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Epidemiological patterns of bacterial meningitis in Niger from 2002 to 2010

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Abstract: Objective: To describe the epidemiology of bacterial meningitis in Niger from January 2002 to June 2010 Methods: A retrospective study of data from the laboratory surveillance of meningitis; cerebrospinal fluid samples from suspected clinical cases were collected and tested using polymerase chain reaction and/or bacteriology for the surveillance of bacterial meningitis in Niger. Data on patients was collected using a questionnaire. Results: The number of CSF samples received was 19,273. Over 80% of the patients were under the age of 15. The overall mean age was 9 years with a range of 0 to 93 years. The mean age was lower for *H. influenzae* (2.4 years, SD=4.8) than for *N. meningitidis* (9.4 years, SD=7.9), *S. pneumoniae* (11.5 years, SD=13.5) and for the other bacteria (7.9 years, SD=10.1). Males were significantly more affected than females (57.4% versus 42.6%, $p < 0.0001$). *N. meningitidis*, *S. pneumoniae* and *H. influenzae* were the three main etiological agents found in 42.4% of the total tested cases. The majority of confirmed cases of the three bacteria were caused by *N. meningitidis* (81.6%). Serogroup A caused 75% of meningococcal meningitis cases during the study period. The highest annual incidence of *N. meningitidis* cases occurred in March and April and was observed in 2008-2009 (15.9 cases per 100,000 inhabitants). The annual incidence rates were most often high in the southeast, near Nigeria. *S. pneumoniae* and *H. influenzae* incidence was higher in Niamey, with 275 and 145 cases, respectively, in this town during the study period. Conclusion: This study revealed the characteristics of the bacteria involved in meningitis, and particularly the serogroups of *N. meningitidis* circulating in Niger, as well as the age groups and areas affected, since 2002. The implementation of the PCR technique considerably improved microbiological surveillance and made it possible to extend its use to the whole country.

Keywords: Bacterial Meningitis, Neisseria Meningitidis, Streptococcus Pneumonia, Haemophilus Influenza, Niger

1. Introduction

Acute bacterial meningitis (ABM) is contracted worldwide, more severely striking Sub-Saharan Africa, where more than half of the meningococcal meningitis cases reported in the world occur. In 1963, Lapeyssonie produced an epidemiological description of the geographical area regularly stricken by meningitis epidemics in Africa, the so-called African Meningitis Belt, extending from Senegal to Ethiopia [1]

In addition to the annual seasonal cases, devastating epidemics are also observed, in which affliction rates reaching 1000 cases for every 100,000 inhabitants arise periodically, in cycles of 5 to 10 years.

Morbidity and mortality remains high in spite of effective and available vaccines and antibiotics. In the 1996 epidemic in Burkina Faso, there were 42,129 cases with a lethality rate of 10%, 7,244 cases in Mali, 16,050 cases in Niger and 75,069 cases in Nigeria. These four countries reported 95% of the cases in Africa in 1996, for an overall case-fatality rate of 10.6% [2]. In 1997 in Ghana, there were 18,551 cases and a lethality rate of 8% [3]. For the year 2003, the WHO estimated the morbidity burden of meningitis at between 394,000 and 497,000 cases, with 8,000 to 12,000 deaths in Africa [4]. In 2005, this organization reported, for 12 countries of the African Meningitis Belt, specific mortality

rates based on reported cases ranging from 4% in Mali to 26% in Benin [5]. In Niger, mortality was recently estimated at 15.7% among laboratory confirmed cases [6].

The most frequent microorganisms causing ABM are *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae*. *N. meningitidis* is the predominant bacteria in Africa, and particularly serogroup A, which leads to large epidemics in the Sub-Saharan region. In 2002 serogroup W135 was scarcely detected in the African Meningitis Belt until it was once detected through routine surveillance in Burkina Faso [7]. Serogroup W135, the vaccine for which is expensive, was also found at the end of the 2001 epidemic in a sample collected during a field investigation in Niamey and Boboye [8]. Henceforth the WHO increased its meningitis surveillance in the meningitis belt by implementing the Multi-Disease Surveillance Center in Ouagadougou, Burkina Faso.

Small epidemics of meningitis due to serogroup X were detected in 1990 [9] and from 1995 to 2000 [10] in Niamey. A significant increase in the incidence of serogroup X, for which a vaccine is not yet available, was also observed in 2006 [11] in Niger. Serogroups C and Y were found occasionally.

