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National Surveillance Data on the Epidemiology of Meningitis in Niger, 2005 - 2020

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Bacterial meningitis is a major public health problem, especially in low-income countries. We analyzed national surveillance data and isolates from Niger to describe the epidemiology of bacterial meningitis from 2005 to 2020.
Methods: We conducted a retrospective study of nationwide case-based surveillance data of all reported meningitis cases in Niger from 2005 to 2020. Modified case definition was used to classify the cases.
Results: A total of 47,953 suspected meningitis cases and 3,276 deaths (CFR=6.83%) were

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reported, corresponding to an incidence of 189.01 cases per 100,000 population. The male represented 55.41% (sex-ratio male : female = 1.30) and 40.52% were 5 -14 y. A total of 29,998 cases were reported through RNL, of which 10,979 (36.60%) were confirmed, of which 6,149 (56.01%), were confirmed by culture. The predominant organism identified was *N. meningitidis* serogroup A (33.91%). All regions reported meningitis cases and a consistent and substantial reduction was seen in confirmed NmA cases, with no cases occurring in the country after the completion of mass campaigns. Nevertheless, other pathogen species and Nm variants, including NmX, NmC, and *Streptococcus pneumoniae*, have become more prevalent.

Conclusion: Increased surveillance of multiple serogroups throughout is necessary, as well as consideration of vaccination with combination vaccines rather than just using a single strain as is currently the case with NmA.

Keywords: Bacterial meningitis; surveillance; epidemiology; outbreaks; Niger.

1. INTRODUCTION

"Bacterial meningitis is a severe acute infection of the fluid surrounding the brain and spinal cord that can rapidly lead to death. It is caused by Nesseria meningitidis (Nm), a Gram-negative bacterium of the family Neisseriaceae that infects humans only. It is transmitted directly from respiratory or salivary projections of patients and especially healthy carriers by prolonged and close contact, presenting It self as diplococcus in the direct examination of pathological products, most often cerebrospinal fluid (CSF) " [1-3].

"This is the only bacterial entity that can occur in sporadic cases, outbreaks, and epidemics. Other serogroups such as *Streptococcus pneumoniae* (Sp), and *Haemophilus influenza* type b (Hib) are also involved but are not responsible for outbreaks" [4-6,1].

"It is a major public health problem, especially in low-income countries, and is associated with a high incidence and mortality in the absence of a rapid and effective response. In Africa, epidemics of meningitis caused by Neisseria meningitidis have been a public health problem for over a century, mainly in the African meningitis belt where the World Health Organization (WHO) estimated that 10 021 suspected cases occurred during the 2021 meningitis season and that 542 were fatal (case-fatality ratio 5%). In this region, Neisseria meningitidis serogroup A (NmA) is associated with seasonal hyperendemic and epidemic meningitis; however, other meningococcal serogroups, pneumococcus, and Haemophilus influenzae type b contribute to the meningitis burden" [7-9].

"Before 2010, serogroup A was responsible for the majority of the epidemics. However, since then, the gradual introduction of a meningococcal A conjugate vaccine (MenAfriVac) in the African meningitis belt through preventive mass vaccination campaigns has led to a significant decrease in the number of Neisseria meningitidis A (Nm A) cases and the elimination of Nm A epidemics in this area. In addition to conferring long-term protection, the safe and highly immunogenic Nm, A conjugate vaccine, decreases carriage rates in immunized populations and provides herd immunity" [10-13].

"To maintain protection levels, it was necessary to introduce MenAfriVac into the routine childhood immunization program within 1–5 years at the end of the preventive campaign.

Although *N. meningitidis* serogroup A has virtually disappeared in countries that have implemented nationwide vaccination campaigns, other serogroups, including *N. meningitidis* serogroup C and serogroup X, have emerged as the prevailing causes of meningitis, and that the patterns and dynamics of meningitis outbreaks has changed" [14].

