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DYNAMICS OF GERMS RESPONSIBLE FOR ACUTE BACTERIAL MENINGITIS IN BURKINA FASO IN THE LAST TEN YEARS (2005-2014)

Absatou Ky-Ba[1,*], Mahamoudou Sanou[2],Juliette -Diallo Tranchot[3], Paul A. Christiasen[4], Abdoul Salam Ouedraogo[3], Mamadou Tamboura[2], Dinanibé Kambiré[2], Kalifa Ouattara[5], Maxime Kienou[5], Idrissa Sanou[6], Isaïe Medah[7], Daouda Koussoubé[7], Rasmata Ouédraogo[2],

Correspondence: Absatou Ky-Ba, Laboratoire National de Santé Publique, Ouagadougou, Burkina Faso, 09 BP 24 Ouagadougou 09. Tel.: (+226) 70 12 05 20/78 89 92 48; Fax: (+226) 25 37 24 30; Email: absetou@yahoo.fr

Lassana Sangaré[5]

[1]Laboratoire National de Santé Publique, Ouagadougou, Burkina Faso ; [2]Centre Hospitalier Universitaire Pédiatrique Charles de Gaulle, Ouagadougou, Burkina Faso ; [3]Universitaire Polytechnique de Bobo Dioulasso, Burkina Faso ; [4]WHO Collaborating Center for Reference and Research on Meningococci, Norwegian Institute of Public Health, Oslo, Norway; [5]Centre Hospitalier Universitaire Yalgado, Ouagadougou, Burkina Faso

[6]Hospitalier Universitaire Blaise Compaoré, Ouagadougou, Burkina Faso ; [7] Direction de la lutte contre la maladie, Ministère de la Santé, Ouagadougou, Burkina Faso

ABSTRACT

The aim of this study was to analyze ten (10) years of epidemiological surveillance data of meningitis in Burkina Faso for high risk germs patterns identification in order to contribute to the strengthening of prevention strategies.

A retrospective study of the past decade (2005- 2014) of cases of acute bacterial meningitis occurred in the thirteen health regions, collected through epidemiological surveillance data meningitis in Burkina Faso. From a total of 88 057 suspected cases of acute bacterial meningitis, we recorded 9134 deaths. From the laboratory confirmed cases, the identified germs were as follows: 56.79% of *Neisseria meningitidis*, 41.09% of *Streptococcus pneumoniae* and 2.13% of *Haemophilus influenzae*. Among the meningococcus isolated, we observed the following distribution: 23.11% of NmA, 58.84% of NmW and 18% of NmX.

Mortality associated with acute bacterial meningitis remains still high in Burkina Faso despite the complete disappearance of NmA since 2012, after the conjugate vaccine A (MenAfriVac) has been introduced in this country. However the emergence of NmX, the reemergence of NmW and the persistence of high prevalence of *Streptococcus pneumoniae* are a major concern in the fight against meningitis in Burkina Faso. So, it is necessary, in addition to the strengthening of surveillance, diagnosis and case management to develop and make available and accessible a conjugate trivalent vaccine against NmA the NmX and NmW serogroups.

Keywords: meningococcal meningitis, W and X serogroups, *Streptococcus pneumoniae*, MenAfriVac.

DYNAMIQUE DES GERMES RESPONSABLES DES MENINGITES BACTERIENNES AIGÜES AU BURKINA FASO DANS LES DIX DERNIERES ANNEES (2005-2014)

RÉSUMÉ

Contexte : l'objectif de cette étude était d'analyser les données de la surveillance épidémiologique des méningites des dix (10) dernières années afin de dégager les profils de germes à risque en vue de contribuer au renforcement des stratégies de prévention

Méthodes: Une étude rétrospective des dix dernières années (2005- 2014) sur les cas de méningites bactériennes aigues des treize régions sanitaires ; recueillies à travers les données de surveillance épidémiologique des méningites du Burkina Faso.

Résultats: Sur un total de 88 057 cas suspects de méningites bactériennes aigues, nous avons enregistré 9134 décès. Parmi les cas confirmés au laboratoire, les germes identifiés se répartissent comme suit : 56.79% de *Neisseria meningitidis*, 41.09% de *Streptococcus pneumoniae* et 2.13% d'*Haemophilus influenzae*. Parmi les méningocoques, nous avons observé 23.11% de NmA, 58.84% de NmW et 18% de NmX.

