DETECTION OF DENGUE VIRUS INFECTION AMONG FEBRILE PATIENTS PRESUMPTIVELY DIAGNOSED WITH MALARIA IN OGUN STATE, NIGERIA

DETECÇÃO DE INFECÇÃO PELO VÍRUS DA DENGUE ENTRE PACIENTES FEBRIS PRESUMIVELMENTE DIAGNOSTICADOS COM MALÁRIA NO ESTADO DE OGUN, NIGÉRIA

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Abstract

Background: In Nigeria, where malaria is endemic, greater than 70% of febrile illnesses are treated presumptively as malaria, often without a laboratory evaluation for other possible causes of fever. Dengue virus infection presents a significant health challenge in tropical regions, often exhibiting clinical symptoms similar to malaria. In Ogun State, Nigeria, febrile patients are frequently presumed to have malaria, potentially overlooking concurrent or alternative infections like dengue. Accurate diagnosis is crucial for appropriate treatment and management. The aim of this study was to determine the prevalence of dengue virus antibodies and antigen among febrile patients attending a state hospital in Ogun State. Methodology: Blood samples from 120 consenting febrile patients suspected of malaria in Ogun state were evaluated for the presence of malaria parasites by microscopic examination of Giemsa-stained blood smears and also tested for the presence of anti-dengue immunoglobulin M (IgM) and immunoglobulin G (IgG), as well as anti-non-structural protein (NS1) using lateral flow chromatographic immunoassay in line with manufacturer's instructions. The study lasted for three months (January- March, 2024). Data analysis was done using the Statistical Package for the Social Sciences (SPSS). A p value <0.05 was considered statistically significant. Results: The percentage occurrence of Dengue IgG Ab only, NS1 Ag, IgM Ab + NS1 Ag and IgM Ab + IgG Ab + NS1 Ag combined were: 4.2%, 0.8%, 3.3% and 6.7%, respectively. In all, 50% tested positive to malaria. A statistically significant association (p=0.026) was found between gender and preventive practice. Females exhibited higher proportions of good preventive practice 45.0% compared to males (20.8%). A significant association (p=0.014) was observed between age range and Dengue NS1 antigen status. Conclusion: These findings imply dengue fever should feature as a prominent differential diagnosis for febrile illnesses and screening for dengue virus should be part of routine tests amongst patients that presents with febrile illness. Given the prevalence of dengue virus infections, there is also a need for a dengue control programme and public education to prevent outbreaks and occurrence of severe dengue complications.
Keywords: Dengue; Malaria; IgG/IgM antibodies; Febrile; NS1 antigen; Ogun State.

Resumo

Na Nigéria, onde a malária é endêmica, mais de 70% das doenças febris são tratadas presumivelmente como malária, muitas vezes sem avaliação laboratorial para outras possíveis causas dA febre. A infecção pelo vírus da dengue apresenta um desafio de saúde significativo em

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regiões tropicais, muitas vezes exibindo sintomas clínicos semelhantes à malária. No estado de Ogun, na Nigéria, presume-se, frequentemente, que pacientes febris tenham malária, potencialmente ignorando infecções simultâneas ou alternativas, como a dengue. O diagnóstico preciso é crucial para tratamentos adequados. O objetivo deste estudo foi determinar a prevalência de anticorpos e antígenos do vírus da dengue em pacientes febris atendidos em um hospital estadual no estado de Ogun. Metodologia: Amostras de sangue de 120 pacientes febris com suspeita de malária no estado de Ogun foram avaliadas quanto à presença de parasitas da malária, via exame microscópico e também por meio de testes para dengue (IgM/IgG), bem como proteína NS1. O estudo durou três meses (janeiro-março de 2024). A análise dos dados foi feita usando o pacote estatístico SPSS, versão. Um valor de p <0,05 foi considerado estatisticamente significativo. Resultados: Os percentuais de ocorrência de Dengue (IgG apenas, NS1, IgM + NS1 Ag e IgM + IgG + NS1) combinados foram de 4,2%, 0,8%, 3,3% e 6,7%, respectivamente. Ao todo, 50% testaram positivo para malária. Foi encontrada associação estatisticamente significativa (p=0,026) entre sexo e prática preventiva. O sexo feminino apresentou maiores proporções de boas práticas preventivas (45,0%) em relação ao masculino (20,8%). Observou-se associação significativa (p=0,014) entre a faixa etária e o status do antígeno NS1 da Dengue. Conclusão: Esses achados sugerem que a dengue deve ser considerada como diagnóstico diferencial proeminente para doenças febris. Ainda, o rastreamento do vírus da dengue deve fazer parte dos testes de rotina entre os pacientes que apresentam doença febril. Dada a prevalência de infecções pelo vírus da dengue, há também a necessidade de um programa de controle da doença e educação pública para prevenir surtos e ocorrência de complicações graves decorrentes.
Palavras-chave: Dengue; Malária; IgG/IgM; Síndromes febris; NS1; Estado de Ogun.

Introduction

Dengue is a rapid-onset viral illness caused by an RNA virus from the Flaviviridae family, transmitted primarily by Aedes mosquitoes, especially *Aedes aegypti*[1–3]. Known as 'breakbone fever,' dengue is the fastest-growing vector-borne viral infection, comprising four serotypes: DEN-1, DEN-2, DEN-3, and DEN-4[4]. It poses a significant public health threat globally, leading to illness and mortality, with diagnosis depending on detecting specific antibodies, IgG and IgM, and the NS1 antigen. The dengue virus is a small, icosahedral-shaped, enveloped virus containing about 11kb of positive single-stranded RNA.[5] It includes seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5) and three structural proteins (capsid [C], envelope [E], membrane [M]). Infection can range from asymptomatic to severe, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS)[6–8].

Dengue is prevalent in tropical and subtropical regions, with an estimated 100 to 400 million cases annually[9–11]. It is endemic in Africa, the Eastern Mediterranean, the Americas, Southeast Asia, and the Western Pacific[11–13]. Rapid urbanization and inadequate infrastructure are significant contributors to its spread, as well as the movement of people for travel[14]. In 2013, a new dengue serotype, DENV5, was identified in Sarawak, Malaysia, initially thought to be sylvatic dengue associated with DENV4[15,16]. Genetic studies revealed it as a new serotype, predominantly found in Southeast Asian forests, possibly due to genetic shifts and environmental changes like deforestation[17–21]. DENV5 has a distinct phylogenetic profile, separate from the other four serotypes, indicating ongoing viral evolution influenced by zoonotic transmission and environmental factors[22]. There are no specific treatments or vaccines for dengue, partly due to cross-reactivity with other flaviviruses, which share similar envelope protein structures.[14, 15–18]

Malaria remains a critical health issue in Africa, with over 200 million cases annually and the majority of deaths occurring in sub-Saharan Africa.[23,24] In Nigeria, where malaria is endemic, over 70% of febrile illnesses are treated as malaria without laboratory confirmation.[25] The first dengue cases in humans were reported in the 1960s, with subsequent cases identified across the country, including recent reports of dengue-malaria co-infection.[3,25] Despite its presence, dengue is not a reportable disease in Nigeria, leading to underdiagnosis and misdiagnosis, often as malaria.[25]

Most healthcare facilities focus on malaria and occasionally enteric fever, neglecting other causes of fever such as dengue.[26] The misclassification of dengue as malaria due to similar symptoms leads to delayed and inappropriate treatment, worsening patient outcomes.[26,27] Resource constraints and reliance on symptomatic diagnoses contribute to this issue.[28, 29] Addressing this requires implementing accurate, accessible diagnostic tools to differentiate between dengue and malaria, ensuring timely and appropriate care and better resource allocation. This study aimed to determine

the prevalence of dengue virus infection among febrile patients presumptively diagnosed with malaria in Ogun State, Nigeria.

Methods

Study Design and area

This was a cross-sectional, epidemiological research. The study was conducted among febrile male and female patients presumptively diagnosed with malaria attending Ijaiye state hospital, Abeokuta, Ogun state. Ijaiye State Hospital, Abeokuta is a government owned general hospital in Ogun state Nigeria, coordinates: 7.1475° N, 3.3619° E.

Duration of Study

The research took place over the course of 3 months (January - March, 2024).

Study Population

This cross sectional institutional based study was carried out among febrile male and female patients presumptively diagnosed with malaria (presenting with high fever) attending Ijaiye state hospital, Abeokuta, Ogun State.

Sample Size Calculation

The sample size for this study was calculated using the formula described by Pourhoseingholi *et al*.[30]:

$$N = \frac{Z^2 \times P(1-P)}{D^2}$$

Where:

N = minimum sample size required

Z = confidence interval (1.96)

P = prevalence rate of Dengue virus among febrile patient in a tested population.

