

## RESEARCH PAPER

### ANTIMICROBIAL UTILIZATION IN INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL

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#### ABSTRACT

**Introduction:** Antimicrobial utilisation in Intensive Care Units (ICUs) is high due to the severity of illness and need for empirical therapy. Evaluation of prescribing patterns using standard indicators is essential to assess drug utilisation and rational prescribing.

**Materials and Methods:** This was a cross-sectional study conducted in ICU for a period of one and half years and the sample size was 650 prescriptions. Patients of either gender, aged 18-80 years, staying in ICU for 1-5 days were included, while those on dialysis, mechanical ventilation or with ICU stay less than 24 hours were excluded. Antimicrobials were classified according to the WHO Anatomical Therapeutic Chemical (ATC) classification. Drug utilisation was evaluated using WHO prescribing indicators, including average number of drugs per encounter, percentage of drugs prescribed by generic name, percentage of encounters with injections and percentage of drugs prescribed from the Essential Medicines List. Antimicrobial consumption was assessed using Defined Daily Dose (DDD) and expressed as DDD per 100 patient-days. Prescribed Daily Dose (PDD) was calculated and compared with DDD. Days of therapy (DOT) were calculated based on duration of antimicrobial use. Antimicrobials were further analysed using WHO AWaRe classification. Cost of antimicrobial and cost per patient was analysed.

**Results :** A total of 650 ICU patient prescriptions were analysed, with a male predominance (64%) and a mean age of approximately  $54 \pm 13$  years. Most patients were from rural areas (52%) and below the poverty line (54%). Chronic obstructive pulmonary disease (46%) and pneumonia (34%) were the most common indications for ICU admission, hypertension was the most frequent comorbidity. Ceftriaxone, meropenem, and piperacillin+tazobactam were predominantly prescribed, and all drugs were administered intravenously along with pantoprazole. The average number of drugs per encounter was 7.35, only 25% were prescribed by generic name and all were from essential medicines list. Ceftriaxone showed the highest utilisation, followed by meropenem and piperacillin+tazobactam. All these medications belonged to the WHO Watch group, while metronidazole belonged to the Access group. Meropenem showed the highest antimicrobial expenditure. PDD/DDD ratio for ceftriaxone and metronidazole was 1 which is as per WHO standard, but lower for piperacillin+ tazobactam and meropenem. A total of 18 adverse drug reactions were reported, with nausea being the most common.

**Conclusion:** Beta-lactam antimicrobials, particularly ceftriaxone, was most frequently used, followed by meropenem and piperacillin+tazobactam. ATC/DDD analysis showed highest utilisation of ceftriaxone. Watch group antimicrobials were commonly used as per AWaRe category. Meropenem treatment cost was high and adverse drug reactions were minimal.

**Keywords:** Intensive care unit, Antimicrobial utilization, Prescribed daily dose, Defined daily dose

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## Introduction

Antimicrobial agents remain central to the management of serious infections in hospitalised patients; however, frequent and inappropriate use has accelerated the emergence and spread of antimicrobial resistance, which has resulted in a worldwide threat. Recent global estimates indicate that bacterial resistance has caused approximately 1.27 million deaths and was associated with nearly 5 million deaths in 2019, with projections suggesting a continued rise in mortality, particularly in low- and middle-income countries. Regions with high infectious disease burden, constrained laboratory capacity, and widespread empirical prescribing, such as South Asia, are expected to experience a disproportionate share of this impact.<sup>1,2</sup>

Intensive Care Units (ICUs) constitute a high-risk environment for both intensive antimicrobial exposure and development of multidrug-resistant (MDR) strains, as critically ill patients require broad-spectrum empirical therapy, invasive devices, and prolonged hospitalization. Surveillance studies have consistently demonstrated that antimicrobial consumption in ICUs, expressed as defined daily doses (DDD) per 100 or 1000 patient-days, is substantially higher than in general wards, often exceeding 150–300 DDD per 1000 patient-days. Data from Indian tertiary care centres show similar findings that ICU antimicrobial utilization, particularly of Watch and Reserve antimicrobials as per the WHO AWaRe (Access watch and reserve) framework, surpasses that in non-ICU settings and highlights the need for tailored stewardship strategies in these units.<sup>3</sup>

