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EPIDEMIOLOGY OF COMMUNITY INVASIVE INFECTIONS IN CHILDREN AT MARRAKECH CHU

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ABSTRACT

INTRODUCTION: Invasive infections include meningitis, bacteremia, and puncture fluid infections. These infections are one of the main causes of severe morbidity and mortality in children. OBJECTIVE: To study the bacteriological profile of documented bacterial invasive infections in children at Marrakech University Hospital including invasive infections caused by Streptococcus pneumoniae, Neisseria meningitidis and Haemophilus influenzae b. MATERIAL AND METHODS: To establish the bacteriological profile of these invasive infections, a surveillance based on data from the microbiology laboratory was carried out including all strains of pneumococcus, meningococcus and Haemophilus influenzae isolated from children hospitalized at the Pediatric Center. Infant from LCS, Hemocultures and pleural fluid during the period January 2010 to December 2018. RESULTS: During this period, 248 bacteriologically confirmed invasive infections were recorded at any infectious site. Pneumococcal IIs ranked first with 55% of the germs responsible for II in children, followed by meningococcus 38% and H.influenzae 7%. The average age of the children was 3 years with a male predominance and one with sex ratio of 1.2. These II mainly affected the child under 4 years in 71% of cases. Meningitis and bacteremia were the two most common infectious sites. Weeds accounted for 13% of these invasive IIs. These invasive infections were more common in winter and early spring. The evolution between 2010 and 2018 showed an increase in these II from 2015 and that continues until 2018 mainly related to the increase in pneumococcal II. Regarding meningitis, a stable prevalence of meningococcal meningitis was found with the predominance of meningococcal serogroup B meningitis (81%), a significant regression of meningitis to H. influenzae b and an increase in pneumococcal meningitis between 2015 and 2018 From 2015, a decrease in pneumococcal meningitis of vaccine serotypes was observed with the progressive increase of pneumococcal meningitis of non-vaccinal serotypes in all age groups. DISCUSSION / CONCLUSION: This work highlights the problem of II in children at the University Hospital of Marrakech which arises mainly with meningococcal serogroup b meningitis and pneumococcal meningitis serotype non-vaccinal. Continuous surveillance of carriage and pneumococcal infection will be essential to monitor the impact of PCV10 use in children, including early detection of alternative serotypes, trends in antimicrobial resistance, and potential indirect effects. . The geographic diversity of pneumococcal serotypes underscores the importance of ongoing surveillance to guide vaccine design and recommendations.

The surveillance of these II is based on clinical, epidemiological and microbiological data, and clinical and biological collaboration is essential for better management of patients.

Keywords : *community invasive infections, Pneumococcal, Meningococcal, Haemophilus influenzae b.*

INTRODUCTION

Invasive infections (II), which include meningitis, bacteraemia, and infections of bacterial punctures, are among the leading causes of severe morbidity and mortality in children. Among the many bacterial species involved, three bacterial species are at the origin of diseases that can be prevented by vaccination: Streptococcus pneumoniae or pneumococcus, Haemophilus influenzae and Neisseriameningitidis or meningococcus.These three bacteria are strictly human bacteria, commensals of the tract respiratory. In poorly understood conditions, these bacteria could be responsible for systemic infections that pose a serious public health problem, because of their epidemic potential and the severity of the sequelae that these infections may cause.

The diagnosis of invasive infections is discussed in front of the clinic and confirmed bacteriologically by laboratory tests, direct examination, culture and molecular biology techniques (PCR). Bacteriological confirmation is important in order to establish the etiological diagnosis of these IIs which includes isolation, bacterial identification, serogroup determination, strain typing and antibiotic susceptibility testing of isolates. Molecular diagnosis by PCR allows rapid diagnosis and has taken an important place in the diagnosis of meningitis.

The objective of this work was to establish the bacteriological profile of bacterial invasive infections documented in children at the University Hospital of Marrakech including invasive infections including meningitis, bacteremia and more rarely infections of puncture fluids; caused by Streptococcus pneumoniae, Neisseriameningitidis and Haemophilus influenza over a period of 8 years.

MATERIALS AND METHODS

To establish the bacteriological profile of these invasive infections, a surveillance based on data from the microbiology laboratory was carried out, including all strains of pneumococcus, meningococcus and Haemophilus influenzae isolated from children hospitalized at the Pediatric Mother Child Division from LCS, Hemocultures and pleural fluid.

