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Epidemiological profile of multi-drug resistant bacteria in pediatric intensive care unit

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Abstract

Multidrug-resistant bacteria are currently a major health problem in our hospitals and a current medical issue due to the morbidity and mortality it causes, especially in intensive care units. The objective of this study is to describe the epidemiological profile, frequency, and resistance status of multidrug-resistant bacteria in pediatric and neonatal intensive care units.

We conducted a retrospective study at the microbiology laboratory of the Hassan II University Hospital in Fez in 2022, where we collected bacterial samples from these two units that identified a multidrug-resistant bacteria (MDR).

We collected 1216 bacterial samples, of which 28% were positive, and among them, we found 148 samples that contained multidrug-resistant bacteria. Gram-negative bacteria (GNB) dominated, with only 4 resistant gram-positive cocci samples, and *Acinetobacter baumannii* was the most prevalent, followed by *Klebsiella pneumoniae*. A high rate of extended-spectrum beta-lactamase (ESBL) was found in infants, estimated at 40% of all samples collected in neonatal intensive care, as well as a high rate of highly resistant isolates of *Acinetobacter baumannii* in pediatric intensive care.

Multidrug-resistant nosocomial bacterial infections are dominated by bacteremia in neonatology and pneumonia in pediatric intensive care, and both are mainly caused by gram-negative bacilli. Knowledge of the bacteriological profiles and antibiotic resistance rates of such bacteria will allow for more tailored and targeted management in each hospital setting.

Keywords: Multidrug-resistant bacteria; MDR; Pediatric intensive care; Extended-spectrum beta-lactamase; ESBL

1 Introduction

Antibiotic resistance is one of the most important public health problems in the world. Infections caused by multidrug-resistant bacteria (MDR) result in up to 700,000 deaths worldwide each year, including 200,000 infants [1]. The prevalence varies depending on geographic distribution, sporadically, and according to the departments of care. In fact, the ecology of the service plays an important role as well as the means of hygiene available to it.

Pediatric intensive care units are experiencing the emergence of multidrug-resistant bacteria, which is associated with an increased risk of morbidity and mortality. Multidrug-resistant bacteria are defined as being resistant to at least one antibiotic in three or more antibiotic families. These infections are more difficult to treat and cause longer hospitalizations, increasing the length of stay by 20% and the risk of mortality by 40% in these patients [2].

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The best way to address this bacterial resistance scourge is to improve knowledge of the germs involved and implement preventive measures. Our research paper aims to study the prevalence of multidrug-resistant bacteria in pediatric and neonatal intensive care units, to reveal their epidemiological and bacteriological profile, and to assess their impact on length of hospital stay and mortality in this pediatric population.

2 Material and methods

Our retrospective study will focus on all bacteriological samples received from the pediatric and neonatal intensive care units during the year 2022 at the microbiology department of Hassan II Hospital in Fez. Data collection was carried out from our department's records as well as an analysis of medical files for epidemiological study and etiological diagnosis elements.

Bacteriological samples include, first of all, blood cultures that are incubated in BD Bactec™ until positivity and then inoculated on blood agar for culture. Secondly, respiratory samples and removed catheters that are done with dilution on blood agar as well as chocolate agar, and finally, pus samples, which can concern severe burns, polytraumatized patients, or postoperative wounds, are inoculated on ordinary media as well as blood agar.

All samples are checked after 24 hours of incubation in an incubator at 37°, and it takes a minimum of 48 hours of incubation to judge them negative. Once a sample is positive, the colonies are identified on BD Phoenix ™ with automated antibiotic susceptibility testing as well as manual testing on Mueller-Hinton.

3 Results

We collected 1216 bacteriological samples from the pediatric intensive care units, including 648 blood cultures, 389 respiratory samples, 151 catheter samples, and 28 pus samples. Out of these samples, only 346 (28%) were positive, including 112 blood cultures, 164 respiratory samples, 55 catheter samples, and 15 pus samples. There were a large number of blood cultures taken compared to positive ones, as they were routinely done upon admission to the neonatology unit. Additionally, the threshold for positivity in other samples was explained by the initiation of empirical antibiotic treatment upon suspicion of sepsis, given the fragile pediatric population, which can result in negative cultures.

Multidrug-resistant bacteria (MDR) were identified in 153 positive samples, corresponding to 44% of positive samples, including 48 blood cultures, 77 respiratory samples, 20 catheter samples, and 8 pus samples, with a slight male predominance at 53% and an average age of 4 years (1 day to 15 years). Gram-negative bacilli (GNB) accounted for 98% of MDR identified in pediatric intensive care units, with only 4 (2%) MDR gram-positive cocci. The most frequently identified GNB were *Acinetobacter baumannii* (A.B) in 97 cases (63%) and *Klebsiella pneumoniae* (K.P) in 32 (21%) patients.