In this context of high incidence and lethality, limited availability of vaccines and unpredictable outbreaks, epidemiological and microbiological surveillance of bacterial meningitis is essential and should be maintained at a high level of efficiency. Over the past 8 years, there have been considerable improvements in the methods for the etiological diagnosis of ABM in Niger through the implementation of the Polymerase Chain Reaction (PCR) test.

This study describes the epidemiology of ABM in Niger from January 2002 to June 2010 using microbiological surveillance data.

2. Methods

Data analyzed in this work was taken from the routine laboratory surveillance of ABM in Niger performed by CERMES from January 2002 to June 2010.

2.1. Data Collection

In Niger, morbidity and mortality of suspected meningitis cases were reported weekly to a national network coordinated by the Direction de la Surveillance, de la Statistique et de la Riposte aux Epidémies (DSSRE) – Ministry of Public Health.

Data collection for microbiological surveillance was described previously (Boisier et al., 2007). Briefly, the Centre de Recherche Médicale et Sanitaire (CERMES) performed a daily collection of cerebrospinal fluid (CSF) samples in Niamey and on a monthly basis within a 250-kilometer radius around the capital. In the remote parts of the country CSF samples were sent by the available means of transportation.

The CSF samples were collected from patients who were clinically suspected of meningitis according to the case definition issued by the WHO [12]. Then, they were tested for confirmation at CERMES. In November 2002, PCR testing was introduced to improve the laboratory surveillance of meningococcal disease. The first PCR test detected *N. meningitidis*, *S. pneumoniae* and *H. influenzae* [13;14], and the second one was performed on positive *N. meningitidis* samples to identify serogroups A, B, C, X, Y / W135 [15; 11]. Finally serogroups Y / W135 were identified into Y or W135 by a confirmation PCR test. Fresh CSF samples or CSF samples kept on trans-isolate medium were tested by conventional bacteriology, including Gram examination, a latex agglutination test [15] and culture.

The descriptive maps of meningitis incidence by department were done on QGIS, version 1.5.0.

The national, regional and departmental demographic data used was from the 2001 general census of the population and was obtained on the website of the Institut National de la Statistique (INS): http: // www.stat-niger.org/.

Exclusion criteria for cases included living in a neighboring country and suspected cases of meningitis without confirmation based on a CSF sample.

2.2. Statistical Analysis

Information on patients and laboratory results was entered daily into an Access database, and later a MySQL database.

The analysis was conducted during an epidemiological year, which is defined from July 1st of the current year to June 30th of the next year. Descriptive statistics and bivariate analyses were done with Epi2000. A chi-square test was performed to study the link between two qualitative variables. An analysis of variance (ANOVA) or a Kruskal-Wallis test was performed to compare quantitative variables in more than two groups. Annual incidence rates were calculated for 100,000 inhabitants based on laboratory confirmed cases, by age group and by department, using the 2001 census population. The p-value was considered significant when < 0.05.

2.3. Ethical Aspects

All the data was collected via the national surveillance system maintained by the CERMES after authorization by the Ministry of Public Health. Therefore, consent was not requested and the preliminary National Ethics Committee agreement was not required. Patients were, however, informed of the reason why their CSF sample was being taken and they received free care during the meningococcal season. Each health structure received the results, identified by patient name, of the samples that it had sent. The retrospective disclosure of information to other partners was done without any mention of the identity of the patient.

3. Results

Over the course of 8.5 years from January 2002 to June 2010, CERMES received 19,273 CSF samples for laboratory confirmation.

The age was available for 17,662 (91.6% of the total of tested) subjects. The overall mean age was 9 years, with a range of 0 to 93 years. The mean age was lower for H. influenzae (2.4 years, SD=4.8) than for N. meningitidis (9.4 years, SD=7.9), S. pneumoniae (11.5 years, SD=13.5) and for the other bacteria (8.6 years, SD=9.8) ($p < 0.0001$). The incidence rates of H. influenzae and S. pneumoniae were higher in the 0-to-11-month age group (Fig. 1).

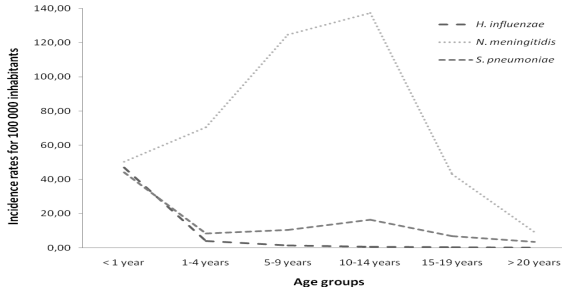

Figure 1. *Incidence rates of main etiologies of bacterial meningitis by age group. Niger, January 2002 to June 2010.*

The 5-9 year and 10-14 year age groups were the most represented every year among meningococcal cases (Fig. 2).

