

Full Length Research Paper

Acute bacterial meningitis ecosystem in Cote D'ivoire from 2012 to 2020

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Bacterial meningitis remains a health concern in meningitis belt countries. The objective of this study was to ascertain the bacterial profiles of meningitis in Côte d'Ivoire from 2012 to 2020. The study, conducted retrospectively at the National Center of Reference of Meningitis of Cote d'ivoire, analyzed 5046 cerebrospinal fluid (CSF) samples from January 2012 to December 2020. Epidemiological data were collected as part of the study. All the samples were subjected to analysis using classic bacteriology, antibiogram, and real-time polymerase chain reaction (PCR) methods. More than 80% of the studied population fell within the age range of 0 to 5 years. The male-to-female sex ratio was 1.45, translating to 2987 men and 2059 women. *Neisseria meningitidis* was the predominant pathogen in 2012 (59%) and 2013 (64%). However, from 2014 to 2020, *Streptococcus pneumoniae* became the most frequently identified pathogen, ranging from 44.74 to 77.30%. *Haemophilus influenzae* type b was observed from 2015 to 2020, with prevalence rates ranging from 14.3 to 16.66%. *H. influenzae* non-b was observed with rates ranging from 10 to 15% from 2018 to 2020. No cases of *N. meningitidis* A were reported. The emergence of bacteria responsible for meningitis, such as pneumococcus and *H. influenzae*, was noted. Microbiological monitoring is deemed essential for the prevention of meningitis.

Key words: Emergence, bacterial, meningitis, ecosystem, monitoring.

INTRODUCTION

Bacterial meningitis remains a significant health concern in meningitis belt countries (Diallo et al., 2017). The highest incidences (per 100,000) were reported in Niger (7.71 in 2015) and Burkina Faso (10.2 in 2012) (Pardo de Santayana et al., 2023). The primary agents responsible for bacterial meningitis include *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* b (Kyaw et al., 2002; Gervais, 2014; Mamadou et al., 2019). In Niger, for instance, *N. meningitidis*

accounted for the highest disease burden, with 4741 (84.8%) confirmed cases, compared to 721 cases of *S. pneumoniae* (12.9%) and 129 cases of *H. influenzae* (2.3%) (Sidikou et al., 2019). These microorganisms, including *S. pneumoniae* (Gram-positive capsulated lanceolate diplococci, or in a candle flame), *N. meningitidis* (a Gram-negative cocci resembling coffee beans), and *H. influenzae* (a bacillus or cocobacillus), are fastidious and thrive in an atmosphere enriched in CO₂

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when cultivated on blood-enriched media. They form part of the normal flora of the mucous membranes in the upper respiratory tracts of both children and adults. Colonization typically commences shortly after birth and persists throughout an individual's life. These bacteria are strictly human pathogens, spreading through the air or direct contact among children or adults via Pflugge droplets. Therefore, when alterations of the mucosa, along with other contributing factors, facilitate the colonization and subsequent multiplication of various bacterial species, infections such as otitis, pneumonia, septicemia, and meningitis can occur (Medical Microbiology Course, 2023).

Approximately, half of all cases are reported in sub-Saharan Africa during the dry season, particularly in an area referred to as the "meningitis belt" (Lapeyssonnie, 1963). In Côte d'Ivoire, meningitis is endemic in two distinct epidemiological zones. Epidemics of meningitis caused by *N. meningitidis* serogroups A, Y, and W have been observed, similar to trends in other countries within this epidemiological zone. In the southern part of the country, which is situated in a humid tropical zone, meningitis occurs sporadically, with serogroup C being predominant. The introduction of the *N. meningitidis* A vaccine has led to a shift in the bacteriological profile of meningitis. In Burkina Faso, for example, *S. pneumoniae* has become the predominant pathogen, accounting for 57%, followed by *N. meningitidis* at 40%, with serogroup W being the most prevalent, and *H. influenzae* at 2% (Diallo et al., 2017). Simonetta's (2022) findings revealed that serogroup A meningococcal disease had disappeared from all age groups in many countries within the meningitis belt. Certainly, Côte d'Ivoire introduced the meningococcal A conjugate vaccine in 2010, along with the *H. influenzae* b vaccine and the pneumococcal conjugate vaccine as part of the Expanded Program on Immunization (EPI). As in other countries, the introduction of these vaccines prompts the question of whether it has contributed to a shift in the microbiological profile. Microbiological monitoring of acute meningitis stands as a crucial component of enhanced surveillance. The objective of this study was to ascertain the bacterial profiles of meningitis in Côte d'Ivoire from 2012 to 2020.

