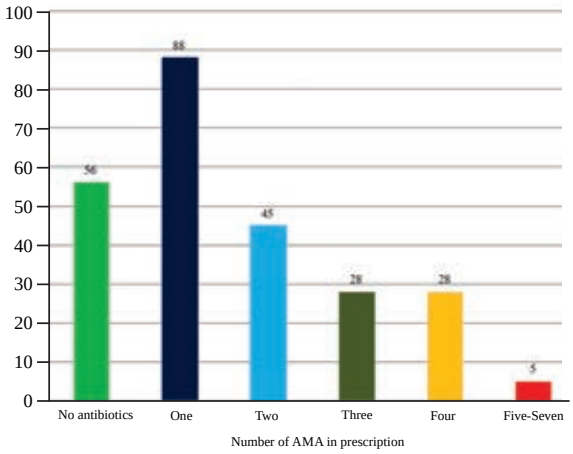

Fig. 1: Distribution of patients according to the number of antimicrobial agents prescribed

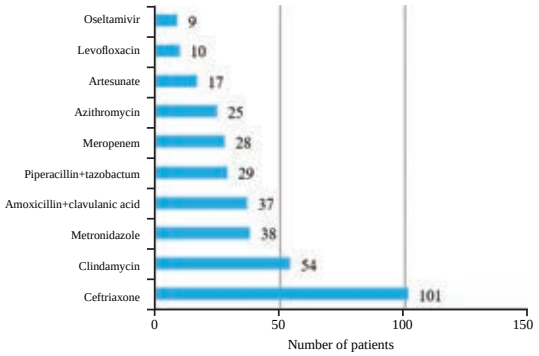

Fig.2: most commonly prescribed antimicrobial agents

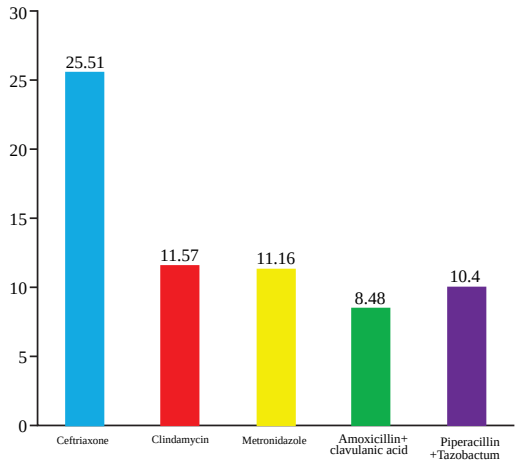

Fig. 3: Antibiotic use density of five frequently used amas according to ddd/100 patient-days

ICU, where patients with complex medical conditions are densely concentrated, often requires frequent administration of broad-spectrum antibiotics to address the acute nature of critically ill patients[34].

In our study, the DDD/100 patient-days for five frequently prescribed drugs were ceftriaxone 25.51, clindamycin 11.57, metronidazole 11.16, amoxicillin +

Table 1: Age and sex distribution of patients admitted in medicine ICU

Age Group (in years)	Male	Female	Total	Percentage
<18	3	0	3	1.2
18-30	29	29	58	23.2
31-45	37	20	57	22.8
46-60	49	26	75	30
>60	35	22	57	22.8
Total	153	97	250	100

Table 2: Distribution of patients according to total number of drug prescribed

Drug prescribed	Number of patients	Percentage
Up to five	16	6.4
Six-Ten	144	57.6
Eleven-Fifteen	81	32.4
More than fifteen	9	3.6
Total	250	100

Table 3: Age wise distribution of patients according to the number of antimicrobial agents prescribed

Drug prescribed	<18year	18-30year	31-45year	46-60year	>60year	Total
One	0	23	24	25	16	88
Two	1	15	7	9	13	45
Three	0	8	7	9	4	28
Four	2	5	5	11	5	28
Five-Seven	0	2	1	2	0	5
Total	3	53	44	56	38	194

Table 4: Number of antimicrobial agents prescribed according to gender distribution

