

Predictors of Poor Prognosis during the 2015 Meningitis Epidemic at Niamey National Hospital

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Summary

The countries of the Peysonnia belt are paying a heavy price for bacterial meningitis. Morbidity and mortality of bacterial meningitis is linked to certain factors.

It is a descriptive and analytical prospective study over a period of two months from April 15 to June 15, 2015 in subjects admitted for suspected meningitis at the National Hospital of Niamey. Identifying predictors of poor prognosis during this outbreak is our goal.

One hundred and five patients were enrolled. The majority were young. Signs of severity were coma (22.9%), seizures (12.4%), signs of focus (9.5%), shock (7.5%). Delay in management and hyperproteinrachia have also been identified as poor prognostic factors. Sequelae were balance disorders (n=20; 19%), hearing loss (n=7; 6.6%), purpura fulminans (n=13; 12.4%). There were 12 deaths or 11.4% of which 11 comas (91.66%), 2 convulsions (16.66%), 1 purpura fulminans (8.3%), 6 shock (50%), 5 signs of focus (41.66%), 8 of these patients (66.66%) came 3 days after the onset of signs.

Poor prognosis factors were related to brain damage, shock and delayed management. Improving Niger's health system will reduce them.

Keywords: bacterial meningitis; poor prognostic factors; Niamey; Niger

Introduction

Meningitis is a global public health problem affecting all continents [1]. The Peysonnie belt is the region of sub-Saharan Africa stretching from Senegal in the west to Ethiopia in the east [2], these countries are prone to sporadic meningitis epidemics; this area experienced in 1996 one of the largest epidemics in recent African history with 250,000 cases and 25,000 deaths. Thus, Niger recorded 45,000 cases with a case fatality rate of 14% [3, 4, 5, 6]. Despite the availability of antibiotic treatments and effective vaccination, bacterial meningitis remains serious in terms of high mortality and the serious sequelae they cause. Even properly managed the disease kills at least 10% of patients within 24 to 48 hours after onset and 20% of those who survive have long-term disabilities such as brain damage, deafness or paralysis of the lower limbs, hydrocephalus at normal pressure due to compartmentalization of the meninges, irreversible dementia [1, 2, 3]. Meningococcal A was responsible for most epidemics in sub-Saharan Africa [7]. With the aim of eliminating meningococcal epidemics a new conjugate vaccine called MenAfriVac has been developed. Pilot studies conducted in Mali, Senegal and Gambia between 2006 and 2008 in adults [8]. These clinical trials with long-term follow-up have proven the efficacy and safety of this vaccine in pregnant women at all stages of pregnancy. It induces 20 times more antibodies than the polysaccharide vaccine [9], the immune response is long-lasting, there are no major side effects reported during clinical trials, and strengthens anti-tetanus immunity because the carrier protein used to conjugate this vaccine against *Neisseria meningitidis A* is tetanus toxoid [10]. In Niger and most countries that have introduced this vaccine, there has been a disappearance of meningitis cases due to serogroup A; of the 275 million Africans living in the Peysonnia belt vaccinated with this conjugate vaccine, to date there have been no reported cases of meningitis due to serogroup A at the time we undertook this study. We are now witnessing the emergence of strains that since then have been responsible for most of the sporadic cases of the disease. This is the case in 2010, which saw a predominance of *NmW135*, especially in Niger, Nigeria, Ghana and Chad [11]. The same trend was observed in 2011 in Niger where *NmW135* was more incriminated [12]. In 2015, Niger experienced an epidemic of meningitis and we wanted to identify the predictive factors of poor prognosis during this epidemic at the national hospital in Niamey.