Conclusion: La mortalité associée aux méningites bactériennes aigues demeure toujours élevée au Burkina Faso malgré la disparition totale du NmA depuis 2012 suite à l'introduction du vaccin conjugué A (MenAfriVac). Cependant l'émergence de NmX, la réémergence de NmW, et la persistance de la forte prévalence du *Streptococcus pneumoniae* constituent une

préoccupation majeure dans la lutte contre la méningite au Burkina Faso. Il s'avère donc nécessaire, en plus du renforcement de la surveillance, du diagnostic et de la prise en charge des cas de mettre au point et de rendre disponible et accessible un vaccin trivalent conjugué couvrant le NmA, le NmX et le NmW.

Mots-clés: méningite à méningocoques, sérogroupes W et X, Streptococcus pneumoniae, MenAfriVac.

INTRODUCTION

Acute bacterial meningitis is a major public health problem in the south-Sahara African area and particularly in Burkina Faso (1). This disease is a serious disease that can cause death within hours or may leave significant neurological sequelae (1, 2). Meningococcus is responsible for major epidemics, usually every 5-10 years, causing many cases of deaths in the population (3). More than half of the cases of meningococcal *Neisseria meningitidis* in the world occur in the African south-Sahara countries (4); they represent the 4th cause of mortality in under 15 years children, after malaria, diarrheal and respiratory diseases (3); according to the reports of the Directorate for the Fight against Disease (DLM), Burkina Faso recorded from 2006 to 2007 a lethality rate of 8% for meningitis (5).

Prevention and response strategies are usually based on epidemiological surveillance, communication, proper case management and mass vaccination. In addition to serogroup A that was most responsible for epidemics before the MenAfriVac vaccine introduction, other serogroups have led to serious epidemics in Burkina Faso. This study aimed to analyze the ten (10) past years ie 2005-2014 data of the epidemiological surveillance of meningitis in order to study trends and identify germs profiles at high risk for the upcoming years. This study could enable the Ministry of Health of Burkina Faso, especially the DLM in strengthening prevention of epidemic outbreaks.

MATERIALS AND METHODS

Study sites

The study was conducted in thirteen (13) health regions of Burkina Faso: the Boucle of Mouhoun, the Cascades, the Centre, the Centre-East, the Centre-North, the Centre-West, the Centre-South, the East, the Hauts-Bassins, the North, the Plateau Central, the Sahel and the South-West regions. The country has a National Reference Laboratory for meningitis (NRL) that is the Charles De Gaulle University teaching Hospital laboratory of Bacteriology-Virology and four (4) national laboratories located in the University teaching Hospital of Yalgado Ouedraogo, the University teaching of Hospital Souro Sanou, the Centre Muraz and the National Laboratory of Public Health. Each region, through its health districts is affiliated to a laboratory for CSF analysis and isolation of germs.

Type and period of the study

The study was descriptive retrospective and was performed for analytical purposes. It covered ten years period, from January 2005 to December 2014.

Sampling and sample

The sampling method was exhaustive: the sample comprised of all cerebrospinal meningitis cases registered in the Ministry of Health database (national epidemiological surveillance system) during the study period.

Cases of cerebrospinal meningitis of all health regions were selected and classified as suspected and confirmed cases, in accordance with the WHO definition of acute bacterial meningitis.

Data collection

Data was collected for analysis purpose on an especially designed form for each case. Clinical records, case filings forms, sampling bulletins and CSF analysis results were the primary tools for data collection.

Results

From 2005-2014, Burkina Faso recorded a lethality rate of 10.37 %. 5775 (6.55 %) of these suspected cases have been laboratory confirmed.

TABLE I- DISTRIBUTION OF MENINGITIS CASES AND DEATHS (LETHALITY) ACCORDING THE YEAR (N = 88,057)

Year	Suspected cases (N)	Deaths (N)	Lethality (%)
2005	3623	751	20.72
2006	19162	1677	8.75
2007	25695	1865	7.25
2008	10345	1068	10.32
2009	4878	693	14.20
2010	6837	989	14.46
2011	3878	588	15.16
2012	7022	739	10.52
2013	2984	367	12.29
2014	3633	397	10.92
Total	88 057	9 134	10.37

The 2010 lethality rate was almost the double of that observed in 2007 or 2006

Prevalence of identified germs from 2005 to 2014

Among the confirmed cases, 3280 (3280/5775, that is to say 56.79%) were *Neisseria meningitidis*. The serogroups distribution was as follows: 23.11% (758/3280) of NmA, 58.84% (1930/3280) of NmW and 18% (591/3280) of NmX. *Streptococcus pneumoniae* and *Haemophilus influenzae* represented respectively 41.09% (2373/5775) and 2.13% (123/5775) of laboratory-confirmed cases.

