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Multidrug-Resistant Organisms and Their Association with Risk Factors; A Study at the Intensive Care Unit of Tertiary Care Hospital, Peshawar

Mariam Sarwar, Fuad Ahmad Siddiqi, Salman Riaz*, Ammad Hasan Chaudhry, Muhammad Hassan, Ashfaq Hussain*****

Combined Military Hospital/National University of Medical Sciences (NUMS) Peshawar Pakistan, *RHQ Hospital, Gilgit Pakistan, **Banazir Bhutto Hospital, Rawalpindi Pakistan, ***Combined Military Hospital/National University of Medical Sciences (NUMS) Mardan Pakistan

ABSTRACT

Objective: To investigate rates of multidrug-resistant organisms (MDRO) infection, their antimicrobial resistance (AMR) patterns, and risk factors for acquisition of such infections at a Tertiary-Care Hospital ICU.

Study Design: Cross sectional study.

Place and Duration of Study: Adult Intensive Care Unit of Tertiary Care Hospital, Peshawar Pakistan, from Jan to Dec 2022.

Methodology: All patients admitted to adult ICU who developed signs/symptoms of infection after 48 hours of admission were investigated. Microbiological diagnosis was done via standard microbiological practices, and if the patient had acquired an MDRO infection, it was included in the study.

Results: During the study, 92 patients acquired MDRO infection in total. The most common source was blood (43.5%). The most common organisms isolated were *Klebsiella pneumoniae* (21.7%), *Acinetobacter baumannii* (20.7%) and *Pseudomonas aeruginosa* (17.4%). The highest percentage of resistance among Gram-positive organisms was exhibited to Penicillin and Co-amoxiclav (91%). Gram-negative isolates exhibited high overall resistance to all used antibiotic classes. The least frequency of resistance was recorded for Tigecycline (1%) against *Klebsiella pneumoniae* and 33% against *Escherichia coli*, while 32% *Acinetobacter baumannii* and 25% *Pseudomonas aeruginosa* were Colistin/Polymyxin resistant; none of the *Klebsiella pneumoniae* showed Colistin resistance.

Conclusion: Antimicrobial resistance in our setup was high among Gram-negative and Gram-positive organisms. The most common risk factor was central line placement among the patients, highlighting the importance of infection control measures and the need to implement infection control bundles to circumvent infections due to invasive devices.

Keywords: Multidrug-resistant organisms (MDRO), Antimicrobial resistance (AMR), Intensive care unit

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INTRODUCTION

Antimicrobial resistance (AMR) is rapidly becoming one of the major healthcare problems globally. It is a vital public health problem worldwide, killing at least 1.27 million people globally and linked with approximately 5 million deaths in 2019.[1] Factors accelerating the rate of AMR include misuse and overuse of antibiotics, irrational use of antimicrobial agents in clinical practice and the agricultural sector, and antibiotic resistance genes, which are a natural component of all environments, help spread the problem.[2,3]

Healthcare-associated infections (HAIs) are increasing at an alarming rate, and according to the World Health Organization, HAIs are the most common adverse event in hospitalized patients, especially due to multidrug-resistant organisms (MDROs).[4,5] MDROs are described as organisms resistant to one or more agents in at least three groups of antimicrobials.[6]

Infection with these MDROs is especially compounded in intensive care units that harbour patients who are in critical condition and usually are relatively immunocompromised.[7] Patients in ICU have multiple risk factors for acquiring infections, such as invasive procedures/devices, lengthy hospital stays, excessive antibiotics usage, and preexisting severe illnesses.[8,9] Acquisition of MDRO infection carries a substantial increase in mortality and morbidity, especially in ICU patients.[10]

There is a need for surveillance of MDRO infection in ICUs and their association with a risk factor to tailor antimicrobial therapy in patients better to help prevent the spread of AMR and for better clinical outcomes. Our study aims to investigate the rates of MDRO infection in the ICU of a tertiary care hospital over one 1-year and assess the aetiology, prevalence, most common organisms isolated and their antimicrobial resistance patterns, and risk factors for acquiring such an infection.