These samples were taken from children under 15 years old and hospitalized at the various pediatric departments of the Mohammed VI University Hospital of Marrakech between January 2010 and December 2018.

The direct gram stained examination allowed a rapid diagnosis of these infertile sites. The culture on enriched media agar and on enrichment media allowed the isolation of these fragile germs. Bacterial identification was made according to conventional morphological, cultural, biochemical and antigenic bacteriological characteristics. This identification was completed by a serogroup determination by serum agglutination of the bacterial bodies with specific sera. The desired serogroups were serogroups A, B, C, W135, and Y. Serogroup b of H.influenzae was determined by seroadministration with a specific serum.

Pneumococcal identification was supplemented by serogrouping and serotyping of the isolates by the Damier method with Pneumotest-latex (StatensSerum Institute antisera, Copenhagen,

Denmark). Serotyping was done by PCR according to the pneumococcal molecular typing protocol.

The study of the sensitivity to antibiotics and the determination of MICs was made according to the standards of the antibiogram committee of the French Society of microbiology CASFM - EUCAST.

The data of each patient was collected on a form, entered on Microsoft Excel.

RESULTS AND DISCUSSION

General distribution of invasive infections in children at the University Hospital of Marrakech between 2010 and December 2018

During this period, 248 bacteriologically confirmed invasive infections were recorded at any confounding site. The average age of the children was 3 years with a male predominance and one with sex ratio of 1.2. These II mainly affected the child under 4 years in 71% of cases, the child between 4 and 10 years in 25% and the child over 10 years in 4% of cases. With regard to the monthly frequency of these II in Marrakesh from 2010 to 2018, all infectious sites combined and all germs combined, these II were more frequent in winter and early spring. The largest number of cases was recorded during the months of March, April and from September, October and December. Pneumococcal IIs ranked first with 55% of the II organisms in children, followed by meningococcus 38% and H.influenzae 7% (Figure 1).

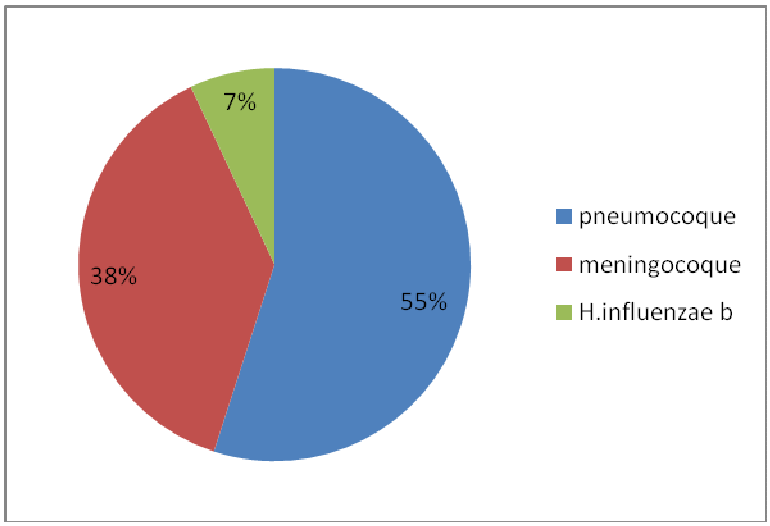

Figure 1: Distribution of invasive infections in children according to species at the University Hospital of Marrakech between 2010 and December 2018 (n = 248)

The most common infectious sites were meningitis and bacteremia (Figure 2).

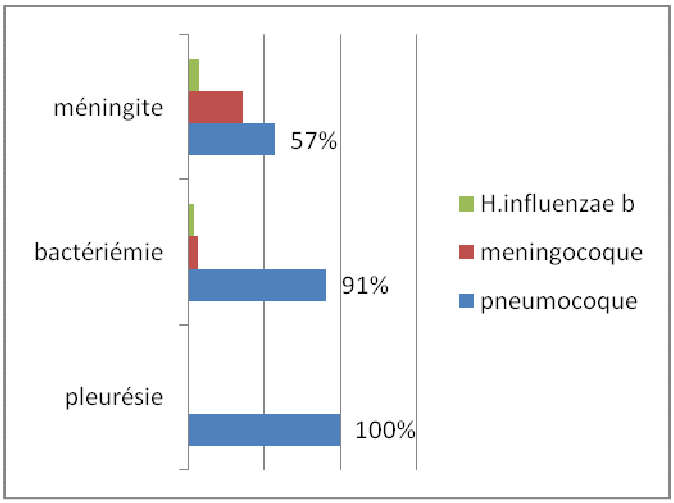

Figure 2: Frequency of invasive infections in children at the University Hospital of Marrakech between 2010 and 2018 according to the infectious site and according to the species (n = 248)

The evolution between 2010 and 2018 showed an increase in these II from 2015 and that continues until 2018 mainly related to the increase in pneumococcal II. Slightly stable variations were found for Meningococcal and H. influenzae IIs. (Figure 3).