The intense and prolonged use of broad-spectrum agents in ICUs has been closely linked to the emergence and dissemination of MDR pathogens, including carbapenem-resistant Enterobacteriaceae, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and methicillin-resistant *Staphylococcus aureus*, which are associated with higher rates of sepsis, extended length of stay, and increased mortality. Infections due to such organisms in critically ill patients have been reported to carry mortality rates in the range of 40–70 percent. This underscores the importance of achieving a balance between prompt initiation of effective empiric therapy and subsequent de-escalation or optimization of regimens. This balance is important in preserving antimicrobial effectiveness while ensuring favourable clinical outcomes in ICU patients.<sup>4</sup>

Rational antimicrobial utilization in ICUs depends on regular quantification and

evaluation of prescribing practices, incorporation of local microbiological and resistance data, and adherence to evidence-based guidelines and national or institutional antimicrobial policies. Antimicrobial stewardship interventions focused on ICUs have demonstrated meaningful reductions in broad-spectrum antimicrobial consumption, often in the range of 15–20 per cent in terms of DDD per 100 patient-days, without adversely affecting patient outcomes. Nevertheless, national and institutional surveillance reports continue to document high use of broad-spectrum Watch and Reserve agents and suboptimal Access-to-Watch utilisation ratios in many tertiary care settings.<sup>5</sup>

## Materials & Methods

This was a cross-sectional study conducted by Department of Pharmacology in the Intensive Care Unit of R.L. Jalappa Hospital, Kolar, over a period of one and half years from May 2024 to October 2025. The study was approved by the Central Ethics Committee and written informed consent was obtained from all the patients willing to participate in the study. The study population included prescriptions of adult patients aged 18–80 years who were admitted to the ICU during the study period.

### Data collection method

A structured pro forma was used to document demographics, diagnosis, comorbidities, length of stay, and each medication order. Generic or brand name, dosage, route of administration, frequency and duration of treatment. Medications used was classified based on ATC Classification, and medication utilisation was studied on the following WHO parameters.

A. Average no of medications per encounter

i. = Total number of different medications prescribed / Number of encounters surveyed

B. Percentage of antimicrobials prescribed by generic name

i. = Number of antimicrobials prescribed by generic name x 100 / Total number of antimicrobials prescribed

C. Percentage of encounters with injection

i. = Number of patients encounters with injection x 100 / Number of encounters surveyed

D. Percentage of antimicrobials prescribed from the essential drug list

i. = Number of Essential medicine list (EDL)listed antimicrobial prescriptions x 100 / Total number of antimicrobials prescribed

E. Days of therapy (DOT) = It will be calculated as difference in date of stoppage and starting of medications

F. Defined daily dose (DDD) will be calculated as : Net quantity of antimicrobials used / DDD

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of antimicrobials as per WHO DDD/100 patient days will be calculated as : DDD of antimicrobials used x 100 / No of patient  
 $G. PDD = \frac{\text{Total amount of drug (mg)}}{\text{No of Patients} \times \text{Average length of stay}}$   
 The cost of antimicrobial therapy will be calculated by

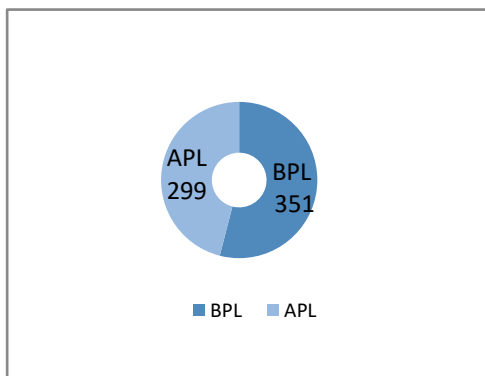
- Total utilisation cost of antimicrobials
- Cost per patient = Total cost / No. of patients

## STATISTICAL METHODS

Descriptive statistics were used to summarise the data, where continuous variables such as age and laboratory parameters were expressed as mean  $\pm$  standard deviation (SD), while categorical variables such as gender, diagnosis, antimicrobial use, and socioeconomic status were presented as frequencies and percentages. Chi-square test was used to assess the association between antimicrobial use and socioeconomic status. A p-value  $<0.05$  was considered statistically significant.

