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Ahmadu Shehu Mohammed, Odekunle Bola Odegbemi, Chinedu Igwe, Nurudeen AA Hussain, Biobelu Abaye & Usman Oladipo Adekanye. Prevalence and Determinants of Dengue Virus Immunoglobulin among Febrile Patients Attending Naval Medical Centre Victoria Island, Lagos State. *Global Biosecurity*, 2020; 3(1).

RESEARCH ARTICLES

Prevalence and Determinants of Dengue Virus Immunoglobulin among Febrile Patients Attending Naval Medical Centre Victoria Island, Lagos State

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Abstract

Background: Dengue fever, (df) is a mosquito-borne disease caused by the dengue virus. Infection with dengue virus is a major cause of morbidity in the tropical and sub-tropical parts of the world. In about 60% of cases, it gives rise to undifferentiated fever which is clinically indistinguishable from other viral infections. Dengue fever is known to occur in Nigeria, but the magnitude of this disease remains unclear. This study was done to determine the prevalence and determinants of df immunoglobulins (Ig) among patients attending a military hospital in Lagos.

Methods: Systematic random sampling was used to recruit participants. Study participants were patients presenting with febrile illness at Naval Medical Centre, Victoria Island, Lagos. A **s**emi-structured, interviewer-administered questionnaire was used to collect data and 3 millilitres venous blood was drawn from each participant. Anti-dengue IgM and IgG was determined from whole blood using lateral flow chromatographic immunoassay in line with manufacturer's instructions. Thick blood film was used for malaria microscopy. Epi-info version 7.2 was employed for data analysis using descriptive statistics and bivariate analysis at 5% level of significance.

Results: Mean age of study participants was 30.1 ± 13.6 years and 182 (59.9%) were males. The prevalence of df IgM and IgG was 8.5% and 18.0% respectively. Malaria-dengue fever co-infection was 10.8%. Individuals with malaria were twice less likely to have df (OR: 0.46, 95%CI: 0.27 - 0.78). Military personnel and their relations were about 3 times less likely to have df (OR: 0.35, 95%CI: 0.18 - 0.66). Joint pain was significantly associated with df (OR: 1.78, 95%CI: 1.05 - 2.99).

*Conclusions***:** A significant proportion of study population had both df IgM and IgG. Screening for df should be part of routine tests amongst patients that presents with febrile illness particularly those with joint pain.

Keywords: Dengue fever, febrile, military, Immunoglobulin

Introduction

Dengue fever is a mosquito-borne disease caused by the dengue virus. The virus is transmitted by female mosquitoes of the Aedes species particularly *Aedes aegypti* and to a lesser extent *Aedes albopictus*. These mosquitoes are also responsible for transmitting Chikungunya, Yellow fever and Zika infections (Afolabi *et al.*, 2016). Dengue fever and the vector is widespread throughout the tropics and sub-tropical regions, with increased risk influenced by rainfall, temperature and unplanned rapid urbanization. Clinical findings in dengue virus infection range from asymptomatic infection to mild or moderately significant, severe disease and sometimes death (Gamil *et al.*, 2015).

Dengue virus is a single-stranded RNA virus of the family Flaviviridae and genus Flavivirus. There are four known serotypes of the virus, all of which can cause dengue infections. These are; DEN-1, DEN-2, DEN-3, and DEN-4. Recent findings suggest that a fifth serotype exists. Infection with any of the serotypes produce similar clinical syndrome, however, some differences may occur in clinical manifestation (Mustafa *et al.*, 2015). All serotypes are known to exist and thrive in the same geographical and ecological areas. Upon recovery from an infection with a particular serotype, an individual may be infected with

another, since infection with one serotype does not confer immunity against others. Some studies however reports that, there can be cross-protection against other serotypes which may last for about 3–4 months (Lee *et al*., 2015; Obaidat and Roess, 2018).

