Epidemiological aspects and follow-up of purulent meningitis sequelae in the Zinder Region, Niger in 2023.

Aspects épidémiologiques et suivi des séquelles des méningites purulentes dans la région de Zinder, Niger en 2023.

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Abstract

Introduction: Objectives: Purulent meningitis is a major public health problem, as it is often responsible for deadly epidemics in the Sahel. This study aims to investigate the epidemiological aspects and assess the sequelae of such meningitis. **Material and methods**: This is a cross-sectional descriptive study of purulent meningitis cases from January 1st to July 31st, 2023, at the Department of Infectious and Tropical Diseases of the National Hospital of Zinder. All patients admitted for febrile meningitis syndrome were included. **Results**: A total of 396 patients were hospitalized for febrile meningitis syndrome, with a prevalence of purulent meningitis at 87.1% (345/396). Most patients, 87.8% (303/345), came from the urban commune of Zinder. The average admission delay was 2.6 days [0-10 days]. The mean age was 14.09 years [3 months-75 years]. Gram staining was performed in 62.4% (216/345), revealing Gram-negative diplococci in 94.9% (205/216). Seventy-seven samples were analyzed by Polymerase Chain Reaction, identifying *Neisseria meningitidis* serogroups. Serogroup C was found in 84.41%, W135 in 1.30%, and *Streptococcus pneumoniae* in 7.79%. The average length of hospital stay was 8 days. The case fatality rate was 10.4% (36/345). Recovery was achieved in 89.6% of patients (309/345), of whom 5.5% presented sequelae (17/309). These sequelae included blindness, deafness, strabismus, hypoacusia, hemiplegia, and neuropsychiatric disorders. The main complications were meningoencephalitis in 11.6% (40/345) and meningococcemia in 38.3% (132/345). **Conclusion**: Meningitis epidemics in Niger are mainly due to serogroup C *Neisseria meningitidis*. Follow-up of sequelae should be associated with the management of these meningitis outbreaks.

Keys words: Purulent meningitis, *Neisseria meningitidis*, epidemiology, sequelae, Sahel.

Résumé

Introduction : Objectifs : Les méningites purulentes sont un problème majeur de santé publique car elles sont souvent responsables d'épidémies meurtrières au sahel. L'objectif était de décrire les aspects épidémiologiques et d'évaluer les séquelles de ces méningites. **Matériel et méthodes** : Il s'agit d'une étude descriptive transversale des méningites purulentes du 1er janvier au 31 juillet 2023 au service des maladies infectieuses et tropicales de l'hôpital national de Zinder. Tous les patients admis pour syndrome méningé fébrile étaient inclus. **Résultats** : Au total, 396 patients étaient hospitalisés pour syndrome méningé fébrile, la prévalence des méningites purulentes était de 87,1% (345/396). La majorité des patients, 87,8% (303/345) provenaient de la commune urbaine de Zinder. Le délai moyen d'admission était de 2,6 jours [0-10 jours]. L'âge moyen était de 14,09 ans [3 mois-75 ans]. La coloration de Gram était réalisée dans 62,4 % (216/345), et avait permis de retrouver des diplocoques Gram négatifs dans 94,9 % (205/216). Soixante-dix-sept échantillons étaient analysés par réaction de polymérisation en chaîne, ce qui a permis l'identification de *Neisseria meningitidis* sérogroupes C dans 84,41%, W135 dans 1,30% et *Streptococcus pneumoniae* dans 7,79%. La durée moyenne d'hospitalisation était de 8 jours. La létalité était de 10,4 % (36/345). La guérison était obtenue dans 89,6 % (309/345), dont 5,5 % avaient présenté des séquelles (17/309). Ces séquelles étaient à type de cécité, surdité, strabisme, hypoacousie, hémiplégie et troubles neuropsychiatriques. Les principales complications étaient les

Conclusion : Les épidémies de méningites au Niger sont principalement dues au sérogroupe C de *Neisseria meningitidis*. Le suivi des séquelles devra être associé à la prise en charge de ces méningites.

Mots clés : Méningite purulente, *Neisseria meningitidis*, épidémiologie, séquelles, Sahel.

INTRODUCTION

Purulent meningitis is an acute inflammation of the meninges caused by pyogenic bacteria. While several bacteria can cause meningitis, *Neisseria meningitidis* (Nm) can trigger large-scale outbreaks. In the meningitis belt, which extends from Senegal to Ethiopia, five Nm serogroups are predominant: A, B, C, W and X. In this region, during the dry season from December to June, populations are facing a significant epidemic risk [1–3]. The disease is transmitted through the air, when infected individuals release large droplets of nasopharyngeal secretions. The incubation period varies from 2 to 10 days.