## RESULTS

The study included 650 prescriptions of patients admitted to Intensive Care Unit (ICU), of which 420 (64%) were males and 230 (36%) females. The mean age of males was  $54.04 \pm 13.38$  and females was  $54.12 \pm 13.35$  years. 340 (52%) were from rural areas and 310 (48%) were from urban areas. A marginal predominance of rural patients was observed.



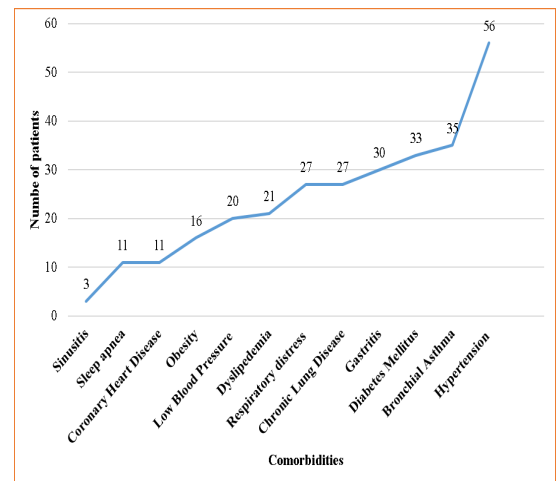
**Figure 1. Socioeconomic status of the patients**

The doughnut chart illustrates the distribution of study patients based on socioeconomic status. Among the 650 patients, 351 (54%) belonged to the below poverty line (BPL), while 299 (46%) were from above poverty line (APL). A higher proportion of the study population was from the BPL (Figure 1). The clinical conditions for admission to ICU are

represented in Table 1 with COPD being most common.

**Table 1. Clinical condition of the patients admitted to the ICU(n=650)**

Diagnosis	No. of patients (%)	Kashyap R et al 2020	Tejas TJ et al. 2025	Oh's Intensive care manual
Chronic obstructive pulmonary disease	300 (46)	54 %	-	16 %
Pneumonia	225 (34)	-	-	5%
Organophosphorus poisoning	65 (10)	25 %		-
Neurological condition (Cerebrovascular accident/Subdural hematoma)	35 (5.3)	-	18.7 %	-
Fracture	20 (3)	42.5 %	-	-
Exploratory laparotomy	5 (0.7)	-	-	-



**Figure 2. Types of comorbidities in the patients**

Figure 2 illustrates the type of comorbidities observed among the patients, with hypertension being the most prevalent 8.62%, followed by bronchial asthma 5.38%, diabetes mellitus 5.08%, gastritis 4.62% and chronic lung disease 4.15%. 361 patients did not have any co-morbidities. The mean total count (TC) was highest in SDH patients and lowest in exploratory laparotomy cases. Neutrophils were increased in pneumonia and subdural hematoma. Patients with pneumonia had an increase in inflammatory markers (Table 2).

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**Table 2. Laboratory investigations in different clinical conditions**

Diagnosis	TC (µL/m) (Mean ± SD)	Neutrophil (%)	Lymphocytes (%)	ESR (mm/hr) (Mean ± SD)
Chronic obstructive pulmonary disease (n=300)	11363.44 ± 2302.89	68	24	32.16 ± 8.24
Pneumonia (n=255)	11334.24 ± 2186.17	72	20	36.88 ± 6.95
Organophosphorous poisoning (n=65)	10729.60 ± 1981.31	64	28	28.63 ± 7.14
Cerebrovascular accident (n=20)	9346.82 ± 1765.84	62	30	25.76 ± 6.88
Subdural hematoma (SDH) (n=15)	12505.33 ± 2476.92	70	22	30.28 ± 5.11
Fracture (n=20)	10765.65 ± 2118.60	65	27	27.41 ± 6.37
Exploratory laparotomy (n=5)	8850.60 ± 1624.52	60	32	24.50 ± 5.03

