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Detection of Antibodies to Dengue Virus Infection among Eligible Blood Donors in Hadhramout Coast/Yemen

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Abstract: Dengue fever is a tropical and subtropical disease, it is one of the most common viral diseases in the world transmitted by the Aeades mosquito. Threat to blood transfusion transmitted dengue virus (DENV) has recently emerged worldwide, and the risk of transfusion transmitted dengue has been increasingly recognized. Blood donors in an endemic area like Hadhramout coast may serve as a potential vehicle for transmission of the DENV infection. So, this cross-sectional study was aimed to determine the seroprevalence of asymptomatic DENV infection and its antibodies among eligible blood donors in Hadhramout coast regions/Yemen. Serum samples were collected from 229 blood donors residents from the main hospitals in Hadhramout coast region. Our results revealed that 23(10%) and 73(32%) were seropositive for anti-DENV IgM and IgG respectively among the tested blood donors. The age group 30-39 years was the most prevalent of DENV infection, followed by the age group 20-29 years, high rate prevalence of DENV infection also was found in the urban areas, as well as all the geographical regions studied showed prevalence of DENV infection. Statistically, study revealed no significant correlation showed between complete blood count (CBC) profile results with positive and negative results of DENV infection among blood donors. In brief, high prevalence of asymptomatic DENV infection and its antibodies among blood donors increasing the importance of establishing blood screening for dengue disease at different blood donation services in Hadhramout coast to improve the guarantee of blood transfusions

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and control DENV dissemination. anti-DENV IgM among the tested donors reflects their ongoing asymptomatic viremic infection stage with DENV during blood donation time, whereas high seroprevalence of anti-DENV IgG reflects the endemicity of dengue disease in Hadhramout coast regions.

Keywords: Dengue Virus, Seroprevalence, Asymptomatic, Eligible Blood Donors, Hadhramout Coast

1. Introduction

Dengue has become a global problem since the Second World War and is common in more than 110 countries [1]. Each year, between 50 and 528 million people are infected and approximately 10,000 to 20,000 are die [2; 3;4].

DENV disease is the most prevalent arthropod-borne viral disease in the world. It is caused by a single-stranded ribonucleic acid (ss-RNA) arbovirus (arthropod-borne viruses) of the genus Flavivirus with five distinct antigen serotypes (DENV1-5) that are transmitted to humans through the bites of infected mosquitoes namely Aedes aegypti (A. aegypti) and Aedes albopictus (A. albopictus) [5;6].

The transmitted DENV replicates in humans within 3 to 14 days after biting [7], and its positive cases have a wider spectrum of clinical manifestations ranging from asymptomatic infection, which is the most common case to potentially fatal cases of DHF and dengue shock syndrome (DSS) due to plasma leakage, increased vascular permeability and homeostasis disorders [8;9].

In addition, the severe clinical forms of dengue disease are more likely to occur during a second infection with a different DENV serotypes from that which caused the primary infection [9;10], and this phenomenon is attributed to the enhancement effect of preexisting heterogeneous antibodies on maturation, virulence and replication of the second heterotopic DENV serotypes [11;12].

According to the World Health Organization (WHO) data, the current worldwide burden of dengue is about 2.5 billion infected people in more than 100 countries with approximately 20.000 fatal cases per year, and its global incidence is predicted to grow dramatically to affect about half of the world's populations [13].

The DENV is currently facing global attention as a potentially transmitted virus that threatens the safety of blood transfusion, and it has been detected in blood and blood products among donors with severe symptoms in parts of the world. Therefore, this study aimed to determine of the seroprevalence of DENV infections without symptoms by detection the antibodies of eligible blood donors serum in the main hospitals of Hadhramout coast-Yemen.

2. Materials and Methods

2.1 Study design

In this cross-sectional study, serum samples were collected from 229 blood donors residents in Hadhramout coast regions in the period from November 2018 to March 2019 obtained from the main hospitals in Hadhramout coast region included: Mukalla city: Ibn-Sina teaching hospital, maternity and child Mukalla hospital, university hospital for GYNOBST and pediatric, Hadhramout modern hospital, Al-Riyan specialized hospital and Al-Borj consultant hospital. Al-Shahr city: Al-Shaher general hospital. Ghail-Bawazer city: Ghail-Bawazer general hospital. All samples were screened for the detection of DENV anti-DENV IgM and IgG using enzyme linked immunosorbent assay.

