



## **Parallel and Concurrent Infection of Dengue Virus and *Plasmodium falciparum* among Patients with Febrile Illnesses Attending Bingham University Health Centre, Karu, Nigeria**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Authors NKS and AOA designed the study, collected samples, performed laboratory and statistical analyses and wrote the first draft of the manuscript. Authors HIM and PGR designed and supervised the study, manage literature searches, wrote the protocols and managed the analyses of the study. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/IJTDH/2020/v41i1230340

#### Editor(s):

(1) Dr. Giuseppe Murdaca, University of Genoa, Italy.

#### Reviewers:

(1) Sudeep Khanna, Indraprastha Apollo Hospital, India.

(2) Riyadi Adrizain, Universitas Padjadjaran, Indonesia.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/60846>

**Original Research Article**

**Received 22 June 2020**

**Accepted 28 August 2020**

**Published 09 September 2020**

### **ABSTRACT**

**Aims:** This study was conducted to determine the parallel and concurrent infection of dengue virus and *Plasmodium falciparum* among patients with febrile illnesses attending Bingham University Health Centre, Karu, Nigeria.

**Study Design:** The study was a cross sectional study.

**Place and Duration of Study:** Department of Medical Microbiology and Parasitology, Jos University Teaching Hospital, Jos, Department of Microbiology, Nasarawa State University, Keffi and 68 Nigerian Army Reference Hospital, Yaba-Lagos, between February and July 2017.

**Methodology:** Blood samples were collected from 400 patients with febrile illnesses at the University Health Centre. The resulting sera was screened for dengue virus seromarkers (IgM, IgG and NS1) using Aria Dou dengue virus RDT kits (CTK Biotech, Inc, San Diego, USA) while malaria parasitemia was detected by Giemsa stained thick and thin film microscopy. Data collected were analysed using Smith's Statistical Package (version 2.8, California, USA) and *P* value of  $\leq 0.05$  was considered statistically significant.

**Results:** Of the 400 patients screened, 12(3.0%) were positive for dengue virus, 20(5.0%) for malaria parasite while 10(2.5%) for dengue/malaria co-infection. Infection with dengue virus and malaria parasite was found to be higher among female subjects aged  $\leq 30$  years. However, age and gender were not significantly associated with both infections in this study ( $P > 0.05$ ).

**Conclusion:** Our findings confirmed the presence of dengue virus infection in the study area which probably may have been misdiagnosed and mistreated. Hence, differential diagnosis of febrile illnesses should not only be limited to malaria and typhoid as is always the case in our health care centres.

*Keywords: Dengue; malaria; infection; febrile illness; Karu; Nigeria.*

## 1. INTRODUCTION

Dengue fever (DF) is a mosquito borne emerging infectious disease [1] caused by dengue virus (DENV), which is a single stranded positive +sense RNA belonging to Family Flaviviridae and genus *Flavivirus* [2]. *Aedes aegypti* and *aedes albopictus* are the day biting vector mosquitoes that are responsible for the transmission of all DENV serotypes which include DENV-1, DENV-2, DENV-3 and DENV-4 [3].

The disease is endemic to more than 100 countries in the tropical and subtropical regions of the world especially tropical Asia, Central and South America, Africa and the Caribbean [4,5,6]. This infection is rapidly expanding and its global footprint is a public health challenge with an economic burden [1,6].

The *Aedes aegypti* mosquito lives in urban habitats and breeds mostly in man-made containers, again unlike other mosquitoes it is a day-time feeder; its biting periods are early in the morning and in the evening before dusk [7]. Early signs and symptoms of dengue virus infection are indistinguishable from those of other tropical disease such as malaria and typhoid. However, infected individuals may be asymptomatic but sometimes they may present with dengue fever (DF), dengue hemorrhagic fever (DHF), or Dengue shock syndrome (DSS) [6,8].

