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Prevalence of Multidrug-Resistant Pathogens among Adult and Paediatric Patients in the Intensive Care Unit in a Tertiary Care Hospital

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Abstract: Multidrug resistance pathogens especially in intensive care hospital settings have emerged as a growing concern in current healthcare scenario. Current study highlights the concerning prevalence of multidrug-resistant (MDR) pathogens in adult and pediatric intensive care units (ICUs) at a tertiary care hospital. The dominance of Gram-negative bacterial infections, coupled with alarmingly high antibiotic resistance rates, underscores the urgent need for effective infection control measures. Implementing local antibiograms, regular surveillance of nosocomial infection rates, and stringent cleaning protocols are crucial steps in combating infections caused by MDR organisms. Tailored infection control strategies are essential for improving patient outcomes and enhancing the quality of care in ICUs facing the growing threat of multidrug resistance.

Keywords: Multidrug resistance, Pathogens, Antibiotic resistance, Nosocomial infections, Control strategies

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Introduction

The prevalence of multidrug-resistant (MDR) pathogens in intensive care units (ICUs) has emerged as a critical concern in modern healthcare. ICUs, which cater to the most critically ill patients, often witness the highest incidence of infections due to the compromised immune status of the patients, invasive procedures, and the frequent use of broad-spectrum antibiotics (Lambert *et al*., 2011; Bereket *et al*., 2012). The proliferation of MDR pathogens poses significant challenges to effective treatment, leading to prolonged hospital stays, increased healthcare costs, and heightened mortality rates.

Nosocomial infections are predominantly caused by a group of pathogens known as ESKAPE pathogens, so named because of their ability to "escape" the biocidal effects of antibiotics. The ESKAPE acronym stands for *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species. These six pathogens are responsible for a significant portion of hospital-acquired infections (WHO, 2002; Santajit and Indrawattana, 2016; Mulani *et al*., 2019). Data from the European Centre for Disease Prevention and Control indicate that 8% of patients who remain in the ICU for more than two days develop at least one ICU-related nosocomial infection. This issue is even more pronounced in developing countries, where the incidence and impact of nosocomial infections are considerably higher (Rice, 2008; De Oliveira *et al*., 2020).

MDR pathogens are characterized by their resistance to multiple classes of antibiotics, making infections caused by these organisms difficult to treat. This resistance often results from the overuse or misuse of antibiotics, which exerts selective pressure on bacterial populations, thereby favouring the survival and proliferation of resistant strains (Blot *et al*., 2007; Carlett *et al*., 2007). In tertiary care hospitals, where advanced medical care is provided, the incidence of MDR infections in ICUs is particularly concerning due to the high-risk nature of the patient population.

Both adult and paediatric patients in ICUs are vulnerable to infections by MDR pathogens, though the epidemiology, risk factors, and outcomes may differ between these groups. Paediatric patients, with their developing immune systems and different physiological responses, may exhibit distinct patterns of infection compared to adults. Understanding the prevalence and characteristics of MDR pathogens in both adult and paediatric ICU populations is essential for developing targeted infection control strategies and optimizing antimicrobial stewardship programs.

This study aims to investigate the prevalence of MDR pathogens among adult and paediatric patients in the ICU of a tertiary care hospital. By identifying the most common MDR organisms and their antibiotic resistance profiles, the study seeks to inform clinical practices and policies to mitigate the impact of these formidable pathogens. Ultimately, the findings of this research will contribute to improving patient outcomes and enhancing the quality of care in ICUs facing the growing threat of multidrug resistance.

Materials and Methods

Study Design and Sample Collection

In this study, we examined 100 non-duplicate positive samples, including blood, respiratory samples and urine, collected from ICUs at our facility. Depending on the infection sites, each patient provided one to three different samples. All samples met the criteria for nosocomial infections, characterized by the onset of infection symptoms at least 48 h after ICU admission, with no signs of infection present at the time of admission. Comprehensive data, including demographic information, antibiotic therapy history, and the duration of ICU stay, were meticulously recorded for all patients (Patricia, 2021).

