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## **Prevalence and Pattern of Antimicrobial Resistance in ICU Patients** with Sepsis in Dhaka City: A Single Center Study

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Abstract: Background: Pathogenic resistance against antibiotics is substantially mounting in the developing countries including Bangladesh. Antimicrobial resistance is a rising concern specially among the critically ill patients who are often treated by multiple antibiotics. *Objective*: To observe the pattern of antimicrobial resistance among the patients diagnosed with sepsis admitted into the intensive care unit (ICU). Method: This observational study took place in the ICU of Bangabandhu Sheikh Mujib Medical University for 1 year. Samples of blood, urine, tracheal aspirate were obtained from 192 patients admitted in ICU with clinically diagnosed sepsis which were cultured and analyzed. *Result*: Mean age of the patients were  $54.29 \pm 19.443$ years and 60.4% were males. The most common sample yielding positive culture was tracheal aspirate [94 (51.6%)]. Out of 530 samples, organisms were isolated from 158 samples. The most frequently isolated microorganisms were Klebsiella spp. 54 (35.29%), followed by Acinetobacter spp. 38 (24.83%), Pseudomonas spp. 19 (12.42%) and Candida spp. 15 (9.80%). Regarding antimicrobials, a range of drugs classified as Penicillins, Cephalosporins, Carbapenems, Fluroquinolones, Macrolides and others such as Trimethoprim/Sulfamethoxazole and Nitrofurantoin were found to be 100.0% resistant to Pseudomonas spp., Klebsiella spp., Acinetobacter spp. and E. coli. Conclusion: A high prevalence of resistance to most antibiotics was detected. Overall, such a revelation of increased antibiotic resistance demands for restrictive and appropriate antibiotic usage in accordance with the updated antibiotic prescribing policy in Bangladesh.

**Keywords:** Antimicrobial resistance; sepsis; ICU; culture; antimicrobial sensitivity testing; specimen; sample; Dhaka.

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## **INTRODUCTION**

Sepsis is a major health emergency and lifethreatening condition which requires effective management. It occurs as a result of dysregulated host response to infection. It is a growing worldwide burden and a significant challenge to clinicians owing to its remarkable pathophysiological, molecular, genetic and clinical complexities [1, 2]. Sepsis can be characterized by fever, increased heart rate, fast breathing, confused states, pain all over the body, low urine output and cold, clammy skin. It can develop septic shock, multiple organ failure and death [1]. It is stated by the presence of two or more of the following parameters: unusual body temperature (<36° C (96.8° F) or >38° C (100.4° F)); heart rate >90 beats/min; respiratory rate >20 breaths/min or partial pressure of carbon dioxide less than 32 mm of Hg; and white blood cell (WBC) count <4000/mm<sup>3</sup> or >12,000/mm<sup>3</sup> [3]. From

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data published in 2020, there were 48.9 million cases and 11 million sepsis-related deaths worldwide, which represents 20% of all global deaths. World Health Organization (WHO) has declared sepsis a global health priority. Significant regional disparities in incidence and mortality are found with the highest rates seen in lower-middle-income countries [1, 3].

In hospital settings, intensive care units (ICUs) have an exceptional environment. Critically ill patients, in combination of existing comorbidities, high risk surgeries and frequent need for invasive devices make them highly vulnerable for acquiring infections [4]. Studies show that, hospital-acquired infections or HAIs were 5 times more commonly found in ICU admitted patients in comparison to patients admitted in other zones of a hospital [5].

Studies suggest that, most commonly isolated pathogens responsible for sepsis were Acinetobacter species. Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Candida species, Streptococcus species, Enterobacter species among others [2]. The most frequently occurring sites of infection related to sepsis are the respiratory tract, the urinary system, the blood and the abdomen [4]. Management of sepsis requires multiple aspects and must be commenced at the earliest. After confirmation of diagnosis from clinical signs and laboratory tests, use of antimicrobials to treat the infection is essential to improve outcomes from sepsis [2]. Rational use of drugs is regarded as the cornerstone in managing these patients. The choice of empiric antimicrobial therapy based on clinical (i.e., site of infection, previous antibiotic use, immunosuppression and risk factors for resistant organisms) and epidemiological criteria is extremely crucial [2]. Appropriate cultural samples are required before antibiotic therapy is started. This treatment should be based on clinical/epidemiological criteria and be administrated abruptly. The second pillar of treatment is fluid resuscitation [2]. Balanced crystalloids are the fluid of choice. In addition, the use of inotropic drugs represents one of the cornerstones of septic shock treatment. Also, oxygen represents the most common treatment administered to any patient with a medical emergency, including those with sepsis [2].

