ORIGINAL RESEARCH   **INTENSIVE CARE**

Antimicrobial resistance patterns in patients admitted in a medical intensive care unit at Rawalpindi, Pakistan

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ABSTRACT

Background & objective: The prevalence of antibiotic resistance has increased with the excessive use of antibiotics in our country. We aimed to examine the patterns of antibiotic resistance in different organisms found in patients admitted to our Medical Intensive Care Unit (MICU). Additionally, the study sought to determine the relationship between the pathogen causing the infection and the outcome of the patients.

Methodology: This retrospective observational cross-sectional study was conducted in the MICU of Farooq Hospital affiliated with Akhtar Saeed Medical College, Rawalpindi, Pakistan, from January 01, 2024 to March 31, 2024. The data was collected from the medical records of adult patients (aged 12-79 y) who were admitted to the MICU during the study period. SPSS 29 was used for data analysis. Analyzed data included information on demographics, culture results, and antibiotic resistance patterns. We included culture results of blood, urine, and Foley catheter tip. The final disposal of the patients was noted and linked to the pathogen responsible for the disease.

Results: The study involved 104 patients admitted to the MICU. The average duration of stay was 5.36 days, the average age was 51.17 ± 18.47 y, and 61.53% of the patients were male. The primary diagnoses were urinary tract infection (18.22%) and sepsis (15.76%). Pre-existing conditions included diabetes mellitus (24.15%) and hypertension (23.59%). Klebsiella pneumoniae was the predominant organism, followed by E. coli. Overall, 58.52% of the isolates showed resistance to the tested antibiotics. Specific drugs, such as ceftazidime and amoxicillin-clavulanic acid, demonstrated absolute resistance (100%), while vancomycin and tigecycline showed no resistance. In this study, patients with infections caused by Enterobacter, Enterococcus faecalis, Proteus, and Salmonella spp. had discharge rates of 100%. In contrast, infections caused by Candida, Acinetobacter species, and Klebsiella pneumoniae were associated with 100%, 75%, and 48.5% mortality rates, respectively.

Conclusion: The study revealed a significant prevalence of antibiotic resistance among microorganisms in our Medical Intensive Care Unit. Klebsiella pneumoniae was the predominant organism, and distinct bacterial infections were linked to diverse patient outcomes.

Abbreviations: MDR - multidrug resistance; MICU - Medical Intensive Care Unit; MRSA - methylene resistant S. aureus XDR - extensively drug resistant

Keywords: Antibiotic, Resistance, Pakistan, Intensive Care Units.

1. INTRODUCTION

Antimicrobial resistance has become a global health challenge especially in third world countries. The main causes of antimicrobial resistance are the improper use or overuse of antibiotics, the lack of skilled public health workers and poor hygiene standards.[1] Resistance to antibiotics reduces the effectiveness of these treatments and has a negative impact on hospital systems especially in intensive care settings.[2,3]

Medical intensive care unit (MICU) is commonly known as a "hotbed of infections" in high-risk healthcare environments. ICU patients are especially prone to infections because of the various invasive procedures they undergo, including vascular access, mechanical ventilation, and intubation.[4] Patients admitted to ICUs are at a higher risk of contracting infections caused by the ESKAPE group of pathogens, which includes bacteria, such as Escherichia coli, Pseudomonas aeruginosa (P. aeruginosa), Acinetobacter baumanii, Klebsiella pneumoniae (K. pneumoniae), Staphylococcus aureus (S. aureus), and Enterococcus spp.[5] ICU patients have a rate of antibiotic resistance that is approximately seven times higher than that of general hospitals.[6] Study by Litwin et al. revealed that 20-30% of patients in the ICU developed nosocomial infections.[7] This indicates a high risk of microbial infections in patients admitted to ICUs.

