

Characterization of Cerebral Spinal Fluid (CSF) in Bacterial Meningitis in Children at the Albert Royer Children's Hospital from January 2022 to June 2023 (18 Months) about 62 Cases

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Abstract

Background: Bacterial meningitis is a diagnostic and therapeutic emergency. The aim was to study the cytological, chemical and microbiological characteristics of cerebral spinal fluid (CSF) during bacterial meningitis. **Methods:** This was a retrospective descriptive and analytical study based on data from patients' hospitalization records, over the period from January 2022 to June 2023 (18 months). All children aged 0 to 14 years with a CSF study including cytochemistry and/or bacteriology in favor of bacterial meningitis were included. **Results:** A total of 62 children, with a sex ratio of 1.69, were included. The median age was 22 months, ranging from one day to 126 months. Immunization status was up to date in 85% of patients. Sixteen children (26%) had received antibiotics prior to hospitalization. The most common clinical signs were fever (85%), convulsions (24%), irritability (23%) and altered consciousness (21%). Lumbar puncture was performed on admission in 66% of cases (n = 41). CSF was clear in 58% of patients; cloudy in about 29%. Cytology ranged from 5 to 5040 elements/mm³, with a median of 136 elements/mm³. Glycorrhachia less than 0.4 g/dl was noted in 26% of patients (n = 16), and the median proteinorachy value was 0.77 g/L. Bacteriology was positive in 32.26% of patients (n = 20), with a positivity threshold of 13% (n = 8) for culture versus 20.1% (n = 13) for PCR. Previous antibiotic therapy was associated with negative CSF culture (p = 0.047). *Streptococcus pneumoniae* was the most frequently found germ (40%; n = 8). **Conclusion:** The study of CSF is essential for the diagnosis of meningitis. Overuse and inadequate use of antibiotics (prior to sampling) make interpretation difficult.

Keywords

Meningitis, Children, Cerebral Spinal Fluid (CSF)

1. Introduction

Bacterial meningitis is the inflammation of the meninges and subarachnoid spaces following an attack by bacteria, most often pyogenic [1]. In 2022, the member states of the African meningitis belt reported 20,843 suspected cases and 1153 deaths for all ages combined, with a case fatality rate of 5.5%. This corresponds to an increase of 28% compared to 2020 and 7% compared to 2021. More specifically, in Senegal in 2022, 943 suspected cases were notified, including 25 deaths [2]. In industrialized countries, the incidence is between 1 and 3.7 per 100,000 inhabitants [3] [4]. Two-thirds of these meningitis cases occur in children under 5 years of age [5] [6]. The largest proportion of meningitis deaths in children under 5 years of age was attributable to *Streptococcus pneumoniae* [7]. The highest proportion of deaths due to meningitis in newborns was attributable to group B streptococci (22.8%), followed by *Klebsiella pneumoniae* (17.1%) and viruses (15.3%) [8]. Epidemiological studies from Africa and Netherlands show that between 2006 and 2014 of 1412 episodes of community-acquired bacterial meningitis, *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Listeria monocytogenes* accounted for 51%, 37%, and 4% of cases, respectively in adults [9]. *S. pneumoniae* and *N. meningitidis* cause up to 90% of cases in infants and children [10]. The diagnosis of bacterial meningitis is based on the study of cerebrospinal fluid. This cytological, biochemical and microbiological study of cerebral spinal fluid (CSF) is systematic for the confirmation of meningitis. Classically, the diagnosis of bacterial meningitis is defined in the presence of hypertensive, cloudy or purulent CSF associated with a CSF cytology > 10 elements/mm³, hyperproteinorachia > 0.5 g/l, hypoglycorachia (CSF/blood glucose ratio < 0.4 g/L) and a direct examination or a positive culture (except in newborns) [11] [12]. However, cases of bacterial meningitis in children have been confirmed by microbiology despite a normal cytological and biochemical study [13]. CSF analysis can be made difficult in the context of excessive use of antibiotics. These are cases of decapitated meningitis. The diagnosis of meningitis therefore requires a rigorous analysis of the different biological parameters of the CSF in a suggestive clinical context. The objective of this work was therefore to study the cytological, chemical and microbiological characteristics of the cerebral spinal fluid (CSF) during bacterial meningitis. The specific objectives were to describe the macroscopic and cytochemical appearance of CSF during bacterial meningitis, to describe the isolated germs in the CSF, as well as to study the factors associated with the different CSF profiles found.

2. Methodology

Study design: This is a retrospective, descriptive and analytical study covering a

period of one and a half years, from January 1, 2022 to June 30, 2023. Data from the registers and medical records of patients hospitalized in the different departments of the hospital for bacterial meningitis were included. Inclusion criteria were age 0 to 14 years, diagnosis made during the study period and the existence of a CSF study in favor of meningitis. The following were excluded from the study: suspected cases not confirmed by CSF analysis, non-bacterial infectious meningitis and incomplete records.

