

## Prognostic Factors of Bacterial Meningitis in Children

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### Abstract

**Introduction:** Children's Bacterial meningitis (BM) is a main cause of death, and serious neurosensory sequelae, permanent and important especially in developing countries.

**Methods:** We carried out a retrospective, descriptive and analytical study including 69 children collected in the Infectious Pediatrics department between January 2015 and December 2021 for BM. Data were collected from hospital files. The statistical analysis was performed by SPSS V21.0 (IBM Inc., Chicago, USA) and Microsoft Excel. The underlying risk factors was made by calculating the Odds Ratio. Difference was considered statistically significant if the P value is  $\leq 0.05$ .

**Results:** The study included 69 patients, 65% are less than 12 months old. The main clinical signs underlined were consciousness disorders (63.76%), seizures (34%), complex seizures (28%) and focal neurological signs (16%). Cerebrospinal fluid (CSF) culture was primarily positive for *S. pneumoniae* (42.8%) and *N. meningitidis* (37.2%). Mortality was noted in 7.25% of the cases. The prognosis factors associated with complicated BM based on multivariate analysis were age  $\leq 12$  months, 3-day progression time before admission, fever with complex seizures, seizures status, focal neurological signs, albuminorrachia  $\geq 2\text{g/l}$ , hypoglycorrachia  $\leq 0.3\text{g/l}$ , involved germs such as pneumococcal and meningococcal as well as anemia.

**Conclusion:** Identifying prognosis factors associated with complicated BM will allow clinicians to better predict BM's evolution of and therefore make treatment decisions

**Keywords:** Complications, infant, prognosis Factors, Bacterial meningitis.

### Introduction

The BM is a main medical emergency, affecting children with preference. It is a public health problem in developing countries, mainly in Africa, where it is responsible for heavy mortality and severe neurosensory sequelae [1]. BM identification prognosis factors at the time of patient's admission or along progression is important in identifying patients at risk for serious complications and which require early management. In Morocco, despite of the progress made by the national immunization program, including pneumococcal vaccine introduction in 2010, BM incidence and mortality is still worrying. Our work is a retrospective, descriptive and analytical study of 69 BM cases with the objective of studying the epidemiological, clinical, para-clinical and developing characteristics of children hospitalized for BM, to identify prognosis factors of complicated BM.

### Patients and Methods

It is a retrospective, descriptive and analytical study held at the Infectious Pediatrics Department of the Abderrahim Harrouchi Mother and Child Hospital in Casablanca. It concerned 69 children hospitalized between January 2015 and December 2021 (7 years) for BM. Patients aged 1 month to 14 years with BM confirmed bacteriologically by culture and/or PCR positive at the CSF were included in our study.

The clinical, biological, radiological, therapeutic and socio-demographic data of all patients included in our study were imported into Microsoft Excel. The statistical analysis was performed by SPSS V21.0 (IBM Inc., Chicago, USA) and Microsoft Excel.

The study population was subdivided into two groups: Group 1 (N=40) with a favourable development and Group 2 (N=29) with an unfavourable development (sequelae or death). The  $X^2$  test was used for a statistical comparison

between different prognosis factors. underlying risk factors was carried out by calculating the Odds Ratio. A difference was considered statistically significant if the P value is  $\leq 0.05$ .

## Results

We identified 69 BM cases. Our patients' average age was 25 months [1 month- 14 years]. BM was found in 87% of the cases in children under 5 years old. A male predominance was noted with a sex-ratio of 1.7. Management time for the clinical signs onset was an average of 3 days [1-20 days].

Fever was the main complaint with an average of 38.4°C [38°-41°C]. It was associated with seizures in 72.46% (n=50) of cases with 19 (38%) were generalized, 14 (28%) were localized, and 17 (34%) with status convulsivus. Vomiting was found in 49.27% (n=34) of cases against suckle refusal in 30 patients (43.47%). First examination found out meningeal syndrome (16%), axial hypotonia (10%), a bulging anterior fontanel (44%). The entrance was found in 11 patients (15.94%) with otitis and pneumonia respectively in 36.36% each.

