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ORIGINAL ARTICLE

Antibiotic Prescription in Critically Ill Patient in Intensive Care Unit of a Tertiary-Level Hospital of a Lower-Middle Income Country

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ABSTRACT

Background and aims: Antibiotic resistance is a major global health concern, particularly in lower-middle income countries. High burden of infections in intensive care units (ICUs) and empirical use of broad-spectrum antibiotics can contribute to the emergence of multidrug-resistant (MDR) organisms. This study aimed to assess the antibiotic prescription pattern in the ICU of a tertiary-level hospital of central Nepal.

Methods: A descriptive, cross-sectional study was conducted over the period of 6months analyzing the records of 249 patients admitted to the ICU. All patients aged 14 years or above admitted to the ICU for a minimum of 24 hours were included in the study. Data on patient demographics, diagnosis, antibiotic prescriptions, culture results, and sensitivity patterns were collected and analyzed.

Results: Among 249 patients, 142 were male, with a mean age of 63.07±16.84 years. The average length of stay (LOS) in ICU was 8.72±6.99 days. The most common diagnoses were acute exacerbation of chronic obstructive pulmonary disease (19.3%), septic shock (16.1%), and pneumonia (14.9%). Cultures were positive in 96 cases. Respiratory specimens were the most frequent source (74.3%), and Acinetobacter species (49%) was the predominant isolate. Empiric antibiotics were prescribed to 234 (94%) patients, with 85.5% receiving two or more antibiotics.

Conclusions: Empirical antibiotic use is highly prevalent with a significant burden of MDR pathogens, notably Acinetobacter species in our setting. Regular surveillance of antibiotic use and resistance patterns, along with ICU-specific antibiotic protocols, are essential to promote rational antimicrobial use and combat rising resistance in Nepalese healthcare settings.

Keywords: *antibiotic, ICU infection, microorganisms, stewardship.*

INTRODUCTION

Antibiotic resistance is widespread globally and it is one of the public health concerns in lower-middle income countries (LMICs) like Nepal.[1] Intensive care unit (ICU) is a specialized unit in the hospital where critically ill patients are managed with various life-saving medical equipment. Multiple medicines are used in treatment of patients in ICU and among them, antibiotics are commonly used for managing infectious conditions in ICU.[2,3] Infection is the most common presentation in hospitalized patients in ICU and regarded as one of the important factors for determining the patient outcomes.[3]

In LMICs, the point-prevalence of infection in ICU was reported as 22.4 per 100 admitted patients.[1,4,6] The risk of acquiring infections in patients admitted to ICUs are high due to multiple antibiotics resistant strains of notorious nosocomial pathogens. The most common pathogens found were *Acinetobacter baumannii* (24%), *Pseudomonas aeruginosa* (16%) and *Klebsiella pneumoniae* (15%).[6]

Overprescribing antibiotics is associated with adverse effects, frequent re-attendance, and unnecessary medicalization of self-limiting conditions.[4] Curbing the overuse and misuse of antibiotics is vital to reduce the number of drug-resistant infections that are compromising health outcomes and increasing the costs and complexities of care.[1,5] Every hospital must have its own antibiotic policy to combat these emergence of new threat, audit of antibiotic use in departments of hospital should be done to support the policy otherwise consequences of multidrug resistance can be grave.[6] Most of admitted patient are presumed to be of infective etiology. Hence, antibiotics are commonly prescribed as prophylactic or definitive therapy. There are studies of antibiotic use in different settings in outpatient and inpatient of tertiary-level hospitals.[1,6-9] Study and data of antibiotic prescription in ICU are very limited and are needed to reveal the fact of antibiotics prescription in ICU of tertiary level hospital and preparation of ICU antibiotic protocol of the hospital. Hence, this study was conducted to identify the antibiotic prescription pattern in the ICU of a tertiary level hospital of central Nepal.