**Table 3. Utilisation of antimicrobials and proton pump inhibitors (PPIs) in different clinical conditions**

Patients	Antimicrobials n (%)	PPIs
Chronic obstructive pulmonary disease	Ceftriaxone 110 (37) Meropenem 104 (40) Piperacillin + tazobactam 86 (29)	Pantoprazole
Pneumonia	Meropenem 138 (53) Ceftriaxone 87 (29)	Pantoprazole
Organophosphorous poisoning	Ceftriaxone 65 (22)	Pantoprazole
Neurological conditions (Cerebrovascular accident/Subdural hematoma)	Ceftriaxone 35 (12)	Pantoprazole
Fracture	Meropenem 14 (5) Metronidazole 6 (100)	Pantoprazole
Exploratory laparotomy	Ceftriaxone 3 (1) Meropenem 2 (0.8)	Pantoprazole

Majority received Beta lactam antimicrobials like ceftriaxone, meropenem and all patients received pantoprazole. All drugs were administered through intravenous route (Table 3). In our study the average number of

medications per encounter was 7.35 which is in ICU setting whereas WHO standard values given in table are for out-patient prescription. Only one antimicrobial was prescribed by generic name (meropenem). All the antimicrobials were given intravenous and 100 % antimicrobials were as per the WHO essential medicines (Table 4).

**Table 4. WHO prescribing indicators**

Indicators	Formula	Value calculated	WHO values
Average number of medications per encounter	Total number of different medications prescribed / Number of encounters surveyed	7.35	1.6-1.8
Percentage of antimicrobials prescribed by generic name	Number of antimicrobials prescribed by generic name x 100 / Total number of antimicrobials prescribed	25%	100%
Percentage of encounters with injection	Number of patients encounters with injection x 100 / Number of encounters surveyed	100%	13-24%
Percentage of antimicrobials prescribed from the essential drug list	Number of Essential medicine list (EDL) listed antimicrobial prescriptions x 100 / Total number of antimicrobial prescriptions	100 %	100%
Days of therapy (DOT)	Difference between the date of stoppage and the start date of medications	5days	-

**Table 5. Defined Daily Dose (DDD) of antimicrobials utilized in the Intensive Care Unit**

Antimicrobial agents	Total Grams (5 Days)	DDD (g/day) as per WHO	Patient-Days	DDD calculated	DDD/100 patient days
Ceftriaxone	3000	2	1500	1500	100
Meropenem	2580	3	1290	860	67
Piperacillin/Tazobactam	3870	14	430	276	64
Metronidazole	45	1.5	30	30	100

Table 5 shows the Defined Daily Dose (DDD) of antimicrobials used in ICU patients in our study, calculated according to the WHO Anatomical Therapeutic Chemical classification (ATC)/DDD methodology. DDD was obtained by using the following formula- Total amount antimicrobial used/WHO assigned DDD value

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for that particular medication. Patient-days were calculated as number of patients multiplied by duration of hospital stay. Ceftriaxone showed the highest utilization (1,500 DDDs) followed by meropenem and piperacillin+tazobactam, while metronidazole showed the lowest use (30 DDDs).

**Table 6. ATC code, WHO Essential medicine and cost**

Antimicrobials agents (unit)	ATC code	Class of antimicrobials	Cost per unit (INR)	No. of units/day	No. of patients received	No. of days of therapy	Cost for 5 days (INR)	Cost/patient (INR)
Ceftriaxone (1gm)	J01D D04	Watch	125	2	300	5	3,75,000	1,250
Meropenem (1gm)	J01D H02	Watch	1123	2	258	5	28,97,340	11,230
Piperacillin+tazobactam (4.5gm)	J01C R05	Watch	336	2	86	5	2,88,960	3360
Metronidazole (500mg)	J01X D01	Access	75.50	3	6	5	6,795	1,132.5

Table 6 shows the comparison of antimicrobial cost per unit and cost / patient. 3 out of 4 antimicrobials prescribed belonged to the Watch category, ceftriaxone being the most frequently used 46.2%, followed by meropenem 39.7% and piperacillin+tazobactam 13.2%. Meropenem was costliest compared to other medications and accounted for 81.2% of total antimicrobial cost. Metronidazole, classified under the Access group, was used in 0.9% patients and accounted for minimal treatment cost of 0.1%.