Regarding blood culture samples, 24 were collected from the pediatric intensive care unit and 24 from the neonatology unit. There were two different ecologies within the two units, with *Klebsiella pneumoniae* (79%), being the most frequently identified organism in neonatal blood cultures. In contrast, *Acinetobacter baumannii* (66%) was dominant in blood cultures from the pediatric intensive care unit.

Respiratory samples were primarily protected distal respiratory samples collected from the pediatric intensive care unit, as this procedure is not done in newborns. They were predominantly gram-negative coccobacilli, specifically *Acinetobacter baumannii* (88%), followed by *Pseudomonas aeruginosa* (6%), of which 3 were carbapenem-resistant and 1 was resistant to ceftazidime. Only one multidrug-resistant gram-positive organism, a *methicillin-resistant Staphylococcus aureus (MRSA)*, was detected in a 1-year-old child who had a long hospital stay and subsequently became infected with A.B, eventually passing away after 64 days of hospitalization.

Catheter samples were also representative of nosocomial infections in the units, with the pediatric intensive care unit predominantly having *Acinetobacter baumannii* (66%) and the neonatology unit having *Klebsiella pneumoniae* (87%). These samples are more indicative of material colonization due to poor hygiene and contamination caused by aseptic errors during catheter placement.

Lastly, pus samples were collected from a severely burned child in the pediatric intensive care unit, in whom *Enterococcus faecium* was identified, and from wound samples of polytraumatized children in the pediatric intensive

care unit contaminated with *Acinetobacter baumannii* or *Pseudomonas aeruginosa*. In the neonatology unit, infections caused by *Klebsiella pneumoniae* and *Escherichia coli* were also observed (Table 1).

Table 1 Distribution of pathogenic agents according to the site of infection and the intensive care unit

	germe	**Pediatric intensive unit care**	**Neonat intensive unit care**
Blood cultures	*Acinetobacter Baumanii*	16	1
	Klebsiella pneumoniae	1	19 (7 ESBL)
	Escherichia coli	2	3 (3 ESBL)
	Enterobacter cloacae	2	
	Citrobacter koseri	1	
	Entérocoque faecium	1	
	MRSA	1	
	Klebsiella oxytoca		1 (1 ESBL)
	Total	24	24
Respiratory samples	*Acinetobacter Baumanii*	68	
	Klebsiella pneumoniae	1	
	Escherichia coli	3	
	MRSA	1	
	Pseudomonas aeruginosa	4	
	Total	77	0
Catheters	*Acinetobacter Baumanii*	8	1
	Klebsiella pneumoniae	2 (1 ESBL)	7 (1 carbapenemase + 2 ESBL)
	Escherichia coli	2 (1 carbapenemase)	
	Total	12	8
Pus samples	*Acinetobacter Baumanii*	3	
	Klebsiella pneumoniae		2 (1 ESBL)
	Escherichia coli		1
	Entérocoque faecium	1	
	Pseudomonas aeruginosa	1	
	Total	5	3

In patients with sepsis, there is a prolonged hospital stay with an average of 20 days and a mortality rate of 52% in neonatology and 30% in pediatric intensive care units. For pneumonia in pediatric intensive care, they were responsible for a longer stay with an average of 36 hospitalization days and an estimated mortality rate of 37%.

Infections related to catheters (either venous, arterial, or urinary) are generally not a cause of mortality because once removed, patients usually recover without the need for antibiotics unless they are associated with pneumonia or sepsis, as was the case for 13 of our patients (65%) where mortality was noted at 45%.

4 Discussion

The rapid emergence of infections associated with multidrug-resistant bacteria (MDR) is an alarming global health problem. Over the past two decades, the number of MDR has quadrupled, causing bacteremia, pneumonia, and skin

infections which were more important in poor regions with defective hygiene and uncontrolled use of antibiotics. In 2013, it was estimated that 6.3 million live-born children in the world died before the age of 5. Among them, nearly half (51.8%) died of infectious causes, with sepsis accounting for 15% of all deaths in children under 5 years of age due to infection [3].

MDR in children and infants are rapidly increasing, the National Healthcare Safety Network NHSN has reported that MDR affects 5-10% of hospitalized children [4], which is comparable to our study where we found 153/1216 samples (12%). The rate of MDR varies by geography and socioeconomic status. In Europe, about 30% of pediatric patients with sepsis have MDR [5], while in the Middle East, specifically in Palestine, this rate rises to 90% for children hospitalized in intensive care units [6], and in the United States, about 20% of children receive colistin to treat multidrug-resistant gram-negative bacteria [7].

