

Neisseria meningitis serogroup X outbreak in Burkina Faso, 2009-2010

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ABSTRACT

Background: Centre MURAZ of Bobo-Dioulasso (Burkina Faso) organized in 2009 and 2010 a system of Cerebro-Spinal Fluid (CSF) collection in eight pilot Districts as an initial step for the future Ministry of Health's led strategy of individual surveillance in a context of meningococcal conjugate A vaccine introduction. **Methods:** CSF samples were analyzed with Polymerase Chain Reaction (PCR). This allowed for meningitis etiologies dynamics studies in the pilot Districts. **Results:** Because of geographical difficulties and lack of means, less than 40% of suspected cases had their CSF analyzed at PCR reference laboratory. In 2009, among confirmed cases at reference laboratory, *Sp* (*Streptococcus pneumonia*), *NmA* (*Neisseria meningitis A*) and *Hib* (*Hemophilus influenzae b*) were responsible respectively for 90%, 6.6% and 4.4% of cases. In 2010, serogroup distribution among confirmed cases was: *Sp* 62.7%, *NmX* 32.2% and *NmA* 5.1%. *Sp* which was continuously present in Burkina Faso takes more significant proportions, just as serogroup X which until there was sporadically encountered. The attack rates of *NmX* were three to twelve times higher than for *NmA* in the two Districts where *NmX* has been notified. **Conclusion:** As a consequence of such results, efforts must be maintained in epidemiologic surveillance field and in reinforcement of laboratory capacities. Fast care should be guaranteed to patients with adequate antibiotics according to country national guideline and chemoprophylaxis measures should be undertaken among contacts of

patients to prevent secondary cases. A plea must be made on one hand for pneumococcal vaccine introduction in Burkina Faso and on other hand towards manufacturers for taking into account serogroup X into meningococcal polyvalent vaccine composition. With this polyvalent vaccine including serogroup X, we suggested to conduct periodically mass campaign vaccination of people before the beginning of meningitis epidemiological season.

Keywords: Epidemiologic Surveillance; Pneumococcal; *NmX* Emergence; Meningitis; Burkina Faso

1. INTRODUCTION

African meningitis belt is characterized by severe meningitis epidemics due to meningococcal. This occurs in a context of high incidence of endemic cases during inter epidemic years. The majority of cases occur during dry season from January to April. In this area, until recently, majority of severe meningitis epidemics due to meningococcal were caused by serogroup A of *Neisseria meningitis* (*NmA*) [1-3]. Serogroup C was rarely involved in recent meningitis except in an epidemic reported in 1979 in Upper Volta, now Burkina Faso [3,4,6], that serogroup was rarely involved in current meningitis epidemics in meningitis belt countries [6,7]. In 2002, the first severe African epidemic of meningitis caused by *Nm* W135 occurred in Burkina Faso [8,9] and there was fear of rapid extension of this epidemic in the African meningitis belt. But eight years after, this extension didn't occur and cases of meningitis W135 were relatively rarely identified in Burkina through national reinforced surveillance

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data system. Sporadic cases of meningitis caused by serogroupe X of *Neisseria meningitidis* (*NmX*) were already reported in Niger in 1990 [10,11] and from 1995 to 2000 [12] and in Ghana in 2000 [13]. Since 2006, sporadic cases of *NmX* were also reported in some health Districts of Burkina Faso (Data from routine surveillance of Health Ministry not published). Burkina Faso was therefore logically engaged in meningitis fight caused by serogroup A. In December 2010, there was a national mass immunization campaign against this serogroup (*NmA*) with conjugate A vaccine. In Parallel, relatively significant proportions of notified case of meningitis during these two last years (2009-2010) were attributed to serogroup X (*NmX*). In addition, it is known that actually no vaccine against this serogroup exists. That could eventually constitute the beginning of acute bacterial meningitis epidemiologic trend change in Burkina Faso during the coming two to three years. The goal of this work is to show the significant increase in serogroup X meningitis case number in the epidemiologic trend of bacterial etiologies of meningitis in Burkina Faso, during 2010 epidemic season.

