Original Research Article

Epidemiological-clinical, therapeutic and evolutionary profile of children treated for bacterial meningitis at CHU-MEL (Benin)

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ABSTRACT

Aims: Bacterial meningitis remains a public health problem due to an unfavorable geographical environment and socioeconomic context. Our study aimed to evaluate the epidemiological-clinical, therapeutic and evolutionary profile of children treated for bacterial meningitis in the pediatric department of CHU-MEL in Benin.
Methodology: The methodology consisted in carrying out a retrospective and descriptive study of children admitted to the pediatric department of the CHU-MEL in Cotonou from January 2019 to December 2020.
Results: Data collection (epidemiological, clinical, paraclinical, therapeutic and evolutionary) was made from registers and files and by telephone call. It was noted that the most represented age group was between 3 months and 3 years with a rate of 52.9%. Most (95.6%) of the children had no particular history. The antibiotics used were ampicillin (17.4%), ceftriaxone (52.2%), cefotaxime (4.3%) and ciprofloxacin (8.7%). For the exploration of cases of meningitis, apart from the cytobacteriological examination of the cerebrospinal fluid (CSF), the blood culture, the complete blood count (NFS) and the C-reactive protein (CRP) were the examinations commonly requested.
Conclusion: It is observed that children treated as meningitis have varying clinical signs. To improve care, it is important to better determine the germs involved, to establish a care protocol and to ensure proper conduct of antibiotic therapy.

Keywords: Bacterial meningitis, Antibiotics, Management, Pediatric, Benin

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1. INTRODUCTION

Bacterial meningitis (BM) is a major pediatric pathology and constitutes a public health problem due to the high mortality associated with it [1]. It causes a diagnostic and therapeutic emergency if not properly diagnosed and managed [2]. Thus, the annually worldwide occur of BM estimated at over 1.2 million cases [3] thought the incidence and case-fatality rates vary by region, country, pathogen and age group [4]. The clinical signs of the BM are not specific but among untreated patients, more than 70% induce case-fatality and 20% of survivors have permanent sequelae [4]. Therefore, this infection is considered as one of the most feared childhood diseases with special recommendations for its detection in endemic countries in Africa [5-6].
The detection of bacterial meningitis is often difficult [7]. This is why several tools have been developed and validated to guide decision-making. These tools will help to limit the prolonged and hazardous use of antibiotics [7–9]. The commonest bacterial meningitis pathogens are mainly *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus*

influenzae [3]. But the incidence of *N. meningitidis* is highest in sub-Saharan Africa region during the dry season [5, 10].
In Benin, as in many other sub-Saharan countries, meningitis suspected children are routinely admitted to hospitals and treated with broad-spectrum antibiotics without any laboratory confirmation. But very few studies have looked into this disease in Benin. To fill this gap, the present study is undertaken with the aim of appreciating not only the epidemiological-clinical profile but also those therapeutic and evolutionary of the children taken care of as bacterial meningitis in the pediatric department of the CHU-MEL in Cotonou (Benin).

2. METHODOLOGY

2.1. Type and period of study

This was a retrospective and descriptive study of children admitted to the pediatric department of the CHU-MEL of Cotonou from January 2019 to December 2020 and treated for bacterial meningitis. Included in the study were all patients aged 1 month to 17 years in whom the diagnosis of bacterial meningitis was retained and who underwent a lumbar puncture. The non-inclusion criterion was the non-availability of a cytobacteriological and chemical examination of the CSF. Recruitment was exhaustive and all patients meeting the inclusion criteria were included.

2.2. Data collection

Data were collected first from registers and files and then by telephone call. Consulting the registers, the collected were epidemiological, clinical, paraclinical, therapeutic and evolutionary. The epidemiological data related to age, sex, treatment before admission and pathological history. With regard to the clinical data, they focused on the presence of fever, neurological signs and signs of meningeal irritation. The assessments made with their results were the substance of the paraclinical data. The therapeutic data took into account the antibiotics used, the duration of the treatments and the poorly followed treatment. We define poorly followed treatment as non-compliance with the dose and/or frequency and/or duration of the prescribed antibiotic and/or the existence of a therapeutic window. Finally, the evolutionary data took into account the short-term evolution, the mode of discharge from the hospital and the medium-term evolution (1 year after hospitalization).

2.3. Data analysis and processing

Data collected was process using Microsoft Excel 2013 software and the IBM SPSS statistics 26 statistical analysis tool. The qualitative variables were expressed as a frequency. Correlations between variables were tested by the chi-square test. We considered a p value < 0.05 to be statistically significant.