2.2 Data collection tool

Data regarding the risk factors for DENV infection were collected using a standardized questionnaire consists of systematic questions schedule about study variables and filled with participants interview

2.3 Test and analysis for the detection of IgM and IgG antibodies

Blood samples were collected from blood donors in the main hospitals in Hadhramout coast and sent to the National Center for Public Health Laboratories to test by ELISA method Positive and negative results were identified in both blood samples. was the examination Performed using the Antibody Detection Kit in Applied Biosystems Tools according to the manufacturer's protocol.

2.4 Statistical analysis

Data statistical analysis were conducted using the software of Statistical Package for Social Sciences (SPSS) version 20. The graphs presented using the software program (Excel for Windows Microsoft) version 10. Descriptive statistics (frequencies, percentage, mean and stander deviation) for study variables were obtained and compared using t-test and one away ANOVA test. The association between different categories of the explanatory variables was measured and compared using Pearson Chi-square ($\chi 2$) test. The level of significance was set at P-value less than 0.05.

3. Results and Discussion

3.1 Results

Data distribution: Among the 229 blood donors samples they have negative results after screening for HIV, HBV and HCV infections, and they were accepted to donate blood, the age groups distribution as the following; 20-29 years 64(28.0%), 30-39 years 137(59.8%) and 40-49 years 28(12.2%). A total of 184(80.3%) and 45(19.7%) of blood donors were urban and rural residence respectively, while 169(73.8%) of blood donors were obtained from Mukalla city, 30(13.1%) from Al-Shehr city and 30(13.1%) from Ghail-Bawazer city.

3.1.1 Rate the prevalence of dengue virus infection

The total seroprevalence of DENV among blood donors was 91(39.7%). The results screening of IgM was 18(19.8%) represents recent infection, 68(74.7%) for IgG represents past infection, while mixed IgM and IgG was 5(5.5%), **Table 1**.

Table 1: Total seroprevalence of dengue virus IgM, IgG and mixed IgM and IgG among blood donors

Dengue antibody screening	No. of infected cases (%)
IgM	18 (19.8%)
IgG	68 (74.7%)
Mixed IgM and IgG	5 (5.5%)
Total	91 (39.7%)

3.1.2 Relationship of dengue virus prevalence with demographic variables

3.1.2.1 Relationship the prevalence of dengue virus infection with age groups and residence

The age group 30-39 years was the most prevalent of DENV infection, 14(61%) for IgM, 40(54.8%) for IgG, followed by the age group 20-29 years, 7(30%) for IgM, 26(35.6%) for IgG. There was no statistically significant association of DENV infection prevalence detected by IgM and, IgG with age groups.

High rate prevalence of DENV infection was found in the urban areas,18(78.0%) for IgM,and 62(85.0%) for IgG compared to the rural areas. There was no significant differences between urban and rural areas with DENV infection prevalence (**Table 2**).

Table 2: Frequencies and percentages the prevalence of dengue virus IgM and IgG antibodies among age groups of blood donors

Demographic Variables	Positive IgM		χ^2 test value	*P-value*	Positive IgG		χ^2 test value	*P-value*
	No.	%			No.	%		
Age groups								
20-29 years	7	10.9			26	40.6		
30-39 years	14	10.2	0.322	0.851	40	29.1	3.318	0.190
40-49 years	2	7.1			7	25		
Total	23	10			73	31.8		
Residence								
Urban	18	9.8			62	33.6		
Rural	5	11.1	0.071	0.790	11	24.4	1.425	0.233
Total	23	10.0			73	31.8		

3.1.2.2 Relationship of dengue virus prevalence with geographical regions

Regarding the geographical regions, all coastal cities enrolled the study showed high prevalence of DENV infection. For IgM detection test results, 19(82.6%), 2(8.7%) and 2(8.7%) were found in Mukalla city, Al-Sheher city and Ghail-Bawazer city respectively. For IgG detection test results, 46(63.0%), 14(19.2%) and 13(17.8%) were reported in Mukalla city, Al-Sheher city and Ghail-Bawazer city respectively. There was no statistical significant relationship between the prevalence of DENV infection and geographical regions of Hadhramout coast, **Table 3**.

Table 3: Frequencies and percentages the prevalence of dengue virus IgM antibody among the hospitals of the coastal Hadhramout cities

Hospital	Positive IgM		χ^2 test value	*P-value*	Positive IgG		χ^2 test value	*P-value*
	No.	%			No.	%		
Mukalla city	19	68			46	160.8		
Al-Shehr city	2	6.7	5.639	0.583	14	46.6	11.642	0.113
Ghail-Bawazer city	2	6.7			13	43.3		

3.1.3 Relationship of dengue virus prevalence and complete blood counts (CBC) profile

The mean and standard deviation of results of CBC profile of a symptomatic IgM and IgG positive and negative for dengue virus infection of blood donors were calculated. Statistically, there was no significant correlation showed between CBC profile results with positive and negative results of dengue virus infection, **Table 4**.

