

Case-by-Case Surveillance for Bacterial Meningitis in Benin: Data Analysis, 2016 to 2018

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Abstract

Background: Bacterial meningitis is an inflammation of the meninges caused mainly by three bacterial species *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae* that are transmitted by nasopharyngeal secretions emitted by carriers. Meningitis is a public health problem in Benin, like all countries in the African meningitis belt. This study aims to analyze the epidemiological surveillance data of meningitis in Benin from 2016 to 2018. **Methods:** Each suspect case of meningitis was recorded and Cerebrospinal Fluid (CSF) samples were collected. CSF collection was accompanied by the Integrated Disease Surveillance and Response form. This sheet provides information on the patient's social-demographic and epidemiological data. CSF specimens were sent to the laboratory for analysis and identification (Gram stain, biochemical parameters, and latex agglutination test) of pathogens according to the WHO standards. **Results:** Of the 2992 patients with suspected meningitis, 2893 were hospitalized with a death rate of 9.4% (281/2992). The sex ratio of registered patients was 1.29 in favor of men. The median age was 4 years (min: 0; max: 90). Patients younger than five years were the most represented (44.8%). During the study period, there was a decrease in the incidence of meningitis per 100,000 inhabitants (6.3 to 3.2 from 2016 to 2018). Of 2928 CSF samples collected we were able to identify 899 pathogenic bacterial species. The most represented species are

S. pneumoniae (63.4%), *N. meningitidis* (24.4%) and *H. influenzae* (12.2%).

Conclusion: The burden of disease is disproportionate in the northern departments as in others. The frequency of bacterial meningitis in the northern region increased during the study period. However, deaths have been recorded in the departments of the South (“Atlantic”, “Plateau”). This suggests an improvement in epidemiological surveillance and case management throughout the national territory.

Keywords

Benin, Meningitidis, Epidemiologic Surveillance, CSF, Bacterial Meningitidis

1. Introduction

Generally caused by infectious agents such as bacteria, fungi, viruses, parasites and rickettsia, meningitis is an acute inflammation of the brain’s meninges. The disease is called cerebrospinal meningitis (CSM) if the meninges of the brain and spinal cord are involved [1]. It is an epidemic-prone disease that affects a significant proportion of the world’s population if it is caused by a *Neisseria meningitidis*. The case fatality rate can reach 50% in the absence of treatment [2]. The most common form of meningitis is bacterial meningitis [3]. Meningococcal meningitis is caused specifically by the type species called *Neisseria meningitidis*. *Haemophilus influenzae* (type b, Hib), *Streptococcus pneumoniae*, *Neisseria meningitidis*, and group B streptococci is common agents of bacterial meningitis [4]. Meningitis is characterized by symptoms ranging from fever, headache, stiff neck, photophobia, and muscle aches to vomiting and diarrhea [2]. The epidemics of meningitis affect about 14 countries in sub-Saharan Africa including Benin, grouped together in the “African meningitis belt” [5]. The disease is a threat to public health in Africa. During the period 1993-2012, nearly one million suspected cases were reported, including 100,000 estimated deaths [6]. The bacterial form, caused by the meningococcal *Neisseria meningitidis* type A, predominates in Africa with 80% to 85% of cases, especially between 1 and 30 years [7]. Infections are particularly serious and can be fatal in the absence of adequate antibiotic treatment. The mortality rate varies from 16% to 37% in adults and the neurological sequelae occur in 30% to 52% of survivors. Children with meningitis attacks die in 2% to 15% of cases and 10% to 15% of survivors have various sequelae [8]. As a result, prompt treatment is recommended, especially in children [9].

In Benin, the incidence of meningitis in the “Atacora” and “Donga” departments was 71 to 619 per 100,000 inhabitants in 2004 with a case fatality rate (CFR) of 3.1% [10]. In 2003, Benin and other African countries were supported by the World Health Organization and the Meningitis Vaccine Project, a joint WHO/PATH initiative in the establishment of a strengthened surveillance network for meningitis [3]. The surveillance system is well organized with standard

