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Invasive *Haemophilus influenzae* Type b (Hib) Infections in Children in the Pediatric Department of the University Hospital Gabriel Touré (UH-GT)

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Abstract

Introduction: According to Mali's National Immunization Center, the *Haemophilus influenzae* b (Hib) vaccine coverage rate was 90% in 2015. Our work aimed to study invasive bacterial infections due to *Haemophilus influenzae* type b in children aged 0 - 15 years hospitalized in the pediatrics department of the UH-GT. **Method:** We carried out a retrospective descriptive study from January 2017 to December 2018 (*i.e.* 2 years) among children aged 0 - 15 years and hospitalized for *Haemophilus influenzae* type b infection confirmed by culture (blood culture, Cerebro-spinal Fluid, and pleural and skin fluid). **Results:** Thirty-three cases of Hib infections were collected giving a frequency of 0.2% and the age group 3 months to 3 years was the most affected (72.73%). Children who received no vaccine accounted for 21.21%. The Cerebro-spinal Fluid culture and other samples (pleural and skin) identified the bacterium in 100% of cases, against 72.72% in the blood culture Meningitis was the most frequent pathology (78.79%) and the lethality was high (21.21%). **Conclusion:** Despite the introduction of the Hib vaccine in the routine immunization program in Mali, Hib infections remain with a high lethality linked to meningitis.

Keywords

Invasive Bacterial Infections, *Haemophilus influenzae* b, Children, Pediatrics

1. Introduction

According to the World Health Organization (WHO) estimates [1], Hib still causes at least 3 millions cases of serious illness and nearly 386,000 deaths yearly, the vast majority of them in developing countries and therefore with low immunization coverage. WHO recommends the inclusion of Hib vaccination in all routine infant immunization programs with a 3-dose primary schedule with or without a booster dose or 2 primary doses plus a booster dose [2]. At the end of 2007, more than 122 countries have introduced the vaccine into their childhood immunization programs according to WHO [2]. The impact of vaccination on the incidence of invasive Hib infections was a dramatic decrease of more than 95% in the first years after its implementation [3]. In fact, invasive Hib pathologies have practically disappeared in many industrialized countries and their incidence has dropped dramatically in countries where vaccination coverage is satisfactory. It is estimated that 92% of children in industrialized countries are immunized against Hib, while the immunization rate is estimated near 42% in developing countries and 8% in least developed countries mainly in sub-Saharan Africa [1] [4].

In Mali, hospital surveillance of invasive bacterial diseases carried out by the Center for the Development of Vaccines (CVD-Mali) since 2002 has revealed a high incidence of invasive disease due to *Haemophilus influenzae* type b [5]. The results of this surveillance led to the introduction of the Hib conjugate vaccine into the Expanded Immunization Program in July 2005.

After the introduction of vaccination annual confirmed Hib hospitalizations in infants from 0 to 11 months decreased from 175/100,000 to 44/100,000 and in infants 6 - 7 months from 377/100,000 to 69/100,000, *i.e.* a decrease of 82% [6]. According to the National Immunization Center of Mali, the Hib vaccination coverage rate was 90% in 2015 [7]. Ten years after the introduction of the Hib vaccine, we thought it appropriate to do a study on invasive bacterial Hib infections in pediatric environment.

2. Methodology

Our study was carried out in the pediatrics department of the UH-GT, a tertiary hospital located in the center of the city of Bamako.

This was a retrospective and descriptive study involving children aged from 0 to 180 months, admitted for a confirmed bacterial infection by Hib between January 1, 2017 to December 31, 2018 (*i.e.* 24 months).

Included were any patient with confirmed bacterial Hib infection either in cerebro spinal fluid (CSF), blood culture, or any other sample. This is a comprehensive sample of all children 0 to 180 months of age hospitalized during the study period for confirmed *Haemophilus influenzae* b infection. We developed a survey formulary that allowed us to collect data from hospitalization records, the inclusion register of participants in the pediatric unit of the Center for Vaccin Development (CVD) and the laboratory results register.

The variables studied were: epidemiological, clinical, biological, therapeutic and evolutionary characteristics.

Data analysis and processing was performed on SPSS software version 20.0. Chi-square and Fisher statistical tests were used. Data confidentiality was respected.

3. Results

3.1. Sociodemographic Characteristics

During the study period 33 cases of confirmed invasive infections with *Haemophilus influenzae* type b were identified out of a total hospitalization of 16 228, giving a frequency of 0.2%.

The 3 - 36 months age group was the most represented (72.73%) with an average age of 6 months and extremes of 2 to 156 months. The Boys:Girls ratio was 1.75. More than half of our sample (55.55%) resided in Bamako. The peak of admission was in December. A proportion of 54.55% was correctly immunized and 21.21% have no vaccine according to the vaccination record

3.2. Clinical and Biological Characteristics

Febrile convulsion was the most frequent reason for consultation with 27.27% followed by respiratory distress with 21.21% and meningeal signs (18.18%). Fever was observed in the majority of patients (72.72%), and the mean temperature at admission was 38.4˚C. Malnutrition was associated with Hib infection in 33.33% of cases, with HIV infection in 6% of cases. Bacterial meningitis was the most common diagnosis (78.79%), followed by sepsis (9.09%) and pneumonia (6.06%).

The rate of isolation of the bacterium in the CSF, pleural effusion and cutaneous lesions was 100%, but it was 72.72% on the blood culture.

3.3. Evolution

The average length of hospital stay was 11 days with extremes of 1 to 31 days. The case mortality was 21.21%.