Correspondence: Dr Mariam Sarwar, Department of Microbiology, Combined Military Hospital, Peshawar Pakistan
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METHODOLOGY

The study was conducted at the adult ICU of a Tertiary Care Hospital, Peshawar, from January to December 2022. We investigated all patients undergoing treatment in the ICU who developed signs and symptoms of infection 48 hours after admission to the ICU. Permission was taken from the Ethical Review Committee. All the patient identification and culture results data included in this study remain confidential.

Inclusion Criteria: All patients admitted to the adult ICU acquiring an MDRO infection after 48 hours of stay in the ICU were included.

Exclusion Criteria: Any patient acquiring an MDRO infection before 48 hours of admission in the ICU was excluded. Repeat isolates from the same patient were also excluded.

During the study, only 92 cases of MDRO infection from the ICU were reported and included using consecutive convenience sampling. Any patient admitted to the ICU who developed signs and symptoms of infection 48 hours after admission in the ICU and then had an infection with an MDRO was included in the study. All relevant information about the patient, including name, age, gender, disease process, brief history, date of admission, and duration of stay, along with the type of culture, the identification of the organism and its susceptibility profile, and risk factors for acquiring the infection were recorded on a predesigned proforma.

The study included various clinical samples including blood, tissue, pus, pus swab, urine, body fluids, and respiratory specimens. All the samples were processed using standard microbiological processes and were inoculated on Blood, MacConkey, Chocolate, and CLED agars accordingly. The samples were incubated for 24-48 hours at 37 C. The identification of the isolate was performed as per the standard operating procedures of our laboratory. The isolated microorganisms were identified according to the colony morphology, Gram staining, and standard biochemical tests. The Gram-positive bacteria were identified by looking at the hemolytic activity on blood agar, and further identification was made using different biochemical tests like catalase reaction, coagulase tests (slide and tube method), and bile esculin hydrolysis. For Gram-negative bacteria, identification was conducted by using API 10S (BioMerieux, France). Antimicrobial susceptibility testing (AST) was performed using a modified Kirby-Bauer disc diffusion method and interpreted according to Clinical & Laboratory Standards Institute (CLSI) guidelines 2022.[10] Colistin susceptibility was tested using the latest CLSI guidelines for the respective isolate. The results of the organism isolated and its antibiotic profile were then noted on the pre-designed proforma.

Statistical Package for Social Sciences version 24.0 was used for the data analysis. Quantitative variables were expressed as Mean ± SD and qualitative variables were expressed as frequency and percentages.

RESULTS

Ninety-two patients acquired MDRO infection in our study period. There was a preponderance of male patients in our study. The mean length of ICU stay was 25 days ± 36.26, ranging from 4-180 days. The most common risk factor was the central line placement, with 58(63%) among the patients, as shown in Table-I. The most common source of the specimen was blood 40(43.5%), followed by tissue 29(31.5%) and then urine 7(7.6%).

Table-I: Clinico-demographic data of patients with Multidrug-Resistant Organisms (MDRO) (n=92).

Variables	n(%)
Gender, n (%)	Male 83 (90%) Female 9 (10%)
Age	33.5 ± 13.17 years
Duration of stay in ICU (days)	25.2 ± 36.26
Systemic illness, n (%)	22 (23.9%)
Immunocompromised	22 (23.9%)
On mechanical ventilation	21 (22.8%)
Central line placement	58 (63%)

Of the 92 isolates identified, 79 were Gram-negative (GNB), accounting for 86% of the pathogens. Among the GNB, the most common organisms isolated were *Klebsiella pneumoniae* 20(21.7%), *Acinetobacter baumannii* 19(20.7%), and *Pseudomonas aeruginosa* 16(17.4%), as depicted in Table-II.

Table-II: Distribution of Organisms Isolated.

Organisms Identified	No. of Organisms	Percentage of all Isolates
Klebsiella pneumoniae	20	21.7
Acinetobacter baumannii	19	20.7
Pseudomonas aeruginosa	16	17.4
Staphylococcus aureus	11	12.0
Escherichia coli	9	9.8
Salmonella typhi	6	6.5
Enterobacter cloacae	5	5.4
Burkhulderia cepaciae	3	3.3
Citrobacter spp	1	1.1
Enterococcus spp	1	1.1
Proteus mirabilis	1	1.1
Total	92	100.0

Among the GNB, all the organisms revealed very high resistance rates to the most commonly used and tested antimicrobials, ranging from 41-100% for almost all antimicrobials tested except *Tigecycline* and *Polymyxin B*. *Acinetobacter baumannii* showed the highest resistance rate to Tigecycline, i.e. 47% and 32% to *Polymyxin B*. The most commonly isolated GPB *Staphylococcus aureus* showed lower resistance rates, with none of the isolates resistant to Vancomycin or Linezolid and only 18% resistance to Doxycycline, as shown in Table-III.