operating procedures to improve the recording and management of data on suspected cases notified each epidemiological week or daily during outbreaks by peripheral health centers and hospitals, to those Responsible for Epidemiological Surveillance Centers (RESC) of the health zones that transmit them by telephone or e-mail to the authorities (national level) through the Departmental Service of Public Health [11]. The collected cerebrospinal fluid (CSF) specimens accompanied by a notice card containing the patient's personal information and the corresponding clinical information are sent by the hospitals' laboratories after manipulation to the bacteriology section of the Ministry's National Public Health Laboratory of Health for confirmation. Despite this structured system, Benin does not have complete epidemiological information on meningitis. It is to remedy this situation, that in collaboration with the Department of Epidemiology and Health Surveillance of the borders, port and airport (DEHS) of the National Direction of Public Health (NDPH), Ministry of Health that we initiated this study. It aims to know epidemiological profile of meningitis in Benin during the period from 2016 to 2018 and to identify the population at risk in the framework of the planning of the best activities of preparation and response to a possible epidemic outbreak.

2. Material and Methods

2.1. Study Area

This study was conducted in Republic of Benin. It is a coastal country of West Africa, with an area of 114,763 km². Annual average temperatures range from 26 to 28°C in the country. The climate is subequatorial in the south, humid tropical transition in the center and tropical dry in the north [12]. The population was estimated at 9,983,884 inhabitants in 2013 [13], including 51.2% of females. About half of the population is over 15 years old. The health system has a pyramidal structure, modeled on the administrative division. It has 3 levels: central, intermediate and peripheral [14]. The peripheral level is represented by the health zone whose head is the Medical Coordinator of the Health Zone while the intermediate level is represented by the department with as head, the Departmental Director of Health. At the central level, it is represented by the Ministry of Health, which is the level of design and decision-making in health sector development policy.

2.2. Methodology

We conducted a prospective, descriptive, targeted surveillance study that relied on data collected from suspected meningitis cases notified to epidemiological surveillance centers across Benin between January 1, 2016 and December 31, 2018.

2.3. Data Collection

Included in the study were all patients with a high sudden-onset fever (rectal

temperature > 38.5°C or axillary > 38.0°C) and one of the following signs: stiff neck, impaired consciousness or other meningeal signs throughout the national territory and from which a sample of Cerebrospinal Fluid was collected.

After identifying a suspected case of meningitis, the collection of Cerebrospinal Fluid (CSF) was sent to the hospital laboratory for analysis; and is accompanied by the completed Integrated Disease Surveillance and Response form. On this form, the social (age, sex and area of origin) and clinical (patient hospitalized or not, the type of case, appearance of CSF samples, vaccinated or non-vaccinated patient) information of the patient was recorded.

In the case where the zone hospital did not have a bacteriology section in its laboratory, the samples were put on Trans-Isolat transport medium and sent to the departmental laboratories having a bacteriology session within 48 hours at most. All samples are then sent to the National Public Health Laboratory (LNSP) for bacteriological analysis for confirmation and identification of bacterial species.

2.4. Bacteriological Analysis of CSF Samples

Macroscopic examination of CSF samples was performed and samples were classified into four categories: clear, turbid, xanthochrome and hemorrhagic. Gram stain was performed on samples for looking for Gram-negative Cocci, Gram-positive Cocci, and Gram-negative Bacilli for the respective presumptive identification of *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*. Bacteriological culture was carried out for isolation of strains of *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae*. CSF samples were streaked onto Columbia blood agar plates and chocolate agar to isolate the pure colonies. After inoculation, the agar plates were incubated at 37°C anaerobically for 24 - 48 hours.

We proceeded to the observation of colonies appeared, the search for catalase, cytochrome oxidase and gram control for identification of bacteria. All cocci and gram-negative catalase and cytochrome oxidase (*Neisseria meningitidis*, *Haemophilus influenzae*) positive strains as well as catalase and cytochrome oxidase (*Streptococcus pneumoniae*) gram-positive cocci strains were selected. The identity of the isolates was confirmed by latex agglutination, as well as serogrouping of *Neisseria meningitidis* species. The latex agglutination was carried out using a Pastorex meningitis kit (Bio-Rad) to detect *H. influenzae*, *S. pneumoniae* and *N. meningitidis* antigens of groups A, B, C, Y and W, and a Directigen meningitis kit (Becton Dickinson) to detect *N. meningitidis* antigens of groups X and Z. The kits were used according to the manufacturer's instructions.