 Microorganisms with multidrug resistance (MDR) cause an increase in morbidity and mortality among individuals. Superbugs such as Acinetobacter spp., Pseudomonas aeruginosa, Klebsiella spp., and S. aureus are associated with pneumonia and other nosocomial infections. Moreover, ICU patients often acquire multiple bacterial infections due to their prolonged hospital stays. These microbial populations, with their evolving sensitivity patterns and resistance, further complicate the treatment process.[8,9]

South Asia is now considered the primary area for antimicrobial resistance and it is predicted that 70% of antimicrobial resistant cases occur in the Asian regions, including Pakistan.[10-13] Over the last ten years, there has been a rise in the quinolone resistance in Enterobacter spp. in Pakistan. Study by Qamar et al. demonstrated 100% resistance to fluoroquinolones to the extensively drug resistant (XDR) Salmonella spp. in the 2016 outbreak.[14] A notable study by Javid et al. spanning 2011-2015 revealed high resistance rates among key

pathogens to essential antibiotics. For instance, over 90% of E. coli strains were resistant to amikacin, while similar resistance levels were observed in Salmonella enterica serovari Typhi to fluoroquinolones, and Acinetobacter spp. to imipenem.[15] Furthermore, a review by Saeed et al. spanning 2006–2018 showed high rates of resistance among hospital-based studies, particularly against third-generation cephalosporins, fluoroquinolones, and cotrimoxazole for both K. pneumoniae and E. coli.[16]

Overcrowding, poor sanitation, limited access to quality healthcare, and the misuse of antibiotics are common factors leading to antimicrobial resistance in third world countries. To ensure effective care of ICU infections, it is critical to know true prevalence of causative agents and their patterns of antibiotic susceptibility. This study is aimed at investigating the patterns of antimicrobial resistance in patients admitted medical ICUs of Farooq Teaching Hospital located in the rural area of Islamabad, Pakistan.

2. METHODOLOGY

This retrospective, observational study was conducted at the MICU in the affiliated hospital of Akhtar Saeed Medical & Dental College, Rawalpindi, Pakistan, from 1st January 2024 to 31st March 2024 after approval from the institutional ethical committee. The study population included all adult patients (aged 12-79 y) admitted to the MICU during the study period. Data were collected from the medical records of the patients. Data on patient demographics, culture results (blood, urine, Foley tip catheter) and antibiotic resistance patterns were extracted from the medical records. Data was analyzed and entered into a password-protected spreadsheet.

The following variables were collected: age, gender, clinical admission date, length of ICU stay: culture site (blood, urine, Foley tip catheter), organism/s identified, and antibiotic resistance profile. Data was analyzed using the Statistical Package for Social Sciences (SPSS) software 29. Descriptive statistics were used to summarize the data, including frequencies and percentages. Trends in organism prevalence and resistance patterns were analyzed over the study period.

3. RESULTS

The study included 104 patients admitted to the MICU. The average age was 51.17 ± 18.47 y; and 61.53% were

Table 1: Clinical profile and baseline characteristics of the study participant

Demographics	n (%)
Age (y) mean ± SD	51.17 ± 18.472
Male	64 (61.53)
Female	40 (38.46)
Discharged from the MICU	77 (74.03)
Duration of stay in days (average)	5.36 ± 2.3
Primary diagnosis at admission	
Urinary tract infection	37 (18.22)
Sepsis	32 (15.76)
Lower respiratory tract infection	25 (12.31)
Acute kidney injury	14 (6.89)
Acute gastroenteritis	14 (6.89)
Infected wound	14 (6.89)
Stroke	13 (6.40)
Comorbids at admission	
Diabetes mellitus	43 (24.15)
Hypertension	42 (23.59)
End-stage renal disease	37 (20.78)
Ischemic heart disease	15 (8.42)
Chronic kidney disease	13 (7.30)
Cerebrovascular accident	12 (6.74)
Chronic liver disease	5 (2.80)

males. The primary diagnoses were urinary tract infection (18.22%) and sepsis (15.76%). Pre-existing conditions included diabetes mellitus (24.15%) and hypertension (23.59%) (Table 1).

The findings revealed that the most prevalent organism in the patient samples was K. pneumoniae followed by E. coli (Figure 1).

Among the isolates, it was observed that 38.88% were sensitive, 2.59% were intermediate, while the majority of isolates (58.52%) showed resistance to the tested antibiotics.

All patients infected with Salmonella spp., Enterobacter, Proteus and Enterococcus faecalis were discharged from the hospital. Those infected with S. aureus, E. coli, methylene resistant S. aureus (MRSA), and P. aeruginosa had discharge rates ranging from 86% to 93%. On the other hand, patients infected with K. pneumoniae and Acinetobacter spp. had significantly lower discharge rates of 51.5% and 25% respectively.