Infection with dengue virus is a major cause of morbidity in the tropical and sub-tropical parts of the world. Dengue virus affects millions of people each year, causing mild to severe clinical manifestations. In some cases, infection with dengue virus may be asymptomatic. However, in about 60% of cases, it gives rise to undifferentiated fever which is clinically indistinguishable from other viral infections. This is otherwise called dengue fever (CDC, 2016). Dengue fever may occur as a primary or secondary infection. In some individuals, the disease progresses to a severe and sometimes fatal form known as Dengue Hemorrhagic Fever (DHF). Dengue Hemorrhagic Fever most often results from secondary infections but may also occur in primary infections, especially in infants and in immunocompromised individuals (Adesina and Adeniji, 2016). In more complicated cases, DHF progresses to Dengue Shock Syndrome (DSS), a condition associated with high mortality following massive plasma leakage. Both DHF and DSS are closely related and are characterized by increase in vascular permeability, hemorrhagic manifestations, progressive leukopenia and low platelet count (Lee *et al*., 2015). Symptomatic management is the main treatment option available in cases of dengue infection. This is because there are no specific effective anti-viral agents against the virus. This must however be accompanied by good supportive care, close monitoring of vital signs and maintenance of fluid balance (Wiwanitkit, 2010; Tian *et al*., 2015).

Over the last three decades, dengue has been the most extensively spread mosquito-borne viral illness and about 3 billion (approximately 40%) of the world's population live in endemic areas (Seema & Jain 2005; Gamil *et al*., 2015; Mustafa *et al*., 2015). Epidemiological data indicate that about 390 million dengue infections occur worldwide each year, with about 96 million resulting in illness, mainly in tropical parts of the world (SAGE, 2016). According to World Health Organization, (WHO, 2012) dengue virus infection causes about 500,000 - 2 million cases of DHF and about 25,000 deaths mainly among children.

Dengue fever is known to occur in Nigeria, but the magnitude of this disease remains unclear. In Africa and Nigeria in particular, df is often mistaken for malaria. This may be because malaria is a prominent endemic disease in the region and both dengue and malaria present with similar symptoms (Mustapha *et al*., 2017). Many patients with fever in the region are sometimes designated as having malaria, typhoid fever or pyrexia of unknown origin, as the attending clinician so desire. Most of these patients remain without a diagnosis even when they test negative to malaria parasite test or when they do not respond to anti-malarial drugs. From the foregoing, df cases are undiagnosed and often misdiagnosed as malaria (Chukwuma *et al*., 2018). The resultant effect of this includes the indiscriminate use of anti-malaria agents and subsequently increasing anti-malaria resistance amongst the populace (Mustapha *et al*., 2017).

Often, df is missed in Nigeria even when patients present with febrile illness because low awareness about dengue virus among healthcare workers makes them ignore the disease. Dengue fever is also not a reportable disease in most African countries as there are no easy and cheap medical diagnostic capacities as it exists for malaria, the supposed most common cause of febrile illness in the country (Ayukekbong, 2014).

There is limited data on the prevalence of dengue fever among Nigerians and Lagos State residents in particular. There is also paucity of data on the risk factors and clinical features of dengue fever among Nigerians who live in Lagos, a water-locked state. The vector for dengue virus transmission is the female mosquito of *Aedes species*. The mosquito is extensively spread throughout the tropics and sub-tropical region (Afolabi *et al*., 2016). Lagos State, being water-locked area is a fantastic breeding ground for mosquitoes. Rapid urbanization in Lagos State has resulted in increase vector density as a result of human practices that promotes mosquito breeding (Gamil *et al*., 2015). There is also lack of proper vector control and good sanitation practices around living quarters and office premises in Lagos State (Fagbohun *et al*., 2021).

Recent studies suggest that "malaria" is one of the leading causes of death in Nigeria (Arthur, 2014; CDC, 2017). These reports, however, may not be completely true as most dengue fever cases in the country are misdiagnosed as malaria (Onyedibe *et al*., 2018). Lee *et al*. (2015) reported that there is presently a shift in the epidemiology of dengue with varying clinical presentation and severity among older population. Despite high levels of dengue infection, few studies have been conducted to explore the risk factors, presenting patterns for dengue virus infection and management among Nigerians. Accordingly, it is hoped that routine serological testing would allow early detection of cases, proper management of infected subjects and reduce misclassification. This study seeks to establish the prevalence of dengue fever among individuals attending Naval Medical Centre, Victoria Island, Lagos State.