METHODS

This descriptive observational study was conducted in the medical ICU of Shree Birendra Hospital (SBH), which is a tertiary level hospital located in central Nepal. The study was approved by the Institutional Research Committee (IRC) of Nepalese Army Institute of Health Sciences (registration number 1114, dated November 22, 2024). The study duration was of six months (Dec 2024 to May 2025). The informed consent was obtained from the patient and/or patient's family.

All patients aged 14 years or above admitted to the ICU for a minimum of 24 hours irrespective of whether antibiotics were prescribed or not were included in the study. Patients who were shifted to other units from ICU during the time of data collection and patients transferred from other hospitals who were already on antibiotics were excluded. The sample size was calculated using following a formula for infinite population; $n = (Z^2 \times P \times (1 - P)) / e^2$, with Z set for 95% confidence interval, estimated proportion (P) of 0.5 and margin of error (e) of 0.05. The calculated sample size of 384.16 was adjusted for a finite population of 700 (ICU admission of the previous year obtained from the hospital records) and using the formula; $n_1 = n / (1 + (n - 1) / N)$, where N is the size of population. A final sample size of 249 was determined.

Information was collected in a structured proforma from a case sheet maintained in ICU. Information of patient's demographics (age and gender), diagnosis, antibiotics prescribed, ICU length of stay (LOS) and outcome (in terms of recovery, ICU discharge, transfer after recovery and death of the patient), and the detail of antibiotics (name and the number of antibiotics prescribed, duration of antibiotics and culture sensitivity test result, whenever available) were collected. Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated by using online APACHE II calculator.[10] APACHE II is a severity scoring system used in ICUs. Applied within 24 hours of admission, it generates a score from 0 to 71, with higher scores indicating more severe illness and higher risk of death.[11]

All data were entered in MS-excel and descriptive statistics like frequency, number, percentages, mean, standard deviations, and range were determined. Data are presented in bar-diagram, table and pie chart. The most frequently used antibiotics are categorized according to Anatomical Therapeutic Chemical (ATC) as the classification system and the Defined Daily Dose (DDD) as a unit of measure.[12] The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.[12]

RESULTS

The prescription of 249 patients admitted into ICU was analyzed. There were 142 males and 107 females with their age ranging from 14 to 96 years. The average age of the patients was 63.07±16.84 years and the most were from age group 61-70 years (n=82).

The most common diagnosis at admission to ICU was acute exacerbation of chronic obstructive pulmonary diseases (AE-COPD, 48 patients) followed by septic shock (40 patients), pneumonia (37), poisoning (11), sepsis (10), decompensated chronic liver disease (9), dyselectrolytemias (8), stroke (7) and heart failure (6). Major organ system and etiological categories involved for ICU admission are shown in figure 1.