AMAs prescribed	Number of male patients	Number of female patients	Total
One	59 (31.41%)	29 (14.95%)	88 (45.36%)
Two	25 (12.89%)	20 (10.31%)	45 (23.20%)
Three	16 (8.25%)	12 (6.19%)	28 (14.43%)
Four	16 (8.25%)	12 (6.19%)	28 (14.43%)
Five-Seven	3 (1.55%)	2 (1.03%)	5 (2.58%)
Total	119 (61.34%)	75 (38.66%)	194 (100%)

Chi-square = 2.263, df = 4, P value = 0.6876 (Not significant)

Table 5: Distribution of Patients and Antimicrobial Agents Prescribed According to Presenting Complain

Presenting complain	Number of patients	AMAs prescribed
Cardiovascular diseases	74 (29.6%)	46 (11.41%)
Central nervous system diseases	36 (14.4%)	64 (15.88%)
Respiratory diseases	41 (16%)	125 (31.02%)
Gastrointestinal diseases	14 (5.6%)	27 (6.70%)
Renal disease	6 (2.4%)	8 (1.98%)
Multiple system	22 (8.8%)	39 (9.68%)
Other	57 (23.2%)	94 (23.32%)
TOTAL	250	403 (100%)

Table 6: Distribution of Patients Prescribed with Number of Antimicrobial Agents According to Presenting Complain

System Affected	One AMAs	Two AMAs	Three AMAs	Four AMAs	Five-Seven AMAs
Cardiovascular disease	20	5	2	1	1
Central nervous system disease	17	6	1	5	2
Respiratory disease	4	9	12	14	2
Gastrointestinal disease	5	4	3	2	0
Renal disease	4	2	0	0	0

Chi-square = 41.57, df = 16, P value = 0.0005 (significant but not valid)

clavulanic acid 8.48 and piperacillin + tazobactum 10.04, closely resembling findings by Williams et al., albeit with differences in clindamycin and amoxicillin + clavulanic acid[23]. Similarly, in the study by Patel *et al*., DDD/100 patient-days for ceftriaxone were nearly identical at 25.44, but varied significantly for other antibiotics[23]. A study from Nepal reported different rates of utilization for various antimicrobial agents[35]. In our study, the majority of antimicrobial agents were administered via the intravenous route, consistent with previous research[36,37]. Respiratory disease patients received the highest proportion of antimicrobial prescriptions (31.02%), followed by central nervous system diseases (15.88%) and cardiovascular diseases (11.41%). This trend mirrors findings by Shrikala *et al.*, where respiratory infections accounted for 50% of all antibiotics prescribed in the ICU[36].

Variability in antimicrobial agent usage for the same indication was observed, possibly due to factors such as concomitant diseases, prescribing physician preferences and lack of standardized treatment guidelines. Respiratory disease patients received the highest proportion of antimicrobial prescriptions despite comprising only 16% of the patient population, while cardiovascular patients received the lowest proportion, likely due to the nature of their admissions, such as myocardial infarction where antimicrobial agents are not typically indicated. Amoxicillin+clavulanic acid was the most commonly

Table 7: Frequency of prescription of Antimicrobial Agents

DRUG	ATC CODE	IV	ORAL	TOTAL
Amoxicillin+clavulanic acid	J01CR02	31	6	37 (9.18%)
Piperacillin+Tazobactam	J01CR05	29	0	29 (7.2%)
Cefuroxime	J01DC02	0	1	1 (0.25%)
Ceftriaxone	J01DD04	101	0	101 (25.06%)
Cefixime	J01DD08	0	4	4 (0.99%)
Ceftazidime	J01DD02	1	0	1 (0.25%)
Cefoperazone+sulbactum	J01DD62	1	0	1 (0.25 %)
Imipenem+cilastatin	J01DH51	1	0	1 (0.25 %)
Meropenem	J01DH02	28	0	28 (6.95%)
Levofloxacin	J01MA12	7	3	10 (2.48%)
Ciprofloxacin	J01MA02	6	1	7 (1.74%)
Ofloxacin	J01MA01	1	0	1 (0.25%)
Moxifloxacin	J01MA14	1	0	1 (0.25%)
Azithromycin	J01FA10	0	25	25 (6.2%)
Gentamicin	J01GB03	2	0	2 (0.5%)
Clarithromycin	J01FA09	0	4	4 (0.99%)
Clindamycin	J01MA14	52	2	54 (13.4%)
Amikacin	J01FA10	2	0	2 (0.5 %)
Metronidazole	J01GB03	36	2	38 (9.43 %)
Vancomycin	J01MA14	8	0	8 (1.99 %)
Linezolid	J01XX08	4	0	4 (0.99 %)
Doxycycline	J01AA02	0	5	5 (1.24 %)
Artesunate	P01BE03	17	0	17 (4.22 %)
Acyclovir	J05AB01	0	6	6 (1.49 %)
Oseltamivir	J05AH02	0	9	9 (2.23 %)
Fluconazole	D01AC15	3	0	3 (0.74 %)
Albendazole	P02CA03	0	4	4 (0.99 %)
Total		331	72	403 (100 %)

