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RESEARCH ARTICLE

DENGUE FEVER IN PORT SUDAN TERTIARY HOSPITAL, SUDAN

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ABSTRACT

Dengue fever (DF) is endemic in the Red Sea State, Sudan. The objective of this study was to describe the clinical and laboratory investigations of dengue in patients of Port Sudan teaching hospital, Sudan, from February 2013 to April 2014. About 334 patients were enrolled in this study. Their mean age was 30±15 years. Males outnumbered females by a ratio 1.9:1. Of them, 289 patients (86.5%) had classic dengue fever. 45 patients (13.5%) had dengue hemorrhagic fever (DHF), classified as 31 patients (9.3%) had DHF I; 12 patients (3.6%) had DHF II and two of them developed dengue shock syndrome (DSS) and died (0.6%). The common clinical demographic findings were high grade fever (100%), headache (84.4%), joint pain (78.4%), backache (59.3%), myalgia (46.7%), retro-orbital pain (20.7%), skin rash (8.4%) and hemorrhagic manifestations (10.5%). The significant laboratory findings were thrombocytopenia in (83.5%) patients, leukopenia in (53%) of patients, prolonged prothrombin time (PT) and partial thromboplastin time (PTT) in (9.0%) and (12.6%) of patients respectively. Reduced fibrinogen (FB) was noted in (18.3%) of patients. A strong positive correlation was showed between prolonged PTT and patients that developed bleeding episodes ($P < 0.000$).

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INTRODUCTION

Dengue fever (DF) is one of the world's major reemerging infections. In recent decades, there is an expanding geographical distribution of the virus and the mosquito vector, increased epidemic activity, and the emergence of dengue hemorrhagic fever (DHF) new geographical regions (Shahin *et al*., 2009). The dengue virus is an arthropod borne virus-arbovirus; belong to the family *Flaviviridae* and genus Flavivirus (Tsai TF, 2005). It is a mosquito borne viral infection which transmitted primarily by *Aedes aegypti* and sometimes by *Aedes albopictus* (Neeraja *et al*., 2006). Dengue (DEN) is composed of single-strand RNA and has five distinct serotypes of viruses, DEN-1, DEN-2, DEN-3, DEN-4, and recently DEN-5 (Mustafa MS, 2015). It is the most common arboviral infection which infects man (Park 2007). It is the second most important mosquito borne infection in terms of morbidity and mortality (Vijaykumar *et al*., 2005). The incidence of dengue fever has increased dramatically 30 fold in the world in recent decades, with over 2.5 – 3 billion people over 40% of the world's population are now at risk from dengue.

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World health organization (WHO) estimates there may be 50 – 100 million dengue infections worldwide every year, the disease now endemic in more than 112 countries in Africa, the Americas, the Eastern Mediterranean, South-east Asia, and the Western Pacific (WHO, 2012). Dengue infections vary in severity, ranging from influenza-like self-limiting illness to life-threatening dengue hemorrhagic fever and dengue shock syndrome (DSS) which, if left untreated, are associated with mortality (Karoli *et al*., 2012). In Sudan the disease presents in Khartoum, South Kurdofan, Kassala, and Port Sudan (Abdallah, 2012). Port Sudan is the main harbor of the Red Sea State, it has a high level of humidity and increasing water storage at homes increased mosquito breeding sites at the State and increasing the rate of transmission of dengue fever (Seidahmed *et al*., 2012). In the last years, Port Sudan faced many outbreaks. The dengue virus serotypes DEN-1 and DEN-2 were first reported in the 1986 in Port Sudan, while DEN-3 was recently identified in an outbreak (Malik *et al*., 2011). Since then, Port Sudan has become an endemic area with dengue virus (Ali, 2012). Unfortunately, due to short facilities serotyping of the virus was not done. This study designed for reporting the demographic, clinical and laboratory data along with the illness outcome of patients admitted to Port Sudan teaching hospital.