Table 4: Complete blood counts (CBC) profile for IgM and IgG results of blood donors

Type of test		Positive IgM	Negative IgM	t-test value	*P-value*	Positive IgG	Negative IgG	t-test value	*P-value*
Hb	Mean	14.65	14.69	0.163	0.871	14.70	14.69	-0.076	0.939
	SD	0.885	1.2			1.175	1.174		
PCV	Mean	42.11	42.54	0.417	0.677	41.69	42.88	1.805	0.072
	SD	4.2	4.7			4.33	4.80		
WBC	Mean	6465	6598	0.356	0.723	6728.7	6517.95	-0.873	0.384
	SD	2106	1657			1520.5	1782.0		
PLT	Mean	275.09	271.80	-0.230	0.819	276.88	269.9	-0.755	0.451
	SD	65.705	65.171			72.95	61.18		

Key: Hb: hemoglobin, PCV: packed cell volume, WBCs: white blood cells, PLT: platelets, SD: standard deviation

3.2 Discussions

Dengue is a neglected disease, and concern is focused on frequent dengue epidemics and crisis management of the disease rather than strategic surveillance to define true disease burden, which could lead to design and implementation of effective control measures. Nevertheless, blood screening tests for dengue disease among the donors have not been approved or established yet in our country. Therefore, this study performed to highlight the seroprevalence of DENV and its antibodies among eligible blood donors.

Our study results showed the seropositivity for anti-DENV IgM 10.0% and anti-DENV IgG 32.0% among the tested blood donors, whereas seropositivity for anti-DENV IgM/IgG was 5.5%. A similar agreement previous study was conducted in the Kingdom of Saudi Arabia using a single step multiplex RT-PCR together with IgM and IgG antibodies in serum samples for the diagnosis of asymptomatic acute dengue infection among eligible Saudi blood donors showed a high rate of previous exposure 32.6% and 5.5% of acute dengue infection among blood donors of IgG and IgM antibodies respectively [14]. So, it can be predicted that donors seropositive antigen DENV IgM antibodies in acute phase of asymptomatic infection at the time of their donation, this cases could act as silent vectors to transmit DENV to their corresponding recipients, while high prevalence of seropositivity of DENV IgG antibodies may indicate the past exposure to dengue virus infection [15].

Seropositivity for DENV IgM antibody among the tested blood donors in this study indicates their ongoing asymptomatic viremic infection stage with DENV during their donation time, whereas high prevalence of anti-DENV IgG seropositivity indicates high endemicity of dengue disease in Hadhramout coast regions. Other studies showed such donors were in a carrier stage of infection [15;16], whereas high prevalence of anti-DENV IgG antibody was 38.9% in the circulation of tested donors indicates the high endemicity of dengue disease [17].

In this study, the prevalence of DENV infection among blood donors in urban areas was higher than in rural areas. Increased prevalence of the DENV has been shown to be associated with areas where the rate of reproduction and the increase of A. aegypti mosquitoes are significant [18].

Securing the safety of blood transfusion and blood products for the recipients is a mandatory medical demand. In that respect, the risk of blood transfusion-transmission of DENV and/or its antibodies from donors to recipients has recently emerged and become an important clinical fact [19; 20; 8]. This is because more than 70% of DENV can be present for about 7 days in the blood of acute infected individuals without appearance of any symptoms of dengue during this period, and such asymptomatic DENV carriers may offer to donate blood [21]. Therefore, screening of DENV and its antibodies among blood donors and blood products at blood donation services may be a global demand to improve blood transfusion safety and control disease spreading and severity around the world [20;22]. With this concept, the Republic of Yemen, particularly, southeastern Yemen is endemic with DENV infection. However, more frequent outbreaks of dengue have emerged since 1994 [23], but some of these outbreaks were not well-documented or published. Yemen lacks quality healthcare service and adequate infrastructure facilities.