Table 8. Commonly prescribed antimicrobial agents according to system

System Disease	Antibiotics	Number of Patients
Respiratory	Clindamycin	27
	Azithromycin	20
	Piperacillin+Tazobactam	16
Central Nervous System	Ceftriaxone	26
	Clindamycin	8
	Metronidazole	7
Cardiovascular System	Ceftriaxone	18
	Amoxicillin+clavulanic acid	11
	Metronidazole	3

Table 9. Antibiotic use density of five frequently used amas according to DDD/100 patient-days along with ATC

Antimicrobial Agent	ATC code	DDD(gm)	UNIT consumed(gm)	DDD/100 patient- days
Ceftriaxone	J01DD04	2	808	25.51
Clindamycin	J01FF01	1.2	330	11.57
Metronidazole	J01GB03	1.5	265.2	11.16
Amoxicillin+clavulanic acid	J01CR02	3	403.2	8.48
Piperacillin+Tazobactam	J01CR05	14	2227.5	10.04

Table 10. FREQUENTLY PRESCRIBED FIXED DOSE COMBINATIONS

Fixed dose combinations	Number of prescription	Percentage
Amoxicillin+clavulanic acid	36	14.4
Piperacillin+Tazobactam	29	11.6
Cefoperazone+sulbactum	1	0.4
Imipenem+cilastatin	1	0.4

Table 11. DURATION OF STAY OF PATIENTS IN MICU

Duration of stay in days	Number of patients	Percentage
One-Five	195	78
Six-Ten	39	15.6
Eleven- Fifteen	10	4
More than Fifteen	6	2.4
TOTAL	250	100

Table 12. Distribution of antimicrobial prescribed according to duration of stay in MICU

Duration of Stay(in days)	One AMAs	Two AMAs	Three AMAs	Four AMAs	Five-Seven AMAs	Total
One-Five	81	32	19	18	1	151
Six-Ten	5	11	7	4	1	28
Eleven-Fifteen	2	1	1	2	3	9
More than Fifteen	0	1	1	4	0	6
Total	88	45	28	28	5	194

Chi-square = 65.24, df = 12, p<0.0001 (significant but not valid)

Table 13. Frequently used combination of drugs in MICU

Combination of drug	Total	Percentage
Clindamycin+(Piperacillin+Tazobactam)	20	8
Clindamycin+(Piperacillin+Tazobactam)+Azithromycin	11	4.4
Clindamycin+Azithromycin	20	8
Ceftriaxone+Metronidazole	18	7.2
Ceftriaxone+Clindamycin	19	7.6

Table 14. Antimicrobial agents in essential drug list

Status in Essential drug list	Yes	No
WHO (2013)	21 (77.8%)	6 (22.2%)
MP State (2018)	18 (66.7%)	9 (33.3%)

Table 15. Distribution of antimicrobial agents (amas) lacking in essential drug list

AMAs lacking in WHO LIST	Antimicrobial agents	Frequency of prescription
	Piperacillin+Tazobactam	29
	Ofloxacin	1
	Cefoperazone+sulbactum	1
AMAs lacking in MP EDL	Ceftazidime	1
	Imipenem+cilastatin	1
	Clarithromycin	4
	Vancomycin	8
	Linezolid	4
	Oseltamivir	9
AMAs lacking in both EDL	Cefuroxime	1
	Meropenem	28
	Moxifloxacin	1

prescribed fixed-dose combination (FDC) of antimicrobial agents in our study, given to approximately 14.4% of patients, followed by Piperacillin+tazobactum in 11.6% of patients. This finding is consistent with Gedam et al.'s observation of amoxicillin+clavulanic acid as the most common FDC.