Methods

Study Area

This study was conducted at the Naval Medical Centre, Victoria Island, (NMC, VI) Lagos State, Nigeria. The NMC, VI is a military health institution located at the Naval Dockyard Limited. The Centre provides quality health care services to naval personnel and their families at primary and secondary levels. Additionally, healthcare services are extended to members and families of sister Services (Nigerian

Army and Nigerian Airforce), the Police and other paramilitary organizations. It also provides medical care for Ministry of Defence civilian staff and the general public within its catchment area as part of Nigerian Navy corporate social responsibilities to the civil populace.

Lagos is a conurbation in the Nigerian State. It is often regarded as the commercial capital of Nigeria and the fastest growing city in Nigeria. It is one of the most populous urban agglomerations in the world (Odegbemi *et al.*, 2016). The state lies in the South-Western part of Nigeria on the Atlantic coast in the gulf of Guinea. Victoria Island, like other parts of Lagos metropolis, is made up of a complex mix of people from various parts of Nigeria. Victoria Island was originally surrounded entirely by water and lies within the boundaries of Eti-Osa Local Government Area (LGA). Victoria Island enjoys heavy annual rainfall and the entire axis is bordered by the Atlantic Ocean on the south (Oyinloye *et al.*, 2016), mouth of the Lagos lagoon on the west, the Five Cowrie Creek to the north, and swamps on the east.

Figure 1. Map of Nigeria showing Lagos State (Oyinloye *et al.*, 2016)

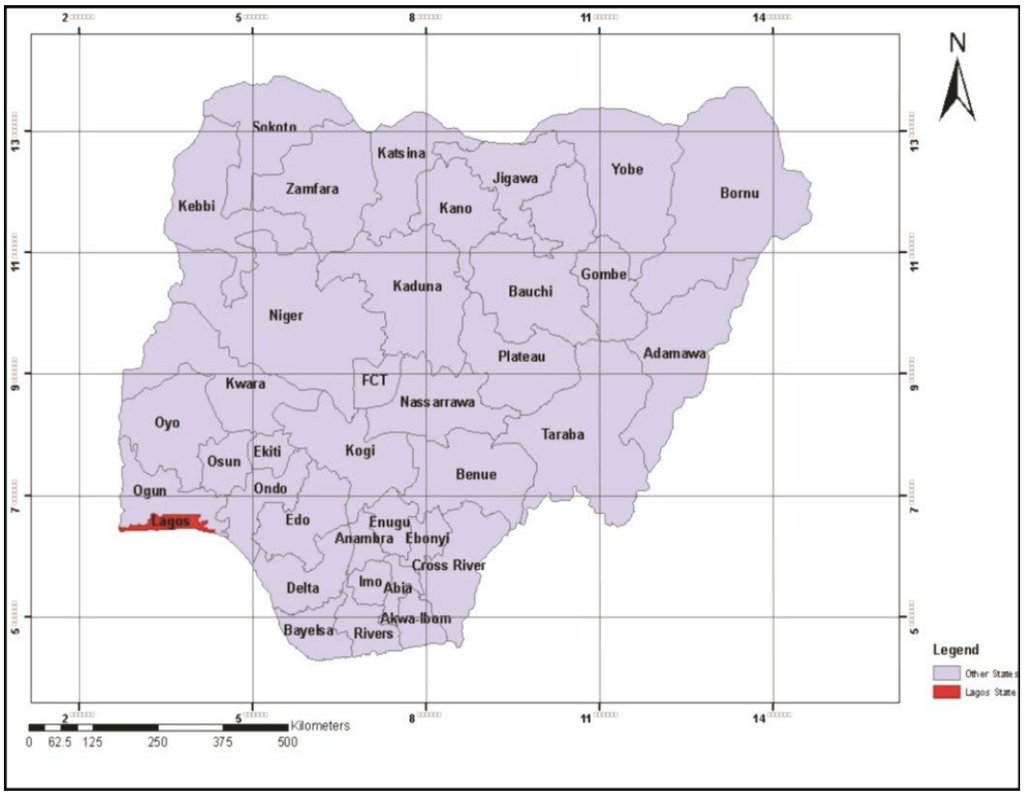

Figure 2. Map of Lagos State, showing Victoria Island in Eti-Osa Local Government Area (Oyinloye et al., 2016)

