

Prevalence and Clinical Outcome of Infections Caused By Multi-Drug-Resistant Organisms In A Critical Care Unit of A Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency and clinical outcomes of infections caused by multidrug resistant organism in a critical care unit.

Study design: Cross-sectional study/ Retrospective Observational study/ Retrospective Cross-sectional study.

Place and Duration of Study: Department of Microbiology, Pak Emirates Military Hospital, Army Medical College (NUMS) Rawalpindi, Pakistan from Mar to Apr 2024.

Methodology: Records of samples from Seven hundred and fifty six patients admitted to the critical care unit were analysed. The microbiology laboratory received and processed 605 paired blood, 498 endobronchial washings, and 50 cerebrospinal fluid specimens for culture and sensitivity. Standard microbiological procedures were followed for sample processing, and antimicrobial susceptibility testing was done following the Clinical and Laboratory Standards Institute guidelines 2023.

Results: Top of Form Out of 605 admitted patients whose samples were sent, 492(81.32%) were male and 113(18.67%) females with a mean stay of 5.6 ± 1.8 days. Among the total specimens analyzed, 365 showed growth, 226(37.35%) of paired blood cultures, 129(29.91%) of endobronchial washings, and 10(20.00%) of cerebrospinal fluid specimens showed bacterial growth. *Acinetobacter baumannii* was the predominant pathogen isolated, with 82(57.74%) were multidrug-resistant and 60(42.25%) were extensively drug-resistant. *Staphylococcus aureus* and *Enterococcus* spp. were the most isolated Gram-positive cocci in blood cultures. Mortality rates due to bacterial meningitis, ventilator-associated pneumonia, and bloodstream infections were observed 4(40.00%), 52(34.89%), and 72(31.85%) respectively.

Conclusion: Rising prevalence of multi drug resistant gram negative bacteria heighten the risk of nosocomial infections among patients of critical care unit.

Keywords: Critical Care Units, Clinical Outcome, Extensively Drug-Resistant, Multi-Drug Resistant Organisms, Pan-Drug-Resistant Organisms. Bottom of Form

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INTRODUCTION

Critical care units present a dual-edged impact within hospitals.¹ On one hand, they provide specialized care and advanced medical interventions, potentially improving the survival prospects of critically ill patients. Whereas on other hand these units can harbor and facilitate the spread of drug-resistant bacteria, also known as multidrug-resistant organisms (MDROs). The emergence of resistant bacteria in these environments poses a significant alarm, leading to life-threatening infections such as bloodstream infections, pneumonia, and meningitis.²

In recent years, bacteria have developed multiple drug resistance mechanisms, transforming initially susceptible bacterial population into multidrug-resistant organisms (MDROs), extensively drug-

resistant (XDR), and even pan resistant bacteria. Multidrug-resistant (MDR) pathogen is defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories.³ Extensively drug-resistant (XDR) is defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories. Pan-drug-resistant (PDR) is defined as non-susceptibility to all agents tested in the laboratory.⁴ This evolution has resulted in a limited arsenal of effective antibiotics to combat infections caused by these resistant bugs, contributing to poor clinical outcomes.⁵ Six nosocomial pathogens namely *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp. have become increasingly resistant to commonly prescribed antibiotics, resulting in a nightmare in critical care units for both clinicians and microbiologists.⁶ These pathogens thrive in the environments of critical care units, especially in lower

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middle-income countries where infection control practices are not widely implemented. As a result, the incidence of ICU-acquired infections is at least 2–3 times higher than in high-income countries.⁷ Top of FormBottom of Form

The World Health Organization (WHO) has recognized antimicrobial resistance (AMR) as one of the top 10 global public health threats facing humanity.⁸ In intensive care units (ICUs), factors such as over prescription of antibiotics and poor infection control practices can exacerbate the problem, potentially leading to widespread havoc.⁹

This study aimed to investigate the distribution and prevalence of multidrug-resistant pathogens isolated from blood, endobronchial washings and cerebrospinal fluid samples collected from critical care unit patients. Additionally, it seeks to evaluate the clinical outcomes of patients infected with these bacteria, shedding light on the impact of MDROs on patient care and healthcare systems.

METHODOLOGY

This study was conducted from March 2024 to April 2024. In our study frequency of multi-drug resistant organisms and clinical outcome of patients infected by these organisms after 48 hours of admission in critical care unit was obtained from January 2023 to December 2023. Sample size was calculated using formula for sample size calculation taking confidence level 95%, margin of error 5%, reported prevalence of MDR bacteria was 57.5%¹⁰. The estimated sample size came out to be 385 patients. A total of 756 patients were admitted in the critical care units. During this period 605 paired blood for culture and sensitivity, 498 endobronchial washings and 50 CSF specimens were received in microbiology laboratory, Pak Emirates Military Hospital Rawalpindi, Pakistan. Ethics Review certificate was obtained from ERC committee (ERC /ID/381 dated 13thMarch 2024).

Data was collected from hospital management system which is designed to save patient's demographic profile and laboratory parameters. Patient's clinical details were obtained from critical care unit records.

