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Prevalence and Risk Factors of Fecal Carriage of Multidrug-resistant Bacteria in Children of Mohammed Vi Hospital Center (Morocco)

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Abstract

Introduction: The emergence of bacterial resistance to antibiotics is a public health issue around the world affecting adults and children. It prolongs the length of stay and worsens the prognosis of hospitalized patients. The objective of the study is to evaluate the prevalence of focal carriage of multidrug-resistant bacteria (MDRB) in children hospitalized at Mohammed VI University Hospital centre in Marrakech, and to identify the risk factors associated with this carriage.

Material and method: This is a cross-sectional prospective study including all children hospitalized on the day of the survey at the four paediatric departments. All children hospitalized in the department on the day of the study were included. Rectal swabbing was performed systematically.

Results: The results of this survey show a prevalence of MDR carriage of 42%, exceeding 75% in Neonatology and Paediatric Resuscitation. Klebsiella pneumonia was dominating (52%), followed by E.cloacae (31%), E.coli (7%) and A.baumannii (7%). These MDRB were resistant to Fluoroquinolones in 70% of cases, Trimethoprim-sulfumethexazole (65%) and Gentamicin (55%). The risk factors were the length of stay more than 48 hours, a prior antibiotic therapy in the last 6 months, and a history of hospitalization.

Conclusion: The colonization of children by MDRB can be explained by the quality of care and the hygiene policy of each establishment, but also by the pressure of selection of antibiotics. This underscores the need to respect hygiene measures during care for patients, to rationalize the prescription of antibiotics and to set up a surveillance system for MDRB bacteria.

Keywords : multidrug-resistant bacteria, risk factors, fecal carriage

Introduction:

Bacterial resistance to antibiotics is a major public health issue, which has been the subject of increased awareness for several years [1].

Surveillance of resistance through observatories and surveys of prevalence or incidence confirms increased resistance and the emergence of multi-resistant strains with epidemic potential. Some strains remain sporadic, while others have become endemic in France and Europe [2].

In Morocco, there is still no national network for monitoring bacterial resistance to antibiotics, but through some national publications, different hospital structures report the recrudescence of

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multidrug resistant (MDR) bacteria in hospitals for all bacterial species but to varying degrees according to cities and departments [3].

Materials and methods:

This is a cross-sectional prospective study including all children hospitalized on the day of the study at thepediatric's four departments: Pediatrics A, pediatrics B, neonatology (resuscitation and premature unit) and pediatric resuscitation. All children hospitalized and present in the department on the day of the survey were included, and each child on the day of the survey received a rectal swab.

Each sample corresponds to a numbered swab and an exploitation sheet containing all the information necessary for the study (age, sex, service, pathological antecedents, history of hospitalization, prior antibiotic intake, day of hospitalization).

The swabs were quickly transferred to the Microbiology department and seeded in two selective culture media: Mac Conkey supplemented with Ceftriaxone: a selective medium for the isolation of C3G-resistant gram-negative bacilli (GNB), and a chromomeric medium (BLSEC from agar), which also isolates C3G-resistant Gram-negative bacilli and facilitates their identification by staining bacterial colonies.

Any positive culture led to bacterial identification and antibiogram.

The identification of strains is based on the study of their morphological, cultural, and biochemical characters by Api 20E galleries, and automated method by BD Phoenix™ which allows at the same time the determination of sensitivity to a panel of antibiotics by minimum inhibitory concentration (MIC)method.

The results were sent to the services concerned to implement the specific isolation measures.

Results:

Prevalence of MDR bacteria digestive carriage

Sixty-six digestive porting samples were taken from all children hospitalized on the day of the survey at the different departments of the Mother and Child Hospital.

(Table I shows the distribution of the samples taken by age and sex in each service).

Among the 66 children sampled on the day of the survey, 28 were carriers of MDR bacteria in their digestive flora, a prevalence of digestive portage of MDRB of 42%.

A different distribution of digestive carriage of MDRB according to the services was found: 73% in neonatal resuscitation, 87.5% in premature unit, 50% in pediatric intensive care unit, 26% in pediatric B and 20% in pediatric A.

No statistically significant relationship was found between gender and digestive carriage of BMR in children sampled on the day of the survey. 54% of MDRB carriers were male.

Distribution of isolated MDRB:

Isolated MDRB were dominated by *Klebsiella pneumonia* (52%) followed by *Enterobacter cloacae* (31%). The rest is shared between *E. coli* (7%) and *A. baumannii* (7%).

These isolated MDRB showed high resistance to the other antibiotics tested, notably Fluoroquinolones 70%, Trimethoprim-sulfumethexazole 65% and Gentamicin 55%.