"In 2017, for example, *Nesseria meningitidis* C (NmC) was responsible for an epidemic wave in Niger with about 790 cases (79.00%) and serogroup X was noted for 204 cases (20.40%)" [15,16]. Sporadic diseases and localized epidemics caused by serogroup X have been well described, but the potential of serogroup X to cause large epidemics remains unclear.

These epidemiological changes and new challenges create a need for surveillance systems to adapt in order to remain relevant, accurate, and efficient so that.

We analyzed national surveillance data and isolates from Niger to describe the epidemiology of bacterial meningitis from 2005 to 2020, and to assess changes and trends in epidemiology after the introduction of MenAfriva.

2. METHODS

In this study, we compiled and analyzed nationwide case-based surveillance data of all reported meningitis cases in Niger from 2005 to 2020 to describe their epidemiological and microbiological features. We collected epidemiological data on reported meningitis cases through complementary aggregate, case-based, and enhanced meningitis surveillance systems.

Meningitis surveillance in Niger is performed on the basis of reporting of epidemiologically suspected cases. Cerebrospinal fluid (CSF) specimens are sent to the Centre de Recherche Médical et Sanitaire (CERMES) in Niamey, which is the National Reference Laboratory (NRL). Culture latex agglutination and Polymerase Chain Reaction (PCR) were performed whenever appropriate. Since 2004, after the addition of a PCR-based nonculture assay that was developed to genogroup isolates of NmX, PCR testing allows for the identification of Nm serogroups A, B, C, X, Y and W.

"We used a modified case definition to classify the cases. Suspected cases of meningitis were defined as a sudden onset of fever with a stiff neck or, in infants, a bulging fontanelle. Probable bacterial meningitis was defined as a suspected case for which gram-stained CSF was positive (gram-negative diplococci, gram-positive diplococci, or gram-negative bacilli). A confirmed case of meningitis was defined as a suspected or probable case for which *N. meningitidis, Haemophilus influenzae* type B or *Streptococcus pneumoniae* was isolated in culture from the blood or CSF, or antigen was detected in the CSF by latex agglutination or PCR. Latex agglutination–positive cases that were later negative by PCR or culture were reclassified as suspected cases" [17].

There is no ethical issue in this study but we have the permission of the Directory of Surveillance and outbreak Response to use the data.

2.1 Analysis

We conducted a retrospective study of all suspected cases of meningitis in Niger between from 2005 to 2020. In our analysis, we did not include meningitis cases without epidemiological data. Demographic information for meningitis itise cases was available from the combined-line lists for 2005–2020. For all other years, the Epidemic Surveillance and Response Directorate (DSRE) database was used. Data were collected and analyzed using Stata 12.0. We calculated the annual national incidence (per 100 000 of the population) using the total number of suspected meningitis cases reported and the population projections from the Niger National Bureau of Statistics (INS) for each year during the analysis period. Population census was conducted in Niger in 2012. We calculated the annual national Case Fatality Rate (CFR) by dividing the total number of miningitis-related deaths by the total number of suspected miningitis cases reported at the national level for each year. Data from 2005 to 2020 were reviewed to determine the number and percentage of CSF specimens tested, with distribution by serotype.

3. RESULTS

From 2005 to 2020, a total of 47,953 suspected meningitis cases and 3,276 deaths, with a CFR of 6.83% were reported through the National case-based minigitis surveillance, corresponding to an incidence of 189.01 cases per 100,000 population.

Of persons, the male represented 55.41% (sex-ratio male/female = 1.30) and 1.40% were <1y of age, 33.27% were 1- 4 y, 40.52% were 5 -14 y, and 19.62% were >15 y (Table 1).