3. RESULTS AND DISCUSSION

3.1. Results

3.1.1. Population size

During the study period, 68 children were treated for bacterial meningitis with a cytobacteriological and biochemical examination of the CSF out of a total of 10,236 hospitalized children, i.e., a hospital frequency of 0.66 %.

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3.1.2. Epidemiological profile

The average age was 31.6 months with extremes of 1 month and 13 years. The most represented age group was between 3 months and 3 years with a rate of 52.9% (Table I). The predominance is male with a sex ratio of 1.1.
Table I: Distribution of the population studied according to age

Age	Number	Percentage (100%)
≤ 3-months	12	17,7
]3-month, 3 years]	36	52.9
]3-years, 5 years]	10	14.7
>5-years	10	14.7
Total	**68**	**100.0**

3.1.3. Clinical profile

Regarding the history, the majority (95.6%) of the children had no particular history. Nevertheless, antibiotic therapy was revealed by 33.8% (23/68) of the children. The antibiotics used were ampicillin (17.4%), ceftriaxone (52.2%), cefotaxime (4.3%) and ciprofloxacin (8.7%).
On admission, the diagnosis of bacterial meningitis was suggested by the deterioration of the general condition, the infectious syndrome, the signs of meningeal irritation and/or the neurological signs. Neurological signs were convulsions or coma rarely incessant crying or bulging anterior fontanel in infants. Table II shows the distribution of children treated for bacterial meningitis according to the clinical signs presented.

Table II: Distribution of children treated as bacterial meningitis according to the clinical signs presented

Signs	Number	Percentage (%)
Fever	68	100
Signs of meningeal irritation	6	9.7
Neurological signs	61	89.7

3.1.4. Reports requested and executed

For the exploration of cases of meningitis, apart from the cytobacteriological examination of the cerebrospinal fluid (CSF), the blood culture, the complete blood count (NFS) and the C-reactive protein (CRP) were the examinations commonly requested. The rate of achievement of the balance sheets is as shown in Table III.

Table III: Distribution of children treated for bacterial meningitis according to the assessments carried out

Reports carried out	Number	Percentage (%)
Blood culture	15	22.1
Complete blood count (NFS)	65	95.6
C-reactive protein	5	7.4

It should be noted that in the case of blood culture, about 20% (3/15) of the analyzes were positive and the germs found were coagulase-negative *Staphylococcus*, *Acinetobacter spp*,

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and *Haemophilus influenzae*. Most of the children had cellulorachy less than 100 cells/mm^3 (55.9%, n=38) high protein ≥ 0.40 g/l (91.2%; n=62) and high glycorrhachia greater than 0.27g/l (82.3%; n=56). A germ was isolated in the CSF in 4.4% of cases (3/68). The germs found were *Haemophilus influenzae*, *Escherichia coli* and a Gram-negative bacillus. Table IV presents the distribution of children treated as bacterial meningitis according to the number of leukocytes, proteinorachia and glycorrhachia.

Table IV: Distribution of children treated as bacterial meningitis according to the number of leukocytes, proteinorachia and glycorrhachia

	Cellulorachy (leukocytes / mm^3)	**Number**	**Percentage (%)**
Cellulorachy	[10 - 50[	31	45.59%
	[50 - 100[	7	10.29%
	[100 - 500[	22	32.35%
	[500 - 1000[	2	2.94%
	≥ 1000	6	8.82%
	Total	**68**	**100.00%**
Proteinorachia	<0.40 g/l	6	8.82%
	≥ 0,40	62	91.1%
	Total	**68**	**100%**
Glycorrhachia	< 0.27	12	17.65%
	≥ 0.27	56	82.35%
	Total	68	100%

3.1.5. Therapeutic profile

The preferred treatment in the department was cefotaxime at 200 mg/kg/24 h three times plus gentamicin at 5 mg/kg/24 h once. In the absence of financial means from the parents, ceftriaxone 100 mg/kg/24 h twice is proposed then the treatment is adapted according to the germ found. In the absence of germs, ceftriaxone or cefotaxime is continued for ten days and gentamicin for 5 days. Finally, in the absence of improvement after ten days of treatment, other antibiotics are proposed. Table V shows the combinations of antibiotics made in hospitalization.