4. Discussion

During the study period 33 cases of confirmed invasive infections with *Haemophilus influenzae* type b were identified out of a total hospitalization of 16,228 giving a frequency of 0.2%. Sow *et al.* [6] in Mali reported a decrease of incidence and hospitalization due to Hib after the introduction of the pentavalent vaccine in July 2005 with hospitalizations going from $377/10^5$ to $69/10^5$. In Egypt, the number of confirmed cases of Hib meningitis is 23/100,000 among children under 5 years [8]. Also David W *et al.* [9], reported that the *Haemophilus influenzae* type b conjugate vaccine reduced the annual number of cases of *H. influenzae* type b meningitis in children. Although the prevalence of *Haemophilus influenzae* infection significantly decreased, 21.21% of the children did not re-

ceive any vaccine according to the vaccination schedule. In 2007, *Haemophilus influenzae* B vaccine coverage was 96.7% in Burkina Faso [10], 68% in the Gambia [11]. This situation urges health authorities to strenghten their efforts to immunize children who still miss the immunization program (Table 1).

Classically the authors divide the ages of children into three groups: less than one year old, one to five years old and more than five years old. We preferred the distribution in less than three months, three months to three years, three years to five years and more than five years. This subdivision is based on the evolution of anti-Hib antibody titers in children (Tables 2-5).

Table 1. Sociodemographic characters in the sample of 33 patients with *Haemophilus influenzae* type b infection.

Sociodemographic characters	Number (n = 33)	%
Age in months		
0 - 3	5	15.15
3 - 36	**24**	**72.73**
36 - 59	2	6.06
60 and more	2	6.06
Sex		
Boys	21	36
Girls	12	64
Residence		
Bamako	18	54.55
Outside Bamako	15	45.45
Immunization according PEV*		
Up to date	**18**	**54.55**
Not up to date	8	24.24
No immunization	7	21.21

*Programme élargi de vaccination: extendend immunization program.

Table 2. Distribution of the patients according to consultation reason in the sample of 33 patients with *Haemophilus influenzae* type b infection.

Reason for consultation	Number	%
Convulsion with fever	**9**	**27.27**
Respiratory distress	**7**	**21.21**
Meningeal signs	**6**	**18.18**
Fever	5	15.15
Skin tumor	2	6.06
Acute severe Malnutrition	2	6.06
Others*	2	6.06
Total	**33**	**100**

Others: 1 case of palor and 1 case of anuria.

Table 3. Patients distribution based on labor assessments in the sample of 33 patients with *Haemophilus influenzae* type b infection.

Labor test	Results in %	
	Positive	Negative
Cultur of meningeal fluid	100	0
Other testz (pleural and skin)	100	0
Blood culture	72.72	27.28

Table 4. Patients distribution according to diagnosis in the sample of 33 patients with *Haemophilus influenzae* type b infection.

Diagnosis	Number	%
Meningitis	**26**	**78.79**
Sepsis	3	9.09
Pneumonia	2	6.06
Pleural effusion	1	3.03
Myositis with abcess	1	3.03
Total	**33**	**100**

Table 5. Distribution of evolution in the sample of 33 patients with *Haemophilus influenzae* type b infection.

Evolution	Number	%
Full recovery	**19**	**57.57**
Death	**7**	**21.21**
Discharge against medical advise	7	21.21
Total	**33**	**100**

The 3 - 36 montha age group was the most represented with 72.73%. This age group was largely found by CISSE in Dakar with 92% [12]. These results confirm that Hib meningitis is typically a disease of young children. In addition, they establish the correlation between anti-Hib antibody titers and the frequency of Hib infections in children. Indeed, before three months the child is protected by maternal antibodies. Between three months and three years of age, the child has lost maternal antibodies and his immune system does not produce enough antibodies. Therefore, they are more exposed to infections including Hib. Between the ages of three and five, a child is still protected because his immune system hasprogressive implementation. After five years, antibody titers are at their maximum and its protection is complete in the absence of any immune deficiency [13].

Hib is endemic with periods of recrudescence without significant impact of temperature and rainfall. Indeed, Sow *et al.* [6], had already reported the non-seasonality of *Haemophilus influenzae* b infection in Mali. On the other hand, Diawara A. *et al.* reported that the distribution of the disease was higher during

the dry season (November-April) (51.0%) than during the rainy season (May-October) (49.0%) [14].

Camara B. *et al.* [15] observed that Hib meningitis is encountered throughout the year with a peak occurring between January and March, that is, during the dry and cold season.

In sub sahara Africa, the cold season is very favorable to the expansion of Ear-Nose-Larynx and respiratory infections which are the beds of bacterial meningitis. In addition, the chronic carriage of Hib in the nasopharynx of children would explain the onset of the disease throughout the year.

The peak at the start of the dry season in the tropics could be attributed to the sudden change in physiological mechanisms of adaptation to the cold.

Bacterial meningitis was the most common diagnosis (78.79%), followed by sepsis (9.09%), and pneumonia (6.06%). The predominance of meningeal localization of Hib has been reported by several authors [8] [16] [17].

Despite the administration of antibiotics in our health structures due to insufficient laboratory tests, all cases of meningitis were diagnosed by culture of the CSF. Pederson *et al.* [18] in Denmark confirm our result with 100% of cases of meningitis confirmed by CSF culture.

We recorded a lethality of 21.21% less than that reported by Cissé *et al.* in Senegal [12], Tall F *et al.* in Burkina Faso [19] with 32.7% and 26% respectively.

Our high lethality could be explained by: the delay in diagnosis, the weakness of the technical equipement (lack of intensive care units) and co-morbidities (malnutrition in 33.33% of cases, HIV infection in 6% of cases).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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