MATERIAL AND METHODS

Study site and population

This study was conducted on 334 patients diagnosed with dengue infection in Port Sudan teaching hospital, Sudan, from February 2013 to April 2014. The Port Sudan city is a coastal area for Red Sea State of Sudan. Red Sea State is located in the eastern part of Sudan having international boundaries with Egypt in the north, Eritrea in the south and the Red Sea in the east. The State also has national borders with Kassala State in the south and River Nile State in the west. It occupies 212000 km. The Total population of the State is estimated at 1.396.110 inhabitants, including the children between 0 to 5 years, numbering 150.104 (According to Sudan 5th census and EPI 2009). The State is divided in 10 localities. The biggest locality in terms of population is Port Sudan locality which divided into 3 administrative units eastern, middle and southern Port Sudan areas with a population of 517.338 according to 2008 estimates. Port Sudan teaching hospital is a governmental hospital which is regarded as tertiary care hospital. The hospital capacity was 380-beds, well-equipped, tertiary-level hospital. All age groups, including the pediatric patients are admitted there.

Study design

This is a descriptive, hospital-based study.

Study subjects

All patients presented to the emergency room with high grade fever, musculoskeletal pain and bicytopenia were admitted and fully investigated. The data studied included age, sex, tribes, clinical findings encompassing the bleeding tendency. The Investigation included platelet count, leukocyte count, hematocrit (Hct), hemoglobin (HB), and coagulation tests (PT, PTT and FB). Tests such as (serology for typhoid, serology for hepatitis A, B, C) was conducted for fever of unknown origin. Thick and thin blood films were examined for detecting malaria parasites. Any patient infected with these diseases was excluded from the research.

Study sample

Samples of all patients were collected into three blood containers. The first was K_3EDTA (tri-potassium ethylene diamine tetra acetic acid) blood containers for hematological parameters using semi-automated hematology analyzer (Sysmex KX-21N, B 7151, and MF 9/2008 Japan), the second was plain containers into which serum was extracted for assessment anti-dengue immunoglobulins (IgM) by enzyme-linked immunoassay technique. The third was the tri-sodium citrate containers from which plasma was used to detect PT, PTT and FB.

Criteria for dengue severity

Patients were classified as dengue fever, dengue hemorrhagic fever or dengue shock syndrome according to WHO guidelines and laboratory diagnosis of dengue was established by demonstration of anti-dengue immunoglobulins IgM (ELISA test Nova Tec Germany). This test had 98% sensitivity and 95% specificity.

Statistical analysis

Differences in laboratory data between patients with DF, DHF and coagulation tests were tested by compare mean and Chi-square test, whichever was appropriate. A *P.value* less than 0.05 were considered statistically significant. The Statistical Package for Social Sciences (SPSS 20.0 version, IBN. Chicago, USA) was used for data analysis.

Ethical considerations

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

RESULTS

Three hundred thirty-four confirmed dengue patients were included in this study. 217 (65%) were males and 117 (35%) were females (male to female ration was approximately 1.9:1. The mean age was 30 ± 15 years (range 3 to 80 years). All age groups, including children were admitted; the percentage of children up to 12 years was only 8.4%. Table 1 shows the different age distribution. Table 2 shows the comparison of different characteristic of study patients. According to the WHO classification system, most of cases in the current study are dengue fever 289 patients (86.5%); followed by dengue hemorrhagic fever I (31) patients 9.3%. 10 patients with DF had an unusual hemorrhage (3.5%) and 25 patients of DHF had clinical significant bleeding (55.6%) (Table 3).