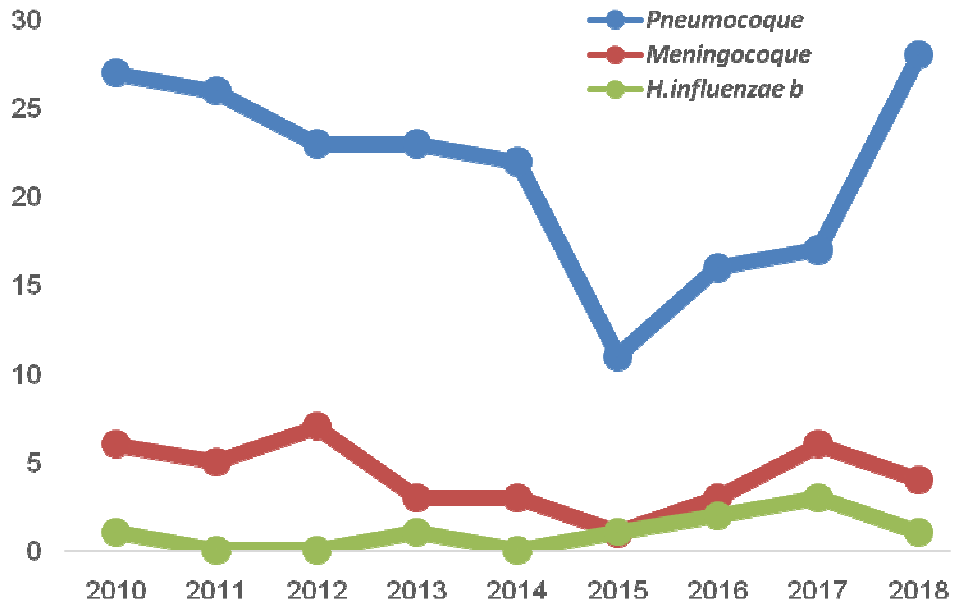

Figure 3: Evolution between 2010 and 2018 according to the species isolated from invasive infections in children at Marrakech University Hospital (n = 248)

Invasive meningococcal infection in children at the University Hospital of Marrakech between 2010 and 2018:

During this period, 42 invasive Meningococcal infections were documented. These meningococcal II were dominated mainly by meningitis in 86% of cases followed by bacteremia in 14% of cases.

The strains were isolated in 86% of cases in meningitis. The evolution between 2010 and 2018 showed a slightly stable fluctuation of meningitis cases with a decrease between 2017 and 2018. These II to MC prevailed in children under one year and from 1 to 4 years in 76% of cases . In fact, these II affected mainly the child of less than 1 years in 48% of cases, the child between 1 and 4 years in 28% the child between 4 and 10 years in 17% and the child over 10 years in 7% of cases.

Group B meningococcal infections accounted for 81% of invasive meningococcal infections at Marrakech CHU in children. The serogroup distribution showed the predominance of serogroup B with 81% of cases. The other serogroups W (4%), C (4%) and A (2%) remained in the minority compared to serogroup B (Figure 4). Only one strain showed resistance to Penicillin G and all strains remained sensitive to cephalosporins. third generation and Fluoroquinolones.

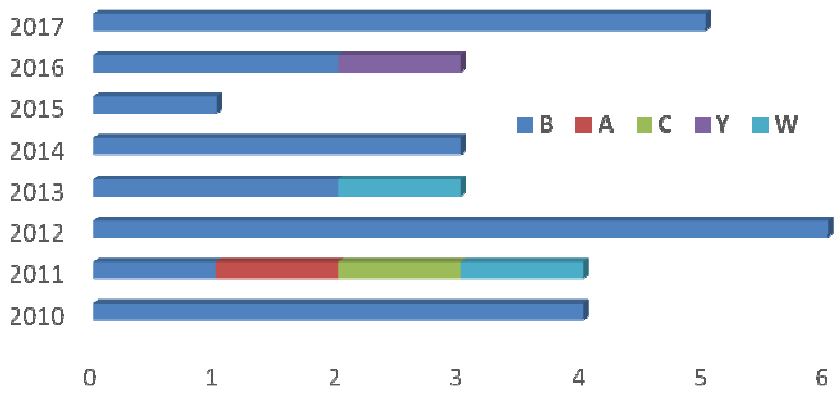

Figure 4: Distribution of meningococcal meningitis in children according to the serogroupes child at the University Hospital of Marrakech (n = 44)