2. METHODS

2.1. Data Collection

Centre MURAZ set up a system of CSF collection in eight pilot Districts of Burkina Faso for contributing to prepare the field individual surveillance promoted by the Ministry of Health (MoH) after meningococcal conjugate A vaccine introduction. This program was set up by Centre MURAZ in collaboration with the Agence de Médecine Préventive (AMP) with a financial support of the French Ministry of Foreign Affairs (MAE) via Institut Pasteur of Paris through the Fonds de Solidarité Prioritaire (FSP). Throughout this system, some dispositions are taken so that all CSF carried out from suspected cases of meningitis on the eight pilot Districts level in the West part of the country can profit from PCR laboratory analysis. CSF conserved at ambient temperature during several days before are conveyed at Centre MURAZ PCR laboratory. Conditioning is done by triple packing system, in an isothermal container with ice boxes and the package is entrusted to conveyors of public transport. A communication network allows the information flow between District teams and laboratory team of Centre MURAZ. In parallel, national system of notification based on national guide of standard clinical meningitis case definition followed its course in the eight pilot Districts level. Biological confirmation of CSF is not necessary before case notification.

2.2. Laboratory Methods

In 2002, acute bacterial meningitis method diagnosis by

PCR was transferred to Centre MURAZ. This diagnosis method by PCR comes in complement from traditional methods of diagnosis such as Gram, latex and Culture. These traditional methods are often not possible to realize at Districts level, on hand because of a lack of reagents in particular concerning latex, and on another hand because of the too long time before CSF arrival at the laboratory for culture. PCR method is used for the diagnosis of the three principal etiologies responsible of meningitis in Burkina: *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae b* according to well defined procedures' [14,15]. An aliquot of each CSF sample or each Trans-Isolate medium supernatant is freeze-thawed, boiled for 5 min and centrifuged at 10,000 g for 10 min. One proceeds by a multiplex single-tube PCR on 10 mL of the supernatant for amplification of the *crpA* genes of *Nm* [16], the *lytA* gene of *S. pneumoniae* [17] and the *bexA* gene of *H. influenzae* [18]. For genogrouping *Nm* positive specimens, a second PCR is performed for the amplification of the *siaD* genes for *Nm* serotypes B, C, Y and W135 and the open reading frame 2 of the gene *mynB* for *NmA* [16]. In 2004, a PCR protocol developed by the *Neisseria* Unit of Institut Pasteur of Paris for the detection of *NmX* was added to our range of genogrouping PCR for *Nm* serogroups A, B, C, Y, and W135. For *NmX* PCR Protocol, two primers were designed in the serogroup X capsule biosynthesis (*xcbA*) gene, one of the *xcbABC* clusters of three genes which are single for *NmX* and were confirmed like essential for the *NmX* capsule expression [19]. These 2 primers are primer X-10 5'-ACAGCCCATAAAAACACCCGTATCATC-3' and primer X-11 5'-GTGATTGGAATCTTGCAATATCGGT-3', and they specifically amplify a 202—base pair DNA fragment. Any amplification was obtained from isolates of a collection of isolates from other serogroups [20].

3. RESULTS

The eight Districts notified at the national surveillance system level 656 of cumulative clinically diagnosed cases of meningitis from January to December 2009 and 695 cumulative cases from January to December 2010. The prevalence of clinical cases in each District is presented in **Figure 1**. During the two years, Solenzo was the most concerned District, followed by Boromo and Sindou Districts. In 2009, CSF samples were performed for 256 (39.0%) of cumulative clinically diagnosed cases, and were analyzed at PCR laboratory of Centre MURAZ. Among theses, 91 cases (35.5%) revealed positive with an etiology of meningitis. *Pneumococcus* (*Sp*), *Neisseria meningitidis* A (*NmA*) and *Hemophilus influenzae b* (*Hib*) accounted for 90%, 6.6% and 4.4% of positive cases respectively. Samples distribution according to District