Study setting: The study took place at the Albert Royer National Children's Hospital, which is an epidemiological surveillance site for bacterial meningitis in children.

2.1. Definitions and Threshold Values

The elements that allowed us to retain the diagnosis of bacterial meningitis were:

- Either a cytology > 10 elements/mm³ or 20 elements/mm³ if newborn associated with hyperproteinorachia > 0.5 g/l in infants or 1.4 g/l in newborns and/or hypoglycorachia (with a glycorachia/glycemia ratio less than 0.4) in a suggestive clinical context.
- Either a positive CSF bacteriology (direct examination, culture and/or PCR).
- Either the association of the 2 criteria.

2.2. Data Collection

Sociodemographic data (age, sex, vaccination status); clinical data (history and comorbidities, psychomotor development, nutritional status, notion of previous antibiotic therapy, clinical signs, duration of hospitalization, time between hospitalization and lumbar puncture, treatment, evolution); and paraclinical data (CSF study: macroscopy, cytology, chemistry and bacteriology as well as blood culture, and CRP) were collected on an Excel 2016 file from medical records.

2.3. Data Analysis

The results are presented as means and standard deviations for quantitative variables and as percentages for qualitative variables. The data were analyzed using SPSS (Statistical Package for Social Sciences) version 25. In bivariate analysis, the significance threshold was set at a p-value < 0.05 (chi-square test). The Shapiro test was used to determine the normality of the distribution of variables. Pearson correlation was used to determine the strengths of association for quantitative variables.

3. Results

3.1. General Characteristics of Patients Diagnosed with Bacterial Meningitis

Of 85 cases of bacterial meningitis recorded at CHNEAR, 62 patients were included (**Figure 1**). The median age was 22 months, with extremes of 1 day and 126 months. In newborns, the mean age was 16 days. There was a male predominance,

63% (n = 39) boys, with a sex ratio of 1.69. 17% of patients had comorbidities. The most frequently found associated pathologies were asthma (5%), dandy walker disease (3%) and spina bifida (3%). Vaccination status was up to date in 85% of patients (n = 53). 71% (n = 44) of patients were vaccinated against pneumococcus and *Haemophilus influenzae*. 23 patients or 37% were vaccinated against meningococcus. The notion of previous antibiotic therapy was found in 26% (n = 16) of patients in our series.

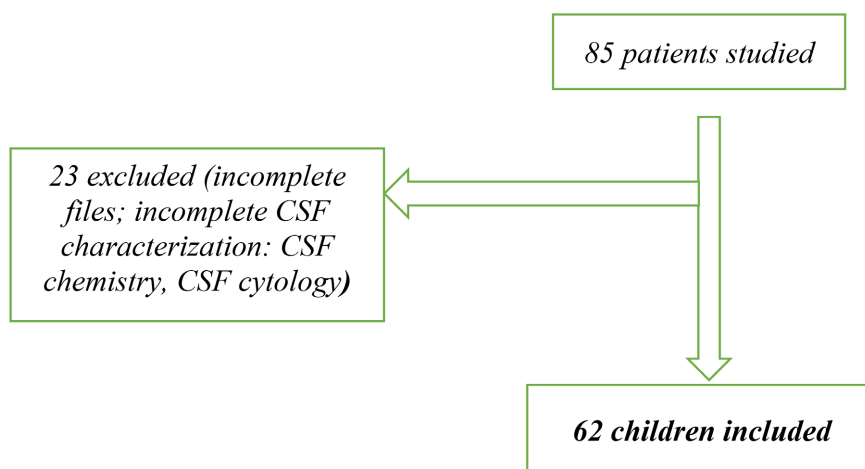


Figure 1. Flow charts of participants.

3.2. Clinical Presentation and Management of Bacterial Meningitis

The average time between the onset of signs and hospitalization was 4 days, with extremes ranging from 0 to 21 days. 47% (n = 29) of patients consulted between 1 and 3 days after the onset of signs. 13% (n = 8) consulted within 24 hours of the onset of signs. Fever was the main reason for consultation in 85% of cases (n = 53). Seizures and irritability followed, which were found in 24% (n = 15) and 23% (n = 14) of patients, respectively. Headaches, vomiting, and refusal to breastfeed were found in 18% of patients. Headaches were present in 66.7% of patients aged between 60 and 120 months. Thirty-six patients (58%) had a normal nutritional status. However, 34% (n = 21) were malnourished, including 8% (n = 5) with severe acute malnutrition (SAM). Of a total of 18 patients over 30 months of age, 66% (n = 12) had neck stiffness and 19% of patients had a Kernig and/or Brudzinski sign present. A soft neck was found in only 1 patient. Fontanelle appearance was described in 39 patients, including 18% (n = 7) with a bulging fontanelle; the rest of the patients had a normal fontanelle. Lumbar puncture was performed at admission in 66% of patients (n = 41). The meningeal bacterial score (BMS) was positive in 51.6% of patients. 75% of patients with positive bacteriology had a positive BMS. The maximum duration between hospitalization and the first lumbar puncture was 2 days. Fifty-six patients (90.3%) received a 3rd generation cephalosporin as treatment. Penicillins, quinolones and glycopeptides were used alone in equal distribution (2%; n = 1). Aminoglycosides and glycopeptides were used