The mean age also varied by serogroup: 9.8 years (SD=7.7) for serogroup A; 8.1 years (SD=6.2) for serogroup X, 8.3 years (SD=9.6) for serogroup W135 and 8.8 years (SD=8.3) for the other serogroups ($p < 0.0001$).

The sex was noted for 18,878 samples (98% of the total of tested subjects). The overall sex ratio of the sample was 1.3 (57.4% male versus 42.6% female, $p < 0.0001$).

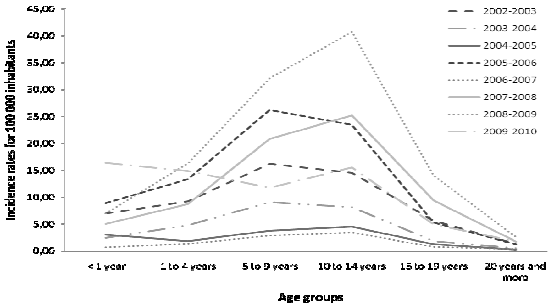

Figure 2. *Incidence rates of meningococcal meningitis by age group and epidemiological year. Niger, 2002 to 2010.*

Table 1. *Distribution of etiological bacteria and serogroups of Neisseria meningitidis on CSF samples received at CERMES. Niger, January 2002 to June 2010.*

Period	Jan-jun02	2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008	2008-2009	2009-2010	All years
CSF samples received	489	2243	1534	1371	3237	1197	2835	4058	2309	19273
CSF samples tested	469	2203	1527	1366	3232	1195	2819	4026	2281	19118
Total positive tests (†)	203 (43.3)	1042 (47.3)	598 (39.2)	427 (31.3)	1383 (42.8)	353 (29.5)	1223 (43.4)	1900 (47.2)	1033 (45.3)	8162 (42.7)
N. meningitidis (††)	100 (49.3)	869 (83.4)	429 (71.7)	201 (47.1)	1181 (85.4)	143 (40.5)	1063 (86.9)	1760 (92.6)	916 (88.7)	6662 (81.6)
A (**)	94 (94.0)	782 (90.0)	369 (86.0)	114 (56.7)	548 (46.4)	126 (88.1)	993 (93.4)	1719 (97.7)	251 (27.4)	4996 (75.0)
X	1 (1.0)	3 (0.3)	13 (3.0)	49 (24.4)	585 (49.5)	11 (7.7)	5 (0.5)	16 (0.9)	1 (0.1)	684 (10.3)
W135	5 (5.0)	72 (8.3)	35 (8.2)	22 (10.9)	26 (2.2)	5 (3.5)	0 (0.0)	10 (0.6)	651 (71.1)	826 (12.4)
C	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.0)
Y	0 (0.0)	4 (0.5)	2 (0.5)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	8 (0.1)
Undetermined	0 (0.0)	8 (0.9)	9 (2.1)	16 (8.0)	21 (1.8)	1 (0.7)	64 (6.0)	14 (0.8)	13 (1.4)	146 (2.2)
S. pneumoniae (††)	56 (27.6)	120 (11.5)	129 (21.6)	185 (43.3)	137 (9.9)	136 (38.5)	119 (9.7)	99 (5.2)	88 (9.6)	1069 (13.1)
H. influenzae (††)	28 (13.8)	553 (5.1)	38 (6.4)	40 (9.4)	62 (4.5)	73 (20.7)	40 (3.3)	21 (1.1)	20 (1.9)	375 (4.6)
Other bacteria (††)	19 (9.4)	0 (0.0)	2 (0.3)	1 (0.2)	3 (0.2)	1 (0.3)	1 (0.1)	20 (1.1)	9 (0.9)	56 (0.7)

†: % of CSF samples tested
††: % of positive results
**: % of N. meningitidis

N. meningitidis, *S. pneumoniae* and *H. influenzae* were identified in 6,662 (81.6%), 1069 (13.1%) and 375 (4.6%) cases, respectively (Table 1). Serogroup A ST7 of *N. meningitidis* was predominant.

3.1. Incidence over Time

The highest annual incidence of positive results was observed in 2008-2009 (17.2 cases per 100,000 inhabitants). The incidence of *N. meningitidis* varied by month and year; the highest number of cases occurred in March and April (Fig. 3).