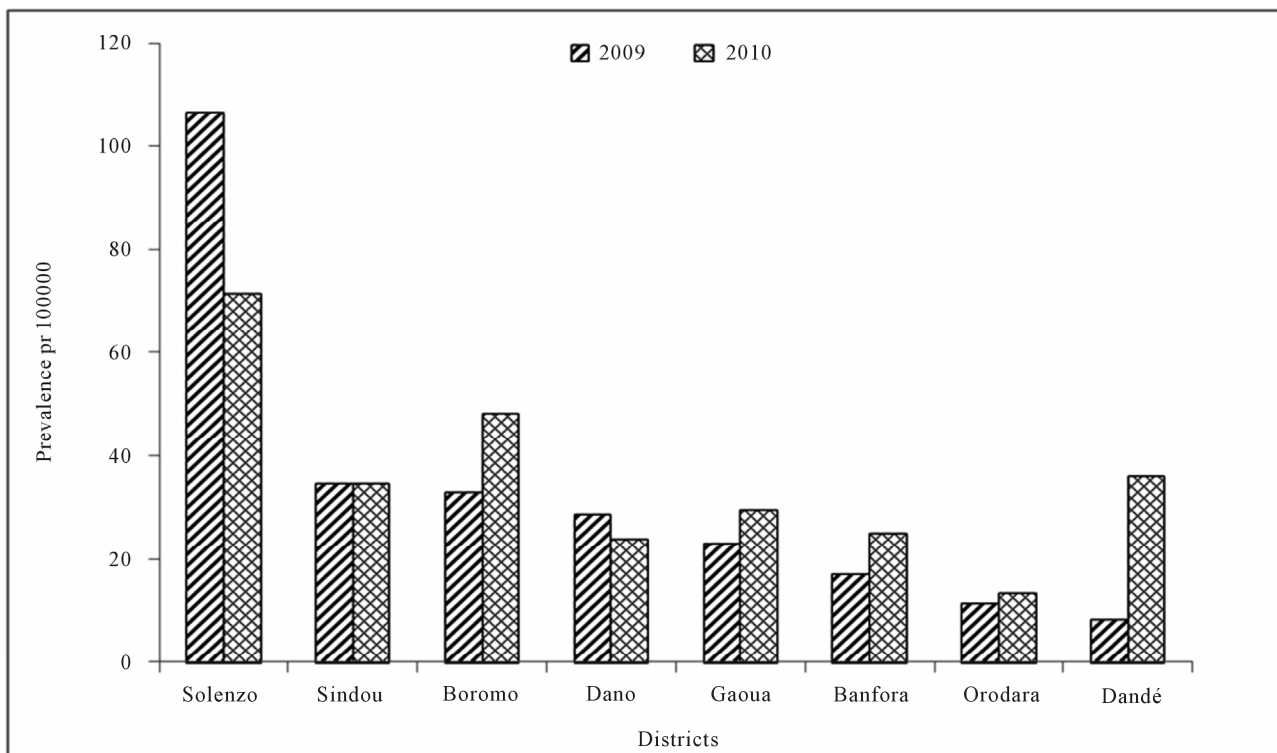


Figure 1. Prevalence of cumulative clinical cases in each District in 2009 and 2010.

source and identified serogroup is presented in **Table 1**. In 2009, no *NmX* case had been identified at the eight pilot Districts level. The comparison between clinically diagnosed cases from national notification system level and cases which were analyzed by PCR according to District source in 2009 is presented in **Figure 2**. The global attack rate of meningitis for the eight Districts was 32.8 for 100,000 inhabitants in 2009 (population size estimated at 1,970,692 inhabitants), with a global lethality of 15.1 per 100. The specific attack rate by serogroup was 4.1, 0.3, and 0.2 for 100,000 inhabitants for *pneumococcus*, *Neisseria meningitidis A* and *Hemophilus influenza b* respectively, when pooling over the eight Districts. Specific attack rate by serogroup and Districts are shown in **Figure 3**. In 2010, from the 695 cumulative clinical diagnosed cases, 213 CSF samples (31.0%) have been sent to PCR laboratory of Centre MURAZ. Of these 213 CSF samples, 59 cases (27.7%) were positive to an etiology of meningitis. *pneumococcus (Sp)*, *Neisseria meningitidis* serogroup X (*NmX*) and the *Neisseria meningitidis* serogroupe A (*NmA*) represented, 62.7%, 32.2% and 5.1% of positive cases respectively. Solenzo District in Boucle du Mouhoun sanitary region has totalized (13 *NmX* cases) which represent twice more cases than Dandé District (6 *NmX* cases) in Hauts Bassins sanitary region. Samples distribution according to the District source and identified serogroup is represented in **Table 2**. From January to December 2010, the global attack rate

of meningitis for the eight Districts was 28.6 for 100,000 inhabitants (population size estimated at 1,988,015 inhabitants) with a global lethality of 20.8 per 100 over the same period. The specific attack rate by serogroup was 1.9; 0.9 and 0.2 for 100,000 inhabitants for the *pneumococcus*, *Neisseria meningitidis X* and *Neisseria meningitidis A*, respectively. Specific attack rates by identified serogroup and by Districts are shown in **Figure 4**. In 2010, the comparison between notified cases on clinical symptom basis and cases which were analyzed by PCR by District are presented in **Figure 5**.