The patients infected with Candida had the highest mortality rates, with a 100% fatality rate. This was followed by patients infected with Acinetobacter spp., with a 75% fatality rate, and K. pneumoniae with a 48.5% fatality rate. P. aeruginosa and MRSA infected patients had a 14% fatality rate. Patients infected with E. coli and S. aureus had the lowest mortality rates of 7.69% and 7% respectively (Table 2).
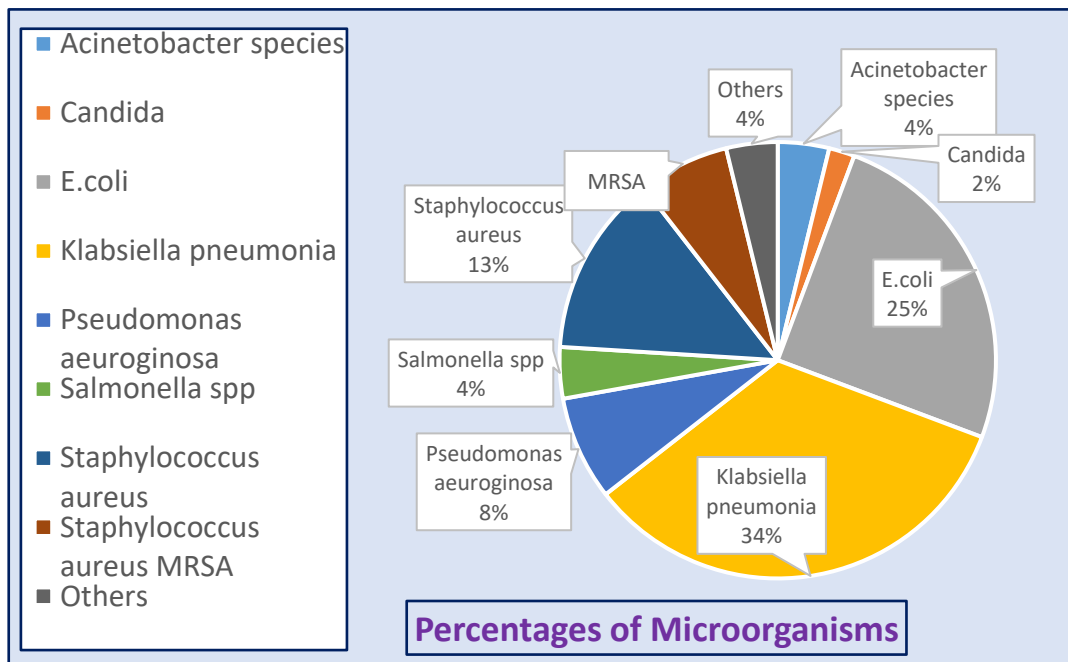

Figure 1: Diagrammatic depiction of the main prevalent microorganisms

Table 2: Pathogens associated with the fate of the patients (n = 104)

Predominantly isolated organism	n (%)
Discharged (77)	
Enterobacter	1 (100)
Enterococcus faecalis	2 (100)
Proteus	1 (100)
Salmonella spp.	4 (100)
S. aureus	13 (93)
E. coli	24 (92.30)
S. aureus, MRSA	6 (86)
P. aeruginosa	7 (86)
K. pneumoniae	18 (51.50)
Acinetobacter species	1 (25)
Expired (27)	
Candida	2 (100)
Acinetobacter species	3 (75)
K. pneumoniae	17 (48.50)
P. aeruginosa	1 (14)
S. aureus, MRSA	1 (14)
E. coli	2 (7.69)
S. aureus	1 (7)

Table 3: Patients resistant to antibiotics (n = 104)