Table V: distribution of children treated for meningitis according to the antibiotics used

Antibiotics	**Number**	**Percentage (%)**
Ceftriaxone + gentamicin	17	25.00%
Cefotaxime + gentamicin	33	48.53%
Ceftriaxone sulbactam + gentamicin	2	2.94%
Ceftriaxone + gentamicin then vancomycin	1	1.47%

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Cefotaxime + gentamicin + ampicillin	2	2.94%
Cefotaxime then ceftriaxone + gentamicin then ciprofloxacin	2	2.94%
Cefotaxime + gentamicin then ciprofloxacin	4	5.88%
Cefotaxime + gentamicin then ciprofloxacin + CTM + phenicols	4	5.88%
Cefotaxime + gentamicin then ceftriaxone	1	1.47%
Cefotaxime + gentamicin then Ceftriaxone sulbactam + vancomycin	1	1.47%
Cefotaxime + gentamicin then ciprofloxacin + ampicillin	1	1.47%
Total	**68**	**100.00%**

The combinations of antibiotics used were diverse and varied. Overall, treatment was poorly followed by 60.3% (41/68) of children treated as bacterial meningitis. Most of the children (69.1%; n=47) completed 10 days of treatment (minimum treatment time for meningitis in the service).

3.1.6. Scalable profile

3.1.6.1 Short-term development

Table VI shows the distribution of children treated for meningitis according to the evolution of clinical signs. It is observed that children treated as meningitis have varying clinical signs. We can note a predominance of children who have a persistence of fever beyond 5 days (33.3%).

Table VI: Distribution of children treated for meningitis according to the evolution of clinical signs

	Number	Percentage (%)	Total
Number of children with persistent fever for more than 5 days	22	33.3	66
Number of children who had persistent signs of meningeal irritation beyond 5 days	1	16.7	6
Number of children with persistence of neurological signs beyond 5 days	9	15.2	59

NB: Two children died before the fifth day

Figure 1 shows the mode of discharge of children treated as bacterial meningitis at CHU-MEL. An intra-hospital lethality of 7.3% (5/68) is noted. Uncured children are children who returned against medical advice or who did not benefit from a PL control before the execution.

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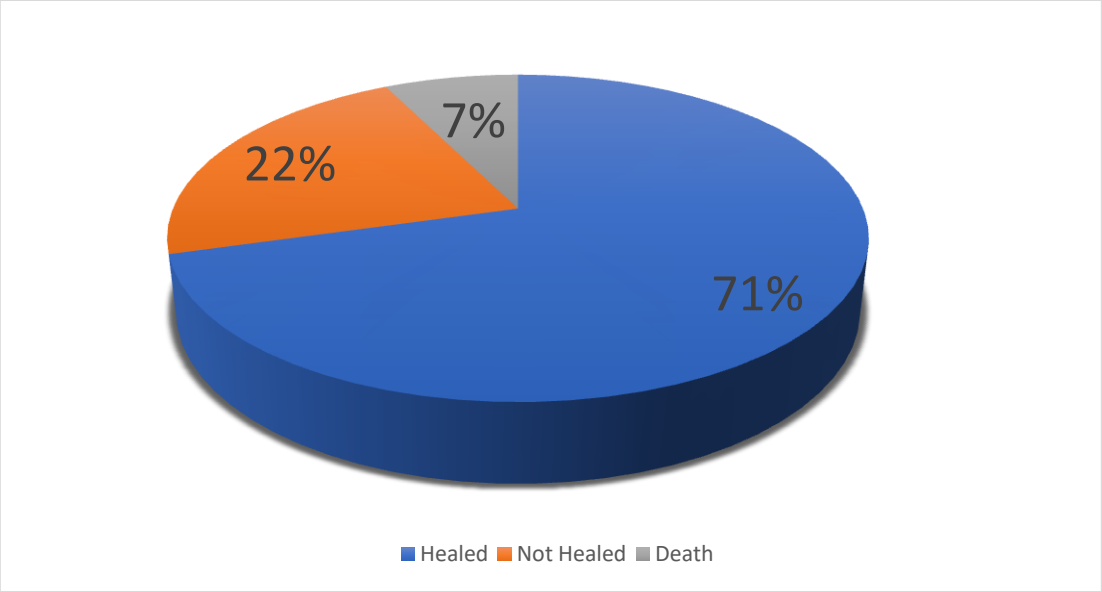

Figure 1: Mode of discharge of children treated as bacterial meningitis at CHU-MEL

Figure 2 shows the duration of hospitalization of children treated for bacterial meningitis. The majority of children (83.8%) spent more than 10 days in hospital with an average hospital stay of 18 days.

