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SEROPREVALENCE OF DENGUE FEVER AMONG FEBRILE PATIENTS IN KASSALA STATE, EASTERN SUDAN

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ABSTRACT

Background: Dengue virus is a significant health threat in Sudan, with recurrent outbreaks affecting tropical and subtropical regions. **Objective:** The study aimed to investigate the epidemiological and serological test of DENV infection in Kassala state. **Methodology:** A cross-sectional study was conducted in 2023 among 273 febrile patients at Kassala state, Eastern Sudan. **Result:** Out of 273 blood samples, 100 (36.63%) tested positive for NS1 Ag. Male participants (70%) and urban residents (92%) exhibited significantly higher infection rates, with statistical associations with P. value < 0.05. Regarding clinical manifestations, certain symptoms were a high prevalent among DENV NS1 Ag-positive patients. Back pain 88(88%), Join pain 87(87%), skin rash 12(12%), sweating 79(79%), chills 71(71%), bleeding 11(11%), and polyarthralgia 69(69%). Moreover, significant correlations were found in headache, back pain, joint pain, skin rash, sweating, chills, bleeding, and polyarthralgia with (X2=43.374, P value = 0,001215), (X2= 18.23, P value = 0.001), (X2=18.749, P value = 0.0013), (X2= 13.404, P value = 0.00230), (X2=14.583, P value = 0.0025), (X2=56.133, P value = 0.001), (X2=19.829, P value = 0.000011), (X2=26,941, P value =0, 0021753), respectively. **Conclusion:** Dengue virus poses a significant health challenge in Kassala state, with 36.63% NS1 Ag positivity, predominantly among male and urban residents. Key clinical manifestations such as back pain, joint pain, and chills showed significant correlations with infection. Enhanced diagnostic efforts and targeted interventions are essential to combat dengue in this region.

KEYWORDS: engue, Seroprevalence, Kassala, Sudan, Fever.

INTRODUCTION

Dengue, identified by the World Health Organization (WHO) in 2019 as one of the most dangerous diseases, is supported by the numerous outbreaks reported in several countries.[1] It is a virus that spreads through mosquitoes and poses a significant risk to public health, causing significant socioeconomic problems in tropical and semi-tropical regions of the world.[2] According to the WHO, over 3.9 billion people in 128 countries are at risk of dengue fever, which has an estimated 390 million cases annually. However, the severity and prevalence of dengue fever can vary greatly by year and location.[3] The increase in dengue virus cases has been attributed to various factors, including insufficient mosquito control, global warming, and the worldwide population. Additionally, inadequate medical facilities have contributed to this increase. According to recent research, the virus infects about 100 million individuals globally yearly, resulting in around 22,000 deaths.[4] Dengue has been documented in 24 of the 54 African nations, and it has become widespread, causing frequent outbreaks. Since 1960, every subregion of Africa has experienced epidemics caused by each of the four-dengue virus (DENV) serotypes (DENV-1-4). In Sudan, Dengue fever was identified in 12 states between 1984 and 2015, with most cases diagnosed in Kassala and Port Sudan in eastern Sudan.[5] Different regions of Sudan have experienced multiple outbreaks of dengue fever (DF), with the eastern region being the most affected, encompassing Kassala and Port Sudan. The nation has

known endemic regions on its eastern coast and the western coast of the Red Sea.[6] In recent years, recurrent outbreaks of dengue fever, particularly its severe form known as dengue hemorrhagic fever, have occurred in various states throughout the year.[7] Dengue fever (DF) was previously confined to eastern Sudan, with documented cases dating back to 1906. However, in the past six years, the disease has spread to the country's western and southern regions due to social, physical, and environmental changes brought on by conflict and humanitarian crises. This has resulted in widespread outbreaks in refugee camps and elevated DENV to a major public health issue throughout Sudan. Various factors, including urbanization, trade, inadequate vector management, and international travel, are believed to contribute to the increase in DENV.[8] Dengue virus infection is influenced by various risk factors, including environmental conditions like standing water that serve as breeding sites for Aedes aegypti. Climate change has escalated transmission rates through increased rainfall and rising temperatures. Geographic location in urban endemic areas with high population density and poor sanitation, along with age and gender factors, contributes to susceptibility, particularly in children and young adults.[9] Additionally, dengue fever is associated with significant hematological changes, including thrombocytopenia, leukopenia, and hemoconcentration, primarily due to increased vascular permeability. Thrombocytopenia arises from immune-mediated destruction and bone marrow suppression, while leukopenia is a result of the virus's impact on bone marrow. Hemoconcentration, marked by elevated hematocrit levels, poses a risk of hypovolemic shock, making these changes vital for early diagnosis and severity assessment.[10]