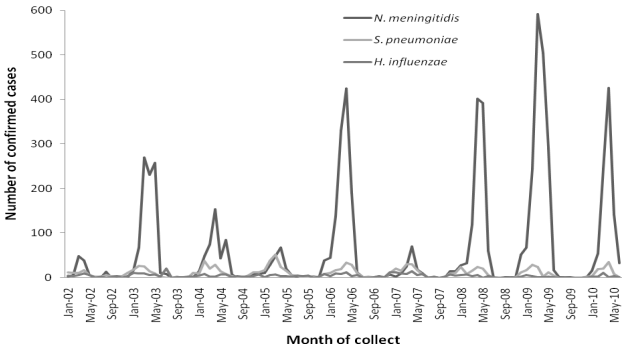

Figure 3. *Monthly detections of N. meningitidis, S. pneumoniae and H. influenzae. Niger, January 2002 to June 2010*

Among the *N. meningitidis* cases, the incidence of serogroup A was higher in 2002-2003 (7 cases per 100,000 inhabitants), 2007-2008 (9 cases per 100,000 inhabitants), and 2008-2009 (15.5 cases per 100,000 inhabitants). The highest incidence of *N. meningitidis* X was observed in 2005-2006. This serogroup was detected in small numbers in the years before its outbreak and in subsequent years. The incidence of *N. meningitidis* W135 increased in 2002-2003 (0.7 cases per 100,000 inhabitants). Then it decreased over the years and rose again in 2009-2010 to reach 5.9 cases per 100,000 inhabitants.

The incidence of *S. pneumoniae* and *H. influenzae* did not vary over the years.

3.2. Geographic Distribution

The CSF samples were sent by all 42 districts of Niger. The annual incidence rates of meningococcal meningitis, by department, are shown in Fig. 4.

They were most often higher in the southeast, near neighboring Nigeria, and increased for the first time in the North of the country (Bilma) in 2008-2009. The regions of Tahoua and Maradi showed the largest outbreaks of meningitis, whereas Agadez and Diffa were almost not involved. *S. pneumoniae* and *H. influenzae* were the highest in Niamey, with 275 and 145 cases, respectively, in this town during the study period.

Serogroup X was more common in the western regions of the country: 262 cases in Niamey, 146 cases in Dosso and 114 cases in Tillabéry out of a total of 684. Serogroup A was high in the regions of Maradi and Tahoua, with 1285 cases and 1265 cases, respectively. Serogroup W135 was more often detected in the regions of Maradi and Tahoua, with 365 and 133 cases.

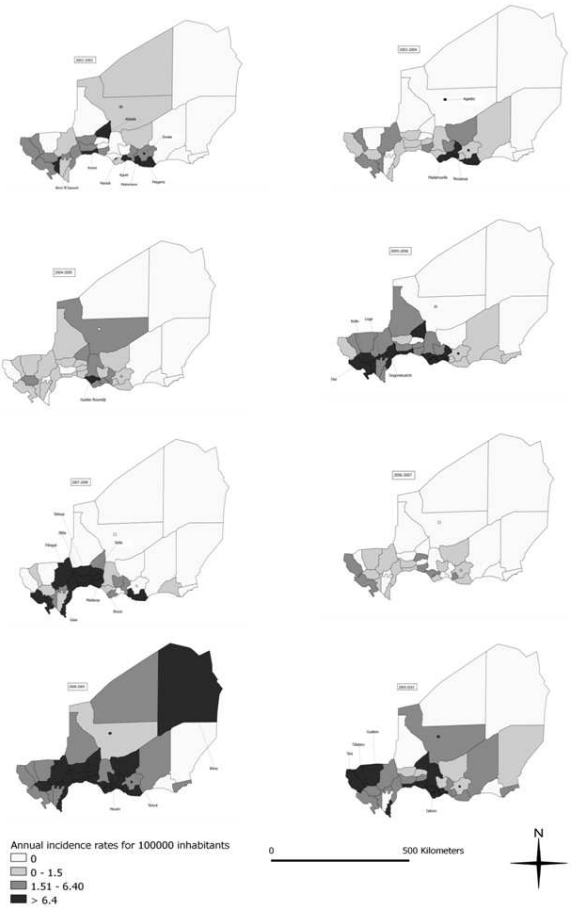

Figure 4. *Annual incidence rates per 100,000 inhabitants of meningococcal meningitis by department. Niger, July 2002 to June 2010.*

4. Discussion

Bacterial meningitis is a major public health issue in children, since the majority of affected subjects were under the age of 15 in this study. A previous study in Niger showed incidence by age group to be clearly more significant among children under the age of 20 [9]. *H. influenzae* was more frequent in children. The highest incidence of *S. pneumoniae* was also found among infants, as shown previously in a study in Togo and Burkina Faso [17].