Invasive infection with H.influenzae in children at the CHU of Marrakech between 2010 and 2018:

During this period, II to H. influenzae b accounted for 7% of all II in children, represented mainly by meningitis, 7% of meningitis and 2% of all bacteremia recorded during this period. period. The most affected age group was the child under 8 months of age in 84% of cases. A single strain responsible for meningitis produced ß-lactamase and also had decreased sensitivity to penicillins. Slightly stable fluctuations were found for these H. influenzae II between 2010 and 2018.

Invasive pneumococcal infection in children at the University Hospital of Marrakech between 2010 and 2018:

During this period, 204 Pneumococcal invasive infections were documented, with 55% of all IIs

taking first place. Pneumococcus was responsible for 84% of bacteremia, 54% of meningitis and 100% of pleurisy.

These Pneumococcal IIs predominated in children under one year of age in 48% of cases followed by children aged 4 to 10 years in 33% of cases, children between 1 and 4 years in 18% and child over 10 years old in 2% of cases. The pneumococcus has touched a little more the child over 4 years old in recent years.

During this period, the frequency of meningitis has increased steadily and continuously since 2015. Between 2010 and 2017, 52 strains isolated from the LCS were serotyped. The relative frequency of different serotypes and the analysis of their distribution was carried out by year of study between 2010 and 2018.

The predominant serotypes in meningitis were serotypes 23F (vaccinal), 15 (non-vaccinal), 19NA NB (non-vaccinal), 3 (PCV13 vaccine), 19A (PCV 13 vaccine). Several other non-vaccine serotypes were increasing compared to 2010, such as serotypes 15, 19NA NB, 11A and 12F. The vaccine serotypes fell sharply between 2010 and 2018 and from 2015, no vaccine serotype was found in meningitis in children. The serotypes included in PCV 13, 3, 19A and 6A remained between 2010 and 2018. (Figure 5)

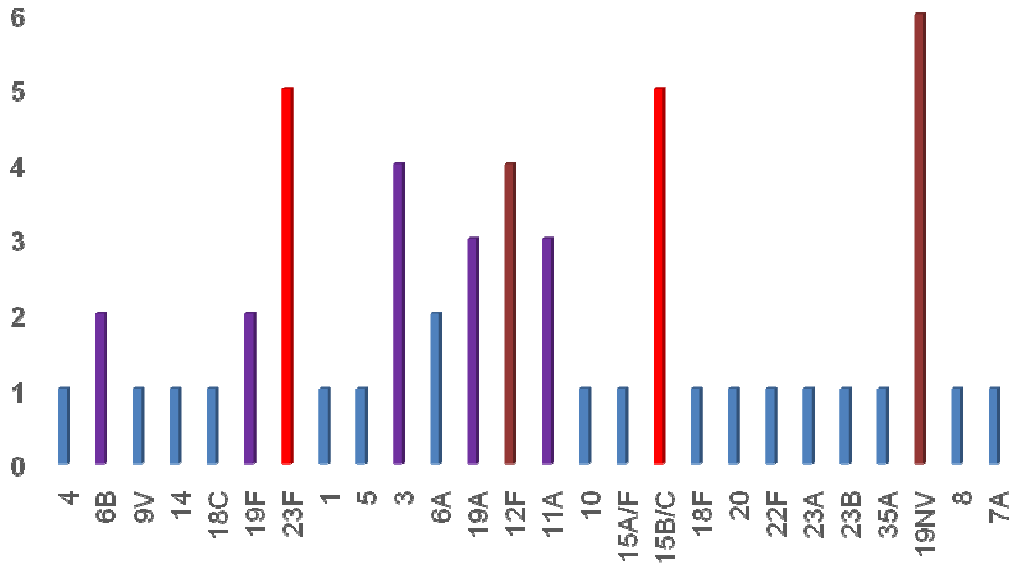

Figure 5 Distribution of Pneumococcal serotypes isolated from meningitis in children at the University Hospital of Marrakech between 2010 and 2018 (n = 54)

In children, a very significant regression of serotypes covered by PCV10 meningitis was found between 2010 and 2014 ranging from 75% in 2010 to 14% in 2014 with a disappearance of serotypes covered by PCV 10 from 2015.