Table-III: Main Pathogen Resistance Rates to Commonly Tested Antimicrobials.

	K. pneumoniae	*A. baumannii*	*P. Aeruginosa*	*E. coli*	*S. aureus*
Penicillin	NT	NT	NT	NT	91
Co-amoxiclav	91	NT	NT	89	91
Ceftriaxone/ Ceftazidime	100	95	81 (Ceftazidime)	89	NT
Piperacillin-tazobactam	88	67	80	56	NT
Ciprofloxacin	100	83	63	100	78
Gentamicin	78	50	88	75	75
Amikacin	80	75	64	63	NT
Doxycycline	80	41	NT	50	18
Cotrimoxazole	89	82	NT	75	82
Meropenem	95	89	63	67	NT
Tigecycline	1	47	NT	33	NT
Polymyxin B	0	32	25	0	NT
Vancomycin	NT	NT	NT	NT	0
Linezolid	NT	NT	NT	NT	0

NT: Not tested, K. pneumoniae: Klebsiella pneumoniae, A. baumannii: Acinetobacter baumannii, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli, S. aureus: Staphylococcus aureus

DISCUSSION

Patients in ICU are often in critical condition, have multi-organ failure, and may even have relative immunosuppression. These patients have an increased likelihood of acquiring infection as the physiological barriers have been breached due to multiple invasive devices like central lines, mechanical ventilation, and urinary catheterization.[11] They are usually on broad-spectrum antibiotics, which add to the problem of developing an MDRO infection.[12]

This study aimed to predict the acquisition of MDRO infection in an ICU setting and identify their major risk factors. Our study revealed that the major risk factor for the acquisition of MDRO infection was placement of a central line observed in 58(63%) of the patients which is comparable to what is reported in a study conducted in Serbia revealing invasive procedures to be the most significant risk factor in ICU patients for contracting an HAI.[13] The lack of employment of proper infection control guidelines and implementation of central line-associated bloodstream infection (CLABSI) prevention practices augments this problem. Implementing CLABSI bundles (prevention practices) has decreased CLABSI events significantly.[14]

In our study, the most common cause of infection in the ICU was septicemia/bacteremia, which is similar to the findings reported in a study conducted at an ICU of a tertiary care hospital in Pakistan.[15] In this study, Gram-negative bacteria 86% (n=79) were the most prevalent pathogens compared to Gram-positive isolates 13 (14%); these are comparable with results found in NICU in Cairo.[16] The most commonly isolated organisms in our study were *Klebsiella pneumoniae* and *Acinetobacter baumannii*, comparable to a study conducted in an ICU in Rawalpindi, Pakistan.[17] In comparison, 32% of *Acinetobacter baumannii* and 25% of *Pseudomonas aeruginosa* were resistant to *Colistin/ Polymyxin* B in our study.[18] The high resistance rate to Colistin/Polymyxin B is an alarming situation as it is considered a drug of last resort.[19]

The study highlights the importance of AMR and the high resistance rates of antimicrobials in a developing country like Pakistan, which is already resource-limited. The alarming rate of MDRO infections, especially in the ICU setup, necessitates the requirement of a robust infection prevention and control program in each ICU to prevent the spread of infection and MDROs. Infection control bundles will also help decrease the incidence of infection in patients, especially those with invasive devices, which is usually required in ICU patients.

CONCLUSION

This study highlights the challenges faced in addressing MDROs in an ICU setup in our country, where HAIs caused by MDR Gram-negative bacteria

are quite common and have a strong impact on patients and outcomes. With the findings of our study, we hope to draw physicians' and policymakers' consideration of the alarming problem of antibiotic resistance and issue a call to action on managing MDROs.

Conflict of Interest: None.

Authors Contribution

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

MS & FAS: Study design, drafting the manuscript, approval of the final version to be published.

SR & AHC: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MH & AH: 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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