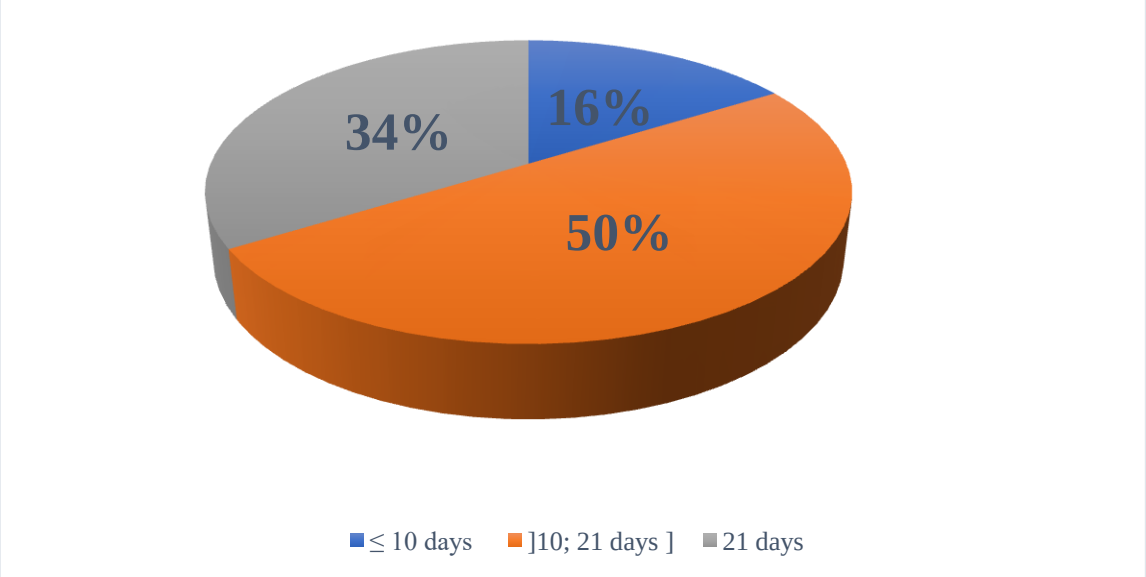

Figure 2: Duration of hospitalization of children treated as bacterial meningitis

3.1.6.2. Medium-term development

Figure 3 presents the medium-term evolution (1 year after hospitalization) of children treated for bacterial meningitis. In this case, we see that 51/68 parents were reachable for the assessment of the medium-term development of the children. Of these parents contacted, the majority were in favor of care.

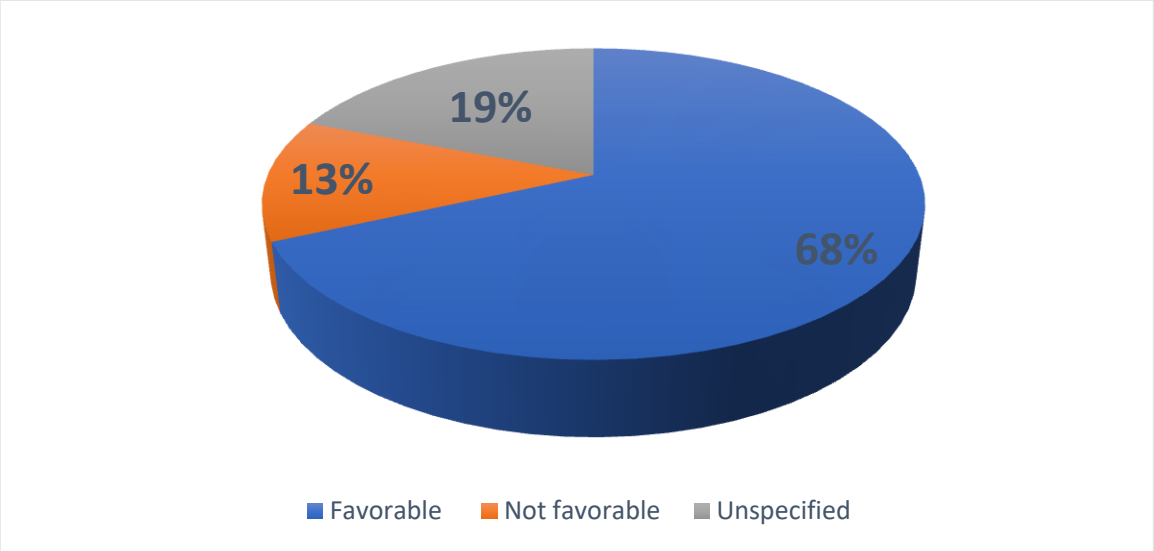

Figure 3. Medium-term evolution of children treated for bacterial meningitis

Table VII below presents the evolutionary modalities of the children who had an unfavorable evolution. The majority (37.5%) had presented a regression of psychomotor acquisitions.

