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RESEARCH ARTICLE

SEROLOGICAL DIAGNOSIS IN SUSPECTED DENGUE CASES AT SAINT CAMILLE HOSPITAL OF OUAGADOUGOU: HIGH PREVALENCE OF INFECTION AMONG YOUNG ADULTS AGED 15 TO 30 YEARS

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ABSTRACT

Dengue fever is currently a major public health problem in Burkina Faso. The aim of this study was to determine seroprevalence and dengue infection evolution during the years 2016 and 2017. The study population consisted of 3572 patients aged 0 to 84 years seen during general medicine consultation from January 2016 to November 2017 and referred to the laboratory of Saint Camille Hospital of Ouagadougou for serological diagnosis of dengue fever. The Dengue Duo Bioline SD Kit (Standard Diagnostic Inc., Korea) was used to detect the presence of dengue virus NS1 antigen and IgM/IgG antibodies in serum or plasma. An overall prevalence of 17.3% (617/3572) of NS1Ag was observed in our study population. Age groups 15 to 30 years were significantly more infected compared to children under 5 years of age. The peak of infection was between mid-October and mid-November corresponding to the end of the rainy season in Burkina Faso. The present study reports a high seroprevalence of acute dengue virus infection in symptomatic patients. The use of effective vector control strategies through the destruction of breeding sites, personal protection and enhanced surveillance from August is needed for dengue fever prevention in Burkina Faso.

INTRODUCTION

Dengue is one of the most common vector-borne viral diseases in the world. It is caused by a single-stranded RNA virus of the genus Flavivirus that is transmitted through the bites of female *Aedes aegypti* and *Aedes albopictus* mosquitoes. Dengue fever is a re-emerging health concerns with increasing geographic expansion in tropical and subtropical populations in the recent decade (Ayukekbong *et al.,* 2017). Because of its morbidity and mortality, the disease is a major public health problem, especially in developing countries (Sorge *et al.,* 2016; WHO, 2017). However, in malaria-endemic areas, more than 70% of febrile illnesses are treated as presumptive malaria, often without proper medical examination and without laboratory diagnosis. In this context, there is a problem of differential diagnosis with a real risk of misdiagnosis of dengue fever as malaria. (Amarasinghe *et al.,* 2011). Dengue fever is a systemic infection with a wide spectrum of clinical presentations. The majority of cases are asymptomatic and clinical signs have no serotypic specificity.

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Two severe forms of dengue can occur especially in children under 15 years, namely dengue hemorrhagic fever (DHF) with or without shock syndrome. There are four dengue serotypes (DEN-1 to DEN-4) and each serotype gives prolonged but uncrossed specific immunity between serotypes. This explains why an individual can present several episodes of dengue infection with more severe symptoms at each new infection by a different serotype (Dellamonica, 2009). Serotypes 2, 3 and 4 of dengue virus have been identified in Burkina Faso (Ridde *et al.,* 2016; Hashimoto *et al.,* 2017). Dengue diagnosis is based on the detection of the viral genome by RT-PCR up to seven days after the onset of symptoms and on serology from the fifth day. The virus detection may also be based on the presence of NS1Ag in the serum. The treatment of dengue is symptomatic, as well as for hemorrhagic forms and/or with shock syndrome. There is currently no specific antiviral treatment for dengue fever. However, a vaccine has recently been licensed in some countries in Latin America and Asia and clinical trials of other vaccine candidates are in progress (WHO, 2016b; Paty, 2014; Carabali *et al.,* 2017; Rabaa *et al.,* 2017). According to recent estimates, 3.9 billion people in 128 countries are exposed to dengue virus infection, with approximately 390 million cases per year and 96 million of the latter have clinical manifestations regardless of the disease severity (Brady *et al.,* 2012; Bhatt *et al.,* 2013). The disease

mortality is estimated at 25 000 deaths/year, or 2 to 10 % of severe dengue (shock or hemorrhage). It mainly concerns children under 15 years and dependent on the ease of access to care (WHO, 2012 ; Sorge *et al.,* 2016). The first dengue epidemics have been reported in Africa since the 19th century while Burkina Faso experienced its first epidemic in 1925 (Amarasinghe *et al.,* 2011; Baronti *et al.,* 2017). In 1982, a second outbreak of dengue fever was reported between September and December; with 30 cases reported in the country (Baronti *et al.,* 2017; Eldin *et al.,* 2016; Gonzalez *et al.,* 1985). Another outbreak was also reported between October and November 2013 (Ridde *et al.,* 2014; Hashimoto *et al.,* 2017). The World Health Organization (WHO) reported 1,061 probable dengue cases out of 1266 suspected cases with a cumulative total of 15 deaths (case fatality rate of 1.2%) between August and November 2016, in Burkina Faso (WHO, 2016a). Dengue fever is a real public health problem in Burkina Faso. After the 2013 outbreak, special attention has been paid to this deadly vector-borne disease by health authorities. However, the epidemiological situation of arboviruses in general and dengue fever in particular is still poorly documented at the national level. The objective of the present study was to evaluate the seroprevalence and the evolution of dengue virus infection during the years 2016 and 2017 in patients attending Saint Camille Hospital of Ouagadougou.

