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Research Article

Dengue Immunological Markers Evolution at Saint Camille Hospital in Ouagadougou (HOSCO) Burkina Faso

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Abstract

Background and Objective: Dengue is a remerging vector-borne viral disease in Burkina Faso since the outbreak of 2013 and requires special attention from health authorities. This study reports the prevalence of dengue fever serological markers (NS1Ag, IgM and IgG) and infection dynamic from January, 2018 to December, 2020 among patients tested for dengue infection at Saint Camille Hospital of Ouagadougou (HOSCO). **Materials and Methods:** The study population consisted of 6414 patients aged 0-97 years. Dengue virus infection was detected in serum or plasma using the SD bioline dengue duo rapid detection kit. **Results:** The prevalence of dengue NS1Ag was 2.25% (45/2003), 18.43% (501/2719) and 2.42% (38/1569) in the study population in 2018, 2019 and 2020, respectively. The age groups over 50 years and 15-20 years were significantly more infected compared to the group 21-30 years respectively in 2019 (p = 0.030) and 2020 (p = 0.035). Patients tested positive for at least one of these markers (NSIAg, IgG and IgM) represented 26.01% (521/2003) and 38.98% (1060/2719). The peak of infection during 2018 and 2019 was observed between October and November. The present study reports a high seroprevalence of acute dengue virus infection. The presence of NS1Ag, IgM and IgG in patients suggests an active circulation of the dengue virus in Ouagadougou. **Conclusion:** Data shows recurrent outbreaks of dengue infection in our country need strong surveillance and a suitable and affordable diagnostic system to clarify the burden, pinpoint the risk factors and for better case management.

Key words: Dengue, NS1Ag, IgG, IgM, seroprevalence, Burkina Faso

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

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INTRODUCTION

Dengue Fever (DF) is one of the most important arthropod-borne viral diseases worldwide with a 30-fold increased incidence over the last 50 years¹.

This positive single-stranded RNA enveloped virus of the genus flavivirus is responsible for the mild undifferentiated fever to life-threatening Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS)^{2,3,4}. Children under the age of 15 are the most affected group by dengue morbidity and mortality⁵. There are so far four distinct dengue serotypes (DENV-1, DENV-2, DENV-3 and DENV-4) sharing around 65% of genome similarity and each of them is divided into several genotypes⁶. Each dengue serotype gives prolonged and uncrossed specific immunity with more severe symptoms at each new infection with a different serotype⁷.

Then on-malaria febrile illness required more attention in the context of such remerging viral disease in malaria-endemic country⁸. Indeed, the real burden of dengue virus infection is underestimated in Sub-Saharan Africa due to the lack of active surveillance although the circulation of the virus since the nineteenth century⁹. Burkina Faso experienced a dengue outbreak in 1925, 1982, 2013 and 2016 with several deaths registered^{10,11}. Previously reported 17.3% of dengue NS1Agamong febrile illness patients seen at Saint Camille Hospital of Ouagadougou from January, 2016 to November, 2017 suggesting the development of adequate strategies for surveillance and control of this deadly viral disease in Burkina Faso¹¹.

Clinical diagnosis of dengue largely depends on the stage of infection in a patient. The Nonstructural (NS) proteins named NS1 can be diagnosed up to 9 days of infection or longer after the disease onset and can be detected as a viral RNA. During the infection, IgM antibodies are usually produced 3-5 days after primary infection. They peak several weeks after recovery and persist in the human patient's body for several months. The IgG antibody produced after IgM can be detected as early as 3 days after onset of illness during secondary infection. They can persist for a more extended period¹².

In line with the previous study, this study reported the prevalence of dengue fever serological markers (NS1Ag, IgM and IgG) and the dynamic of infection from 2018-2020 among patients tested at Saint Camille Hospital of Ouagadougou, Burkina Faso.

MATERIALS AND METHODS

Type, period and population study: A retrospective study was conducted from January, 2018 to December, 2020 among

febrile illness tested patients for dengue infection at Saint Camille Hospital of Ouagadougou. Sociodemographic information such as age and sex and results of dengue serological markers were extracted from the patient register according to the Institutional Ethics Committee of Saint Camille Hospital of Ouagadougou. A total of 6.414 patients were tested for dengue virus infection during the study period.

