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# Characteristics of *Haemophilus influenzae* Meningitis Cases in Children Aged 0 to 15 Years in Burkina Faso from 2008 to 2018

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

**Introduction:** Bacterial meningitis done represent a major public health concern especially within the meningitis belt. In 2019, *Hemophilus influenzae (Hi)* was responsible for 8% of meningitis cases in the ECOWAS zone. In Burkina Faso, the vaccine against type b *Hi* was introduced in the broad vaccine program since 2006. The purpose of this study was to study the characteristics of *Hi* meningitis from 2008 to 2018 in Burkina Faso.
**Methods:** We conducted a cross-sectional repetitive study between June and December 2020. We collected all cases of bacterial meningitis due to *Hi* that were confirmed through culture, Gram coloration, PCR, or latex agglutination, and were recorded in the database of the epidemiologic surveillance from January 2008 to December 2018 in Burkina Faso.
**Results:** An overall number of 177 cases of *Hi* meningitis was recorded; *Hi* (4.04%), was the third cause of meningitis after pneumococcus (59.85%) and meningococcus (35.01%). The number of *Hi* meningitis cases declined through the years but still remained high despite a vaccine coverage that almost reaches 100%. The disease is present throughout the year with an outburst during the dry season. The children from 3 months to three years were mostly affected (55.93%) and the "Boucle du Mouhoun" was the region that reported the highest number of cases (18.08%). The stereotypes that were identified included *Hib* (55.38%) and non b *Hi* (14.69%). The disease prognosis was unfavorable in the absence of treatment in 33.39% of cases.
**Conclusion:** Despite the good vaccine coverage, there is a persistence of *Hi meningitis* cases with a number of regions more affected than others. It appears useful to supervise vaccine campaign and conduct immunologic studies on vaccine efficacy on this fragile population that carries the burden of other diseases such as malaria, besides *Hi* meningitis.


*Keywords: Characteristics; meningitis; Hemophilus influenzae; children; Burkina Faso.*

## 1. INTRODUCTION

Bacterial meningitis are dreadful cosmopolite affections; they constitute a major public health concern due to their frequency, mortality rate and dramatic sequalae [1]. They are more concerning in developing countries especially those that are located in the « meningitis belt » where their incidence rate is ten-fold more compared to developed countries [2-4]. Three bacterial species do represent the majority of bacterial meningitis: *Streptococcus pneumoniae*, *Neisseria meningitidis* and type b *Hemophilus influenzae* (*Hi*b) [5-8]. In fact, laboratory results which were reported in 2009 by countries located in the African meningitis belt showed that the pathological germs were mostly made of: *Neisseria meningitidis* (56%), *Streptococcus pneumoniae* (34%), type b *Hemophilus influenzae* (8%) [6]. According to the estimations from World health Organization (WHO), *Hib* has caused 370 000 deaths worldwide, among children below age five during the year 2000 and prior to the vulgarization of the vaccine [9].

In Bobo-Dioulasso, between 1986 and 1990, it was reported that *Hemophilus influenzae* (*Hi*) was the second cause of bacterial meningitis among children as it was isolated in 39.6% in cerebrospinal fluid analysis [10]. Between January 2004 and June 2008, *Hib* meningitis accounted for 42.3% of all diagnosed bacterial meningitis [11]. The WHO recommended that each country may systematically use the vaccine against *Hemophilus* (anti-*Hi*) in the child vaccination program since 2006 and reinforced that statement in 2013 [12,13]. The impact of such vaccination program on the incidence of invasive *Hib* infections was spectacular from the very first years following its implementation [14].

A study assessing the impact of anti-*Hib* vaccine on the incidence course of *Hi*b acute bacterial meningitis in Burkina Faso from 2003 to 2011, reported 48 cases per year in the pre-vaccine period and 6 cases per year in the post vaccine period [15]. In the pediatric ward of Yalgado Ouedraogo University Hospital (YOUH), the annual frequency of *Hib* meningitis went from 35 cases in 2005 to 8 cases in 2006, twelve months after the beginning of vaccination, and down to one case in 2010 [16].