Methods

This was a descriptive prospective study conducted over two months, from 15 April 2015 to 15 June 2015, during the meningitis epidemic in Niger in Niamey in 2015. Patients hospitalized in the Infectious Diseases Department "Raymond Madras Pavilion" of the National Hospital of Niamey were included, whose diagnosis of meningitis was confirmed by the study of cerebrospinal fluid (cytobacteriological examination, biochemical, presence of soluble antigen, PCR). For data collection, we developed a support with a questionnaire structured in seven parts. A first part where we collected socio-demographic parameters including age, sex, origin, and mode of admission. A second part deals with an interrogation in order to constitute the history of the disease. For this part we focused on the time between the onset of symptoms and admission. A third part is devoted to the search for a history of vaccination against meningitis, medical history and the concept of contagion. In addition, we also looked for a history of otitis, sinusitis, nasopharyngitis for possible contiguous meningitis. A fourth part is devoted to the physical examination of the patient. At this level, we looked for general signs, neurological signs in children and adults, especially coma, convulsions and signs of focus; Other signs were sought, including cutaneous, articular. A fifth part devoted to the results of the CRF examinations. The sixth part concerns the antibiotic treatment received before admission but also the specific treatment of the service, inspired by the WHO protocol, possible corticosteroid therapy and the duration of treatment. The last part is devoted to the evolution under treatment. It is at this level that we looked for complications and sequelae observed in certain patients such as hearing loss, deafness, dementia, neurological deficit, balance disorders, behavioral disorders. The results of our work are entered on a computer into a database that we have developed in the Epi info 2012 version 3.5.4 software. The processing and analysis of this data was carried out with Epi info version 3.5.4, Excel 2007 and Word 2007.

Results

The study involved 105 patients. The average age of patients was 18.7 years ranging from 6 months to 81 years. The 15-29 age group was the most represented with 37.1% of cases. In sum, patients aged 0 to 29 years account for 82.9% of reported cases (See Table 1).

<i>Age range</i>	<i>Number of cases</i>	<i>Percentage</i>
≤ 5	22	21,0
6 – 14	26	24,8
15 – 29	39	37,1
30 – 44	8	7,6
≥ 45	10	9,5
Total	105	100,0

Table 1: Distribution of patients by age group.

The female gender represented the majority of our patients with 56 cases or 53.30%. The sex ratio was 0.88.

The mean time from onset of symptomatology to admission was 2.3 days ranging from 0 to 14 days. Of our patients, 19 (18.1%) had received antibiotic treatment prior to admission, of which 14 were on ceftriaxone or 73.7% of cases, 3 patients or 15.8% reported receiving amoxicillin and the remaining 2 were unaware of the molecule used.

The general condition was impaired in 40 patients or 38.10%. The majority of patients had a temperature between 37.9 and 39.4°C: 66 cases or 62.8%. Thirteen (13) patients had a temperature greater than or equal to 39.5°C or 12.4%. In children we found: incessant crying in 13 cases or 12.4%; digestive signs (jet vomiting, abdominal pain and diarrhea) in 11.4% of cases; refusal to suck in 11 cases or 10.5%; signs of focus in 6 patients or 5.7% of cases; neck stiffness in 5 cases or 4.8%; bulging fontanelle in two (2) infants or 1.9% of cases. In adults: headache was present in 81 cases or 77.1%; sixty-five (65) patients or 61.9% experienced jet vomiting; thirty patients (32) patients reported vertigo; seizures were present in 11 patients or 10.5%; Twenty (20) patients experienced agitation (19%); neck stiffness was found as a physical sign in adults in 74 cases (70.5%) of cases; Kernig and Brudzinski's signs were present in 64 and 58 patients respectively; four (4) patients showed signs of focus.

Signs of severity were coma, brain signs, purpura fulminans, shock in 22.9%, 24.9%, 12.4% and 7.6%, respectively (See Table 2).

<i>Signes of gravity</i>	<i>Actual</i>	<i>Percentage</i>
Comma	24	22,9
Brain signs	23	24,9
Purpura Fulminans	13	12,4
Shock	8	7,6
No sign of severity	37	35,2
Total	105	100,0

Table 2: Distribution of patients by signs of severity.