D = desired level of significance (0.05)

In order to calculate the minimum sample size needed, a 95% confidence interval, a prevalence rate of 8.5% from an earlier study by Ayolabi *et al*.[31] and margin of error (d) set at 0.05 will be utilized.

$$N = \frac{Z^2 \times P(1-P)}{D^2}$$

Z = 1.96

P = 8.5% (Ayolabi *et al*. [31])

D = 0.05

$$N = \frac{(1.96)^2 \times 0.085(1-0.085)}{(0.05)^2}$$

$$N = \frac{0.29878044}{0.0025}$$

N = 119.51

N = 120

Sample size is, therefore, 120. Hence, 120 blood specimens were used for this study.

Sample Size

A total of 120 blood specimens was collected at random from 120 consenting febrile patients (presenting with high fever) attending Ijaiye state hospital, Abeokuta, Ogun State.

Eligibility of Subjects

Inclusion Criteria

The inclusion criteria included all consenting patients of all ages presented with symptoms of fever (>38^{0}C) and were

clinically diagnosed or suspected to have malaria infection attending Ijaiye state hospital, Abeokuta, Ogun state, Nigeria. For children, procedures were as follows: children whose parent(s) gave consent and were presenting with fever and were clinically diagnosed or suspected to have malaria infection was included in the study.

Exclusion Criteria

The exclusion criteria included all consenting patients of all ages presented with no symptoms of fever (>38^{o}C) and were not clinically diagnosed or suspected to have malaria infection attending Ijaiye state hospital, Abeokuta, Ogun state, Nigeria. For children, criteria were children whose parent(s) did not give consent and were not presenting with fever and were not clinically diagnosed or suspected to have malaria infection was excluded from this study.

Consent

Informed consent was distributed to each study participant. The purpose and nature of the study, as well as the method of sample collection was explained to them properly, afterwards, participants were required to voluntarily complete the consent form in their own handwriting and endorsed by their signatures as proof of willingness to provide samples for the test. They were assured of the confidentiality.

Data Collection

Prior to specimen collection, demographic and clinical information of the participants were obtained using prepared questionnaires which were administered to the participants. Each questionnaire had a unique participant identification number (PIDN). Data collection lasted for an average of twenty-eight (28) days in the study location. This period was used for the selection of the subjects, distribution and retrieval of the questionnaires, and collection of samples. The pre-test questionnaires were administered to the participants directly. The first part of the questionnaires contained the biodata of the participants such as their age, religion, tribe, educational level, and sex. The second section comprised of clinical data from the individuals relating to a brief history of symptoms of dengue fever such as headache, fever, Bone pain, Rash, muscle aches, vomiting, eye pain etc. All completed questionnaires were checked for accuracy and stored in a secure locker each day, with data input taking place the next day. For the sake of secrecy, only the PIDN were recorded on the specimen bottles and result sheet.

Measurement of body temperature

A battery powered digital clinical thermometer was used to measure the participants' body temperature.

Specimen Collection

Each participant's blood was drawn via venous puncture with the help of a certified phlebotomist.

Venous Blood Collection

With the help of a competent phlebotomist, five (5) mls of venous blood

were collected into an EDTA sample bottle labelled with each PIDN.

Sample Transportation and Storage

The blood samples were transported to the laboratory unit of the department of medical laboratory science at Babcock University and analysed there within 2 hours of collection. Every sample was transported swiftly and without delay to the laboratory, where it was processed at the same day it was collected. The specimens collected from each participant were labelled with their unique identification number on the specimen container. Specimens were not stored due to the need for immediate processing. However, in cases when a delay was anticipated, the sera were kept at 2-8℃ for up to 3 days. The specimens were stored below -20℃ for extended periods of time. Prior to testing, frozen samples were fully thawed and well mixed. Repeated freezing and thawing of sera were avoided. To prevent interfering with the interpretation of results, samples displaying turbidity, gross lipedaemia, or gross haemolysis were not used.

Laboratory Analysis

Detection of Malaria Parasite

The presence of malaria parasite was done using the microscopy (Gold Standard).

Principle

Giemsa stain is a Romanowsky stain composed of eosin and methylene blue. The eosin component stains the parasite nucleus red while methylene blue stains the parasite nucleus blue. Dehemoglobinasation of the thick film and staining takes place at the same time simultaneously with an ideal pH of 7.2 buffered water.

Procedure

A thin and thick blood film were made on a labelled clean grease free slide. The slide was placed horizontally on a staining rack. A small drop of absolute methanol was applied to the thin film, making sure the alcohol does not touch the thick film as this will prevent lysis of the red cells. The thin film was allowed to fix for 1 minutes. The thick film was allowed to air dry. Blood films were stained for 10 minutes using 10% Giemsa stain solution. The stain was flushed from the slide using buffered water with 7.2 pH to avoid the films being covered with a fine deposit of stain. The back of the slide was wiped clean with cotton wool and placed in a draining rack for the preparation to air-dry.

They were viewed under the microscope using immersion oil and x100 (oil immersion) objective lenses with the light microscopy. The diagnosis of malaria was based on the identification of asexual stages of *Plasmodium* on the thick blood smears. Thin blood smears were used to identify species of *Plasmodium*. If no parasite is seen, blood films were declared negative. Each slide was read independently. In the event of discordant results, the slide was examined by two microscopists independently.

Detection of Dengue Virus

The detection of Dengue Virus was diagnosed with the use of the Aria duo

Dengue Ag-IgG/IgM lateral flow Immunochromatographic immunoassay rapid test cassette according to the manufacturers' instruction.

Principle of the RDT KIT

The Aria Duo Dengue Ag-IgG/IgM Rapid test contains two test strips (left side: Dengue IgG/IgM test; right side: Dengue Ag test). The Dengue IgG/IgM Rapid Test on the left side is a lateral flow chromatographic immunoassay. The test strip consists of: 1) a coloured conjugate pad containing recombinant dengue envelope antigens conjugated with colloidal gold (dengue Ag conjugates) and a control antibody conjugated with colloidal. 2) a nitrocellulose membrane strip containing two test lines (G and M) and a control line (C line).

The G line is pre-coated with antibodies for the detection of anti-dengue virus IgG, the M line is pre-coated with antibodies for the detection of anti-dengue virus IgM, and the C line is pre-coated with a control line antibody. The Dengue Ag Rapid test on the right side is a lateral flow chromatographic immunoassay.

The test strip consists of: 1) a coloured conjugate pad containing antibodies to dengue NS1 antigen, conjugated with colloidal gold (dengue Ab conjugates) and a control antibody conjugated with colloidal gold, 2) a nitrocellulose membrane strip containing a test (T line) and a control line (C line). The T line is pre-coated with antibodies to dengue NS1, and the C line is pre-coated with a control line antibody. The antibodies to dengue NS1 recognize the NS1 antigens from all four dengue virus serotypes.

When an adequate volume of specimen is dispensed into the sample well of the test cassette, the specimen will migrate by capillary action across the cassette. Dengue NS1 antigen, if present in the specimen, will bind to the dengue Ab conjugates. The immunocomplex is then captured on the membrane by the pre-coated antibodies to dengue NS1 antigen forming a coloured T line. Anti-dengue virus IgG and IgM, if present in the specimen, will bind to the dengue Ag conjugates. The immunocomplex is then captured by the pre-coated reagent forming a coloured G and/or M line respectively.

Procedure of Test

The whole blood was centrifuged at 1500g for five (5) minutes to obtain the plasma. The test cassette was brought out of the pack, opened and placed on a clean work bench. The specimen's unique identification number were accurately labelled on the test cassette. About 30 microliters - 45 microliters (1 drop) of plasma from the specimen were collected using a plastic dropper and dropped into well of the sample on the cassette. Then, two drops of buffer (sample diluent) were added. The test samples were ran alongside external positive and negative controls provided by the manufacturer. The results were read after 20 minutes with the aid of a timer.

Interpretation of results

Positive Result

When 'M' line for IgM is produced, test confirms the presence of IgM anti-

DENV in the specimen, in addition to the presence of the 'C' line (control). The outcome is either positive or negative. When just the IgG "G" line is produced, test confirms the presence of IgG anti-DENV in the specimen, in addition to the presence of the C line. When the NS1 antigen 'T' line is produced, test confirms the presence of NS1 antigen in the specimen, in addition to the presence of the C line. The outcome is either negative or positive. In addition to the presence of the C line, the test confirms the presence of both IgG and IgM anti-DENV and NS1 antigen in the samples if both the "M", "G" and 'T' lines are formed. The outcomes were either positive or negative.

Negative Result

When just the C line is present, the absence of any pink hue in both test lines (M and G) and NS1 line indicates that DENV antibodies and antigen are absent respectively. The outcome is either unfavorable or non-responsive.

