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Frequency of Multidrug-Resistant Organisms Among the Pediatric Intensive Care Unit Patients in Minia University Hospital

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ABSTRACT

Background: One of the biggest problems with healthcare-associated infections is multidrug-resistant organisms (MDROs).

Objective: To determine the frequency and the outcome of MDRO infections among pediatric intensive care unit (PICU) patients at Minia University Hospital, Egypt.

Patients and Methods: This retrospective cross-sectional study was conducted on 202 pediatric patients who were admitted during the period from December 2021 to July 2022 in the pediatric intensive care unit in Minia University Children's Hospital.

Results: The culture results revealed that out of the 202 evaluated patients, 70 (34.7%) were MDROs carriers, and 30.0% of these MDROs were Klebsiella species. The majority of MDROs were isolated from endotracheal tubes in 32 (45.7%) followed by blood culture in 27 (38.6%). Extended-spectrum beta-lactamase (ESBL) among MDROs was 25 (35.7%). A statistically significantly higher mortality was detected in patients with MDROs 44/70 (62.9%) versus non-MDRO patients 20/132 (15.1%) (p=0.005). Moreover, MDROs infection has increased in frequency among patients with chest infections 27 (38.6%). Additionally, patients infected with MDROs had significantly greater PICU stay compared to the non MDROs patients (Mean ± SD of 11.59±4.80, p=0.006).

Conclusion: The frequency of MDROs (34.7%) was high among PICU cases in Minia University Hospital. Klebsiella species were the most prevalent MDROs, followed by Staph aureus species. Infection brought on by Gram-negative organisms occurs significantly more frequently than infection brought on by Gram-positive species. Programmes for strict infection control should be adopted.

Keywords: MDROs, PICU, Antimicrobial resistance.

INTRODUCTION

Illnesses that people get while receiving medical care are known as healthcare-associated illnesses (HCAIs) [(1)]. The term "HCAIs" originally referred to infections associated with admission to an acute-care hospital (previously known as "nosocomial infections"), but it is now used to describe infections that develop in a variety of patient care settings, such as long-term care facilities, family medicine clinics, ambulatory care centres, and homes. HCAIs are infections that initially manifest 48 hours or more after admission to the hospital or within 30 days of receiving medical care [(2)].

Due to the enormous number of vulnerable special groups and the unique diagnosis and treatment environment in the ICU, particularly in the PICU, it has become a high-risk region for hospital acquired infection and drug-resistant pathogens [(3)]. Hospital pathogenic diseases attack patients in critical care units (ICUs). Due to their weakened immune systems, use of broad-spectrum antibiotics, and medical interventions that disturb the host's natural defences, such as the use of invasive devices like urinary catheters (UC) and intubation (e.g., nasogastric tubes) [(4)].

In areas with inadequate sanitation and unchecked antibiotic usage, the antimicrobial resistance is fast rising [(5)]. The prevalence of MDR organisms varies by country and location, with the poor world seeing a larger prevalence than the industrialised world (65.1% vs. 23.5%, respectively) [(4)].

Gram-negative bacteria (GNB), which are on the rise globally and are linked with increased mortality and morbidity, are the primary cause of MDROs, one of the most serious issues in HCAIs and community-acquired infections [(6)].

Due to widespread antibiotic resistance and the critically ill patients, the death and morbidity rates are notably greater in certain illnesses. To allow the quick organisation of measures linked to preventative, control, and therapeutic activities, it is crucial to monitor pathogenic microorganisms in ICUs and keep track of their antimicrobial resistance [(7)].

The purpose of the present work was to determine the frequency and the outcome of MDRO infections among PICU patients at Minia University Hospital, Egypt.

PATIENTS AND METHODS

This retrospective cross-sectional study was conducted on 202 pediatric patients admitted to the pediatric intensive care unit in Minia University Children's Hospital during the period from December 2021 to July 2022.

The characteristics of the patient were documented by a thorough history and physical examination. Vital signs included temperature, respiration rate, pulse, and blood pressure. A detailed examination of the heart, respiratory system, abdomen, and nervous system was performed.

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The enrolled patients were further subdivided into two groups (based on the antibiotic susceptibility patterns): **Group I:** those with MDRO, and **Group II:** The non-MDRO cases.
MDR is described as acquired non-susceptibility to at least one antimicrobial in ≥3 antimicrobial classes by the Centre for Disease Control & Prevention (CDC) [(8)].

