International Journal of
Virology & Infectious Diseases

Research Article

Characterization of Dengue Infections by Using Hematological and Serological Markers -

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Submitted: 27 January 2020; **Approved:** 18 February 2020; **Published:** 26 February 2020

Cite this article: Salim S, Ahmad R, Hussain W, Afzal K, Munir T, et al. Characterization of Dengue Infections by Using Hematological and Serological Markers. Int J Virol Infect Dis. 2020;5(1): 001-004.

ABSTRACT

Methods: Two groups were selected by non-probability random sampling technique including case group of 154 patients with suspected dengue (fever>2days and <10days) and control group of 146 patients with febrile illness other than dengue. Clinical, hematological and serologic markers of cases and control groups were analyzed. The frequency distribution was used to compare categorical serologic markers and paired sample T test was applied for hematologic variables before and after treatment of dengue using SPSS version 21.

Results: A total of 154 cases of dengue (by using WHO calculator 154 suspected cases were defined fever >2 days and < 10days having hematologic and NS 1positive in earlier phase of disease) and 146 control cases were observed. Serology markers using NS1 dengue were detected positive in (85/154) 55%, dengue IgM in (46/154) 30% and both NS1 and dengue IgM in 15%(23/154) cases. Control group included malaria, enteric fever and febrile illness 103(71%), 30(20%), 13(9%) respectively. In cases 70(45%) were females and 85(55%) males with significant *p* value, while in control group 80(55%) were females and 66(45%) males with *p* value of < 0.05. For Hematological markers including platelets count, hematocrit and WBCs, paired sample T test showed high significant difference in value of platelets counts and hematocrit , while no significant difference in WBCS was observed.

Conclusion: Serological markers (NS1, IgM and IgG) greatly helps in diagnosis as well as prognosis of dengue infection, thereby helping not only in reducing the morbidity and mortality in patients but also helps controlling the epidemic by observing early preventive measures by using Hematological markers in earlier phase of disease. These marker will make utilized by other Asian and tropical African countries.

Keywords: Dengue fever; serologic markers; hematologic markers; Dengue infection; NS-1 antigen; IgM; IgG

INTRODUCTION

Dengue is febrile illness caused by four Dengue Viruses (DENV 1-4). This illness is transmitted by Aedes aegypti, Aedes albopictus [1,2]. World Health Organization (WHO) in 1997 first published 3 categories of classification of this disease as symptomatic dengue infection, Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) [3]. DF is break bone fever. The main symptoms of this fever are headache, myalgia retro-orbital pain, arthralgia, rash, leukopenia, hemorrhagic manifestations (petechial, Purpura, gum bleeding, epistaxis, hematuria, hematemesis, stool and vaginal bleeding) [4]. DHF is plasma leakage due to increase vascular permeability (hematocrit rise above baseline). DHF is classically characterized by fever, thrombocytopenia and hemorrhagic manifestation [4]. DSS is characterized by DHF plus circulatory failure manifestation by weak pulse, pulse pressure < 20mmhg and shock with hypotension. Dengue is also classified without warning signs as vomiting / nausea, rash, headache, myalgia, retro-orbital pain and leukopenia. And With warning signs of dengue areas abdominal pain, persistent vomiting, mucosal bleed, and fluid accumulation (ascites and pleural effusion), increase in hematocrit due to decrease in platelet count and organ failure [3]. Dengue fever is an infection effecting millions of people around the globe, particularly South East Asia. According to WHO, 2.5 billion people have DF and 1.3 billion people are at risk of DHF and DSS [5]. Aedes aegypti is widely distributed in South East Asia specially Pakistan, India and Sri Lanka where hyper endemic distribution of all dengue serotypes has been established [6]. Factors effecting transmission of DF are over population, poor urbanization, poor sanitation and increase in vector breeding places [7]. Diagnosis of DENV is done clinically and by laboratory testing. Clinical diagnosis is made by febrile illness manifestation and relevant epidemiological exposure (travelling from vector borne transmission area for week or 2). Laboratory diagnosis of DENV direct by viral component seen in serum (RT - PCR) and indirectly by serology (IgM and IgG). Non Structural Protein 1 (NS1) is positive in first week of infection and start declining after resolution of viremia [8,9]. Our research study is based on clinical assessment of dengue virus by using hemodynamic and serologic marker causing the epidemic in Pakistani population. We recently analyzed the dengue virus among local population in Pakistan and providing the better outcomes of patient management and disease control.

MATERIALS AND METHODS

This study was carried out at District Head Quarter Hospital (DHQ) Attock after approval by ethical research committee, DHQ Attock. The time duration was 10 months from January 2019 to October 2019.

All the suspected dengue patients confirmed by serology (NS1, IgM /IgG) were included in this research study as cases (dengue group) and, all other febrile illness (<7 days) like malaria, enteric fever, pyrexia of unknown origin were included in control group. Patients having prolonged fever (more than7 days) due to other viral/bacterial illness were excluded. Sampling technique was non probability random sampling.

Sample size according to WHO calculator was 300 as further divided 154 as cases and 146 as control group. Data including demographic data, clinical symptoms and hematological parameters including platelets count, WBC count and hematocrit (Pre and post treatment) were collected and compared between dengue group and control group patients admitted at DHQ Attock.

OPERATIONAL DEFINITION

Thrombocytopenia was defined as total platelets less than 100,000/ cu, mm. Leukopenia was defined as WBC less than 4000/ cu, mm. hematocrit determined when haemoconcentration is rise >20% above normal range.