The surveillance of dengue virus infection in Nigeria is affected by the lack of routine laboratory diagnosis which may include culture, polymerase chain reaction (PCR) and serological assays [9]. The true incidence and impact of

dengue fever in Nigeria is unknown and this could be attributed to the fact that it is not a reportable disease in Nigeria. Most cases are often, misdiagnosed as malaria or referred to as pyrexia of unknown origin [10]. In Nigeria where malaria is highly endemic most cases of febrile illness are likely to be treated as presumptive malaria some of which often resist anti-malaria and antibiotic treatment [11].

Dengue and malaria infections have similar geographical areas of distribution, and similar factors encourage the spread of both infections [7,12]. For instance, due to poor drainage system, poor environmental sanitation of the villages surrounding the University, the University is in its self-surrounded by bush and streams which may result in infestation of the day-biting mosquitoes that transmit dengue infection and night biting mosquitoes that spread Malaria. Thus an existence of high dengue burden where malaria is endemic may be expected. It is in view of this, that this study was carried out in Bingham University Health Centre, Nigeria to determine the Parallel and concurrent infection of dengue virus and *Plasmodium falciparum* among patients with febrile illnesses.

## 2. MATERIALS AND METHODS

### 2.1 Study Area

The study was conducted among patients that visited Bingham University Health Centre, Karu, Nigeria. This is a facility that provides health care services majorly to students and staff of the University and also to people living in the neighboring communities.

Bingham University is located around kilometer 25 Keffi-Abuja express way, Auta-Baleifi in Kodape District, Karu Local Government Area of Nasarawa State [13].

## 2.2 Study Population

The study population consisted of male and female adults Bingham University students, staff and members of the neighboring communities that accessed the University Health Centre from February to July, 2017.

## 2.3 Sample Size Determination

The sample size for this study was determined using the formula, Naing et al. [14] for sample size calculation a 0.05 level of precision.

## 2.4 Sample Collection, Processing and Storage

A total of 400 blood samples were collected from febrile in and out patients seeking medical care at Bingham University Health Centre, from February through July, 2017. About 3 ml of venous blood sample was collected from each participant aseptically into an EDTA container. The serum was obtained after centrifugation at 1,200 revolutions per minute for 5minutes [15]. The plasma was stored at -20°C until ready for use.

## 2.5 Laboratory Analysis

### 2.5.1 Detection of dengue virus seromarkers

All samples were screened for the presence of dengue virus Immunoglobulin G (IgG), Immunoglobulin M (IgM) and dengue virus antigen (NS1 Ag) using Aria Dou dengue virus rapid diagnostic test kit (CTK Biotech, Inc, San Diego, USA). The test was conducted and interpreted according to manufacturer's instructions.

### 2.5.2 Detection of malaria parasite

Malaria parasitemia was determined by Giemsa stained thick and thin film microscopy. Thick and thin blood films were prepared using clean grease-free non-silicate glass slides. The films were air dried without convection, and stained with 10% freshly prepared Giemsa stain. Thin blood films were fixed with 100% methanol prior to staining. The stained blood films were viewed under a light microscope at x1000 magnification

(X100 oil immersion lens). The diagnosis of malaria was based on the identification of asexual stages of *Plasmodium* on the thick blood smears, while thin blood smears were used to identify species of *Plasmodium*. If no parasite was seen, blood films were declared negative [15].

## 2.6 Data Analysis

The information obtained from the questionnaires and results of laboratory tests were analysed using Smith's Statistical Package (version 2.8, California, USA). Descriptive Statistics were presented in table and figure. Chi-square test was used to determine the relationships between the socio-demographic data and the prevalence of dengue fever and malaria. *P* value of  $\leq 0.05$  was considered statistically significant at 95% confidence interval.