4. DISCUSSIONS

Among suspected cases of meningitis notified at national surveillance system level by the eight Districts, less than 40% of CSF samples collected arrived at PCR laboratory of Centre MURAZ. This proportion is relatively weak owing to the fact that within this pilot project framework, some mechanisms had been set up to facilitate CSF collection and it's routing on the eight Districts level. In 2006 epidemic season in Niger, on 4185 suspected cases notified by national surveillance system, the reference laboratory had received 2905 CSF Samples, which represented approximately 70% of suspected cases [20]. Within our study framework, CSF proportion from suspected cases of meningitis which profited from a PCR analysis is definitely better than the previous years where

Table 1. Distribution of serogroup within each District, January to December 2009.

Districts	Samples analyzed by PCR		Identified serogroup		
	Number	Positive (%)	Sp (%)	NmA (%)	Hib (%)
Dande	11	6 (54.5)	5 (83.3)	0 (0)	1 (16.7)
Orodara	9	7 (77.5)	6 (85.7)	1 (14.3)	0 (0)
Solenzo	151	32 (21.2)	29 (90.6)	3 (9.4)	0 (0)
Boromo	17	5 (29.4)	3 (60.0)	1 (20.0)	1 (20.0)
Banfora	11	6 (54.6)	6 (100)	0 (0)	0 (0)
Sindou	25	8 (32.0)	7 (87.5)	0 (0)	1 (12.5)
Gaoua	10	8 (80.0)	7 (87.5)	0 (0)	1 (12.5)
Dano	22	19 (86.4)	18 (94.7)	1 (5.3)	0 (0)
Total	256	91 (35.5)	81 (89.0)	6 (6.6)	4 (4.4)