Penicillin-reduced susceptibility strains accounted for 23% of all isolates. These strains were mainly found in non-vaccine serotypes. No C3G resistant strain was isolated. (Table I)

Year	strain of SDP	Penicillin-sensitive strain	Serotypes of SDP strains
2010	2	8	19A*-15C
2011	1	4	11A
2012	3	3	14-5-19A
2013	1	6	12F
2014	3	4	3*-20-23F
2015	-	3	-
2016	-	4	-
2017	2	4	15-10
2018	0	8	-

Table I: Distribution of Serotypes isolés of Pneumococcal Meningitis by Penicillin Sensitivity

DISCUSSION

II due to Pneumococcal, Meningococcal or H. influenzae is the consequence of carriage in the upper airways and in the normal state, the natural defenses quickly rid us of these carriers bacteria. When the invasive infection is going to settle, it will be done in several stages: the translocation of the mucous membrane towards the blood, the resistance to the defenses of the organism, the multiplication in the blood and the eventual crossing of the blood barrier meningeal with multiplication in the cerebrospinal fluid.

The main risk factor is to carry a strain in which the subject does not have natural or vaccinal immunity and especially if it is hyper-invasive. Only encapsulated strains are responsible for these II. The capsule protects the strain against desiccation, phagocytosis and complement-mediated bactericide, which promotes colonization and transmission.

The other risk factors are represented by young age, immune immaturity, concomitant respiratory infections that weaken the respiratory mucosa and promote colonization and invasion.

The objectives of bacteriological confirmation are of a diagnostic and epidemiological nature. This diagnosis confirms the bacterial etiology of these II by identifying the bacterium in question to better adapt the treatment. These bacteria can be extremely virulent and some may be associated with increased severity of infection, which may influence the patient's load.

The bacteriological diagnosis makes it possible to determine the preventive measures to take in the entourage of the patient vaccination or chemo prophylaxis. It also helps to identify the epidemic risk of cluster cases or when there is an increase in the incidence of cases.

The diagnosis of II is discussed in front of the clinic and confirmed bacteriologically by laboratory examinations, direct examination, culture or molecular biology.

It is important to establish the etiological diagnosis of II which involves the isolation and identification of the bacterium, the study of antibiotic sensitivity, serogroup determination and strain typing.

This monitoring, based on data from the Microbiology laboratory, recorded 248 cases of bacteriologically confirmed invasive infections. Pneumococcal II took first place with 55% of the germs responsible for II in children, followed by meningococcus. Meningitis and bacteremia were the two most common infectious sites.

These invasive infections were more common in winter and early spring. This seasonal variation of these infections would be related to seasonal viral infections, which would play a facilitating role. It is commonly accepted that these II occur, at the same time or slightly offset in time, with winter epidemics (1). These II mainly affected the child under 4 years in 71%. This is consistent with literature data or incidence is higher in young children.

Invasive meningococcal infections are serious and epidemic. They mainly include meningitis, acute meningococcemia including purpura fulminans. These are infections that are very often life-threatening and require treatment in extreme urgency. During this period, meningococcal II accounted for 38% of all II and were predominantly meningococcal in 86% of cases, which is consistent with literature data, or meningococcal meningitis accounts for 77% of II meningococcus (2). A slightly stable fluctuation of cases of confirmed meningitis on culture was found with a decrease in cases between 2017 and 2018. They mainly affected children under one year and 1 to 4 years. Several studies report that the most affected age group is between 0 and 1 years (2,3,4). Group B meningococcal infections accounted for 81% of invasive meningococcal infections at Marrakech CHU in children. Similar data are reported in a French study where serogroup B accounted for 64% of serogroups diagnosed with meningitis (3). All strains isolated from 2017 were serogroup B. Only one strain showed resistance to Penicillin G and all strains remained susceptible to third generation cephalosporins and fluoroquinolones. Several studies also report percentages of penicillin-like resistance and conserved susceptibility to cephalosporins (3).