METERIAL AND METHODS

Type and period of study

This was a descriptive analytical study to determine the seroprevalence and evolution of dengue virus infection during the period from January 1, 2016 to November 23, 2017 in patients attending Saint Camille Hospital of Ouagadougou.

Study population

The population of this study consisted of 3572 patients of various ages and sex seen at general medicine consultation during the study period and referred to the laboratory of Saint Camille Hospital of Ouagadougou for the serological diagnosis of the dengue. The institutional ethics committee of Saint Camille Hospital in Ouagadougou gave its approval for the exploitation of the data.

Sampling

The samples consisted of venous blood samples in dry tubes or EDTA. After centrifugation at 4000 rpm/min for 5 minutes, the serum or plasma was used to perform the dengue test. Serological tests were performed immediately after collection for quick availability of results.

Diagnosis of dengue fever

Detection of dengue virus infection was performed from serum or plasma using the SD Bioline Dengue Duo Rapid Detection Kit (Standard Diagnostic Inc., Korea) according to the protocol provided by the manufacturer. The test allows the detection of nonstructural protein (NS1) and anti-dengue virus IgG/IgM antibodies in serum, plasma or whole human blood.

Statistical analyzes

The data was saved on Microsoft Excel 2016 and analyzed using SPSS 21.0 and Epi info version 7.0 software. Multivariate logistic regression was used to determine the effect of age and gender of patients on dengue virus infection. The difference in statistical tests was considered significant for $p < 0.05$.

RESULTS

Sociodemographic characteristics

Our study population consisted of 43.8 % (669/1527) men and 56.2 % (858/1527) women in 2016 compared to 42.7% (874/2015) men and 57.3% (1171/2045) women in 2017. Patients age ranged from 0 and 80 years with an average of 26.1 ± 15.9 years in 2016 while it was 27.9 ± 15.9 in 2017 (ranged from 0 and 84 years of age). Children under 15 accounted for 24.1% (368/1527) and 17.8% (364/2045) of the study population in 2016 and 2017 respectively (Table I).

Prevalence of dengue virus infection

The prevalence of dengue NS1Ag was 22.5% (344/1527) and 13.3% (273/2045) in our study population, in 2016 and 2017 respectively. Prevalences of 2.6% (39/1527) and 20.4% (312/1527) was observed respectively for IgM and IgG in the study population in 2016. These prevalences were respectively 4.5% (92/2045) and 17.8% (363/2045) in 2017. Men were significantly more infected with the dengue virus (NS1Ag+) compared to women ($p = 0.040$, OR = 0.774, CI = [0.606-0.988]) in 2016, while no difference in infection according the gender was observed in 2017 (Table II). The age groups of 15 to 50 years were significantly more infected ($p < 0.05$, Table II) compared to children under 5 years of age in 2016 while the most infected age groups compared to the latter group were patients aged 15 to 30 in 2017 ($p < 0.002$).

Different serological profiles of dengue in the study population

In our study population, 40.1% (613/1527) of patients were positive for at least one of three serological markers of dengue fever (NS1Ag, IgM and IgG) in 2016. A prevalence of 0.3% (4/1527) positive individuals at all of these markers was observed during the same year. In 2017, there were 28.0% (573/2045) of patients positive for at least one of the three serological markers, while the prevalence of NS1Ag+/IgG+/IgM+ patients was 1.6% (33/2045). Individuals positive for two dengue serologic markers in 2016 accounted for 3.4% (52/1527), 1.1% (17/1527) and 0.3% (5/1527) of the study population respectively for NS1Ag+/ IgM+, NS1Ag+/IgG+ and IgM+/IgG+. In 2017, this prevalence was 0.6% (12/2045) for NS1Ag+/IgM+, 2.0% (41/2045) for NS1Ag+/IgG+ and 1.8% (36/2045) for IgM+/IgG+ patients (Table III).