TABLE II: GERMS DISTRIBUTION OF ACCORDING TO THE YEAR (N =5775)

	NmA (%)	NmW (%)	NmX (%)	Spn (%)	Hib (%)	Total
2005	41 (68.33)	0 (0)	0 (0)	17 (28.33)	2 (3.33)	60
2006	244 (89.37)	3 (1.09)	0 (0)	20 (7.32)	6 (2.19)	273
2007	253 (89.71)	4 (1.58)	0 (0)	23 (8.15)	2 (0.70)	282
2008	156 (89.14)	0 (0)	0 (0)	19 (10.85)	0 (0)	175
2009	40 (27.21)	4 (2.72)	0 (0)	100 (68.02)	3 (2.04)	147
2010	20 (7.46)	2 (0.74)	207 (77.23)	36 (13.43)	3 (1.11)	268
2011	4 (0.35)	111 (9.96)	158 (14.18)	798 (71.63)	43 (3.86)	1114
2012	0 (0)	1357 (64.95)	201 (9.62)	502 (24.03)	29 (1.38)	2089
2013	0 (0)	236 (37.76)	23 (3.68)	351 (56.16)	15 (2.40)	625
2014	0 (0)	213 (28.70)	2 (0.27)	507 (68.32)	20 (2.69)	742
Total	758 (13.12)	1930 (33.42)	591 (10.23)	2373 (41.09)	123 (2.13)	5 775

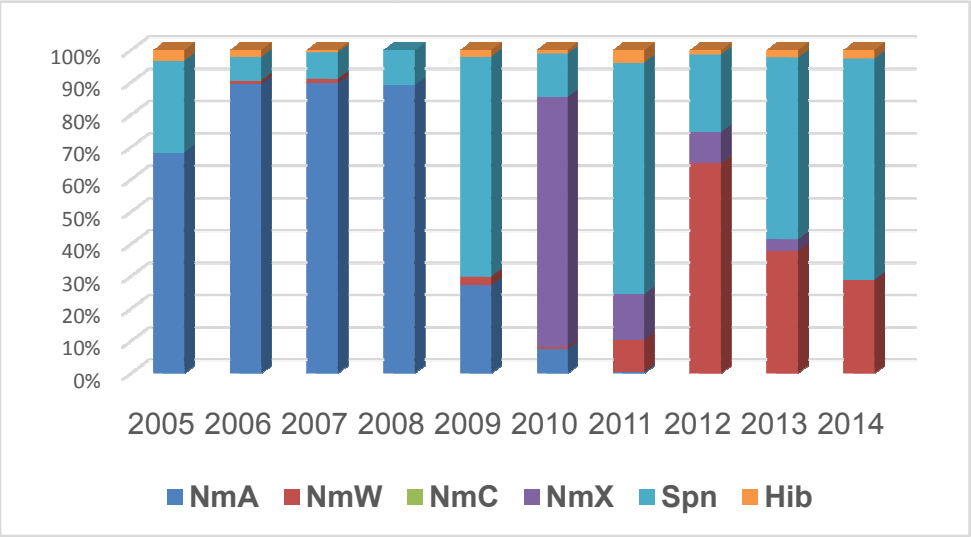

FIGURE 1: GERMS DISTRIBUTION ACCORDING TO THE YEAR, FROM 2005 TO 2014

TABLE III: DISTRIBUTION OF GERMS ACCORDING TO HEALTH REGIONS FROM 2005 TO 2014 (N = 5775)

Health region	NmA	NmW	NmX	Spn	Hib	Total
Boucle of Mouhoun	57	254	55	271	8	**645**
Cascades	9	140	20	98	3	**270**
Centre	149	24	16	93	8	**290**
Centre-East	10	262	70	272	18	**632**
Centre-North	75	77	29	168	11	**360**
Centre-West	80	148	25	236	13	**502**
Centre-South	47	140	63	124	5	**379**
East	16	154	24	214	17	**425**
Hauts-Bassins	61	353	81	311	3	**809**
North	88	204	149	231	13	**685**
Plateau Central	94	75	43	220	11	**443**
Sahel	9	60	4	70	12	**155**
South-West	63	39	12	65	1	**180**
TOTAL	**758**	**1930**	**591**	**2373**	**123**	**5 775**