Since January 1st, 2006, the ministry in charge of health in Burkina Faso did introduce the anti-*Hi*b vaccine in the Broad Vaccine Program (BVP). More than 10 years after introducing the anti-*Hi*b vaccine in the BVP, there are few data that show the impact of the vaccine on the

incidence trend of Hemophilus Influenzae meningitis nationwide. We initiated this study in order to show the impact that anti *Hi*b vaccine introduction has on the incidence trend of *Hi*b meningitis in Burkina Faso from 2008 to 2018, by describing the characteristics of the infection during that period.

## 2. METRIALS AND METHODS

### 2.1 Type and Period of Study

we conducted a cross-sectional repetitive survey between June 6th 2020 and December 31st 2020.

### 2.2 Study Population

The study population was made of all children from 0 to 15 years, who had available data in the database of the epidemiologic surveillance section of the department of Population Health Protection (DPHP) of the Ministry of Health and Public Hygiene of Burkina Faso.

### 2.3 Sample and Sampling

We recorded all children meeting the inclusion criteria and the non-inclusion criteria of the study. We included each case of acute bacterial meningitis confirmed through culture, Gram coloration, PCR, or latex agglutination in children aged 0 to 15 years and recorded in the database of the epidemiologic surveillance section of the DPHP from January 1st 2008 to December 31st 2018. We excluded all incomplete recordings from the study (seventeen).

### 2.4 Variables

The variable of interest in our study was the meningitis status (presence or absence). The other variables were made of sociodemographic data (age, gender, health region), clinical data (vaccinal status), paraclinical data (microscopic aspect of the cerebrospinal fluid "CSF", identified stereotypes, methods of identification), and evolutive data (outcoming).

### 2.5 Data Collection

Data were extracted from the database of the epidemiologic surveillance section the DPHP using an anonymous questionnaire. The collected data were typed-in using the Epi-Info software version 7.2.3.

### 2.6 Data Analysis

We first estimated the period prevalence of *Hi* meningitis dividing the compiled number of *Hi* meningitis cases between 2008 and 2018 by the overall number of meningitis cases recorded during the same period. Secondly, we draw a chart of cases per region using the QGIS software. Thirdly, we made a monthly distribution of cases during the period. Fourthly, we made a distribution of cases according to sociodemographic features and vaccinal status. In order to have a better assessment of the impact of vaccine introduction during the period, we built two trend curves that showed the evolution of cases according to children vaccinal status.

## 3. RESULTS

### 3.1. Global Prevalence

During the period of study, 4 380 confirmed cases of bacterial meningitis were reported by the epidemiologic surveillance section (giving a prevalence of 12.42 %; 4380/35 253) with 194 cases of *Hi* meningitis (4.43%) (Fig. 1). Overall, 177 (4.04%) cases of *Hi* meningitis were included.

Overall, 177 (4.04%) cases of *Hemophilus influenzae* meningitis were included. The etiologies of meningitis were dominated by meningococci (59.84%) (Fig. 2).

### 3.2 Distribution of *Hi* Meningitis According to Location

The "Boucle du Mouhoun" region was the most affected (Fig. 3).

### 3.3 Monthly Distribution of Compiled *Hi* Meningitis

The *Hi* meningitis is prevalent throughout the year with outbursts during the first trimester (corresponding to the dry and cold season) and the second trimester (corresponding to the hot season) (Fig. 4).

### 3.4 Distribution According to Sociodemographic Features and Vaccinal Status

The median age for *Hi* meningitis was 12 months; the mode was 3 months with

extremes at 0.17 and 156 months. The age range from 3 months to 48 months was the most affected (47.46%). The sex ratio (H/F) was 0.96. The information on vaccinal status was available for 124 patients. Thirty-two cases of meningitis with completed vaccinal status were notified (Table 1).