However, antimicrobial resistance (AMR) has emerged as one of the significant and urgent threats to public health; not just in developing countries but throughout the world [6]. Antimicrobial resistance occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to drugs making infections harder to treat increasing the risk of disease spread, severe illness and ultimately death [6]. The scenario is such that, frequent and irrational use of broadspectrum antibiotics in critically ill patients who stay in the ICU for more prolonged periods have increased microbial resistance over time [7]. Furthermore, in many developing countries where there are deficiencies in proper diagnostic tools, patient management is predominantly contingent upon the prescription of medicine, particularly antibiotics. Many antibiotics are of poor quality and sold over the counter in the developing countries [7]. Moreover, antibacterial resistance can develop because physicians unnecessarily prescribe lengthy courses of antibiotics. Studies have implicated that; clinicians consider the perceived patient request for antibiotics as one of the major barriers to adhere to standard guidelines for antibiotic prescriptions [6]. Antimicrobial resistance mechanisms fall into four main categories: limiting uptake of a drug; modifying a drug target; inactivating a drug; active drug efflux [6, 7].

Additionally, sustained increases in antimicrobial resistance have led to fewer treatment options for patients and an associated increase in morbidity and mortality [7]. Antimicrobial resistance has become a global concern with economic and social implications worldwide [7]. The combination of diseases like HIV/AIDS, Tuberculosis or Malaria with antimicrobial resistance will make the scenario extremely worse [7]. As much as the issue with HAIs in ICUs, adding the multidrug antimicrobial resistance flares up the burden [8]. Considering the risk profile of the patients admitted in ICUs, this zone is known to be the epicenter of development of resistance [8].

According to the updated country report on antimicrobial resistance of 2022, there were 1,037,002 culture records from 2016 to 2020, of which 299,786 (28.90%) records reported bacterial growth. A total of 736.077 records were reported as no growth or negative. while 1.139 records were missing culture results [9]. Among the records with bacterial growth, 23,888 records reported no significant findings or did not yield a pathogen (no significant growth, normal flora, mixed bacterial species, no pathogens found etc.) [9]. The most common bacteria isolated in the dataset obtained was Escherichia coli (nearly 34.71% of positive records with pathogen identified) followed by Klebsiella spp., Pseudomonas spp., Staphylococcus aureus and Enterococcus spp. (approximately 14.51%, 10.14%, 8.83%, and 6.86%, respectively) [9]. In addition, high levels of resistance were observed in the pathogens associated with hospital acquired infections, and Salmonella Typhi resistant to aminoglycosides and decreased susceptibility to Ciprofloxacin was also observed [9]. Furthermore, the Bangladeshi data illustrates that there have not been any significant changes in antimicrobial susceptibility trends in the region over the last 4 years [9]. A number of critical priority bacteria, including carbapenem resistant Acinetobacter spp. (56%) and ceftriaxone/cefotaxime resistant Escherichia coli (up to 61%) were observed [9].

The global rise in antibiotic resistance poses a significant threat, diminishing the efficacy of common antibiotics against widespread bacterial infections [10]. The 2022 Global Antimicrobial Resistance and Use

Surveillance System (GLASS) report highlights alarming resistance rates among prevalent bacterial pathogens [10]. Median reported rates in 76 countries of 42% for third generation cephalosporin-resistant E. coli and 35% for methicillin-resistant Staphylococcus aureus are a major concern [10]. For urinary tract infections caused by E. coli, 1 in 5 cases exhibited reduced susceptibility to standard antibiotics like ampicillin, co-trimoxazole, and fluoroquinolones in 2020 [10]. This is making it harder to effectively treat common infections. Klebsiella pneumoniae, a common intestinal bacterium, also showed elevated resistance levels against critical antibiotics [10]. Increased levels of resistance potentially lead to heightened utilization of last-resort drugs like carbapenems, for which resistance is in turn being observed across multiple regions [10].

AMR is a complex problem that requires both sector-specific actions in the human health, food production, animal and environmental sectors and a coordinated approach across these sectors. A lot of strategies, plans and policies have been on implementation to combat this global challenge. The present study has been designed to determine the prevalence of micro-organisms isolated from cultures from ICU-admitted patients with clinically suspected sepsis and the resistance of these bacteria to the commonly prescribed antibiotics in patients. The antibiotic sensitivity patterns may guide the physicians for initiation of empiric therapy with antibiotics, thus increasing the chance of successful recovery of patients with sepsis, ultimately reducing mortality, morbidity and healthcare cost which is very essential for this country with limited resources. This study will also help to improve the antibiotic policy of this country.

