

Vol No: 04, Issue: 01

Received Date: November 11, 2020
Published Date: December 21, 2020

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Seroprevalence of Dengue Fever among Febrile Patients Attending Kura General Hospital Kano, Nigeria

Dengue is the most rapidly spreading mosqui-to-borne viral disease with an estimated inci-dence of millions of cases per years. The study was aimed to determine the seroprevalence of dengue fever among febrile patients attending Kura General Hospital Kano, Northern Nigeria. Five milliliter (5 ml) of blood samples were collected from a total of 137 subjects (male, n= 63 and female, n=74) of all ages presenting febrile conditions suggestive of malaria or related diseases for testing of malaria parasites and antibody detection against dengue virus from May, 2018 to October, 2018. Examination of blood samples for detection of malaria parasite was conducted with thick blood film using Giemsa Staining technique while dengue virus antigen was detected using Dengue virus IgM/IgG antibody ELISA kits. The result showed that 13 subjects out of 103 were positive for dengue virus fever which accounted for 9.4% of the tested samples. Highest incidence of dengue virus fever was recorded among subjects of 21 – 40 years with total of 5 (3.6%) positive cases. On the basis of gender, 9 samples were men (6.5%) while females recorded only 4 positive samples (2.9%). From the result, 8 samples were infected for both malaria and dengue virus fever and this represents 5.8% of the total samples examined. No significant differences on the prevalence of dengue virus among age categories and sex of the subjects at $p < 0.05$. It is concluded that dengue virus fever is an emerging infection among the population in the study area.

KEYWORDS: Dengue fever; Febrile patients; Kano; Kura; Seroprevalence

INTRODUCTION

Over the last few decades, dengue fever has become the most important and widespread vector-borne human viral infection [1,2]. Dengue is otherwise called break-bone fever, it is the fastest spreading vector-borne viral infection transmitted between humans by the female *Aedes aegypti* mosquito [3]. Dengue fever is caused by one of four dengue virus serotype namely DENV-1, DENV-2, DENV-3 and DENV-4 belonging to Flaviviridae family and genus flavivirus. The virus has a non-segmented, positive-strand RNA genome of about 10,700 nucleotides with a 5' cap structure and a non-polyadenylated 3' end [4].

Infection with any of the dengue virus sub-types may result either in an asymptomatic infection or a febrile illness of varying severity ranging from mild illness to more severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [5]. Dengue as the most rapidly spreading mosquito-borne viral disease has an estimated inci-dence of 390 million cases per years [1,6]. It is

regarded as the most important arboviral disease worldwide [7] and it is estimated that every year between 2.5-3.6 billion people in over 125 endemic countries are at risk including 120 million travelers to these regions [8]. About 2 million cases evolve to dengue hemorrhagic fever and about 20,000 may culminate to death [9]. Factors responsible for the global transmission of dengue fever include unplanned urbanization, rapid population growth, agricultural development, increase international travel, ineffective mosquito control.

The first isolated case of dengue in Nigeria was in the 1960s [10], but dengue is not a reportable disease in this country with most cases often undiagnosed, misdiagnosed as malaria or referred to as fever of unknown cause. This is due to the lack of awareness of health staff and unavailability of diagnostic tools in health institutions [11]. Recent reports suggest that dengue viruses are a major cause of acute fevers in Nigeria [12]. To emphasize the growing importance of dengue in Nigeria, several studies were conducted to determine the seroprevalence of dengue fever among febrile patients. A recent seroprevalence surveys conducted in Maiduguri [13] and in Ilorin [14] showed that 10.1% and 30.8% of participants respectively, were sero-positive for dengue subtype-3 virus (DENV-3). Additionally, dengue IgM sero-prevalence among febrile Nigerian children in South-Western Nigeria has been reported to be 17.2% [15]. Adeleke et al. [16] reported that there is high density of *Aedes aegypti* mosquito in highly populated Nigerian city. In order to bring the attention to possible sources of febrile illness, other than malaria and typhoid fever in tropical countries such as Nigeria, the study was aimed to determine the seroprevalence of dengue fever among febrile patients attending Kura General Hospital Kano, Northern Nigeria.

MATERIALS AND METHODS

Study Area

Kura is one of the Local Government areas of Kano State. It is located in the southern part of the state along Kano-Zaria express with a distance of about 35 Kilometer from the state capital. Geographically, it is located at latitude 11°25'N. and Longitude 8°25' E. It covers an area of about 206 Km² of land. According to 2006 population census, it has a total population of 144,601 and the projected population of 199,002 as of 2016 [17]. Kura Local Government shares common boundaries with Garun-Mallam (West), Dawakin-kudu (East), Bunkure (South)

and Madobi Local Government (North). Farming and irrigation remain the major occupations in the area. However many educated indigenes in the area are employed in the formal sector while others engaged in various trading activities.