Invalid Result

The assay is inaccurate if no control "C" line develops, regardless of any pink hue in the test bands as shown. A complete lack of colour in either region or the appearance of only one colour band on the test region suggests a technique error and/or deterioration of the test reagent. When this happens, the assay was repeated using a different rapid kit.

Data Analysis

The data gathered from the serum antibody testing and the questionnaires were entered into Microsoft Excel. The statistical analysis was done with the SPSS-18.0 statistical tool (Statistical programs for Social Sciences, version 18.0). To test for significant differences in the percentage occurrence of DENV NS1 antigen, IgG and IgM antibodies, as well as the percentage occurrence of past and present DENV infection, a one-way analysis of variance (ANOVA) and P-Values < 0.05 and Turkey-Kramer Multiple Comparisons Test were used. Data analysis outputs were represented using tables and charts.

Results

This current study investigated the prevalence of Dengue virus infection among febrile patients presumptuously diagnosed for malaria. Table 1 shows the socio-demographic characteristics of the study participants. In terms of gender, the majority were female, comprising 60% of the study participants, while males constituted 36.7%, and a smaller percentage identified as "Others." Regarding age distribution, the largest proportion fell within the 25-40 years range, accounting for 42.5%, followed by those aged 42-49 years at 23.3%. Marital status shows that the majority were married (55.0%), followed by singles (40.0%). Christianity was the predominant religion among study participants (75.0%), with Islam representing 22.5%. Educational status varied, with the highest percentage having tertiary education (56.7%), followed by secondary education (30.0%). Geographically, the majority

resided in urban areas (77.5%). Occupationally, civil servants were the largest group (46.7%), while a small percentage identified as farmers or unemployed.

Table 1. Socio-demographic characteristics of the study participants

Variable	Categories	Frequency (N)	%
Gender	Female	72	60.0
	Male	44	36.7
	Others	4	3.3
Age range	<18yrs	21	17.5
	>50yrs	9	7.5
	18-25yrs	11	9.2
	25-40yrs	51	42.5
	42-49yrs	28	23.3
Marital status	married	66	55.0
	single	48	40.0
	widow	6	5.0
Religion	Christianity	90	75.0
	Islam	27	22.5
	others	2	1.7
	Traditional	1	0.8
Tribe	Hausa	2	1.7
	Igbo	24	20.0
	others	10	8.3
	Yoruba	84	70.0
Educational Status	None	8	6.7
	Primary	8	6.7
	Secondary	36	30.0
	Tertiary	68	56.7
Residential location	Rural	9	7.5
	Semi-Urban	17	14.2
	Semi-Urban	1	0.8
	Urban	93	77.5
Occupation	Civil servant	56	46.7
	Farmer	1	0.8
	Self-employed	35	29.2
	Student	14	11.7
	Teacher	4	3.3
	Unemployed	10	8.3

Table 2 shows Dengue awareness and symptoms among the study participants. Alarmingly, all of the study participants (100%) reported not having heard of the Dengue virus, indicating a significant lack of awareness about this disease.

Similarly, all participants who were aware of Dengue were unaware of its transmission by *Aedes spp* mosquitoes. Notably, 100% of study participants had no idea about the mode of transmission of Dengue. Furthermore, none of the participants reported a history of Dengue virus infection. However, a significant proportion of study participants reported experiencing symptoms associated with

Dengue, with fever being the most prevalent symptom (33.3%), followed by fever/headache (51.7%). Other reported symptoms included muscle pain, vomiting, and eye pain. Additionally, a substantial majority (75.8%) of participants had taken some form of drug medication in the last two weeks, which could potentially mask Dengue symptoms or interact with treatments.

Table 2. Dengue Awareness and Symptoms among the study participants

Variable	Categories	Frequency (N)	%
Have you heard of Dengue Virus?	No	120	100.0
If yes, are you aware that Dengue Virus is transmitted by *Aedes spp* mosquito?	No	120	100.0
What is the mode of transmission of Dengue Virus?	No Idea	120	100.0
Do you have any history of Dengue Virus?	No	120	100.0
Which of the following signs/symptoms do you have currently?	Fever	40	33.3
	Fever/Headache	62	51.7
	Fever/Headache/Muscle Pain	4	3.3

	Fever/Headache/vomiting	8	6.7
	Fever/Headache/Eye pain	6	5.0

Table 3 shows the factors influencing mosquito exposure and health practices among the surveyed population. The majority of study participants reported the presence of mosquitoes in their environment (92.5%) and having been bitten by mosquitoes before (100.0%), highlighting a widespread exposure to mosquitoes. A small proportion of participants (10.0%) reported a history of blood transfusion. Regarding preventive measures, 36.7% reported using mosquito nets, while 20.8% admitted to staying outdoors late. Among those who stayed outdoors late, the majority (80.0%) reported wearing full clothing as a protective measure. Additionally, approximately half of the study participants (51.7%) reported having stagnant water sources around them, which can serve as breeding grounds for mosquitoes. In terms of health practices, the majority (57.5%) reported going for medical check-ups or laboratory tests often, while a significant proportion (37.5%) practiced self-medication often.

Figure 1 is a pie chart showing the prevalence of Dengue virus antigen and antibodies among the study participants. The occurrence of Dengue virus infection was found to be low in this study. Only 5 (4.2%) tested positive to Dengue virus IgGAb only, 1 (0.8%) tested positive to Dengue virus NS1 Antigen, 4 (3.3%) tested positive to both Dengue virus IgM antibodies and NS1 Antigen; while 8 (6.7%) tested positive for a combination of Dengue virus IgM antibodies, IgG antibodies, and NS1 Antigen. The majority of the study participants tested negative for Dengue IgG antibodies (95.8%), Dengue NS1 Antigen (99.2%), and the combination of Dengue IgM antibodies and NS1 Antigen (96.7%).

Figure 2 illustrates the practice associated with the occurrence of Dengue virus infection among febrile patients presumptively diagnosed with malaria. Among the surveyed participants, 33.3% were classified as having poor practices, while 66.7% exhibited good practices. A statistically significant association was found between gender and practice ($\chi^2 = 7.295$, df = 2, $p = 0.026$). Females exhibited higher proportions of good practice (45.0%) compared to males (20.8%). No significant association was observed between age range and practice ($\chi^2 = 4.435$, df = 4, $p = 0.350$).

There was no significant association between marital status and practice ($\chi^2 = 1.739$, df = 2, $p = 0.419$). No significant association was observed between educational status and practice ($\chi^2 = 5.243$, df = 3, $p = 0.155$). While there were variations in practice across educational categories, these differences were not statistically significant, suggesting that educational status may not be a significant determinant of practice associated with Dengue virus infection occurrence. No significant association was found between residential location and practice ($\chi^2 = 1.429$, df = 3, $p = 0.699$).

Table 3. Factors influencing mosquito exposure and health practices

Variable	Categories	Frequency (N)	%
Do you have mosquitoes in your environment?	No	9	7.5
	Yes	111	92.5
Have you ever been bitten by mosquito before?	Yes	120	100.0
Any history of blood transfusion before?	No	108	90.0
	Yes	12	10.0
Do Use Mosquito net>	No	76	63.3
	Yes	44	36.7
Do you stay outdoor late?	No	95	79.2
	Yes	25	20.8
If yes, full clothing or not	Full clothing	12	10.0
	Not full clothing	1	0.8
	Not applicable	96	80.0
	Not full clothing	11	9.2
Any source of stagnant water around you?	No	58	48.3
	Yes	62	51.7
How often do you go for medical check-up/laboratory test?	Less often	28	23.3
	Much often	23	19.2
	Often	69	57.5
How often do you practice self-medication?	Less often	33	27.5
	Much often	28	23.3
	Never	14	11.7
	Often	45	37.5

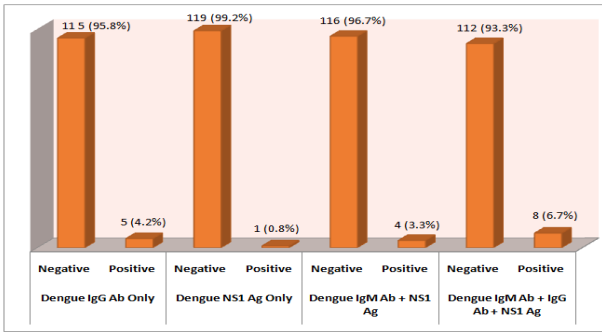

Figure 1: Prevalence of Dengue virus antigen and antibodies among the study participants