This antibiotic resistance phenomenon is mainly caused by overconsumption and improper use of antibiotics, which contributes to the selection of MDR bacterial strains. These prescriptions are observed in 30 to 60% of antibiotic therapies administered to ambulatory or hospitalized patients in some studies [8].

Infections caused by MDR are more difficult to treat and are associated with a more severe and longer illness that leads to prolonged hospitalization, with a 20% increase in length of stay and a more unfavorable prognosis, increasing mortality up to 40% in nosocomial MDR contracted during hospitalization.

One can observe a dominance of gram-negative bacteria in MDR, which is comparable to the results of the 2011-2016 antibiotic plan conducted in France. The assessment of actions taken since the early 2000s to preserve the effectiveness of antibiotics is mixed, showing successes and limitations, both in urban and healthcare settings. Results have been obtained on the control of consumption and on the control of the cross-transmission of certain multidrug-resistant bacteria or MDR (MRSA, VRE), but there has been an emergence and dissemination of other MDR (ESBL or carbapenemase-producing enterobacteria - CPE) [9].

Newborns have weaker immune systems and are more prone to bacterial infections, making it urgent to intensify efforts to manage antibiotics and address infection control and MDR prevention in pediatric units. High rates of resistance have been reported in neonatal infections with early onset, which can be linked to either maternal-fetal infection or nosocomial infection.

Adequate management of sepsis in children first requires rapid diagnosis and appropriate treatment, which are the main determinants of patient outcomes. However, these interventions must be performed before a definitive etiological diagnosis is available. Empirical antibiotic therapy in case of suspected sepsis should be initiated with broad-spectrum antibiotics based on age group and local epidemiology, and should be administered at doses capable of achieving bactericidal concentrations in the blood. Once a pathogen has been identified, antibiotic therapy should be restricted and targeted to the isolated bacteria. In our study, sepsis in newborns reported a rate of ESBL of 41%, which is comparable to a study in Brazil that found 34% [10].

Data on the use of β-lactam-β-lactamase inhibitors (BL/BLI) for the treatment of ESBL infections are still inconsistent, as many organisms are capable of producing multiple ESBLs simultaneously, thereby reducing the efficacy of the inhibitor [11]. However, carbapenems have shown excellent in vitro activity and are currently considered the treatment of choice for invasive ESBL infections in children. All of these efforts are necessary to decrease the mortality rate, which continues to increase and reaches 33.3% for MDR sepsis, although in our study, it was estimated at 41% [10].

In pediatric intensive care, blood cultures were dominated by *Acinetobacter baumannii*, as reported in other hospitals in Asia [12], with a reported mortality rate of 38% in A.B carriers, whereas in our study, 50% of those with A.B sepsis died.

Pneumonia caused by *Acinetobacter baumannii* is a real problem in critically ill children. Studies have identified risk factors such as prolonged stay, mechanical ventilation, anemia, and hypoalbuminemia. Furthermore, the intensive care environment is conducive to many opportunistic pathogens that colonize it, as well as the skin and mucous membranes of medical personnel, and this germ is even found on computer keyboards and condensed water that is part of the mechanical ventilation system according to a Korean study [13].

In a study conducted in China, 77% of identified *Acinetobacter baumannii* (A.B) had highly resistant profiles. In our setting, this rate is even higher as almost all of our isolates are resistant, which is consistent with an increase in carbapenemases in A.B isolates from 53% in 2006 to 90% in 2013 in Byun et al. study [13]. This pathogen is also the

most incriminated agent in ventilator-associated pneumonias. Due to the limited effectiveness of antibiotics against this pathogen, ampicillin/sulbactam, colistin, tigecycline, and minocycline were used alone or in combination. In our study, colistin was the most commonly used antibiotic, either intravenously or intratracheally.

The mortality rate in Cai et al. study was estimated at 18.26% [14], although a more recent study showed an increase to 29% [12], which is comparable to our study where the death rate was 37%.

Catheter specimens are often due to the duration of placement and colonization by nosocomial germs from the relevant unit, and any devices used can be a formidable reservoir of biofilms and bacteria that are practically inaccessible by antibiotics. The only way to treat the patient is by removing the device [2].

5 Conclusion

Our study has demonstrated the emergence of multidrug-resistant bacteria (MDR) in pediatric intensive care units dominated by *Acinetobacter baumannii* and *Klebsiella pneumoniae*. These two pathogens are heavily incriminated in intensive care units in the literature. The high prevalence of MDR carriers in children poses a major public health problem, especially in developing countries such as Morocco where the health system is already overburdened. Our results call for recommendations on the main prevention and control measures in hospital settings, as well as improvements in early diagnosis and targeted treatment of MDR bacterial infections.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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