Evolution of dengue virus infection in 2016 and 2017

Approximately 97.0% (1477/1527) of dengue suspicions were recorded in the last four months (September - December) of 2016. Patients positive for NS1Ag antigen during this period accounted for 99.7% (343/344) of all positive cases during the year. In 2017, 85.6% (1750/2045) of the examinations for suspicion of dengue were recorded between the months of August and November. It should also be noted that 97.4% (266/273) of all cases positive for NS1 antigen were observed during this period of 2017.

Table 1. Sociodemographic characteristics and prevalence of dengue in 2016 and 2017

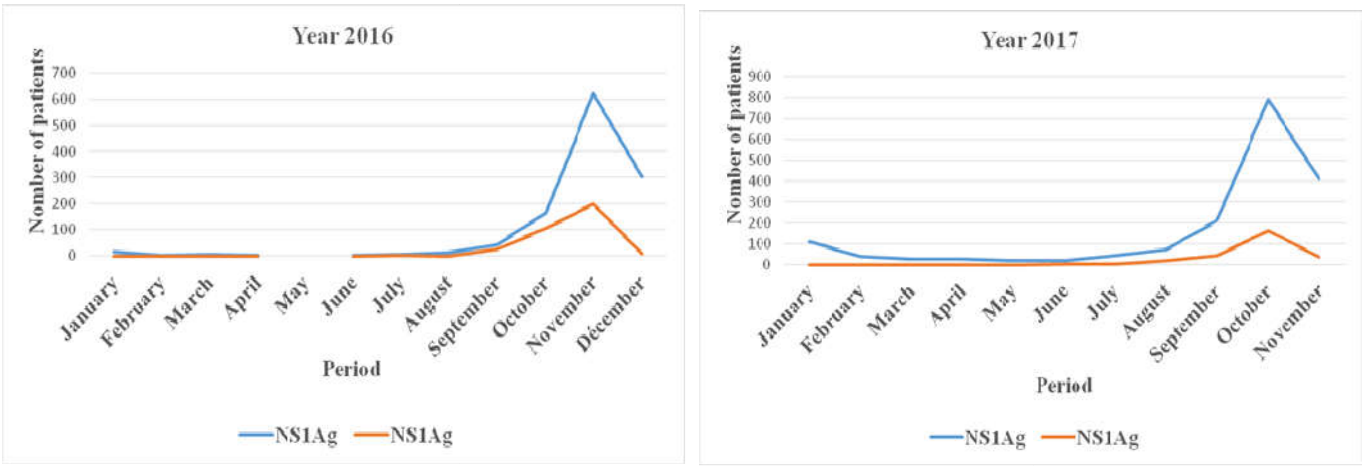
	Year 2016 (January - December)				Year 2017 (January - November)			
		Serology of dengue fever				Serology of dengue fever		
Characteristics		Ns1Ag+	IgM+	IgG+		NS1Ag+	IgM+	IgG+
Gender	N (%)	n (%)	n (%)	n (%)	N (%)	n (%)	n (%)	n (%)
Male	669 (43.8)	167 (25.0)	23 (3.4)	179 (20.9)	874 (42.7)	126 (14.4)	42 (4.8)	148 (16.9)
Female	858 (56.2)	177 (20.6)	16 (1.9)	133 (19.9)	1171 (57.3)	147 (12.6)	50 (4.3)	215 (18.4)
Total	1527 (100.0)	344 (22.5)	39 (2.6)	312 (20.4)	2045 (100.0)	273 (13.3)	92 (4.5)	363 (17.8)
Age, mean ± SD	26.1 ± 15.9	26.4 ± 13.6	Min - max = [0 - 80]		27.9 ± 15.9	26.9 ± 12.6	Min – Max = [0 – 84]	
Age group								
< 5	129 (8.4)	14 (4.1)	1 (0.8)	13 (10.1)	183 (8.9)	14 (7.3)	8 (4.4)	26 (14.2)
5 - 14	239 (15.7)	40 (11.6)	4 (1.7)	25 (10.5)	181 (8.9)	16 (8.8)	8 (4.4)	26 (14.4)
15 - 20	179 (11.7)	62 (18.0)	7 (3.9)	28 (15.6)	230 (11.2)	42 (18.3)	14 (6.1)	49 (21.3)
21 -30	469 (30.7)	123 (35.8)	16 (3.4)	116 (24.7)	717 (35.1)	123 (17.2)	36 (5.0)	122 (17.0)
31 - 40	277 (18.7)	63 (18.3)	5 (1.8)	62 (22.4)	367 (17.9)	42 (11.4)	12 (3.3)	70 (19.1)
41 - 50	103 (6.7)	21 (6.1)	3 (2.9)	26 (25.2)	183 (8.9)	24 (13.1)	6 (3.3)	35 (19.1)
> 50	131 (8.6)	21 (6.1)	3 (2.3)	42 (32.1)	184 (9.0)	12 (6.5)	8 (4.3)	35 (19.0)
Total	1527 (100.0)	344 (22.5)	39 (2.6)	312 (20.4)	2045 (100.0)	273 (13.3)	92 (4.5)	363 (17.8)

