

# Seroepidemiological Study of Dengue Virus Infection Suspected Cases in Burkina Faso

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## Abstract

Dengue fever is a mosquito-borne disease caused by four related but antigenically distinct dengue viruses. In the last half-century, the prevalence of dengue fever has increased dramatically (up to 30%) worldwide, especially in Sub-Saharan Africa. In Burkina Faso, the last dengue epidemic occurred in 2016, and the epidemiological situation is still poorly documented at the national level. Therefore, the present study aimed to conduct a sentinel seroepidemiology of suspected dengue virus infections from 2017 to 2020 at Charles de Gaulle University Pediatric Hospital Center of Ouagadougou. This investigation was designed to be a descriptive and analytical study. Patients with suspected cases of dengue fever were recruited from January 2017 to December 2020 during general medicine consultation and referred to Charles de Gaulle University Pediatric Hospital Center of Ouagadougou for the serological diagnosis of dengue. Venous blood was collected in dry or EDTA tubes and tested for DENV NS1 antigen, anti-dengue IgM, and anti-dengue IgG using SD Bioline Dengue Duo Rapid Detection Kit (Standard Diagnostic Inc., Korea). A total of 3400 blood samples from clinically suspected dengue cases were analyzed, of which 1784 (52.5%) were males, and 1616 (47.5%) were females. Among the 3400 patients included in the study, 661 (19.4%) were tested at least positive for NS1 antigen, anti-dengue IgM or anti-IgG. Among them, individuals positive for IgG suggesting past dengue virus infection were found in more than a third of 262 (7.7%) of the cases. Approximately, 80.0% (2705/3400) dengue suspected cases and 85.5% (341/399) early or primary dengue infections were recorded in the last four months of the study (September to December 2020), with a peak in mid-October and mid-November. There was no statistically significant difference in seroprevalence between males and fe-

males ( $p = 0.7$ ), but an increasing seropositivity trend with age, from 11.6% for the patient under 5 years group to 39.7% for 30 years and over age group were noted. This study puts in evidence a considerable level of transmission of dengue viruses in Burkina Faso and provides baseline seroprevalence data. The recurrent outbreaks of dengue infection in multiple geographical areas need comprehensive surveillance and a diagnostic system to identify the actual burden and pinpoint the risk factors. A larger study is, therefore, needed to determine the actual prevalence of dengue in Burkina Faso and map the serotypes.

## Keywords

Dengue, Seroepidemiology, Ouagadougou, Burkina Faso

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## 1. Introduction

Dengue fever is a mosquito-borne disease caused by four related but antigenically Distinct Dengue Viruses (DENVs, Serotypes 1 - 4) [1]. The viruses are transmitted through the bite of infected *Aedes aegypti* and *Aedes albopictus* female mosquitoes. Recovery from one episode of infection provides lifelong immunity against that particular serotype. However, the cross-immunity to the other serotypes is temporary and partial. Currently, there is no specific treatment for dengue virus infections [2] [3]. The clinical manifestations of dengue virus infections range from asymptomatic and mild flu-like symptoms to severe life-threatening complications such as Dengue Shock Syndrome (DSS) and Dengue Hemorrhagic Fever (DHF) [4]. The mosquito vectors of the dengue virus are widely spread, and dengue cases have been reported in 34 African countries [5] [6]. In western Africa, DENV-1, 2, and 3 were isolated for the first time in the 1960s from samples collected from humans in Nigeria [7]. Subsequent dengue outbreaks have been reported in different countries, for example, in Burkina Faso (1982, DENV-2) [8] and Senegal (1999, DENV-2) [9]. In the last half-century, the prevalence of dengue fever has increased dramatically (up to 30%) worldwide [5] [10], especially in Sub-Saharan Africa [11] [12] [13]. In Sub-Saharan Africa, dengue fever represents an added but underestimated burden to a landscape dominated by malaria [14] [15]. In this context, febrile illnesses, including dengue, are likely misdiagnosed and treated as malaria. The confusion between dengue fever and malaria negatively impacts the evaluation of dengue fever epidemiology [16]. Many dengue fever cases were reported in Burkina Faso since 1980s and 2000s, but the country is facing more serious outbreaks in the last decade [17] [18] [19].

The World Health Organization (WHO) reported 1061 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 [20]. The majority of the cases (86.23%) were recorded in Ouagadougou [21]. Because of its mor-

bidity and mortality, the disease has become an alarming public health problem, especially in developing countries like Burkina Faso [22] [23]. Unfortunately, the epidemiological situation of dengue fever is still poorly documented in Burkina Faso. Therefore, a sentinel seroepidemiological analysis of dengue infections was conducted from 2017 to 2020 at Charles de Gaulle University Pediatric Hospital Center of Ouagadougou to determine the baseline prevalence of dengue infection in patients clinically suspected.