Study population

The study populations were patients presenting with febrile illness at the outpatients department of Naval Medical Centre, Victoria Island, Lagos State between November, 2018 and May, 2019.

Inclusion criterion

Male and female Nigerians presenting febrile illness and body temperature of ≥ 37.5°C who consented to

participate in the study were recruited irrespective of age group.

Exclusion criterion

Patients under management for any other viral infection were excluded from this study.

Sample Size

The number of participants required for the study was calculated using the formula below

$$n = \frac{Z^2pq}{d^2}$$

where:

n = sample size,
Z = standard normal deviate for a two tail test,
p = prevalence of exposure of factors of interest,
q = 1-p and
d = level of precision (5%).

Prevalence rate of 77.0% according to (Adeleke *et al.*, 2016) was used to calculate sample size for number of subjects required.

Z=1.96, p= 77%, q=1-77.0%, d=5%

$$n = \frac{(1.96)^2 \times 0.77 \times 0.23}{(0.05)^2}$$

n= 272.1 subjects

Non-response rate = n/1-f, (where f is non-response rate=10%)

Sample size (n) =272/1-0.1,

n=272/0.9,

n = 302 subjects

A total of 305 subjects were recruited for the study.

Sampling technique

Systematic random sampling technique was employed in this study to recruit study participants. The sampling interval was determined using the projected outpatient attendance for febrile illness and the calculated minimum sample size.

Sampling interval = Projected outpatient attendance for febrile illness

Calculated sample size = 1800/302 = 6

Participants that met the inclusion criteria were then recruited using the calculated sampling interval. Simple random sampling was used to pick the first subject and subsequently every sixth patient with febrile illness until the minimum sample size was achieved. Available resources enabled us to accommodate three more subjects to make 305 participants.

Data collection

Quantitative Component (Structured Questionnaire)

A structured interviewer administered questionnaire was used to obtain information from selected study participants who consent to participate in the study. The questionnaire consists of three sections, viz:

a. Socio-demographic characteristics (Sex, Age in years, Level of Education, Occupation and Marital Status)
b. Risk factors for acquiring dengue infection
c. Clinical features suggestive of dengue fever

Laboratory Component (Blood Sample Collection and Preparation)

Three mililitres (3ml) of whole blood samples were aseptically collected by venipuncture and dispensed into an Ethylene Diamine Tetra-acetic Acid specimen bottle. Blood sample collection was done by Medical Laboratory Scientists and Medical Laboratory Technicians at NMC, VI medical laboratory using sterile disposable syringes and needles from subjects.

Screening for malaria parasite

Thick blood films were made by placing a drop of whole blood on a pre-labeled, clean, grease-free slide. Applicator stick was used to spread the drop in a circular pattern until the size of a dime was achieved. The smears were air dried by laying the slide flat on the work bench. Dried smears were stained with Giemsa stain and microscopically examined by oil immersion objective to detect malaria parasites.

Determination of Dengue IgM and IgG

Detection and differentiation of anti-dengue IgM and IgG was determined from human whole blood using Micropoint lateral flow chromatographic immunoassay in line with manufacturer's instructions. The relative sensitivity and specificity of the kit were 95.8% and 96.1% respectively. The presence of IgM antibodies which may become detectable 3-7 days after infection and may remain in circulation for about 6 months is consistent with acute infection. Absence of same means lack of infection. Detection of anti-dengue IgG on the other hand is consistent with previous exposure to the virus. It is present in immunocompetent persons after about 3 weeks after infection.