There are different laboratory approaches that can be used to detect the acute stages of dengue infection [20] In that regard, using direct virus isolation is a time-consuming, complex, and fastidious process that demands specialized viral isolation units, cells, and highly experienced staff. Similarly, application of PCR for quantitative detection of DENV-RNA and for diagnosis of early DENV infections is relatively expensive and also requires specialized equipment and difficult technical skills that make it an unaffordable routine diagnostic tool for large-scale blood banks or may not be available in resource-poor settings and in countries with limited financial resources [24].

Laboratory diagnosis of dengue disease is also done using antibody screening in the serum samples. The diagnostic window period is about 3 to 5 days for anti-DENV IgM antibodies and anti-DENV IgG antibodies are detectable after approximately 9 to 10 days [20].

Some studies revealed that the DENV is transmitted through blood products to prove that the DENV infection is endangering blood safety. A study in Hong Kong showed that a 76-year-old woman had low fever after two days of blood transfusion at Hospital. The fever was resolved automatically after 3 days and the patient recovered calmly, the blood product received by a non-accidental patient was donated at the time of donation but the symptoms of dengue appeared after one week of blood donation. An archived sample of the donation was positive for the DENV-1, post-infection blood transfusion. The women receiving the blood test were called IgM antibodies and was the first documented cases of DENV transmitted by blood transfusion [25].

Tambyah et al., (2008) conducted a study in Singapore consisting of three cases contaminated by a blood donor without symptoms of fever after donation of blood. An investigation of the blood product of the donor confirmed that it was positive for DENV type-2, In the stored blood sample, two days after blood transfusion, two of the three recipients had positive infection and were positive for type-2 DENV, whereas platelet recipients had no symptoms, but showed satisfactory evidence of DENV infection. Another study found that a rare case of DENV transmitted by blood transfusion. A 37 year old woman who had been shown to have a Hb concentration 10 days after hospitalization was treated with red blood cells RBCs. After four days of blood transfusion, the patient became infected with fever and continued for two days, showing that the patient showed thrombocytopenia. The serum test revealed that they had dengue. More tests showed that donor blood samples were positive for DENV-2 infection as transmitted by blood transfusion [26]. Another study showed blood recipients admitted to hospital and symptoms of dengue appeared three days after blood transfusion during the outbreak of dengue in Sao Paulo. The donor was found to be positive for the DENV a few days after the donation. It has already been transmitted to two patients, one of whom has developed DENV symptoms with high viral load laboratory evidence has shown that he acquired dengue virus infection through blood transfusion [27].

Other study conducted to evaluate the diagnosis of DENV by ELISA and compare it with IC test, the sensitivity was 84% and 94% for detection of IgM and IgG antibodies respectively, while specificity was 98% and 92% respectively [28]. Another study showed sensitivity to immunoglobulin assays to detect antibodies IgM and IgG was 100% in diagnosis of DENV and to distinguish between primary and secondary infection of the virus. Rapid IC was used to detect the antigen of NS1 virus and the IgM antibody in acute infection, and these tests showed high sensitivity and specificity in early diagnosis of the virus [29]. The ELISA technique was used to detect the IgM and IgG antibodies produced in the body during the viral infection of dengue with excellent sensitivity. The IgG standard classification of primary and secondary infections can be used for 100% primary infection and 96% for secondary infection. The ELISA technique is useful in the clinical diagnosis of DENV infection [30].

4. Conclusion

Our study revealed that there is a high prevalence of asymptomatic DENV infection and its antibodies among blood donors. The percentage of IgG titer was high, the IgM titer ratio was average. And 30-39 years old were the age groups of more prevalent with DENV infection among blood donors. Furthermore, urban areas were more prevalent of DENV infection. Also we found that Mukalla city was the most prevalent compared to other cities due to the population density and the presence of more blood transfusion centers.

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References

[1] S. Ranjit et al., " Dengue hemorrhagic fever and shock syndromes," Pediatric Critical Care Medicine, vol. 12, no.1, pp. 90–100, 2008.

[2] Whitehorn et al., " Dengue," British Medical Bulletin, vol. 95, pp. 161–173, 2010.

[3] J. et al., "The global burden of dengue: an analysis from the Global Burden of Disease Study 2013," The Lancet Infectious Diseases, vol. 16, no.6, pp. 712–723, 2016.

[4] M. Carabali et al., "Why are people with dengue dying? A scoping review of determinants for dengue mortality," BMC Infectious Diseases, vol. 15, pp. 301, 2015.

[5] A. Ashshi et al., "Sero-detection of Dengue virus and its antibodies among blood donors in the western region of Saudi Arabia: a preliminary study," Blood Transfusion, vol. 13, pp.135-238, 2015.