The Hematological parameters collected from the patient samples at 1st day and 7thday of fever whereas performed at DHQ hospital laboratory Attock by using automated hematology analyzer (Siemen's ADVIA 2120).

The serological tests NS1, Dengue IgM/IgG were performed by using rapiGEN BIOCREDIT (an *in vitro* immunochromatographic assay) as per manufacturer instruction. Serological confirmation of dengue is done by positive NS1 antigen or seroconversion of IgM or fourfold rise in IgG.

RESULTS

Out of total of 154 patients in cases group, 55%(85/154) were positive for NS 1 antigen, 30%(46/154) for dengue IgM antibody and 15%(23/154) for both NS1 and IgM antibody. The control group included 71%(103/146) patients having malaria followed by 20%(30/146) enteric fever and 9%(13/146) were febrile illness other than these.

(Table1) Illustrates the clinical characterization of Dengue and control groups according to age and gender. Slightly high male ratio with low mean age with some significant difference were seen in case (dengue) group as compared to control group and mean ages in groups with higher in males and lower in females.

When compared the clinical symptoms between cases and control groups, dengue group and control group had Headache (48.7% *vs* 6%), Myalgia (34% *vs* 1%), Abdominal pain (6% *vs* 4%), Diarrhea (2% *vs* 4%), Chills 2(1% *vs* 34%), sore throat (9% *vs* 51%) as shown in table 2.

In table 3 statistical analyses of paired samples taken before and after treatment for hematological markers including platelet count, hematocrit and WBC count is shown. Mean, standard deviation, standard error of mean, T test of paired samples and *p* value for platelets, hematocrit and white blood cells were also shown in table 3. Statistically significant *p* value for platelets and hematocrit was obtained, while non-significant *p* value was noted for WBC count.

Table 1: Comparison of clinical characterization between cases and control groups.

	Cases (Dengue) Group (*n* = 154)	Control Group (*n* = 146)	*p* Value
Gender Female Male	 70 (45%) 84(55%)	 80(55%) 66 (45%)	 <0.05
Mean age (years)	27(15-67)	45(15-83)	<0.001

Table 2: Comparison of clinical presentation / symptoms between cases and control groups.

	Dengue (Cases) (*n* = 154)%Ages	Control Groups (*n* = 146)% Ages
Fever	154(100%)	146(100%)
Myalgia	53(34%)	2(1%)
Chills	2(1%)	53(34%)
Headache/Retro-Orbital Pain	75(48.7%)	10(6%)
Sore Throat	14(9%)	75(51%)
Diarrhea	4(2%)	3(4%)
Abdomen Pain	10(6%)	3(4%)

DISCUSSION

Dengue is one of the big challenges in tropical regions specially under developed countries, while travel-associated infections occur in developed countries like America [10].

It is most widely and rapid spreading disease in south East Asia specially Pakistan, Bangladesh region where tropic season is very common among July to September. The World Health Organization (WHO) reports it as emerging challenge of public health awareness [11].

The present study conducted at DHQ hospital Attock, Pakistan. Dengue patients and control patients were checked for both hematologic markers (Platelets, Hematocrit, WBCS) before and after treatment) and serologic markers to confirm dengue in clinical course of illness. Using demographic data of this research study, most of patients of dengue were male 84(55%) and less frequent were female 70(45%). In contrast to control group where female patients 80(55%) were observed more than males 66(45%) with high significant *p* value that was <0.005 in both groups.

Using clinical symptoms of cases and control group fever, myalgia, chills, headache, sore-throat, diarrhea and abdominal pain were 100% each, 34% and 1%. 1% and 34%, 48.6% and 6%, 9% and 51%, 2% and 4%, 6% and 4% respectively. Myalgia, headache and retrorbital pain were most common observed symptoms in dengue case group as compared to control group with other febrile illnesses in our study. Similar symptoms/findings has also been reported in patients with dengue fever in other retrospective study conducted at Thailand in 2018 by Juthatip [12].

In our study, serologic markers for diagnosis of dengue patients, including NS1antigen and IgM antibodies were detected positive either alone in 53% and 29% respectively or both (15%) in same patient. Similar results were also reported in other study conducted at Indonesia [13].

In this research study, control group comprised malaria cases (71%), enteric (21%) and febrile illness cases.

Hematologic markers platelets count, hematocrit and WBCs analysed before and after treatment revealed thrombocytopenia in dengue cases before treatment that recovered after treatment during convalescence and become within normal ranges. Mean, standard deviation, standard error of mean for platelets, hematocrit and, WBCs were observed and paired sample T test applied. The *p* value was observed significant for platelets and hematocrit (< 0.05) but not for WBCS (> 0.05). Similar results were also observed by other studies conducted at Indonesia by Alametal [14] and at Thailand by Chaloewong J, et al. [12] with significant *p* value or platelets and hematocrit. At the end we conclude that by evaluating dengue infection using simple, easily available serological and hematologic markers before and after treatment not only helps in diagnosis and

Table 3: Statistical Analysis by SPSS.

	Mean	Standard Deviation	Standard Error of Mean	95% Confidence Interval Lower	95% Confidence Interval Upper	T	Dif	*p* Value
Platelets counts	-192921	114904	9259	-211213	-174628	-20	153	0.00
Hematocrit	-6.5	33.57	2.7	-11.9	-1.253	-2.4	153	.016
WBCS	-1608766	4675	376.73	-905.39	583.3	-427	153	.670

prognosis of patients but also indirectly helps in limiting its spread by observing early preventive measures thereby reducing the epidemic and decreasing the.

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