**Table 7. Comparison of prescribed daily dose and WHO DDD of antimicrobials**

Antimicrobial agents	Prescribed dose/day (g)	WHO DDD (g/day)	PDD/DDD	Observation
Ceftriaxone	2	2	1.00	Standard dose followed
Meropenem	2	3	0.67	33% below DDD; based on renal function
Piperacillin+tazobactam	9	14	0.64	36% below DDD
Metronidazole	1.5	1.5	1.00	Standard dose followed

Ceftriaxone and metronidazole were prescribed at doses equivalent to their WHO DDDs, indicating conformity with standard adult dosing recommendations. Ceftriaxone and

metronidazole indicate guidelines-based empiric therapy as it showed PDD/DDD ratio of 1. Meropenem and piperacillin+ tazobactam was administered at lower doses than WHO DDD. PDD was less than DDD for meropenem and piperacillin + tazobactam (Table 7).

**Table 8. Association of antimicrobials based and economic status**

Antimicrobial	APL(%)	BPL(%)	Total	P value
Ceftriaxone	130 (43)	170 (48)	300	0.2
Meropenem	112 (37)	146 (42)	258	0.4
Piperacillin+tazobactam	53 (18)	33 (9)	86	0.001*
Metronidazole	4 (1)	2 (0.5)	6	0.42
Total	299	351	650	

\* Chi-square test of association

Table 8 shows there is no association between the medications ceftriaxone, meropenem, metronidazole and socioeconomic status. However, piperacillin+tazobactam showed a statistically significant association with economic status. It was prescribed in more percentage of APL (18%) patients than BPL (9%).

A total of 18 adverse drug reactions were documented, nausea (meropenem-3, piperacillin+tazobactam-6), vomiting (2,1) and diarrhea (ceftriaxone-6).

### Discussion

The present study was conducted to evaluate the utilisation pattern of antimicrobials in patients admitted to the Intensive Care Unit (ICU) of a tertiary care hospital. The study analysed 650 patients prescriptions and assessed the antimicrobial use based on WHO prescribing indicators.

In this study, patients admitted to our ICU were in the 5<sup>th</sup> decade of life. This aligns with findings from Indian ICU studies, where adult patients were in the range of 40–60years.<sup>6,7</sup> Approximately two-thirds were males, more than 50% from rural areas and below-the-poverty-line (Figure 1) which is similar to another study.<sup>8</sup> The tertiary care hospital is the referral centre located in the rural region providing health care to surrounding villages and semiurban areas. The clinical conditions for admission to ICU are represented in Table 1 with COPD being more common followed by pneumonia which collectively represented 80%. This is similar to a

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multicentre Indian data indicating that severe lower respiratory infections are the primary reason for ICU admissions.<sup>9</sup> The other studies have shown 54% and 21% respectively (Table 1).<sup>10,11</sup> Organophosphorous poisoning was 10% compared to 25% in Kashyap et al. study.<sup>10</sup> Admission due to neurological conditions and fracture was less in our study compared to Kashyap et al. and Tejas et al.<sup>10,12</sup>

The comorbidities observed (Figure 2), commonest was hypertension followed by bronchial asthma and more than 50% did not have any comorbidities. A similar observation by Mithal et al., who reported hypertension and diabetes mellitus as the most prevalent comorbid conditions.<sup>13</sup> The complete blood count revealed elevated total count, neutrophils and lymphocytes indicating inflammation similarly, Ghosh et al. showed high total leukocyte counts and neutrophil levels, reflecting increasing systemic inflammation with disease severity.<sup>14</sup> This co-relates with infectious condition and COPD being the commonest indication for admission to ICU.

Table 3 shows antimicrobials used in ICU patients in different clinical conditions. All are beta lactam antimicrobials, ceftriaxone was used in 46%, meropenem in 40% and piperacillin + tazobactam in 13% of patients, this indicates the organisms were responsive to cephalosporins in different clinical situations. Similar findings were reported by Anand et al., John M S et al., who evaluated antimicrobial utilisation in a teaching hospital ICU and reported that third-generation cephalosporins were the most commonly used antimicrobials for empirical therapy.<sup>6,15</sup>

Pantoprazole was used in all the patients as prophylactic measure as patients in ICU will be receiving multiple other medications and patients are subjected to a lot of stress both physical and mental, the environmental factors like seeing other terminal ill patients will also contribute. The patients will have limited interaction with their dear ones to express their psychological concerns as well. This practice aligns with the findings of Dabiri et al., who reported routine use of proton pump inhibitors as prophylactic measure.<sup>16</sup>

The WHO prescribing indicators are defined for out-patient prescriptions, we have used these formulas for in-patient analysis. Table 4 represents the details, 7.35 is the average medication which is more than WHO out-patient value because in ICU the patients will be receiving many medications, due to their

critical condition. Twenty five percent of drugs were prescribed by generic name and all medications were given as injections, similar to a study by Karthik K et al., where 34.9% antimicrobials were prescribed in generic name and 88.2 % were given as injectables.<sup>17</sup> In our study, all the medications prescribed were from essential medicines list. Patients received medications for 5 days.