## 2. Materials and Methods

### 2.1. Study Type

This study is a sentinel surveillance of the seroprevalence and evolution of dengue virus infections in Burkina Faso. The study is designed as cross-sectional and descriptive epidemiology.

### 2.2. Study Population and Ethics Clearance

The study included patients suspected to have dengue fever and referred to the laboratory of Charles de Gaulle University Pediatric Hospital Center between January 2017 and December 2020. The ethics committee of the hospital gave its approval for the data exploitation.

### 2.3. Biological Samples

Venous blood samples were collected in dry or EDTA tubes and immediately centrifuged at 4000 rpm/min for 5 minutes. The sera or plasmas were used to perform the test according to the manufacturer instructions as soon as possible for punctual results' delivery.

### 2.4. Dengue NS1 Ag and IgG/IgM Test

SD Bioline Dengue Duo Rapid Detection Kits (Standard Diagnostic Inc., Korea) were used to detect the presence of DENV NS1 antigen, anti-dengue IgM, and anti-dengue IgG in the patient sera. All tests in this study were carried out following the manufacturer's instructions. The test contains two *in vitro* immunochromatographic assays for analysis of dengue infection in human serum, plasma or whole blood (left side: Dengue NS1 Ag assay, right side: Dengue IgM/IgG assay). NS1 positive line indicates an early dengue infection, and IgM positive result reveals a primary dengue infection. IgG positive result denotes a secondary or past dengue infection. Simultaneous IgM and IgG positive suggests a late primary infection or early secondary dengue infection.

### 2.5. Statistical Analysis

The data were recorded in Microsoft Excel 2016 sheet and analyzed using Epi Info version 7 software developed by the Center for Disease Control (CDC) and Prevention Atlanta, Georgia, USA. The chi-squared test was used for comparisons, and each value was considered statistically significant for  $p \leq 0.05$ .

### 3. Results

#### 3.1. Demographic Characteristics

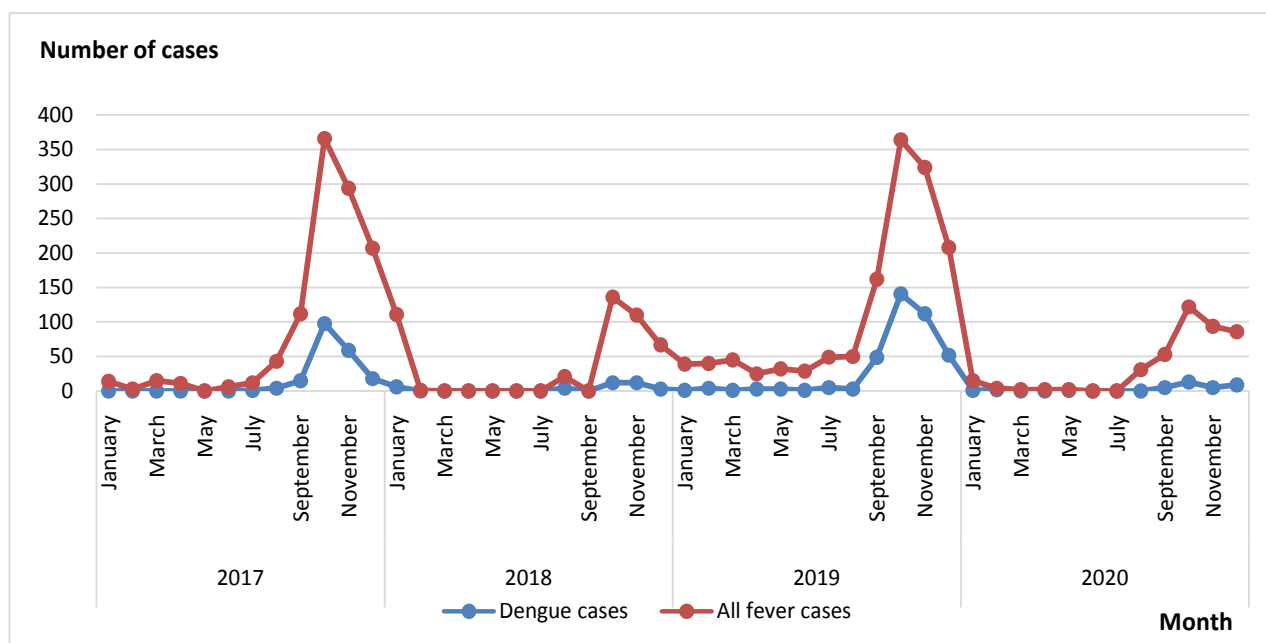
The demographic characteristics of suspected dengue cases from 2017 to 2020 at Charles de Gaulle University Pediatric Hospital Center of Ouagadougou are reported in **Table 1**. A total of 3400 blood samples from clinically suspected dengue cases were recorded from January 2017 to December 2020, of which 1784 (52.5%) were males and 1616 (47.5%) were females. The ages of the patients were between 0 and 90 years, with a median age of 4 years and a mean of 11 years. According to the age group, 1995 (58.7%) were children under 5 years, 738 (21.7%) were children between 5 - 14 years, 380 (11.2%) were young adults aged 15 to 30 years, and 287 (8.4%) were adults 30 years and over. The difference in the percentage of seropositivity between men (18.8%) and women (20%) was not significant ( $p = 0.7$ ). On the other hand, the age of the patients was associated with an increased risk of being seropositive for dengue virus. Seroprevalence increases significantly with age, ranging from 11.6% for patient under 5 year to 39.7% for those over 30 years old ( $p = 0.005$ ,  $p < 0.0001$ ).