Microbiological Cultures

Clinical samples collected for microbiological cultures included blood, urine, and respiratory samples. These cultures were processed following standard microbiological procedures. Blood cultures were conducted using the automated blood culture system. Bacterial identification was performed through automated Vitek 2 Compact system.

Identification and Antibiotic Resistance Analysis

The isolated bacterial strains were identified, and their antibiotic resistance patterns were analyzed using the Vitek 2 Compact system. For the identification of fermentative and non-fermentative Gram-negative bacilli, the VITEK 2 GN card was utilized, while the VITEK 2 GP card used for Gram-positive bacteria identification. Antimicrobial susceptibility testing was conducted in accordance with the guidelines established by the Clinical Laboratory Standards Institute (CLSI) (Kouchak and Askarian, 2012; CLSI, 2020).

Definitions and Analysis of Multidrug-Resistant Pathogens

Multidrug-resistant (MDR) pathogens are defined as organisms that have acquired resistance to at least one antibiotic in three or more antimicrobial categories. Extensively drug-resistant (XDR) pathogens show resistance to all but two or fewer antimicrobial categories. Pan-drug-resistant (PDR) pathogens are resistant to all antimicrobial agents tested in the hospital.

In this study, we analyzed the prevalence of MDR strains among clinical isolates from the ICU. The criteria for MDR included resistance to at least three different classes of antibiotics, namely aminoglycosides, cephalosporins, carbapenems, tetracyclines, and fluoroquinolones. The analysis also included the identification of various microorganisms and their antibiotic susceptibility profiles. Coagulase-negative staphylococci (CoNS) were included, with the recognition that a high presence of these organisms might indicate sample contamination. In such cases, it was necessary to repeat the sampling and correlate treatment with the clinical situation and results from other laboratory tests.

Statistical Analysis

Data entry and analysis were performed using Microsoft Excel. Continuous variables, such as age, are presented as mean ± standard deviation. The distribution of microorganisms was analyzed and expressed in percentages. For categorical data, the χ^2 test was used, with a p-value of less than 0.05 considered indicative of a statistically significant difference.

Results

A total of 300 samples were collected from various patients during the study period. Of these, 100 samples (33.33%) exhibited bacterial growth. The culture positivity rates were 70% for adult patients and 30% for paediatric patients. The most frequently isolated organisms were Gram-negative Enterobacteriaceae and non-fermenters, followed by Gram-positive cocci.

The highest culture positivity was observed in blood samples (47%), followed by lower respiratory tract samples (33%), and urine samples (20%). Upon analyzing the culture-positive data, we observed that in the adult ICU, culture positivity was higher in samples from female patients (55%) compared to males (45%). Conversely, in the paediatric ICU, male patients exhibited a higher culture positivity rate (57%) compared to female patients (43%).

In the adult population, *Staphylococcus aureus* was the most commonly isolated bacterium causing bacteremia (19%), followed by *Acinetobacter spp.*, *Enterococcus spp.*, *Klebsiella pneumoniae*, and other non-fermenters with prevalence rates of 15%, 13%, 12%, and 10%, respectively. Conversely, in paediatric ICUs, *Escherichia coli* was the predominant cause of bacteremia (26%), followed by *Acinetobacter*, *Klebsiella*, other non-fermenters, and *Staphylococcus aureus*, with prevalence rates of 16%, 13%, 10%, and 5%, respectively (Table 1).

Among both adult and paediatric patients, the leading pathogens causing respiratory tract infections are non-fermentative bacteria, with prevalence rates of 31% and 27%, respectively. In adults, these are followed by *Klebsiella spp*. (27%), *Acinetobacter spp*. (18%), and *Pseudomonas spp.* (13%). Conversely, in paediatric patients, the sequence is *Acinetobacter spp.* (25%), *Pseudomonas spp.* (20%), and *Klebsiella spp.* (13%).