Ethical Clearance

Ethical approval for the study with reference number HMB/GEN/488/VOL.1/009 was obtained from Kano State Hospital Management Board based on the consent of ethical committee of Kura General Hospital, Kano.

Study Population

A completely randomized design was used in the study. A total of 137 subjects (male, n= 63 and female, n=74) of all ages presenting febrile conditions suggestive of malaria or related diseases such as typhoid fever at Kura Specialist Hospital, Kano from May, 2018 to October, 2018 were used in the study. All the sampled patients used for the study gave their consent to be involved in the research.

Questionnaire Administration

A total of one hundred and thirty seven (137) simple structured questionnaires were designed using open ended questions to provide information about the socio-demographic factors of participants and predisposing factors to both infections. Informed consents were obtained from all participants before inclusion.

Collection of Blood Samples

Five milliliter (5 ml) of blood samples were collected from the participant for testing for malaria parasites and antibody detection against dengue virus from a period of May, 2018 to October, 2018. Samples of blood were stored in test tubes and refrigerated at 4°C prior to laboratory analysis

Examination of Malaria Parasites

Examination of blood samples for detection of malaria parasite was conducted with thick blood film using Giemsa Staining technique [18] Giemsa stain was diluted 1 in 10 by adding 5 ml of stain to 45 ml buffered distilled water (pH 7.0) and mixed. The blood films were flooded with freshly diluted Giemsa stain for 30 minutes. The stain was then washed off and slide allowed to air dry in a draining rack after the underside was cleaned using cotton wool. The dried smear was examined using X100 objective

Determination of IgM Antibody against Dengue Virus

The serums of the samples were obtained by centrifugation of the blood samples at 2000 rpm for 10 minutes and were used for detection of DENV antibody. An IgM capture ELISA was used for the process using RicombiLISA Dengue virus IgM/IgG antibody ELISA kits (CTK Biotech Inc. USA), according to manufacturer's instructions

Statistical Analysis

Data were analyzed using basic descriptive statistics such as percentages. The data on the incidence of Malaria, dengue fever and their co-infection was analyzed using Chi-square (X²) test to assess relationships between selected categorical variables such as age, gender and residential area. The level of significance was set at $p < 0.05$.

RESULTS

Socio-demographic Distribution of the Subjects

A total 137 subjects participated in the study with 63 (46%) males and 74 (54%) females of all ages. Majority of the participants were 20 to 40 years age bracket. Participant from rural area accounted for 56.9% (78 subjects) while 43.1% (59 subjects) are from urban area. Most female participants are house wives (36.5%) while males participant are mostly students, civil servant and farmers.

Parameter	Male (n)	Female (n)	Total (n)
Age (Years)			
0 – 20	17 (12.4%)	20 (14.6%)	37 (27.1%)
21 – 40	26 (19.0%)	25 (18.2%)	51 (37.2%)
41 – 60	13 (9.5%)	18 (13.1%)	31 (22.6%)
61 – Above	07 (05.2%)	11 (08.0%)	18 (13.1%)
Settlement			
Urban	27 (19.7%)	32 (23.4%)	59 (43.1%)
Rural	36 (26.3%)	42 (30.6%)	78 (56.9%)
Occupation			
Student	18 (13.1%)	13 (9.5%)	31 (22.6%)
Civil servant	13 (9.5%)	02 (01.5%)	15 (11.0%)
Farming	15 (10.9%)	06 (04.4%)	21 (15.3%)
Trading	09 (06.6%)	03 (02.2%)	12 (08.8%)
House wives	00 (00.0%)	50 (36.5%)	50 (36.5%)
Others	08 (05.8%)	00 (00%)	08 (05.8%)

Table 1: Socio-demographic Factors of the Participants with Percentage Frequency.

Seroprevalence of Dengue Virus Fever

The seroprevalence of dengue virus fever among febrile patients attending Kura General Hospital Kano is presented in Table 2 below. The result showed that out of 137 participating subjects, 13 were positive for dengue virus fever which accounted for 9.4% of the tested samples. Based on the age category of the subjects, highest incidence of dengue virus fever was recorded among subjects of 21 – 40 years with total of 5 positive cases which accounted for 3.6%, this is followed by those of age category 41 – 60 years with 4 positive cases (2.9%), then subjects of 0 – 20 years with 3 positive cases (2.2%). Least cases were recorded among subjects above 60 years with only 1 positive case. On the basis of gender of the subjects, 9 out of the 13 positive samples were men (6.5%) while females recorded 4 positive samples (2.9%). According to the result, higher prevalence of dengue virus fever was found among rural dwellers with 9 positive cases (6.5%) when compared to urban dwellers with total of 4 positive cases (2.9%).