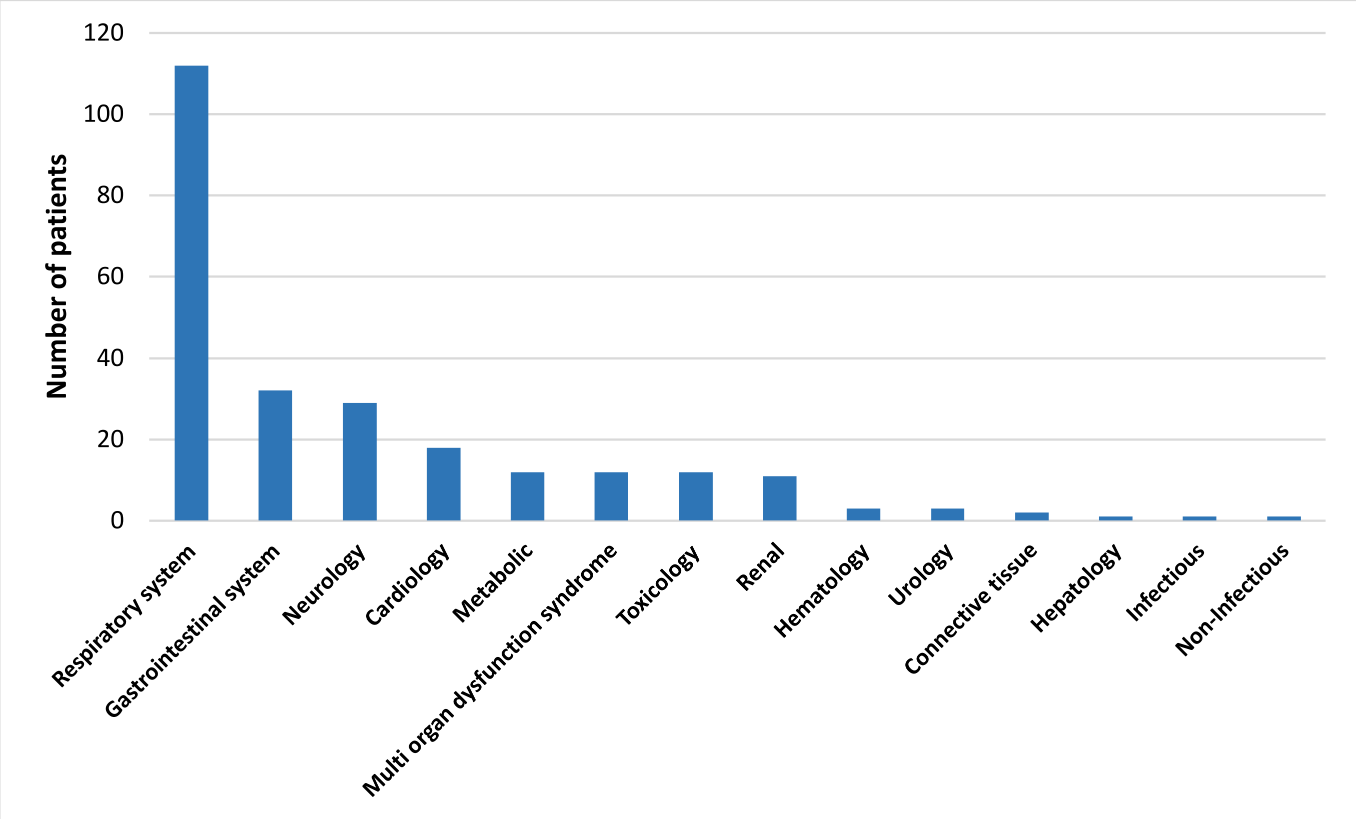

Figure 1. Major organ system and etiological categories of ICU admission

The average length of stay (LOS) in ICU was 8.72±6.99 days with median of 7 days. The minimum duration of stay was one day and maximum duration was 60 days.

Out of 249 patients, 96 patients had organisms growing in culture for which sensitivity test was done. The major culture positive specimen was respiratory specimen (75) followed by blood (17), cerebrospinal fluid (3) and urine (1). The most commonly isolated organism was *Acinetobacter species* (47) followed by *Klebsiella species* (18) and *Pseudomonas species* (7) (Table 1).

The antibiotics were prescribed in 234 patients. Total number of antibiotics used was 451 with the average number of antibiotics prescribed per patient of 1.92. The most frequently used antibiotics are given in table 2. The least prescribed antibiotics in ICU were amikacin (7), cefepime (7), cefotaxime (2), colistin (2), flucloxacillin (2), ampicillin (1), ceftazidime (1), cefuroxime (1), ciprofloxacin (1) and clarithromycin (1).

The empirical treatment was started in 234, and culture was sent for all patients. The antibiotic therapy was changed for 37 patients with 86% of them growing MDR organisms. The commonly isolated organism (*Acinetobacter species)* was mostly susceptible to doxycycline (Table 3). Acinetobacter species and *Klebsiella pneumoniae* had the highest susceptibility to doxycycline whereas Pseudomonas to piperacillin-tazobactam and levofloxacin.