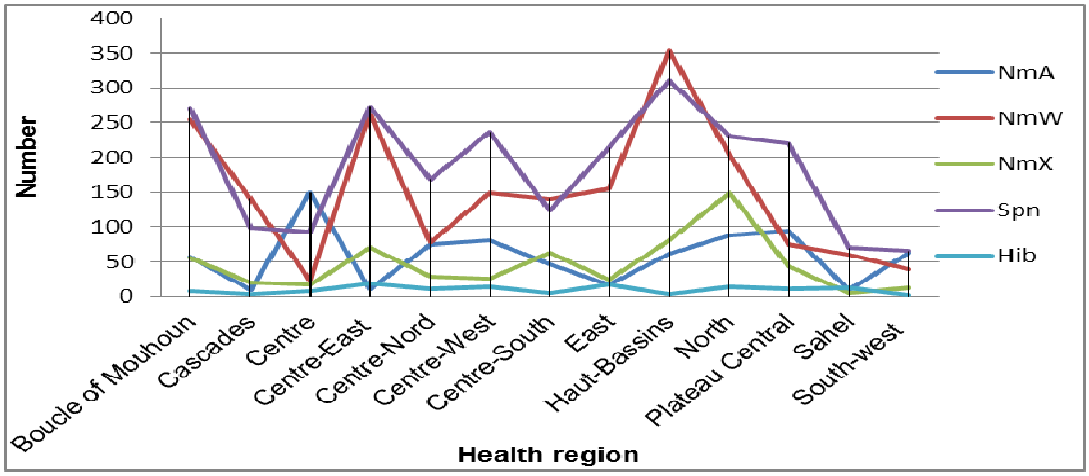

FIGURE 2: DYNAMICS OF GERMS DISTRIBUTION ACCORDING TO THE HEALTH REGION

DISCUSSION

Among the suspected cases, the bacterial meningitis were laboratory-confirmed for 5775 patients, equivalent to about one patient in 15. One limitation of our study is related to the low rate of laboratory confirmed cases: less than 7% of cases have been laboratory confirmed. Several studies reveal the insufficient use of the laboratory in meningitis surveillance in the meningitidis belt countries (6, 7). This situation could be explained by the integrated surveillance system set up in Burkina Faso before the introduction of the serogroup A anti meningococcal conjugate vaccine, the MenAfriVac in 2010. Since mass vaccination with MenAfriVac, the country adopted a surveillance system in which the CSF analysis of each suspected case is mandatory. In addition, since 2010 the use of real-time PCR increased the laboratories capacities for *N. meningitidis* detection.

During the 2005 to 2014 period, 88 057 meningitis suspected cases have been recorded in the 13 health regions of Burkina Faso. The years 2013 and 2014 were relatively calm with fewer cases (6617) in contrast to years 2006 and 2007 when the number of reported cases was 6 times higher (44,857).

Analysis of epidemiological surveillance data from 2005 to 2014 showed that *Neisseria meningitidis* was the most responsible of meningitis in Burkina Faso, about 57% of laboratory-confirmed cases. So this finding confirms what Leon Lapeyssonnie described since 1963 on germs that cause acute bacterial meningitis in the countries of the meningitidis belt in which Burkina Faso is entirely included (4, 8).

The NmA has been the dominant serogroup till 2008 with its peak in 2007: about 90% (253/282) of NmA was recorded among confirmed cases of the year. In addition to Burkina Faso, other countries located in the meningitidis belt were hit hard in 2007 by the NmA including Sudan and Uganda that notified from January 1st to March 16th, 2007, respectively 7149 and 3297 cases, mainly due to NmA (7).

Of all NmA isolated over the past 10 years, the Centre health region which houses the capital of Burkina Faso is one that recorded the highest prevalence of serogroup with about 20% (149/758) of NmA. This observation could be explained by the fact that this region is the main convergence area for both local and foreign populations in order to engage in economic activities.

Of note, the country experienced from 2010 to 2012 an abrupt emergence of a new serogroup, the NmX that was, until that period absent from the country where 566 cases of NmX with 207 cases in 2010 and 201 serogroup 2012 have been recorded. This serogroup had been reported in other countries of the belt meningitidis since 2006 including Niger, Togo, Ghana and Kenya (9, 10, 11, 12, 13). A part from Kenya, Niger, Togo and Ghana are Burkina border countries at the east and the south and thus, population movement between Burkina Faso and its border countries could explain the spread of this serogroup in almost all the 13 health regions that have been affected. Contrarily to the other epidemic serogroups, no vaccine is yet available against the NmX; in effect since December 2010, Burkina Faso, like other countries of the meningitidis belt introduced nationwide a conjugate vaccine against serogroup A, the MenAfriVac. Since 2011 we have seen the almost total disappearance of NmA: only 0.35% of NmA (4/1114) and no case of this serogroup have been reported since this year. Several studies have shown the impact of this

vaccine on cerebrospinal meningitis as well as on the NmA asymptomatic carriage.(14, 15, 16, 17).