Table 1. Distribution of meningitis cases by age group from, 2005-2020

Variables	n(%)
Age group (y)	
< 1	419 (1.40)
1 - 4	9,981(33.27)
5 - 14	12,156(40.52)
>15	5,885(19.62)
Unknown	1,557(5.19)
Sex	
Male	16,622(55.41)
Female	13,242(44.14)
Unknown	134(0.45)

A total of 29,998 cases were reported through RNL, of which 10,979 (36.60%) were confirmed, 18,888 (62.96%) were negative, and 131 (0.44%) were unspecified. Of the 10,979 confirmed cases, 6,149 (56.01%), 4, 693 (42.74 %), and 137 (1.25%) were confirmed by culture, PCR, and latex agglutination, respectively. The predominant organism identified was N. meningitidis serogroup A (33.91%) (Table 2).

More meningitis cases were reported during 2009, with 13,934 cases (annual incidence of 39.92 cases/100,000 population) and an estimated 589 deaths (CFR 4.23%). A higher CFR was recorded in 2012 (17.83%) (Fig. 1), and most of the serogroups were detected between January and June (Fig. 2).

Table 3 shows the notifications by region. All regions reported meningitis cases between 2005 and 2020. The region of Niamey recorded the highest number of cases (9,813) and deaths (728), while the region of Agadez had the highest CFR (10.06%).

The weekly trend of meningitis incidence shows a similarity in the curves, with a first peak between the 7th and 19th epidemiological weeks and a second peak between the 16th and 21st epidemiological weeks. The notification persisted until the end of the year, although at a decreasing rate (Fig. 3).

Table 2. Distribution of the number of strains of *meningitidis serogroup* isolated, tested, and confirmed at the NRL for Niger, 2005–2020

Variables	n(%)
Laboratory results	
Confirmed	10,979(36.60)
Negative	18,888(62.96)
Not specified	131(0.44)
Method used	
Conventional culture	6,149(56.01)
PCR	4,693(42.75)
Latex agglunitation	137(1.25)
Serogroup idenfied	
H. influenzae b	200(1.82)
H. influenzae non b	180(1.64)
N. meningitidis A	3,723(33.91)
N. meningitidis B	1(0.01)
N. meningitidis C	2,803(25.53)
N. meningitidis W135	1,439(13.11)
N. meningitidis X	1,114(10.15)
N. meningitidis Y	1(0.01)
S. pneumoniae	1,518(13.83)

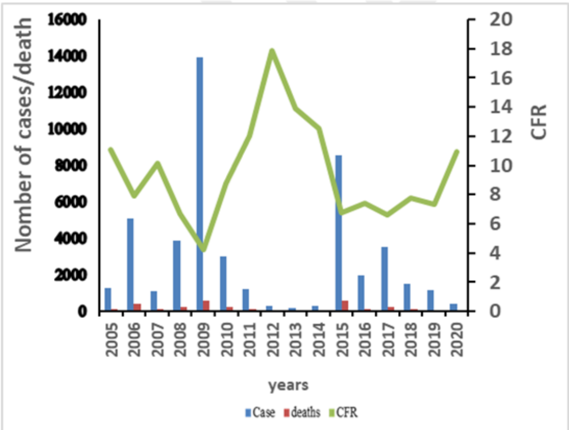

Fig. 1. Trend of meningitis cases, deaths and CFR in Niger, 2005-2020

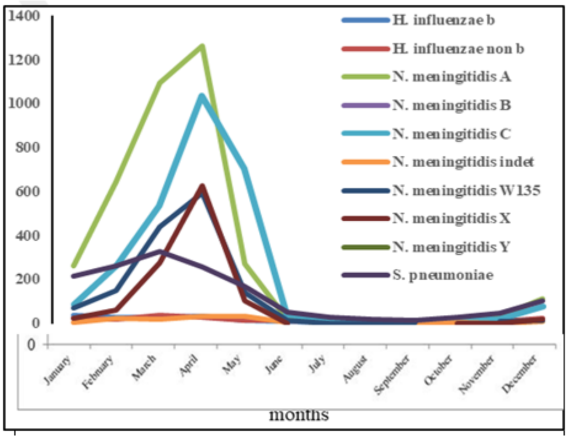

Fig. 2. Monthly trend of serogroup of Nm and others serogroups in Niger, 2005-2020