Table 1. Organisms isolated from culture

Organism	Number of cultures
Acinetobacter species	47
Klebsiella pneumoniae	18
Pseudomonas aeruginosa	7
Escherichia coli	5
Enterobacter	4
Methicillin resistant *Staphylococcus aureus* (MRSA)	4
Methicillin resistant coagulase negative *Staphylococcus aureus* (MRCNS)	4
Methicillin sensitive *Staphylococcus aureus* (MSSA)	3
Candida	2
Citrobacter freundii	1
Aspergillus	1
Total	**96**

Table 2. List of most frequently used antibiotics

Antibiotic	ATC Code*	DDD (gm)	Number of prescriptions
Piperacillin + Tazobactam	J01CR05	14	73
Meropenem	J01DH02	2	61
Linezolid	J01XX08	1.2	35
Levofloxacin	J01MA12	0.5	34
Azithromycin	J01FA10	0.3	25
Ceftriaxone	J01DD04	2	23
Vancomycin	J01XA01	2	20
Clindamycin	J01FF01	1.8 (oral), 1.2 (intravenous)	19
Aztreonam	J01DF0	4	17
Moxifloxacin	J01MA14	0.4	17
Ceftazidime + Avibactam	J01DD52	6	15
Teicoplanin	J01XA02	0.4	15
Metronidazole	J01XD01	2	12
Amoxycillin Clavulanate	J01CR02	1.5 (oral), 3 (intravenous)	11
Minocycline	J01AA08	0.2	11
Doxycycline	J01AA02	0.2	10
Imipenem/Cilastatin	J01DH51	2	10
Polymyxin B	J01XB02	0.0756	10

*ATC codes classified under J (anti-infectives for systemic use); DDD, defined daily dose.

Table 3. Antibiotics sensitivity in commonly isolated organisms form ICU

Antibiotic	Micro-organisms		
	Acinetobacter (n=53)	Klebsiella (n=17)	Pseudomonas (n=7)
Doxycycline	9	4	-
Tobramycin	1	-	1
Imipenem	1	-	-
Piperacillin-tazobactam	1	1	2
Levofloxacin	-	1	2

Average duration of antibiotics use was 8.38 ± 5.72 days with a median of 7 days. Majority of the patients were prescribed antibiotics for 1-10 days (220 cases) followed by 11-20 days (186 cases).

Maximum number of patients (75) were prescribed with two antibiotics, 56 received three antibiotics, 47 patients received four, 35 patients had five or more antibiotics, 21 cases were treated with a single antibiotic and 15 patients were not prescribed any antibiotics. The most common interventions done in patients admitted in ICU were mechanical ventilation (86) followed by non-invasive ventilation (53) and hemodialysis (11) and tracheostomy (11) (Table 4).

Table 4. Interventions done

Intervention	Number of patients
MV	86
NIV	53
HD	11
MV & Tracheostomy	12
MV & HD	6
Diagnostic Laparotomy	1
MV, HD & Angiography	1
UGI Endoscopy	1
Temporary Pacemaker Implantation	1

MV, Mechanical ventilation; NIV, Non-invasive ventilation; HD, Hemodialysis; UGI, Upper Gastro Intestinal

The median APACHE II Score was 18 (IQR 1-41). Out of 249 patients, 160 were transferred to wards, 85 died in ICU, and 4 left the ICU against medical advice (LAMA).

DISCUSSION

This study analyzed the clinical profiles, antimicrobials usage, microbiological patterns, interventions and outcome of the patients admitted to the ICU of a tertiary level hospital.

Our study showed slight male predominance (57%) in ICU admission which is lower than the findings of study by Alharthi et al. (71.7%) and Williams et al. (65.5%) but higher than that reported by Gedam S et al (52.7%) and Kayambankadzanja et al. (51%).[13-16] This is in contrast to the female predominance on ICU admission reported by Marasine et al (58%) from Nepal.[8] This disparity might be due to differences in population demographics, disease prevalence or ICU admission criteria and healthcare-seeking behavior. Similarly, our study setting is primarily focused on family of military, military veterans and few serving military population where the number of males is significantly higher. The average age of the patients and higher number of patient's age group in our study (63.07 ± 16.84 years, age group 61-70 years) is higher than findings of study by Kayambankadzanja et al. (32), Chatterjee et al. (41-60 years) from India, Williams et al (49 ± 19.5 years, age group 15-30 years), Marasine et al. (50.60 ± 20.18 years, age group 18-94 years).[8,14,16,17] The higher prevalence of age-related chronic illnesses (including sepsis, heart failure, and COPD) that need urgent care, combined with delayed hospital presentations in settings with inadequate resources, may be the cause of our older cohort. Furthermore, our ICU admissions were older than those in studies conducted in populations with younger demographics or with different healthcare infrastructures, which could be explained by differences in life expectancy and access to long-term disease management.