In Sudan, the seroprevalence of DENV was reported to be approximately 27%, while estimates of dengue prevalence from cross-sectional studies conducted in communities and hospitals were 26% and 30%, respectively. The regional analysis found that seroprevalence estimates varied by 23%, 24%, 36%, and 43% in East, North, West, and Central Sudan, respectively.[11] Over the past several years, dengue epidemics have been more frequent in eastern Sudan, particularly in the Kassala state. Severe illness manifestations and fatalities have also been documented among some patients. The prevalence of dengue IgG and IgM antibodies in Kassala state was 9.4% and 0.6%, respectively.[12] According to recent findings, the results of enzyme-linked immunosorbent assays (ELISA) testing revealed that nonstructural (NS1) antigen (Ag) was present in approximately 23% of patients in Kassala state.

Dengue viruses (DENVs) belong to the Flaviviridae family, which comprises several viruses that pose a significant threat to public health, such as tick-borne encephalitis virus (TBEV), yellow fever virus (YFV), West Nile virus (WNV), and Japanese encephalitis virus (JEV). The DENV genome is composed of approximately 11 kilobases of positive-sense RNA.[13] Five serotypes of the DENV virus, namely DENV1, DENV2, DENV3, DENV4, and DENV5, are distinguished based on their antigenic features.[14]

Dengue virus (DENV) possesses a smooth surface, measures 40–60 nm in diameter, and features a nucleocapsid protein that spans 25–30 nm in size, encased within a lipid bilayer, as observed through electron microscope imaging. As a positive-sense, single-stranded RNA virus, DENV can directly translate its genetic material into proteins. The virus's genome, approximately 11 kilobases, encodes for three structural and seven nonstructural proteins. Approximately 65% of the amino acid sequences are shared among the different DENV subtypes. The structural proteins comprise Pre-membrane/membrane (prM/M), E, and C, while the nonstructural (NS) proteins include NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5. Additionally, the genome of DENV contains two untranslated 5 and 3 terminal segments. The virus consists of three domains that primarily interact with the host cell to facilitate invasion, and it is structured with the 495 amino acid Envelope (E) protein.[4]

Dengue fever, transmitted primarily by Aedes mosquitoes, has become a significant public health challenge worldwide. The WHO has categorized dengue as one of the most critical vector-borne diseases, particularly in tropical and subtropical regions.[15] The disease's resurgence in recent decades can be attributed to several reasons, including urbanization, climate change, and increased international travel. The WHO estimates that about 390 million dengue infections occur annually, with a substantial proportion leading to severe manifestations, including dengue shock syndrome and dengue hemorrhagic fever.[16]

Dengue fever outbreaks have been detected in previously non-endemic areas, raising concerns about its geographical expansion. This change emphasizes the need for a deeper understanding of the virus's transmission dynamics and the variables that affect its dissemination. Dengue fever is a global health and socioeconomic concern, with epidemics disrupting local economies and putting a straining on healthcare systems.[17,18]

Dengue virus (DENV) and other flaviviruses are capable of causing severe illnesses that range in severity from mild fever to life-threatening symptoms such as hemorrhagic, neurologic, and gastrointestinal issues. Following an incubation period of 4-10 days, during which an infected mosquito bites an individual, DENV infections can result in 2-7 days of clinical features. These features can include asymptomatic or undifferentiated fever, dengue fever (DF), or dengue hemorrhagic fever (DHF) with plasma leakage that may result in hypovolemic shock and dengue shock syndrome

(DSS). In the past, symptomatic DENV infections were classified into DF, DHF, and DSS according to the 1997 World Health Organization (WHO) classification guidelines until 2009.[19] Dengue fever, commonly referred to as "dengue without warning signs," often exhibits mild symptoms. In contrast, dengue hemorrhagic fever, which is characterized by severe symptoms and is commonly referred to as "dengue with warning signs," is characterized by severe symptoms.[20]