N. meningitidis, *S. pneumoniae* and *H. influenzae* were responsible for about 42.06% of the cases of suspected meningitis. *N. meningitidis* was the main agent responsible for bacterial meningitis in Niger. Serogroup A was the predominant serogroup of *N. meningitidis*, as has been the case in the other countries of the African Meningitis Belt over the last 70 years [18].

The distribution of the three etiologic agents of bacterial meningitis was similar to those previously observed in Niger. In 2010, *N. meningitidis* was the predominant pathogen, followed by *S. pneumoniae* and *H. influenza* [19]. In Niamey from 1981 to 1996, *N. meningitidis* was identified in 57.7% of CSF samples, *S. pneumoniae* in 13.2% and *H. influenzae* in 9.5% [9]. This study confirms the exceptional emergence of serogroup X in 2006 (51% of 1139 confirmed cases of meningococcal meningitis), as described by Boisier [11] and

in an epidemic that occurred in the northern and central regions of Burkina Faso, with cumulative incidence reaching 130/100,000 in March-April [20]. Serogroup W135 was identified every year except in 2007-2008, with a decreasing number of cases, followed by a significant increase in 2009-2010. It belonged to the ST-11 sequence type [19].

During the study period, 5 major epidemics of meningitis occurred in Niger: 2002-2003, 2005-2006, 2007-2008, 2008-2009 and 2009-2010. Three of these outbreaks (2002-2003, 2007-2008 and 2008-2009) were due to *N. meningitidis* A, one (2005-2006) to both serogroup A and X, and one (2009-2010) to serogroup W135. During this time, other countries reported meningococcal meningitis to be the major cause of bacterial meningitis. In Togo from 2006 to 2009, 61% of cases were confirmed for *N. meningitidis*, in which serogroup A was predominant (31%), followed by *N. meningitidis* X (16%) [20]. In Ghana, from 2001 onward, serogroup A meningococcal meningitis cases reemerged, causing annual outbreaks until 2004 [21]. From March 2007 to December 2009, Bobo-Dioulasso, Burkina Faso reported, among confirmed bacterial meningitis cases, 63% from *N. meningitidis*, 35% from *S. pneumoniae* and 2% from *H. influenzae* [20]. In Greece, *Neisseria meningitidis* was found to be the leading cause of childhood bacterial meningitis from 1974 to 2005. The main serogroups isolated throughout this study were A, B and C [22]. In Brazil, from 1995 to 2003, 69.8% of cases were caused by *Neisseria meningitidis* serogoup C [23].

Neisseria meningitidis was found in all of the districts that sent samples to the CERMES. For reasons not understood, serogroup A caused outbreaks only in restricted areas. Tahoua and Maradi exhibited the highest incidences every year from *N. meningitidis* A and they are the most populated regions of the country. In these regions, the risk of a meningococcal cluster occurring was found to be higher for the cantons of Konni and Tibiri-Guidan-Roumdji [24]. The exceptionally high number of cases in the department of Bilma in 2008-2009 was probably due to migrants from other countries (Nigeria, Senegal, Ghana and others), on their way to Europe via the Sahara, since the mean age (21.29 years) is higher than the average of the population studied (9 years). In 2005-2006, Nm X was predominant in the southwest region of Niger, whereas serogroup A was predominant as usual in the southeast. In 2009-2010 serogroup W135 was predominant in the region of Maradi, located in southeast of the country.

The collection of CSF samples did not cover the entire population of Niger affected by meningococcal meningitis. Indeed, it could vary within departments or regions due to the unequal availability of human and financial resources, how easy or difficult it was to transport CSF samples, or due to geographical remoteness, accessibility of health care centers, and variability of meningitis diagnosis practices among Health Care Workers. Furthermore, it is possible that selection bias could have caused an underestimation of incidence rates because CSF samples were not available for all cases, and some of the samples could not be tested because of poor quality.

In spite of the above limitations, the results are consistent with those already published. They also show the quality of meningitis surveillance in Niger. This one is coordinated by 2 institutions, CERMES for laboratory surveillance and DSSRE for epidemiological surveillance. The analysis of a significant number of CSF samples from all parts of the country made it possible to detect the majority of circulating serogroups.

5. Conclusion

The epidemiology of bacterial meningitis is better understood through the serogroups circulating in Niger, and the age groups and areas of the country most affected since 2002. It was made possible by detailed routine surveillance which is important both to monitor the effectiveness of vaccines and to help identify the most appropriate vaccine for a response campaign.

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