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Seroprevalence of Dengue Virus in Febrile Patients in Parts of North East Nigeria

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Abstract **Original Research Article**

Dengue virus, an arthropod – borne arbovirus of the genus *Flavivirus*, is the causative agent of dengue fever. Presently the virus has four distinct serotypes, known as DENV-1, 2, 3 and 4, are transmitted by the *Aedes* mosquito. Over 50% of the global population are at risk of dengue transmission with the vast majority in Asia, then Africa and America. Recent studies have shown an increase in dengue virus prevalence in Nigeria. This study was carried out in four states in the North East region of Nigeria and involved five government tertiary health institutions. The four states included Bauchi, Gombe, Adamawa and Taraba states. Dengue virus seroprevalence of 34% was recorded among the 400 participants who took part in the study. Of the three different serological markers tested in this study, dengue virus seroprevalence of 7.8%, 32.3% and 7.5% was recorded for NS1, IgM and IgG, respectively. The study showed a high rate of acute/current infection among the study population with IgM of 32.3%. Results from this study showed dengue seroprevalence P value of < 0.001, which is statistically significant; inferring that dengue virus could be an emerging cause of fever in this region. Study participants from Taraba state showed the highest seroprevalence of 56.6% for IgM. Indicating that Taraba and neighbouring states are particularly vulnerable to acute and current infection with dengue. There is therefore a need for the government to address the situation before it becomes a national emergency.

Keywords: Non-Structural 1(NS1), Immunoglobulin M (IgM), Immunoglobulin G (IgG), Seroprevalence.

INTRODUCTION

Dengue Virus (DENV), the etiological agent of dengue, is an arthropod-borne arbovirus of the family *Flaviviridae,* genus *Flavivirus,* and consists of four serologically related but antigenically distinct serotypes designated as DENV-1, 2, 3, and 4 [1-4]. These serotypes progressed from a mutual ancestor, and are considered as the causative agent of approximately similar disease spectrum in humans due to DENV selecting different receptors based on cell and virus strains [5]. Developed viral particles have a spherical shape with 11 kb in length and 40-50nm in diameter, containing a single-stranded and positive-sense RNA molecule, which has a 5-methyl cap with a single open reading frame [6]. Dengue fever spreads from the bite of an infected female *Aedes* mosquito; including *Aedes aegypti* and *Aedes albopictus* [7], to people, and both vectors are present in Africa [8]. It is more common in tropical and subtropical climates and remains one of the most common mosquito-transmitted viral infections worldwide, with growing numbers of cases in recent years [7].

While the annual incidence is unclear owing to incomplete global reporting and misclassification of illness, approximately 3.2 million individuals were infected globally in 2015 [9]. Over 50% of the global population are at risk of dengue transmission, with the vast majority in Asia, then Africa and America [10, 11]. Annually, an estimated 400 million cases of dengue occur with majority of them in the urban and semi-urban areas of tropical and subtropical regions [12]. In 2023, the first global landmark of 6.5 million cases of dengue infection and greater than 6,800 deaths was recorded. South America reported the highest number of dengue cases (3.9 million) with Brazil reporting the highest number of cases (3.1 million), and Bangladesh reporting the highest number of deaths (1,705) [13].

Studies on the prevalence of dengue virus in Nigeria has shown the presence of the virus in different parts of the country. In a study in Dutse, Jigawa State, North West Nigeria, a seroprevalence of 33% dengue immunoglobulinaemia was reported among the study population [14]. Another study in South East Nigeria also revealed a dengue seroprevalence by NS1

antigenemia, IgM and IgG antibodies as 9.5%, 5.6% and 8% respectively [15].

Detection of NS1 in combination with IgM and IgG in patients' samples helps in differentiating between primary and secondary infections and assists in identifying acute/current dengue infections. The NS1 antigen is usually found after the onset of fever from day one to day seven, in primary or secondary dengue infection. At the same time, IgM is detected by day four to five in primary dengue infections and can continue for several months. IgG appears after IgM and could persist for life with a higher titre in secondary infections. The presence of dengue NS1/IgM in a patient with a positive IgG test could cause severe symptoms if the current infection is from a different strain from that the patient had previously suffered, leading to dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). Primary infections are usually generally mild, with some cases being asymptomatic and could resolve on their own. The use of IgM- and IgG-capture ELISAs for serologic diagnosis in the confirmation of dengue virus infection is considered reliable [16].