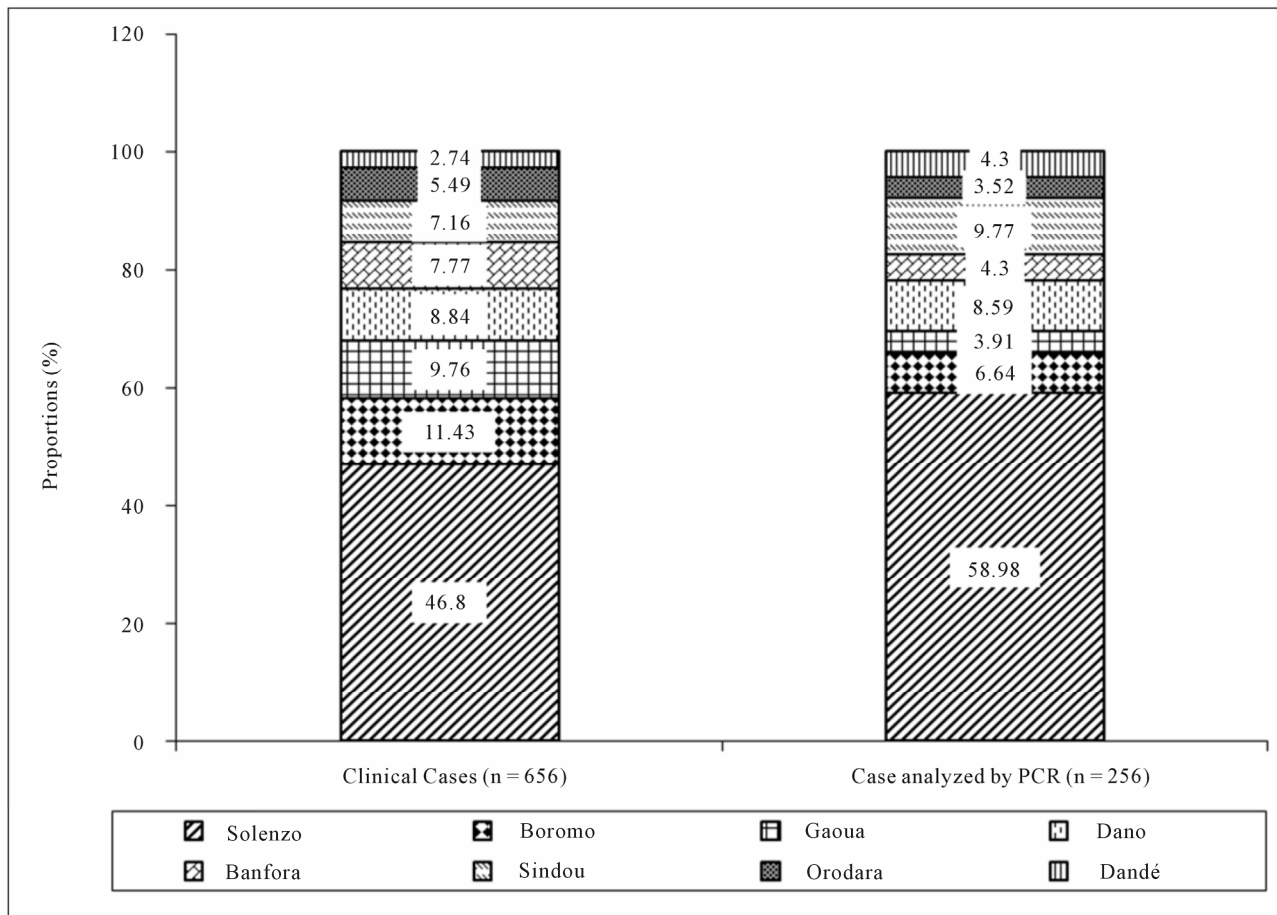


Figure 2. Distribution of notified cases and case analyzed by PCR across District, 2009.

the national directives recommended confirming the first ten cases to make it possible to take response measures. It remains however insufficient in the perspective of individual surveillance strategy after conjugate vaccine introduction whereby all CSF sample perform from any

suspected case must necessary be analyze by a laboratory. It is possible to have difficulties to obtain CSF on the field from a suspected case by lumbar puncture, which is not an easy medical act. In this case, notification can be made without there being CSF sample to analyze by the

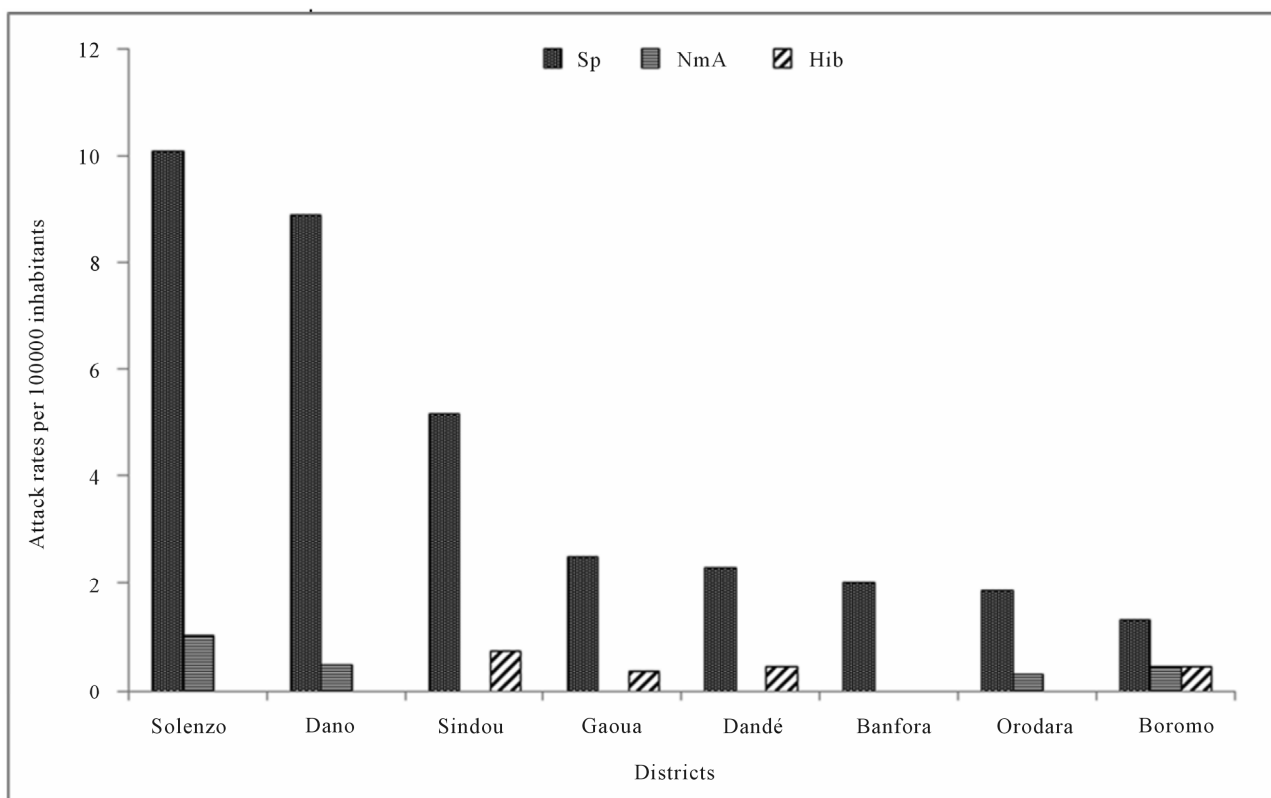


Figure 3. Attack rates by identified serogroup in each Districts, 2009.

