

ZIKA VIRUS AND MALARIA PARASITE INFECTIONS IN FEBRILE PATIENTS' ATTENDEES AT PLATEAU SPECIALIST HOSPITAL, JOS, NIGERIA

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ABSTRACT

Febrile illnesses caused by mosquito-borne pathogens such as Zika virus (ZIKV) and *Plasmodium falciparum* remain a significant public health concern in sub-Saharan Africa, particularly in Nigeria, where surveillance for arboviral infections is limited. This study aimed to determine the seroprevalence of ZIKV and malaria parasite infections among febrile patients attending Plateau Specialist Hospital, Jos, Nigeria. A total of 100 febrile patients were enrolled in this study. Serum and blood samples were screened for anti-ZIKV IgG/M and *Plasmodium falciparum* antigen, respectively, using rapid diagnostic test kits. Socio-demographic and risk factors were also assessed through structured questionnaires. Out of the 100 participants, 3 (3.0%) tested positive for anti-ZIKV IgG, while 0.0% tested positive for anti-ZIKV IgM. *Plasmodium falciparum* antigen was detected in 17 (17.0%) of the patients. Socio-demographic variables such as sex, occupation, marital status, and educational level revealed the distribution of disease burden and were statistically significantly associated with ZIKV and malaria infections. Similarly, environmental and behavioral factors, including the use of mosquito nets, the application of insecticides, and the presence of stagnant water around the home, were significantly associated with ZIKV and malaria infections ($p < 0.05$). The low seroprevalence of ZIKV antibodies and the relatively high prevalence of *P. falciparum* highlight the continued endemicity of malaria in Nigeria. Furthermore, the presence of ZIKV antibodies signals the need for enhanced arboviral surveillance. Vector control measures and improved public health education remain critical in reducing the burden of mosquito-borne diseases in Nigeria.

Keywords: Zika, Malaria, Infections, Jos, Nigeria

INTRODUCTION

The worldwide spread of vector-borne diseases, especially in tropical and subtropical regions, has recently increased, with these diseases accounting for 17% of all infectious diseases and causing over 1 million deaths worldwide (Padilla et al., 2017; Osarumwense et al., 2022). Malaria and other mosquito-borne arboviruses (such as Dengue and Zika) are common vector-borne diseases of the tropical and subtropical regions, and due to similarity in onset symptoms, they are mostly misdiagnosed (Nassar et al., 2019; Mubashir et al., 2020; Katnap et al., 2020; Miri et al., 2021; Osarumwense et al., 2022). Approximately 40% of the global

population resides in malaria-endemic regions. The disease results in an estimated 1 to 3 million deaths annually, with African children representing 75% of total mortality (Duru et al., 2024). ZIKV infection and malaria are transmitted through the bites of mosquitoes of the genus *Anopheles* and *Aedes*, respectively. While these mosquitoes transmit infections that cause immense human suffering, they are not affected by these infections (WHO, 2021).

Zika virus has attracted global public health attention, especially following recent outbreaks across more than 50 countries in Africa, Asia, and the Americas, where it was linked to serious health outcomes (WHO, 2021). The virus has been associated with congenital abnormalities, most notably microcephaly, in neonates born to infected mothers, as well as fetal loss, stillbirths, and severe neurological deficits in infants (Plourde & Bloch, 2016). In adults, ZIKV infection has also been linked to neurological disorders such as Guillain-Barré syndrome, meningoencephalitis, and myelitis, underscoring its public health importance beyond mild febrile illness (Musso & Gubler, 2021). The World Malaria Report in 2021 published by WHO (2022) revealed 241 million cases of malaria in 2020, marking a 14 million increase from the previous year. Also, malaria caused an estimated 627,000 deaths in 2020, with more than half of the deaths in Africa, and Nigeria had the highest death rate at 31.9% (WHO, 2022). The risk of spontaneous abortions, premature births and stillborn children is 30% higher in pregnant women who contract malaria, because malaria parasites compete favourably with the foetus for nutrients in the mother's blood in the placenta. This leads to severe anaemia, which may result in poor oxygen supply to the unborn baby, causing low birth weight and a reduced chance of survival for the child. Pregnant women can transmit the dengue virus to their foetuses during pregnancy or around the time of birth, and this can lead to low birth weight, premature birth and foetal death (CDC, 2024).