Quality control

Clinicians at the outpatient department of NMC, VI were trained on how to identify and select probable subjects. Research assistants were trained on how to administer questionnaires on respondents. Questionnaire was pre-tested before the study in order to ascertain its validity at another Military Hospital in Ikoyi, Lagos State. Quality control was ensured while using latex kits for determining anti-dengue IgM and IgG. External positive and negative controls provided by the kit manufacturer were assayed along with each batch of blood samples analyzed. Data obtained was cleaned before analysis.

Data Management and Analysis
Dependent variable

The dependent variable in this study was the presence or absence of anti-dengue IgM and IgG and presence or absence of malaria parasite.

Independent variables

These includes age, gender, marital status, religion, level of education, socio-economic status, ethnicity, smoking status, neck pain, fatigue, fever, cough, headache and sensitivity to light.

Data analysis

Data obtained were entered and analyzed using Epi info software version 7.2. Data was summarized using mean and standard deviation for quantitative variables. Qualitative variables were summarized using frequencies and proportions. Bivariate analysis and logistic regression was used to test the association between dependent and independent variables.

Ethical Considerations

Ethical approval for this study was obtained from Ministry of Defence Health Research Ethics Committee (MODHREC/APP./14/26/10/20/8/NHEREC/15/05/2009). Administrative approval was also obtained from the management of Naval Medical Centre, VI before the commencement of the study. The following ethical principles were maintained during the study;

i. A written informed consent was attached to the questionnaire for each participant to fill in order to obtain individual consent to participate in the study.
ii. Confidentiality of data: the content was not disclosed to anybody except the co-investigators and data will only be used for research purposes.
iii. Beneficience: results of screening were given to the managing clinical team free of charge to enable them ensure appropriate management.
iv. Voluntariness: every target participant had the right not to participate in the study when approached or otherwise.

Results

A total of 305 subjects participated in this study which was conducted between November, 2018 and May, 2019. Blood sample was collected from all the participants while some sections of the questionnaire were not answered by all. The results of the study are presented in this section in line with the objectives of the study. The results are presented in frequencies, mean and standard deviation and statistical significance difference at $P < 0.05$ of the variables are also shown.

Characteristics of Study Participants

Table 1 shows that the age of all study participants ranged from 2 to 65 years. The mean age of all study participants was 30.1 ± 13.6 years. Male participants constitute majority 182 (59.9%) of the study participants. Most of our study participants 147 (48.2%) are single and 264 (86.6%) are from monogamous family set up. Different minority tribes, 121 (39.7%) accounted for the majority ethnic group. One hundred and sixty one respondents (52.8%) had tertiary education, 51 (16.7%) had secondary education and 46 (15.1%) had postgraduate education. Civil service was their major occupation 115 (37.7%) while unemployed constitutes 5 (1.6%) and only 2 (0.7%) were farmers.

Malaria Microscopy Screening Results among Subjects

Table 2 shows the results of malaria microscopy among subjects with febrile illness at NMC VI. The table shows the gender distribution of malaria parasite screening. A total of 176 persons (57.9%) tested positive for malaria parasite by microscopy and majority (58.5%) were males.

Dengue fever screening results among subjects with febrile illness

Table 3 shows findings of dengue fever screening among subjects with febrile illness at NMC, VI. In all, 76 (24.9%) of the subjects tested positive for df. Fifty (16.4%) persons of our study participants tested positive for dengue fever IgG, 6.9% were positive for IgM while about 1.6% had both IgG and IgM.

Association between the prevalence of Dengue fever Immunoglobulin and Malaria among Subjects

Comparison between the prevalence of dengue fever immunoglobulins and malaria among subjects with febrile illness is shown on Table 4. Thirty three participants tested positive for both df immunoglobulins and MP while 86 subjects neither tested positive for df immunoglobulins nor MP. Subjects with malaria were twice less likely to have df immunoglobulins (OR: 0.46, 95%CI: 0.27-0.78) and the association was statistically significant.