#### 3.2. Monthly Distribution of Dengue Fever Infection from 2017 to 2020 in Ouagadougou

The monthly distribution of dengue fever infection from 2017 to 2020 in Ouagadougou (Burkina Faso) indicated that approximately 80.0% (2705/3400) of dengue suspected cases were recorded in the last four months (September to December 2020) with a peak in mid-October and mid-November (**Figure 1**). At the same period, 85.5% (341/399) of early or primary dengue infection were reported with respectively annual distribution, 2017 (89.9%), 2018 (58.7%), 2019 (77.4%), 2020 (86.4%). During the study period, it were noticed a significant fluctuation in the number of annual cases distributions. In 2017 (1089) and 2019 (1367) overall reported were at least twice as high than 2018 (533) and 2020 (411). Overall seroprevalence 2017 (18.2%) and 2019 (27.9%) were also at least twice as high than 2018 (7.9%) and 2020 (9.2%) (**Table 2**).

**Table 1.** Multivariate logistic regression of independent predictors for dengue fever positives cases in Burkina Faso from 2017 to 2020.

Gender	Number of tested samples	Number of positive samples	Percentage of positivity	95% CI	p-value
Male	1784	335	18.8	(17.01 - 20.69)	(ref)
Female	1616	324	20	(18.1 - 21.9)	( $p = 0.7$ )
Age groups (years)					
<5	1995	232	11.6	(10.2 - 13.1)	(ref)
5 - 14	738	167	22.6	(19.6 - 25.8)	( $p = 0.005$ )
15 - 30	380	148	38.9	(33.9 - 40.0)	( $p < 0.0001$ )
>30	287	114	39.7	(33.9 - 45.6)	( $p < 0.0001$ )



**Figure 1.** Monthly distribution of dengue fever infection from 2017 to 2020 in Burkina Faso.

**Table 2.** Comparison of annual dengue fever positivity rate from 2017 to 2020 in Ouagadougou.

Years	Total		Male		fEmale	
	Tested samples	Positivity rate (%)	Tested samples	Positivity rate (%)	Tested samples	Positivity rate (%)
2017	1089	18.2	587	19.6	502	16.5
2018	533	7.9	281	6.0	252	9.9
2019	1367	27.9	711	26.6	656	29.3
2020	411	9.2	205	6.8	206	11.6

### 3.3. Seroepidemiology of Dengue NS1Ag, IgM and IgG Antibodies from 2017 to 2020 in Ouagadougou

Seroprevalence markers of dengue fever are in **Table 3**. Out of the 3400 suspected samples collected, 661 were positive for any of NS1 antigen, IgM, or IgG antibodies by SD BIOLINE immunochromatographic assay, for an overall seroprevalence of 19.4%. Early dengue infection (NS1+), primary dengue infection (IgM+), secondary or past dengue infection (IgG+) prevalences were 4.2%, 2.1%, and 7.7%, respectively, during the study period. Primary dengue infection IgM antibodies incidence decreased with age group and ranged from 16.4% (<5 years) to 4.4% (>30 years). Also, late primary or early secondary dengue infection (IgM+/IgG+) decreases with age group and ranged from 27.1% (<5 years) to 11.4% (>30 years). In contrast, the incidence of IgG antibodies increases with age group and ranged from 34.5% (<5 years) to 52.6% (>30 years).