2.5. Statistical Analysis

The epidemiological data of the patients were recorded in an Excel spreadsheet and analyzed with the SAS software. Quantitative variables were presented as

mean \pm standard deviation with the max/min range. Qualitative variables were presented as numbers and percentages. The graphs were made with Graphpad Prism 7 software.

2.6. Ethical Considerations

In Benin, ethical approval was not required for routine surveillance of meningitis, as it had been approved as part of the systematic diagnosis algorithm in the Ministry of Health. However, informed consent was sought from parents or guardians of surveillance participants.

3. Results

3.1. Demographic and Clinical Characteristics

We identified 2992 individuals suspected of meningitis, of whom 2893 admitted (96.7%) to the hospital from 2016 to 2018. The sex ratio of the individuals included in our study is 1.29 in favor of men, with a median age of 4 years (min: 0; max: 90). Individuals under five represent the most represented age group 44.8% (1339 individuals). The least represented age group is 55 to 59 years old (0.8%). More than half of the individuals (77.1%) included in this study came from a rural area with 281 deaths (9.4%) identified throughout the three years of study. Of the 2992 suspected meningitis cases included in this study, CSF samples were collected from 2928 patients, for a sample rate of 97.9%. CSF samples were taken from 98.4% hospitalized patients. One thousand six hundred and thirty-nine (56%) CSF samples were collected from men and 1285 (43.9) from women. 273 (9.3%) patients died with disease, but 2529 (86.4%) survived (**Table 1**).

Table 1. Characteristics of patients with suspected bacterial meningitis in the Republic of Benin, 2016-2018.

Characteristics	Number of suspect cases (%)	Number of collected CSF samples (%)	Number of CSF sample not collected (%)	p-value
Age group				-
[0 - 5[1339 (44.8)	1326 (45.3)	13 (20.3)	
[5 - 10[397 (13.3)	392 (13.4)	05 (7.8)	
[10 - 15[235 (7.9)	231 (7.9)	04 (6.2)	
[15 - 20[111 (3.7)	107 (3.7)	04 (6.2)	
[20 - 25[70 (2.3)	69 (2.4)	01 (1.6)	
[25 - 30[54 (1.8)	54 (1.8)	00	
[30 - 35[54 (1.8)	53 (1.8)	01 (1.6)	
[35 - 40[67 (2.2)	65 (2.2)	02 (3.1)	
[40 - 45[45 (1.5)	45 (1.5)	00	
[45 - 50[36 (1.2)	36 (1.2)	00	
[50 - 55[43 (1.4)	42 (1.4)	01 (1.6)	

Continued

[55 - 60[24 (0.8)	24 (0.8)	00	
60+	72 (2.4)	71 (2.4)	01 (1.6)	
Unknown	445 (14.9)	413 (14.1)	32 (50.0)	
Sex				-
Male	1661 (55.5)	1639 (56.0)	22 (34.4)	
Female	1292 (43.2)	1285 (43.9)	07 (10.9)	
Unknown	39 (1.3)	04 (0.1)	35 (54.7)	
Area of residence				-
Urban	554 (18.5)	546 (18.6)	08 (12.5)	
Rural	2307 (77.1)	2290 (78.2)	17 (26.6)	
Unknown	131 (4.4)	92 (3.1)	39 (60.9)	
Place of consultation				
Hospital	2893 (96.7)	2880 (98.4)	13 (20.3)	0.03
External	57 (1.9)	42 (1.4)	15 (23.4)	
Unknown	42 (1.4)	06 (0.2)	36 (56.3)	
Outcome				-
Death	281 (9.4)	273 (9.3)	08 (12.5)	
Living	2571 (85.9)	2529 (86.4)	42 (65.6)	
Unknown	140 (4.7)	126 (4.3)	14 (21.9)	
Total	2992 (100)	2928 (100)	64 (100)	

Source: DEHS/NDPH (2016, 2017, and 2018).

The annual distribution of suspected meningitis cases with incidences per 100,000 population and annual lethality rates are shown in **Table 2**. In 2017, we recorded more suspect cases (1148) than in 2016 and 2018. In 2016, the number of suspect cases was 1060 and 748 in 2018. However, the highest lethality (13.4%) was observed in 2016, with an incidence of 6.3 per 100,000 inhabitants. In 2017, the incidence was 6.8 with a case fatality rate of 7.1%. The lowest incidence (3.2) was observed in 2018 with a lethality of 7.6% (**Table 2**).