The highest attack rates are observed in children under 15 years of age [2,4]. Common symptoms include high fever, headache, neck stiffness, vomiting, photophobia, and swelling of the fontanels in infants [2,5]. Several bacteria can cause purulent meningitis (PM), with *Nm*, *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) being the most common in Africa [2,6]. The well-established treatment, based on third-generation cephalosporins, has proven effective in the management of cases. Mortality rates generally range from 8 to 15% in treated patients and exceed 70% without treatment [1,3,7].

Before 2010, serogroup A was responsible for the majority of epidemics in the meningitis belt. Since 2010, the gradual introduction of a meningococcal A conjugate vaccine (MenAfriVac) in Africa has led to a dramatic decrease in the number of cases of meningitis caused by *N. meningitidis* A and the elimination of epidemics associated with this serogroup [2,5]. At the same time, the relative proportion of cases due to other serogroups (W, X and C) and *S. pneumoniae* has increased [1,2,4,6].

Meningococcal meningitis can lead to severe brain damage and death in 50% of cases without treatment [1,2,6]. Worldwide, 1.2 million cases of PM are recorded each year. Developing countries have the highest mortality, reaching around 240,000 [2]. From 2010 to 2018, Niger reported 5,994 cases of purulent meningitis, including 5,144 cases of *N. meningitidis*, 721 cases of pneumococcus and 129 cases of *H. influenzae* [7,8]. In the Zinder region, the epidemiological situation was relatively calm in 2015 and 2016. However, from 2017, several health districts exceeded the alert threshold of 5 cases per 100,000 inhabitants for one week [2,5,8]. At the Zinder National Hospital (HNZ), 143 and 122 cases of meningitis were recorded in 2021 and 2022 respectively [9,10].

Despite the heavy burden of meningitis after-effects on affected individuals, their families and communities, access to care and support services is often insufficient, particularly in low- and middle-income countries [11]. Since the start of 2023, there has been an increase in suspected cases of meningitis with a high rate of deaths both in the community and in hospitals. This study aims to investigate the epidemiological aspects of purulent meningitis and to describe the short-term sequelae.

MATERIALS AND METHODS

This is a descriptive cross-sectional study of cases of purulent meningitis carried out over a period of seven months from January 1, 2023 to July 31, 2023, at the Infectious Diseases Department (SMIT) of the Zinder National Hospital (HNZ).

Inclusion criteria

All patients of all ages hospitalized for febrile meningeal syndrome at HNZ SMIT were included in this study.

Exclusion criteria

Patients without febrile meningeal syndrome were not included in this study.

Study variables

Qualitative variables were examined based on their frequencies and quantitative variables were analyzed based on their means. The variables measured concerned the following data:

- Socio-demographic information (age, gender, profession, origin, time to admission, point of entry, method of admission)
- Clinical signs (fever, nasolabial herpes, purpura, headache, vomiting, constipation, diarrhea, convulsions, phonophobia, photophobia, cervical hypotonia, bulging fontanelle, agitation, neck stiffness, Kernig and Brudzinski signs, consciousness)

- Paraclinical data (cerebrospinal fluid)
- Results (healing, complications, death)

This data was collected using a data collection form. Free and informed consent was obtained, and data confidentiality was respected.

Data entry was carried out using an Excel input mask, and data analysis and processing were carried out using Epi Info software.

Declaration of ethical approval

This study was conducted in accordance with ethical principles and received approval from the Institutional Review Board (IRB) of Faculty of Health Sciences, André Salifou University, Zinder (FSS-UASZ), Niger. The IRB reviewed the research plan, ensuring that it adhered to ethical standards and guidelines for conducting research involving human subjects. The approval from the IRB signifies compliance with the principles of confidentiality, informed consent, and the protection of participants' rights.

RESULTS

Of 396 patients hospitalized at the Infectious and Tropical Diseases Department of the Zinder National Hospital for febrile meningeal syndrome, 345 cases presented cerebrospinal fluid with purulent aspects, or 87.1%. This analysis focused on data from these 345 cases of purulent meningitis.

Epidemiology

Most patients came from the urban commune of Zinder, 87.8% (303/345). Students represented the most affected social group with 57.4% (198/345) (Table 1). The average age of the population was 14.09 years [3 months - 75 years], and the most affected age group was 0 to 14 years, including 64.6% (223/345). The average time to admission was 2.6 days [0-10 days]. The direct admission method was predominant at 94.2% (325/345). The entry point through the ENT (Ear, Nose, Throat) was found in 4.1% (14/345).

Clinical and Paraclinical Aspects

Clinical aspects

The analysis covered all patients included in the study (n=345). All patients presented with headaches and vomiting. The classic triad of meningitis (Headaches, Vomiting, and Constipation) was found in 48.9% (169/345) of cases. Physical signs (neck stiffness, Brudzinsky's sign, and Kernig's sign) were present in 96.2%, 96.2%, and 95.9% of cases, respectively (Table I).