[6] S. Mardekian et al., "Diagnostic options and challenges for dengue and chikungunya viruses," BioMed research International, 83431, 2015.

[7] S. Stramer et al., "Dengue viremia in blood donors identified by RNA and detection of dengue transfusion transmission during the 2007 dengue outbreak in Puerto Rico," Transfusion, vol. 52, pp.1657–1666, 2012.

[8] E. Sabino et al.,"Transfusion-transmitted dengue and associated clinical symptoms during the 2012 epidemic in Brazil," Journal of Infectious Diseases, vol.213 no.5, pp.694-702, 2016.

[9] C. Vicente et al.,"Serotype influences on dengue severity: a cross-sectional study on 485 confirmed dengue cases in Vitória, Brazil," BMC Infectious Diseases, vol.16, no.320, 2016.

[10] J. Heilman J et al., "Dengue fever: a Wikipedia clinical review," Open Medicine, vol. 8, p. 105–115, 2014.

[11] W. Dejnirattisai et al., "Cross-reacting antibodies enhance dengue virus infection in humans," Science, vol. 328, p. 745–748, 2010.

[12] A. Schmidt et al., "Response to dengue fever—the good, the bad, and the ugly? The New England," Journal of Medicine, vol. 363, pp. 484–487, 2010.

[13] World Health Organization (WHO), Dengue and Severe Dengue, 2016.

[14] A Ashshi., " The prevalence of dengue virus serotypes in asymptomatic blood donors reveals the emergence of serotype 4 in Saudi Arabia," Virology Journal, vol.14, no.1, pp. 107, 2017.

[15] H. Faddy et al.,"Implications of dengue outbreaks for blood supply, Australia," Emerging Infectious Diseases, vol.19, pp.787–789, 2013.

[16] N. Harif et al., "Seropositive status of dengue virus infection among blood donors in North Malaysia," Asian Journal of Transfusion Science, vol. 8, no. 64, 2014.

[17] G. Jamjoom et al.,"Seroepidemiology of asymptomatic dengue virus infection in Jeddah, Saudi Arabia," Virology: Research and Treatment, vol.7, pp. 1-7, 2016.

[18] N. Gratz., "Critical review of the vector status of Aedes albopictus," Medical and Veterinary Entomology, vol. 18, pp. 215–227, 2004.

[19] P. Tambyah et al.,"Dengue hemorrhagic fever transmitted by blood transfusion," The New England Journal,vol. 359, no. 14, pp.1526-1527, 2008.

[20] M. Schmidt et al., "Emerging pathogens-how safe is blood? ," Transfusion Medicine and Hemotherapy, vol.41,pp.10-17, 2014.

[21] L. Dias et al .,"Detection of dengue virus in sera of Brazilian blood donors," Transfusion, vol.52, no.8, pp. 1667–1671, 2012.

[22] B. Pozzetto et al.,"Is transfusion-transmitted dengue fever a potential public health threat? ," World Journal of Virology, vol.4, pp. 113-123, 2015.

[23] A. Bin-Ghouth et al., "Dengue Outbreak in Hadhramout, Yemen, 2010," An Epidemiological Perspective, vol.86, no.6, pp. 1072-1076, 2012.

[24] S. Mangwana.,"Dengue viremia in blood donors in Northen India: challenges of emerging dengue outbreaks to blood transfusion safety," Asian Journal Transfusion Science, vol.9, pp. 177-180, 2015.

[25] V. Chuang et al.,"Review of dengue fever cases in Hong Kong during 1998 to 2005," Hong Kong Medical Journal, vol.14, pp.170-177, 2008.

[26] H. Oh et al.,"Bitten by a bug or a bag? Transfusion-transmitted dengue: a rare complication in the bleeding surgical patient," Transfusion, 55, 1655-1661, 2015.

[27] J. Levi et al.,"Real-time symptomatic case of transfusion-transmitted dengue," Transfusion, vol.55, no5, pp.961-964, 2015.

[28] M.Parida et al., "Evaluation of a dipstick ELISA and a rapid immunochromatographic test for diagnosis of Dengue virus infection," Acta Virololgy, vol.45, no.5-6, pp. 299-304, 2001.

[29] J. Karia et al., "Evaluation of commercial newer rapid test for detection of early acute dengue infection," National Journal of Medical Research, vol.1 no.2, pp.31-33, 2011.

[30] R.Narayan, et al., "Anovel indirect ELISA for diagnosis of dengue fever," Indian Journal of Medical Research, vol.144, no.1, pp.128-133, 2016.