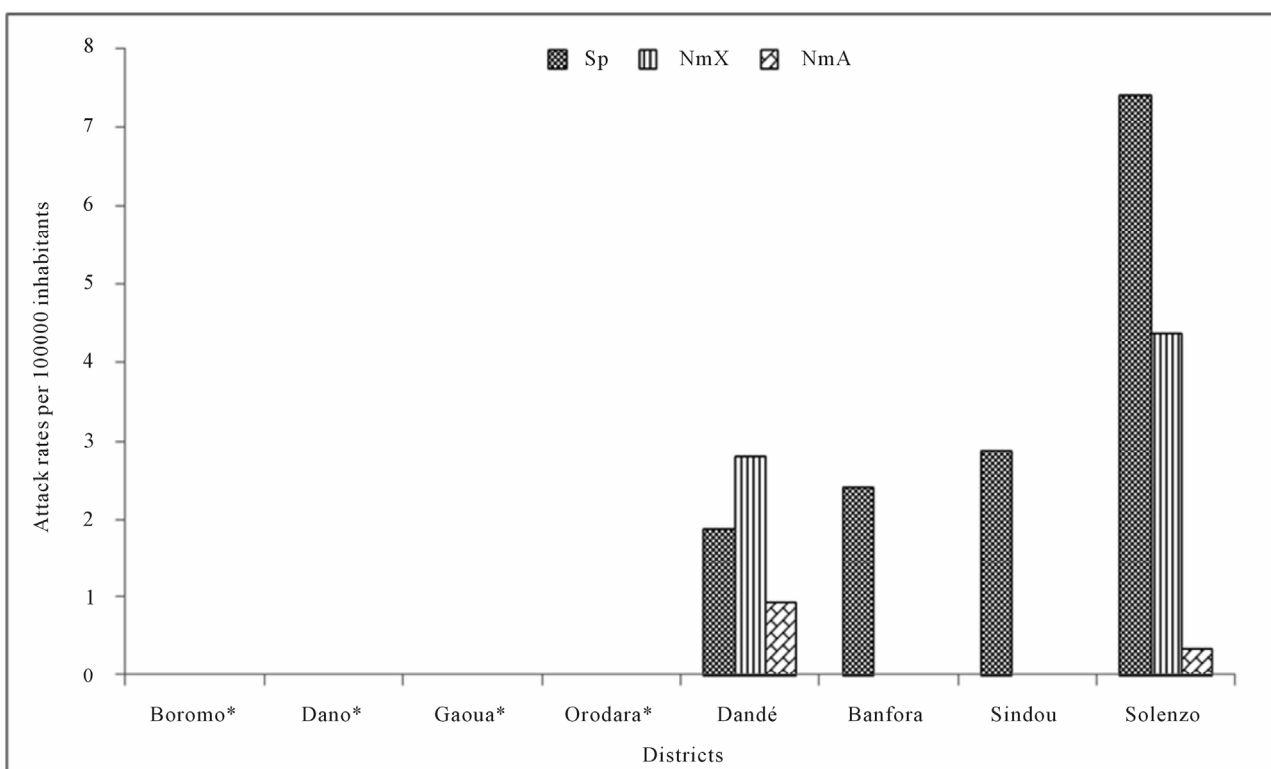


Figure 4. Attack rates by identified serogroup in each Districts, 2010. *Dano, Gaoua, Orodara and Boromo didn't send CSF for PCR in 2010.

Table 2. Distribution of serogroup within each District, January to December 2010.

Districts	Samples analyzed by PCR		Identified serogroup		
	Number	Positive (%)	Sp (%)	NmX (%)	NmA (%)
Dande	41	12 (29.3)	4 (33.3)	6 (50.0)	2 (16.7)
Orodara*	0	0	0	0	0
Solenzo	127	36 (28.3)	22 (61.1)	13 (36.1)	1 (2.8)
Boromo*	0	0	0	0	0
Banfora	25	7 (28.0)	7 (100)	0	0
Sindou	20	4 (20.0)	4 (100)	0	0
Gaoua*	0	0	0	0	0
Dano*	0	0	0	0	0
Total	213	59 (27.7)	37 (62.7)	19 (32.2)	3 (5.1)

*Dano, Gaoua, Orodara and Boromo didn't sent CSF for PCR in 2010.