MATERIALS AND METHODS

Study design and sampling

This retrospective cross-sectional study utilized data collected at the National Center of References for Meningitis (NCRm), situated at the Institut Pasteur of Côte d'Ivoire (IPCI), spanning from January 2012 to December 2020. The NCRm is the recipient of cerebrospinal fluid (CSF) samples from suspected cases of bacterial meningitis, sourced from all health districts across Côte d'Ivoire. The NCRm is responsible for diagnosing and confirming suspected cases of meningitis. The study included all CSF samples received at the NCRm between 2012 and 2020, encompassing both adults and children, provided they were accompanied by a properly completed epidemiological form or an analysis report.

CSFs lacking an analysis sheet or bulletin were excluded from the study. Ethical approval was obtained from the appropriate authorities before the data analysis process commenced.

Epidemiological and laboratory data collection

All epidemiological data were collected from the epidemiological sheets accompanying the samples. Data analysis was performed using Microsoft Excel 2007. The variables used for the study were laboratory number, month of sample collection and year, patient age, sex, microscopy, culture, latex test, and polymerase chain reaction (PCR).

Cytobacteriological examination

The analysis was conducted employing conventional bacteriological methods, including macroscopy, microscopy (both in the fresh state and using Gram stain), cultures on blood-enriched agar media, bacterial identification based on biochemical characteristics, and the detection of soluble antigens (utilizing the Pastorex meningitidis kit from Biorad®, Marnes-la-Coquette, France).

Additionally, all CSF samples underwent molecular analysis through real-time PCR. The molecular study involved DNA extraction using the heat shock method, preparation of reaction mixtures, amplification, and gene detection. The targeted genes included *Lyt A* (*S. pneumoniae*), *Hpd* (*H. influenzae*), *sodC* C, and *ctrA* (*N. meningitidis*).

For *N. meningitidis* serotyping, the following targets were tested: *csaB* (*N. meningitidis* A), *csb* (*N. meningitidis* B), *csc* (*N. meningitidis* C), *csy* (*N. meningitidis* Y), *csw* (*N. meningitidis* W), and *csxB* (*N. meningitidis* X) (WHO, 2011).

RESULTS

For epidemiological characteristics, a total of 5046 CSF samples were analyzed at the National Center of Reference for Meningitis (CNRm) at the Institut Pasteur de Côte d'Ivoire. The mean age of the patients was 12 years, ranging from 0 to 86 years, with over 80% of the population falling between 0 and 5 years of age. The male/female sex ratio was 1.45, comprising 2987 males to 2059 females. Confirmed cases accounted for 476 or 8.3% of the total. The average age of confirmed patients was 10.2 years, with extremes ranging from 0 to 56 years, and the male/female sex ratio was 1.76. For the microbiological characteristics of CSF, Figure 1 illustrates the proportions of positivity by culture and PCR from 2012 to 2020.

The PCR technic detected the majority of positive meningitis cases from 2012 to 2020. In 2015, PCR-positive cases accounted for the majority, with 72%, compared with 11.59% in 2017. The culture-positive rate was low until 2020. From 5.4% in 2014 to 0 in 2020. Figure 2 represents the distribution of germs identified in CSF.

From 2012 to 2013, *N. meningitidis* was the most frequent pathogen, accounting for 59% in 2012 and 64% in 2013. Subsequently, from 2014 to 2020, *S. pneumoniae* became the most common germ, with rates