Parameter	No. of sample examined (n)	Dengue virus positive (n)	Prevalence (%)	P-value
Age (Years)				
0 – 20	37	3	2.2	.875794a
21 – 40	51	5	3.6	
41 – 60	31	4	2.9	
61 – Above	18	1	0.7	
Gender				
Male	63	9	6.5	.10888a
Female	74	4	2.9	
Settlement				
Urban	59	4	2.9	.39063a
Rural	78	9	6.5	

Table 2: Seroprevalence of Dengue Virus Fever among study subjects. Key: a = the result is not significant at $p < 0.05$;

Prevalence of Malaria Parasite

The prevalence of malaria among febrile patients attending Kura General Hospital Kano is presented in Table 3 below. The result showed that 84 out of 137 subjects were positive for malaria parasite and this accounted for 61.3% of the total samples tested. Highest incidence of malaria parasite was

found among subject aged between 21 – 40 years (24.8%), followed by 0 – 20 years (19.7%). Based on the gender of the subject, males have the highest incidence of malaria, which consist of 46 out of the 84 positive samples, and this accounted for 33.6% whereas females recorded 38 out of the 84 positive samples (27.7%). The results revealed that majority of the malaria infected individual are from rural area i.e. 51 positive cases which stood as 37.2%. On the other hand, 33 positive cases (24.1%) were recorded from subjects inhabiting urban areas.

Parameter	No. of sample examined (n)	Malaria parasite positive (n)	Prevalence (%)	P-value
Age (Years)				
0 – 20	37	27	19.7	.479291a
21 – 40	51	34	24.8	
41 – 60	31	17	12.4	
61 – Above	18	06	4.4	
Gender				
Male	63	46	33.6	.20524a
Female	74	38	27.7	
Settlement				
Urban	59	33	24.1	.580027a
Rural	78	51	37.2	

Table 3: Prevalence of Malaria among study subjects. Key: a = the result is not significant at $p < .05$.

Malaria and Dengue Virus Fever Co-infection

Table 4 represents the result of malaria and dengue virus fever co-infection among the study subjects. The result showed that only 8 samples were infected for both malaria and dengue virus fever and this represents 5.8% of the total samples examined (137 samples). Participants within age categories 0 – 20 and 21 – 40 years have 3 subjects each while 2 subjects were found among those of 41 – 60 years. Based on gender, 6 male and 2 female subjects were positive for both malaria and dengue virus fever. Majority of the subjects with co-infection are from rural area which comprises of 5 out of the 8 positive samples.

Parameter	No. of sample examined (n)	Malaria and dengue fever co-infection (n)	Prevalence (%)	P-value
Age (Years)				
0 – 20	37	3	2.2	.979934a
21 – 40	51	3	2.2	
41 – 60	31	2	1.4	
61 – Above	18	0	0.0	
Gender				
Male	63	6	4.4	.110209a
Female	74	2	1.4	
Settlement				
Urban	59	3	2.2	.757097a
Rural	78	5	3.6	

Table 4: Malaria and Dengue Virus Fever Co-infection among study subjects. Key: a = the result is not significant at $p < .05$.

DISCUSSION

The incidence of dengue virus fever has been increasing rapidly around the world with over 40% of the world population at risk from the infection. World Health Organization estimated that there may be 50 – 100 million dengue infection worldwide annually. In the present study, the seroprevalence of dengue virus fever among febrile patients was 9.4%. This finding was in conformity with the finding of Idris AN, et al. [13] who investigate Sero-prevalence of dengue type-3 Virus among patients with febrile illnesses attending a tertiary hospital in Maiduguri, Nigeria and found that 10.1% were positive. This result is higher than the results of Idoko MO, et al. [19] and Out AA, et al. [20] who found the seroprevalence percentage of Dengue virus fever in Kaduna (Northern Nigeria) and Cross River (Southern Nigeria) as 1.8 and 6.0% respectively. On the other hand, the result of this finding is lower than those of Adedayo F, et al. [14] and Oladipo EK, et al. [15] who found the seroprevalence percentage of Dengue virus fever in Ilori (North Central, Nigeria) and Ogbomosho, Oyo State (South western, Nigeria) as 30.8 and 17.2% respectively. Finding of this study was also contrary to that of Nagi AG, et al. [21] in Pakistan who reported 73% anti-dengue IgM positive patients in 2011. Finding from the present and previous study indicated that dengue virus has been presently and actively circulating in Nigeria with high prevalence of the infection in southern part of the country than Northern part. Differences in the prevalence