All our patients had received a lumbar puncture. The appearance of the fluid was cloudy in 96 patients or 91.40% of cases, purulent in one patient, clear in another and hemorrhagic in two patients or 1.90%. The WBC count in the CSF showed that 54 (51.4%) were between 1000 and 5000 leukocytes/mm³, 32 (30.5%) between 5000 and 10,000/mm³ and 19 (18.1%) greater than 10,000/mm³. In all cases there was hyperproteinachia ranging from more than 0.41 g / l to 9.08 g / l; the majority (53 cases or 50.5%) was between 0.41 to 1 g / l. There was hypoglycorachia in 59 patients (56.2% of cases), it was normal in 31 cases or 29.5% and elevated in 15 patients or 14.3%. *Neisseria meningitidis* C was isolated from 69 patients or 65.7%, *Neisseria meningitidis* W135 in 29 or 27.6% of patients and no germs were isolated in 7 cases or 6.7%.

All but one of our patients had received ceftriaxone who had been on dual therapy ceftriaxone + gentamicin. Dexamethasone was prescribed to 51 patients or 48.6% of cases and was in patients 0 to 15 years of age. The majority of patients (73 cases or 69.5%) had been treated for less than 7 days. The average duration of treatment was 6.1 days ranging from 1 to 35 days. In the majority of cases (64 cases or 61.0%), the clinical course was favorable, nevertheless we recorded 12 deaths or 11.40% of cases. The clinical outcome was more favourable in women than in men. We also recorded as many deaths among women as among men. The course of patients does not vary significantly by sex ($p = 0.9$). Forty-two (42) of our patients had sequelae, or 40% of cases (See Table 3).

<i>Aftermath</i>	<i>Number of cases</i>	<i>Percentage</i>
Balance disorders	20	19,04
Hearing loss/Deafness	7	6,6
Motor deficit	5	4,7
Dementia	5	4,7
Skin sequelae	3	2,8
Decreased visual acuity	2	1,9
No sequelae	63	60
Total	105	100

Table 3: Distribution of cases by sequelae.

In comatose patients there were 11 deaths, 11 cases of recovery with sequelae and 2 patients cured without sequelae. It should be noted that most of the deceased patients had a coma-shock association. Of the 13 cases of convulsions, there are 2 cases of death and 8 cases of recovery with sequelae. Of the 13 cases of purpura fulminans, there was one death and 8 cases of recovery with sequelae. This case of death had a combination of coma-purpura fulminans. No healing without sequelae was noted in patients who had signs of focus. A statistically significant relationship was found between signs of severity and prognosis ($p = 0.007$).

Of the 53 patients who had a proteinorachia between 0.41 and 1 g/l, there was 1 death and 8 recoveries with sequelae; 4 deaths and 6 recoveries with sequelae were noted in patients who had hyperproteinrachia between 1.1 and 3 g / l. We also note that among the 7 patients who had hyperproteinrachia between 6 and 9.08 g / l there were 3 deaths and 2 recoveries with sequelae. A statistically significant relationship was found between hyperproteinrachia and prognosis ($p = 0.004$).

All our patients have more than 1000 leukocytes per^{mm3} in the CSF. We found 29.63% of cures with sequelae and death in patients with leukocytosis between 1000 and 5000 elements per mm³, 40.62% in those with leukocytosis between 5000 and 10000 elements per mm³ had sequelae and death. The same observation was made in patients who had leukocytosis in the CSF greater than 10000 elements per mm³; sequelae and death rate: 63.15%. In view of these observations we retain that a very high number of leukocytes in the CSF could be a factor of poor prognosis. A statistically significant relationship was also found between white blood cell cytology of CSF and patient prognosis ($p=0.048$).

There were no deaths among the patients who consulted immediately after the onset of signs but two were cured with sequelae; For those (58 patients) who consulted between days 1 and 3, there were 4 deaths and 19 cured with sequelae; those (18 patients) who consulted between days 4 and 6, there were 6 deaths and 7 cured with sequelae. A statistically significant relationship was found between time to consultation and prognosis ($p = 0.003$).