Specimens' collection: Different samples were obtained according to the patient's condition including blood cultures, sputum, urine samples, central venous catheter, and endotracheal tube. All samples were collected under complete aseptic conditions to perform culture and antimicrobial sensitivity.
In the Microbiology Laboratory, all obtained samples underwent antibiotic susceptibility testing and organism identification using standard microbiological techniques.

Processing of Specimens

After being delivered to the clinical microbiology laboratory, BACTEC blood culture vials BACTEC BD (Becton, Dickinson and company (continuous monitoring blood culture system)) [(9)], were immediately incubated at 35±1^{o}C in the BACTEC fluorescence series device. All urine, sputum, and blood samples that had positive signals were inoculated on blood agar and Maconkey agar. Overnight, all plates underwent incubation at 35±1^{0}C. Additionally, blood and sputum samples were inoculated on chocolate agar plates then incubated overnight at 35±1^{o}C in a 5-10% CO_2 jar [(10)].

Several typical conventional microbiological techniques, such as colony macroscopic morphology, microscopic inspection, and other biochemical assays, were used to confirm the identities of the recovered isolates. An automated identification method called Vitek® 2 (Biomerieux, France) was utilized for further identification [(11)].

According to the Clinical and Laboratory Standards Institute (CLSI) 2015 Guidelines and Interpretative Criteria, MIC determination was utilized for determination of the antimicrobial susceptibility of all isolates [(12)].

The following antimicrobial classes (Oxoid, UK) including penicillins, tetracyclines, cephalosporins, quinolones, carbapenems, lincomycins, macrolides, sulfonamides, aminoglycosides, glycopeptide antibiotics, and oxazolidinones, were tested against gram-positive and gram-negative isolates: ampicillin/sulbactam (10/10 μg), cefoxitin (30 μg), ceftazidime (30 μg), cefpodoxime (30 μg), cefotaxime (30 μg), ceftriaxone (30 μg), imipenem (10 μg), meropenem (10 μg), amikacin (30 μg), gentamicin (10 μg), tobramicin (10 μg), ciprofloxacin (5 μg), levofloxacin (5 μg), tetracycline (30 μg), doxycycline (30 μg), piperacillintazobactam (100/10 μg), oxacillin (1 μg), vancomycin (30 μg), erythromycin (15 μg), and norfloxacin (10 μg).

Methicillin resistance staphylococcus aureus (MRSA) and ESBL identification:

MRSA was discovered using the cefoxitin disc test (30 g; Oxoid, UK), which is approved by the CLSI [(12)] for predicting MecA gene-mediated methicillin resistance in staphylococcus species.

When Gram-negative bacilli are resistant to three or more antibiotic classes, they are classified as multidrug-resistant (MDR) organisms [(12)]. The Vitek® 2 automated system (Biomerieux, France) was utilized to identify ESBL-producing Enterobacteriaceae [(11)].

Ethical consent:

The Ethics Committee of Minia University's Faculty of Medicine granted the study approval. All the caregivers of all the participants signed an informing consent to use their data for medical research. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

Using the SPSS programme version 25, the acquired data were coded, tabulated, and statistically examined. Descriptive statistics were performed using the mean ±standard deviation for parametric quantitative data, the median and interquartile range (IQR) for non-parametric quantitative data, and the number and percentage for categorical data. For analyses of qualitative data, either the Fisher's exact test (more than 20% of cells have anticipated 5) or the Chi-square test (if less than 20% of cells have expected count less than 5) were used. For comparison of quantitative data between the groups, an independent sample T-test was used. The level of significance was at a p-value of < 0.05.

RESULTS

The study comprised 202 pediatric intensive care unit patients; their demographic and clinical data are shown in Table 1**.**

Table (1): Demographics and some clinical characteristics of enrolled patients.

	Characteristic	Total (n =202)
Age (years)	Mean ± SD	25.42 ± **30.75**
Sex	• Male • Female	104(51.5%) 98(48.5%)
Fate	• Discharged • Died	151(74.8%) 51(25.2%)
Length of stay (Days)	Median (IQR)	7 (5-10)
Sample type:	• Blood culture • Central venous catheter • Endotracheal tube • Sputum • Urine	63(31.2%) 11(5.4%) 106(52.5%) 17(8.4%) 5(2.5%)
Multi drug resistance	• Yes • No	70(34.7%) 132(65.3%)

There was significant difference among the studied groups regarding the outcome of the cases and the type of the organisms and ESBL frequency in PICU (Table 2).