Antibiotics tested	Total	Resistance observed
Amikacin	22	16 (72.72)
Amoxicillin/clavulanic acid	5	5 (100)
Ampicillin	3	1 (33.33)
Azithromycin	5	3 (60)
Aztreonam	4	3 (75)
Ceftazidime	31	31 (100)
Ceftriaxone	53	47 (88.67)
Chloramphenicol	19	9 (47.36)
Ciprofloxacin	90	70 (77.77)
Clindamycin	8	3 (37.5)
Colistin	28	2 (7.14)
Doxycycline	90	54 (60)
Ertapenem	24	20 (83.33)
Gentamycin	17	10 (58.82)
Imipenem	83	30 (36.14)
Linezolid	22	6 (27.27)
Meropenem	73	30 (41.09)
Methicillin	17	10 (58.82)
Moxifloxacin	5	5 (100)
Nitrofurantoin	42	19 (45.23)
Piperacillin/tazobactum	30	22 (73.33)
Teicoplanin	18	6 (33.33)
Tigecycline	6	0 (0)
Trimethoprim/ sulfamethoxazole	31	27 (87.09)
Vancomycin	7	0 (0)
Total	**733**	**429 (58.52)**

Data presented as n (%); Some patients received multiple antibiotics, either simultaneously or in sequence.

The organisms displayed a significant level of antibiotic resistance, with an overall resistance rate of 58.52% for all tested antibiotics. Notably, amoxicillin/clavulanic acid, ceftazidime, and moxifloxacin all had resistance rates of 100%. Ceftriaxone had a resistance rate of 88.6%, while ceftazidime, ciprofloxacin, cefepime, and levofloxacin had resistance rates of 80%, 77%, 75%, and 72% respectively. Out of the total samples tested, 93% showed antimicrobial resistance to at least one drug. The majority of these samples (87%) demonstrated resistance to two or more drugs (Table 3).

4. DISCUSSION

Drug resistance, especially antimicrobial resistance, has become a global issue that affects people worldwide, particularly those in impoverished countries. Our study also revealed high rates of microbial resistance in patients admitted to medical intensive care, similar to the study conducted by Tran et al. in ICU settings of a Vietnam hospital, which showed resistance of 80 percent to antibiotics. P. aeruginosa, Klebsiella species, Escherichia coli, Enterococcus, and S. aureus, a pattern similar to the current study.[17-21] It causes predominant infections identified in ICU patients in studies from several Asian nations. Regarding antibiotic resistance,

our study revealed a high level of antimicrobial resistance to ceftriaxone, ceftazidime, amikacin and ciprofloxacin in patients infected with Gram-negative organisms of E. coli, P. aeruginosa and klebsiella reaching up to 90 to 100 percent similar to results shown by other studies done in ICU settings of other Asian countries.[22,23] An increasing trend of resistance pattern to meropenem, piperacillin and tazobactam is also observed against E coli, P. aeruginosa reaching 40 to 70 percent, respectively. High level of antimicrobial resistance against P. aeruginosa.[22] Our study revealed high sensitivity of Colistin to these Multidrug resistance Gram-negative bacteria. Vancomycin has high sensitivity against Gram-positive streptococcus and staphylococcus, including MRSA.[23]

Although the occurrence of K. pneumoniae has decreased in the United States, it is still a concern. It remains prevalent in Asian countries, especially among patients with ventilator-associated pneumonia.[24,25] In our study, we identified K. pneumoniae as the deadliest organism, resulting in the death of 17 patients. This gram-negative pathogen belongs to the family Enterobacteriaceae and is widely recognized as one of the most prevalent and deadly nosocomial pathogens globally.[25]

Infection with multidrug-resistant (MDR) Gram-negative bacteria, such as Acinetobacter baumanii, is a leading cause of death among patients in the ICU. Our study also revealed high mortality (75%) with Acinetobacter species.[19]

5. LIMITATIONS

The retrospective nature of our study limits the ability to establish causal correlations between the components. Furthermore, the generalizability of the findings is constrained by the very small sample size obtained from a single medical center. The study is constrained for not considering the isolation of multiple microbes, and the use of multiple antibiotics in the same patient, either simultaneously or in sequence.

6. CONCLUSION

There is significantly high antibiotic resistance among microorganisms in the patients admitted to intensive care unit (ICU) in Rawalpindi, Pakistan. K. pneumoniae was the predominant organism, and distinct bacterial infections were linked to diverse patient outcomes. The highest resistance was found with amoxicillin/clavulanic acid, ceftazidime and moxifloxacin; and highest sensitivity was found to tigecycline and vancomycin.

7. Data availability

The numerical data generated during this research is available with the authors.

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9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

All authors contributed in the concept, data acquisition, data analysis, literature search and manuscript preparation. All authors approved the final draft of the paper.

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