Of the 12 departments in Benin, 10 were included in our study. Department of “Atacora” was the department with the highest number 2095 of suspected cases of meningitis, followed by Borgou with 392 suspected cases and Alibori with 286. With lethality rates ranging from 8.4% to 10.5%. “Atlantique” and “Plateau” departments with low numbers of suspect cases (**Figure 1**), respectively, have the highest CFR (12.5%). The age group under 5 years has recorded more deaths (130) with a lethality of 9.7%, survival of the group of 5 to 9 years with 37 cases of death recorded and a CFR of 9.3%.

There is no significant difference ($p > 0.05$) between suspected cases and deaths among male and female. But there was a higher CFR (9.8%) among male than female (**Figure 2**). Distribution of suspect cases and deaths by months of

Table 2. Estimated annual incidence and case-fatality rate (CFR) of meningitis bacteria in Benin, 2016-2018.

Years	Population ^a	Number of suspect cases	Number of death	Incidence/100,000 inhabitants	CFR (%)
2016	11.027.717	1060	142	6.3	13.4
2017	11.485.270	1148	82	6.8	7.1
2018	11.496.140	748	57	3.2	7.6

^a: National Institute of Statistics and Economic Analysis [13].

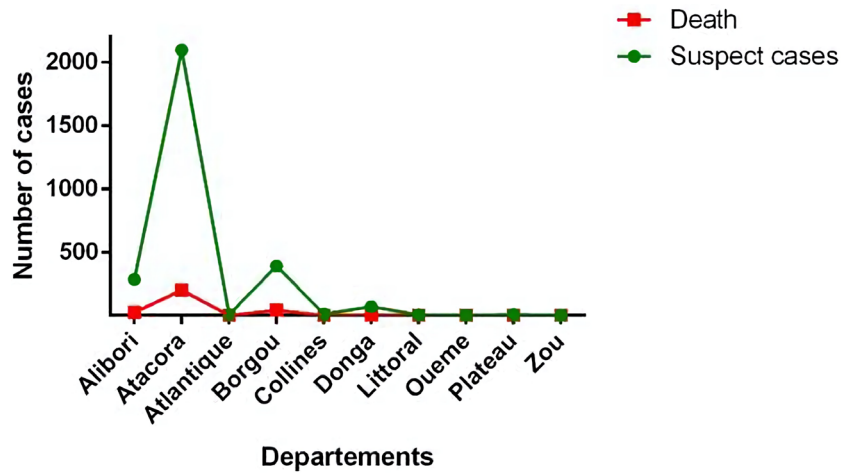


Figure 1. Distribution by department of suspected cases and deaths due to bacterial meningitis in the Republic of Benin, 2016-2018.

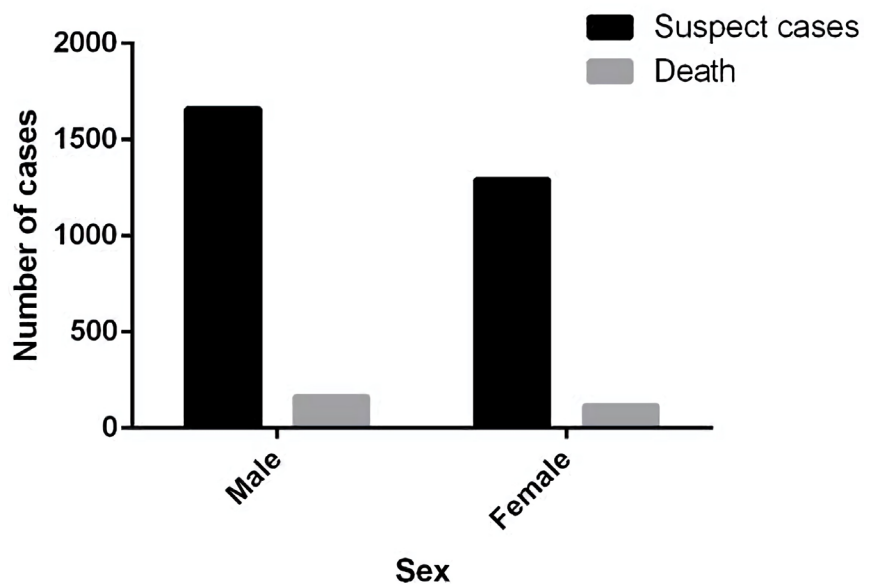


Figure 2. Sex distribution of suspected meningitis cases and deaths due to bacterial meningitis in the Republic of Benin, 2016-2018.

the year (Figure 3). It has been noted a suspicious case increase from January to April.