percentage of the infection between the present and previous studies may be attributed to differences in the density of the vector (*Aedes aegypti* mosquito) among the major cities under study. The prevalence of 9.4% from the present study suggested that dengue is a growing public health problem in Nigeria, the magnitude of which needs to be more clearly defined. In addition, rapid urbanization in Africa has resulted in increase in vector density as a result of human practices that promote mosquito breeding [22]. Based on the age category of the subjects, highest incidence of dengue virus fever was recorded among subjects of 21 – 40 years with total of 5 positive cases which accounted for 3.6% (result not significant at $p < 0.05$). This finding is in agreement with the finding of Adesina and Adeniji [23] who reported higher prevalence of dengue was observed in the age category 21 – 30 years. Higher prevalence among this age category is because the mosquito vector is diurnal animal and predominantly day biting and outdoor vector, as a result, people of age 21 – 40 are at higher risk of infection because they spend most of their time outdoor. The seropositivity of dengue virus fever in this study is greater in male (6.5%) when compared to female (2.9%). This finding was in conformity with those of Chukuma GO, et al. [24] and Faneye A, et al. [25] who both reported a higher prevalence rate of Dengue virus infection in male than female children. This is however not in agreement with the study conducted by Adesina and Adeniji [23] who found the prevalence of dengue fever infection among male and female approximately in ratio 1:1. Higher prevalence in male is due to the fact that they spent much of their time outdoor while most of female in the study area remain indoor hence at lower risk of the infection.

The prevalence percentage of malaria infection from the present study obtained using microscopy method is 61.3%. The prevalence rate is higher than that of Idoko MO, et al. [19] and Nas FS, et al. [26] with prevalence of 46% and 55% in Kaduna (Northern Nigeria) and Kano (Northern Nigeria) respectively. High prevalence of malaria in the present study may be attributed to the fact that the study was conducted during rainy season. Rainy season has been marked as a period of high transmission of malaria [27]. High rainfall and humidity increases mosquito longevity and give room to the collection of clear, still, sun exposed waters, all of which enhance malaria transmission, serving as good vector breeding sites [28]. Secondly, the area under study is surrounded by many rivers and water channels for irrigation purposes which may

also provide breeding ground for the vector. The prevalence of malaria in an area is governed by the density of mosquito population, presence of environment that supports mosquito breeding [29].

With the regard to malaria and dengue virus co-infection, out of 137 cases examined, only 8 samples were infected for both malaria and dengue virus fever and this represents 5.8% of the samples. This result is higher than those of Idoko MO, et al. [19] and Tchuandom [30] who found the prevalence of malaria dengue virus co-infection as 1.2% and 4.6% in Kaduna Nigeria and Cameroon respectively. This result suggested that dengue virus may cause febrile disease especially in tropical and sub-tropical region of Africa. The result will also be vital in Nigeria because most of the hospitals limit the investigation of febrile illness to malaria only. The diagnosis of dengue in Nigeria is further complicated by evidence of high co-infection rates of malaria and dengue. A recent report revealed a 10% active dengue co-infection rate among confirmed malaria cases in Ibadan, South-Western Nigeria [31].

CONCLUSION

The study determined seroprevalence of dengue virus fever among febrile patients attending Kura General Hospital Kano. It has been found that 9.4% of the febrile patients examined were seropositive for dengue virus fever while 5.8% of the subjects had malaria and dengue virus fever co-infection. The findings indicated a potential endemicity of dengue virus fever among population in the study area in addition to malaria and typhoid fever. It is recommended that there is a need for the improvement of facilities for diagnosis of the infection. More intensive routine surveillance for the detection and characterization of the virus should also be promoted to enhance understanding of the serotype diversity which will in turn aid the production of vaccine against the virus.

ACKNOWLEDGEMENT

The authors wish to acknowledge the Department of Health Kura Local Government area of Kano state for their support and cooperation. Thanks to the technical staff of Kura General Hospital for guidance and samples provision.

CONFLICT OF INTEREST

The authors declared that no conflict of interest exist.

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Citation: Nas FS, et al. (2020). Seroprevalence of Dengue Fever among Febrile Patients Attending Kura General Hospital Kano, Nigeria?. *Mathews J Immunol Allergy.* (4)1:10.

DOI: <https://doi.org/10.30654/MJIA.10010>