## 3. RESULTS AND DISCUSSION

The epidemiology of dengue virus in most developing countries such as Nigeria is not clear [16]. This is because, most cases are often misdiagnosed and/or mistreated as presumptive malaria or typhoid some of which often resist anti-malaria and antibiotic treatment [10,11]. In this study, 400 patients with febrile illnesses attending Bingham University Health Centre were screened for dengue and malaria infection. Dengue virus IgM, IgG and NS1 were used as surrogates for the detection of dengue virus infection unlike most Nigerian studies [9,17,18,19] which were based on IgM seropositivity or positive NS1 antigenaemia.

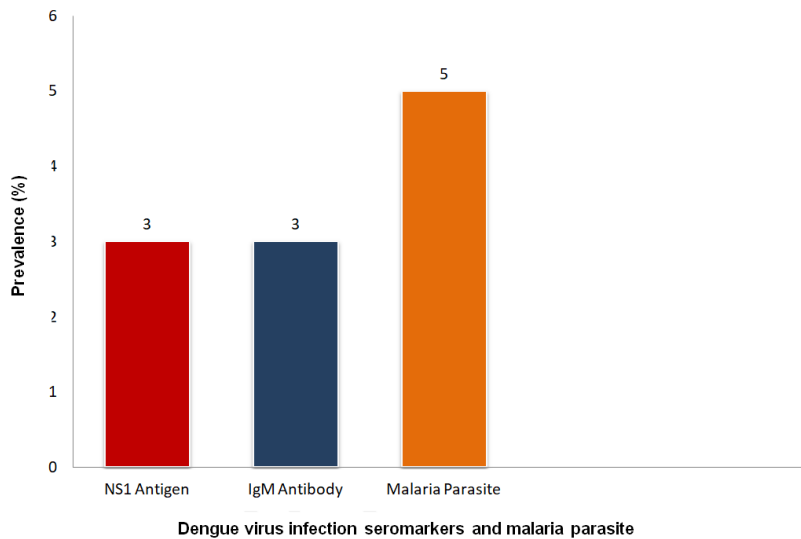
However, of the 400 patients screened in this study, 12(3.0%) were positive for both NS1 antigen and IgM antibody while none of the patient was positive for IgG antibody (Fig. 1). This is an indication that there was no past exposure to the virus in the study population (since IgG antibody was negative) rather positive cases (3.0%) were of acute and recent infection [10].

The recorded 3.0% prevalence of dengue virus infection in this current study is higher than most reports of studies conducted in the same region of the country (Northern region). For instance, the 2.3% reported by Onyedibe et al. [10] in febrile patients presumptively diagnosed of malaria in Maiduguri and Jos, 2.2% by Dawurung et al. [20] among febrile patients attending Specialist Hospital Jos and 1.8% by Idoko et al.

[9] among febrile patients in Kaduna. However, much higher prevalence rates were reported especially from the Southern region of the country. These include the 17.2% among apparently healthy individuals in Ogbomoso [17], 25.7% among febrile patients in Ile-Ife [19] and 35.0% among febrile patients in Ibadan [18]. Reports from other parts of Sub-Saharan Africa also showed higher prevalence between 21-26.3% of the viral infection [21,22,23]. The climatic conditions in the rainforest region of Southern Nigeria which support increased mosquito breeding than the dry Sahel region of Northern Nigeria may possibly account for the higher prevalence reported in Southern Nigeria and other parts of Africa [24]. The disparity in the

reported prevalence in different studies could also be as a result of the different methods of viral detection employed. Because while other studies [9,10,20] use RDT kits, others [21,23] uses molecular technique by PCR.

The lack of statistical significant association of dengue virus infection with age and gender in this study ( $P > 0.05$ ) is an indication that regardless of age and gender, all patients are equally susceptible to the virus (Table 1). However, the higher prevalence recorded among females of  $\leq 20$  years old in this study is consistent with the reports of other previous studies [19,25].