Consciousness disorders were found in 44 cases (63.76%). They were predominant by somnolencia in 31 cases (44.93%) while 12 patients (17.39%) were obsessed with one patient (1.44) in coma. The Glasgow score (GCS) evaluated in all patients showed an average of 13.74 [ 7 to 15]. Fulminant purpura was found in 13 patients (18.84%). Motor deficit was noted in 7 cases (10.14%). Prior antibiotic therapy was administered before hospitalization in 17 patients (24.63%) with Amoxicillin-clavulanic acid (11.76%), Amoxicillin (29.41%) and 3rd-generation cephalosporins (C3G) in 41.17%.

Cerebrospinal fluid study (CSF) underlined a cloudy appearance in 90% of cases. Cellulorachia greater than 500/mm<sup>3</sup> and predominantly PNN (100%) was found in 52 patients (75.36%). Hyper-albuminorachia was constant

while deep hypo-glycorachia below 0.29g/L was noted in 79.71% (N=55) of cases. CSF examination with Gram stain was positive in 24 cases (34.78%), culture was positive in 35 cases, the germs found were S Pneumoniae (15 cases), N Meningitidis (13 cases), H Influenzae b (6 cases), E Coli (1 case). Blood culture was positive in 17 cases. N. meningitidis and S. pneumoniae were the most isolated species in 8 cases (47%) and 6 cases (35.29%) respectively.

As far as radiology is concerned, the transfontanellar ultrasound and the cerebral scan had made it possible to identify the main abnormalities: an empyema (23.18%) a hydrocephalus (8.69%), an abscess (5.79%). Cases of ventriculitis, presuppurative encephalitis, cerebral edema, vasculitis, thrombophlebitis and sinusitis were also found.

For treatment, first-line antibiotic therapy was ceftriaxone (100mg/kg/d) in all patients. For complicated BM, vancomycin was associated in 23.18% (n=16) and ciproxin in 18.84% (n=13). Term average of antibiotic treatment was 20 days [8-60 days]. This time was variable depending on the germ and the presence or absence of complications. An anticonvulsant was administered in 41 patients (59.42%).

Recovery without sequelae was noted in 40 patients in our series (57.97%) while 24 (34.78%) patients had neurological sequelae. The latter had motor deficit in 8 cases (33.3%), hydrocephaly in 7 cases (29%), deafness in 5 cases (20.8%), epilepsy in 2 cases (8.3%), hearing loss in 1 case (4.1%), blindness in one case (4.1%) and psychomotor retardation in one patient (4.1%).

Death underlined in 5 patients (7.25%), with an average age of 6 months, with 3 (60%) were due to pneumococcal and 2 (40%) were due to meningococcal disease. Prognosis factors associated with complicated BM are shown in Table 1. (P-value 0.05).

**Table 1:** Multivariate analysis of prognosis factors.

	G1(N=40)	G2(N=29)	P-value	Odds Ratio	IC95%
Age $\leq 12$ month	30	15	0,0001	21	(7-32,2)
Time development before admission $\geq 3$ days	19	15	0,05	1	(0,4-2 ,3)
Prior antibiotic therapy	9	9	0,142	1,2	(0,83-3)
Complex seizure	5	9	0,0238	3	(1,2-9)
Seizure status	5	12	0,0145	40	(12-100)
impaired consciousness	25	19	0,2	0,98	(5-26)
focal neurologic Signs	2	9	0,0477	8,23	-
Albuminorrachia $\geq 2$ g/l	31	19	0,0072	11	(6,42-
Glycorrachia $\leq 0, 3$ g/l	31	24	0,0385	3,15	(1,32-10)
pneumococcus	13	15	0,00012	26	(12-68)
meningococcus	14	14	0,0001	30	(10-98)
anemia	24	11	0,05	9	(3,2-15)

## Discussion

Our study concerned 69 cases of BM in children between 1 month and 14 years old in the infectious pediatrics department. Age average was 25 months and over 65% of our children were under 12 months old. This could be explained by the high frequency of promiscuity (nursery) and low antibody levels at this age, especially in cases of meningitis to *Haemophilus influenzae b* [1,2]. both sexes are concerned [3,4,5].