Sampling: Venous blood samples were collected in dry tubes or EDTA. After centrifugation at 4000 rpm min⁻¹ for 5 min, the serum or plasma was used for the detection of dengue virus infection. All data were compiled in the laboratory archive.

Dengue diagnostic: The 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 instructions for AgNS1 and IgG/IgM immunochromatographic tests were followed as described previously by Wang and Sekaran¹³. The one-step immunochromatographic assay allows the detection of non-structural protein (NS1) and anti-dengue virus IgG/IgM antibodies in these blood samples. Current or recent dengue infection was defined based on a positive result for NS1Ag and/or IgM. Past infection was defined by the positive result of IgG alone.

Statistical analysis: Analyzes were performed using STATA version 16. Excel software was also used for data entry and table formatting. The bivariate analysis makes it possible to verify the association between two variables. The frequencies of the various parameters were calculated and compared utilizing the Chi2 (Chi-squared) test at the 5% threshold. Chi-square provides information on the degree of association between 2 categorical variables.

RESULTS

Sociodemographic characteristics of patients: The global study population was a total of 6291 patients with 2003 patients (31.84%) in 2018, 2719 (43.22%) in 2019 and 1569 (24.94%) in 2020. Besides, 55.68 and 44.32% were women and men, respectively in Table 1.

For each year this study population was consisted of 56.52% women and 43.48% men in 2018 compared to 55.68% women and 44.32% men in 2019, in 2020 women were

Table 1: Baseline	characteristics	of the study	population

Year	Effective (N)	Percentage
2018	2003	31.84
2019	2719	43.22
2020	1569	24.94
Total	6291	100.00
Gender		
Female	3503	55.68
Male	2788	44.32
Total	6291	100.00
Age groups, years		
<5	589	9.36
5-14	729	11.59
15-20	1097	17.44
21-30	1954	31.06
31-40	1040	16.53
41-50	388	6.17
>50	494	7.85
Total	6291	100.00

54.62% and men 45.38%. Patient's average age was 28.62 ± 16.96 years in 2018, 24.85 ± 16.41 in 2019 and 28.27 ± 19.27 in 2020. Individuals aged from 15-40 years and children under 5 years, were most concerned by dengue infection. People from 15-20 and 21-30 were 20.37, 31.75% in 2018, respectively. In 2019, 17.10% were aged from 15-20 and 33.91% from 21-30 years. In 2020, 25.24% were 21-30 years and 19.25% from 31-40 years. Children under 15 accounted for 15.83, 23.35 and 23.33% of the study population in 2018, 2019 and 2020, respectively.

Prevalence of dengue virus infection: The prevalence of dengue NS1Ag was 2.25, 18.43 and 2.42% in the study population, in 2018, 2019 and 2020, respectively. Prevalence of 1.00 and 23.91% was observed, respectively for IgM and IgG in 2018. These prevalences were, respectively 6.80 and 19.82% in 2019. In 2020, 1.59% for IgM and 34.10% for IgG in Table 2. Men were significantly more infected with the dengue virus (NS1Ag+) compared to women, 20.58% versus 16.71% (p = 0.011) in 2019, while no difference in infection according to the gender was observed in 2018 and 2020 in Table 3. The age groups >50 years were significantly more infected (p = 0.030) compared to people 21-30 years of age in 2019 while the most infected age groups compared to the latter group were patients aged 15-20 in 2020 (p = 0.035). No significant difference was found in 2018.