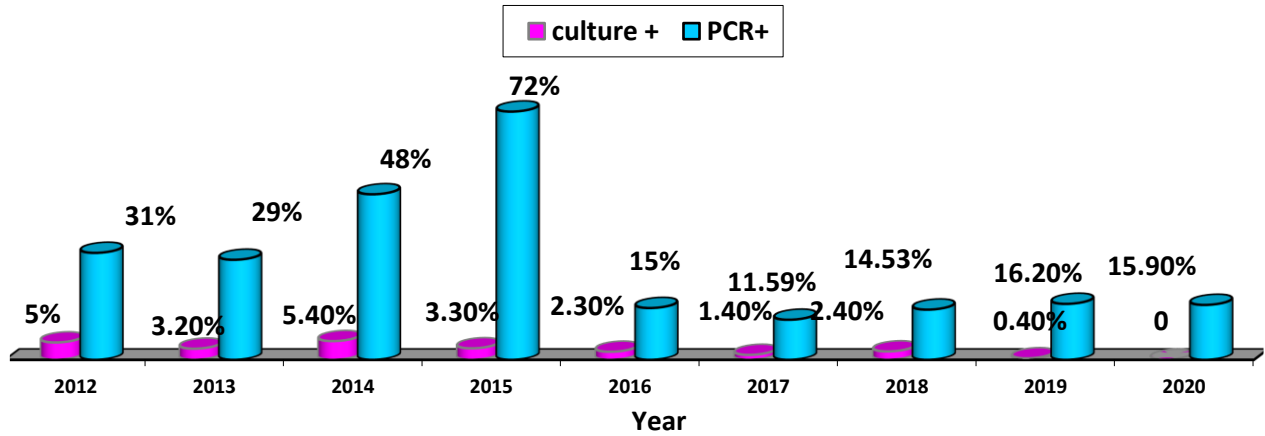


Figure 1. Proportions of positivity by culture and PCR from 2012-2020.

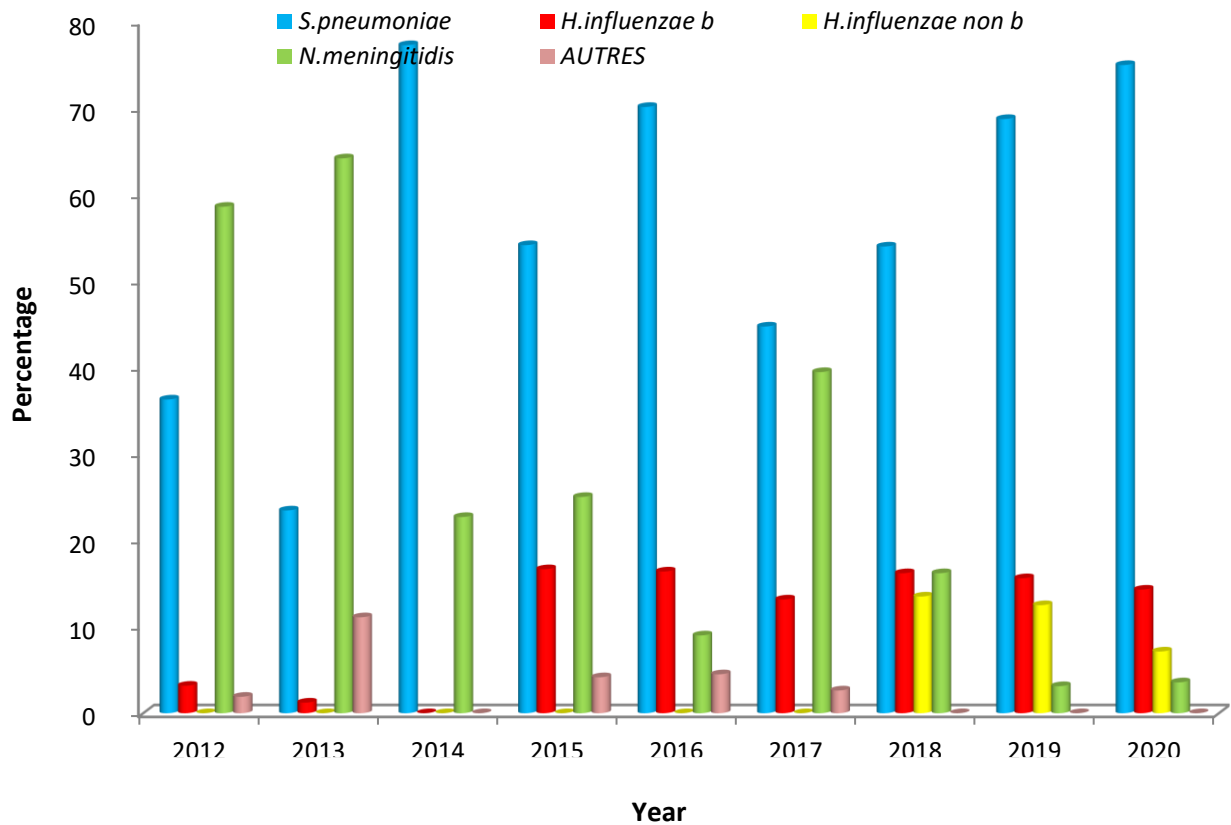


Figure 2. Distribution of germs identified in CSF from 2012-2020. (Others): *S.pneumoniae* *H.influenzae b* *H.influenzae non b* *N.meningitidis*

ranging from 44.74 to 77.30%, followed by *N. meningitidis*. An emergence of *H. influenzae b* meningitis cases occurred from 2015 to 2020, with respective rates of 16.66 and 14.3%. Additionally, there was an emergence of cases of *H. influenzae non-b* meningitis, observed with rates ranging from 10 to 15% from 2018 to