The ATC/DDD analysis (Table 5) revealed that ceftriaxone had the highest utilisation (1500 DDD) followed by meropenem among the antimicrobials used in ICU patients. Comparable results were reported by Chatterjee et al., Sah K A et al., who conducted an observational study on antimicrobial utilisation and reported ceftriaxone as the most frequently utilised antimicrobial based on DDD analysis.<sup>18,19</sup>

Table 6 describes the ATC code and classification of antimicrobials as per the AWARe framework. All the antimicrobials used in our patients were according to WHO list and are within the AWARe framework, each carrying distinct stewardship implications. Seventy five percent belonged to Watch and twenty five percent Access, none of our patients received the Reserve category. Ceftriaxone, meropenem and piperacillin+tazobactam are categorized under Watch antimicrobials due to their wider spectrum, useful in severe infections and higher potential for resistance whereas, metronidazole is recognised as an Access agent commonly used for anaerobic and intra-abdominal infections.<sup>20</sup> The antimicrobial utilisation pattern in our study demonstrates strong alignment with EML-based national and international policy where ceftriaxone, piperacillin+tazobactam, and meropenem were frequently prescribed in ICU settings.<sup>21</sup> A significant dependence on Watch group medications as reflected from recent data from India indicating a less-than-ideal Access:Watch ratio, which has become a primary concern in AWARe-based stewardship assessments.<sup>22</sup>

The observation from cost analysis in the present study showed that meropenem contributed to the highest proportion of antimicrobial treatment cost. Similar findings were reported by Axente et al., who evaluated antimicrobial consumption and costs in an ICU and reported that carbapenems significantly increased antimicrobial expenditure due to their high cost per unit.<sup>23</sup>

Table 7 compares the prescribed daily dose and DDD where ceftriaxone and metronidazole showed concordance with WHO

DDD, therefore had a PDD/DDD ratio of 1, whereas lower (<1) PDD/DDD ratios for meropenem and piperacillin+tazobactam, reflecting dose adjustments based on clinical factors such as renal function and severity of illness, similar findings were reported by Birendra et al., where PDD/DDD ratios for most antimicrobials were close to unity, indicating adherence to standard dosing practices.<sup>24</sup> Table 8 shows association between the antimicrobial use and economic status of the patients categorised as above poverty line (APL) and below poverty line (BPL), where a significant association was found for the use of piperacillin+tazobactam and patients economic status indicating more proportion of patients received it in the APL.

Adverse drug reactions (18) reported in the present study were commonly gastrointestinal disturbances such as nausea, vomiting, and diarrhoea associated with antimicrobial therapy. Similar adverse drug reactions were reported by Ansari et al., where the most frequently reported adverse drug reactions associated with beta-lactam antimicrobials in ICU patients were gastrointestinal symptoms.<sup>25</sup>

### Conclusion

Antimicrobial use remains high in Intensive Care Units (ICUs), which are high-risk settings due to the extensive use of these agents in critically ill patients. This study evaluated antimicrobial utilisation in ICU patients using WHO prescribing indicators. There was predominance of middle-aged patients, males and individuals from rural and lower socioeconomic background. The most common indications for ICU admission were COPD and pneumonia, highlighting the burden of respiratory illnesses in critical care. Ceftriaxone was the most frequently used antimicrobial, followed by meropenem and piperacillin+tazobactam, reflecting  $\beta$ -lactam antimicrobials use for empirical therapy. WHO prescribing indicators revealed average of 7.35 drugs per patient, all were administered through intravenous route and 25% were prescribed by generic name but all medications used were from essential medicines list. Commonly used was Watch group followed by Access category and no Reserve antimicrobials were used. Adverse drug reactions were mild gastrointestinal effects.

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