Inclusion Criteria: Records of paired blood samples, Endobronchial washing samples and Cerebro Spinal Fluid specimens were included, also those patients who had confirmed hospital acquired infections were included in the study.

Exclusion Criteria: Records of Patients who stayed less than 48 hours in the critical care units, incomplete sample details and duplicate specimens from the same patient were excluded from the study.

All the paired blood, endobronchial washings and CSF specimens were processed according to microbiological guidelines. The specimens were inoculated on 5% sheep blood agar, MacConkey and chocolate agar according to the requirements of the specimen. Culture plates were incubated in $35 \pm 2^\circ\text{C}$ in ambient air for 24 to 48 hours for bacterial growth otherwise reported negative. On the bases of Gram stain results and colony morphology catalase and coagulase tests were done on Gram positive cocci which were further identified by biochemical reactions on Analytical Profile Index (API) for Staphylococci and Streptococci. For Gram negative rods, oxidase test was done and exact identification was done by API20E for Enterobacterales and API20NE for non-Enterobacterales.

Antibiotic susceptibility testing was done using modified Kirby Bauer disc diffusion method on Mueller Hinton Agar (Oxoid UK) for all antimicrobials except for colistin for which agar dilution method was done. For Staphylococcus aureus vancomycin susceptibility was determined using vancomycin agar.¹¹ Results of antimicrobial susceptibility was interpreted according to CLSI 2023.

Statistical analysis was performed using Statistical Package for Social Sciences SPSS version 26. Mean and Standard Deviation was calculated for quantitative variable, frequency and percentages for qualitative variables. *p* value was calculated using chi-square test for association between outcome and clinical diagnosis.

RESULTS

A total of 756 patients were admitted in the critical care units in a year which included 492 (81.32%) male and 113 (18.67%) female with mean age of 42.20 years \pm 17.00. Mean length of stay in critical care unit was 5.60 ± 1.70 days.

The critical care unit submitted 605 paired blood samples, 498(82.31%) endobronchial washings, and 50(8.26%) cerebrospinal fluid (CSF) specimens for analysis. Of these, 528(87.27%) came from the medical critical care unit and 77(12.72%) from the surgical unit. 226(37.35%) paired blood cultures, 149(29.91%) endobronchial washings and 10(20.00%) CSF specimens had growth of pathogens.

As shown in figure 1. *Acinetobacter baumannii* was the most frequently isolated organism from the blood, endobronchial washing and CSF specimens. Among Gram positive cocci, *Staphylococcus aureus* and *Enterococcus spp* were most commonly isolated from blood cultures.

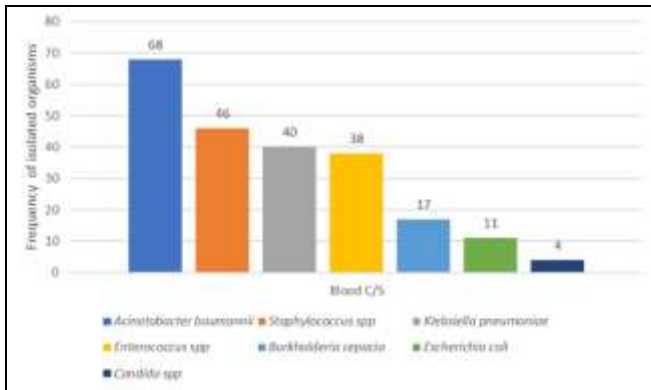


Figure-1: Frequency of isolated pathogens from blood cultures

Whereas in Figure 2 EB washing and CSF *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* respectively were the second most isolated organisms. *Candida spp* detected from blood, endobronchial washing and CSF specimens included *Candida glabrata*, *Candida krusei* and *Candida albicans*.

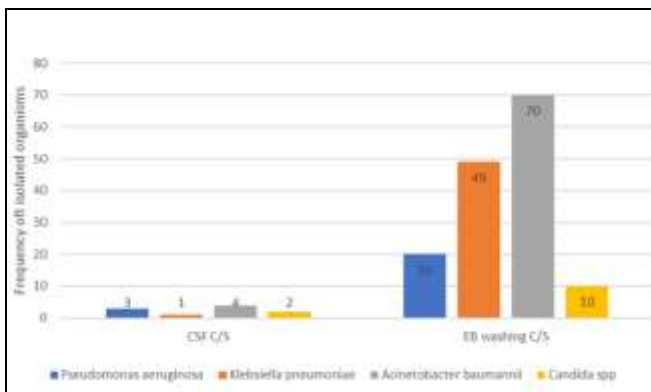


Figure-2: Frequency of pathogens isolated from cerebrospinal fluid (CSF) and endobronchial (EB) washing

Mortality of patients due to bacterial meningitis, ventilator associated pneumonia and blood stream infections were 4(40.00%), 52(34.89%) and 72(31.85%) respectively, as shown in Table II. Patients diagnosed with bacterial meningitis had history of neurological intervention before developing infection. Intrathecal along with intravenous antibiotic therapy was suggested for these patients.