Factors associated with Dengue fever immunoglobulins among subjects in Lagos State, Nigeria, 2019

Table 5 shows association between probable risk factors and results of dengue fever screening. Individuals with direct military relationship were about three times less likely to have df (OR: 0.35, 95%CI: 0.18 - 0.66).

Clinical features associated with Dengue fever immunoglobulins among subjects with febrile illness in Lagos State, Nigeria, 2019

Table 6 shows some of the clinical features for df assessed among our respondents. Our study highlighted joint pain is significantly associated with df. Those with joint pain were about two times likely to have df (OR: 1.78, 95%CI: 1.05 - 2.99).

Table 1. Demographic Characteristics of Study Participants

Variables	Frequency (n = 305)	Percentage (%)
Age Group (years)		
≤10	34	11.1
11-20	25	8.2
21-30	93	30.5
31-40	92	30.1
41-50	42	13.8
>60	19	6.2
Mean ± SD	30.1 ± 13.6	
Gender		
Male	182	9.7
Female	122	40.3
Marital Status		
Single	147	48.2
Married	142	46.6
Co-habiting	5	1.6
Widowed	6	2.0
Divorced/separated	3	1.0
Missing	2	0.7
Type of family		
Monogamy	264	86.6
Polygamous	36	11.8
Missing	5	1.6
Ethnic Group		
Fulani	10	3.3
Hausa	28	9.2
Yoruba	61	20.0
Igbo	85	27.9
Others	121	39.7
Religion		
Christianity	229	75.1
Islam	72	23.6
Traditional	4	1.3
Missing	5	1.6
Educational Level		
Primary	20	6.6
Secondary	51	16.7
Tertiary	161	52.8
Postgraduate	46	15.1
None	20	6.6
Missing	7	2.3
Occupation		
Student	53	17.4
Civil servant	115	37.7
Farmer	2	0.7
Business/Trader	37	12.1
Unemployed	5	1.6
Others	87	28.5

Table 2. Results of Malaria Microscopy among subjects with febrile illness

Gender	Positive	Negative
Male	103 (56.6)	79 (43.4)
Female	73 (59.8)	49 (40.2)
Total	176 (57.9)	128 (42.1)

Table 3. Results of Dengue fever screening among subjects with febrile illness

Gender	IgG	IgM	Both	Neg
Male	29 (15.9)	14 (7.7)	3 (1.6)	136 (74.7)
Female	21 (17.2)	7 (5.7)	2 (1.6)	92 (75.4)
Total	50 (16.4)	21 (6.9)	5 (1.6)	228 (75.0)

Table 4. Comparison between the prevalence of Dengue fever Immunoglobulins and Malaria screening among Subjects

		Result of Dengue Screening		Odds Ratio	95% CI	Chi-square	P-value
		Positive	Negative				
Malaria	Positive	33	143	0.46	0.27 - 0.78	8.4341	0.0036
	Negative	43	86				
	Total	76	229				

Table 5. Risk factors for Dengue fever among respondents in Lagos State, Nigeria, 2019

Variables		Dengue fever		OR(95% CI)	p-value
		Positive	Negative		
Age	≤30	32	120	0.66 (0.39-1.11)	0.07
	>30	44	109		
Gender	Female	30	92	0.96 (0.56-1.63)	0.44
	Male	46	136		
Marital Status	Single	33	114	0.85 (0.49-1.46)	0.283
	Others	36	106		
Military link	Yes	15	104	0.35 (0.18 – 0.66)	0.0003*
	No	51	125		
Travel history	Yes	17	52	0.98 (0.52-1.82)	0.48
	No	59	177		
Live by refuse dump site	Yes	37	101	1.23 (0.73-2.08)	0.21
	No	38	128		
Reside by stationary H_2O	Yes	33	114	0.85 (0.49-1.64)	0.28
	No	36	106		
Mosquito bite last 2 months	Yes	72	221	1.30 (0.27 – 6.27)	0.39[a]
	No	2	8		

[a] = Fisher exact
* = Statistical significance

Table 6. Clinical features for Dengue fever among respondents in Lagos State, Nigeria, 2019