Table 3. Cumulative suspected meningitis cases, deaths, and CFRs by region, 2005–2020

Regions	Case,n	Death,n	CFR,%
Agadez	666	67	10,06
Diffa	262	25	9,54
Dosso	7341	652	8,88
Maradi	9238	564	6,11
Niamey	9813	728	7,42
Tahoua	7244	417	5,76
Tillaberi	5330	501	9,40
Zinder	8059	322	3,99
Total	47953	3276	6,83

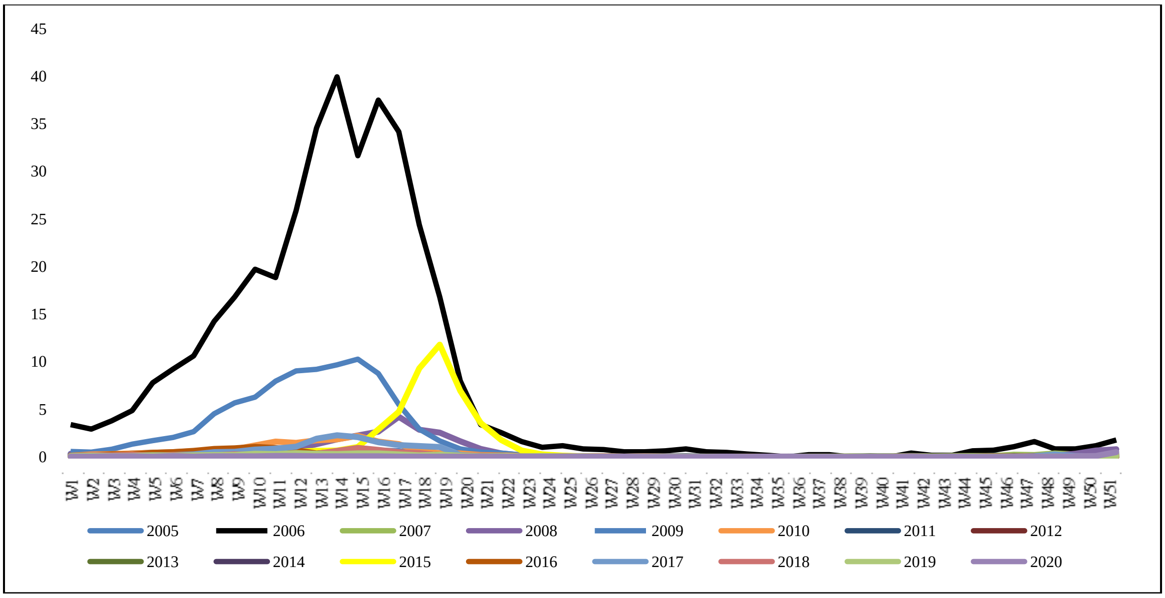

Fig. 3. Weekly trend of meningitis incidence in Niger, 2005-2020

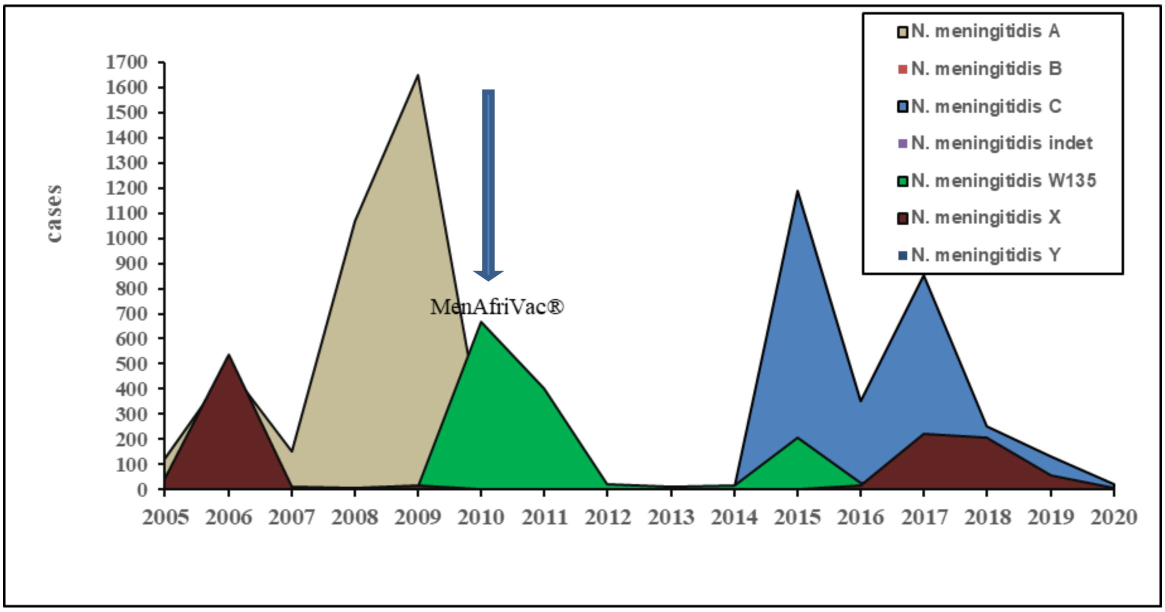

Fig. 4. Trend of serogroup of *Neisseria meningitidis*, 2005 à 2020

Neisseria meningitidis (Nm) was recorded over the entire period from 2005 to 2020. In 2006, Nm A and Nm X were recorded at high proportions. NmX reappeared in 2016 and continued to decrease gradually until 2020. Prior to 2010, Nm A was the dominant cause of meningitis before the introduction of MenAfriVac. Nm W135 appeared in 2009, disappeared in 2013, and reappeared in 2014. From 2013 to 2014, NmC appeared and caused a major epidemic in 2015 and 2017, and continues to dominate meningitis aetiology until 2020.

4. DISCUSSION AND CONCLUSION

"N. meningitidis is an aerobic Gram (-) diplococcus species whose only host is human. It is found in the respiratory tract of healthy human beings but can cause devastating diseases in vulnerable individuals. It is recognized as one of the three leading causes of meningitis worldwide despite the presence of vaccines against almost five of its serotypes" [17].

"The meningitis belt experiences the greatest burden of meningococcal diseases worldwide. The area at risk includes 21 countries with a population of over 300 million people" [18-20].