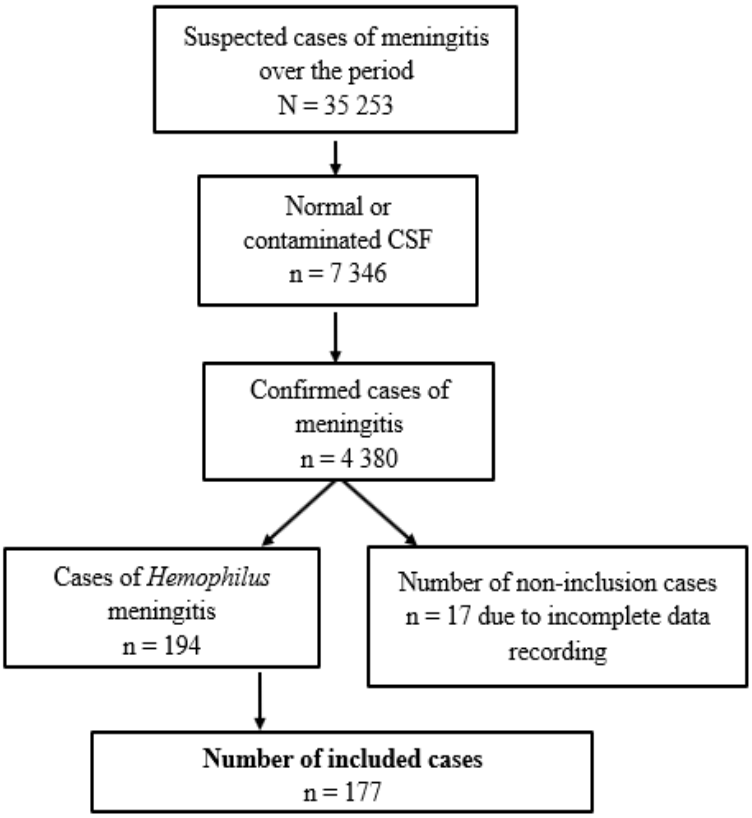


**Fig. 1. Study flow diagram**

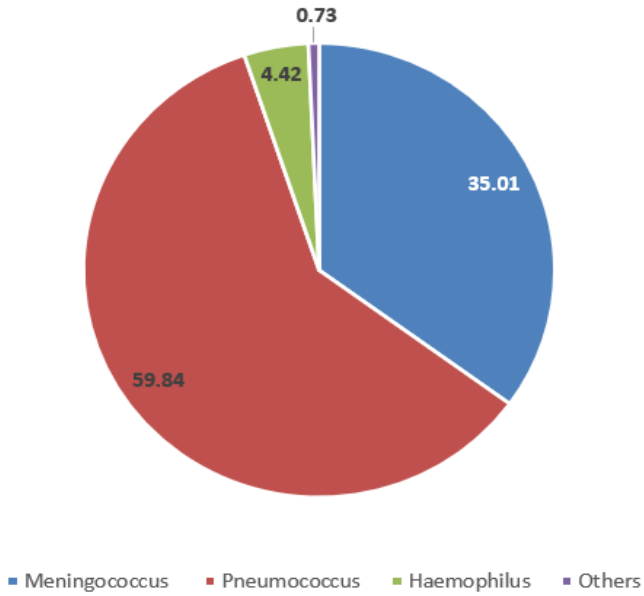


**Fig. 2. Distribution of bacterial meningitis according to identified germs between 2008 and 2018, Burkina Faso**

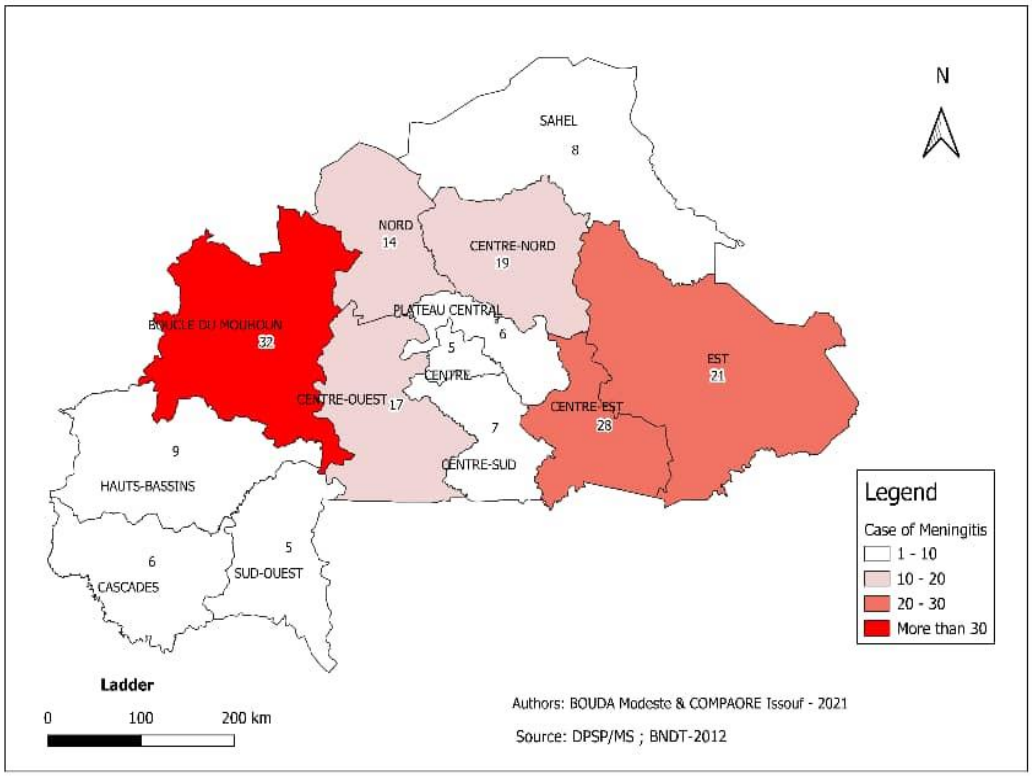


**Fig. 3. Cartography of compiled cases of *Hi* meningitis according to regions from 2008 to 2018**

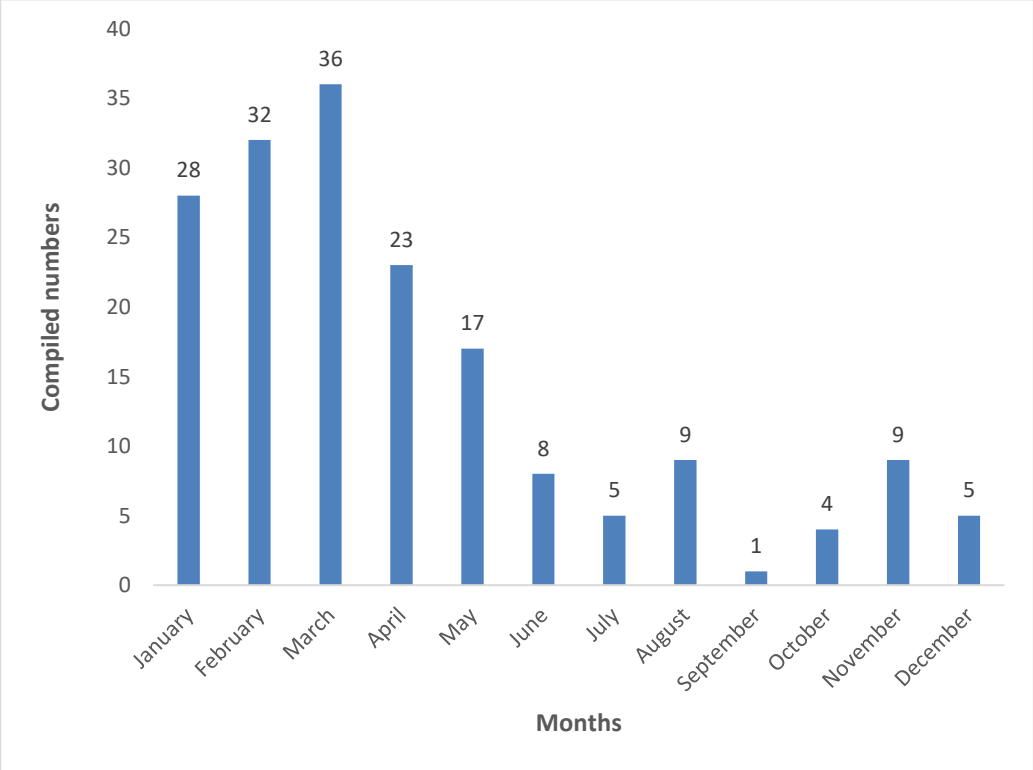


**Fig. 4. Monthly distribution of the 177 compiled cases of *Hi* meningitis from 2008 to 2018**

**Table 1. Distribution of 177 cases of *Hi* meningitis according to age, gender, vaccinal status and serotype**

| Age range | Serotype | | | Overall number |
|---|---|---|---|---|
