Demographic Manifestations and Laboratory Findings among Patients with Dengue Infection in Port Sudan, Eastern Sudan

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Abstract: *Dengue fever (DF) is considered a non-severe manifestation of dengue, recently demonstrated a heterogeneous group of patients with varied clinical bleeding episodes. This is a case-control study was conducted to assess the bleeding manifestations in patients with dengue infection in Red Sea State, Sudan. Blood count, coagulation tests, and biochemical test markers were evaluated. Out of 334 patients confirmed dengue fever enrolled, 289 (86.5%) patients had classical dengue fever, 31(9.3%) patients had DHF I, 12(3.6%) patients had DHF II, and 2(0.6%) patients had DSS. Bleeding episodes were present in 35 (10.5%) patients. The commonest bleeding manifestations were haematuria (5.7%), haematamesis (0.3%), haemoptysis (0.3%), epistaxis (1.5%), and gum bleed (2.7%). Patients with severe bleeding episode had severe thrombocytopenia (P. value 0.000).*

Keyword: Dengue, dengue hemorrhagic fever, bleeding, Port Sudan

1. Introduction

Dengue virus is a mosquito-borne human viral pathogen, has recently become a major public health concern particularly in tropical and subtropical countries, predominantly in urban and periurban areas [1]. The incidence of dengue has grown dramatically over the world in recent decades. Over 2.5 billion people – over 40% of the world's population – are now at risk from dengue. WHO currently estimates there may be 50-100 million dengue infections worldwide every year. There are efforts continual on fundamental research on the genetic susceptibility of the host; pathogenesis of Dengue virus (DENV) associated thrombocytopenia, bleeding and plasma leakage [2]. Following DENV infection, bleeding can be fatal and severe thrombocytopenia contributes to it. Recently there have been reports of successful control of massive bleeding due to thrombocytopenia in two DENV patients [3]. Moreover, DENV infection can even lead to bone marrow failures [4]. The resurgence of dengue has been observed in Port Sudan, Red Sea State, Sudan and dengue outbreak have been frequently reported from different part of the states in both urban rural populations [5 - 6]. Dengue virus (DENV) is a mosquito-borne Flavivirus that is transmitted by mosquitoes such as *Aedes aegypti* or *Aedes albopictus*. Based on the antigenic difference, DENV can be divided into four different serotypes, DENV 1 – 4. DENV might lead to an influenza-like illness, which is called dengue fever or cause more severe dengue hemorrhagic fever (DHF) or dengue shock

syndrome (DSS). DHF is a severe febrile disease characterized by abnormalities in hemostasis and increased capillary leakage that can progress to blood pressure decrease, and hypovolemic shock (DSS) [7]. The various manifestations of dengue may not have a district line of demarcation: apart from the classic features, reports of rare presentations have recently become more frequent [8, 9]. Therefore, this prospective study has been undertaken to determine the demographic features and some laboratory findings between DF and DHF.

2. Material and Method

This study was conducted prospectively for a period from Feb/2013 to June/2014 during the recent outbreak of dengue in Port Sudan teaching hospital, Red Sea State, Sudan. This study consisted of three hundred thirty four patients positive with dengue infection. The inclusion criteria were all patients with clinical features and serologically positive dengue infection included. The exclusion criteria were includes patients with thrombocytopenia but serologically negative, patients with thrombocytopenia and no fever, and if routine laboratory testing suggested a bacterial, parasite or any viral infection other than dengue infection or any other disease. Hundred and one, apparently healthy normal individuals with no any clinical sign for dengue infection were selected randomly to be the control group. Blood sample were collected from all of the studied population. About 3 ml blood was placed in potassium ethylene diamine tetra

acetic acid (EDTA), 3 ml in citrate buffer and 3 ml was allowed to colt. Platelet and white cell counts were done using automated hematology analyzer (Sysmex KX-21N, B 7151, and MF 9/2008). Coagulation test were examined within 4 hours of collection using a semi-automated blood coagulation analyzer (bio bas-1 manufactured by RAL for SPINREACT, SN 536, Spain-European Community). Aspartate transaminase (AST) and alanine transaminase (ALT) were examined using spectophotomery (WP21B Tough biochemistry analyzer, mindary, China).

Patients were classified as dengue fever, dengue hemorrhagic fever or dengue shock fever according to WHO guidelines and laboratory diagnosis of dengue was established by demonstration of IgM and IgG Rapid strip test (BioTracer/BioFocus, REF: 17112, Exp.12/2015, Korea), sensitivity 95.6 and specificity 96.