In Nigeria, most cases of zika infection are underdiagnosed or misdiagnosed as malaria, typhoid or referred to as fever of unknown cause (Isa et al., 2021; Oderinde et al., 2024); as such, greater than 70% of febrile illnesses are treated presumptively as malaria, often without a laboratory evaluation for other possible causes of fever (Onyedibe et al., 2018). Arboviral infections and malaria are prevalent in Nigeria due to the established presence of mosquito vectors that transmit them and published reports on their prevalence, mostly reporting them as single infections (Ayorinde et

al., 2021; Duru et al., 2024); therefore, there is a need to explore different localities for an in-depth understanding of the infection rate. Generally, Infants, children under 5 years, pregnant women, travellers and people with HIV or AIDS are at higher risk of severe infection with malaria (CDC, 2024); hence, this study aims to determine the prevalence of zika and malaria infections among febrile patients attending Plateau Specialist Hospital, Jos, Nigeria.

MATERIALS AND METHODS

Study Area and Design

This was a hospital-based cross-sectional study conducted at the Plateau Specialist Hospital (PSH) in Jos, Plateau State, Nigeria. Plateau State is the twelfth largest state in the country by land mass, with an area of 26,899 km² and an estimated population of about three (3) million people (NPC, 2006). Plateau State sits at an average altitude of approximately 1,280 meters above sea level. Kaduna and Bauchi States border it to the North, Taraba State to the East, and Nasarawa State to the South and East. The state is situated in the Guinea Savannah zone and is characterized by a tropical climate with distinct rainy and dry seasons. These factors influence the prevalence of mosquito-borne diseases. Plateau Specialist Hospital is a tertiary healthcare facility serving the immediate population of Jos and surrounding local government areas.

Ethical Consideration and Consent

Ethical approval for the study protocol was obtained from the Health Research Ethics Committee of Plateau Specialist Hospital (NHREC/09/23/2010b). Written informed consent was obtained from all adult participants prior to enrolment in the study. For participants under the age of 18, assent was obtained in addition to informed consent from their parents or legal guardians. Participation was entirely voluntary, and confidentiality was maintained throughout the study.

Inclusion and Exclusion Criteria

Patients presenting with acute fever ($\geq 37.5^{\circ}\text{C}$ axillary) or a history of fever within the last 48 hours, who provided informed consent, were included, while patients who were critically ill and unable to give consent, and those who had received antimalarial or antiviral treatment in the preceding two weeks, were excluded.

Sample Collection and Processing

Approximately 5 mL of venous blood was collected from each enrolled participant by venipuncture using sterile, disposable syringes and transferred into EDTA and plain tubes (for serum separation). Blood samples were transported immediately to the Microbiology Laboratory of the Department of Microbiology, Faculty of Natural Sciences, University of Jos, for processing. Blood collected in plain tubes was allowed to clot at room temperature, and the serum was separated by centrifugation at 3000 rpm for 10 minutes. The resulting serum was aliquoted and stored at -200°C until serological analysis for ZIKV.

Serological Screening of Malaria Parasite and Zika Virus Infection

Malaria parasite infection was determined using a commercial Rapid Diagnostic Test (RDT) kit (SD Biosensor, Inc., India, Cat. No. 09MAL10D) following the manufacturer's instructions, with sensitivity between 99.4% and 99.7% and specificity between 99.5% and 100%. Briefly, a small volume of whole blood was

applied to the sample well, followed by adding 2 drops of the specified buffer solution. The results were read after 15 minutes. The RDT results were interpreted as positive (indicating the presence of *Plasmodium* antigen) or negative. Any result showing an invalid control line was repeated. At the same time, ZIKV infection was determined by screening for ZIKV-specific Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibodies in the collected serum samples. Commercially available rapid chromatographic kits were used following the manufacturer's instructions (Evancare Medical (Nantong) Co., Ltd., China), with sensitivity and specificity $>99.9\%$. A sample was considered positive for ZIKV infection if IgM antibodies were detected, and positive for past exposure if IgG antibodies were detected.

Data Analysis

Data collected were entered into SPSS version 27.0, and descriptive statistics, including frequencies and percentages, were used to summarize the socio-demographic and clinical characteristics of the study participants. The prevalence of ZIKV and malaria was calculated as a percentage. The association between infection status and demographic factors (age, sex) was assessed using the Chi-square (χ^2) test. Statistical significance was defined as a p-value < 0.05 .

RESULTS

A total of 100 febrile patients consented and were enrolled in this study. The results showed that 3.0% of the patients were seropositive for Zika virus IgG and 0.0% for IgM, while *P. falciparum* antigen was recorded in 17 (17.0%) of the patients (Figures 1 and 2).