| | ***Hib*** | **non b *Hi*** | **Undetermined Serotype** | |
| 0 - 5 years | 73 | 23 | 38 | 134 |
| 5 - 10 years | 19 | 02 | 14 | 35 |
| 10 - 15 years | 06 | 01 | 01 | 08 |
| **Gender** | | | | |
| Male | 50 | 16 | 21 | 87 |
| Female | 48 | 10 | 32 | 90 |
| **Vaccinal status** | | | | |
| Completed | 27 | 5 | 13 | 45 |
| Unknown | 20 | 4 | 14 | 38 |
| Uncompleted | 51 | 17 | 26 | 94 |

**Table 2. Features of cerebrospinal fluid**

| Features of CSF | Numbers(n) | Percentage (%) |
|---|---|---|
| **Macroscopic aspect** | | |
| Clear | 21 | 11.86 |
| Bloody | 15 | 8.47 |
| Purulent | 19 | 10.73 |
| Troubled | 126 | 71.18 |
| **Gram Coloration** | | |
| Positive | 128 | 72.31 |
| Negative | 19 | 10.73 |
| Not performed | 30 | 16.94 |
| **Germ identification** | | |
| Culture | | |
| Positive | 93 | 52.54 |
| Negative | 5 | 02.82 |
| Not performed | 78 | 44.06 |
| **Latex agglutination** | | |
| Positive | 113 | 63.84 |
| Negative | 10 | 5.64 |
| Not performed | 54 | 30.50 |
| **PCR** | | |
| Positive | 124 | 70.05 |
| Negative | 0 | 0.00 |
| Not performed | 53 | 29.94 |

**Table 3. Distribution of 177 cases of *Hi* meningitis according to the evolution in relation to their vaccinal status**

| Evolution | Vaccinal status | | | Total |
|---|---|---|---|---|
| | **Completed** | **Uncompleted** | **Unknown** | |
| Favorable | 28 | 50 | 25 | 103 |
| Ongoing | 5 | 8 | 2 | 15 |
| Deceased | 2 | 13 | 2 | 17 |
| Unknown | 10 | 23 | 9 | 42 |