The prognosis of patients (death and recovery with sequelae) is acceptable for patients (one death, 19 cured with sequelae) who had a temperature between 36 and 37.8 °C, compared to those with a temperature between 37.9 and 41 °C in whom there were more deaths (7/66) and recoveries with sequelae (41/66). No statistically significant relationship was noted between temperature and prognosis ($p=0.2$).

Discussion

The average age of the patients was 18.7 years. Sanon Adama [13] had found an average age of 36.97 years. Indeed our study had taken place during a period of epidemic while that of Sanon Adama had taken place over a year which could explain this difference in average age.

The sex ratio of our sample was 0.88 in favor of women or 53.30%. Our result is close to that observed by Dembélé A. [14] with a sex ratio of 0.90. Our results are different from those of Towa Djungoué [15] and Abdoukarim Sabo [16] who found respectively 1.38 and 1.68 in favor of the male sex. Campagne et al. [17] had also found that men were in the majority.

The majority of patients (58 patients, 55.2%) consulted between 1 and 3 days, 5 patients (4.8%) of patients consulted at least one week after the onset of symptomatology. Our result is consistent with that of Amadou Oumarou [18] in whom 80.43% of patients are hospitalized within 72 hours of the onset of the disease; ours being 78.1%. Our results are different from those of Barbach Youness [19] in which this duration varies from 0 to 2 months.

Otitis was the most prevalent morbidity with 14.3%. Our result is close to that of Barnach Youness [19]. Other pathologies have been found including sinusitis and nasopharyngitis. Twenty-three patients or 21.90% reported cases of meningitis in their surroundings.

At the end of our study, 8 patients or 7.8% of cases presented a state of shock. This result is practically identical to that observed by Sanon Adama [13] who obtained 7.6% of cases of shock. Impaired consciousness was present in 22.9% of cases. This result is very close to that obtained by Julie Chaix [20] in her Nancy cohort (21.2%). Sanon Adama [13], on the other hand, obtained in his sample 46.36% of cases of disorders of consciousness, a result much higher than ours. Convulsive seizures are found in 10.46% of our patients. This result is lower than that obtained by Sanon Adama [13] in whom 20.1% of patients presented with seizures. In our sample, 12.4% of cases of purpura fulminans were identified. This figure is much higher than those of Julie Chaix [20] and Sanon Adama [13] who obtained respectively despite the long duration that marked their work 2.3% (Senegalese cohort) and 0.6%. Ten of our patients or 9.5% of the sample showed a sign of focus. This is the case of Sanon Adama [13] who identified 5 cases with signs of focus (2.8%) several days after hospitalization.

CSF was cloudy in 91.4% of patients. Our result is much higher than those obtained by Sanon Adama [13] and Abdoukarim Sabo [16] in whom CSF is cloudy in 19.66% and 37.1% of cases respectively. Indeed, the murky aspect of CSF comforts us about the bacterial origin of germs linked to this 2015 epidemic. All our patients had hyperproteinachia, Abdoukarim Sabo [16] obtained a result almost identical to ours since nearly 99% of his patients had hyperproteinachia. Hyperproteinachia is indicative of inflammatory involvement of the meninges, especially if it is associated with hypoglycorachia. Leukocyte cytology was very high in all our patients. A proportion of 51.4% of our sample has a leukocyte cytology between 1000 and 5000 elements / mm³. What interests us is of course the influence of this hypercytosis on the patient's prognosis. *Neisseria meningitidis C* was the most identified in patients in our study with 65.7%. *NmW135* was also identified in 27.6% of cases. Our results are higher than those of Sanon Adama [13] who identified *NmW135* in 20.7% of cases and *NmA* in 3.44% of cases. Before the 2000s, countries in the meningitis belt were facing epidemics of meningitis due to *NmA*. *NmW135* appeared in the belt in 2002, which justifies its frequency in our sample and in that of Sanon Adama whose study was made in 2003. The high proportion of *NmC* in our sample is of concern to us because it is for the first time that this serogroup is involved in a large-scale meningitis epidemic in the country.