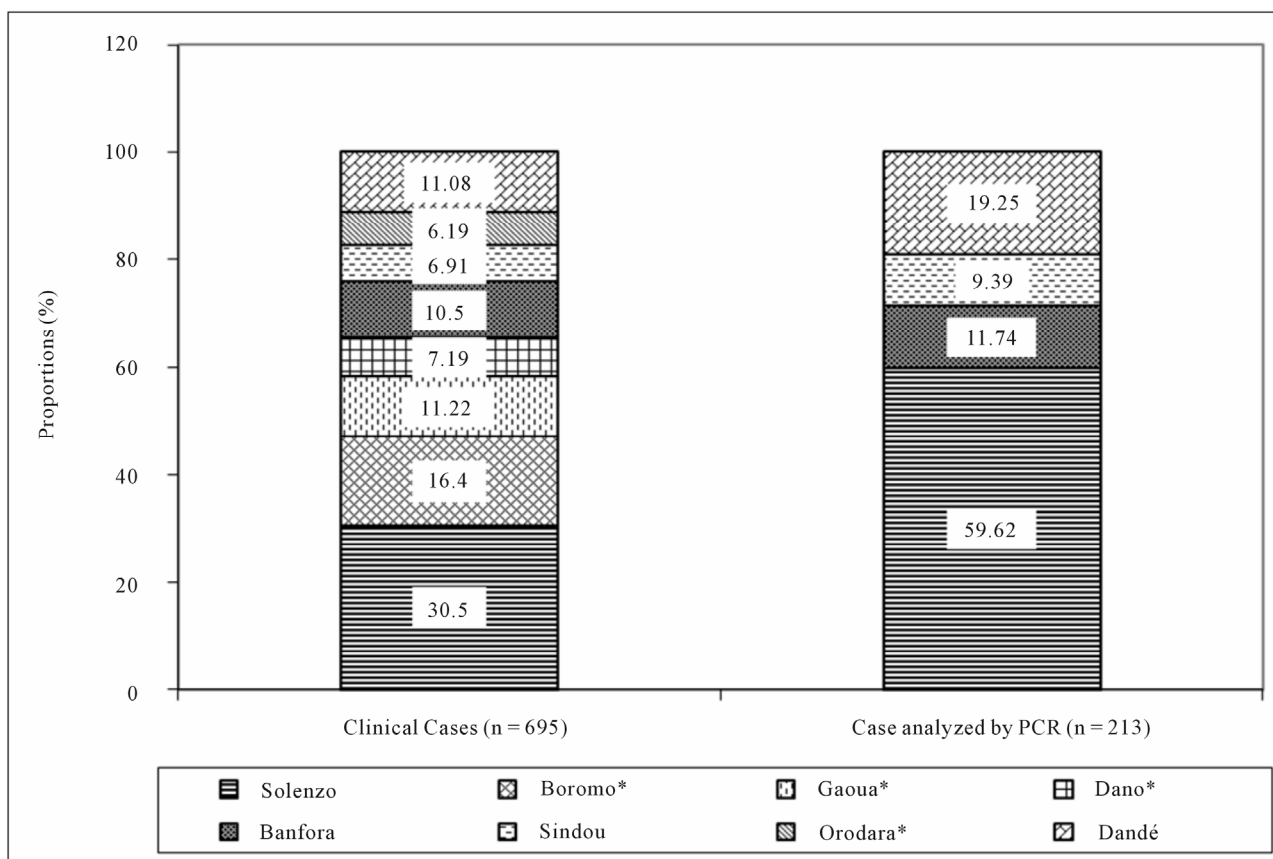


Figure 5. Distribution of notified cases and case analyzed by PCR across District, 2010. *Dano, Gaoua, Orodara and Boromo didn't sent CSF for PCR in 2010.