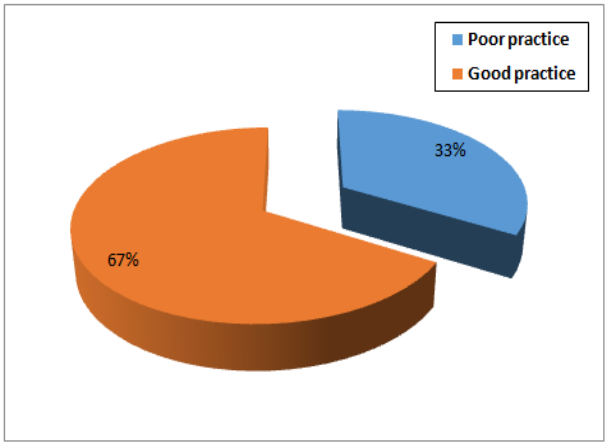

Figure 2: Practice pattern associated with occurrence of Dengue virus infection among the study participants

Table 4 (at the end of the document) examines the association between Dengue IgG antibody status and sociodemographic factors among the study participants. The table provides frequencies and percentages of patients testing negative and positive for Dengue IgG antibodies across various demographic categories, alongside the results of the Pearson Chi-Square test assessing the association between each demographic variable and Dengue IgG antibody status. Regarding gender, the data show that 58.3% of females tested negative for Dengue IgG antibodies, while only 1.7% tested positive. Among males, 34.2% tested negative, and 2.5% tested positive. However, the association between gender and Dengue IgG antibody status was not statistically significant (χ^2 = 1.296, df = 2, p = 0.523). Age range did not demonstrate a significant association with Dengue IgG antibody status (χ^2 = 1.289, df = 4, p = 0.863), indicating that age might not be a determining factor in Dengue IgG antibody positivity among febrile patients. Marital status also

showed no significant association with Dengue IgG antibody status (χ^2 = 0.996, df = 2, p = 0.608), suggesting that marital status may not influence the likelihood of Dengue IgG antibody positivity. Similarly, religion (χ^2 = 0.162, df = 3, p = 0.983) and educational status (χ^2 = 2.517, df = 3, p = 0.472) did not exhibit significant associations with Dengue IgG antibody status, indicating that these factors may not play a substantial role in Dengue IgG antibody positivity among febrile patients. In contrast, tribe (χ^2 = 11.031, df = 3, p = 0.012), residential location (χ^2 = 25.032, df = 3, p = 0.000), and occupation (χ^2 = 24.477, df = 5, p = 0.000) demonstrated significant associations with Dengue IgG antibody status. Specifically, patients from certain tribes, urban residential areas, and civil servants showed higher rates of Dengue IgG antibody positivity compared to other groups.

Table 5 (at the end of the document) shows the relationship between Dengue NS1 antigen status and various sociodemographic factors among febrile patients. The table presents the frequencies and percentages of patients testing negative and positive for Dengue NS1 antigen across different demographic categories, along with the results of the Pearson Chi-Square test evaluating the association between each demographic variable and Dengue NS1 antigen status. The data indicate that 59.2% of females tested negative for Dengue NS1 antigen, while only 0.8% tested positive. Among males, 36.7% tested negative, and none tested positive. However, the association between gender and Dengue NS1 antigen status was not statistically significant (χ^2 = 0.672, df = 2, p = 0.715). A significant association was observed between age range and Dengue NS1 antigen status (χ^2 = 12.437, df = 4, p = 0.014). Patients aged 25-40 years exhibited the highest proportion of Dengue NS1 antigen positivity, while those aged <18 years and >50 years showed lower positivity rates. Marital status, religion, tribe, educational status, residential location, and occupation did not show significant associations with Dengue NS1 antigen status, as indicated by their respective p-values exceeding the significance threshold of 0.05.

Table 6 (at the end of the document) presents the association between Dengue IgM Antibody + NS1 Antigen status and various sociodemographic factors among febrile patients. The table includes the frequencies and percentages of patients testing negative and positive for Dengue IgM Antibody + NS1 Antigen across different demographic categories, along with the results of the Pearson Chi-Square test evaluating the association between each demographic variable and Dengue IgM Antibody + NS1 Antigen status. Among females, 57.5% tested negative for Dengue IgM Antibody + NS1 Antigen, while 2.5% tested positive. For males, 35.8% tested negative, and 0.8% tested positive. The association between gender and Dengue IgM Antibody + NS1 Antigen status was not statistically significant (χ^2 = 0.447, df = 2, p = 0.800). There was no significant association between age range and Dengue IgM Antibody + NS1 Antigen status (χ^2 = 5.830, df = 4, p = 0.212). Patients aged 25-40 years had the highest proportion of Dengue IgM Antibody + NS1 Antigen

positivity. Marital status, religion, tribe, educational status, residential location, and occupation did not show significant associations with Dengue IgM Antibody + NS1 Antigen status, as indicated by their respective p-values exceeding the significance threshold of 0.05.

Table 7 (at the end of the document) presents the association between Dengue IgM Antibody + IgG Antibody + NS1 Antigen status and various sociodemographic factors among febrile patients. The table includes the frequencies and percentages of patients testing negative and positive for Dengue IgM Antibody + IgG Antibody + NS1 Antigen across different demographic categories, along with the results of the Pearson Chi-Square test evaluating the association between each demographic variable and Dengue IgM Antibody + IgG Antibody + NS1 Antigen status. Among females, 55.0% tested negative for Dengue IgM Antibody + IgG Antibody + NS1 Antigen, while 5.0% tested positive. For males, 35.0% tested negative, and 1.7% tested positive. The association between gender and Dengue IgM Antibody + IgG Antibody + NS1 Antigen status was not statistically significant ($\chi^2 = 0.925$, df = 2, p = 0.630). There was no significant association between age range and Dengue IgM Antibody + IgG Antibody + NS1 Antigen status ($\chi^2 = 2.377$, df = 4, p = 0.667). Patients aged 25-40 years had the highest proportion of Dengue IgM Antibody + IgG Antibody + NS1 Antigen positivity. Marital status, religion, tribe, educational status, residential location, and occupation did not show significant associations with Dengue IgM Antibody + IgG Antibody + NS1 Antigen status, as indicated by their respective p-values exceeding the significance threshold of 0.05.

Table 8 (at the end of the document) shows the relationship between Dengue IgG antibody status and associated risk factors, presenting frequencies for both negative and positive Dengue IgG antibody statuses within each category of the variables. The Pearson Chi-Square statistic (χ^2), degrees of freedom (df), and p-values are provided to assess the significance of these associations. Results indicate no significant association between travel history and Dengue IgG antibody status ($\chi^2 = 0.275$, p = 0.600), nor between awareness of Dengue Virus, including knowledge of its transmission and history, and Dengue IgG antibody status. Similarly, no significant association is found between drug medication in the last two weeks and Dengue IgG antibody status ($\chi^2 = 1.663$, p = 0.197). Additionally, the presence of mosquitoes, history of mosquito bites, history of blood transfusion, use of mosquito nets, staying outdoors late, presence of stagnant water sources, frequency of medical check-ups/laboratory tests, and frequency of self-medication do not exhibit significant associations with Dengue IgG antibody status.

Table 9 (at the end of the document) presents the association between Dengue NS1 Antigen status and various associated risk factors. It indicates that travel history is not significantly associated with Dengue NS1 antigen status, nor does awareness of Dengue Virus, including its mode of transmission and history. While no

significant association between drug medication in the last two weeks and Dengue NS1 Antigen status is found, there is a suggestive trend ($\chi^2 = 3.164$, $p = 0.075$). The presence of mosquitoes in the environment exhibits a significant association with Dengue NS1 Antigen positivity ($\chi^2 = 12.437$, $p < 0.001$), indicating a potential risk factor. Moreover, having a history of mosquito bites is significantly associated with Dengue NS1 Antigen positivity. Conversely, there was no significant association between a history of blood transfusion and Dengue NS1 Antigen status, nor with the use of mosquito nets or the presence of stagnant water sources. However, staying outdoors late demonstrates a marginal association with Dengue NS1 Antigen positivity ($\chi^2 = 3.832$, $p = 0.050$). Furthermore, while there was no significant association between the frequency of medical check-ups/laboratory tests and Dengue NS1 Antigen status, there was a marginally significant association between the frequency of self-medication and Dengue NS1 Antigen positivity ($\chi^2 = 7.635$, $p = 0.054$), suggesting a potential risk factor.

Discussion

Malaria and dengue fever are leading causes of acute undifferentiated febrile illness. Dengue fever infection has always been considered an emerging public health problem in several African Countries and tropical regions with risk of severe infections.[1-5] Most febrile cases are routinely diagnosed and tested for malaria without proper investigation for other conditions including viral infections. This study was carried out to determine the incidence rate of dengue fever among patients presenting with fever (a major symptoms of malaria) at a state hospital in Abeokuta, Ogun State. This study found an overall dengue fever IgM, IgG& NS1Ag prevalence of only which 4.2% (5) tested positive to Dengue virus IgGAb only, 0.8% (1) tested positive to Dengue virus NS1 Antigen, 3.3% (4) tested positive to both Dengue virus IgM antibodies and NS1 Antigen; while 6.7% (8) tested positive for a combination of Dengue virus IgM antibodies, IgG antibodies, and NS1 Antigen. The majority of the study participants tested negative for Dengue IgG antibodies 95.8%, Dengue NS1 Antigen 99.2%, and the combination of Dengue IgM antibodies and NS1 Antigen 96.7%, 4.2%, 0.8%, respectively. The occurrence of Dengue virus infection was found to be low in this study.