Table 1 shows the seroprevalence of Zika virus infection and *P. falciparum* antigen based on socio-demographic variables. By age in the study population, Zika virus IgG was recorded in the 31–40 years age group. The seroprevalence of *P. falciparum* antigen was highest (50.0%) among those aged over 61 years, while the 21–30 age group had the lowest seroprevalence at 14.29%. Females showed higher cases of Zika virus IgG at 3.39%, while malaria parasite prevalence was higher in males at 19.51% compared to females. Married patients had a higher incidence of malaria parasites (21.67%) than singles (10.00%), whereas Zika virus infection was more common among single patients, with 75.00% getting infected. Those with primary education had the highest prevalence (13.33%) of Zika virus infection, while individuals with tertiary education exhibited a higher prevalence of malaria parasite infection at 20.75%. Based on occupation, Zika virus infection was more prevalent among students (12.50%), and malaria parasite infection was higher among patients in business (21.43%).

About 75% of patients reported regularly sleeping under an insecticide-treated bed net (ITN); 28% reported using indoor insecticides. 92% reported no stagnant water around their homes, and 46% were unsure of their genotype. Except for "type of genotype", all other risk factors assessed were statistically associated with Zika virus and malaria parasite infection at $P < 0.05$ (Table 2).

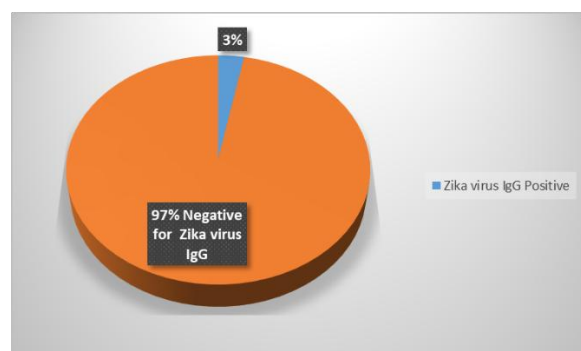


Figure 1: Seroprevalence of Zika Virus IgG antibodies among Febrile Patients in Jos, Nigeria

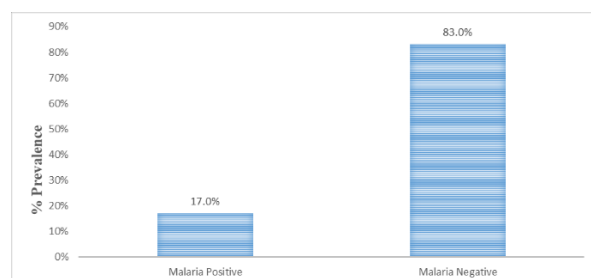


Figure 2: Prevalence of *Plasmodium falciparum* Antigen among Febrile Patients in Jos, Nigeria

Table 1: Socio-demographic Variables Associated with Zika virus Infection and Malaria among Febrile Patients in Jos, Nigeria

Variable	No. Examined	%Positive for Zika IgG	% Positive for Malaria Antigen
Age (Years)			
11-20	16	0(0.00)	1(6.25)
21-30	21	0(0.00)	3(14.29)
31-40	19	3(15.79)	4(21.05)
41-50	19	0(0.00)	7(36.84)
51-60	5	0(0.00)	1(20.00)
61>	2	0(0.00)	1(50.00)
χ^2		18.064	23.549
P-value		0.925	0.705
Sex			
Female	59	2(3.39)	9(15.25)
Male	41	1(2.44)	8(19.51)
χ^2		11.286	11.468
P-value		0.024	0.022
Marital Status			
Married	60	0(0.00)	13(21.67)
Single	40	3(7.50)	4(10.00)
χ^2		104.609	13.770
P-value		0.001	0.008
Educational Level			
7		0(0.00)	1(14.29)
None Formal	15	2(13.33)	2(13.33)
Primary	25	0(0.00)	3(12.00)
Secondary	53	1(1.89)	11(20.75)
Tertiary		16.348	12.279
χ^2		0.038	0.139
P-value			

Occupation			
Business	42	2(4.76)	9(21.43)
Civil Servant	36	0(0.00)	7(19.44)
Student	8	1(12.50)	1(12.50)
Unemployed	14	0(0.00)	0(0.00)
χ^2		15.978	16.862
P-value		0.043	0.032

Table 2: Risk Factors Associated with Zika Virus Infection and Malaria among Febrile Patients in Jos, Nigeria

Factor	No. Examined	%Positive for Zika IgG	% Positive for Malaria Antigen
Do you use a long-lasting insecticide-treated net?			
Yes	75	1(1.33)	12(16.00)
No	25	2(8.00)	5(20.00)
χ^2		13.554	11.383
P-value		0.009**	0.023**
Do you make use of Insecticides?			
Yes	28	1(3.57)	6(21.43)
No	72	2(2.78)	11(15.28)
χ^2		11.301	12.236
P-value		0.023**	0.016**
Do you have stagnant water close to your house?			
Yes	92	3(3.26)	3(37.50)
No	8	0(0.00)	14(15.23)
χ^2		11.714	13.281
P-value		0.020**	0.010**
What is your Genotype?			
AA	10	0(0.00)	1(10.00)
AS	44	2(4.55)	9(20.45)
Not Sure	46	1(2.17)	7(15.22)
χ^2		12.327	12.296
P-value		0.055	0.056