The burden of dengue virus in Nigeria has remained undetermined due to lack of systematic studies, limited data, insufficient diagnostic capabilities and misdiagnosis as malaria [17]. Urbanization, climate change, susceptible vector – host, migration, are some of the reasons for possible increased incidence of the disease. In Nigeria, measures to combat the disease have been grossly inadequate; if not absent. This study therefore aimed to determine the seroprevalence of DENV disease in the study area through the use of NS1 antigen (colloidal gold test kit), ELISA IgM and ELISA IgG tests, in the detection of both current and past infections with DENV among febrile patients in parts of North East Nigeria.

MATERIALS AND METHODS

Four of the six states which make up the North East geopolitical zone of Nigeria was randomly chosen for this study. These states include Taraba State, Adamawa State, Bauchi State and Gombe State. Five tertiary medical facilities were used for this study. They include Modibbo Adama University Teaching Hospital, Yola, Adamawa State; Federal Medical Centre, Jalingo, Taraba State; Taraba State Specialist Hospital, Jalingo, Taraba State; Abubakar Tafawa Balewa University Teaching Hospital, Bauchi, Bauchi state and Gombe State Specialist Hospital, Gombe, Gombe state. These are all government health care institutions that provide specialized services to their state populace and also serve as referral centres to other neighboring states. The study utilized a cross sectional study design. Ethical approvals for this study was obtained from the hospitals and state ministries of health (where applicable). Informed consent was obtained from each participant or their parent/ legal guardian (where applicable), followed by administration of a well-structured questionnaire. Four hundred patients were recruited for this study using a simple random sampling technique. Consenting patients within the ages of one (1) year to eighty (80) years with acute febrile symptoms (temperature of 37.5˚C and above) attending any of the enlisted health care facilities in parts of North East, Nigeria, were recruited into the study.

Samples were collected from participant between October 2023 and October 2024 at varying intervals from the various facilities. Five milliliters of whole blood sample were collected from each patient that met the acceptable criteria. Serum was extracted through centrifugation at 8000 rpm for 3 minutes, placed in cryovial tubes and transported in cold chain (2 – 8^{0}C) to reference laboratory where they were stored at - 20^{0}C until required number of samples where obtained for analysis. Serological analysis for current/previous dengue virus (DENV) infection using Non- Structural 1 antigen (NS I) rapid test, IgM ELISA and IgG ELISA were done using kits from Hunan Runmei Gene Technology Co., Ltd., China. Antibody assay for ELISA were read on BioTek ELx800 (USA) Microplate Reader, at 540 nm wavelength. Data from this study was analyzed using SPSS version 30.0 at statistical significance ($P < 0.05$; 95% confidence interval [CI])

SAMPLE SIZE DETERMINATION

Sample size was determined using Fisher's formula [18], and a prevalence rate of 37.4% % [19], with an attrition rate of 10%. A sample size of 395.73 was obtained, and then approximated to 400 samples. Therefore, 100 samples were collected from each of the four participating states.

RESULTS

Of the 400 patients tested for DENV, 264 (66%) were seronegative and 136 (34%) were seropositive for dengue virus.

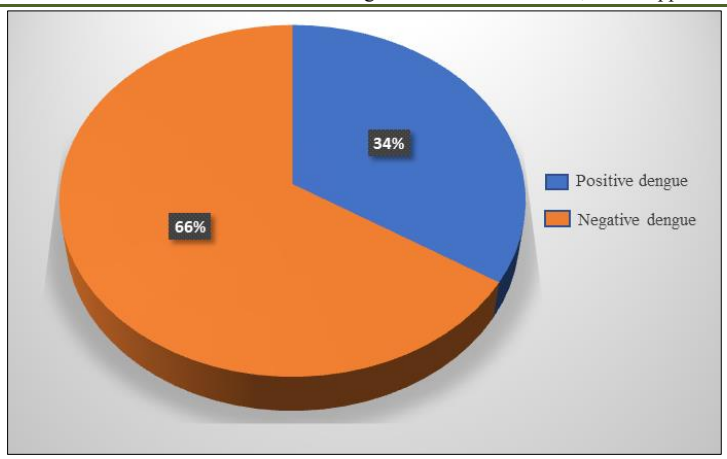

Figure 1: Prevalence of dengue virus in febrile patients in North East Nigeria

Dengue virus seroprevalence of 7.8%, 32.3% and 7.5% were observed for NS1, IgM and IgG respectively from the study population.