In our study, 78% of patients were discharged or transferred to medicine wards within 1-5 days, with an average MICU stay of 4.14 days, similar to previous research[29]. A higher number of antimicrobial agents were used in patients with longer MICU stays. Various drug combinations were used in MICU treatment, with Clindamycin+ (Piperacillin+tazobactum) and Clindamycin+Azithromycin being the most common, particularly in respiratory diseases.

Guidelines recommend antibiotics such as ß-lactam plus ß-lactamase inhibitor, clindamycin and carbapenem for treating pneumonia, particularly aspiration pneumonia[36]. Piperacillin/tazobactam has shown sustained potency against problematic nosocomial and community-acquired pathogens, making it suitable for empiric treatment in settings with emerging resistance[37]. Essential medicines, as defined by the WHO, address priority healthcare needs based on disease prevalence, efficacy, safety and cost-effectiveness.

In our study, 77.8% of antimicrobial agents (AMAs) align with the WHO Essential Drug List (2013), while 66.7% correspond to the Madhya Pradesh Essential Drug List (2018). Notably, AMAs used in the ICU but absent from the WHO list include piperacillin+tazobactam, cefuroxime, cefoperazone+sulbactum, meropenem, ofloxacin and moxifloxacin. Meropenem, used in 6.95% of cases, merits inclusion in the Madhya Pradesh list. Generic names were used in 96.3% of antimicrobial prescriptions, with only amoxicillin+clavulanic acid and oseltamivir occasionally referred to as Augmentin and Tamiflu, respectively.

Only nine patients underwent blood/urine/sputum culture, with no organism growth detected except for two cases of *E. coli*. This suggests prevalent use of empirical treatment in patient management. Bacterial resistance to antibiotics poses a significant threat to patient health in ICUs, often stemming from antibiotic misuse. Strategies to mitigate resistance include rational antibiotic prescribing, periodic changes in antibiotic preferences and temporary withdrawal and reintroduction of antibiotic classes[33].

ICUs should develop protocols tailored to local pathogens and resistance patterns, in collaboration with microbiology departments. Enhancing pharmacovigilance awareness through training programs can facilitate reporting of adverse drug reactions (ADRs) in ICUs, thereby reducing patient morbidity and mortality[38,39]. ADRs are more common in ICUs compared to other hospital areas, often resulting from drug interactions. ICU clinicians must remain vigilant about potential drug interactions to minimize complications[40].

Procalcitonin serves as a biomarker to guide antibiotic treatment duration in hospital settings, particularly for conditions like community-acquired pneumonia (CAP) and sepsis. Elevated procalcitonin levels indicate systemic inflammation, often of bacterial origin. Numerous randomized controlled trials have demonstrated that procalcitonin-based algorithms can safely reduce antibiotic usage, duration of therapy and ICU length of stay in patients with CAP and sepsis. Procalcitonin dynamics within 72 hours of sepsis onset correlate with both the appropriateness of empirical antibiotic therapy and overall survival. Clinical algorithms incorporating procalcitonin measurements have been shown to decrease antibiotic courses by 25-65% in hospitalized patients with CAP and sepsis[33,41,42].There are some limitations of present study, first and foremost it is observational study, no intervention has been done. It is single centric study, observation may not be same for other region and in the same region at different time. There is known regional and seasonal variation in the causative agent.

CONCLUSION

Based on our study in the Medicine ICU of Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, it's clear that antimicrobial agents are extensively utilized, particularly among

middle-aged male patients. While cardiovascular emergencies were the primary reason for admission, patients with respiratory diseases received the highest antimicrobial prescriptions. Ceftriaxone was the most commonly prescribed antimicrobial, often in combination with amoxicillin+clavulanic acid. Parenteral administration was prevalent and most patients had short hospital stays. Notably, a significant proportion of prescribed antimicrobials belonged to the essential drug list. To address these findings, we recommend comprehensive studies across all hospital departments to understand antimicrobial utilization, routine bacterial culture and sensitivity testing for timely therapy initiation, establishment of hospital-specific antimicrobial guidelines, regular monitoring of culture sensitivity patterns and integration of antimicrobial stewardship training into medical education curricula.

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