Ceftriaxone, a molecule recommended by WHO for the treatment of bacterial meningitis, was used for all patients in our sample. This is not the case for Sanon Adama [13] in whom ceftriaxone was used in only 10.6% of cases. In order to reduce the auditory sequelae observed at the beginning of the 2015 meningitis epidemic, we undertook corticosteroid therapy in patients aged 0 to 15 years. As a result, 48.6% of our patients benefited from dexamethasone administration within the first 48 hours of admission. The result is very satisfactory because it has probably avoided auditory sequelae. Indeed, several studies report the beneficial effect of corticosteroid therapy during acute bacterial meningitis if administered within a short time after the onset of infection [21, 22, 23].

We recorded 12 deaths (11.40%). Our result is acceptable compared to those of Sanon Adama [13] and Abdoukarim Sabo [16] who recorded respectively 30.17% and 46.66% of deaths in their samples.

In our series, balance disorders were the most encountered sequelae (69% of sequelae); hearing loss and deafness, neurological deficit, dementia, decreased visual acuity and skin sequelae were also found. Abdoukarim Sabo [16] found mainly neurological and auditory sequelae. Sanon Adama [13] recorded only auditory and neurological sequelae and only in 3.2% of his patients.

A statistically significant relationship was also found regarding the time elapsed between the onset of symptomatology and the date of consultation; and patient prognosis ($p=0.003$). The same observation was made by Amadou Oumarou [18] who also noted a co-relationship between a long delay before the consultation and the occurrence of sequelae.

A statistically significant relationship was found between signs of severity and prognosis ($p = 0.007$). Thus, we note that signs of severity have an important influence on the prognosis of patients during the epidemic. Some studies have mentioned this observation in particular: V. Des Portes [24] reports neurological impairment and disorders of consciousness as factors of poor prognosis. E. Forestier [25] also mentioned shock, disorders of consciousness and neurological disorders as factors of poor prognosis. H. Ben Hamouda et al [26] cited shock as a factor in poor prognosis as well as respiratory distress and low birth weight.

Julie Chaix [20] in her Senegalese cohort also found that mortality increases with the proteinorachia observed; the death rate varies from 13.3% for proteinorachia between 0.41 and 1 g / l to 50% for proteinorachia greater than 5 g / l. V. des Portes [20] goes in the same direction by evoking that a very high proteinorachy is in favor of a poor prognosis. Indeed, a statistically significant relationship was noted between hyperproteinorachia and prognosis ($p=0.004$) in our study. We can retain that a very high proteinorachy could be a predictor of poor prognosis.

Conclusion

Meningitis epidemics remain severe despite all WHO strategies to reduce morbidity and mortality. The time between the first signs and the consultation can be an important factor in the patient's prognosis; The longer it is, the lower the chances of recovery. Signs of severity such as impaired consciousness, neurological deficit, shock and seizures are predictors of poor prognosis in that they may be the basis for significant mortality. Purpura fulminans, which is recognized as a sign of severity, was not a poor prognosis in our sample. Hyperproteinorachia and leukocyte hypercytosis in CSF may be poor prognostic factors. We found through our results that there were more deaths and cures with sequelae in patients who had very high proteinorachy. It should be noted that corticosteroid therapy performed early in patients from 0 to 15 years of age reduces neurosensory complications including hearing loss and deafness.

Authors' Contributions

- Gado Amadou Mahamadou: data collection, data analysis and article writing.
- Boulama Malam Mamadou: data collection, data analysis and article writing.
- Amadou Mahamane Laouali Harouna: data collection, data analysis and article writing.
- Akilou Abdoulsalam: data collection, data analysis and article writing.
- Mamane Daou: data collection, data analysis and article writing.
- Ayouba Ismael Tanni: data collection and analysis.
- Moussa Sahada Salèye: correction of the article.
- YacoubaNouhou: correction of the article.
- Hanki Yahayé: correction of the article.
- Adehossi Eric: supervision of the works.

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