## METHOD

#### Study Settings, Design and Participants

This observational study took place in the ICU of Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, Bangladesh. It was conducted to determine the prevalence of microorganisms isolated from cultures from patients admitted in ICU with clinically diagnosed sepsis and the resistance of these organisms to the commonly prescribed antibiotics. The study duration was April 2023 to March 2024, roundabout 12 months after approval from Institutional Review Board (IRB) of BSMMU.

Sample size was determined by using the formula n=  $(z^2) *(pq)/d^2$ .

Where, n= Desired sample size; z= The standard normal deviate (usually set at 1.96 at 5% level which corresponds to 95% confidence level); p= suppose, proportion of patient is more than 50%, so p=0.5 (in last year 2022, on the basis of hospital record, more than 50% patients were septic or history of sepsis); q= 1-p =1-0.5

=0.5 and d= acceptable error (it is usually set at 5% (0.05).

So,

 $n = (1.96)^2 * 0.5 * 0.5/(0.05)^2$ 

= 3.8416 \* 0.5 \* 0.5/0.0025

= 384 = 384/2 = 192 (As the sample collection time was six months, the targeted sample size was considered half of total). Therefore, the total number of respondents who took part in this study was 192.

## Eligibility Criteria

Inclusion Criteria

- Patients with sepsis aged 18 years and above.
- Patients admitted in ICU of BSMMU referred from another ICU after failed treatment.
- Patients who became acutely ill in another ward in BSMMU during treatment.
- Patients who developed sudden emergency during intra-operative or post-operative period.

#### **Exclusion Criteria**

- Pregnant women.
- Patients with any existing malignancy.
- Patients who are diagnosed with HIV/AIDS and Tuberculosis.

A case record form or structured questionnaire was used to collect all the information required to perform this study which were demographics (such as age, gender, body weight), blood pressure, heart rate, respiratory rate, temperature, leukocyte count, arterial blood gas, lactate level, primary diagnosis and so on.

The guardian accompanying the patient were interviewed. The nature, objective, procedure, risks and benefits and implications of the study were explained. Informed written consent was obtained.

# Bacterial Isolation and Antibiotic Susceptibility Testing

Samples of blood, urine and sputum/tracheal aspirate were collected. The collected samples were cultured in standard culture media for isolation of potential pathogens using standard methods. For each isolated pathogen, antibiotic susceptibility was performed by a standard microbiological procedure which was disc diffusion method.

Sites selected for blood sampling were swabbed with 70% alcohol. Five to ten milliliters were collected in bactec bottles, transported to the laboratory and placed in the bactec 91.20 instruments. Positive bottles were Gram stained, sub-cultured and tested for sensitivity by the microbiologist.

Tracheal aspirates were obtained by suctioning the endotracheal or tracheostomy tubes using a sterile suction catheter and the tip cut off with a sterile surgical blade, placed in sterile containers and were sent to the laboratories. The most purulent part of the aspirate was used by the laboratory technician to inoculate the plates with specimen, chocolate and MacConkey agar. Chocolate and specimen plates were inoculated in carbon dioxide at 35-37° C and MacConkey agar in ambient air for 24 hours.

Urine was taken in the form of mid-stream urine or from a sampling port on an indwelling catheter using an aseptic technique in a sterile container. The samples were used to inoculate blood and MacConkey agar, which were incubated at 35-37° C for 18-24 hours. Positive cultures were Gram stained, sub-cultured and tested for sensitivities. Bacterial pathogens were identified using standard bacteriological procedures.

Isolates showing sensitivity to all antibiotics and isolate identified as commensals, colonization or contaminants were excluded. Isolates with intermediate susceptibility were considered resistant.

#### **Statistical Analysis**

The data, after being collected and organized, were input in Microsoft Excel and Statistical Package of Social Sciences (SPSS, Version 25) for statistical analysis. The data were presented in the forms of frequency and percentages using relevant tables and figures.

#### Ethics

Proper safety measures were taken in every step of the study. According to Helsinki Declaration for Medical Research involving Human Subjects 1964, all the patients were informed about the study design, the underlying hypothesis and the right of the participants to withdraw themselves from the research at any time and for any reason whatsoever.