**Fig. 1. Prevalence of dengue virus infection seromarkers and malaria parasite among patients with febrile illnesses attending Bingham University Health Centre, Karu, Nigeria**

**Table 1. Parallel and concurrent infection of dengue virus and *Plasmodium falciparum* among patients with febrile illnesses attending Bingham University Health Centre, Karu, Nigeria in relation to age and gender**

Parameter	No. examined	No. positive (%)		
		Dengue	Malaria	Dengue/malaria co-infection
<b>Age (Years)</b>				
$\leq 20$	242	9(3.7)	12(5.0)	7(2.9)
21-30	116	3(2.6)	6(5.2)	2(1.7)
$\geq 30$	42	0(0.0)	2(4.8)	1(2.4)
Total	400	12(3.0)	20(5.0)	10(2.5)
p-value		0.1480	0.1305	0.2757
<b>Gender</b>				
Male	204	3(1.8)	8(3.9)	2(0.9)
Female	194	9(4.6)	12(6.2)	8(4.1)
Total	400	12(3.0)	20(5.0)	10(2.5)
p-value		0.0506	0.1916	0.1330

Nigeria suffers the world's greatest malaria burden [26]. Surprisingly, the result of this current study shows that only 5.0% of the study population was infected with malaria parasite (Fig. 1). Nevertheless, most previous studies reported higher prevalence of the parasitic infection in Nigeria [27,28,29]. The lower prevalence of the infection recorded in this study may be attributed to the fact that the study population is comprised of staff and students of a tertiary institution who may have some level of awareness about malaria and hence, may have taken some proactive measures in its prevention. It may also be because the study was conducted during the dry season which is unfavorable for the breeding of mosquito.

We also recorded higher prevalence of malaria among female patients of  $\leq 30$  years old (Table 1). Although there is no significant association between the infection with age and gender of the participants ( $P > 0.05$ ), there is no scientific evidence documented to prove the higher prevalence among younger female. However, other studies also reported similar observations [28,29].

In this current study, the prevalence of concurrent dengue and malaria infection was 2.5% (Table 1). However, the prevalence of concurrent infection in other Nigerian studies has been quite variable and range from 1.3% in Kaduna [30] to 2.8% within Ilorin metropolis [31] to 5.0% in Maiduguri and Jos and 10.7% in Uyo [32]. The result of this current study is very important because Nigeria is one of the countries that limit investigation of febrile illnesses to malaria and perhaps typhoid neglecting other viral infections. Generally, viral infections suppress the natural immunity of the host and this often allows opportunistic infections to set in [20]. Hence, the concurrent infection of dengue and malaria as observed in this study could be very devastating to the host. Therefore, by implication, it means that medical personnel need to distinguish between dengue virus infection and other causes of fever especially malaria for appropriate management as both infections have clinically indistinguishable symptoms [33].

Similarly, the concurrent dengue and malaria infection in this study was found to be higher among females aged  $\leq 20$  years (Table 1). However, just like the report of other previous researchers [10,31,32], this study did not recorded significant association between

concurrent dengue and malaria infection with age and gender ( $p > 0.05$ ). This is an indication that regardless of age and gender, all patients are equally at risk of the infections.

#### 4. CONCLUSION

This study recorded 3.0%, 5.0% and 2.5% prevalence of dengue virus, malaria and dengue/malaria co-infection respectively among patients with febrile illnesses attending Bingham University Health Centre, Karu, Nigeria.

The dengue virus and malaria parasite concurrent infection observed in this study which was found to be higher among females of  $\leq 20$  years calls for concern since both infections have clinically indistinguishable symptoms. Hence, there is need to include dengue virus infection in the differential diagnosis of febrile illnesses to avoid misdiagnosis and mistreatment of febrile infections.

#### CONSENT

Each participant was consented and socio-demographic information was obtained from them by the use of a designed questionnaire.

#### ETHICAL APPROVAL

Ethical clearance to conduct this study was obtained from Research and Ethical Committee of Bingham University Teaching Hospital Jos, Plateau State, Nigeria.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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