3. Statistical Analysis

Statistical analysis was performed by frequencies, compare mean, and Chi Square test by using the Statistical Package for Social Sciences (SPSS 20.0 version, IBN. Chicago, USA). $P< 0.05$ considered significant.

4. Ethical Considerations

This study was approved by the regional Ethical Review Committee (ERC) and written informed consent was obtained from all the patients.

5. Result

This is a case control analytical study conducted in Port Sudan teaching hospital, Red Sea State, Sudan. The total number of the confirmed diagnosed dengue patients was 334. The age of the patients in this study was between 3 – 80 years (mean age 30 years). 101 individuals, age and sex matched, were selected as control group. The control individual aged between 6 – 76 years (mean age 22 years). Of the 334 clinical patients, (217) 65% were males and (117) 35% were female. In control group, (64) 63.4% were males and (37) 36.6% were females. Demographics data were obtained from patients with dengue virus infection include residence, tribes, and occupation. 27.25% was noted with high incidence of dengue virus infection in the eastern neighborhood (Selalab) (Figure1). The student was the most segment of occupational affected (34.74%), followed by traders (18.73%), and the house wife (18.13%). Table 1 illustrates that the overwhelming majority of dengue virus infection is among the Northern Sudan tribe (43.1%), followed by the Hadandwa tribe (21%), Bani amer tribe (18.3%), western Sudan tribe (14.7%), and the immigrants tribe (3%). The clinical demographic manifestations of the DF/DHF are summarized in table 2. Thrombocytopenia was found more severe with bleeding (P.value 0.000). Bleeding manifestations was observed in both DF and DHF patients (P.value 0.000) (Table 3). Severe bleeding was recorded in 35 (10.5%) cases of all dengue patients (Table 4). Bleeding manifestations included haematuria in 19(5.7%) cases, haematamesis in 1 (0.3%), haemoptysis in 1 (0.3%), epistaxis in 5 (1.5%) cases, and gum bleed in 9 (2.7%)

cases. The degree of thrombocytopenia along with bleeding clearly shows in table 5. Most of cases in the current study are dengue fever; followed by dengue haemorrhagic fever I (Table 6). In our study, per laboratory parameters, 177 (53%) patients had leukopenia; 279 (83.5%) had thrombocytopenia; 44 (43.6%) had raised AST and 22 (21.8%) had raised ALT enzymes; an altered coagulation profile (prothrombin time/partial thromboplastin time) and fibrinogen (FB) were found in 76(22.8%) and 61(18.3%) of the patients respectively shows in table 7.
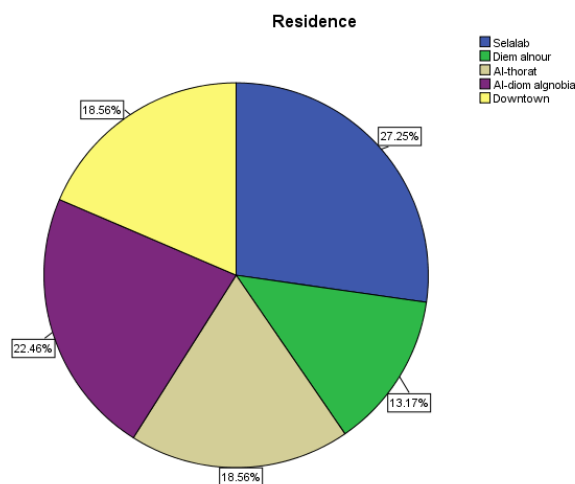
Figure 1: Residence distributions among the test group of the study

Table 1: Frequency of DF/DHF in different (Red Sea State) tribes

Tribe	Number	Frequency%
Western Sudan	49	14.7
Bani Amer	61	18.3
Northern Sudan	144	43.1
Hadandwa Immigrants	70 10	21.0 3.0
Total	334	100

Table 2: Clinical manifestations among the DF/DHF patients

Clinical data	Number of patients	Frequency	P. value
Rash (Purpura)	28	8.4 %	0.000
Fever	334	100 %	0.000
Joint Pain	262	78.2 %	0.000
Backache	198	59.3 %	0.000
Headache	282	84.4 %	0.000
Myalgia	156	46.7 %	0.000
Retro-orbital pain	69	20.7 %	0.000