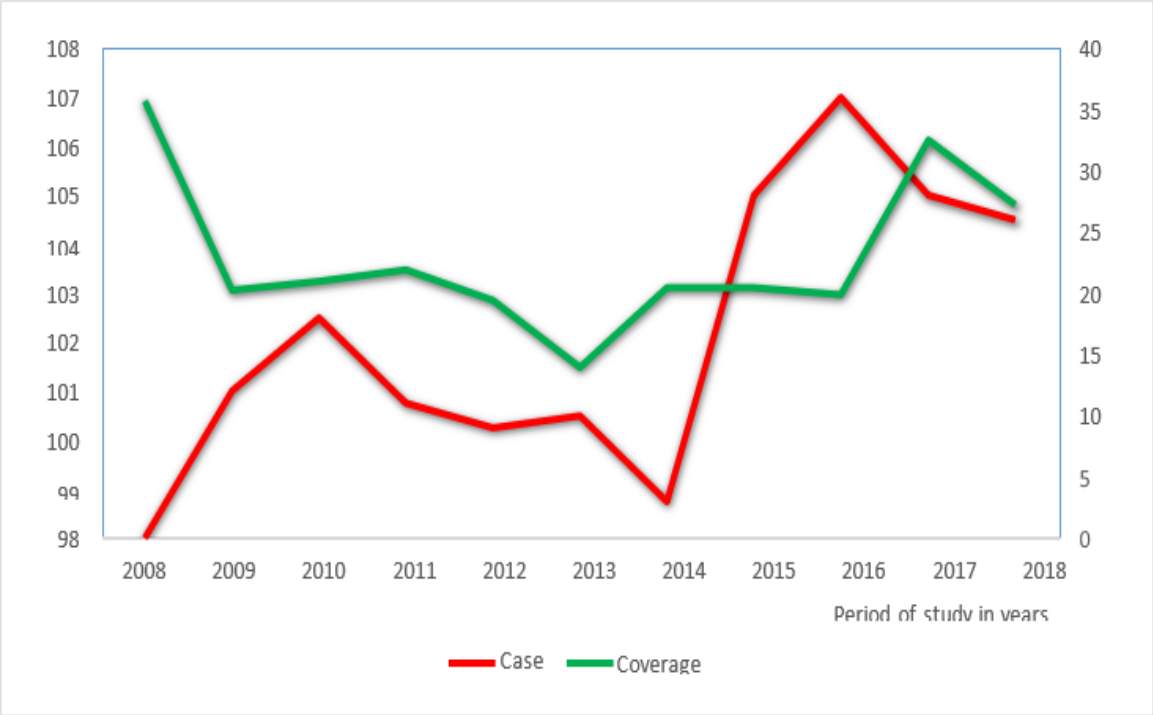


**Fig. 5. Trend curve of vaccine coverage and cases of *Hi* meningitis**

### 3.5 Distribution According to Vaccinal Status of Hi meningitis Cases

The number of cases were increasing as the vaccine coverage went down such as in 2008 but not always (Fig. 5).

### 3.6 Distribution According to Biological Features

The analysis of CSF showed: a troubled aspect in 69.49% of cases (n = 123), Gram negative bacilli (GNB) in 72.31% of cases. Many techniques were used for identification: culture (93/98 positive cultures giving 94.89%), detection of soluble *Hi* specific antigens (113/123 giving 91.86%), PCR (124 cases giving 70.05%) (Table 2).

### 3.7 Distribution According to Evolution

Seventeen patients passed away (9.04 %) and were mainly from the range of 3 month to 2 years (12/17). The outcoming was unknown in 42 cases (23.73%). (Table 3).

## 4. DISCUSSION

During this study that assessed the characteristics of *Hib* meningitis cases after the introduction of anti-*Hib* vaccine in the BVP of Burkina Faso in 2006, we have shown that *Hib* meningitis is still occurring and represents the third cause of meningitis despite the decrease in incidence over time. The disease is prevalent throughout the year with an outburst during the dry season; it affects mainly children from 3 months to 3 years of age. On the geographic hand, the “Boucle du Mouhoun” region was the most affected one.

The mains limitations of this study were the uncomplete data (antibiograms, received treatment …), the differences data collecting forms.

### 4.1 Global Prevalence

The meningitis due to *Hi* germ represented 4.43% of all bacterial meningitis and were ranked the third etiology after pneumococci and meningococci. Its frequency was of 10.22% according to Kaboré [17].

The Hemophilus meningitis is prevalent on an endemic mode with periods of outburst. The majority of *Hi* meningitis cases in our study was observed during the first trimester of the year. Camara et al. [18] in Dakar also reported that seasonal feature.