The widespread use of Hib vaccination has upset recognized epidemiological patterns, resulting in a significant decrease in the incidence of invasive manifestations, particularly meningitis. In terms of invasive infections in children, H. influenzae b occupies only a discrete place or 7% of meningitis of the child at the University Hospital of Marrakech, which is consistent with the data from the literature which also report an almost disappearance of meningitis due to H. influenzae b in children (5,7)

During this period, 9 strains of H. influenzae b were isolated in children less than 1 year old, and one strain in a 4-year-old child, 7 in meningitis and 3 in bacteremia. A French study of meningitis in H. influenzae ba found that these Hib infections were observed mainly in children between 3 months and 3 years (6). Indeed, Hib meningitis can be observed either before vaccination in children who have not yet received the first injection or after the injection of one to 3 doses of vaccine within 1 month. These meningitis have not been explored immune.

A single strain responsible for meningitis produced ß-lactamase and also had decreased sensitivity

to penicillins.

Pneumococcal II are also common and severe. Pneumococcal infections are often severe and severe. The serotypes in question are preferentially "porting" serotypes that colonize the nasopharynx of young children and these strains are responsible for more than 75% of severe pneumococcal infections in children. During this period, Pneumococcal IIs were the first placard in the II in children and were dominated mainly by bacteremia followed by meningitis.

The introduction of VPC13 vaccine in October 2010 and VPC10 in July 2012 in the National Infant Immunization Program was followed by a decrease in invasive pneumococcal infections between 2010 and 2015. This during a gradual increase was observed from 2015 and continued until 2018.

These pneumococcal meningitis have mainly affected young infants, in particular less than 6 months old, too young to be vaccinated or given an insufficient number of doses. In recent years, their frequency has increased among those over 4 years old.

The vaccine serotypes fell sharply compared to the period 2010 - 2014. The serotypes of PCV 13 are maintained in particular serotype 3 and 19 A. In fact, serotypes3, 6A and 19A are no longer covered by the vaccine since 2013.

Several other non-vaccine serotypes were increasing compared to 2010, such as serotypes 19 No A and No F, 11A, 12F and 15.

As of 2015, no PCV10 vaccine serotype was found in meningitis. On the other hand, an increase in the number of non-vaccinal serotypes has been found with a high serotypic diversity. Streptococcus pneumoniae reacts to the vaccine pressure by a phenomenon of "capsule switching" or "capsule replacement". The vaccine puts pressure on the new bacteria that have switched and will select virulent and invasive variants. There is a major serotypic replacement that has been observed.

Strains of penicillin-reduced susceptibility accounted for 23% of all isolates and were found mainly in non-vaccine serotypes, which is consistent with a 2011 study in France of invasive pneumococcal infections in which the percentage of Pneumococcal strains of susceptibility decreased to penicillins was 16% (8).

All pneumococcal strains isolated during this time were C3G sensitive, consistent with the results of the same study (8)

This epidemiological surveillance of the identified serotypes made it possible to evaluate the impact of the 10-valent pneumococcal conjugate vaccine (valences 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) introduced in the immunization schedule. since July 2012 that replaced the 13-valent vaccine introduced in October 2010.

Globally, pneumococcal infections dominated the profile of these II and meningitis accounted for a large proportion, mainly affecting children under 4, which is not consistent with the 2011 French study on Pneumococcal II was noted with a marked decrease in pneumococcal II in children aged between 0 and 2 years after the introduction of the 7-valent conjugate vaccine (8).

Between 2010 and 2018, there was an increase in the prevalence of invasive pneumococcal infections from 2015. However, a gradual and significant decrease in invasive infections with serotype vaccines was found over this period. Thus, there was a decrease in pneumococcal meningitis serotype (PCV10) and a replacement related to the progressive increase in pneumococcal meningitis of non-vaccinal serotype in all age groups. The serotypes of invasive infections are now quite different non-vaccine serotypes (23A, 3, 15, 10, 19 No A and No F and 12F) which is

consistent with data from the literature where there is a replacement in France for vaccine serotypes by non-vaccine serotypes including 24F and 19 Non A and Non F (8,9).

CONCLUSION

In the field of invasive infection in children at the University Hospital of Marrakech, the problem mainly arises with Pneumococcal meningitis with non-vaccine serotype and meningococcal meningitis with serogroup B.

Continuous surveillance of carriage and pneumococcal infection will be essential to monitor the impact of PCV10 use in children, including early detection of alternative serotypes, trends in antimicrobial resistance, and indirect effects. potential.

The geographical diversity of serotypes and the evolution of Pneumococcal epidemiology underscore the importance of this continuous surveillance of pneumococcal serotypes in order to guide vaccine recommendations.

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