Different serological profiles of dengue in the study **population:** In 2018, 26.01% (521/2003) of patients were tested positive for at least one of the three serological markers of dengue fever (NSIAg, IgG and IgM). During the same year of 2018, 0.1% (2/2003) of patients were positive

let NSIAg+ IgM+ IgG+ NSIAg+ NSIAg+ NSIAg+ IgG+ NSIAg+ NSIAg+ NSIAg+ NSIAg+ NSIAg+ NSIAg+ NSIA		Year 2018 (Jan	Year 2018 (January-December)	(Year 2019 (Jan	Year 2019 (January-December)			Year 2020 (Jan	Year 2020 (January-December)	(
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tics N(%) n(%) n(%) n(%) n(%) n(%) n(%) n(%) n			NSIAg+	lgM+	lgG+		NSIAg+	lgM+	lgG+		NSIAg+	lgM+	lgG+
1132 (56.52) 21 (1.86) 10 (0.88) 238 (25.44) 1514 (55.68) 253 (16.71) 871 (43.48) 24 (2.76) 10 (1.15) 191 (21.93) 1205 (44.32) 248 (20.58) 2003 (100) 45 (2.25) 20 (1.00) 479 (23.91) 2719 (100) 501 (18.43) 246 (20.37) 10 (2.00) 10 (0.00) 16 (12.50) 272 (10.00) 27 (9.93) 128 (6.39) 0 (0.00) 0 (0.00) 16 (12.50) 272 (10.00) 27 (9.93) 189 (9.44) 1 (0.53) 0 (0.00) 39 (20.63) 363 (13.35) 81 (22.31) 10 (2.45) 7 (1.72) 103 (25.25) 465 (17.10) 104 (22.37) 10 (2.45) 7 (1.72) 103 (25.25) 465 (17.10) 104 (22.37) 10 (2.45) 20 (3.14) 9 (1.42) 152 (23.90) 922 (33.91) 181 (19.63) 133 (6.44) 2 (1.50) 0 (0.00) 37 (27.82) 138 (5.08) 27 (19.57) 160 (7.99) 5 (31.33) 1 (0.63) 60 (37.50) 170 (6.25) 21 (35.50) 20 (3.17) 20 (3.13) 10 (3.25) 2	Characteristics	(%) N	n (%)	(%) u	n (%)	(%) N	u (%)	(%) u	n (%)	(%) N	n (%)	n (%)	(%) u
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128 (6.39) 0 (0.00) 0 (0.00) 16 (12.50) 272 (10.00) 27 (9.93) 189 (9.44) 1 (0.53) 0 (0.00) 39 (20.63) 363 (13.35) 81 (22.31) 408 (20.37) 10 (2.45) 7 (1.72) 103 (25.25) 465 (17.10) 104 (22.37) 636 (13.75) 20 (3.14) 9 (1.42) 152 (23.90) 922 (3.91) 181 (19.63) 133 (6.44) 2 (1.50) 0 (0.00) 37 (27.82) 138 (5.08) 27 (19.57) 100 (7.99) 27 (1.50) 0 (0.00) 37 (27.82) 138 (5.08) 27 (19.57) 100 (7.99) 27 (19.57) 20 (3.13) 1 (0.63) 60 (37.50) 27 (10.00) 27 (3.91) 27 (19.57) 20 (3.13) 20 (3.13) 20 (3.10) 47 (2.20) 27 (1.50)	Total	2003 (100)	45 (2.25)	20 (1.00)	479 (23.91)	2719 (100)	501 (18.43)	185 (6.80)	539 (19.82)	1569 (100)	38 (2.42)	25 (1.59)	535 (34.10)