Table I: Epidemiological, clinical, paraclinical and evolutionary data in this population

Epidemiology (n=345)		**Clinical data (n=345)**		**Paraclinical data (n=345)**		**Complications (n=345)**		**Sequelae (n=17)**	
	%		%		%		%		%
Sex		Fever	100	**Pleocytosis $\geq$5**	100	Coma	1.4	Hypoacusis	52.9
Male	68.7	Headaches	100	**Gram staining**		Intracranial suppuration	2.3	Blindness	17.6
Female	31.3	Vomiting	100	DGN	59.4	Hydrocephalus	0.9	Behavioral disorders	17.6
Residence		Constipation	49.0	DGP	2.9	Altered consciousness	11.6	Hemiplegia	11.8
Urban commune of Zinder	12.2	Diarrhea	7.2	BGN	0.3	Purpura	35.4	Deafness	11.8
Outside Zinder commune	87.8	Restlessness	7.8	Normal	37.4	Arthritis	4.1	Neuropsychiatric disorders	11.8
Occupation		Convulsions	3.5	**PCR**		Spontaneous miscarriages	0.6	Strabismus with diplopia	5.9
Student	57.4	Fontanelle bulging	3.8	Nm C)	18.8	Facial Zoster (shingles)	0.3		
Talibé (religious student)	20.9	Gaze fixation	4.1	Nm W135)	0.3				
Child	7.8	Neck stiffness	96.2	Sp	1.7				
Homemaker	4.9	Cervical hypotonia	3.2	Negative	1.4				
Farmer	3.8	Kerning's sign	95.9						
Others	5.2	Brudzinski's sign	96.2						

Gram-negative diplococci (DGN) ; Gram-positive diplococci (DGP) ; Gram-negative bacilli (BGN) ; Neisseria meningitidis C (Nm C); Neisseria meningitidis W135 (Nm W135); Streptococcus pneumoniae (Sp).

Paraclinical aspects

The study of cerebrospinal fluid revealed a pleocytosis (white blood cell count) of ≥ 5 cells/mm3 in all patients. Gram staining was performed in 62.4% (216/345) of cases, and it revealed Gram-negative diplococci in 94.9% (205/216). Culture was performed in 37.7% (130/345), isolating *Neisseria meningitidis* in 94.6%, *Streptococcus pneumoniae* in 4.6%, and *Haemophilus influenzae* in 0.8%. Seventy-seven samples were sent for further analysis, with Neisseria meningitidis C being the most prevalent serogroup in 84.4% of cases, followed by *Streptococcus pneumoniae* in 7.8% of cases (Table I).

Therapeutic aspects

Third-generation cephalosporins, particularly ceftriaxone, were the most administered antibiotics (100%). Systematic corticosteroid therapy (dexamethasone) was administered to all patients before antibiotic treatment. This was followed by analgesic-antipyretic treatment (paracetamol) with rehydration with physiological saline at a dosage of 30 to 40 ml/kg/day for all patients. Sedatives were added for patients suffering from seizures. aminoglycosides (gentamicin) were used in 167 patients showing signs of severity. amoxicillin-clavulanate was administered to 14 patients with identified ENT entry points. Oxygen was administered to 29 patients. Systematic and preventive chemoprophylaxis with ciprofloxacin for all contact subjects was initiated upon admission.

Evolutionary aspects

Healing was achieved in 89.6% of cases (309/345), with 5.5% of sequelae (17/309). The mortality rate was 10.4% (36/345). The sequelae identified included blindness, deafness, strabismus, hypoacusis, hemiplegia and neuropsychiatric disorders (Table I). The main complications included meningococcemia (purpura, arthritis) in 38.3% (132/345) (figure 1 et figure 2) and meningoencephalitis in 11.6% (40/345) (Table I). The follow-up of the after-effects was carried out over a short period of one month and revealed late behavioral problems in 3 patients.

Figure 1: Purpura fulminans in a 3-year-old child hospitalized for meningitis (Nm was isolated).

Figure 2: Osteoartritis secondary to invasive meningococcal infection, and Nm was isolated

Purpura fulminans was the prognostic factor associated with mortality in this study (Table II).

Table II: Prognostic factors associated with mortality

Signs	Numbers	Deceased	Recovered
Admission delay >48 hours	147	24	123
Coma	5	3	2
Altered consciousness	40	19	21
Fulminant purpura	5	4	1
Spontaneous miscarriages	2	1	1

DISCUSSION

During the 2023 epidemic, 396 patients were hospitalized for febrile meningeal syndrome, with a prevalence of purulent meningitis of 87.1% (345/396). In this study, over half (64.6%) of purulent meningitis cases occurred in children under 15 years of age. This observation is consistent with epidemiological studies on purulent meningitis, even though the main causative agents may vary by country. These findings are supported by observations in Mali by Dao S et al and in Côte d'Ivoire by Akoua-Koffi et al[12,13]. The male predominance noted in this study aligns with most other studies [13].