In dengue fever infection, the NS1protein antigen is typically the first to be produced in the infection, which ensures the first early window is not missed in DENV infection; the IgM antibody is the first to be produced in response to an infection, and their presence is a strong indicator of an ongoing Dengue Virus infection. IgM antibodies can be detected in eight (8) to nine (9) days following infection. On the other hand, IgG antibodies are produced later in the course of the infection and can persist for several years remaining in convalescence. The presence of NS1 Ag and both IgG and IgM antibodies in a single serum sample suggests a current infection or reinfection. The findings from this study are in agreement with similar

studies conducted in Jos, Plateau state by Bukbuk *et al*.[32], using febrile patients and immunochromatographic assay technique who reported a prevalence of 2.2% (4) of 182 samples examined, with female having 2.9 % (3) and male 1.3% (1). Also, a study conducted by Ayorinde *et al*.[33] in a town close to Simawa, Ogun state reported a prevalence of 3% among sixty (60) febrile patients using immunochromatographic assay.

Furthermore, the findings from this study show that there was a significant association between dengue fever and age. Patients aged 25-40 years exhibited the highest proportion of Dengue NS1 antigen positivity, while those aged <18 years and >50 years showed lower positivity rates. This association is also in agreement with Bukbuk *et al*.[32] where age range 11-40yrs showed high positivity. A study carried out by Mohammed *et al*.[34] in Lagos, Nigeria also affirm that age has a significant association with Dengue fever occurrence. In their study, high dengue positivity was found in febrile patients >30yrs of age.

Onyedibe[25] in his studies documented a seroprevalence of 2.8% amongst febrile patients in Jos and Maiduguri using ELISA technique. The study conducted by Linda *et al*.[35] in Awka, Anambra amongst HIV infected patients reported a prevalence of 20.2% among the 188 HIV patients included in the study using ELISA technique. The study showed significant association with some haematological parameters which suggest that Dengue maybe the emerging cause of fever of unknown origin among this population. The study by Ayolabi *et al*.[36] detected Dengue viruses among febrile patients in Lagos, Nigeria and phylogenetics of circulating Dengue serotypes in Africa is in agreement with this study's findings. Ayolabi *et al*.[36] reported a low prevalence of 8.5% (11) among the 130 febrile patients examined in the study. In contrast, a recent study conducted by Okonko *et al*.[37] amongst HIV Infected patient using ELISA technique to detect Dengue virus IgM among 94 patients reported a high prevalence as high as 35.1%. Among the participants who tested positive, females had higher positivity percentage (43.6%), while the males had a lower percentage (23.1%). This is in contradiction to the work of Linda *et al*.[35]. The possible reason could be due to sample size variation.

Additionally, Miri[38] reported a prevalence of 55.3% among 94 consenting febrile patients suspected of malaria attending health centre in Jos, Nigeria using ELISA technique with females having higher percentage of positivity 39(75%) within the age range of 20-29yrs. Miri's study[28] focused on both IgM and IgG alone and was conducted in Jos, Nigeria. The reason for this high prevalence could be because the study coincides with the warm temperatures and rainy season (April - October) in that region, a suitable condition for the breeding of mosquito that transmits the virus.

Furthermore, the study by Sule *et al*.[39] in Osun State found a prevalence of 33.7% and 41.6% for Dengue IgG and IgM antibodies, respectively using ELISA technique. Eighty-nine (89) newly admitted students were recruited for the study with 46 females and 43 males. The

age range of the participants was between 15-33years. The study was conducted during the rainy season and thus may contribute to its high prevalence. The study carried out by Abdulaziz*et et al*.[40] among febrile patients attending secondary health facilities in Kano metropolis, Nigeria' reported a high seroprevalence of 78.3% among the 440 patients included in their study using ELISA technique. This high prevalence of Dengue IgM could possibly be because of the rapid unplanned urbanization in Kano metropolitan; a good condition for mosquito breeding.

The rates reported in the studies show the disparity that exists between different studies in the prevalence of dengue fever. The possible reasons for this variation are the sample size of participants, researchers whose sample size were larger and higher prevalence rate, differences in detection method. This study made use of a rapid diagnostic kit, similar studies like that of Mohammed *et al*.[24] that also made use of rapid diagnostic kit had a low prevalence, although with lower sample size. Studies like that of Abdulaziz *et al*.[40] that made use of the ELISA technique had higher prevalence percentage hence, this could be a reason.

Regional variation is another possibility. The period this study was conducted was during the dry season with reduced humidity and cooler temperature. Rainfall is minimal during this season which does not favour the breeding of mosquitoes compared to other studies with high prevalence in which majority of those studies were carried out during the wet season with higher humidity, frequent rainfall and lush vegetation a condition that favours the breeding of mosquitoes.

One major statistically significant factor in this study associated with the risk of developing DF was age. A significant association was observed between age range and Dengue NS1 antigen status (χ^2 = 12.437, df = 4, p = 0.014). Patients aged 25-40 years exhibited the highest proportion of Dengue NS1 antigen positivity, while those aged <18 years and >50 years showed lower positivity rates. There were significant correlations found between Dengue IgG antibody status and tribe (χ^2 = 11.031, df = 3, p = 0.012), residential location (χ^2 = 25.032, df = 3, p = 0.000), and occupation (χ^2 = 24.477, df = 5, p = 0.000). A possible risk factor is the substantial correlation between the presence of mosquitoes in the surroundings and Dengue NS1 Antigen positive (χ^2 = 12.437, p < 0.001). As evidenced by their respective p-values surpassing the significance threshold of 0.05, marital status, religion, and educational status did not exhibit significant relationships with Dengue Virus infection. According to this study, gender did not appear to be related to the dengue fever virus (p>0.05). Although, there was no-correlation between gender and dengue fever virus, it was shown that female participants had a greater prevalence of dengue virus than male participants. This study revealed that sex is a possible predisposing factor, with more females than males contracting the infection. This finding is consistent with

the work of Okonko *et al*.[37] who observed that sex was a predisposing factor with more females contracting the disease than males.

Limitations of the study

This study has several limitations, including the relatively small sample size, which might have influenced the statistical power to detect significant associations. Additionally, the cross-sectional nature of the study limits our ability to establish causation and temporal relationships between variables. Nonetheless, the findings of this study underscore the importance of continuous surveillance and awareness campaigns to educate the public about Dengue and its associated risk factors. While certain risk factors did not show significant associations in this study, the complex interplay between various factors cannot be overlooked. Future research endeavours with larger sample sizes and longitudinal designs could provide a more comprehensive understanding of these relationships.

Conclusion and recomendations

In conclusion, this study contributes to the growing body of knowledge regarding the seroprevalence of Dengue antibodies and antigen among patients attending a hospital in Nigeria. The lack of significant associations with gender, religion, and several risk factors emphasizes the need for a multifaceted approach to Dengue prevention. This study suggest that Febrile illness is not only limited to malaria and as such serological screening for dengue virus using NS1 antigen and anti-dengue IgG and IgM antibodies for all febrile patients, as part of fever diagnostic protocols in Nigeria. Adequate training of clinicians and laboratory workers on laboratory diagnosis and case management of dengue should be ensured. Community based public enlightenment programmes for preventive measures will also help in reducing the transmission of dengue and other mosquito-borne diseases in our environment. Future research with enhanced study designs will contribute to a more comprehensive understanding of the factors influencing Dengue seropositivity and inform effective preventive strategies.

Recommendations

The findings of this study provide valuable insights into the detection of dengue virus among febrile patients in a hospital in Nigeria. Building upon these findings, we offer the following recommendations to guide future research and public health initiatives aimed at addressing the challenges posed by Dengue: 1) Enhanced Surveillance and Awareness Campaigns, 2) Longitudinal Studies with Larger Sample Sizes, 3) Interdisciplinary Collaboration, 4) Improvement in Hygiene and Sanitation Practices and 5) Investment in Infrastructure and Education.