128 (6.39) 0 (0.00) 0 (0.00) 16 (12.50) 272 (10.00) 27 (9.93) 17 (6.25) 3 189 (9.44) 1 (0.53) 0 (0.00) 39 (20.63) 363 (13.35) 81 (22.31) 19 (5.23) 408 (20.37) 10 (2.45) 7 (1.72) 103 (25.25) 465 (17.10) 104 (22.37) 36 (7.74) 103 (25.25) 20 (31.4) 9 (1.42) 152 (23.90) 922 (33.91) 181 (19.63) 70 (7.59) 13 (0.86) 72 (20.63) 389 (14.31) 60 (15.42) 27 (6.94) 9 133 (6.44) 2 (1.50) 0 (0.00) 37 (27.82 138 (5.08) 27 (19.57) 5 (3.62) 106 (7.99) 5 (3.13) 1 (0.63) 60 (37.50) 170 (6.25) 21 (35) 11 (6.47) 45 (5.25) 20 (1.00) 47 (7.25) 30 (1.00) 47 (7.20) 30 (10.00) 47 (7.20) 47 (1.20)	Mean age±SD	28.62 ± 16.96	33.32±17.19	Minimum-N	1aximum = (0-91)	24.85 ± 16.41	23.99±13.76	Minimum-M	aximum = (0-85)	28.27 ± 19.27	25.81 ± 23.45	Minimum-M	Minimum-Maximum = (0-84)
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15 408 (20.37) 10 (2.45) 7 (1.72) 103 (25.25) 465 (17.10) 104 (22.37) 36 (7.74) 15 (36.31.75) 20 (3.14) 9 (1.42) 152 (23.90) 922 (33.91) 181 (19.63) 70 (7.59) 17 (3.01) 3 (0.86) 72 (20.63) 389 (14.31) 60 (15.42) 27 (6.94) 9 17 (1.50) 0 (0.00) 37 (27.82 138 (5.08) 27 (19.57) 5 (3.62) 160 (7.99) 5 (3.13) 1 (0.63) 60 (37.50) 170 (6.25) 21 (35) 11 (6.47) 4 5 (3.75) 20 (1.00) 470 (73.91) 2710 (100) 5013 (100) 5013 (100) 470 (73.91) 2710 (100) 5013 (100) 5013 (100) 470 (73.91) 2710 (100) 5013 (10	5-14 years	189 (9.44)	1 (0.53)	0 (0.00)	39 (20.63)	363 (13.35)	81 (22.31)	19 (5.23)	48 (13.22)	177 (11.28)	5 (2.82)	0 (0:00)	42 (23.73)
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15 349 (17.42) 7 (2.01) 3 (0.86) 72 (20.63) 389 (14.31) 60 (15.42) 27 (6.94) 15 133 (6.64) 2 (1.50) 0 (0.00) 37 (27.82 138 (5.08) 27 (19.57) 5 (3.62) 160 (7.99) 5 (3.13) 1 (0.63) 60 (37.50) 170 (6.25) 21 (35) 11 (6.47) 2003 (100) 45 (7.25) 20 (1.00) 470 (73.91) 7710 (100) 50 (11.843) 187 (8.80)	21-30 years	636 (31.75)	20 (3.14)	9 (1.42)	152 (23.90)	922 (33.91)	181 (19.63)	70 (7.59)	174 (18.87)	396 (25.24)	5 (1.26)	8 (2.02)	142 (35.86)
rs 133 (6.64) 2 (1.50) 0 (0.00) 37 (27.82 138 (5.08) 27 (19.57) 5 (3.62) 160 (7.99) 5 (3.13) 1 (0.63) 60 (37.50) 170 (6.25) 21 (35) 11 (6.47) 2003 (100) 45 (7.25) 20 (1.00) 470 (73.91) 7710 (100) 50 (1.18.43) 187 (6.80)	31-40 years	349 (17.42)	7 (2.01)	3 (0.86)	72 (20.63)	389 (14.31)	60 (15.42)	27 (6.94)	91 (23.39)	302 (19.25)	5 (1.66)	3 (0.99)	118 (39.07)
160 (7.99) 5 (3.13) 1 (0.63) 60 (37.50) 170 (6.25) 21 (35) 11 (6.47) 3003 (100) 45 (7.25) 20 (100) 479 (73.91) 2719 (100) 501 (18.43) 18F (8.80)	41-50 years	133 (6.64)	2 (1.50)	0 (0.00)	37 (27.82	138 (5.08)	27 (19.57)	5 (3.62)	33 (23.91)	117 (7.46)	3 (2.56)	3 (2.56)	55 (47.01)
2003 (100) 45 (2.25) 20 (1.00) 479 (23.91) 2719 (100) 501 (18.43) 185 (6.80)	>50 years	160 (7.99)	5 (3.13)	1 (0.63)	60 (37.50)	170 (6.25)	21 (35)	11 (6.47)	46 (27.06)	164 (10.45)	4 (2.44)	2 (1.22)	76 (46.34)
(0.0) (0.1) (Total	2003 (100)	45 (2.25)	20 (1.00)	479 (23.91)	2719 (100)	501 (18.43)	185 (6.80)	539 (19.82)	1569 (100)	38 (2.42)	25 (1.59)	535 (34.10)