"The persistence of long dry seasons and the effect of desert aerosols made of dust and sand particles are important environmental and ecological determinants that have been put forward to explain the epidemic development phases of meningitis epidemics within the belt" [21-26].

During epidemic waves that span several districts and countries every 5 -10 years, incidence rates vary from region to region, ranging from less than 2 cases per 100,000 inhabitants per year to more than 10 cases per 100,0000 population [27]. In case of sporadic localised epidemics, community case based surveillance can report weekly peak incidence rates of suspected cases of over 1,000 cases per 100,000 population [28].

From 2005 to 2020, 47,963 cases were reported in the surveillance system of Niger. Unfortunately, 3,276 deaths patients with suspected meningitis died, resulting in a case fatality rate (CFR) of 6.83%. As in Niger, surveillance is passive, and it remains to be seen how representative these data are of epidemiological reality. Indeed, it is clear that there is a high level of underreporting, which could be explained by a lack of knowledge of case definitions, low use of health facilities, and poor health coverage in certain areas. As a result, all suspected cases and deaths that do not occur in health facilities are not included in the report, which underestimates the burden of meningitis. Therefore, the implementation and/or reinforcement of active surveillance should be favored, as in a study carried out in Kenya, which revealed that the number of cholera cases increased by 46% and the number of deaths by 200% due to active case finding [29]. Nevertheless, these figures suggest that meningitis is a public health problem that requires an in-depth exploration of the determinants of its persistence and recurrence in Niger.