The following ethical issues was addressed accordingly:

- Strict confidentiality and security of data related to the patient was maintained.
- The presentation of data and information related to the patient was documented anonymously.

## **Results**

This study involved 192 patients admitted to the ICU of a specialized hospital, all clinically diagnosed with sepsis. The mean age of the patients was  $54.29 \pm 19.443$  years; 60.40% of them were males; 82.50% (151) of them had been hospitalized within the last 90 days and 81.40% (140) had undergone surgery prior to their ICU admission. The majority of the patients had hypertension 75.2% (106) followed by diabetes mellitus 69.5% (98), chronic kidney disease 39.0% (55), COPD 10.6% (15), cerebrovascular disease 9.9% (14) and bronchial asthma 8.5% (12).

 Table 1: Sample profile and rate of positive culture from different samples

Samples	Total No. of the Sample	Samples yielding growth of organisms		
		Number (n)	Percentage (%)	
Tracheal Aspirate	182	94	51.6	
Blood	192	34	17.7	
Urine	156	30	19.2	
Total	530	158	29.81	

Table above demonstrates distribution of samples and growth of organisms in the culture of the samples. It is evident that, 192, 182 and 156 samples of blood, tracheal aspirate and urine were sent for culture

and sensitivity testing respectively. Highest culture positive was found in tracheal specimen [94 (51.6%)]. Out of 530 samples, organisms were isolated from 158 samples (Table 1).

Table 2: Patterns of microorganisms isolated from uniferent samples					
Specimen	Blood	Urine	Tracheal Aspirate	Total (%)	
Gram Positive Bacteria					
Staphylococcus					
Staphyloccus aureas	5	0	0	5 (3.26)	
Staphylococcus haemolyticus	2	0	0	2 (1.31)	
MRSA	4	0	0	4 (2.61)	
Streptococcus					
Streptococcus pneumoniae	2	0	0	2 (1.31)	
Streptococcus pyogenes	1	0	0	1 (0.65)	
Enterococcus faecalis	0	2	0	2 (1.31)	
Gram Negative Bacteria					
Cocci					
Acinetobacter	2	1	35	38 (24.83)	
Acinetobacter baumannii complex	2	0	0	2 (1.31)	
Bacilli					
Facultative Anaerobe					

 Table 2: Patterns of microorganisms isolated from different samples

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Total	34 (21.51%)	30 (18.98%)	94 (59.49%)	158
Filamentous Fungi	0	0	1	1 (0.65)
Candida species	0	12	3	15 (9.80)
Fungus				
Stenotrophomonas maltophilia	2	0	0	2 (1.31)
Elizabethkingia meningoseptica	1	0	0	1 (0.65)
Pseudomonas	5	4	10	19 (12.42)
Aerobe				
Proteus	0	1	0	1 (0.65)
Enterobacter	0	0	1	1 (0.65)
Serratia marcescens	3	0	0	3 (1.96)
E. coli	1	4	0	5 (3.26)
Klebsiella	4	6	44	54 (35.29)

Table 2 illustrates the detailed pattern of organisms isolated from various types of samples. The commonest microorganism isolated from all samples was *Klebsiella* 54 (35.29%), followed by *Acinetobacter* 38 (24.83%), *Pseudomonas* 19 (12.42%) and *Candida spp* 15 (9.80%).

Figure 1 describes the prevalence of microorganisms isolated from the various samples. It is

clearly evident that, *Klebsiella* (46.8%) and *Acinetobacter* (37.2%) were the most commonly encountered pathogens in respiratory specimen; *Pseudomonas* (14.7%) and *Staphylococcus aureus* (14.7%) were frequently detected in blood samples; the most prevalent microorganisms found in urine specimens were *Candida spp* (40.0%) and *Klebsiella* (20.0%).

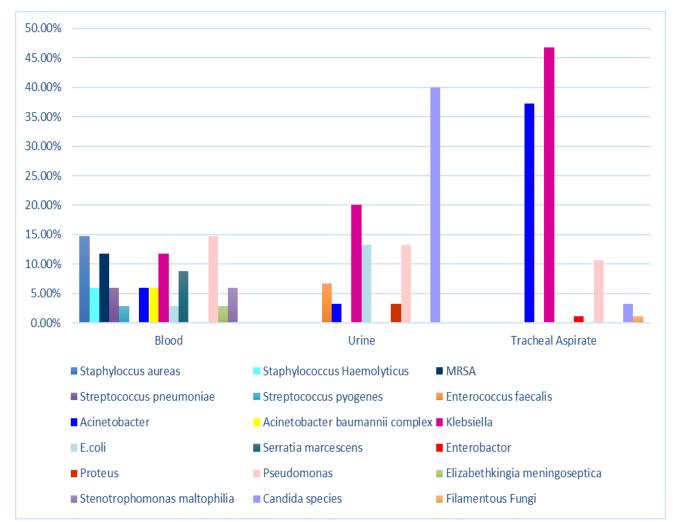


Figure 1: Prevalence of the microorganisms isolated from different samples.