Table (2): Comparison between the two studied groups as regards the multidrug resistance status

Characteristic	Group I N=70	Group II N=132	P-value
Sex			
Male	32(45.7%)	72(54.5%)	0.232
Female	38(54.3%)	60(45.5%)	
Outcome			
Improved	26(37.1%)	125(94.7%)	<0.0001*
Died	44(62.9%)	7(5.3%)	
Organism			
Acinitobater	14(20.0%)	7(5.3%)	
Alcaligenes	1(1.4%)	1(0.8%)	<0.0001*
Burkholderia	3(4.3%)	0(0.0%)	
Citrobacter	0(0.0%)	4(3.0%)	
E.coli	6(8.6%)	11(8.3%)	
Enterobacter	0(0.0%)	5(3.8%)	
Enterococcus	0(0.0%)	4(3.0%)	
Klebsiella	21(30.0%)	77(58.3%)	
Pseudomonas	14(20.0%)	5(3.8%)	
Serratia	0(0.0%)	1(0.8%)	
staph aureus	10(14.3%)	16(12.1%)	
streptococcus	1(1.4%)	1(0.8%)	
Sample			
Blood culture	27(38.6%)	36(27.3%)	
Central venous line	5(7.1%)	6(4.5%)	0.339
Endotracheal tube	32(45.7%)	74(56.1%)	
Sputum	4(5.7%)	13(9.8%)	
Urine	2(2.9%)	3(2.3%)	
Extended spectrum beta lactamase			
Yes	25(35.7%)	41(31.1%)	
No	3(4.3%)	53(40.2%)	<0.0001*
Not tested	42(60.0%)	38(28.8%)	
Methicillin resistance staphylococcus aureus			
Yes	9(12.9%)	8(6.1%)	0.098
No	61(87.1%)	124(93.9%)	

There was significant difference among the studied groups regarding the type of organisms in group I patients according to the site of culture (Table 3).

Table (3): Type of organisms in group I patients according to the site of culture

Characteristic	Acinitobater N=13	Alcaligenes N=1	Burkholderia N=3	E.coli N= 6	Klebsiella N= 21	Pseudomonas N=15	staph aureus N=10	Streptococcus N=1	P- value
Blood culture	2(14.3%)	1(100.0%)	3(100.0%)	0(0.0%)	12(57.1%)	1(7.1%)	8(80.0%)	0(0.0%)	
Central venous line	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	2(9.5%)	3(21.4%)	0(0.0%)	0(0.0%)	
Endotracheal tube	12(85.7%)	0(0.0%)	0(0.0%)	6(100.0%)	7(33.3%)	5(35.7%)	1(10.0%)	1(100.0%)	0.0001*
Sputum	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	3(21.4%)	1(10.0%)	0(0.0%)	
Urine	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	2(14.3%)	0(0.0%)	0(0.0%)	

There was no significant difference among the studied groups regarding the diagnosis of the enrolled patients (Table 4).

Table (4): The multidrug resistance according to the diagnosis of the enrolled patients

Diagnosis	Group I N=70	Group II N=132	P-value
Cardiac	15(21.4%)	38(28.8%)	0.156
Chest	27(38.6%)	61(46.2%)	
GIT	1(1.4%)	4(3.0%)	
Hematological	2(2.9%)	1(0.8%)	
Metabolic	3(4.3%)	1(0.8%)	
Neurological	3(4.3%)	2(1.5%)	
Renal	3(4.3%)	8(6.1%)	
Sepsis	14(20.0%)	13(9.8%)	
Surgical	2(2.9%)	4(3.0%)	

There was significant difference among the studied groups regarding the hospital stay in PICU based on the multidrug resistance (Table 5).

Table (5): The hospital stays duration of the enrolled patients based on the multi-drug resistance

Length of hospital stay	Group I N=70	Group II N=132	P-value
Mean ± SD	11.59±**4.80**	9.77±**3.49**	0.006*

There was no significant difference among the studied groups regarding the type of organism among multi-drug resistance cases based on the outcome (Table 6).

Table (6): Type of organism among multi-drug resistance cases based on the outcome.