MATERIALS AND METHODS

A cross sectional study investigated the prevalence of DENV Kassala state, eastern. The study was carried out the outbreak in 2023. All patients with a fever were considered the population. The Health Research Ethics Committee approved this study in the Ministry of Health and Social Development, Kassala state. Informed consent was obtained from adult patients, parents, or legal guardians of children. Regarding the sample size, the report stated that 23% of febrile patients during the disease outbreak in Kassala state had DENV.[21]

The study involved obtaining acute-phase blood samples from individuals suspected of having dengue fever and seeking treatment and diagnosis at in Kassala state facility, Eastern Sudan. Participants provided their approval for the collection of blood samples. A volume of 5 ml of venous blood was collected strictly following aseptic measures and transferred immediately to a sterile ethylenediaminetetraacetic acid (EDTA) vacutainer tube. The plasma was then separated by centrifugation at 3000 rpm for 5 minutes at room temperature and placed in duplicate labeled eppendorf tubes.

SN1 Ag detection by rapid cassette: Samples were tested using On Site, Dengue Ag rapid test SD BIOSENSOR the device was labeled with the specimen ID number and 60µl of plasma or two drops were added to the specimen well. Immediately, 40µl or one drop of sample diluent was added to the center of the sample well with the bottle positioned vertically. Then, a period of 15 - 20 min was patiently waited to read the colored red lines, understanding the importance of this waiting period in the accuracy of the test.

Interpretation of Assay Result

Negative Result: If only the C lines were present, the test indicates that no detectable dengue NS1 Ag was present in the specimen. The result was non-reactive or negative.

Positive Control: If both lines were developed, the test indicates the presence of detectable dengue NS1 Ag in the specimen. The result was reactive or positive.

Invalid: If no lines develop, the assay was invalid, regardless of color developments on the T lines.

Statistical Analysis: The collected data in this study was computerized and analyzed using the statistical package for social sciences (SPSS) program version 28, Inc., based in Chicago, IL, USA. The results were interpreted using binary and logistic regression analyses, with a test employed to evaluate the relationship between variables. Odds ratios (OR) were calculated with a 95% confidence interval (CI), and statistical significance was established at $P < 0.05$. Numerical data was expressed in frequencies and proportions, while quantitative data was measured through recurrent responses and the calculating of the mean and standard deviation.

RESULT

Two hundred seventy-three participants from Kassala state were included in this study, and all of whom had experienced fever. The mean age with standard error of the participants was 30.4 ±0.84 years, ranging from 2 to 74 years.

All participants were included in the study and underwent NS1 Ag rapid testing to detect early infection during the acute phase of the disease. Among these participants, 100 (36.63%) tested positive for NS1Ag (Figure 1).

70 (70%) of the positive cases were male and 30 (30%) were female. The results indicated that male individuals had a significant correlation and a higher proportion of positive NS1Ag cases than female individuals ($X2 = 6.032$, $P = 0.015$) (Table 1). Regarding the age group and positive DENV NS1 Ag results, most patients (32%) were in the 30-40-year age group, followed by the 20-30-year age group (30%). No significant correlation was observed between the age group and DENV NS1 Ag ($X2= 6.782$, P value = 0.999) (Table 1). Most patients testing positive for DENV NS1 Ag resided in urban areas, accounting for 92(92%) of cases, while only 8(8%) lived in rural areas. Furthermore, a statistically significant correlation was observed ($X2=4.615$, P value = 0.03) (Table 1).

Regarding clinical manifestations, certain symptoms were a high prevalent among DENV NS1 Ag-positive patients. Headache 88 (88%), joint pain 87 (87%), back pain 88 (88%), skin rash 12 (12%), loss of appetite 80 (80%), sweating 79 (79%), chills 71 (71%), vomiting 9 (9%), bleeding 11 (11%), and polyarthralgia 69 (69%) were also observed. Moreover, significant correlations were found in headache, back pain, joint pain, skin rash, sweating, chills, bleeding, and polyarthralgia with ($X2=43.374$, P value = 0,001215), ($X2= 18.23$, P value = 0.001), ($X2=18.749$, P value = 0.0013), ($X2= 13.404$, P value = 0.00230), ($X2=14.583$, P value = 0.0025), ($X2=56.133$, P value = 0.001), ($X2=19.829$, P value = 0.0011), ($X2=26,941$, P value =0 ,0021753), respectively (Table 2).