In contrast to the paediatric intensive care unit, isolates obtained from urine in the adult intensive care unit displayed a predominance of Gram-positive bacteria. The most common isolate from urinary tract infections in paediatric patients was *Escherichia coli* (45%), followed by *Klebsiella spp*. (21%) and *Enterococcus spp.* (18%). Similarly,

Table 1: Showing the most common pathogens causing bacteraemia, respiratory tract infections, and urinary tract infections in both adult and pediatric ICUs, along with their respective prevalence rates

Infection Type	Population	Most Common Pathogen	Prevalence (%)
Bacteremia	Adult ICU	*Staphylococcus aureus*	19
		Acinetobacter spp.	15
		Enterococcus spp.	13
		Klebsiella pneumoniae	12
		Other non-fermenters	10
	Pediatric ICU	*Escherichia coli spp.*	26
		Acinetobacter	16
		Klebsiella	13
		Other non-fermenters	10
		Staphylococcus aureus	5
Respiratory Tract Infection	Adult ICU	Non-fermentative bacteria	31
		Klebsiella spp.	27
		Acinetobacter spp.	18
		Pseudomonas spp.	13
	Pediatric ICU	Non-fermentative bacteria	27
		Acinetobacter spp.	25
		Pseudomonas spp.	20
		Klebsiella spp.	13
Urinary Tract Infection	Adult ICU	*Escherichia coli*	48
		Klebsiella spp.	22
		Enterococcus spp.	18
	Pediatric ICU	*Escherichia coli*	45
		Klebsiella spp.	21
		Enterococcus spp.	18

in adults, the predominant pathogen was *Escherichia coli* (48%), *Klebsiella spp.* (22%) and *Enterococcus spp.* (18%).

Gram-negative bacterial isolates exhibited high levels of antibiotic resistance against various antibiotic classes. In adult patients, *Escherichia coli* showed resistance to aminoglycosides (74%), second-generation cephalosporins (93%), beta-lactams (97%), fluoroquinolones (96%), carbapenems (70%), and cotrimoxazole (87%). Paediatric ICU *Escherichia coli* isolates exhibited resistance to second-generation cephalosporins (95%), beta-lactams (69%), fluoroquinolones (84%), and cotrimoxazole (75%).

Klebsiella spp. isolated from adult patients showed resistance to aminoglycosides (71%), second-generation cephalosporins (100%), beta-lactams (95%), fluoroquinolones (90%), carbapenems (86%), and cotrimoxazole (81%). *Proteus spp.* from adult patients were resistant to cephalosporins (100%), while those from paediatric patients showed resistance to aminoglycosides (100%), second-generation cephalosporins (100%), beta-lactams (100%), and

Table 2: Resistance rates of different Gram-negative bacteria in both adult and paediatric ICUs against various antibiotic classes

Bacteria	ICU Type	Aminoglycosides (%)	2nd Gen. Cephalosporins (%)	Beta-lactams (%)	Fluoroquinolones (%)	Carbapenems (%)	Cotrimoxazole (%)
Escherichia coli	Adult ICU	74	93	97	96	70	87
Escherichia coli	Pediatric ICU	-	95	69	84	-	75
Klebsiella spp.	Adult ICU	71	100	95	90	86	81
Proteus spp.	Adult ICU	-	-	100	-	-	-
Proteus spp.	Pediatric ICU	100	100	100	100	100	-
Enterobacter spp.	Pediatric ICU	-	98	-	-	-	-
Acinetobacter baumannii	Adult ICU	-	-	-	-	-	-
Acinetobacter baumannii	Pediatric ICU	-	-	-	-	-	-
Pseudomonas spp.	Adult ICU	-	-	75	73	87	-
Other non-fermenters	Adult ICU	-	-	-	-	-	-
Other non-fermenters	Pediatric ICU	-	-	-	-	-	-

carbapenems (100%).

Enterobacter spp. isolated from paediatric ICUs exhibited full resistance against second-generation cephalosporins (98%) only. *Acinetobacter baumannii* isolated from both adult and paediatric patients displayed high resistance to all antibiotic classes.