As shown in Table-II, 82(57.75%) MDR and 60(42.25%) XDR *Acinetobacter baumannii* were isolated from blood, CSF and EB washings of patients admitted in the critical care unit. Extensively drug resistant *Acinetobacter baumannii* and *Klebsiella pneumoniae* were only sensitive to colistin and tigecycline.

For MDR *Pseudomonas aeruginosa*, treatment options included colistin, meropenem, piperacillin-tazobactam, and amikacin. Among Gram-positive cocci, *Enterococcus spp* exhibited high resistance, with six isolates of *Enterococcus faecium* being vancomycin-resistant (VRE). The remaining treatment choices for these patients were limited to linezolid and tigecycline.

Table-I: Clinical Diagnosis and Outcome of Patients in Critical Care Unit (n=385)

*Clinical diagnosis	*Treated	Treatment Failure	p value
Ventilator associated pneumonia (n=149)	75(50.33%)	52(34.89%)	< 0.001
Bacterial Meningitis (n=10)	6(60.00%)	4(40.00%)	< 0.001
Blood stream infections (n=226)	129(57.07%)	72(31.85%)	< 0.001

Table-II: Multidrug and Extensively Drug-Resistant Organisms Detected from Blood, EB Washing and Cerebro Spinal Fluid Specimens (n=333)

Gram negative rods	MDR	XDR
<i>Acinetobacter baumannii</i> (n=142)	82(57.74%)	60(42.25%)
<i>Klebsiella pneumoniae</i> (n=90)	50(55.55%)	29(32.22%)
<i>Pseudomonas aeruginosa</i> (n=23)	4(17.39%)	9(39.13%)
Gram positive cocci		
<i>Enterococcus spp</i> (n=32)	18(56.25%)	6(18.75%)
<i>Staphylococcus spp</i> (n=46)	21(45.65%)	9(19.56%)

MDR: Multidrug resistant, XDR: Extensively Drug Resistant

DISCUSSION

In our study multidrug resistant *Acinetobacter baumannii* was the most frequently isolated organism from blood, EB washing and CSF specimens. Out of which 82(57.75%) were MDR and 60(42.25%) were XDR followed by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Similar results were seen in another study from Egypt and India.^{12,13} EURO-BACT-2, a cohort study from Europe also showed that Gram negative bacteria are leading pathogens in critical care setting however in contrast to our study *Klebsiella pneumoniae* with 40(27.90 %) was most prevalent.¹⁴

Staphylococcus aureus and Coagulase-negative Staphylococci were most prevalent organism in critical

care units in United States.¹⁵ Data from 2017 from The European Centre for Disease Prevention and Control for ICU shows Gram positive pathogens are leading causing of hospital acquired infections i.e. 23.6% Coagulase-negative Staphylococci and 14.9% Enterococcus spp, followed by 12.4% Klebsiella pneumoniae.¹⁶ Non-adherence to infection control practices ,lack of antimicrobial stewardship polices , increased work load of critical care workers and limited availability of resources all contributed to increased prevalence of highly resistant Gram negative bacteria in our settings. This situation is concerning because it negatively affects patient outcomes, increases management costs, and exacerbates the broader issue of antimicrobial resistance (AMR).

Hospital-acquired infections (HAIs) in critical care unit are increasing as bacteria are becoming more resistant with increase in antibiotic resistance globally leading to significant morbidity and mortality. In our study the majority of patients had blood stream infections i.e. bacteremia followed by ventilator associated pneumonia and then by bacterial meningitis. Similar results were seen in studies conducted in Egypt, India and Pakistan due to similar demographic and socioeconomic status and infection control practices.^{12,17,18}

The results of our study are in contradiction with study conducted in Poland where VAP 54.1 % was leading diagnosis followed by blood stream infections in critical care settings.¹⁹ In our setting majority of deaths were due to bacterial meningitis. Mortality due to bacterial meningitis, ventilator associated pneumonia and blood stream infections were 40.00%, 34.89%and 31.85% respectively.

Infection management in critical care settings require a multifaceted approach as these infections not only have individual consequences but also have broader consequences in terms of prolong hospital stay and treatment cost and emergence of resistant pathogens. Prompt diagnosis and appropriate treatment should be started as soon as possible to avoid emergence of MDROS.

CONCLUSION

Multidrug resistant Acinetobacter baumannii was the most frequently isolated organism from blood specimens, EB washings and CSF specimens. The findings of this study show a heightened risk of nosocomial infections among patients admitted to critical care units due to the rising prevalence of Multi-Drug Resistant Gram-Negative Bacteria (MDR-GNBs). Particularly concerning are strains resistant to

Cephalosporin and Carbapenems, which can lead to increased morbidity and mortality as standard antibiotics prove ineffective, necessitating the use of Colistin. To address this issue, we advocate in adopting a comprehensive strategy, encompassing care bundles, ongoing education, surveillance, and performance feedback on infection control practices to mitigate the occurrence of hospital-acquired infections.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

WF & FH: Data acquisition, data analysis, critical review, approval of the final version to be published.

JU & RI: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AN & QF: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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