References

1. World Health Organization (WHO). Dengue guidelines for diagnosis, treatment, prevention and control: new edition. 2009. Available from: https://iris.who.int/handle/10665/44188
2. World Health Organization (WHO). Dengue and severe dengue. 2019. Available from: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue
3. Adesola RO et al. Addressing the Dengue fever challenges in Nigeria: A narrative review and recommendations for control. Le Infezioni in Medicina. 2024;32(2):157. doi: 10.53854/liim-3202-5
4. Hasan S et al. Dengue virus: A global human threat: Review of literature. J Int Soc Prev Community Dent. 2016;6(1):1. doi: 10.4103/2231-0762.175416
5. Clyde K, Harris E. RNA Secondary Structure in the Coding Region of Dengue Virus Type 2 Directs Translation Start Codon Selection and Is Required for Viral Replication. J Virol. 2006;80(5):2170–82. doi: 10.1128/jvi.80.5.2170-2182.2006
6. Otu A et al. Dengue fever – an update review and implications for Nigeria, and similar countries. Afr Health Sci. 2019;19(2):743–53. doi: 10.4314/ahs.v19i2.23
7. Soto-Garita C et al. Epidemiological, virological and clinical characterization of a Dengue/Zika outbreak in the Caribbean region of Costa Rica 2017–2018. Front Cell Infect Microbiol. 2024 Jun 26;14:1421744. doi: 10.3389/fcimb.2024.1421744
8. Khosla S et al. Dengue encephalitis–An unusual case series. J Fam Med Prim Care. 2024 Aug 1;13(8):3420-3. doi: 10.4103/jfmpc.jfmpc_413_24
9. World Health Organization (WHO). Treating malaria. 2023. Available from: https://www.who.int/activities/treating-malaria
10. Mohamed MA et al. Epidemiological investigation of dengue fever outbreak and its socioeconomic determinants in Banadir region, Somalia. BMC Infect Dis. 2024 Apr 11;24(1):393. doi: 10.1186/s12879-024-09276-2
11. Nigussie E, Atlaw D, Negash G et al. A dengue virus infection in Ethiopia: a systematic review and meta-analysis. BMC Infect Dis. 2024 Mar 6;24(1):297. doi: 10.1186/s12879-024-09142-1
12. Chaturvedi UC, Shrivastava R. Dengue Haemorrhagic Fever: A Global Challenge. Indian J Med Microbiol. 2004;22(1):5-10. doi: 10.1016/s0255-0857(21)02943-1
13. Adu EA et al. (Sero) Prevalence of (Re) Emerging Major Arbovirus Infections in Africa: A Systematic Review and Meta-Analysis Protocol. 2024. Available from: https://doi.org/10.21203/rs.3.rs-3906474/v1
14. Kraemer MUG et al. The global distribution of the arbovirus vectors Aedes aegypti and Ae. albopictus.

eLife. 2015;4:e08347. doi: 10.7554/elife.08347

15. Normile D. Surprising New Dengue Virus Throws a Spanner in Disease Control Efforts. Science. 2013;342(6157):415. doi: 10.1126/science.342.6157.415
16. Mustapa MA et al. Bio-Functionalized Tapered Multimode Fiber Coated With Dengue Virus NS1 Glycoprotein for Label Free Detection of Anti-Dengue Virus NS1 IgG Antibody. IEEE Sens J. 2018;18(10):4066–72. doi: 10.1109/jsen.2018.2813385
17. Mustafa MS et al. Discovery of fifth serotype of dengue virus (DENV-5): A new public health dilemma in dengue control. Med J Armed Forces India. 2015;71(1):67-70. doi: 10.1016/j.mjafi.2014.09.011
18. Vasilakis N et al. Fever from the forest: prospects for the continued emergence of sylvatic dengue virus and its impact on public health. Nat Rev Microbiol. 2011;9(7):532–41. doi: 10.1038/nrmicro2595
19. Monath TP. Dengue: the risk to developed and developing countries. Proc Natl Acad Sci U S A. 1994;91(7):2395–400. doi: 10.1073/pnas.91.7.2395
20. European Centre for Disease Prevention and Control (ECDC). Geographical distribution of dengue cases reported worldwide, 2022. Available from: https://www.ecdc.europa.eu/en/publications-data/geographical-distribution-dengue-cases-reported-worldwide-2022
21. Rudel TK et al. Changing drivers of deforestation and new opportunities for conservation. Conserv Biol. 2009;23(6):1396–405. doi: 10.1111/j.1523-1739.2009.01332.x
22. Joob B, Wiwanikit V. Comment on: definitive tests for dengue fever: when and which should I use? Singapore Med J. 2018;59(1):60. doi: 10.11622/smedj.2018008
23. World Health Organization (WHO). World Malaria Report 2019. Available from: https://www.who.int/news-room/feature-stories/detail/world-malaria-report-2019
24. World Health Organization (WHO). How can malaria be prevented? Available from: https://www.who.int/news-room/questions-and-answers/item/malaria?gclid=Cj0KCQiApKagBhC1ARIsAFc7Mc4OL9rVSzFArHHOBeGw7dsz34
25. Onyedibe K. A cross sectional study of dengue virus infection in febrile patients presumptively diagnosed of malaria in Maiduguri and Jos plateau, Nigeria. Malawi Med J. 2018;30(4):276. doi: 10.4314/mmj.v30i4.11
26. Onoja BA et al. Whole genome sequencing unravels cryptic circulation of divergent dengue virus lineages in the rainforest region of Nigeria. Emerg Microbes Infect. 2024 Dec 31;13(1):2307511. doi: 10.1080/22221751.2024.2307511
27. Cerilo-Filho M et al. Worldwide distribution, symptoms and diagnosis of the coinfections between malaria and arboviral diseases: a systematic review. Mem Inst Oswaldo Cruz. 2024 Jun 24;119. doi: 10.1590/0074-02760240015

28. Agüero-Echeverría W et al. Validity of diagnostic tools in pediatric patients hospitalized with a presumptive diagnosis of dengue in a Reference Hospital in Paraguay. Anales Fac Cien Med (Asunción). 2024 Apr;57(1):26-36. doi: 10.18004/anales/2024.057.01.26
29. Frazer JL, Norton R. Dengue: A review of laboratory diagnostics in the vaccine age. J Med Microbiol. 2024 May 9;73(5):001833. doi: 10.1099/jmm.0.001833
30. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. Hepatol Bed Bench. 2013;6(1):14-17. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4017493/
31. Ayolabi CI et al. Detection of Dengue viruses among febrile patients in Lagos, Nigeria and phylogenetics of circulating Dengue serotypes in Africa. Infect Genet Evol. 2019 Nov;75:103947. doi: 10.1016/j.meegid.2019.103947
32. Bukbuk DN et al. Serological evidence of acute Dengue virus infection among febrile patients attending Plateau State. ResearchGate. 2016 Feb 29. Available from: https://www.researchgate.net/publication/296319684_Serological_evidence_of_acute_Dengue_virus_infection_among_febrile_patients_attending_Plateau_State_Specialist_Hospital_Jos_Nigeria
33. Ayorinde AF et al. A survey of malaria and some arboviral infections among suspected febrile patients visiting a health centre in Simawa, Ogun State, Nigeria. J Infect Public Health. 2016 Jan;9(1):52–9. doi: 10.1016/j.jiph.2015.06.009
34. Mohammed AS et al. Prevalence and Determinants of Dengue Virus Immunoglobulin among Febrile Patients Attending Naval Medical Centre Victoria Island, Lagos State. Glob Biosecurity. 2021;3. doi: 10.31646/gbio.110
35. Linda OE, Violet Chimere E, George OC. Determination of Dengue Virus IGM Seroprevalence, Malaria Parasitaemia and Some Haematological Parameters of HIV Infected Individuals in Awka, Nigeria. J Adv Microbiol. 2021 Nov 30;17–29. doi: 10.9734/jamb/2021/v21i1230410
36. Ayolabi CI et al. Detection of Dengue viruses among febrile patients in Lagos, Nigeria and phylogenetics of circulating Dengue serotypes in Africa. Infect Genet Evol. 2019 Nov;75:103947. doi: 10.1016/j.meegid.2019.103947
37. Okonko I et al. The first serological evidence of recent dengue virus infection among HIV-infected patients attending the University of Port Harcourt Teaching Hospital, Rivers State, Nigeria. Scientia Africana. 2023 May 31;22(1):1–12. doi: 10.4314/sa.v22i1.1
38. Miri NF. Detection of IgM and IgG Dengue antibodies in febrile patients suspected of malaria attending health center in Jos, Nigeria. Ann Med Lab Sci. 2021 Mar 20;1(1):27–35. doi: 10.51374/annalsmls.2021.1.1.0018
39. Sule WF et al. Probable primary and secondary dengue viral infections and associated host factors among

university undergraduates in Osun State, Nigeria. Alexandria J Med. 2019 Jan 2;55(1):25–30. doi: 10.1080/20905068.2019.1592935

40. Abdulaziz M et al. Prevalence and factors associated with dengue fever among febrile patients attending secondary health facilities in Kano metropolis, Nigeria. Afr J Clin Exp Microbiol. 2020 Aug 25;21(4):340–8. doi: 10.4314/ajcem.v21i4.11

List of Abbreviations

Ab: Antibody
Aedes spp - Aedes species
Ag: Antigen
BUHREC - Babcock University Health Research Ethics Committee
DEN-1, DEN-2, DEN-3, DEN-4: Dengue virus serotype 1-4
DENV: Dengue Virus
df: Degrees of Freedom
DF: Dengue Fever
DHF: Dengue Hemorrhagic Fever
DSS: Dengue Shock Syndrome
ECDC: European Centre for Disease Prevention and Control
ELISA: Enzyme-Linked Immunosorbent Assay
HIV: Human Immunodeficiency Virus
IgG: Immunoglobulin G
IgM: Immunoglobulin M
IRB - Institutional Review Board
kb: Kilobases
NS1: Non-structural Protein 1
p - p-value
PIDN - Participant Identification Number
RDT - Rapid Diagnostic Test
SPSS - Statistical Package for the Social Sciences
WHO: World Health Organization
χ^2: Chi-square

Ethical approval

Ethical approval for this study was granted by the Babcock University Health Research Ethics Committee (BUHREC) with ethical approval registration number: BUHREC 884/23. BUHREC is the Institutional Review Board (IRB) of the university.