The climatic conditions during the dry season (cold and dry wind) are favorable to the occurrence of meningitis including *Hib* ones [10].

In our series, the population was mainly made of children. In fact, *Hi* meningitis does affect children between 3 months and 3 years of age. The decrease in the titer of the anti-PRP in the infant, from two months after birth up to three years, do favor the occurrence of the disease [19].

### 4.2 Distribution of Meningitis Cases

The “Boucle du Mouhoun” region had recorded the highest number of *Hi* meningitis cases and the central north region the highest number of non-b *Hi* meningitis during the period of our study. Although the “Boucle du Mouhoun” region was reported to be the most affected in the study of Bocoum in 2008 [20-22], a socio-anthropological study would be helpful in order to assess the reasons of such findings. The variation in vaccine coverage could be explained by the closure of centers for health and social promotion due to insecurity.

### 4.3 Vaccine Coverage

A number of cases had received zero anti-*Hi* vaccine (53.11%). In the survey from Kaboré [17], 58.82% of children did not receive a single dose of anti-*Hi* vaccine. In Italy, Giufrè and coll [23-25] had found the same pattern (a diminution of vaccine coverage between 2014 and 2016 and an increase in incidence from 2016 to 2018). The campaigns that seek to mobilize and increase vaccine acceptation should be duplicated in order to have the adhesion of populations. The security concerns in Burkina Faso make it difficult to conduct vaccine campaigns properly. Moreover, 25.42% of immunized patient according to their age had received 3 doses and the vaccine coverage during the study period was above 100% in almost every zone. Adegbola in Gambia [26] reported an efficacy of 94% [62 - 99%] after the secund dose of anti-*Hi*b vaccine. The occurrence of *Hi*b meningitis in children who were properly immunized could be due to vaccine failure, or the emergence of non b serotype or simply an overestimation of vaccine coverage. Few cases have been reported in the literature [14].

### 4.4 Biological Aspect

The trouble aspect of CSF which is typical of bacterial meningitis is related to the increase in number of destroyed neutrophils. Our results showed that more than 50% of CSF had a troubled aspect just as reported in the literature [6]. We also found polymorphic GNB in 71% of patients in our series. Ouedraogo [16] had noticed that the gram coloration was positive in 90.47% of cases in his series. The lower performance of gram coloration could be linked to the technique used by the performer, the time lag before consulting, the fluid draw after the onset of an antibiotic treatment.

The detection of *Hib* specific soluble antigens (91.86%), the culture (94.89%) and the PCR (70.05%) were the labs exams performed for etiologic diagnosis. They had different level of performance and were combined for more efficacy given that PCR was not readily available in our context. In fact, Kaboré [17] had reported a performance of 66.67% through the detection of *Hib* specific soluble antigens, and Pop-Jora and Coll reported 100% through sample culture [27,28]. The lab performer, the antibiotic treatment prior to lumbar punction could have an influence on the results of etiologic diagnosis depending on the technique that was used.

### 4.5 Evolution

We recorded 17 cases of death (9.60%). This death rate varies according to study authors: 21% for Kaboré [17], 27% for Tall [10]. The improvement of vaccine coverage throughout the country could help reduce the number of *Hi* meningitis cases as well as related death rate.

## 5. CONCLUSION

Despite the reduction of the *Hi* meningitis prevalence thanks to immunization, the disease is still occurring in Burkina Faso. The regions of “Boucle du Mouhoun” and Central North were the most affected places. Additional investigations are necessary to determine the causes of such findings in middle term. A broader vaccine coverage could help reduce the disease prevalence in short term despite the security concerns.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

## CONSENT

As per international standards, parental written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

The study received the approval of the YOUH institutional committee. We were also granted an administrative authorization from the Ministry of Health and Public Hygiene in order to use the database of the epidemiologic surveillance section of the DPHP. Throughout the process of extracting and using the data, we worked anonymously in order to guarantee the confidentiality of data from the database.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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