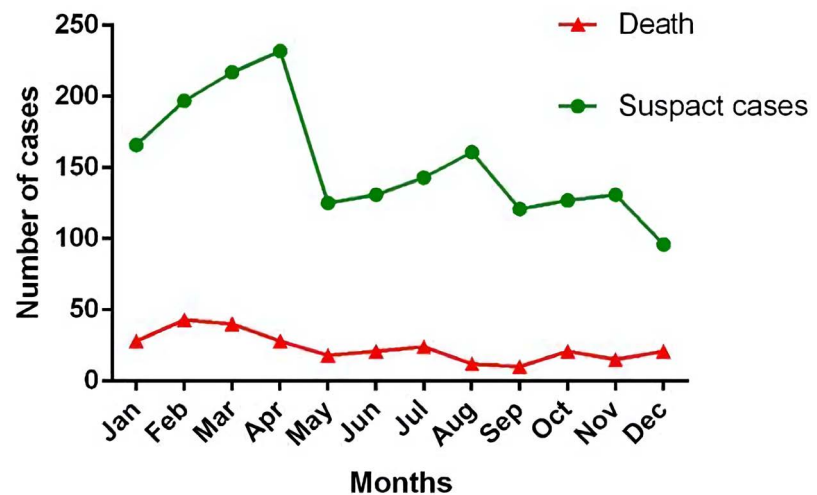


Figure 3. Number of suspected cases of bacterial meningitis and deaths by month of the year in the Republic of Benin from 2016 to 2018.

3.2. Pathogen Distribution

Of 2928 CSF samples analyzed in this study, 899 pathogens were identified, representing a 30.7% prevalence of meningeal bacteria. The number of pathogens identified increased during the first two years of study (312 to 318 from 2016 to 2017) and decreased over the last year (2018). During the present study, we observed a dominance of *S. pneumoniae* strains in patients. We identified more pathogens in patients (male) than in patients (female). Of the 2928 CSF samples, 54.4% were clear and 29.9% had a turbid appearance. From CSF turbid samples, was identified the highest proportion of pathogen (77%) with a dominance of *S. pneumoniae* (60.2%) and *N. meningitidis* (27%) (Table 3).

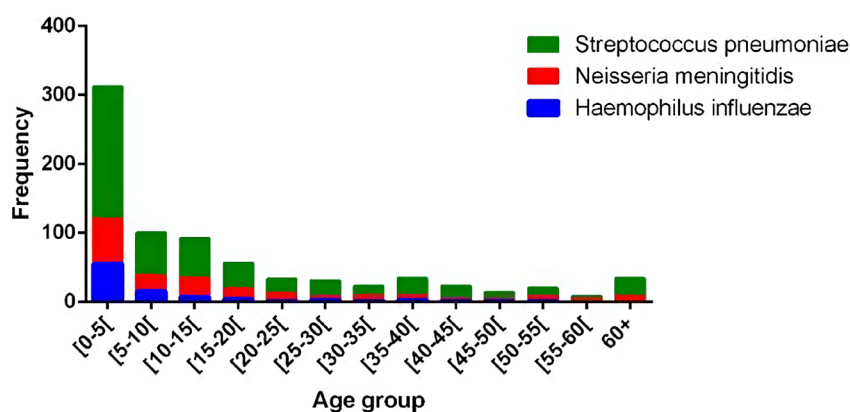
A high proportion of pathogens was noted in patient under 5 years of age with *S. pneumoniae* (192) and *N. meningitidis* (65) being dominant. Similarly, in subjects over the age of 50, there is an absence of *H. influenzae* and a high proportion of *S. pneumoniae* (42) and *N. meningitidis* (19) (Figure 4).