Characteristic	Acinitobater N=13	Alcaligenes N=1	Burkholderia N=3	E.coli N= 6	Klebsiella N= 21	Pseudomonas N=15	staph aureus N=10	Streptococcus N=1	P- value
Improved	7(53.8%)	0(0.0%)	0(0.0%)	4(66.7%)	7(33.3%)	4(26.7%)	4(40.0%)	0(0.0%)	0.409
Died	6(46.2%)	1(100.0%)	3(100.0%)	2(33.3%)	14(66.7%)	11(73.3%)	6(60.0%)	1(100.0%)	

DISCUSSION

MDR microbes provide a global hazard in ICU hospitalized children, with substantial fatality rates. The prevalence of resistant infections necessitates more expensive medicines, which raises treatment costs [13].

The culture results in the current investigation indicated that 70 isolates (34.7%) were MDROs and the remaining 42 (61.8%) were non-MDROs. When these findings were compared to other Egyptian hospital PICUs, only 26 (38.2%) of the 68/282 isolates were MDROs. Although this rate was lower compared to the rate revealed in Egyptian previous studies, **Eyada *et al.*** [14], 98/106 (92.45%), and in Beni-Suef University Hospital's Neonatal and Paediatric Intensive Care Units, 145/169 (85.8%) [13]. Our percentage, however, was lower than the prevalence at King Chulalongkorn Memorial Hospital Thailand, which was 30/58 (52%) [15]. Furthermore, in another investigation by **Qureshi *et al.*** [16], the total MDRO carriage was found to be quite high, at 68.3%.

Variation in sample size, distinct demographic areas, and the effectiveness of infection control strategy implementation might all be used to account for these significant disparities [13].

With a wide range of patient acceptances, university hospitals and tertiary referral hospitals in Egypt tend to have higher infection rates and, as a result, higher MDROs [15].

Antibiotic overuse in outpatient settings, incorrect dosage, inadequate antibiotic courses, and the use of antibiotics to treat viral infections can all be factors in the high prevalence of MDROs in some PICUs [13].

A thorough systematic review and meta-analysis research discovered 569 (29%) antimicrobial-resistant pathogens. MRSA, carbapenem-resistant A. baumannii, and Klebsiella pneumoniae were the most often detected MDR microorganisms [14].

The proportion of MRSA carriage among MDRO in this study was 9/70 (12.9%), which corresponded with a study by **Qureshi *et al.*** [16] where the percentage of MRSA carriage was likewise elevated (14.2%), in contrast to a study by **Kiddee *et al.*** [17] in China where MRSA carriage was 6.4%.

The proportion of MDRO carrying ESBL was 25/70 (35.7%) in the current research. ESBL E. coli was 47.7% and K. pneumonia was 15.8% in previously published research from Guinea-Bissau, Madagascar (ESBL E. coli and K. pneumonia were 36.9%), Lebanon (ESBL Enterobacteriaceae 24.9%), and Thailand (ESBL E. coli 67.5% and K. pneumoniae 19.4%).

Age, antibiotic usage [18], past hospital admission, particularly to ICU [19], and overall length of stay in hospital are also risk factors for MDRO transmission[20, 21]. The length of hospital stay was shown to be statistically significantly linked with MDRO carrier versus non-MDRO (p-= 0.006) in our research. Previous research has found that patients with MDRI spend much more time in the ICU and have poorer survival rates than other patient groups [22].

In **Rezk *et al.*** [23] study, patients receiving transplants and those who have underlying lung diseases are more susceptible to get nosocomial infections from resistant pathogens.

The length of ICU stay is associated with increased need for drugs, invasive procedures, and patient cross-infection. Additionally, endogenous infections may result from the body's own germs spreading to different tissues and organs [24].

Regarding the relationship between MDRO carriage and gender, there was no statistically significant association between MDRO carrier versus non-MDRO (p-value =0.232). Similarly, **Tarchouna *et al.*** [21] showed no association with age and gender.

CONCLUSION

The frequency of MDROs (34.7%) was high among PICU patients in Minia University Children's Hospital. Klebsiella species were the most prevalent MDROs, followed by Staph aureus species. Gram-negative bacteria are substantially more prevalent than Gram-positive bacteria. Worldwide, it has been found that antibiotic resistance is rising along with PICU patient mortality and morbidity, even for new categories. As a result, strong infection control programmes need to be put in place.

There are limitations to the current study: The prevalence of MDRO in Minia as a whole may not be accurately represented by the existing findings from a single-center investigation. To further comprehend the problem, multicenter research is required to evaluate various healthcare facilities in our region's urban and rural settings.

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