Consent

Informed consent was obtained from each participant. The purpose and nature of the study, as well as the method of sample collection was explained to them properly. Afterwards, participants were requested to voluntarily complete the consent form in their own handwriting and endorsed by their signatures as proof of willingness to provide samples for the test. They were assured of the confidentiality.

Competing Interests

The authors declare no competing interests.

Data Availability

Data supporting the findings of this study are available on reasonable request from the corresponding author [Seyi Samson Enitan], exclusively for non-commercial use and under a Data Usage Agreement.

Conflict of Interest

There is no conflict of interest reported by the authors.

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Author contribution

Study concept and design: TOA, OATA; Literature search: TOA, OATA, SSE, MOD & EJE Acquisition of data: TOA, SSE, MOD & EJE; Analysis and interpretation of data: TOA, OATA, SSE; Statistical analysis: SSE & EJE Study supervision: TOA & SSE; Drafting of the manuscript: TOA & SSE; Critical revision of the manuscript for important intellectual content: OATA, SSE, MOD & EJE; Final approval of the manuscript: TOA, OATA, SSE, MOD & EJE.

LARGE TABLES ARE PRESENTED IN THE NEXT PAGE

Tables

Table 4. Association between Dengue IgG antibody status and sociodemographic factors among the study participants

Variable	Categories	Negative	Positive	Total	Pearson Chi-Square (χ^2)	Df	p-value
Gender	Female	70(58.3)	2(1.7)	72(60.0)	1.296[a]	2	0.523
	male	41(34.2)	3(2.5)	44(36.7)			
	Others	4(3.3)	0(0.0)	4(3.3)			
Age range	<18yrs	20(16.7)	1(0.8)	21(17.5)	1.289[a]	4	0.863
	>50yrs	9(7.5)	0(0.0)	9(7.5)			
	18-25yrs	11(9.2)	0(0.0)	11(9.2)			
	25-40yrs	48(40.0)	3(2.5)	51(42.5)			
	42-49yrs	27(22.5)	1(0.8)	28(23.3)			
Marital status	married	64(53.3)	2(1.7)	66(55.0)	.996[a]	2	0.608
	single	45(37.5)	3(2.5)	48(40.0)			
	widow	6(5.0)	0(0.0)	6(5.0)			
Religion	Christianity	86(71.7)	4(3.3)	90(75.0)	.162[a]	3	0.983
	Islam	26(21.7)	1(0.8)	27(22.5)			
	others	2(1.7)	0(0.0)	2(1.7)			
	Traditional	1(0.8)	0(0.0)	1(0.8)			
Tribe	Hausa	1(0.8)	1(0.8)	2(1.7)	11.031[a]	3	0.012
	Igbo	23(19.2)	1(0.8)	24(20.0)			
	others	10(8.3)	0(0.0)	10(8.3)			
	Yoruba	81(67.5)	3(2.5)	84(70.0)			
Educational Status	None	8(6.7)	0(0.0)	8(6.7)	2.517[a]	3	0.472
	Primary	8(6.7)	0(0.0)	8(6.7)			
	Secondary	33(27.5)	3(2.5)	36(30.0)			
	Tertiary	66(55.0)	2(1.7)	68(56.7)			
Residential location	Rural	8(6.7)	1(0.8)	9(7.5)	25.032[a]	3	0
	Semi-Urban	17(14.2)	0(0.0)	17(14.2)			
	Semi-Urban	0(0.0)	1(0.8)	1(0.8)			
	Urban	90(75.0)	3(2.5)	93(77.5)			
Occupation	Civil servant	54(45.0)	2(1.7)	56(46.7)	24.477[a]	5	0
	Farmer	0(0.0)	1(0.8)	1(0.8)			
	Self-employed	33(27.5)	2(1.7)	35(29.2)			
	Student	14(11.7)	0(0.0)	14(11.7)			
	Teacher	4(3.3)	0(0.0)	4(3.3)			
	Unemployed	10(8.3)	0(0.0)	10(8.3)			

Table 5. Association between Dengue NS1 Antigen status and socio-demographic factors among the study participants

Variable	Categories	Negative	Positive	Total	Pearson Chi-Square (χ^2)	df	p-value
Gender	Female	71(59.2)	1(0.8)	72(60.0)	.672[a]	2	0.715
	Male	44(36.7)	0(0.0)	4436.7)			
	Others	4(3.3)	0(0.0)	4(3.3)			
Age range	<18yrs	21(17.5)	0(0.0)	21(17.5)	12.437[a]	4	0.014
	>50yrs	8(6.7)	10.8)	9(7.5)			
	18-25yrs	11(9.2)	0(0.0)	11(9.2)			
	25-40yrs	51(42.5)	0(0.0)	51(42.5)			
	42-49yrs	28(23.3)	0(0.0)	28(23.3)			
Marital status	Married	65(54.2)	1(0.8)	66(55.0)	.825[a]	2	0.662
	Single	48(40.0)	0(0.0)	48(40.0)			
	Widow	6(5.0)	0(0.0)	6(5.0)			
Religion	Christianity	90(75.0)	0(0.0)	90(75.0)	3.473[a]	3	0.324
	Islam	26(21.7)	1(0.8)	27(22.5)			
	others	2(1.7)	0(0.0)	2(1.7)			
	Traditional	1(0.8)	0(0.0)	1(0.8)			
Tribe	Hausa	2(1.7)	0(0.0)	2(1.7)	.432[a]	3	0.934
	Igbo	24(20.0)	0(0.0)	24(20.0)			
	Others	10(8.3)	0(0.0)	10(8.3)			
	Yoruba	83(69.2)	1(0.8)	84(70.0)			
Educational Status	None	8(6.7)	0(0.0)	8(6.7)	2.353[a]	3	0.502
	Primary	8(6.7)	0(0.0)	8(6.7)			
	Secondary	35(29.2)	1(0.8)	36(30.0)			
	Tertiary	68(56.7)	0(0.0)	68(56.7)			
Residential location	Rural	9(7.5)	0(0.0)	9(7.5)	.293[a]	3	0.961
	Semi-Urban	17(14.2)	0(0.0)	17(14.2)			
	Semi-Urban	1(0.8)	0(0.0)	1(0.8)			
	Urban	92(76.7)	1(0.8)	93(77.5)			
Occupation	Civil servant	56(46.7)	0(0.0)	56(46.7)	2.449[a]	5	0.784
	Farmer	1(0.8)	0(0.0)	1(0.8)			
	Self-employed	34(28.3)	1(0.8)	35(29.2)			
	Student	14(11.7)	0(0.0)	14(11.7)			
	Teacher	4(3.3)	0(0.0)	4(3.3)			
	Unemployed	10(8.3)	0(0.0)	10(8.3)			

Table 6. Association between Dengue IgMAb + NS1 Ag antigen status and sociodemographic factors among the study participants