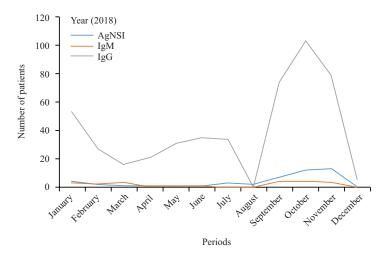


Fig. 1: Evolution of dengue infection during 2018

AgNS1: Antigen NS1, IgM: Antibody M and IgG: Antibody G

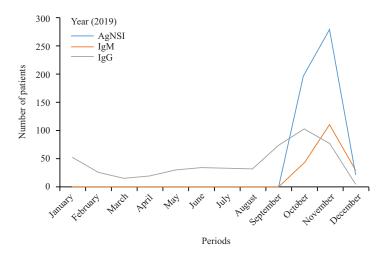


Fig. 2: Evolution of dengue virus during year 2019 AgNS1: Antigen NS1, IgM: Antibody M and IgG: Antibody G

Table 3: Multinomial logistic regression of the prevalence of NS1 antigen

	Year 2018	(January-December)		Year 2019	(January-December	·)	Year 2020	(January-Decembe	er)
	NSIAg stat	us							
Characteristics	OR	CI 95%	p-value	OR	CI 95%	p-value	OR	CI 95%	p-value
Gender									
Female	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Male	1.669	0.918-3.034	0.093	1.291	1.061-1.570	0.011	0.853	0.443-1.641	0.634
Age group									
>5 years	1	-	-	0.443	0.288-0.681	0.000	3.029	0.948-9.679	0.061
5-14 years	0.148	0.019-1.116	0.064	1.157	0.860-1.556	0.334	2.283	0.652-7.992	0.196
15-20 years	0.730	0.337-1.583	0.427	1.181	0.899-1.551	0.230	3.280	1.085-9.913	0.035
21-30 years	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
31-40 years	0.626	0.262-1.498	0.294	0.754	0.548-1.039	0.085	1.314	0.376-4.581	0.668
41-50 years	0.466	0.107-2.019	0.308	1.000	0.637-1.572	0.997	2.050	0.482-8.710	0.331
>50 years	1.008	0.015-0.044	0.987	0.584	0.180-0.262	0.030	1.941	0.514-7.327	0.327

NSIAg+: Antigen NSI positive

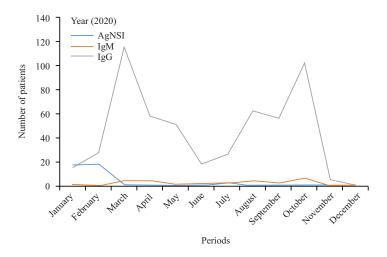


Fig. 3: Evolution of dengue virus in 2020 AgNS1: Antigen NS1, IgM: Antibody M and IgG: Antibody G

Table 4: Serological profile of dengue virus infection in the study population in 2018, 2019 and 2020