Pseudomonas spp. isolated from adult patients were resistant to third-generation cephalosporins (100%), fourth-generation cephalosporins (76%), beta-lactams (75%), fluoroquinolones (73%), and carbapenems (87%). Other non-fermenters from both adult and paediatric patients showed high resistance to all antibiotic classes (Table 2).

Regarding Gram-positive bacteria, *Enterococcus spp.* isolated from adult and paediatric ICUs exhibited resistance rates of 95% and 91% against ampicillin, and 96% and 72% against fluoroquinolones, respectively. Methicillin-resistant *Staphylococcus aureus* (MRSA) strains from adult patients showed 53% resistance against cotrimoxazole and 62% resistance against fluoroquinolones. MRSA strains from paediatric patients showed 55% resistance against fluoroquinolones.

Discussion

Infections caused by multidrug-resistant organisms present a significant global challenge, posing life-threatening risks to critically ill patients and contributing to increased healthcare expenses. It is imperative to prioritize prevention strategies for these infections within the ICU setting. This necessitates a comprehensive understanding of local infection rates and the bacteriological profile specific to the region, including patterns of antibiotic resistance.

This study offers insights into antibiotic resistance within the adult and paediatric ICUs of a tertiary care hospital located in Haryana, India. Through our analysis, we have examined a range of pathogens and antibiotic regimens, enabling a thorough documentation of antibiotic resistance patterns among ICU patients.

Out of 100 various positive samples collected from adult and paediatric patients. Gram-negative bacterial infections prevailed among adult and paediatric patients, with non-fermentative Gram-negative rods being the most frequent. Consistent with prior research, more than half of the nosocomial infections in the hospital ICU were attributed to Gram-negative bacteria, aligning with the present study findings. The substantial presence of Gram-negative bacteria within hospital settings may contribute significantly to the recurrent occurrence of ICU infections worldwide (Vincet *et al*., 2012; Richards *et al*., 2000). Biofilm formation triggered by wet environments and waste materials disposed of in hospital sinks or drains can harbor multidrug-resistant (MDR) bacteria, contributing to nosocomial infections (Chia *et al*., 2020). The incidence of these infections varies based on hospital settings and surveillance methods used. A large-scale multicentric study revealed that 18.9% of patients acquired at least one ICU infection, with frequencies ranging from 2.3% to 49.2% across different centers (Gastmeier, 2002). Previous studies have reported prevalence rates between 9% and 37%, influenced by the specific patient population studied (Rebolo *et al*., 1996; Papia *et al*., 1999; Alberti *et al*., 2002). An international study involving 1265 ICUs across 76 countries found that 51% of patients had nosocomial infections, though rates varied significantly by country (Vincet *et al*., 2009). Patients within a single hospital may face multiple infection risks, influenced by factors such as illness severity (Richards *et al*., 2000).

In the adult population, bacteremia was predominantly caused by *Staphylococcus aureus*, with a prevalence of 19%, followed by *Acinetobacter spp*., *Enterococcus spp*., *Klebsiella pneumoniae*, and other non-fermenters, with prevalence rates of 15%, 13%, 12%, and 10%, respectively. Conversely, in paediatric ICUs, *Escherichia coli* emerged as the primary causative agent of bacteremia, with a prevalence of 26%. Following *Escherichia coli* were *Acinetobacter*, *Klebsiella*, other non-fermenters, and

Staphylococcus aureus, with prevalence rates of 16%, 13%, 10%, and 5%, respectively. A recent study by Negm *et al*. (2021) conducted in Zagazig University Hospitals, Egypt, highlighted that bacteremia was the most prevalent infection among ICU patients, affecting 32% of individuals. In both adult and pediatric patients, respiratory tract infections are primarily caused by non-fermentative bacteria, with prevalence rates of 31% and 27%, respectively. In adults, *Klebsiella spp*. (27%), *Acinetobacter spp*. (18%), and *Pseudomonas spp*. (13%) follow as the leading pathogens. Conversely, in pediatric patients, *Acinetobacter spp*. (25%), *Pseudomonas spp*. (20%), and *Klebsiella spp*. (13%) are the predominant causative agents.