Efficient and reliable surveillance and notification systems are vital for the monitoring of public health and disease outbreaks. However, most surveillance and notification systems are affected by the degree of underestimation (UE). Therefore, uncertainty surrounds the « true » incidence of diseases affecting morbidity and mortality rates. Surveillance systems fail to capture cases at two distinct levels of the surveillance pyramid: from the community, because not all cases seek healthcare (under-ascertainment), and at the healthcare level, representing a failure to adequately report symptomatic cases that have sought medical advice (underreporting). When routine data are used to make decisions on resource allocation or to estimate epidemiological parameters in populations, it becomes important to understand when, where, and to what extent these data represent the true picture of the disease, and in some instances (such as priority setting), it is necessary to adjust for underestimation.

"The case-fatality rate of 6.83% is well below the WHO threshold (10%-15%). This recorded rate may still underestimate the actual rate recorded during epidemics due to underreporting of cases to the national case-based surveillance system as well as delays in setting up response mechanisms, particularly those involving patients who die in the community before seeking care. The diversity of bacterial strains and species responsible for meningitis epidemics in Africa is another important explanatory factor for the uncertainty surrounding CFR. Indeed, in a study of meningitis epidemics of the meningeal belt published in 2002, Chippaux and his collaborators showed that lethality due to meningitis varies according to bacterial strains and species" [30].

The study showed (Table1) that all ages can be affected by bacterial meningitis as described by Oordt-Speets and al. in a meta-analysis in which they stated that the most common pathogens in the all age group, for most regions, were *N. meningitidis* and *S. pneumoniae*, with weighted means for frequency ranging from 9.1±36.2%, and from 25.1±41.2%, respectively [31]. This is in accordance with our study witch found that *N. meningitidis and S. pneumoniae* were the most notified (Table 2).

The weekly trend of miningitis incidence showed a similarity in the curves with outbreaks occurring between the 1st and 24th epidemiological weeks (Fig. 3), which included the dry season (January-June) corresponding to the miningitis epidemic season and favorable to the meningitis outbreak (Fig. 2). Outbreaks in the sub-Saharan regions coincide with the dry season, which has led to a hypothesis for the potential role of low humidity and seasonal dust winds blowing from the Sahara (Harmattan) in damaging the mucosa and producing irritant coughing that aids transmission [32].

According to laboratory confirmation, substantial efforts have been made to improve data quality, as evidenced by the increasing proportion of suspected cases that were confirmed ((56.01%) by culture and 4,693 (42.74%) by PCR). Nevertheless, data quality remains a concern and poses challenges for the interpretation of laboratory surveillance data (18,888 (62.96%) were negative, and 131 (0.44%) were not specified).

The introduction of MenAfriVac® into the meningitis belt through mass immunization campaigns of 1-29 year olds has had a dramatic impact on the incidence of suspected and confirmed meningitis cases. A consistent and substantial reduction was seen in confirmed NmA cases, with no cases occurring in the country after the completion of mass campaigns (Fig. 4). Caroline L.T and col estimated that the incidence of suspected meningitis cases fell by around 60% in vaccinated compared to the unvaccinated population [33]. We observed a similar decline in the number of districts that reached the epidemic threshold. Nevertheless, other pathogen species and Nm variants, including NmX, NmC, and Streptococcus pneumoniae, have become more prevalent (Fig. 4). This reflecting a greater diversity of bacterial strains causing meningitis epidemics in Africa today.

The increasing trend of other strains of *N. meningitidis* (other than NmA) is currently worrying, in particular because it seems that the elimination of NmA by vaccination may have led to its almost immediate replacement in human populations by other bacterial strains, as in an ecological process of occupation of ecological niches rendered empty or the existence of ecological interference and competition across bacterial strains [34,35]. Increased surveillance of multiple serogroups throughout the African region is necessary, as well as consideration of vaccination with combination vaccines rather than just using a single strain as is currently the case with NmA.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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