		2018 (N =	2003)		2019 (N =	2719)		2020 (N =	1569)	
Parameters	IgG	NSIAg-	NSIAg+	Total	NSIAg-	NSIAg+	Total	NSIAg-	NSIAg+	Total
lgM			-							
Negative										
	Negative									
	Number	1482	27	1509	1659	399	2058	1003	30	1033
	Percentage	73.99	1.35	75.34	61.02	14.67	75.69	63.93	1.91	65.84
	Positive									
	Number	463	11	474	425	51	476	504	7	511
	Percentage	23.12	0.55	23.66	15.63	1.88	17.51	32.12	0.45	32.57
	Total									
	Number	1945	38	1983	2084	450	2534	1507	37	1544
	Percentage	97.10	1.90	99.00	76.65	16.55	93.20	96.05	2.36	98.41
Positive										
	Negative									
	Number	10	5	15	98	24	122	0	1	1
	Percentage	0.50	0.25	0.75	3.60	0.88	4.49	0.00	0.06	0.06
	Positive									
	Number	3	2	5	36	27	63	24	0	24
	Percentage	0.15	0.10	0.25	1.32	0.99	2.32	1.53	0.00	1.53
	Total									
	Number	13	7	20	134	51	185	24	1	25
	Percentage	0.65	0.35	1.00	4.93	1.88	6.80	1.53	0.06	1.59

NSIAg+: Antigen NSI positive, IgM: Antibody IgM and IgG: Antibody IgG

for all 3 markers of dengue. As for the year 2019, Table 4 showed that 38.98% (1060/2719) of patients were positive for at least one of the three serological markers, while the prevalence of NS1Ag+/lgG+/lgM+ patients was 0.99% (27/2719). In 2020, there were no patients positive for all 3 markers at the same time.

Individuals positive for 2 dengue serologic markers (both markers NS1Ag+/lgM+,NS1Ag+/lgG+ and lgM+/lgG+.) accounted for 0.25, 0.55 and 0.15% in 2018, respectively. In 2019, the proportions were, respectively 0.88, 1.88 and

1.32%. For the NS1Ag+ and IgM+markers, only 0.06% of the patients were tested positive for both at the same time in 2020 against 0.45 and 1.53%, respectively for the NS1Ag+markers/IgG+ and IgM+/IgG+ Table 4.

Evolution of dengue virus infection from 2018 to 2020:

Approximately 63.35% (1273/2003) of dengue fever suspicions were recorded in the last 6 months (July-December) of 2018. Patients positive for NS1Ag antigen during this period accounted for 77, 77% (35/45) of all positive cases during the

year. Figure 1 shows a high prevalence of dengue virus infection between September and December with a peak during that period.

The suspicions of dengue were recorded each year, especially in 2019 during the last 4 months from September, to December. In fact, in 2019, 99.92% (2717/2719) of examinations for suspected dengue fever were recorded between these months. It should also be noted that 100% (501/501) of all NS1 antigen positive cases were seen during this period of 2019. We noted a high prevalence of dengue virus infection between September and December, with a peak during that period (Fig. 2).

In 2020, about 39.64% (622/1569) of examinations for suspected dengue fever were recorded during this year. It should also be noted that 5.26% (2/38) of all NS1 antigen positive cases were seen from January to March, in Fig. 3. A high prevalence of dengue virus infection was observed between September and December, with a peak during that period.

DISCUSSION

The global study population was a total of 6 291 patients with 2003 patients (31.84%) in 2018, 2719 (43.22%) in 2019 and 1569 (24.94%) in 2020. Besides, 55.68 and 44.32% were women and men, respectively, so the population of this study was predominantly women. This difference can be explained by the fact that women attend health centres much more than men.

The prevalence of dengue NS1Ag was 2.25% (45/2003), 18.43% (501/2719) and 2.42% (38/1569) in our study population, in 2018, 2019 and 2020 respectively. These high seroprevalences of dengue found in this study that confirms the high endemicity of dengue infection in Burkina Faso^{11,14,15}. Ouattara *et al.*¹¹ showed an overall prevalence of 17.3% of NS1Ag in the study population in Saint Camille Hospital of Ouagadougou.