Previous research by Hazra *et al*. (2015) identified pneumonia as the most frequently encountered infection (62.07%) in the intensive care unit. Shao *et al.* (2016) reported that respiratory tract infections comprised 64.75% of total nosocomial infections at the First Affiliated Hospital in Zhejiang Province, China. Variation in the frequency of nosocomial infections across different studies and hospital settings has also been noted by the United States National Nosocomial Infections Surveillance System (De Oliviera *et al*., 2020).

A significant finding of this study was the alarming level of antibiotic resistance observed among key pathogens. Notably, the majority of bacterial isolates displayed exceptionally high resistance across various classes of antibiotics This poses a serious public health concern, as these antibiotics are crucial for treating nosocomial infections. Antibiotic-resistant ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter species*) pose a global threat to both human health and healthcare systems. The acquisition of antibiotic resistance genes by ESKAPE pathogens has significantly limited treatment options for severe nosocomial infections, leading to increased disease burden and mortality rates due to treatment failure in hospitals (De Oliviera *et al*., 2020).

Tran *et al*. (2017) recently investigated antibiotic resistance patterns in ICU patients admitted to a tertiary hospital in Vietnam, focusing on Ventilator-associated pneumonia (VAP). Their findings revealed resistance of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* to ceftazidime, ceftriaxone, piperacillin, imipenem, meropenem, ertapenem, ciprofloxacin, and levofloxacin. Additionally, they observed high rates (>70%) of ceftriaxone and ceftazidime resistance among *Klebsiella spp*.

Recently, Yadav *et al*. (2020) reported the emergence of multidrug-resistant non-fermentative Gram-negative bacterial infections among hospitalized patients in a tertiary care center in Nepal. These MDR bacteria can spread easily to different patient groups within ICUs, either originating from contaminated surfaces or transmitted via contaminated hands or equipment used in the hospital. Cross-infections resulting from bacterial transmission can contribute significantly to the escalation of nosocomial infections during prolonged hospital stays. The increase in MDR bacterial strains within ICUs in hospital settings may be attributed to inappropriate antibiotic usage, inadequate maintenance of hygiene, insufficient cleanliness of the hospital environment, and the development of newer antibiotic-resistant mechanisms by opportunistic pathogenic bacteria (Uc-Cachon *et al*., 2019). Therefore, establishing local antibiograms, conducting regular surveillance of nosocomial infection rates, and implementing thorough cleaning protocols for the ICU environment are essential strategies for combating infections caused by multidrug-resistant organisms.

The present study was conducted at a single tertiary care hospital, limiting the generalizability of our findings to other healthcare settings. Additionally, the sample size was relatively small, which may affect the robustness of our conclusions. Furthermore, our study focused primarily on bacterial infections and did not address other potential sources of nosocomial infections, such as fungal or viral pathogens. Finally, our study did not assess the impact of specific interventions or infection control measures on the prevalence of MDR pathogens in ICUs, which warrants further investigation in future studies.

Conclusion

Our study highlights the concerning prevalence of multidrug-resistant (MDR) pathogens in adult and paediatric intensive care units (ICUs) at a tertiary care hospital. The dominance of Gram-negative bacterial infections, coupled with alarmingly high antibiotic resistance rates, underscores the urgent need for effective infection control measures. Implementing local antibiograms, regular surveillance of nosocomial infection rates, and stringent cleaning protocols are crucial steps in combating infections caused by MDR organisms. Tailored infection control strategies are essential for improving patient outcomes and enhancing the quality of care in ICUs facing the growing threat of multidrug resistance.

Ethical Statement

The authors confirm that all ethical issues have been dealt with the research ethics guidelines provided by the Department of Biotechnology, Amity University, Mohali140306, Punjab, India

Author Contributions

Each author has contributed equally to the study's planning, analysis, writing, and editing. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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