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Study of the risk factors related to the digestive portage in children at the Mother Child Hospital of the University Hospital of Marrakech

1. Service and age:

The statistical analysis by the Chi-square test confirms that the difference between these services is very significant with a probability equal to 0.0018 (P = 0.0018).

The distribution of MDRB digestive portage by department and age showed a statistically confirmed relationship with a very significant value **($p= 6,6.10^{-05}$),** in fact, the two units of the neonatology department (in particular premature unit) had the highest MDRB rectal carriage rate compared to other services that participated in the survey.

2. Length of stay:

Prolonged length of stay at the hospital is at risk for BMR digestive carriage (P = 0.002) (figure 1)

3. Previous ant biotherapy:

The prevalence of carriage was higher in children who received prior antibiotic treatment compared to children who did not receive prior antibiotic therapy in the 6 months prior to hospitalization(p0.0014).

4. History of Hospitalization

The prevalence of MDRB carriage was higher among children with a history of hospitalization than children who had never been hospitalized before. These observed differences were statistically significant by the Khi 2 test (P = 0.0008)
(Figure 2)

Discussion

Antibiotic resistance is a natural phenomenon, but it is accelerated by the misuse of antibiotics in humans and animals. This often abusive use of antibiotics favors the evolution towards the bacterial resistance leading frequently to therapeutic failures (4). This situation is even more worrying given the slow discovery of antibiotics, and the limited available therapeutic choices [5].

Bacteria are multi drug resistant (MDR) when they are sensitive only to a small number of antibiotics used in therapeutics, due to the accumulation of natural and acquired resistance to several families of antibiotics [6].

Rates of colonization and infection by multidrug-resistant bacteria are increasing worldwide. Different major facts are to be highlighted in the evolution of bacterial epidemiology. First, the decrease in the incidence of MRSA in health care facilities, the sharp increase in the incidence of ESBL-producing nitrobacteria. This increase is largely related to the high proportion of Escherichia coli CTX-M strains that have been widely disseminated in recent years, both in hospital and in out-of-hospital settings. Finally, the occurrence of sporadic cases of enterbacteria producing carbapenemases.

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The problem of bacterial resistance is more emphasized in children for several reasons: a fragile field, a high susceptibility to the selection of bacterial resistance by the excessive use of antibiotics in viral infections in children and the difficulty of confirming the bacterial origin, as well as the pressure imposed by the parents on pediatricians. Half of the antibiotic treatments prescribed in children are unnecessary or inappropriate [7,8].

This study reports a high prevalence of MDRB in children affecting 42% of samples. This rate is important, and is higher than what is reported in an Algerian study in pediatrics (26%) and another Tunisian in neonatology (34.2%) [9, 10]. Studies in adults in Tunisia and Morocco have reported a lower prevalence of 17 to 20% in intensive care settings [11,12].
Multidrug-resistant nitrobacteria accounted for 93% of the isolated MDRB, representing 39% of all samples taken, a very high rate compared to what was observed in a French study studying the fecal and nasal carriage of MDRB in newborns. , and where 9.8% of the samples were positive for multi-resistant nitrobacteria [2], and in a study conducted in Israel that reported a lower rate of ESBL Enterobacteriaceae in fecal carriage (10.8% of samples) [13]; a difference that can be explained by the difference in sample sizes, antibiotic prescription and hygiene practices.
However, a study done in adults at a university hospital in Morocco shows a 42.8% carry rate of ESBL enterobacteriaceae; and 12.8% of carbapenemase-producing nitrobacteria [14].

In isolated enterobacteria, *Klebsiella pneumonia* was the predominant species exceeding half of the positive samples, which is consistent with a study done in a resuscitation department in Marrakech [10]. *E. coli* is isolated to a lesser extent in our study. These two species are among the germs followed by the European network "the European Antimicrobial Resistance Surveillance System (EARSS)" which reports a high percentage of *E. Coli* and *Klebsiella pneumonia* resistant to C3G. This high prevalence of ESBLs in nitrobacteria significantly limits the treatment options for patients with life-threatening infections. In addition, the increase in associated resistance and the spread of ESBL may lead to increased use of carbapenems, promoting the subsequent diffusion of carbapenemase-producing nitrobacteria (CPE) [15].

The emergence of carbapenem resistance in *Acinetobacter baumannii* has become a worldwide concern as these molecules are often the only effective treatment against multi-resistant strains.

There is no exhaustive list of risk factors for multidrug resistance, but the age of the patient [16] and the prior use of an antibiotic are considered as the risk factors for bacterial resistance, whatever the infected site, and the bacterial flora involved are. Recent hospitalization is also responsible for infections with resistant bacteria because, in this case, it is a nosocomial infections.