Respiratory diseases (COPD 19.27%, pneumonia 14.85%) were the most common system involved, followed by septic shock (16.065) in our study which is similar to the findings of study done by Priyankara D et al. (pneumonia 49.1%, AE-COPD 4.6%) and Alharthi et al. (respiratory tract infection 29.35%).[13,18] According to Gedam S et al. (cardiovascular diseases along with sepsis and multiorgan dysfunction 51.35% and respiratory diseases 17.57%) were more common diagnosis than AE-COPD (4.7%) in lieu with findings from study of Chatterjee et al., cardiac diseases including hypertension, arrhythmias, heart block (11.3%).[15,17] This variation might be attributed to regional disease pattern, seasonal variation of diseases, higher smoking rates and air pollution in the region of our study settings. This finding highlights the need for region-specific critical care policies because local disease frequency, healthcare infrastructure, and access to preventative care have a significant impact on ICU admission patterns.

The LOS at ICU (mean 8.72 ± 6.99 days, median 7 days, interquartile range 1- 60 days) is longer than data reported by Marasine et al. (median LOS 5 days, range 2-16 days), Alharthi et al. (mean LOS 7.4 days, range 2-5 days), Williams et al. (mean LOS 5.75 days, range 1 to 15 days), Kayambankadzanja et al. (median LOS 2 days, range 1 to 4 days) and Chatterjee et al. (mean LOS 5.43 days).[8,13,14,16,17] The longer length of stay in our study might be related to our institutional factors (free of cost treatment), delay in hospital presentation with severe form of diseases, limited availability of step-down units or high dependency units and high prevalence of complex chronic conditions like COPD and septic shock in our cohort. To maximize ICU bed usage in our setting, these systemic issues underscore the necessity of bolstering pre-hospital care, intermediate care facilities, and discharge planning.[19,20]

Among 96 culture and sensitivity tests done, with the most frequent source being respiratory specimens, the most common organisms isolated were *Acinetobacter species* (47 isolates) and almost all common isolates were resistant to meropenem, gentamycin and all generation cephalosporins. Marasine et al from Nepal in 2021 reported *Escherichia coli* (10 isolates) and *Acinetobacter* (2 isolates) which were resistant to meropenem but sensitive to piperacillin/tazobactam, polymyxin-B, ceftriaxone and ceftazidime.[8] We found that most frequently prescribed antibiotics were piperacillin-tazobactam (31.19%), meropenem (26%), linezolid (14.96%) and levofloxacin (15.53%). Alharthi et al from Saudi Arabia found prescription of piperacillin-tazobactam in 17.7% & meropenem in 9.56% of their patients. Similarly Priyankara et al. from Sri Lanka found meropenem prescribed in 32.91% and piperacillin-tazobactam in 22.36 % of their patients which is similar to ours.[13,18] In contrast, Gedam S et al. and Williams et al. from India reported cefotaxime (17.5%) and cefoperazone (26%) respectively and Kayambankadzanja et al. from Malawi reported ceftriaxone 50.4% and metronidazole 38% as most commonly used antibiotics in ICU.[14-16] Our study's findings on the widespread use of broad-spectrum antibiotics, such as meropenem and piperacillin-tazobactam, are consistent with those of other ICUs in South Asia and the Middle East, indicating comparable antimicrobial prescribing trends in response to common multidrug-resistant organisms. In contrast to research from Nepal, the significant incidence of carbapenem-resistant *Acinetobacter species* in our context indicates a more severe resistance pattern, suggesting that the landscape of antimicrobial resistance is changing and getting worse with time. It's possible that variations in local resistance trends, antimicrobial stewardship strategies, or the availability of healthcare resources in Indian and African intensive care units account for the variable antibiotic usage patterns, where narrower-spectrum drugs were more frequently utilized.[1,4,21]