**Table 3.** Seroprevalence of dengue fever markers in Ouagadougou.

	NS1+	IgM+	IgG+	NS1+ IgM+	NS1+ IgG+	IgM+ IgG+	NS1+ IgM+ IgG+	Total
	Age groups (years)							
<5	30 (0.9)	38 (1.1)	80 (2.3)	8 (0.25)	3 (0.09)	63 (1.8)	10 (0.3)	232 (6.8)
5 - 14	43 (1.3)	20 (0.6)	60 (1.8)	4 (0.12)	4 (0.12)	30 (0.9)	6 (0.2)	167 (4.9)
15 - 30	41 (1.2)	09 (0.3)	62 (1.8)	3 (0.09)	5 (0.15)	21 (0.6)	7 (0.2)	148 (4.3)
>30	30 (0.9)	05 (0.1)	60 (1.8)	1 (0.03)	3 (0.09)	13 (0.4)	2 (0.06)	114 (3.4)
<b>Total</b>	144 (4.2)	72 (2.1)	262 (7.7)	16 (0.5)	15 (0.4)	127 (3.7)	25 (0.7)	661 (19.4)

(%): (total number/3400) × 100; NS1+: early dengue infection; IgM+: primary dengue infection; IgG+: secondary or past dengue infection; IgM+/IgG+: late primary or early secondary dengue infection.

#### 4. Discussion

The present study found that 19.4% of dengue suspected cases were positive for at least one of three serological markers of dengue fever (NS1Ag, IgM and IgG) from 2017 to 2020 in Ouagadougou. Our data agrees with the reports of Lim JK *et al.*, 2021 in Lambaréné in Gabon who found a prevalence of 17.4% [24]. Before the 2016 outbreak, dengue was a neglected disease in Burkina Faso. Although the seroprevalence of dengue in this study is high, Ouattara (2017) and Tarnagda (2016) reported more higher seroprevalence in Ouagadougou (Burkina Faso) respectively 28.0% and 68.2% between 2016 and 2017 [21] [25]. The lower seroprevalence found in the present study, compared with these previous report, could be explained by the awareness of the disease among the populations and the prevention strategies implemented by the health authorities since the last 2016 dengue outbreak. Nevertheless, seroprevalence remains important, probably due to some risk factors such as demographic growth. Ouagadougou's population grew annually by 6% from 2015 to 2020 [26]. It is well established that rapid and unplanned demographic and societal changes, such as population growth, urbanization, and modern transportation, could lead to increased transmission of DENV by increasing the vector population and changing the ecological balance of different species [26] [27]. The rapid urbanization increases the population density and the promiscuity, which favor risk of dengue infection as stagnant waters inside and out of the concessions and poor sanitation provide an environment for *Aedes aegypti* proliferation close to human hosts. The recent increase in dengue virus infections may also be directly linked to climatic factors such as increased rainfall, floods that promote vector breeding and disease transmission efficiencies [28]. Otherwise children under 5 years had fewer dengue virus infection with the dengue virus compared to other's group ( $p < 0.0001$ ). Ouattara study indicated similar that age groups of 15 to 50 years were significantly more infected ( $p < 0.05$ ), compared to children under 5 years of age. Other's studies in other countries showed that adults are reported to be much more at risk of infection with the dengue virus than children under 5 years of age [29] [30]. The increase of seroprevalence in these age groups could be attributed to the age effect in terms of time as an opportunity for exposure. Older people have had

more time to be exposed than young people. The infection cases culminated between September to December, with the peak between mid-October and mid-November. These findings agree with previous studies that reported dengue outbreaks between September and December in Burkina Faso and suggested a superposition of dengue transmission season with *Plasmodium falciparum* infections [18] [25]. Dengue outbreak occurred at the end of the rainy season as for *Plasmodium falciparum* infection in the population of Burkina Faso. The overall prevalence for each individual marker was 4.2% for NS1Ag and 2.1% for dengue-specific IgM *versus* 7.7% for IgG antibodies. According to the previous reviews, antibodies of class IgM are detectable from the 5th day of illness and for 3 - 6 months following initial infection. Antibodies of class IgG arise several days later than IgM and probably persist for life. Therefore, individuals found positive for IgG were classified as those with past dengue virus infection, while those found positive for IgM were classified as recent dengue virus infection [31] [32] [33]. Our data clearly show a late diagnosis of dengue fever. Other cases of primary and secondary infections (Ns1Ag+/IgM+, Ns1Ag+/IgG+ and IgM+/IgG+) reflect the endemic-epidemic character of DENV in Ouagadougou. These findings suggest an active circulation of the dengue virus in Ouagadougou and eventually in Burkina Faso in general severe cases [34].

## 5. Conclusion

Our data on dengue seroprevalence revealed that 19.4% of suspected dengue cases were positive for any of NS1Ag, IgM, or IgG antibodies. Children under 5 years were significantly more infected and dengue fever was late diagnosed. This study provides baseline seroprevalence data of dengue fever in Ouagadougou, Burkina Faso, after the 2016 outbreak. The recurrent outbreaks of dengue infection in multiple geographical areas in Burkina Faso need comprehensive surveillance and a diagnostic system to clarify the burden and pinpoint the risk factors. Further studies should include more districts and more participants to seize the dengue fever epidemiology in Burkina Faso.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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