However, in this present study, this seroprevalence of NS1Ag varies according to gender. Men were significantly more infected with the dengue virus (NS1Ag+) compared to women, 20.58% versus 16.71% in 2019 while no differences were found in 2018 and 2020. The prevalence of dengue NS1Ag was 22.5 and 13.3% among patients attending Saint Camille Hospital of Ouagadougou in Burkina Faso, in 2016 and 2017, respectively. Men were significantly more infected compared to women in 2016, while no difference in infection according to gender was observed in 2017¹¹. These findings are following other studies from India. Indeed, Garg *et al.*¹⁶ and

Patankar *et al.*¹⁷ reported a higher prevalence of dengue infection among males than females, respectively at Kanpur in North India and Delhi^{16,17}. The high prevalence amongst males is probably due to more outdoor activities by males in comparison to females, which results in more exposure to day-biting mosquitoes. The high prevalence of AgNS1 in our study population confirmed the high endemicity of dengue infection, active transmission of disease and proved that dengue fever was also a public health concern in Burkina Faso in addition to malaria.

In addition, children under 15 and individuals aged from 15-40 years were most concerned by dengue infection. Children under 15 accounted for 15.83, 23.35 and 23.33% of the study population in 2018, 2019 and 2020, respectively. This age group is the most affected by severe cases and dengue mortality according to several authors 18,19. In 2018, the risk of dengue infection among people aged 21-30 (31.75%) was 2-fold higher compared to children under 5 years of age (15.83%). In 2019, this is 1.5-fold (33.91%) versus 23.35% for children under 5 years. But in 2020, the risk of infection among children under five (23.33%) is almost the same compared to people aged 21-30 (25.24%). In sum, age groups 15-40 years remained more infected with dengue fever than children under 5 years of age. Current results are similar to those reported by Ridde et al.15, in Ouagadougou16. Adults are much more at risk of infection with the dengue virus than children under 5 years of age^{20,21}. Besides age and gender, do not observe an important decrease in this seroprevalence from 2018 to 2020 instead the awareness of the disease among the populations and the prevention strategies implemented by the health authorities since the 2013 dengue outbreak.

The diagnosis of acute infection of dengue virus in this study was based on the presence of AgNS1 and/or dengue specific IgM. Past infection was defined on a basis of a positive result of IgG alone²².

In 2018 and 2019, 26.01% (521/2003) and 38.98% (1060/2719) of patients were tested positive for at least one of the 3 serological markers of dengue fever (NSIAg, IgG and IgM), respectively. These results were respectively similar to those found by Ouattara *et al.*¹¹ who found 28.0% (573/2045) in 2017 and 40.1% (613/1527) in 2016. The dengue outbreak in 2016 was deathful in Burkina Faso. From 2016-2020, dengue prevalence in each year is still high and means the endemicity of dengue in our country.

In this present study, the prevalence of NS1Ag+/lgG+/lgM+ patients were 0.1% (2/2003) in 2018 and 0.99% (27/2719) in 2019, respectively. While a high prevalence of NS1Ag+/lgG+/lgM+ patients was found 1.6% (33/2045)¹¹. The

presence of NS1Ag+/IgG+/IgM+ means a recent infection over a probable old infection so the dengue virus is active in Burkina Faso. A prevalence of 22.7% probable past flavivirus infection has been reported in children aged 6 months to 12 years in Ouagadougou²⁰. These observations suggest an active circulation of the dengue virus in Ouagadougou and Burkina Faso. In 2020, there were no patients positive for all three markers at the same time.

In addition, in this study, individuals positive for two dengue serologic markers (both markers NS1Ag+/lgM+, NS1Ag+/lgG+ and lgM+/lgG+.) accounted for 0.25% (5/2003), 0.55% (11/2003) and 0.15% (3/2003) in 2018, respectively. In 2019, the proportions were, respectively 0.88% (24/2719), 1.88% (51/2719) and 1.32% (36/2719). In 2020, the proportions were, respectively 0.06% (1/1569), 0.45% (7/1569) and 1.53% (24/1569), respectively. The presence of AgNS1 and IgM means an acute infection with the dengue virus, these cases of primary and secondary infections (Ns1Ag+/lgM+, Ns1Ag+/lgG+ and lgM+/lgG+) reflect the active transmission of the dengue virus in our populations with a risk of severe cases²². So, the presence of IgG in addition to AgNS1 allowed to distinguish the acute phase of secondary infections from past infection serological scars. The simultaneous detection of AgNS1 and IgG means secondary infections that reflected an active transmission of the dengue virus in our populations with a risk of severe cases. 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^{14,23,24}.