2020. Other pathogens, such as *S. agalactiae*, *Escherichia coli* and *Salmonella* species, were found from 2012 to 2017, with rates ranging from 0 to 4%. Figure 3 represents the distribution of *N. meningitidis* by serogroup.

In 2012, *N. meningitidis* serogroup W135 was the

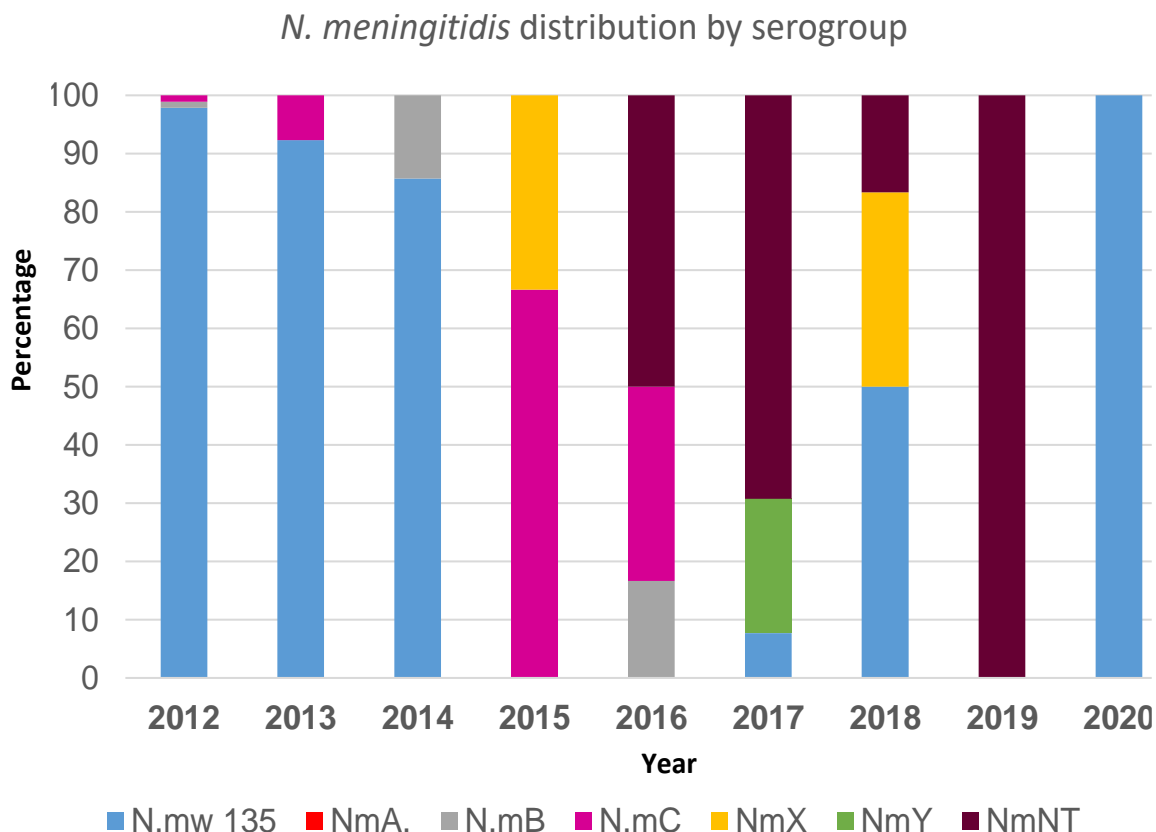


Figure 3. *N. meningitidis* distribution by serogroup from 2012-2020.

predominant pathogen until 2014, and then it appeared sporadically in other years, notably in 2018. No cases of *N. meningitidis* serogroup A were detected. There was an emergence of serogroup X in 2015 and 2017, and serogroup C persisted from 2012 to 2017. Serogroup X was reported in 2015 and 2018, while non-typeable *N. meningitidis* was observed from 2016 to 2020.