Table 1. Age distribution of dengue fever patients

Age(Years)	Number of Patients (%)(Total = 334)
Up to 12	28 (8.4%)
13 – 20	69 (20.7%)
21 – 30	103 (30.8%)
31 – 40	60 (18.0%)
41 – 50	42 (12.6%)
> 50	32 (9.6%)

Table 2. Characteristics of patients in study

Characteristics	Patients *n=334*
Age (mean ± SD)	30 ± 15
(range)	3 – 80 y
Sex (male)	217 (65%)
(female)	117 (35%)
Demographic data	
Residence	
Selalab	91 (27.2%)
Diem alnour	44 (13.2%)
Al-thorat	62 (18.6%)
Al-diomalganobia	75 (22.5%)
Downtown	62 (18.6%)
Tribe	
Hadandwa	70 (21%)
Baniamer	61 (18.3%)
Northern Sudan	144 (43.1%)
Western Sudan	49 (14.7%)
Immigrants	10 (3%)
Occupation	
Students	115 (34.4%)
Traders	65 (19.5%)
House wife	60 (18%)
Other jobs	94 (28.1%)

Table 3. Classification results 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 4. Clinical findings among the DF/DHF patients

Clinical manifestations	n (%)
Fever	334 (100 %)
Headache	282 (84.4 %)
Joint Pain	262 (78.4 %)
Backache	198 (59.3 %)
Myalgia	156 (46.7 %)
Retro-orbital pain	69 (20.7 %)
Bleeding manifestations	35 (10.5%)
Hematamesis	1 (5.9%)
Hemoptysis	1 (5.9%)
Epistaxis	2 (11.8%)
Hematuria	10 (58.8%)
Gum bleed	3 (17.6%)
Rash (Purpura)	28 (8.4 %)
Mortality (two patients)	2 (0.6%)

Table 5. General findings among DF and DHF patients

Parameter	DF*n = 289*	DHF*n = 45*
Thrombocytopenia	234 (81%)	45 (100%)
Hemoconcentration	12 (3.6%)	12 (3.6%)
Anemia	40 (12.0%)	8 (2.4%)
Bleeding manifest	10 (3.5%)	25 (55.6%)
Prolong PT	27 (9.3%)	3 (6.7%)
Prolong PTT	32 (11.1%)	10 (22.2%)
Reduced FB	48 (16.6%)	13 (28.9%)
High FB	40 (13.8%)	8 (17.8%)
Leukopenia	156 (54%)	21 (47%)

Table 6. The significant test in studied parameters

Parameters	Test group Mean ± SD	Median test	Range test	P.value
TWBCsX10^9/l	4344±31	1	1-17	0.000
Platelet count X10^9/l	95.691± 57	95	3 – 443	0.000
Hematocrit (%)	34.89±7.0	36.0	10 – 49.7	0.002
Hemoglobin (gm/dl)	12.3±2.4	12.7	4 – 19.0	0.023
PT (second)	14.1±2.1	13.8	10–20.4	0.000
PTT (second)	33.5±9.7	32.4	15–80.7	0.000
FB (g/dl)	4.15±6.99	2.60	0.5 – 63.96	0.000

Table 7. Association of bleeding with thrombocytopenia

Platelet count	No bleeding	Patients with bleeding	No. of patients
< 25.000	7 (29.2%)	17 (70.8%)	24 (7.2%)
25 – 50.000	47 (87%)	7 (13%)	54 (16.2%)
50 – 100.000	109 (94.8%)	6 (5.2%)	115 (34.4%)
> 100.000	136 (96.4%)	5 (3.6%)	141 (42.2%)
Total	299 (89.5%)	35 (10.5%)	334 (100%)

The clinical demographic findings of the studied were fever (334,100%), headache (282, 84.4%), joint pain (262, 78.2%), backache (198, 59.3%), myalgia (156, 46.7%), retro-orbital pain (69, 20.7%), and rash (28, 8.4%). Bleeding manifestations were observed higher in DHF than in DF patients. Bleeding was recorded in 35 (10.5%) cases of all dengue patients. Bleeding manifestations included hematuria in 19(54.3%) cases, hematemesis in 1 (2.9%), hemoptysis in 1 (2.9%), epistaxis in 5 (14.2%) cases, and gum bleeds in 9 (25.7%) cases. Two patients presented with shock, both patients had gastrointestinal bleeding. Those patients died after three days in the intensive care unit because of irreversible shock (Table 4). The hematological parameters abnormalities were thrombocytopenia, anemia, hemoconcentration, leukopenia, prolonged prothrombin time, prolonged partial thromboplastin time, reduced and high fibrinogen are summarized in (Table 5). The significant were found to be in leukocyte count, platelet count, hematocrit, hemoglobin, prothrombin time, partial thromboplastin time, and fibrinogen level (Table 6). Severe thrombocytopenia was associated with bleeding (P< 0.000) and the degree of thrombocytopenia along with bleeding clearly shows in (Table 7).