Bacterial meningitis Clinical signs are very variable mainly in children. The younger the child is, the more atypical the symptoms are. Fever is the most common and earliest symptom. However, although the suggestive signs of meningitis are well known to date, their low specificity is still suggestive of diagnosis errors, and consequently inadequate antibiotic therapy. Looking for entrance during meningitis is important because, depending on its nature, it will require special monitoring and treatment [6]. In a study in France on pneumococcal meningitis in children, clinical data showed that 35.6% of children had acute otitis media prior to hospitalization [7]. The most frequently found entry were otitis [8,9]. In our series, respiratory infections and ear infection represented 36.36% each.

Lumbar puncture (LP) is the diagnosis key during meningitis. It is urgent and essential to underline meningitis diagnosis. In addition to LP, blood cultures are essential because they can be positive even if the CRL culture is negative. In our series, blood culture was positive in 89.47% of the cases. Three main bacterial species dominate purulent meningitis etiology: *H. influenzae*, *S. pneumonia* and *N. meningitidis* [10]. In our series there were three main identified germs: pneumococcus (42.8%), meningococcal (37.2%) and *H. influenzae* (17.2%). In a study held in Tunisia by Thabet and al, *H. influenzae* type b (Hib) was the main bacteria isolated in their series because vaccination was not yet part of the immunization schedule [10]. In countries where Hib vaccination is systematic, such as Morocco, there is a collapse in the rate of meningitis in Hib [11, 12, 13], which is consistent with our study. This is because vaccination against pneumococci and meningococci does not cover all pathogenic strains.

The antibiotic treatment we initiate in emergency is probabilistic in all cases. In infants, it includes a bi-antibiotic bactericidal and synergistic combining ceftriaxone and aminoglycoside. This association benefit is proven in the 0–3-month age group. But beyond this age group, this benefit remains questionable because aminoglycoside does not or slightly cross the blood-meningeal barrier. When the child is over 24 months old, ceftriaxone monotherapy is used in most of the cases. The three main germs are sensitive to ceftriaxone in most cases [14].

Meningitis is a severe affection responsible for high mortality and many sequelae in children cured in practice. We found an overall mortality of 7.25% which is comparable to others of pediatric cases in the USA (6.9%) [15]. Other authors reported high rates [16,17] The 34.78% sequelae rate we report is similar to the 34.5% reported by Thabet and al. [18] in Tunisia. These mortality and sequelae's high rates in our study could be explained by the clinical condition severity of these children at admission who underwent early complications in nearly third of the cases. Besides therapeutic management difficulties due to shortage of diagnostic means and resuscitation. Our study shows that the sequelae are dominated by neurosensory disorders and tone (motor deficit, hydrocephalus, deafness, epilepsy, hearing loss, blindness and psychomotor retardation) and are caused by *S. pneumoniae* in 36.36% of the cases. These sequelae can affect the patients' life quality, related to learning, adaptability and social integration disabilities.

In our series, the multivariate analysis has made it possible to identify ten significant prognosis factors related to complicated BM: age  $\leq 12$  months, development time before admission  $\geq 3$  days, a complex febrile convulsion, status convulsivus, focal neurological signs, albuminorrachia  $\geq 2\text{g/l}$ , hypoglycorrachia  $\leq 0.3\text{g/l}$ , germs including pneumococcus and meningococcal, and anemia. Indeed, S. Namanie and al. [19] have identified in a retrospective series of 77 patients, prognosis factors such as age  $\leq 12$  months, impaired consciousness state, seizures, prior antibiotic therapy, focal neurological signs, Massive cellulorrachia, glycorrachia/glycemia ratio  $\leq 0.2$ . In a retrospective series of 44 cases in Argentina, Sergio A. Antoniuk and al found out as prognosis factors convulsions, impaired consciousness state, focal neurological signs, irritability, use of ventilation, albuminorrachia  $\geq 2\text{g/l}$ , Deep glycorrachia, neutropenia, *S. pneumoniae*. [20]. In contrast to our series, some authors have found that impaired consciousness and prior antibiotic therapy are associated with complicated BM [18,21,22,23].

## Conclusion

The underlying prognosis factors associated with complicated BM from admission and/ or during hospitalization aims to improve management's quality of our patients. It will allow clinicians to better predict the BM's evolution and thus help in treatment decisions in emergencies as well as in medium and long-term follow-up.

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