Table 3: Hemorrhagic manifestations between DF and DHF*

Diagnosis	Bleeding manifestations		Total	P. value
	Yes	No		
DF	11 (31.4%)	279 (93.3%)	290 (86.8%)	0.000
DHF	24 (68.6%)	20 (6.7%)	44 (13.2%)	0.000
Total	35 (10.5%)	299 (89.5%)	334	

DF = dengue fever; DHF = dengue hemorrhagic fever

Table 4: Bleeding manifestations among thrombocytopenic patients

Platelet count	Patients with bleeding	Haematuria	Haematamesis	Haemoptysis	Epistaxis	Gum bleed ed	No bleeding
< 25.000	17	10	1	1	2	3	7
25 – 50.000	7	5	0	0	1	1	47
50 – 100.000	6	3	0	0	0	3	109
>100.000	5	1	0	0	2	2	136
Total	35	19	1	1	5	9	299

Table 5: Association of bleeding with thrombocytopenia

Platelet count	No. of Patients	Patients with bleeding	No bleeding
< 25.000	24	17	7
25 – 50.000	54	7	47
50 – 100.000	115	6	109
> 100.000	141	5	136
Total	334	35	299

Table 6: Demographic data of studied patients

Diagnosis	Number of Patients	Sex	
		Male	Female
DF	289 (**86.5**%)	190	99
DHF I	31 (**9.3**%)	16	15
DHF II	12 (**3.6**%)	11	1
DSS (DHF III)	2 (**0.6**%)	0	2
Total	334 (**100**%)	217	117

Table 7: Comparison of hematological parameters between DF and DHF

	DF	DHF	P value
Thrombocytopenia	234 (83.9%)	45(16.1%)	0.000
Leukopenia	156(88.1%)	21(11.9)	0.000
Abnormal PT/PTT	59(77.6%)	17(22.4%)	0.000
Fibrinogen level	46(75.4%)	15(24.6%)	0.000

6. Discussion

In this study, bleeding complication is the most common complication reported in patients with DF. Particularly, adult patients may present more bleeding manifestation than children [10], and bleeding manifestations in the adults may occur in the absences of plasma leakage [11]. These observations would raise at least two questions: first, that bleeding manifestations and plasma leakage may be two independent complications of dengue. Second, that the dengue hemorrhagic fever classification may underestimate some severe cases of dengue. In our study we are concentrating on the bleeding complication in patients with DF. Thrombocytopenia has been considered as a common important factor responsible for bleeding events in DF/DHF [12]. The current study showed that thrombocytopenia was strongly associated with bleeding; raising the hypothesis that thrombocytopenia is not only a laboratory changing in DF but also an important cause of bleeding, these fact explain the difference of those thought thrombocytopenia in DF is only a laboratory changed [12, 13]. Hematuria, bleeding gum, and epistaxis were more commonly with DHF patients during the acute phase of the illness, although previous studies reported conflicting data on the frequency of bleeding manifestations. Since hematuria, gum bleed, and epistaxis were also found in DF, a diagnostic value of these symptoms for the severity of the disease is limited [14]. Some limitations that may be found in this study, it is possible that some results have been influenced by the selection process and sample size. This is a case-control study and patients have been included as they presenting or not the outcome of interest. However, a greater number of patients could not be enrolled; this posed a problem to the selection process because some patients' possibly important clinical manifestations may have been missed. Of note, all patients with bleeding complications were selected from the hospital and presented potentially severe manifestations of dengue; less severe cases were not detected among patients with bleeding. Because of that, it is possible that the severity of the coagulopathy associated with DF with bleedings may have been overestimated. Liver enzyme elevation, a common feature in dengue fever [15] was also apparent in our study. In this study, AST levels were equal to or greater than those of ALT level in all of dengue infected patients, a finding that has also been reported earlier [16]. Viral hepatitis, rarely reported manifestation of dengue hemorrhagic fever [17], was not diagnosed in our patients. Deranged liver function in dengue infection can be a result of the direct effect of the virus on liver cells or the unregulated host immune response against the virus. An altered coagulation profile was observed in patients indicate the activation of both coagulation and fibrinolysis during dengue infection [18]. Although, there are common manifestations have been reported in this study. There are

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rare atypical manifestations should be considered in the future.

7. Conclusion

Our present data demonstrated a low incidence of DSS. Our data also show the differences in the frequency of clinical demographic symptoms, such as hematuria, epistaxis, bleeding gum in DF /DHF. Bleeding manifestations in patients with dengue infection was associated with thrombocytopenia.

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