Additionally, the link between mosquito net usage was 44 (44%), mosquito control 13 (13%), Disease awareness 12 (12%), family with the same signs 24 (24%), and past infection 5 (5%), among the NS1 Ag positive patients were not significant (Table 2).

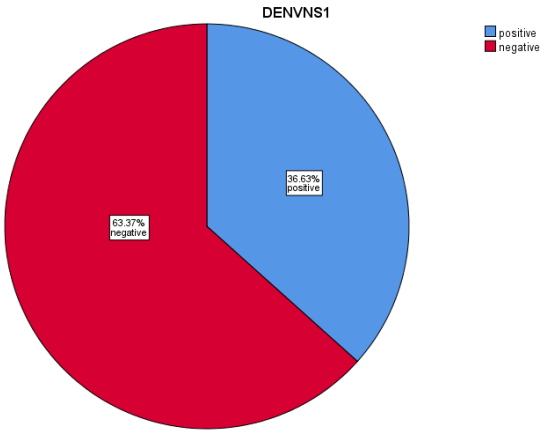

Figure: 1 Incidence of positive and negative results for the DENVNS1 Ag test.

Table: 1 Associations of Sociodemographic Variables of Participants and NS1 Ag in Kassala state.

Variables	Types	DENV NS1 Ag		Total 273 (100%)	X2	P
		Positive N (%) = 100	Negative N (%) = 173			
Gender	Males	70(70)	95(54.9)	165(51)	6.032	0.015
	Females	30(30)	78(45.1)	108(49)		
Age group	1-10	5(5)	13(7.5)	18(6.6)	6.782	0.999
	10-20	10(10)	21(12.1)	31(11.4)		
	20-30	30(30)	57(32.9)	87(31.9)		
	30-40	32(32)	41(23.7)	73(26.7)		
	40-50	14(14)	25(14.5)	39(14.3)		
	50-60	4(4)	11(6.4)	15(5.5)		
	60-70	5(5)	3(1.7)	8(2.9)		
	70-80	0(0)	2(1.2)	2(0.7)		
Educational Level	Illiterate	5(5)	10(5.8)	15(5.5)	1.848	0.78
	Primary	19(19)	35(20.2)	54(19.8)		0.97
	Secondary	43(43)	78(45.1)	121(26)		0.9 03
	University	30(30)	43(23.7)	73(28.3)		0.88
	Informal education	3 (3)	9(5.2)	12(4.4)		0.745
Residence	Urban	92(92)	143(82.7)	235(86.1)	4.615	0.032
	Rural	8 (8)	30(17.3)	38(13.9)		
Occupation	Self-employed	49(49)	67(38.7)	116(42.5)	4.920	0.076
	Housewife	22(22)	57(32.9)	79(28.9)		0.273
	Student	20(20)	33(19.1)	53(19.4)		0.538
	Farmer	1(1)	4(2.3)	5(1.8)		0.142
	Others	8(8)	12(6.9)	20(7.3)		0.208
Marital status	Single	31(31)	58(33.5)	89(30.4)	0.184	0.690
	Married	69(69)	115(66.5)	184(67.4)		

Table: 2 Associations of Symptoms of participants and NS1 Ag in Kassala State.

Variables	Clinical outcome		Total 273 (100%)	X2	P
	Positive N (%) = 100	Negative N (%) = 173			
Symptoms					
Headache	88(88)	83(48)	171(62.6)	43.374	0,001215
Fever	100(100)	173(100)	273(100)	0.155	1.000
Join pain	87(87)	108(62.4)	195(71.4)	18.749	0.0013
Vomiting	9(9)	7(4)	16(5.9)	2.819	0.111
Back pain	88(88)	172(99.4)	260(95.2)	18.229	0.001
Skin rash	12(12)	55(31.8)	67(24.5)	13.404	0.00230
Loss appetite	80(80)	136(78.6)	216(79.1)	0.074	0.878
Sweating	79(79)	163(94.2)	242(88.6)	14.583	0.0025
Chills	71(71)	173(100)	244(89.4)	56.133	0.001
Bleeding	11(11)	0(0.0)	11(6.6)	19.829	0.0011

Polyarthraglia	69(69)	63(36.4)	132(48.4)	26.941	0,0021753
Mosquito net use	44(44)	139(80.3)	183(67)	37.883	1.89
Mosquito control	13(13)	39(22.5)	52(19)	3.743	0.056
Disease awareness	12(12)	80(46.2)	92(33.7)	33.257	2.67
Family with same signs	24(24)	59(34.1)	83(30.4)	3.058	0.208
Past infection	5(5)	19(11)	24(8.8)	2.829	0.121

DISCUSSION

The objective was to assess serological prevalence of DENV infection and examine its correlation with various demographic, clinical, and hematological parameters. To achieve this, serological diagnostic method was utilized: NS1Ag rapid testing, which facilitated early detection of DENV during the acute phase.