Table 2. Multinomial logistic regression of the prevalence of NS1 antigen

	Year 2016 (January - December)			Year 2017 (January - November)		
Caractéristiques		NS1Ag status			NS1Ag status	
Gender	OR	CI 95 %	p-Value	OR	CI 95 %	p-Value
Male	Ref.	-	-	Ref.	-	-
Female	0.774	[0.606 - 0.988]	0.040	0.841	[0.649 – 1.089]	0.188
Age group						
< 5	Ref.	-	-	Ref.	-	-
5 - 14	1.698	[0.885 - 3.257]	0.111	1.181	[0.558 - 2.497]	0.664
15 - 20	4.441	[2.352 - 8.386]	< 0.001	2.740	[1.445 - 5.199]	0.002
21 -30	2.994	[1.655 - 5.417]	< 0.001	2.532	[1.419 - 4.518]	0.002
31 - 40	2.489	[1.335 - 4.641]	0.004	1.572	[0.835 - 2.961]	0.161
41 - 50	2.173	[1.042 - 4.529]	0.038	1.849	[0.923 - 3.703]	0.083
> 50	1.623	[0.785 - 3.356]	0.191	0.860	[0.386 - 1.916]	0.713

Table 3. Serological profile of dengue virus infection in the study population in 2016 and 2017

			Year 2017 (January - November)			Year 2017 (January - November)		
			N = 1527			N = 2045		
Variables		IgG	NS1Ag- n (%)	NS1Ag+ n (%)	Total N (%)	NS1Ag- n (%)	NS1Ag+ n (%)	Total N (%)
IgM	Negative	Negative	914 (59.9)	271 (17.7)	1185 (77.6)	1472 (72.0)	187 (9.1)	1659 (81.1)
		Positive	13 (0.8)	17 (1.1)	30 (2.0)	253 (12.4)	41 (2.0)	294 (14.4)
	Total		927 (60.7)	288 (18.8)	1215 (79.6)	1725 (84.4)	228 (11.1)	1953 (95.5)
	Positive	Negative	251 (16.4)	52 (3.4)	303 (19.8)	11 (0.5)	12 (0.6)	23 (1.1)
		Positive	5 (0.3)	4 (0.3)	9 (0.6)	36 (1.8)	33 (1.6)	69 (3.4)



(a) **(b)**

Figure 1. Evolution of dengue infection (A) during 2016 and (B) during 2017

Figure 1 shows a high prevalence of Dengue virus infection between the months of September and December with a peak during October and November.

DISCUSSION

Sociodemographic characteristics

The population of this study was predominantly women (56.2% and 57.3% respectively in 2016 and 2017). This difference reflects the national situation (INSD, 2009) and can also be explained by the fact that women attend health centers much more than men. The mean age was 26 and 28 years ± 15.9 years with a prevalence of 40.1 % (613/1527) of patients positive for at least one of the three serological markers of dengue in 2016 compared to 28.0 % (573/2045) in 2017. On the one hand, the high seroprevalence of dengue in our study population confirms high endemicity of dengue infection in Burkina Faso (Ridde *et al.,* 2014; Ridde *et al.,* 2016). On the other hand, the decrease in this seroprevalence observed from 2016 to 2017 could be explained by the awareness of the disease among the populations and the prevention strategies implemented by the health authorities since the 2013 dengue outbreak (Ministère de la santé, 2017). Children under 15 represented 24.1% (368/1527) of the study population in 2016 compared to 17.8 % (364/2045) in 2017. This age group is the most affected by the severe cases and dengue mortality according to several authors (Dellamonica, 2009; Gerardin, 2010; Tarnagda *et al.,* 2014).

Prevalence of dengue virus infection

The prevalence of dengue NS1 antigen was 22.5 % (344/1527) in 2016 and 13.3 % (273/2045) in 2017 among patients in this study. The presence of this antigen means an acute infection with the dengue virus. Men were significantly more affected by acute dengue infection (OR = 0.774, 95% CI [0.609-0.988], p = 0.040) than women in 2016. Previous studies in India have also reported a higher prevalence of dengue virus infection in men (Patankar *et al.,* 2014; Garg *et al.,* 2011). Age groups 15 to 30 years remained significantly more infected with dengue fever in both years compared to children under 5 years of age. Our results are similar to the national rate (Ministère de la santé, 2017) with more than 80,0 % of cases aged 15 and over, as well as the results reported by Ridde et *al.* in Ouagadougou (Ridde *et al.,* 2016). Indeed, the authors found that the risk of dengue infection among people aged 15 to 20 and those over 50 years of age was 4 and 8 fold higher, respectively compared to children under 5 years of age. The increase in the odds ratio of seroprevalence in these age groups could be attributed to the risk of exposure. Adults are much more at risk of infection with dengue virus than children under 5 years of age (Fournet *et al.,* 2016; Carabali *et al.,* 2017).