4. Discussion

The occurrence of a meningitis epidemic in Benin is a very complex public health problem. It is a temperate climate country and belongs to the African meningitis belt. The burden of bacterial meningitis is distributed disproportionately by location, age, and almost equally by sex. While the case-fatality rates are high, the laboratory confirmation rate is low. This low confirmation rate in the laboratory shows a high sensitivity of the case-by-case surveillance system for bacterial meningitis in the pediatric departments of hospitals in the Republic of Benin, since the results of this study showed that individuals under five accounted for the largest proportion (44.8%) of suspected cases with 46.3% of deaths, in contrast to individuals over 60 who accounted for only 2.4% of suspected cases with 2.9% of deaths. These results are somewhat similar to those obtained by several authors [1] [4]. Kaburi *et al.* [1] Showed after the evaluation

Table 3. Distribution of cerebrospinal fluid characteristics and proportion of pathogens identified by sex in the Republic of Benin from 2016 to 2018, 2016-2018.

Characteristics	Number of CSF samples (%)	Number of pathogens identified (%)	Number of bacterial species identified (%)		
			<i>H. influenzae</i>	<i>S. pneumoniae</i>	<i>N. meningitidis</i>
Appearance of CSF samples					
Clear	1594 (54.4)	129 (8.1)	14 (10.9)	91 (70.5)	24 (18.6)
Turbid	875 (29.9)	674 (77.0)	86 (12.8)	406 (60.2)	182 (27.0)
Hemorrhagic	199 (6.8)	38 (19.1)	7 (18.4)	30 (79.0)	1 (2.6)
Xanthochromic	112 (3.8)	52 (46.4)	1 (2.0)	41 (78.8)	10 (19.2)
Unknown	148 (5.1)	6 (4.1)	2 (33.3)	2 (33.3)	2 (33.3)
Sex					
Male	1639 (56.0)	531 (32.4)	58 (10.9)	342 (64.4)	131 (24.7)
Female	1285 (43.9)	366 (28.5)	52 (14.2)	227 (62.0)	87 (23.8)
Unknown	4 (0.1)	2 (50.0)	-	1 (50.0)	1 (50.0)
Years					
2016	1069 (36.5)	312 (29.2)	52 (16.7)	175 (56.1)	85 (27.2)
2017	1127 (38.5)	318 (28.2)	35 (11.0)	182 (57.2)	101 (31.8)
2018	732 (25.0)	269 (36.7)	23 (8.6)	213 (79.2)	33 (12.3)
Total CSF analyzed	2928 (100)	899 (30.7)	110 (12.2)	570 (63.4)	219 (24.4)

**Figure 4.** Distribution of meningitis bacteria according to the age group of patients in the Republic of Benin from 2016 to 2018.

of surveillance data for bacterial meningitis in northern Ghana from 2010 to 2015, that cases of meningitis suspects were significantly higher in children under five (27.4%) than in patients 60 years and older (4.8%). This vulnerability of children to meningitis is attributed to their immature immune system [15]. Exposure of babies to perineal bacteria at the time of delivery would also increase the risk of bacterial meningitis early in the neonatal period [1]. Our study showed that 77.1% of suspected meningitis cases were from rural areas with

84.3% (237/281) deaths during the study period. This high CFR among individuals living in a rural area would be related to several factors or behaviors. At numbers of these, malnutrition, overcrowding of households, lack of vaccination, waiting to be very sick before going to hospital, home treatment and self-medication [16]. In their study of identifying the social, economic, and behavioral factors that may contribute to meningitis transmission, Hayden *et al.* [17] found that in rural areas of northern Ghana only 33.3% Respondents reported vaccination as a means of protecting themselves or their family from meningitis. In addition, 42.8% of respondents said they go to the hospital when they are very sick and 18% provide home treatment by self-medication. This confirms the influence of social and behavioral factors in the occurrence of meningitis epidemics in rural areas. Our results showed a decrease in CFR of meningitis during the study period. From 13.4% in 2016, it rose to 7.6% in 2018. This decrease CFR of meningitis has also been observed in several studies in Benin (2011 to 2016) and in the sub-region [1] [18] [19]. For example, CFR of meningitis in recent years has decreased in Benin and in most countries of the African meningitis belt (lapeyssonnie) [5], it is now comparable to that of developed countries [20]. Investments in prevention (introduction of new polysaccharide and conjugate vaccines) of bacterial meningitis over the last decade are justified by this improvement in morbidity and mortality [21]. The implementation of robust immunization programs and high-quality clinical care has contributed significantly to reducing the burden of disease in the region [22].