With an average of 1.92 antibiotics per patient, 451 antibiotics were prescribed in total. The most commonly used top three antibiotics were piperacillin-tazobactam (31.19%), meropenem (26%) and linezolid (14.96%). Alharthi et al. (one antibiotic in 40.2% and two antibiotics in 39.1%), Williams et al. (1-2 antibiotics in 70%), Priyankara D et al. (two antibiotics in 39.24% and one antibiotic in 35%) and Kayambankadzanja et al. (two antibiotics in 50.2%) also showed similar findings to ours (two antibiotics in 32.05% and three antibiotics in 23.93%).[13,14,16,18] The number of days of antibiotic use (median 7 days) and 170 antibiotics used for 6 to 10 days is higher than that reported by Kayambankadzanja et al. (median 2 days).[16] Our study showed preferences of two or more antibiotics combination aligning with findings from other LMICs suggesting that empirical treatment covered wide range of organisms. The differences in duration of antibiotic therapy indicate the differences in patient severity, local resistance patterns and antimicrobial stewardship practices necessitating the need for context-specific antibiotic protocols based on local antibiogram in developing or resource constrained healthcare settings.[1,4,22]

APACHE II scores in our study (41.76% with score 10-19, median 18, mean 18.80 ± 8.53, IQR 1-41) is similar from the study from Chitwan, Nepal (51.6% with score 11-20) and with the findings of Williams et al. from India (46.5% with score 10-19).[8,14] Consistent patterns of critical illness severity among intensive care unit patients in South Asian healthcare settings are suggested by the similar APACHE II score distributions between our study, the Chitwan study, and the Indian study. Shared regional characteristics including delayed healthcare presentation, similar illness load, and equivalent critical care admission requirements among various healthcare systems are probably the cause of this resemblance. Our findings (ICU mortality 34.14%, discharge percentage 64.3% and LAMA 1.6%) are comparable with the findings of the studies from India by Williams et al. (discharged 60.5%, ICU mortality 39.5%) and Chatterjee et al. (discharge 68.8%,transferred out and referred 18.7% ICU mortality 9.5%, LAMA 3%).[14,17] The prevalence of severe respiratory disease (COPD, pneumonia) and septic shock cases, which have worse prognoses, is probably the reason for our high fatality rate and maximum dependency on mechanical ventilation (34.53%) and non-invasive ventilation (21.28%). Limitations in ventilator availability, dialysis, or sophisticated monitoring in our context may cause delays in interventions, which could decrease outcomes when compared to ICUs with adequate resources. Our reduced LAMA percentage indicates improved financial support or family involvement, notwithstanding cultural perceptions about essential care.

This study has a few limitations. This single center ICU based study with small number of patients limit the generalizability of the antibiotic's patterns and resistance profiles to other healthcare settings across Nepal. The observation study design prevents the actual establishment of causal relationships between antibiotic choices and clinical outcomes with the lack of long-term follow up data. This also limits the overall assessment of clinical effectiveness and outcomes.

This study highlights the further need of long-term multicentric study with focus on infectious disease pattern, organisms' growth, availability of culture-sensitivity test, antimicrobial sensitive spectrum and resistance pattern to develop the evidence-based antimicrobial stewardship program of a country like Nepal.

CONCLUSION

In our setting, empiric use of antibiotic is highly prevalent in ICU with a significant burden of MDR pathogens such as Acinetobacter species. Regular surveillance of antibiotic use and resistance patterns, along with antibiotic prescription guidelines, are essential to promote rational use of antimicrobial use and combat antimicrobial resistance.

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DECLARATIONS

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CONFLICT OF INTEREST

None.

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