Antibiotics	Percent Isolates Showing Antibiotic Resistance						
	Klebsiella Spp.	Acinetobacter Spp.	Pseudomonas Spp.	E coli			
Beta-Lactam Antibiotics							
Penicillin							
Amoxicillin	100.0	-	-	50.0			
Ampicillin	100.0	-	-	-			
Mecillinam	100.0	-	100.0	50.0			
Cephalosporin							
Ceftriaxone	94.34	100.0	-	80.0			
Cefuroxime	95.83	100.0	-	80.0			
Ceftazidime	80.0	100.0	72.22	80.0			
Cefixime	75.0	-	-	66.67			
Cefotaxime	97.56	100.0	-	100.0			
Cefepime	76.92	-	75.0	0			
Aztreonam	-	100.0	90.90	100.0			
Carbanem							
Meropenem	92.30	94.73	44.44	50			
Imipenem	100.0	-	25.0	-			
Ertapenem	100.0	-	-	-			
Beta Lactamase inhibitor							
Piperacillin/Tazobactam	96.15	97.22	55.56	0			
Amoxicillin/Clavulanic Acid	95.83	-	50.0	66.67			
Cefoperazone/Sulbactam	100.0	-	-	-			
Aminoglycosides							
Amikacin	88.88	94.73	77.78	66.67			
Tigecyclines	8.33	0	0	-			
Gentamicin	77.77	66.67	100.0	66.67			
Netilmicin	100.0	66.67	88.89	50			
Fluoroquinolones							
Ciprofloxacin	98.15	97.37	66.67	80.0			
Levofloxacin	100.0	-	66.67	-			
Nalidixic acid	100.0	-	100.0	100.0			
Macrolides							
Azithromycin	100.0	-	-	-			
Polymyxin	100.0	-	0	-			
Colistin	2.17	0	28.57	-			
Others							
Trimethoprim/Sulfamethoxazole	66.66	-	100.0	-			
Nitrofurantoin	83.33	-	100.0	0			
Fosfomycin	33.33	-	-	-			
Cotrimoxazole	89.58	94.74	50.0	80.0			

 Table 3: The antibiotic resistance pattern of major organisms isolated from the patients in ICU

The table 3 highlights the pattern of antimicrobial resistance of 4 major organisms that were isolated from the patients from ICU namely Klebsiella spp, Acinetobacter spp, Pseudomonas spp and E. coli. For Klebsiella spp, Amoxicillin, Ampicillin, Mecillinam, Imipenem, Ertapenem, Cefoperazone/Sulbactam, Netilmicin, Levofloxacin, Nalidixic acid, Azithromycin, Polvmixin showed 100.0% resistance. For Acinetobacter, Aztreonam, Cefuroxime, Ceftriaxone, Ceftadizime, Cefotaxime revealed 100.0% resistance. In Pseudomonas Nitrofurantoin. case of spp, Trimethoprim/Sulfamethoxazole, Nalidixic acid, Gentamicin and Mecillinam exposed 100.0% resistance. Lastly, for Escherichia coli, Nalidixic acid, Aztreonam and Cefotaxime were found to have 100.0% resistance.

## DISCUSSION

Antimicrobial resistance is a worldwide problem and Bangladesh is a significant contributor owing to its poor healthcare standards, along with the misuse and overuse of drugs. This study was performed to determine the prevalence of microorganisms isolated from cultures from patients admitted in ICU with clinically diagnosed sepsis and the resistance of these organisms to the commonly prescribed antibiotics.

Our study reported the mean age of the patients to be  $54.29 \pm 19.443$  years and 60.4% were males. Previous study [11] found 21.0\% of the patients were within 61-70 years and 66.0% were males.

We found tracheal aspirate to be highest culture positive. Findings are consistent with a study [11] done in Bangladesh in 2021 where the most common locations for infection were tracheal aspirate (67.2%); urine (16.0%) and blood (10.4%).