Further, the study revealed the re-emergence of the NmW serogroup after vaccination. From 2011, a progressive increase in this serogroup was observed with a peak in 2012: approximately 65% (1357/2089) of germs confirmed during this year (2012). The number of cases declined in 2013 and 2014 but remained still high: respectively 236 and 213 cases. Out of all the affected regions, the regions of Hauts Bassins, Center-East and boucle du Mouhoun were the most affected with respectively 18.29% (353/1930), 13.57% (262/1930) and 13.16% (254/1930) of meningitidis cases caused by NmW from 2005 to 2014. Of note, in addition to Burkina Faso, countries such as, Benin, Mali, Nigeria, Gambia, Guinea and Sudan have experienced epidemics due to the NmW after MenAfriVac vaccination (18, 19, 20, 21). The proximity of some health regions with neighboring countries such as Hauts Bassins and Boucle du Mouhoun regions that are adjacent to Mali as well as the center-East region, that is near to Benin; could explain their high exposure to the NmW. Of note, this serogroup was isolated for the first time in Burkina Faso in 2002 - 2003 causing high morbidity and mortality (22, 23). Our study showed a very high lethality rate in 2012 where about 65% of the isolates have been identified as NmW. Indeed in 2012, we recorded a lethality rate 10.52% with 739 deaths out of 7022 cases as well as in 2010 when the lethality rate was 14.46% with 989 deaths out of 6837 cases of meningitis. This year, 77.23% (207/268) of the isolates were related to NmX. In general, we found that the lethality due to NmX and NmW is equivalent or even higher than that caused by NmA; this finding has been revealed by other authors (21, 24, 25).

Besides the *Neisseria meningitidis*, the study has shown the significant proportion of *Streptococcus pneumoniae* (41.09%) in the occurrence of cerebrospinal meningitis during the past decade in Burkina Faso. This germ, well-known for its high lethality (26, 27) has been observed since 2009; however it had a net increase after vaccination with MenAfriVac. In 2011, it represented almost 72% (798/1114) of the isolates; during the same year we have recorded 3878 cases of meningitis with 588 deaths, that is to say a lethality rate of 15.16%. Since 2011, there has been noticed a decrease of cases but the number of cases remained high from 2012 to 2014: it was respectively 502 cases in 2012, 351 in 2013 and 507 cases in 2014.

In addition to the three (03) most affected health regions by the NmW, other regions such as the Centre-West, North and Plateau Central regions had shown a high number of cases Spn.

CONCLUSION

Cerebrospinal meningitis continues to cause high mortality in Burkina Faso population although no NmA case has been isolated since 2011, reflecting effective action of MenAfriVac vaccination against this serogroup. However the emergence of NmX serogroup in 2010 and re-emergence of NmW serogroup since 2012 remain a major concern in the fight against meningococcal meningitis. In addition, the study has identified *Streptococcus pneumoniae* as a significant cause of high mortality of cerebrospinal meningitis in Burkina Faso. If a vaccine against NmX has not yet been developed , a conjugate vaccine against pneumococcus, which takes into account most of Spn serotypes encountered in Burkina Faso has been introduced in the childhood immunization program since 2013,. Similarly, polysaccharide vaccine against the NmW serogroup exists but has a limited access for developing countries populations such as Burkina Faso. Given this change in the epidemiological situation that is heterogeneous and dynamic geographically and through years, highlighting the emergence of NmX, the reemergence of NmW, and the persistence of high prevalence of *Streptococcus pneumoniae*, it appears imperative to reinforce preventive and case management strategies.

Thus, in addition to the strengthening of the surveillance which is essential to monitor these changes and remain able to detect epidemics caused by every serogroup of Nm; it is imperative to develop a trivalent conjugated vaccine covering NmA, NmX, and NmW serogroups and to make it available to the population. Such vaccine would be particularly useful for the prevention of meningococcal disease in the African meningitis belt and could protect against more than 90% of invasive cases of meningococcal meningitis. The major challenge after the vaccine development would be for the country to integrate it systematically into the national immunization program.

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