Table VII. Evolutionary modalities of children who had an unfavorable evolution.

Unfavorable development	**Number**	**Percentage (%)**
Death after enforcement	2	25.0
Hydrocephalus	1	12.5
Recurrent bacterial meningitis	1	12.5
Regression of psychomotor acquisitions	3	37.5
Deafness + blindness	1	12.5
Total	**8**	**100**

The factors associated with an unfavorable evolution of children treated as bacterial meningitis are presented in table VIII

Table VIII. Factors associated with the unfavorable evolution of children treated for bacterial meningitis

Risk factors		**Favorable evolution**	**Unfavorable evolution**	***p***
Age (n=56)	0- 3 months	7	1	0.197
	]3 months – 3 years]	21	10	
	]3 years -5 years]	6	2	
	> 5 years	9	0	
Cellulorachia (n=56)	0-50	25	3	0.083
	50-100	3	2	
	≥ 100	15	8	
Proteinorachia (n=56)	< 0.40	4	1	0.858
	≥ 0.40	39	12	
Glycorachia (n=56)	≤ 0.27	4	5	**0.012**
	> 0.27	39	8	
Poorly followed treatment (n=56)	Yes	21	13	**0.001**
	No	22	0	
Duration of treatment (n=56)	10 days	33	6	0.094

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	21 days	6	5	
	> 21 days	4	2	
Disappearance of fever (n=51)	< 5 days	33	2	**0.004**
	≥ 5 days	10	6	
Disappearance of neurological signs (n=46)	< 5 days	35	4	**0.027**
	≥ 5 days	4	3	
Mode of exit (n=51)	Healed	37	2	**0.000**
	Not Healed	6	6	

3.2. Discussion

3.2.1. Epidemiological characteristics

In our study, the hospital frequency of meningitis treated as bacterial was 0.66%. This prevalence is lower than the 1.07% found at the CHU Gabriel Touré in Mali by Maiga et al. [11] and the 1.4% reported by Kané et al. [12] in their study conducted in the pediatric department of the Mali hospital from 2012 to 2018. However, this value is higher than the 0.3% found by Tfifha et al. [13]. In this last study, only 61 cases of bacterial meningitis had been recruited at Sahloul University Hospital (Sousse-Tunisia) over a period of 11 years (2006 to 2016). Thus, the most represented age group is between 3 months and 3 years (52.9%) and the majority (85.3%) were under 5 years old. This observation corroborates that found by Maiga et al. [11] when they found a similar prevalence to ours; which shows the immune fragility of this age group.

3.2.2. Biological characteristics

Regarding the biological characteristics, in our series, a germ was isolated in the CSF in 4.4% of cases. Previous studies have reported much higher values with positivity thresholds of 39% in Mali [11], 66% in Morocco [14] and 67.2 in Tunisia [13]. The absence of germs in the Cerebrospinal Fluid (CSF) despite bacterial meningitis may be related to taking antibiotics before performing the lumbar puncture. But only 33.8% of the children in our study had received an antibiotic compared to the series by Maiga et al. [11] of which 66% of children had received antibiotic therapy before admission. CSF and PCR can be very helpful in the diagnosis of bacterial meningitis. Along the same lines, Kané et al. [12], in their study on the diagnosis of meningitis in children used PCR (59.1%), Gram stain (39.8%), agglutination test (29.5%) and cultivation (5.7%). The absence of germs in the CSF in the event of bacterial meningitis, perhaps also linked to the conditions of transport and storage. Indeed, given the fragility of certain germs such as pneumococcus, CSF must reach the laboratory without delay at room temperature for immediate processing. The study of transport and storage conditions and the performance of PCR on CSF samples would help us at the CHU-MEL to better detect the germs involved in presumed bacterial meningitis. Additionally, in low-resource settings, many children may present with bacterial meningitis, but laboratory capacity may not be sufficient to isolate the causative agent and confirm the diagnosis [15]. Unless this is an overestimate of cases of bacterial meningitis by clinicians, because most of the children in our series had a cellulorachy less than 100 cells/mm3 (55.9%, n=38) and a higher high glycorrhachia to 0.27g/l (82.3%; n=56) or bacterial meningitis is often considered when the leukocytes are greater than 100 cells/mm3 and the glycorrhachia is less than 0.27g/l [16].