In this study, a total of 273 blood samples were collected from febrile patients at Kassala Teaching Hospital, and NS1Ag rapid testing was conducted using an ICT test, with 100 samples (36.63%) testing positive for dengue fever. Several studies have reported varying rates of DENV NS1 Ag detection across different regions. Some areas showed lower prevalence rates when compared to other research. According to,[12] the prevalence was 9.4% in Kassala State; however,[22,23] found percentages of 16.3%, and 14.1% respectively, in India. Elduma et al.[11] estimated a dengue virus prevalence of 27% in Sudan, whereas Abbas et al.[24] and Eldigail et al.[21] found rates of 27.9% and 23.0%, respectively, in Red Sea State and Kassala State. In contrast, higher prevalence rates were found in several studies. One study in India found a significantly higher percentage of 62.8%[25], while another study in the nearby El-Gadarif State found a prevalence of 47.6%, as recorded via Eldigail et al.[26] The study revealed a notably high seroprevalence of dengue in Kassala, likely due to ongoing epidemics and favorable conditions for mosquito reproduction and disease transmission. Heavy rainfall in Kassala State further contributes to the surge in dengue cases.[26]

The present study found that most of the participants who tested positive for NS1 Ag were male (70%), with a significant correlation between gender and infection rate. This gender disparity aligns with studies conducted in Pakistan,[27–30] Males are more likely to be infected with DENV, possibly due to increased exposure to mosquito bites during outdoor activities and the differences in lifestyle of males and their greater exposure to the environment may lead to the infection more than females. Additionally, our data indicate that the majority of NS1 Ag-positive patients fell within the 30–40 year age group, followed closely by the 20–30 year group. These findings contrast with another study, conducted in Kassala state, which was higher among children and adolescents.[12] Other studies in India and Pakistan showed similar findings of a high disease rate in young people compared to children and elderly people.[30,31] This could be attributed to higher mobility and environmental exposure. The lack of a significant correlation between age and DENV infection in this study may be due to regional differences in mosquito exposure and population demographics. Studies in Africa have demonstrated a wider age range of dengue infections, which supports our finding of more evenly distributed age-related pattern.[32]

Interestingly, the findings showed that most (92%) of DENV NS1 Ag-positive individuals resided in urban areas, with a statistically significant correlation between urban residency and infection. This observation is consistent with other studies that have identified urban environments as high-risk areas for dengue transmission due to higher population density, stagnant water, and poor waste management, which create ideal breeding grounds for Aedes mosquitoes.[33–36] As observed in this study, rural typically report lower infection rates, likely due to reduced mosquito habitats and human-vector interaction.

Of note, all participants exhibited fever, and additional symptoms like headache, joint pain, back pain, and loss of appetite were also prevalent among NS1 Ag-positive patients. The high prevalence of these symptoms agrees with classical dengue presentation observed in endemic regions[37] Significant correlations were found for joint pain, back pain, skin, and bleeding, consistent with the systemic inflammatory response to DENV infection.[38] However, skin rash and bleeding observed in 12% and 11% respectively, of patients, are lower than in other studies, where it is a more common manifestation, suggesting possible regional or genetic variability in clinical presentation.

On the other hand, preventive measures such as mosquito net use, awareness campaigns, and mosquito control were recorded but showed no significant correlation with NS1 Ag positivity. This lack of association contrasts with studies in other endemic areas, where awareness and preventive strategies have been shown to reduce dengue incidence.[39,40] The discrepancy may be due to differences in the implementation and effectiveness of public health campaigns in Kassala compared to other regions.

CONCLUSION

NS1 Ag testing enhances DENV detection, with NS1 Ag identifying 36.63%. Dengue virus (DENV) remains a critical public health threat in Kassala, Sudan, with a significant infection rate, particularly among males and urban residents. Fever was universally present due to study criteria, significant correlations were observed between DENV infection and specific symptoms such as back pain, joint pain, skin rash, sweating, chills, and bleeding.

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