Table 1: Prevalence of Dengue virus NS1/ IgM/IgG in febrile patients in parts of North east Nigeria.

Dengue Test	Total Number of Patients Tested	Number Positive	Percentage Positive
NS1	400	31	7.8
IgM	400	129	32.3
IgG	400	30	7.5

$\chi^2 = 119.85$, df=3, $p < 0.001$

Thirty of the participants in this study were positive for more than one dengue serological marker (figure 2). Seven participants showed acute and current infection (primary infection), while 23 participants showed secondary infection.

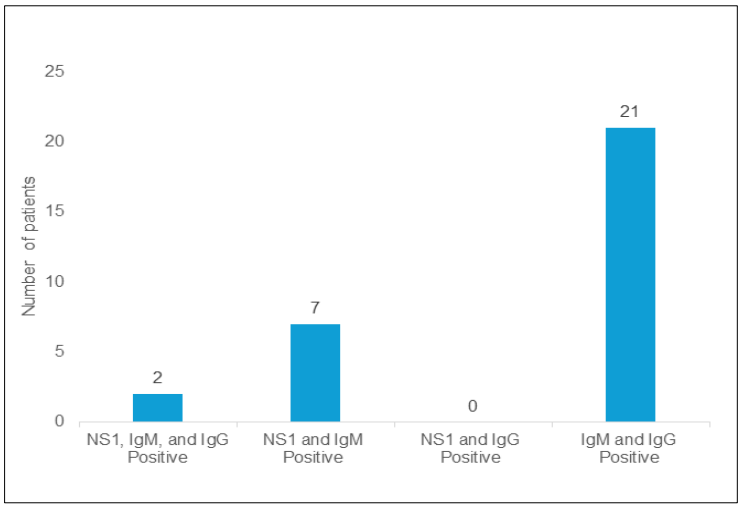

Figure 2: Prevelence of two or more dengue serological markers in febrile patients in parts of North east Nigeria

The states in the study showed significant association to dengue seroprevalence (P – value <0.001). Adamawa state had 9(29%), 9(7.0%) and 0(0.0%) for NS1, IgM and IgG dengue seropositivity respectively. Indicating a low rate of current/acute infection. Bauchi state had 0(0.0%), 35(27.1%) and 11(36.1%) for NS1, IgM and IgG dengue seroprevalence respectively. Though none of the participant from this state showed NS1 positivity, there was evidence of a high acute/recent dengue infection among the participants (27.1% IgM) with a high dengue immunity among the participants (36.1% IgG). Gombe state had 19(61.3%), 12(9.3%) and 0(0.0%) for NS1, IgM and IgG seropositivity to dengue respectively. Signifying acute and recent dengue infection. While, Taraba state had 3(9.7%), 73(56.6%) and 19(63.3%) for NS1, IgM and IgG seropositivity to dengue respectively. Indicating that Taraba state is particularly vulnerable to current and previous/past infections with dengue, as evidenced by its high number of IgM and IgG-seropositive cases.

Table 2: Prevalence of Dengue NS1, IgM and IgG in febrile patients in North East Nigeria in relation to states

State n = 400	Number of NS1 Positive (%)	Number of IgM Positive (%)	Number of IgG Positive (%)	p- value
Adamawa	9(29.0)	9(7.0)	0(0.0)	<0.001
Bauchi	0(0.0)	35(27.1)	11(36.1)	
Gombe	19(61.3)	12(9.3)	0(0.0)	
Taraba	3(9.7)	73(56.6)	19(63.3)	

p-value < 0.001; $\chi^2 = 29.48$; df =3

DISCUSSION

This study was carried out in four states in the North East region of Nigeria and in five government tertiary health institutions, which gave a wide range of area coverage in this study. Our finding in this study is in agreement with the contemporary systemic review on previous studies carried out in Nigeria from 2009 to 2020 by Emeribe *et al*., [20], that dengue virus is actively circulating in the country.

Dengue virus seroprevalence of 136 (34.0%) was observed from this study; which was similar to the finding of Mahmoud *et al.,* [14], in North west Nigeria, with a seroprevalence of dengue immunoglobulinaemia of 33% and slightly higher than the findings of Kingsley *et al*., [21], among febrile patients attending a tertiary hospital in Jos, Nigeria, where 27.9% of participants were found to be positive for anti-DENV antibodies.