Furthermore, the study detected Klebsiella spp, Acinetobacter spp, Pseudomonas spp. and Candida spp to be the most prevalent microorganisms in the specimens. Recent research [12] by Salam et al., says, Pseudomonas spp. (30.59%), Escherichia coli (24.71%), Acinetobacter spp. (20.0%), and Klebsiella spp. (14.12%)were the most frequently isolated microorganisms. Meanwhile, a similar study [13] in Vietnam in 2017 found that, the three commonly isolated microorganisms were Acinetobacter spp. (n = 75), Klebsiella spp. (n = 39), and Pseudomonas spp. (n = 29).

Besides, we found that, Klebsiella spp. and Acinetobacter spp. were the most prevalent microorganisms in respiratory specimen; Pseudomonas spp. and Staphylococcus Aureus in blood and Candida spp. and Klebsiella spp. in urine. Previous paper [11] saw that, Acinetobacter spp. (n=22) and Pseudomonas spp. (n=21) were the commonest in tracheal specimen; blood detected Pseudomonas spp. (n=8) and Staphylococcus Aureus (n=4) most frequently; and in urine, the most prevalent organisms were E. coli (n=7) and Pseudomonas spp. (n=6).

In this investigation we found that, among the four microorganisms Klebsiella spp., Pseudomonas spp., coli and Acinetobacter spp., the following E. antimicrobials namely Amoxicillin, Ampicillin, Mecillinam. Ceftriaxone. Cefuroxime. Ceftadizime. Cefotaxime, Aztreonam, Imipenem, Ertapenem, Cefoperazone/Sulbactam, Gentamicin, Netilmicin, Levofloxacin, Nalidixic acid, Azithromycin, Polymyxin, Trimethoprim/Sulfamethoxazole, Nitrofurantoin were 100.0% resistant to at least one of the species.

Relevant paper [12] highlighted that, the following antibiotics were shown to have the highest overall patterns of resistance: Levofloxacin (68.24%), Amikacin (64.71%), Meropenem (49.41%), Ceftazidime (75.29%), Ciprofloxacin (78.82%) and Gentamicin (82.35%). Furthermore, findings from another study [14] by Dutta et al., done in selected areas of Dhaka, Bangladesh report that most of the Gram-negative bacilli were found resistant against Ciprofloxacin, Tetracycline and Cotrimoxazole. Furthermore, a review paper [15] which includes studies about AMR in Bangladesh from 2004 to 2018 suggests that, a high prevalence of resistance was detected in most tested pathogens, and many of the common first-line drugs were mostly ineffective. Resistance to carbapenems was low in most cases. The presence of extended-spectrum betalactamase (ESBL)-producing organisms was indicated by the high resistance to beta-lactams. A study [16] in

India illustrated that, most of the Klebsiella species and Acinetobacter species were resistant to beta lactam group of antibiotics such as cephalosporins and piperacillin-tazobactam.

The study reflects that, Tigecycline and Colistin are the only types of antibiotics which have implications to be used for ICU patients.

Our findings have important therapeutic implications for the management of patients in ICU. The high rate of multidrug resistance shown in this study raises serious concerns about the management of patients in intensive care units. To optimize drug distribution and enable a more customized treatment plan, a drug monitoring system also needs to be implemented. Nonetheless, the study's benefits and drawbacks should be considered when interpreting the findings. Furthermore, the lack of newer drugs means resistance must be contained before we run out of options to tackle it.

However, our study had certain limitations. The study is a one-center investigation with a small sample size. As such, the results may not be generalizable. Moreover, the disc diffusion method was utilized to determine the antibiotic sensitivity instead of the broth dilution approach, which leaves out information on the lowest inhibitory concentration of antibiotics. In addition, since the study was carried out at a tertiary hospital and the data only included ICU patients, the findings might not correctly reflect community-acquired illnesses in this region. The study's minute sample size prevented it from having the power to detect rare events or smaller effect sizes. It was unknown what specifically caused the infections and comorbidities. Furthermore, we did not thoroughly look into every aspect of our patients' care that might have resulted in the prescription of needless antibiotics.

## CONCLUSION

The prevalence of antibiotic resistance is high among the ICU patients and the majority of the isolated organisms are resistant to conventional antibiotics. Based on the findings, we recommend appropriate initiatives to monitor and control the use of antibiotics, as well as nationwide surveillance following standardized methodologies.

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