Variables		Dengue fever		OR(95%CI)	p-value
		Positive	Negative		
Fever	Yes	72	208	1.96 (0.55-6.88)	0.14[a]
	No	3	17		
Headache	Yes	65	187	1.32 (0.64-2.73)	0.22
	No	11	42		
Vomiting	Yes	5	15	1.00 (0.35-2.85)	0.48
	No	70	210		
Nausea	Yes	15	44	1.03 (0.54 – 2.0)	0.44
	No	60	183		
Joint pain	Yes	41	91	1.78 (1.05-2.99)	0.04*
	No	35	138		
Body ache	Yes	49	132	1.35 (0.78-2.33)	0.33
	No	26	95		
Abdominal pain	Yes	17	48	1.08 (0.58-2.03)	0.92
	No	59	181		
Temperature	<37.4°C	51	168	1.53 (0.86 – 2.69)	0.19
	≥37.5°C	25	54		

[a] = Fisher exact
* = Statistical significance

Discussion

We conducted this study to determine the prevalence of dengue fever among febrile patients attending NMC VI. Dengue fever immunoglobulins were present in varying proportions among subjects with febrile illnesses in this study. The observed cumulative prevalence of dengue fever (24.9%) among our subjects is similar to findings in Jordan where a prevalence of 24.6% was reported (Obaidat and Roess, 2018). Our findings confirmed the assumption that *Aedes* species exists in Lagos State and that df virus is in circulation among Nigerians. This finding affirms the thought that dengue fever prevalence is higher in densely populated accommodation areas of tropical countries (CDC, 2016; Otu *et al.*, 2019).

Our finding is however lower than IgG prevalence of 77% reported by (Adeleke *et al.*, 2016) in Osogbo, Southwestern Nigeria and IgM 77.1% reported by Chukwuma *et al.*, 2018 in Southeastern Nigeria. The discordance in the observations may be due to differences in environmental conditions, sample size as well as presence and rate of use malaria preventive intervention services. Additionally, study location and subject distribution appears to influence the incidence of Dengue fever (Gamil *et al.*, 2014; Afolabi *et al.*, 2016).

Over the years, there has been less attention on dengue fever occurrence among Nigerians. The observed prevalence of higher proportion of IgG among our subjects shows they have been exposed in the past and may have recovered. The presence of IgM in some of our subjects shows current infection and detection of both IgG and IgM indicates fresh infection in sensitized subjects. This shows the need for improved intervention measures towards vector control and entomology studies in Nigeria to ascertain circulating mosquito species.

The prevalence of dengue fever immunoglobulin was lower than the prevalence of malaria parasite among our subjects. This finding is at variance with findings from the work by Adeleke *et al.*, 2015, Mustapha *et al*, 2017 and Chukwuma *et al.*, 2018 in Southwestern, Northcentral and Southeastern Nigeria respectively where higher dengue fever prevalence was reported among their subjects. Variations in the observations may be due to differences in the distribution of df vector, varying environmental conditions, sample size as well as presence and rate of use malaria preventive intervention services. Our finding of lower prevalence of df corroborates findings from other studies (Ayolabi *et al.*, 2019, Otu *et al.*, 2019). Some of our subjects had both malaria parasite and df immunoglobulins. This finding is similar to df-malaria co-morbidities as reported by Adeleke *et al.*, 2016, Chukwuma *et al.*, 2018 and Akaninyene *et al.* 2019 in different parts of Nigeria. This confirms the assumption that there is df-malaria co-infection among febrile patients in Nigeria.

From our study, there was a statistically significant association between the prevalence of df immunoglobulins and malaria. Subjects with malaria were twice less likely to have df immunoglobulins. This suggests that the vector for malaria is more common in

the locality. However, the vector for both malaria and df may be found in the environment in Nigeria (Olufisayo and Johnson, 2016). Malaria remains a disease with significant morbidity and mortality in tropical countries of the world and the relative burden of df infection remains underestimated. It is therefore important to initiate df surveillance to increase the gains of malaria control interventions. This will also reduce patient misclassification as individuals with pyrexia of unknown origin.