In our study, 7.4% of children performed CRP; 22.1% blood culture and 95.6% NFS. These assessments are not systematically carried out because they are the responsibility of the parents and their realization depends on their financial means. However, these assessments and especially the blood procalcitonin and the lactate level in the CSF have an orientation

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interest in the diagnosis of bacterial meningitis. In the case of a CSF lactate assay, a value below 3.2 mmol/l makes the diagnosis of bacterial meningitis very unlikely and a value below 0.5 ng/ml for the procalcitonin assay serum level makes the diagnosis of bacterial meningitis highly unlikely [17]. Blood procalcitonin is considered to have higher diagnostic accuracy for detecting bacterial meningitis than serum C-reactive protein, leukocyte count, neutrophil count, CSF protein and glucose levels [18-19]. Often the combination of the results of these tests allows an accurate prediction of the likelihood of bacterial meningitis versus viral meningitis.

3.2.3. Therapeutic characteristics

In the case of bacterial meningitis, antibiotic therapy should ideally be initiated within one hour of arrival at the hospital, regardless of the time that has already elapsed since the presumed start of the meningitis [20]. In our investigation, all our patients received ceftriaxone or cefotaxime either in combination with gentamicin or other antibiotics. This corresponds to the recommendations for the management of bacterial meningitis, which recommend the use of a third-generation cephalosporin in the event of bacterial meningitis [21]. Unfortunately, 60.3% of the children treated for bacterial meningitis in our study did not follow the treatment well. This poor compliance is probably linked to the cost of antibiotics, the duration of treatment and the low purchasing power of populations. Poorly followed treatment is statistically associated with the development of children treated as bacterial meningitis ($p = 0.001$). Health insurance for all would be a great contribution to overcoming the therapeutic non-compliance of our patients. In addition, the combinations of antibiotics used are diverse and varied. It would be more appropriate to establish a protocol of antibiotics to be used in the service in the event of bacterial meningitis.

3.2.4. Scalable Features

In the event of meningitis, surveillance focuses on fever and neurological signs. The fever often disappears after 48 hours and the neurological signs within 2 to 5 days [20]. About 1/3 of the children (33.3%) had a persistence of fever beyond 5 days and this is associated with an unfavorable outcome ($p=0.004$). Similarly, 15.2% of children had persistence of neurological signs beyond 5 days and this was also associated with an unfavorable outcome ($p=0.027$). The medium-term evolution was assessed after phone calls to parents, this underlines a lack of follow-up of children hospitalized for bacterial meningitis. In addition, sequelae were observed in 8.9% of children (5/56). These sequelae were of the hydrocephalus type (1.8%), regression of psychomotor acquisitions (5.3%) and deafness + blindness (1.8%). In addition, one child had a recurrence of bacterial meningitis (1.8%). The sequelae rate is lower than the 13% reported by El Fakiri et al. [14] and 12.5% by Kané et al. [12]. The overall lethality was 12.5% (7/56). This rate is similar to that of Merabet et al. [22] who recorded a case fatality rate of 11.7% in the Tangier region of Morocco. Nevertheless, this rate is lower than that found in the pediatric department of the Mali Hospital where it was 18.2% [12] and that found by El Amrani et al. [23] who found a rate of 19.2% but it is on the other hand much higher than that found by El Fakiri et al. [14] which was 1%.

Despite the limitations of our study with regard to the epidemiological data obtained from medical records, which did not allow us to study the socio-economic level of the parents and the vaccination status of the children and the evolution in the medium term which could not be appreciated in all the children (12 parents of children were unreachable by telephone), our study tried to objectively assess the state of play on the management of supposedly bacterial meningitis in our center while indicating some areas for improvement.

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4. CONCLUSION

Bacterial meningitis is a serious condition characterized by high mortality and significant sequelae. In our study, 23.2% of children treated for presumed bacterial meningitis experienced an unfavorable evolution with an overall lethality of 12.5% and sequelae in the order of 8.9%. To improve care, it is important to better determine the germs involved, to establish a care protocol and to ensure proper conduct of antibiotic therapy.

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