Vaccination coverage is significantly compromised due to population movements.

Several studies have highlighted low vaccination rates among migrants and refugees. The efforts to combat meningitis have also diminished with the COVID-19 pandemic crisis [14,15].

The urban area of Zinder was the epicenter of this epidemic due to the concentration and gatherings in modern schools and Quranic schools. Simultaneous outbreaks of other diseases in this region, coupled with insecurity in a humanitarian crisis context, actively contribute to the spread of these epidemics [14].

All patients presented with febrile meningeal syndrome; a rate comparable to that reported by Seydi et al at 86% [16]. *Neisseria meningitidis* was predominantly found in 94.91%, as reported by Djeungoue T et al [20]. In contrast, in Côte d'Ivoire, Akoua-Koffi et al reported a higher rate of pneumococcus (14.1%) [12].

The predominance of *Neisseria meningitidis* cases can be explained by the epidemic context. *N. meningitidis* is currently the species capable of causing large-scale epidemics in the meningitis belt of Lapeysonnie, an area where meningococcal meningitis regularly leads to outbreaks. Meningococcal meningitis occurs worldwide as isolated cases (sporadic) or epidemics. However, many uncertainties related to a limited understanding of the epidemic process weigh on the evolution of meningitis epidemiology in sub-Saharan Africa. From a scientific perspective, many mysteries are yet to be unraveled. Over 100 years after the first major epidemic described in the belt, the epidemiology of meningococcal meningitis in Africa is still poorly understood. Numerous factors seem to be involved in the occurrence of epidemics, with a combination of risk factors involving the microorganism, the host (immunity and susceptibility), and the environment (dry climate, Harmattan winds laden with dust, living conditions, population clustering, etc.) likely necessary to trigger an epidemic in a specific location and time [17].

Microbiological diagnosis of meningitis relates primarily on direct examination (cytology and Gram staining) and culture of cerebrospinal fluid. In addition to conventional tests, PCR has proven highly specific in identifying causative microorganisms [18]. The severity of such infections emphasizes the importance of not only diagnostic criteria but also comprehensive antibiotic treatment strategies, complemented by preventive measures such as chemoprophylaxis and antimeningococcal vaccination [19].

Third-generation cephalosporins, with their broad-spectrum activity at low concentrations, and sufficient penetration into the meninges, are the cornerstone of antibiotic therapy. Corticosteroids are often co-administered to reduce inflammation and prevent excessive inflammatory reactions [20]. Otogenic routes were identified as the major entry points in 81.81% of cases, contrasting with findings in Côte d'Ivoire, where sinus routes predominated [21]. Brain imaging was requested for persistent meningitis and recurrent cases. In addition to intracranial suppuration, complications included hydrocephalus [22]. Patients with septic arthritis responded well to fluoroquinolones, while those with reactive arthritis benefited from a more extended corticosteroid therapy resulting in complete recovery. Lethality rates were higher in pneumococcal meningitis compared to meningococcal cases [23].

Following hospital discharge, 121 consenting patients were monitored for a short one-month period. According to WHO, approximately 20% of meningitis patients present with sequelae upon discharge [24]. The observed 5.5% prevalence is comparable to findings by Seydi et al in Senegal. However, a study by Konaté in Mali in 2007 reported a prevalence of 46.2%, suggesting that meningitis sequelae may manifest later [25]. A recent study in Niger reported that among 521 evaluated survivors, 62 (12%) had sequelae, and among 138 confirmed NmC cases, 25 (18%) developed sequelae [26]. In cases of pneumococcal meningitis, neurological sequelae are significant, affecting 34.5% of survivors [16,27]. These results align with observations by other authors [28,29]. Sequelae may emerge long after hospitalization, ranging from 3 to 60 months, and include hypoacusis, mental retardation, and various neurological disorders. The data presented here underestimate the true significance of purulent meningitis in Zinder and its impact, as they rely on the detection of individuals seeking hospital care. Some patients may be affected by a fulminant form of meningitis and may not have sought hospital care. Others might not be referred in time or refuse hospitalization due to socio-cultural and financial reasons. Preceding self-medication with antibiotics, common in this context, has sometimes complicated the diagnostic process [30].

CONCLUSION

In conclusion, purulent meningitis leads to deadly epidemics in the Sahel, primarily caused by *Nm* C and *Streptococcus pneumoniae*. The results of this study sufficiently demonstrate the emergence of *Nm* C cases. Combating these meningitis outbreaks requires an improvement in epidemiological surveillance to detect small changes in serogroup distribution. This surveillance could have significant implications for public health strategies in the coming seasons, emphasizing the importance of comprehensive patient follow-up for sequelae management.

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