in combination with a 3rd generation cephalosporin in 5% of cases (n = 3). Three patients were given antituberculosis drugs. The median duration of antibiotic therapy was 10.5 days. Thirty-one patients (50%) had antibiotic therapy between 8 and 14 days and 9 patients (15%) had antibiotic therapy for less than 7 days. Corticosteroid therapy was administered in 50% (n = 31) of patients, including 77% (n = 24) based on betamethasone and 10% based on dexamethasone (n = 3). Lumbar puncture control was performed in 67.7% of patients (n = 42) with a median time of 7.5 days. The outcome was favorable in 78% (n = 48) of patients. Four deaths were recorded and 12 patients (19.3%) developed complications, the most common of which was hydrocephalus (58%; n = 7).

3.3. Analysis of the CSF

The macroscopic appearance of the CSF was reported in all patients. It was mostly clear in 58% (n = 36) of patients, and cloudy in 29.03% (n = 18) of patients. The cytology of our patients varied between 5 and 5040 elements/mm³ with a median of 136 elements/mm³. Patients with cytology less than 100 elements/mm³ represented 48% (n = 30), as shown in **Table 1**. An average of 22.07% of altered polymorphonuclear cells and 28.46% of unaltered polymorphonuclear cells were found. For lymphocytes, the average found was equal to 50.18%. The predominance of altered polymorphonuclear cells in the CSF (>50%) was found in 12.9% of patients. The minimum glycorachia was equal to 0.04 g/l and the maximum to 1.36 g/l. Capillary blood glucose concomitant with the PL was reported in only 46.8% of patients, of which 26% (n = 16) returned less than 0.4 g/l. CSF protein levels ranged from 0.21 g/l to 5.9 g/l with a median of 0.77 g/l. Among newborns, 33% had a protein level greater than 1.5 g/l. Among infants and older children, approximately 25% had a protein level greater than 1.2 g/l. Direct examination was positive in 11.29% (n = 7) of patients. Culture was positive in 8 patients, or 13% of our series. The search for soluble antigens in the CSF was positive in 2 patients, or 3.2%. Both positive results were in favor of *Streptococcus pneumoniae*. PCR was positive in 20.1% of patients (n = 13). *Streptococcus pneumoniae* was the most common germ and represented 40% of the germs isolated. *Mycobacterium tuberculosis* was identified in 2 patients with CSF GNxpert. *Neisseria meningitidis* was isolated from one patient. The overall microbiological yield was 32%. **Table 2** shows the distribution of germs found in bacteriology tests. Since blood culture is a paid test, it was only performed on 4 patients, 3 of whom had negative incomes. The only positive blood culture isolated *Escherichia coli* from a one-month-old patient.

3.4. Factors Associated with the CSF Profiles Found

Among the 16 patients who had received prior antibiotic therapy, 14 had no germs on culture. The p-value was statistically significant, p = 0.047 (χ^2 test). Prior antibiotic therapy was associated with a negative CSF culture. Among the 6 patients with normal chemistry, none had received prior antibiotic therapy. There was no

relationship between prior antibiotic therapy and normal CSF chemistry.

Table 1. Distribution of patients according to their CSF cytology.

Cytology	Effective	Percentage
5 - 100	30	48%
100 - 500	18	29%
500 - 1000	1	2%
>1000	13	21%
Total	62	100%

Table 2. Distribution of patients according to bacteria isolated in the CSF.

Germ isolated by bacteriology	Effective	Percentage
<i>Streptococcus pneumoniae</i>	8	40%
<i>Mycobacterium tuberculosis</i>	2	10%
<i>Streptococcus A</i>	2	10%
<i>Pseudomonas SP</i>	2	10%
<i>Staphylococcus epidermidis</i>	1	5%
<i>Staphylococcus SP</i>	1	5%
<i>Streptococcus mitis</i>	1	5%
<i>Streptococcus suis</i>	1	5%
<i>Escherichia coli</i>	1	5%
<i>N. meningitidis</i>	1	5%
Total	20	100%

4. Discussion

Acute bacterial meningitis is one of the deadliest forms of meningitis and the cause of the most disabling forms of this disease. It is a diagnostic and therapeutic emergency. The main objective of our work was to study the cytological, chemical and microbiological characteristics of cerebral spinal fluid (CSF) during bacterial meningitis at CHNEAR.