Different serological profiles of dengue in the study population

Of all the patients positive for at least one of the three serological markers of the dengue virus, 2.1% (13/613) were only positive for IgG antibodies in 2016 against 44.2 % (253/573) in 2017. Positivity to IgG antibodies only, indicates a past dengue infection (Najioullah *et al.,* 2012; Lima *et al.,* 2012). A prevalence of 22.7% probable past flavivirus infection has been reported in children aged six (6) months to 12 years in Ouagadougou (Fournet *et al.,* 2016). These observations suggest an active circulation of the dengue virus in particular in Ouagadougou and Burkina Faso in general (Ministère de la santé, 2017). The lack of awareness among the population and health professionals about the disease, limited resources available for dengue diagnosis, as well as environmental factors such as waste management are all risk factors associated with flavivirus infection (Ridde *et al.,* 2014; Jaenisch *et al.,* 2014; Eldin *et al.,* 2016). Other cases of primary and secondary infections (Ns1Ag+/ IgM +, Ns1Ag+/IgG+ and IgM+/IgG +) reflect active transmission of dengue virus in our populations with a risk of severe cases (Mamoudou and Boushab, 2016). Indeed, the three DENV-2, DENV-3 and DENV-4 serotypes of the dengue virus have been identified in Burkina Faso (Baronti *et al.,* 2017; Ridde *et al.,* 2016; Hashimoto *et al.,* 2017).

It should also be noted that the different serotypes of the virus have no cross-immunity with more severe symptomatology at each infection of a patient with a different serotype. According to the Ministry of Health about 0.4% (6/1661 suspected cases) death cases due to dengue fever were recorded between January 1 and October 7, 2017 in Burkina Faso (Ministère de la santé, 2017). Although ethnicity and African descent are considered protective factors against severe forms of dengue fever, a study of the prevalence of different serotypes and their clinical implications is needed for a better understanding of the epidemiology of dengue and adequate management of patients (Rodriguez-Roche and Gould, 2013; Halstead and Cohen, 2015).

Evolution of dengue virus infection in 2016 and 2017

In our study population, acute dengue infection was sporadic from January to August, with a slight increase in infections. Patients positive for NS1 antigen during the last 4 months of 2016 accounted for 99.7% (343/344) of all positive cases throughout the year compared to 97.4% (266/273) cases registered between August and November during the year 2017. The peak of infection during the two years was between mid-October and mid-November (Figure 1). These findings are similar to previous studies that reported dengue outbreak between September and December in Burkina Faso and suggest a superposition of dengue transmission season with *Plasmodium falciparum* infection in Burkina Faso (Gonzalez *et al.,* 1985; Tarnagda *et al.,* 2014; Eldin *et al.,* 2016). Indeed, dengue outbreak occurred at the end of the rainy season as for *Plasmodium falciparum* infection in the population of Burkina Faso.

Conclusion

Dengue fever is a major public health problem in Burkina Faso. This study reports a high seroprevalence of acute dengue virus infection with an outbreak during October and November 2017. It also suggests a superposition between dengue virus and malaria parasite transmissions with peaks at the end of the rainy season. Strengthening surveillance of dengue through several actions such as vector control, determination of the prevalence of different serotypes, availability and accessibility of diagnostic tests and adequate management of patients are needs for a considerable reduction in the morbidity and mortality due to dengue in Burkina Faso. The study also suggests the need for the destruction of breeding sites and a strengthened vector control from the month of August for the prevention of dengue virus infection in our country.

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Authors contributions

JS, AKO, CWMN, BD, study concept and design; AKO, CWMN, BD, TMZ, sample collection and processing; AKO, CWMN, statistical analysis and interpretation of data; AKP, CWMN, BD, TMZ, AY, DO-Y, MB, PO, VP, JS, drafting of the manuscript; AKO, CWMN, BD, JS, Critical revision of the manuscript for important intellectual content; AKO, CWMN, BD, JS, administrative, technical, and material support; JS, CWMN, study supervision.

Conflict of interests

The authors declare no potential conflict of interest

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