Dengue seroprevalence of 31(7.8%), 129(32.3%) and 30(7.5%) for NS1, IgM and IgG respectively were observed from this study population, showing that there are both current and previous infections due to dengue in the area. Our finding was slightly lower than that of Hamisu *et al*., [19], in a similar study conducted among febrile patients in Maiduguri, Northeast Nigeria, with a dengue seroprevalence of 9.9% for NS1 and 37.4% for IgM. Suggesting that dengue virus is circulating in this region and could be a probable cause of fever among others in febrile patients in this region. Our finding is however, lower in IgG compared to that reported by Adeleke *et al.*, 2016 in Osogbo, Southwest Nigeria, with a prevalence of 77%.

Our study showed close similarity in NS1 and IgG, but vast difference in IgM from a study in South East Nigeria where dengue seroprevalence by NS1 antigenemia, IgM and IgG antibodies were 9.5%, 5.6% and 8% respectively [15]. With an IgM seroprevalence of 32.3%, there is a far higher rate of acute/current infection in this study which may be due to morbidity, insurgency, urbanization and global warming.

Seroprevalence of 7.8% for NS1 was obtained in this study, which was similar to the result from a systematic review of dengue in Nigeria from 2009 to 2020 by Emeribe *et al*., [20], where the detection rate of DENV infection by NS1 was 7.7% suggesting a steady rate of infectivity in the country.

Thirty of the participants in this study were positive for more than one dengue serological marker (figure 2). Seven participants showed acute and current infection (primary infection), while 23 participants showed both primary and secondary infection; indicating a current and previous infection. This usually could have a devastating effect on the patient if they were currently infected by a different serotype from which he/she was previously infected.

Dengue virus (DENV) may be an emerging cause of fever in this region as results from this study showed significant statistical association to seroprevalence of dengue (p – value <0.001) in the states studied.

Adamawa state had NS1 of 9(29%), IgM of 9(7.0%) and IgG of 0(0.0%) dengue seropositivity respectively. This showed a low rate of current/acute infection, perhaps due to the hot and arid weather observed in that state during the period of sample collection (March to July, 2024), which discouraged the breeding of mosquitoes and their breeding sites.

Bauchi state had NS1 of 0(0.0%), IgM of 35(27.1%) and IgG of 11(36.1%) dengue seroprevalence respectively. Though none of the participant from this

state showed NS1 positivity, there was still evidence of a high acute/recent dengue infection among the participants (27.1% IgM) with a high dengue immunity among the participants (36.1% IgG).

Gombe state had NS1 of 19(61.3%), IgM of 12(9.3%) and IgG of 0(0.0%) dengue seropositivity respectively. Signifying acute and recent dengue infection among the study participants.

Taraba state had NS1 of 3(9.7%), IgM of 73(56.6%) and IgG of 19(63.3%) dengue seropositivity respectively. Suggesting that Taraba state is particularly vulnerable to current and previous/past infections with dengue, as evidenced by its high number of IgM and IgG seropositive cases.

These findings confirm the presence of dengue virus in these states and therefore call for collaborative efforts from both government and private agencies to combat the disease in this region and in the country at large. This can be done through public enlightenment campaigns, advocacy programs, vector control and surveillance programs aimed at dengue virus eradication. The need for government to train more medical personnel and provide testing sites is crucial to averting possible epidemic.

CONCLUSION

We have reported acute and current dengue seropositivity among our study population at some of the tertiary health care facilities in parts of North East Nigeria. The study established the presence of DENV in four of the states that were covered, revealing its endemicity and as a possible cause of fever in this region. Up until now, dengue is still being neglected, and often misdiagnosed as malaria in Nigeria due to its overlapping symptoms and lack of screening facilities. The need for health care strategies for the diagnosis and management of dengue disease in Nigeria is long overdue. This study therefore calls for public health initiatives from both government and non- governmental organisations in the prevention and control of dengue vector, as well as an increased surveillance and research into dengue epidemiology and circulating serotypes to help give informed interventions in cases of outbreaks.

Conflict of Interest: The authors declare no conflict of interest in this publication.

Ethical Approval

Ethical approval was obtained from the Ethical committees of Abubakar Tafawa Balewa University Teaching Hospital (ATBUTH) Bauchi; Moddibo Adama University Teaching Hospital (MAUTHY), Yola; Gombe State Ministry of Health and Taraba State Ministry of Health, respectively.

Informed Consent: Informed consent was obtained from all individual participant included in the study.

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