**Significant association.

DISCUSSION

Zika virus and malaria parasites are febrile-causing pathogens and a major public health burden in tropical and subtropical countries. In recent times in Nigeria, it is common to find patients receiving malaria and typhoid treatment as the major or the only cause of febrile illness. Zika virus is one of the flaviviruses associated with febrile sicknesses in the tropics and subtropical regions of the world. The use of rapid diagnostic test kits has the benefit of identifying the nonstructural protein 1 (NS1) antigen, as well as differential IgM/IgG antibodies to ZIKV and other viruses, in human blood (Gubler, 1996). In this study, out of the 100 participants, 3.0% tested positive for anti-ZIKV IgG, while none (0.0%) tested positive for anti-ZIKV IgM, indicating past exposure to the virus. This prevalence is lower than the 12% prevalence of ZIKV IgG reported

in Cross River State by Otu *et al.* (2020). The variation in the prevalence rate could be associated with differences in the sample size, study location and period of sample collection. The overall prevalence of malaria parasites in this study was 17 (17.0%). This is lower than 40.5% reported in South Eastern Nigeria (Uneke *et al.*, 2006), 43.1% reported in Rivers (Wogu *et al.*, 2018), 43.4% in Cameroon (Achonduh-Atijegbe *et al.*, 2016), and 27% reported by Abdulahi *et al.* (2009). Additionally, higher prevalence has also been documented: 85.7% in Enugu (Ayogu *et al.*, 2016), 71.4% in Cross River (Udoh *et al.*, 2013); 76% by Aribodor *et al.* (2003) and 62% by Onyido *et al.* (2011) in Azia and Umudioka communities in Anambra State, respectively. The disparity in prevalence could be related to changes in sample size and sampling procedures, as well as environmental parameters such as the research area's temperature and humidity. Also, variation could be attributed to government malaria intervention programmes or the distribution and use of Long-Lasting Insecticidal Treated Nets (LLINs). These LLINs are known to reduce malaria cases by 50% and decrease child mortality by 15-30% in settings with high coverage (Neeta *et al.*, 2009). The co-circulation of ZIKV alongside *Plasmodium* highlights the inadequacy of relying solely on clinical symptoms for diagnosis. Misattributing viral fever to malaria or typhoid leads to unnecessary usage of artemisinin-based combination therapies (ACTs), accelerating drug resistance and inflating healthcare expenditure. Even low-level circulation of Zika virus poses significant public health risks due to its capacity for teratogenic outcomes, including congenital Zika syndrome and severe neurological defects, which can compound the severe maternal anemia and adverse gestational risks associated with placental malaria. The concurrent presence of both pathogens underscores the need for integrated vector management strategies targeting both daytime-biting *Aedes* and nighttime-biting *Anopheles* vectors.

Socio-demographic factors, such as age, sex, occupation and marital and educational status, revealed a burden of ZIKV and malaria in Nigeria. The high prevalence of IgG in the 31–40-year age group is consistent with results from earlier studies by Matthew *et al.* (2016) and Kumar *et al.* (2015). A possible explanation for this observation could be the activity of the 31–40 age group during the early hours of the day, which exposes them to bites from Zika virus-carrying *Aedes* spp. mosquitoes more frequently. This could also suggest that adults manifest the disease less, as they become immune to the Zika virus. Considering the findings of Matthew *et al.* (2016) and the present study, there may be gender-related differences in Zika virus infection incidence, possibly due to differences in exposure (Kaplan, 1983; Ankrah *et al.*, 2019). The activity of females during the early hours of the day exposes a greater proportion of females to Zika virus-carrying *Aedes* spp. mosquitoes either at work or while travelling to and from work. This may also be attributed to possible differences in who sought medical care following symptomatic Zika virus infection. About 9 out of 10 participants reported stagnant water around their homes, and 72% did not use mosquito repellent or insecticide. These characteristics might predispose them to ZIKV and malaria parasite infections, as the immature forms of *Aedes aegypti* and *Aedes albopictus* mosquitoes are primarily found in water-filled artificial containers around habitats. Further research is required in this regard. Only 75% of participants reported regular use of LLINs, which falls short of the global target of greater than 80% of individuals in at-risk populations.

Conclusion

This study reported co-circulation of ZIKV alongside *Plasmodium*. This highlights the inadequacy of relying solely on clinical symptoms for diagnosis. The concurrent presence of both pathogens underscores the need for integrated vector management strategies targeting both daytime-biting *Aedes* and nighttime-biting *Anopheles* vectors.

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