The median age in our study was 22 months and the male sex was predominant with a sex ratio of 1.69. In our study, CSF macroscopy was clear in 58% of cases. These results were superimposable with those of Sonko *et al.* in 2019 [14]. In a study carried out in Bangladesh, on bacterial meningitis, the CSF was clear in 38% of cases [15]. The proportion of clear fluid found could be explained by the fact that 26% of patients had benefited from antibiotic therapy prior to LP. Dupeyron reports that clear fluid can be observed in purulent meningitis decapitated by insufficient oral or injectable antibiotic treatment, with a variable proportion of polymorphonuclear cells and lymphocytes [16].

Cytology greater than 10 elements or 20 in the newborn was in favor of meningitis in our study. The usual number of cells in the CSF in bacterial meningitis is approximately 1000 cells/mm³ [17] [18]. In our study, 48% of patients had a cytol-

ogy between 5 and 100 elements/mm³. Davis shows that the CSF cells deteriorate within 30 minutes after the puncture, hence the need for urgent analysis of the CSF. The time between the performance of the lumbar puncture and the study of the CSF in the laboratory was not specified in our study [17] [19].

In Davis's study, 23.2% (n = 13) of patients had a diagnosis of bacterial meningitis by positive culture but with atypical CSF cytology that was normal or increased with lymphocyte predominance, suggesting antibiotic therapy prior to LP. In our study, in addition to the 26% (n = 16) of patients who received antibiotic therapy before hospitalization, LP was performed in 44% of patients beyond 24 hours after admission, *i.e.*, after the start of antibiotic therapy. Protein levels during the study varied between 0.21 and 5.9 g/l with a median of 0.77, which is superimposable on the diagnostic criteria for protein levels according to the BMS [18]. In our study, we did not find an association between previous antibiotic use and CSF chemistry, which makes it a discriminating diagnostic element in our context, where uncontrolled prescription of antibiotics could explain the atypical CSF profiles that we found, as well as the low rate of compliance with the BMS, which was positive in only 51.6% of all patients. In our study, *Streptococcus pneumoniae* was the most frequently found germ in 40% of cases (n = 8). These results are close to 72% found in a systematic review by Rodrigo Hasbun [20]. In Nigeria, Obaro *et al.* also found *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae* as the most common germs. In this study, PCR isolated 24.5% of germs (n = 90) for which the culture was negative [21]. In our study, the culture was positive in 8 patients (13%) versus 13 patients (20.1%) for PCR. The pathogen detection rate in our study was 32%, similar to Obaro *et al.*, who had 27.2% (109/400). Belayneh *et al.*, working in CARD8 polymorphisms among bacterial meningitis patients in Ethiopia in 2024, found 7/400 positive culture versus 39/400 positive PCR [22]. In addition, we found an association between previous antibiotic therapy and the absence of germs in the culture.

Our study allowed us to identify the different CSF profiles during bacterial meningitis. Our results demonstrate the variability of cytological, chemical and bacteriological characteristics of CSF, particularly in the context of antibiotic misuse. It also highlights the importance of accessibility to molecular diagnosis in resource-limited countries in order not to underdiagnose this serious condition. However, the limitations of our study were the absence of data concerning the conditions of CSF study in the laboratory, the absence of data concerning the serotypes of the isolated germs in comparison with those targeted by vaccination and the absence of measurement of the lactate level in CSF, which is also an element helping to diagnose bacterial meningitis.

5. Conclusion

Bacterial meningitis is a diagnostic and therapeutic emergency. It is a rigorously monitored condition, particularly in countries within the meningitis belt, such as Senegal. Its diagnosis is based on the study of CSF, the cytological and chemical

characteristics of which provide guidance, confirmed by the isolation of a bacterium during bacteriological study. The systematic use of molecular biology platforms, on the one hand, and the proper use of antibiotics, on the other, will ensure that patients are not underdiagnosed.

Declaration

The medical data was collected following informed consent from the parents of the study participants.

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Lack of funds.

Authors' Contributions

Writing: Awa Kane, Maryam Aida Kane, and Eva Sophie Sène. Reading: Awa Kane, Amadou Lamine Fall, Papa Moctar Faye, Aminata Mbaye, Marie Paula Absa Di-one, Mame Awa Ndao, Ndeye Astou Diop, Laeticia Béatrice Takam, Guilaye Di-agne, Ndeye Fatou Sow, Amadou Sow, Yaye Joor Dieng, Djenaba Fafa Cissé, Ibrahim Diop, Indou Deme-Ly, Idrissa Demba Ba, and Ousmane Ndiaye. Recruiting: Awa Kane, Maryam Aida Kane, Eva Sophie Sène, and Aminata Mbaye.

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Conflicts of Interest

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

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