DISCUSSION

This study indicates the special pattern of dengue fever in eastern parts of Sudan. The epidemics of dengue have been reported in different parts of the Sudan (Sohaier *et al*., 2014). Dengue virus (DEN) serotypes DEN-1 and DEN-2 were first reported in the 1986 in Port Sudan (Hyams *et al*., 1986), while DEN-3 was recently identified in an outbreak as a fatal case of DHF (Malik *et al*., 2011). Since then, Port Sudan has become an endemic area with sporadic outbreaks of dengue virus (Ali, 2012).The mean age of patients was 30±15 years. Internationally, dengue fever considered an infectious disease of children. So, the percentage of infected children in our study was 7.1%. Other reports from different area such as India, Indonesia and Thailand indicated that children may represent up to 95% of cases which is different from our findings and this may be due to our smaller sample size (Shahin W *et al*, 2009). The age pattern of dengue fever infection in Port Sudan is higher in adults, which is consistent with report from Brazil that dengue serotype happens more in adults (Teixeira Mda *et al*., 2005). This may be related to the genotype present. Females are less commonly affected than males (ratio 1: 1.9); while reports from different endemic area showed that males and females are affected equally (Nimmannitya, 1997; Chairufatah *et al.,* 2003). This may be due to their wearing hijab outdoors which covers the whole body. Regards to clinical demographic findings, high grade fever, headache, joint pain, and backache were the most common symptoms followed by gastrointestinal complication. Similar findings have been reported internationally (Shahin *et al*., 2009). Bleeding manifestations happened in 35 patients (10.5%). Similar reports were recorded internationally (Sung *et al*., 2003; Shahin *et al*., 2009). In the current study two patients presented with DHF III (DSS) and GI bleeding and died (0.6%). The lower percentage of incidence of DSS is perhaps attributed to limited number of cases. Bleeding has developed as a result from a combination of factors such as thrombocytopenia, coagulation defects andvasculopathy (Hoffbrand *et al*., 2011). Patients who showed bleeding were not necessarily those who had thrombocytopenia. Many factors con contribute to the onset of thrombocytopenia in dengue from a reactive immune response against platelets to decreased production (Saito *et al*., 2004). However, in this outbreak the majority of patients (279 (83.5%)) had thrombocytopenia a finding which is similar to Karoli *et al*. (2012). Leukopenia in our study was developed in both DF and DHF, this result is

positively correlated with Nimmannity (1999). Prolonged PT was demonstrated in (30/334; 9.0%) a result which agrees with Wills *et al*. (2009). Whereas prolonged PTT was observed in (42/334; 12.6%) a finding which is consistent with Wills BA *et al.* (2002). Fibrinogen (FB) also was observed to be reduced in 18.3% of patients and increased in 14.4% of patients. Wills B *et al*. (2009) in their study detected a reduction FB concentration in patients with dengue infection. The prevalence of dengue fever in Sudan is still not unique. Studies have described the presence of dengue in other areas of eastern Africa in Zanzibar (1870), Egypt (1927), Somalia (1982), Sudan (1986), Djibouti (1991), Ethiopia (1999), and Eretria (2005). The limitation of this study is due mainly to limit number of cases, no any ideas about virus sero-type or entomological picture are present. These issue should be taken into consideration in the future for further studies.

Conclusion

Dengue fever is considered an endemic disease in Port Sudan, Red Sea State, Sudan. Prevention and control to curb the spread of this disease should be taken.

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