laboratory. However, there are obviously insufficiencies in cases notification and also difficulties on field level to ensure CSF collected routing towards reference laboratory. On reference laboratory level, it can be some difficulties per moment to ensure CSF analysis because of

reagents ruptures in relation to disease extent. Serogroup X of *Nesseria meningitis* was described for the first time in years 1960 and was implied in sporadic cases of invasive meningitis through North America, Europe and Africa [21]. Meningococcal serogroup X was responsible

for sporadic cases on some health Districts level of Burkina (Surveillance data not published). Since 2006, a report is made through surveillance system of relative fall of serogroup A case number of meningitis. On another hand, case number caused by pneumococcus which was always present in any season these last years [22], get important proportions, just as ascribable case number of serogroup X. Beside of isolated cases described more than ten years ago in Ghana (9 cases over a period of two years from 1998 to 2000) and in Niger (134 cases from 1995 to 2000), it is case number described during 2006 epidemic season in Niger which was most impressive where more half of confirmed cases of meningitis was due to serogroup X [20]. Niger is moreover a West African country which had described the greatest number of meningitis serogroup X cases, with the first cases isolated in 1982 [23]. Then after a silent of 8 years, 22 cases were described in 1990 [12,24]. Between 1995 and 2000, serogroup X meningitis cases were annually detected, with a peak of 83 cases in 1997 [12,25,26]. In 2005-2006, serogroup X meningitis cases were confirmed in the West of Kenya [23], but before this period no case due to this serogroup X had been described in East Africa [27]. The cases described in Ghana between 1998 and 2000 coincided with the significant increase in carriage of serogroup X [13,21,26]. This increase in carriage and outbreak of serogroup X meningitis cases coincided with significant reduction in dominating serotype A in the epidemic plan. Later, a new serotype A took the top again, while the carriage and the number of serogroup X cases dropped [26].

In Africa, the outbreak of meningitis epidemics due to less frequent serogroup were often charged to mass campaigns immunization against the prevalent serogroup which is *NmA*. What would result in to facilitate outbreak and diffusion of others serogroups [21,28,29]. However, this hypothesis seems moderate, because in 2006, maximum of serogroup X meningitis cases occurred in a South western area of Niger who didn't know an epidemic these last years and from which last immunization campaign goes back to before 2001 [20]. Molecular biology investigations have shown that *NmX* cases which have occurred in Kenya into 2006, was of sequence type ST5403 and differed from those described in Niger and Ghana which were sequences type ST181, ST5789 and ST751 [21,23,27]. *NmX* serotypes were described in Africa in the last forty years, during which they were responsible for sporadic cases particularly in Senegal in 1981, Niger in 1982, Chad in 1995 and Burkina Faso in 2003 [20]. Sequencing of cases described in 2010 in Burkina Faso is ongoing and will make it possible to see whether there is a bond with sequences which circulated in the Sub Saharan region or in East Africa. It is probable that evolution of serogroup X in Burkina Faso will be

similar to that of W135. This serogroup emerged between 2000 and 2002 [8,30], then it remained limited to Burkina Faso, without epidemiological dissemination in the other neighboring countries, and knew a fast reduction in time in particular from 2003 [23,31]. Burkina Faso had known a similar situation in 1979 [4,6] with an emergence of serogroup C, geographically limited and which disappeared quickly in time. The proportion of serogroup X cases of meningitis noted in Burkina Faso into 2010 is a significant concern. Although this serogroup don't have the same epidemic potential which is recognized to serogroup A until there [20,23], the reports observed, on one hand, during 2006 epidemic season in Niger [20] and on another hand, into 2010 in Burkina Faso, particularly in some health Districts such as Solenzo and Dandé make fear an epidemic risk of serogroup X explosion in African meningitis belt. In the image of what was made for the serogroup C and W135, potential epidemic of serogroup X took significant dimension to take into account within the conjugate A vaccine framework introduction in Burkina Faso, and in the other Sub Saharan countries [20,23,32]. A strong plea is necessary to be made so that vaccines manufacturers take into account this serogroup X in polyvalent vaccines composition. Otherwise, similar situations could be observed with the pneumococcal conjugate vaccine introduction, where serotypes not taken into account in vaccine composition replaced those eliminated by immunization [33]. In this context, it would be significant to reinforce surveillance in general and particularly the reinforcement of laboratories capacities to follow dynamics etiologies responsible of meningitis after conjugate A vaccine introduction in Burkina Faso.

5. CONCLUSION

The significant increase of serogroup X case number in 2010 challenges the decision makers in regards of epidemic control strategies. The reinforcement of laboratories capacities is essential with complementarities between bacteriology and molecular biology, while the development of an epidemiologic prompt and powerful surveillance system based on all available means techniques of communication. Fast care should be guaranteed to patients with adequate antibiotics according to country national guideline and chemoprophylaxis measures should be undertaken among contacts of patients to prevent secondary cases. A strong plea will be made in favor of obtaining and introducing of meningococcal polyvalent vaccine including serogroup X. With this polyvalent vaccine including serougruop X, we suggested to conduct periodically mass campaign vaccination of people before the beginning of meningitis epidemiological seasons.

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