Benin is subdivided into 12 departments. During the present study, we recorded suspected cases of meningitis in only 10 departments. At the numbers of these, the departments of “Alibori”, “Atacora” and “Borgou” represent the departments where we recorded more cases and deaths (Figure 1), with incidences/100,000 population of 13.9; 51.2 and 18.9 respectively. These three departments are found in the northern zone of Benin. This area is the part of Benin that is found in the Lapeyssonnie. This is justified by the high proportion of meningitis cases and deaths recorded in these three departments. However, we have recorded suspected cases of meningitis and deaths in other departments outside of the region. There was CFR of 12.5% in the Atlantic and Plateau departments, respectively, and 8.3% in the “Collines” department. These results show that, apart from the northern part of the country, the disease can occur in all departments from North to South and from East to West.

In this study, the majority of meningitis cases were recorded from January to April with a peak in April and 68.6% of deaths (Figure 4). In Benin, and more precisely in the northern zone, two seasons are well defined and known. The rainy season (May to October) and the dry season with harmattan (November to April). During the dry season, the heat, the dry and dusty wind during the day, increases the risk of communicable respiratory diseases [23] [24]. Meningitis could result, if these respiratory infections are poorly managed. During the harmattan, nights are cold and people close their windows to warm up. This leads to poor ventilation. These conditions facilitate the spread of infections from one

person to another, in an overcrowded room [17].

The prevalence of meningeal bacteria identified during this study is 30.7% with a decrease in number of pathogens over the three years of study (312 in 2016 and 218 in 2018). Our results showed a predominance of *S. pneumoniae* (63.4%), followed by *N. meningitidis* (24.4%) and *H. influenzae* (12.2%). This predominance of *S. pneumoniae* on *N. meningitidis* and *H. influenzae* was also reported by several authors [1] [18] [19] [20]. The decrease in the proportion of *N. meningitidis* may be due to the introduction of MenAfriVac through mass vaccination campaigns of 1 to 29 years in 2010, but also to the improvement of the surveillance system [21]. Similarly, in 2011, Benin introduced the influenza B conjugate vaccine, which also justifies the drastic decline in *H. influenzae* involved in meningitis [21]. The proportion of *S. pneumoniae* identified in children under five in our study was 21.4% in 2016 compared to 32.4% [18]. This predominance of *S. pneumoniae* involved in cases of pneumococcal meningitis in children under five is still relevant in 2019 [18] despite the introduction of conjugate pneumococcal vaccine (PCV) in the Expanded Program on Immunization in the Republic of Benin since 2011 [21]. As a limitation, during our study, we did not record the information that registered patients were on antibiotics or not. Moreover, we have not tested the susceptibility of meningeal bacteria to antibiotics. This information could allow us to evaluate the impact of self-medication on treatment failures in terms of the management of probable cases.

5. Conclusion

The present study showed that the highest proportion of meningitis cases reported was in the dry season, in patients under 5 years old and predominant in boys. The burden of disease is disproportionate in the northern departments as in the rest of the country. However, deaths have been recorded in the departments of the South (Atlantic, Plateau). This suggests an improvement in epidemiological surveillance and case management throughout the national territory. This study showed the success of the PsA-TT vaccine against *N. meningitidis* A in the Republic of Benin. Overall, pneumococcus remained an important cause of infantile meningitis in the Republic of Benin, despite a gradual decline in prevalence after the PCV era. This suggests the need for closer monitoring to determine any change in disease progression soon after a decade after the introduction of PCV.

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Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets supporting the conclusions of this article are included within the article.

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Author's Contributions

TPG, MNP, AJA, HB wrote the protocol. TPG and AJA Field work, protocol implementation, data analysis, interpretation and wrote the draft of the manuscript. TVD, CD and AA made substantial contributions to conception and study design, data analysis and interpretation. MNP, LB-M, HB participated in the critical revision of the manuscript.

Conflicts of Interest

The authors declare that they have no competing interests.

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