Two studies studying colonization by multidrug-resistant nosocomial bacteria in newborns, reported as risk factors: prematurity, parenteral nutrition [2, 17], prior hospitalization, and history of assisted ventilation [2]. Furthermore, in a four-year case-control study, the authors found that the prior use of fluoroquinolones, a third-generation cephalosporin, is one of the independent risk

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factors associated with ESBL *E- coli* type CTX-M infections [18, 19]. This finding was also reported in the Kaiser et al study [20].

A history of hospitalization, prolonged hospitalization, prior antibiotic therapy, and corticosteroid treatment are the risk factors for acquiring *klebsiella pneumonia* producing carbapenemases studied in a Spanish study [21]. No cases of Pseudomonas aeruginosa resistant to impanel were isolated in this study. The risk factors for acquiring this bacterium with nosocomial potential found in the studies are almost the same as ESBL: prematurity (gestational age below 32 weeks), low birth weight and prior antibiotic intake (C3G and impanel) [22, 23]. There is no doubt that it is the considerable increase in selection pressure due to the excessive use of antibiotics that leads to the selection of bacteria that combine the various resistance mechanisms.

Conclusion:

Antibiotic resistance leads to an increase in medical expenses, an increase in hospitalizations and an increase in mortality [24]. As a result, at the 2016 meeting of the United Nations General Assembly, the leaders pledged to adopt a coordinated approach to address the root causes of antimicrobial resistance in several sectors. Prevention measures aim to limit the selection pressure by means of a reasoned strategy of the prescription of antibiotics and to break the chain of transmission of MDRB thanks to adapted hygiene measures: hand hygiene, screening and detection of carrier patients, isolation of colonized patients.

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Tables and figures:

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Service	Pediatric A	Pediatric B	Neonatology (resuscitation)	Neonatology (premature)	Pediatric intensive care unit
Newborns	0	0	11	8	3
Infant	11	9	0	0	2
Children	9	10	0	0	3
Females	9	11	4	4	2
Males	11	8	7	4	6

Table I: Overall Distribution of Levies taken by Service by Age and Gender (n = 66)

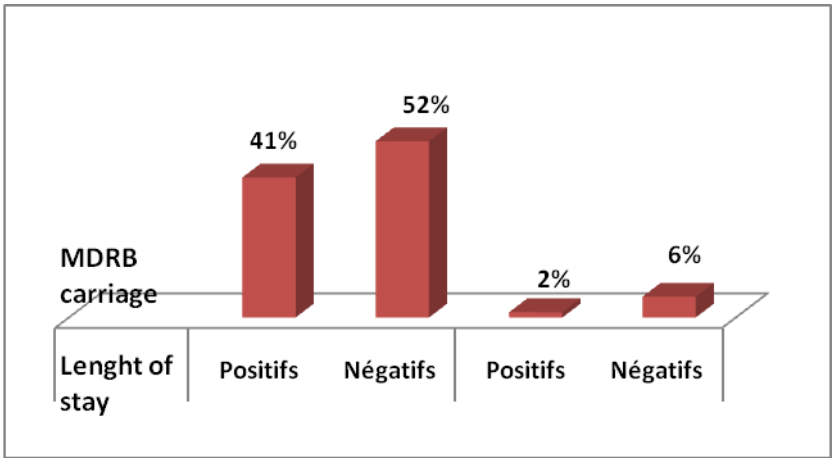

Figure 1: BMR Wear Risk Analysis by Length of Stay

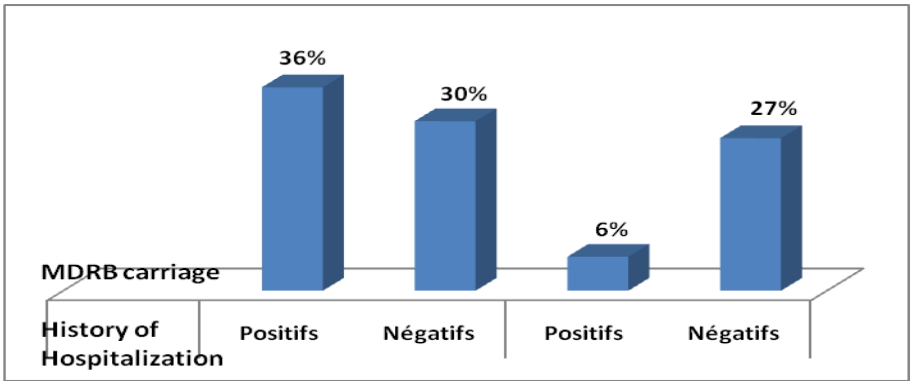

Figure 2: Risk analysis of MDRB rectal carriage according to history of hospitalization