DISCUSSION

This study observed that more than 80% of the population with suspected meningitis cases were between 0 and 5 years of age, a result in agreement with Berthe (2020) findings in Mali. The male/female sex ratio was 1.45, closely aligned with the results of Savadogo et al. (2014) in Burkina Faso. Meningitis epidemics in African countries within the "meningitis belt" were predominantly caused by group *N. meningitidis* A (Lapeysonnie, 1963). In 2012, *N. meningitidis* serogroup W135 was the predominant strain, comprising over 90% of cases. This could likely be attributed to the circulation of the same epidemiogenic clone responsible for meningitis epidemics in Senegal, Burkina Faso, Côte d'Ivoire, and 16 other belt countries in 2012 (Mustapha

and Lee, 2018; WHO, 2013). Additionally, the observed shift may be attributed to the introduction of the meningococcal conjugate vaccine A, which may not provide protection against this serogroup (Mazamay et al., 2021; Mariagrazia et al., 2020). Subsequently, there was a progressive decline in *N. meningitidis* W from 2013 to 2019, decreasing from 93 to 0%, aligning with the findings of Ouangraoua in Burkina Faso in 2014 (Ouangraoua et al., 2014). However, serogroups X and Y emerged in 2015 and 2017, respectively. Hlozek et al., (2018) revealed that the similarity in the primary structures of the two polysaccharides suggests that serogroup A vaccination may offer cross-protection against serogroup X disease, yet some outbreaks caused by serogroup X have been reported. It should be noted, however, that non-typable serogroups existed from 2016 to 2019. Indeed, according to the World Health Organization (WHO), the introduction of the meningococcal conjugate vaccine A (MenAfriVac) strengthens the strategy for combating epidemics by improving prevention, but it also presents new challenges (WHO, 2013). Doumbia in Mali further revealed that after the introduction of MenAfriVac, *N. meningitidis* W became predominant, accounting for 66.10%, followed by pneumococcus at 22.88%, and *H. influenzae* b at 4.24%

(Doumbia, 2013). The global study by Pardo de Santayana, in summary, indicated that changes in invasive meningococcal disease over time were likely influenced by natural fluctuations, the emergence of virulent meningococcal clones (such as W:cc11), social trends, and immunization programs (Pardo de Santayana et al., 2023).

Furthermore, the rate of *S. pneumoniae*, which in 2012 was less than *N. meningitidis* W at 36%, underwent an increase with a frequency ranging from 23 to 70.15% from 2013 to 2016. These results align with the findings of Boni-Cisse et al. (2019) in 2019. From 2017 to 2020, it predominated over other pathogens with a rate ranging from 44.74 to 75%.

This shift is likely attributed to the introduction of the PCV10 conjugate vaccine in the Expanded Vaccine Program (Nhantumbo et al., 2015). Indeed, Kellner, (2011) noted that the marked decline in conjugate vaccine serotype infections was offset, to some extent, by an increase in infections attributable to a limited number of non-vaccine serotypes. Similarly, there was an increase in cases of *H. influenzae* b meningitis observed from 2015 to 2016. This surge in cases could be explained by the fact that the EPI only covers children aged 0 to 11 months. Booster doses are not being administered correctly, possibly due to the cost of vaccines and challenges in adhering to the vaccination calendar. Despite the availability of vaccines to protect against these serogroups, existing immunization programs do not cover all affected age groups (Clark, 2020). It is noteworthy that Slack (2021) in Australia affirmed that the Hib (*H. influenzae* b) conjugate vaccine has been successful in reducing the incidence of meningitis due to this germ to a very low level in countries where vaccination is well established in the EPI. However, much remains to be done in the case of non-immunized or partially immunized children. On the other hand, the emergence of non-b serotypes has become an important cause of meningitis in our populations, and these results are similar to those found among North American natives (Sadeghi-Aval et al., 2013; Ashley et al., 2019; Slack et al., 2021).

Conclusion

Bacterial meningitis constitutes a significant source of mortality and morbidity in Côte d'Ivoire. Vaccination against *N. meningitidis* has substantially altered the epidemiology of bacterial meningitis in high-risk regions. Meningitis-causing bacteria, such as *S. pneumoniae* and *H. influenzae*, have emerged. These bacteria, once regarded as non-epidemiogenic, were the primary isolates following the 2016 epidemic. Comprehensive epidemiological and microbiological surveillance, encompassing all age groups and types, is imperative to thoroughly document these changes and tailor vaccine

regimens accordingly.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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