Variable	Categories	Negative N (%)	Positive N (%)	Total N (%)	Pearson Chi-Square (χ^2)	Df	p-value
Gender	Female	69(57.5)	3(2.5)	72(60.0)	.447[a]	2	0.8
	Male	43(35.8)	1(0.8)	44(36.7)			
	Others	4(3.3)	0(0.0)	4(3.3)			
Age range	<18yrs	19(15.8)	2(1.7)	21(17.5)	5.830[a]	4	0.212
	>50yrs	8(6.7)	1(0.8)	9(7.5)			
	18-25yrs	11(9.2)	0(0.0)	11(9.2)			
	25-40yrs	50(41.7)	1(0.8)	51(42.5)			
	42-49yrs	28(23.3)	0(0.0)	28(23.3)			
Marital status	married	64(53.3)	2(1.7)	66(55.0)	.329[a]	2	0.848
	single	46(38.3)	2(1.7)	48(40.0)			
	widow	6(5.0)	0(0.0)	6(5.0)			
Religion	Christianity	87(72.5)	3(2.5)	90(75.0)	.115[a]	3	0.99
	Islam	26(21.7)	1(0.8)	27(22.5)			
	others	2(1.7)	0(0.0)	2(1.7)			
	Traditional	1(0.8)	0(0.0)	1(0.8)			
Tribe	Hausa	2(1.7)	0(0.0)	2(1.7)	2.291[a]	3	0.514
	Igbo	24(20.0)	0(0.0)	24(20.0)			
	others	9(7.5)	1(0.8)	10(8.3)			
	Yoruba	81(67.5)	3(2.5)	84(70.0)			
Educational Status	None	8(6.7)	0(0.0)	8(6.7)	3.646[a]	3	0.302
	Primary	7(5.8)	1(0.8)	8(6.7)			
	Secondary	34(28.3)	2(1.7)	36(30.0)			
	Tertiary	67(55.8)	1(0.8)	68(56.7)			
Residential location	Rural	8(6.7)	1(0.8)	9(7.5)	2.314[a]	3	0.51
	Semi-Urban	17(14.2)	0(0.0)	17(14.2)			
	Semi-Urban	1(0.8)	0(0.0)	1(0.8)			
	Urban	90(75.0)	3(2.5)	93(77.5)			
Occupation	Civil servant	56(46.7)	0(0.0)	56(46.7)	6.059[a]	5	0.301
	Farmer	1(0.8)	0(0.0)	1(0.8)			
	Self-employed	32(26.7)	3(2.5)	35(29.2)			
	Student	13(10.8)	1(0.8)	14(11.7)			
	Teacher	4(3.3)	0(0.0)	4(3.3)			
	Unemployed	10(8.3)	0(0.0)	10(8.3)			

Table 7. Association between Dengue IgMAb + IgGAb + NS1 Antigen status and sociodemographic factors among febrile patients

Variable	Categories	Negative N (%)	Positive N (%)	Total N (%)	Pearson Chi-Square (χ^2)	df	P-value
Gender	Female	66(55.0)	6(5.0)	72(60.0)	.925[a]	2	0.63
	Male	42(35.0)	2(1.7)	44(36.7)			
	Others	4(3.3)	0(0.0)	4(3.3)			
Age range	<18yrs	19(15.8)	2(1.7)	21(17.5)	2.377[a]	4	0.667
	>50yrs	9(7.5)	0(0.0)	9(7.5)			
	18-25yrs	10(8.3)	1(0.8)	11(9.2)			
	25-40yrs	49(40.8)	2(1.7)	51(42.5)			
	42-49yrs	25(20.8)	3(2.5)	28(23.3)			
Marital status	Married	61(50.8)	5(4.2)	66(55.0)	.530[a]	2	0.767
	Single	45(37.5)	3(2.5)	48(40.0)			
	Widow	6(5.0)	0(0.0)	6(5.0)			
Religion	Christianity	84(70.0)	6(5.0)	90(75.0)	.238[a]	3	0.971
	Islam	25(20.8)	2(1.7)	27(22.5)			
	Others	2(1.7)	0(0.0)	2(1.7)			
	Traditional	1(0.8)	0(0.0)	1(0.8)			
Tribe	Hausa	2(1.7)	0(0.0)	2(1.7)	4.745[a]	3	0.191
	Igbo	24(20.0)	0(0.0)	24(20.0)			
	Others	8(6.7)	2(1.7)	10(8.3)			
	Yoruba	78(65.0)	6(5.0)	84(70.0)			
Educational Status	None	8(6.7)	0(0.0)	8(6.7)	1.355[a]	3	0.716
	Primary	8(6.7)	0(0.0)	8(6.7)			
	Secondary	33(27.5)	3(2.5)	36(30.0)			
	Tertiary	63(52.5)	5(4.2)	68(56.7)			
Residential location	Rural	8(6.7)	1(0.8)	9(7.5)	1.682[a]	3	0.641
	Semi-Urban	17(14.2)	0(0.0)	17(14.2)			
	Semi-Urban	1(0.8)	0(0.0)	1(0.8)			
	Urban	86(71.7)	7(5.8)	93(77.5)			
Occupation	Civil Servant	53(44.2)	3(2.5)	56(46.7)	2.736[a]	5	0.741
	Farmer	1(0.8)	0(0.0)	1(0.8)			
	Self-Employed	32(26.7)	3(2.5)	35(29.2)			
	Student	12(10.0)	2(1.7)	14(11.7)			
	Teacher	4(3.3)	0(0.0)	4(3.3)			
	Unemployed	10(8.3)	0(0.0)	10(8.3)			

Table 8. Association between Dengue IgGAb and associated risk factors among the study participants

Enquiries	Categories	Negative	Positive	Pearson Chi-Square (χ^2)	Df	P-value	LR
Travel history	Ever lived abroad	6(5.0)	0(0.0)	.275[a]	1	0.6	0.524
	Never lived abroad	109(90.8)	5(4.2)				
Have you heard of Dengue Virus?	No	115(95.8)	5(4.2)				
What is the mode of transmission of Dengue Virus?	No Idea	115(95.8)	5(4.2)				
Do you have any history of Dengue Virus?	No	115(95.8)	5(4.2)				
Do you have mosquitoes in your environment?	No	9(7.5)	0(0.0)	.423[a]	1	0.515	0.797
	Yes	106(88.3)	5(4.2)				
Have you ever been bitten by mosquito before?	Yes	115(95.8)	5(4.2)				
Any history of blood transfusion before?	No	104(86.7)	4(3.3)	.580[a]	1	0.446	0.469
	Yes	11(9.2)	1(0.8)				
Do Use Mosquito net?	No	72(60.0)	4(3.3)	.624[a]	1	0.43	0.683
	Yes	43(35.8)	1(0.8)				
Do you stay out-door late?	No	91(75.8)	4(3.3)	.002[a]	1	0.963	0.002
	Yes	24(20.0)	1(0.8)				
Any source of stagnant water around you?	No	57(47.5)	1(0.8)	1.677[a]	1	0.195	1.803
	Yes	58(48.3)	4(3.3)				
How often do you go for medical check-up/laboratory test?	Less Often	26(21.7)	2(1.7)	.901[a]	2	0.637	0.827
	Much Often	22(18.3)	1(0.8)				
	Often	67(55.8)	2(1.7)				
How often do you practice self-medication?	Less Often	30(25.0)	3(2.5)	4.296[a]	3	0.231	5.63
	Much Often	27(22.5)	1(0.8)				
	Never	13(10.8)	1(0.8)				
	Often	45(37.5)	0(0.0)				

Table 9. Association between Dengue NS1 Ag and associated risk factors among the study participants

Enquiries	Categories	Negative	Positive	Pearson Chi-Square (χ^2)	Df	P-value	LR
Travel history	Ever Lived Abroad	6(5.0)	0(0.0)	.053[a]	1	0.818	0.103
	Never Lived Abroad	113(94.2)	1(0.8)				
Have you heard of Dengue Virus?	No	119(99.2)	1(0.8)				
What is the mode of transmission of Dengue Virus?	No Idea	119(99.2)	1(0.8)				
Do you have any history of Dengue Virus?	No	119(99.2)	1(0.8)				
Do you have mosquitoes in your environment?	No	8(6.7)	1(0.8)	12.437[a]	1	0	5.288
	Yes	111(92.5)	0(0.0)				
Have you ever been bitten by mosquito before?	Yes	119(99.2)	1(0.8)				
Any history of blood transfusion before?	No	107(89.2)	1(0.8)	.112[a]	1	0.738	0.212
	Yes	12(10.0)	0(0.0)				
Do use mosquito net?	No	75(62.5)	1(0.8)	.584[a]	1	0.445	0.918
	Yes	44(36.7)	0(0.0)				
Do you stay out-door late?	No	95(79.2)	0(0.0)	3.832[a]	1	0.05	3.169
	Yes	24(20.0)	1(0.8)				
Any source of stagnant water around you?	No	58(48.3)	0(0.0)				
	Yes	61(50.8)	1(0.8)				
How often do you go for medical check-up/laboratory test?	Less Often	28(23.3)	0(0.0)	4.253[a]	2	0.119	3.34
	Much Often	22(18.3)	1(0.8)				
	Often	69(57.5)	0(0.0)				
How often do you practice self-medication?	Less Often	33(27.5)	0(0.0)	7.635[a]	3	0.054	4.362
	Much Often	28(23.3)	0(0.0)				
	Never	13(10.8)	1(0.8)				
	Often	45(37.5)	0(0.0)				