Findings from our study indicate that being military personnel or living with military personnel is an important protective factor against df immunoglobulins. This finding has not been previously reported in the literature. This may not be far-fetched from the availability, as well as compliance and adherence to use malaria preventive measures among military personnel and their relatives. Our study however shows that gender, marital status, low socio-economic status and travel history are not enough predictors of df immunoglobulin. Therefore, other factors that were not yet explored may exist. The non-significant statistical differences in df seroprevalence in the factors assessed may suggest that everyone within the study area, irrespective of status, age and sex is at risk of infections.

Our study findings were similar to what (Ayukekbong, 2014b; Adeleke *et al.*, 2016) reported in df review and in a study with high df seroprevalence rate among subjects with febrile illness in Southwest, Nigeria respectively. Our findings were however at variance with report by (Obaidat and Roess, 2018) in a study in Jordan. Their findings showed that age, socio-economic status and travel history were significantly associated with df sero-positivity. The discordance observed may be due to differences in lifestyles, subject sampling, diagnostic methods of sample analysis and period of sample selection. Study location and subject distribution also appears to influence df seroprevalence (Gamil *et al.*, 2014).

Globally and particularly in tropical countries of the world, several factors have been described to predict df seroprevalence in humans globally. Living in endemic areas of the tropics is a major predisposing factor. Other predictors of df infection include history of exposure to Aedes mosquito and low socio-economic status (Afolabi *et al.*, 2016; Oladejo *et al.*, 2016). Although, 24.6% who of our subjects gave history of mosquito bite tested positive to df immunoglobulin, the species of mosquitoes in the environment and the ones they were exposed to could not be ascertained. There was no record that any of our subjects degenerated to DSS. This may be because all subjects got necessary treatment. The presence of df immunoglobulins among our subjects even among those without any history of foreign travels further affirms the presence of *Aedes spp*. in our study area (Gamil *et al.*, 2014; CDC, 2016; A. Otu *et al.*, 2019).

Dengue fever infection is a viral infection that presents diversely and clinical symptoms may range from mild febrile illness to severe plasma leakage with hemorrhagic manifestations. Common symptoms may include non–specific fever, with two or more of any of the following: headache, retro-orbital pain, arthralgia, muscle pain, rash with no localized signs or symptoms (Gamil *et al.*, 2014). Complications in infections may however due to different factors such as age, infecting viral serotype as well as viral load (Chee-fu yong, et al 2015). Some of these features were seen in our subjects for this study; however, only joint pain was found to be significantly associated with having serum df immunoglobulins among febrile patients. This finding was similar to report by Chee-fu yong, 2015 in a study in Singapore. However, our finding was contrary to what Chukwuma *et al.*, (2018) reported, that anemia is an important predictor of df among febrile subjects in Southeastern, Nigeria. Their findings may be because their study was conducted among children who require special care.

Study Limitation

This study is an institution-based study and the period of sample collection was not all year round. Hence, generalization of findings needs careful consideration. Dengue fever Immunoglobulin prevalence could be greater among the population than assessed as our study focused on subjects that presented with febrile illness. An all year study and a surveillance system with focus on population at risk is needed for the detection of actual prevalence.

Conclusion and Recommendations

A significant proportion of our subjects had df Immunoglobulins. Dengue fever-Malaria co-infection was confirmed amongst Nigerians in Lagos State. This is a threat to rational drug use and may be promoting anti-malaria resistance since df is not routinely detected among febrile Nigerians. Based on our findings, we recommended inclusion of df screening among patients presenting with febrile illness in Lagos State. Findings from this study confirmed the assumption that *Aedes* species exists in Lagos State and that df virus is in circulation. Future entomological study in Lagos State is also recommended to confirm this assumption. For better characterization of circulating virus, df strain classification study would be required to ascertain circulating species.

Public Health Actions

As part of our public health actions, we shared df screening results with members of clinical team at NMC, VI and we sensitized the hospital community on df screening.

Acknowledgement

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Conflict of Interest
The authors have no conflict of interest to declare.

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