The acute dengue infection increases slightly and we observed a pic from September-December, in the two first years. Patients positive for NS1 antigen from July-December, (during the last 6 months of 2018) accounted for 77, 77% (35/45 of all positive cases throughout the year compared to 100% (501/501) cases registered between September and December, of 2019. The peak of infection during the two first years was between October and November. These findings similar to previous studies that reported dengue outbreaks between September and December, in Burkina Faso and suggest a superposition of dengue transmission season with Plasmodium falciparum infection in Burkina Faso²⁴. Indeed, the dengue outbreak occurred at the end of the rainy season as for *Plasmodium falciparum* infection in the population of Burkina Faso. Dengue is an important emerging disease in tropical and sub-tropical regions where malaria is still endemic. Since the last decade, dengue has been occurring regularly with periodic surges in several

cases²⁵. In Burkina Faso, several outbreaks of dengue infection have been reported and malaria transmission is stable and seasonal. The high peak of malaria transmission is observed during the rainy season between May and November (in Banfora and Niangologo), June and October, in Ouagadougou^{26,27}. Dengue occurs mostly in parallel with malaria with high morbidity. In fact, because of its morbidity and mortality, the disease is a major public health problem²⁸, especially in developing countries.

The comparative analysis of these 3 Figures shows that the year 2019 saw a dengue epidemic from September, to December, 2019 characterized by recent infections with a positive peak of AgNS1 accompanied by a peak of IgM. The period from August to December, of each year shows the presence of at least one of the three markers of dengue (either AgNS1 or IgM or IgG). The pic of infection is usually observed during the last months of the year. The 2016 outbreak in Burkina Faso peaked on November²⁹.

Furthermore, the fact that we have some cases where we only have AgNS1 positive is because we are at the very beginning of the infection, >4 days. From the 4th day, the IgM appear. And on day 7 it is mainly the IgM, then from the 10th day, the IgG appears. AgNS1 positive is the onset of dengue infection. AgNS1+ and IgM+ means a recent infection. AgNS1+ and IgM+ and IgG+ means that is a recent infection over a probable old infection and only marker IgG positive (AgNS1 and IgG negative and IgG positive) indicate an old infection. Positivity to IgG antibodies only indicates a past dengue infection²³. A prevalence of 22.7% probable past flavivirus infection has been reported in children aged 6 months to 12 years in Ouagadougou²⁰. Even if we did not observe a very high prevalence in 2020, it should also be noted that 5.26% (2/38) of all NS1 antigen positive cases should take into account in the dengue global fight in Burkina Faso. All these observations in this study suggest an active circulation of the dengue virus in Ouagadougou.

CONCLUSION

Study data provide evidence for high seroprevalence of acute dengue virus infection with an outbreak during October and November, after the 2016 outbreak. The recurrent outbreaks of dengue infection in Burkina Faso need comprehensive surveillance and a diagnostic system to clarify the burden and pinpoint the risk factors. This study also suggests a superposition between dengue virus and malaria parasite transmissions with peaks at the end of the rainy season. So, it is important to well diagnosis the virus presence for best treatment, dengue and malaria co-infection

requires special attention because delayed diagnosis and inappropriate treatment may result in fatal complications. Strengthening surveillance of dengue in Burkina Faso is needed for a considerable reduction in the morbidity and mortality due to dengue in Burkina Faso. Indeed, the determination of the prevalence of different serotypes, availability and accessibility of diagnostic tests and adequate management of patients constitute important actions to undertake.

SIGNIFICANCE STATEMENT

This study on three successive years has shown that dengue outbreaks every year in our country. The active circulation of this dengue virus with a seasonal pic between September and December, can be beneficial for national dengue fight strategy development. Strategies based on vector control before each outbreak could be important to prevent life-threatening. This study will inspire the researchers to uncover the critical areas of dengue research that many researchers were not able to explore. Thus, some more efforts are needed to control or eliminate dengue infection in the dengue-endemic country like Burkina Faso.

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