CHARACTERISTICS OF DENGUE FEVER IN A LARGE PUBLIC HOSPITAL, JEDDAH, SAUDI ARABIA

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Background: This study aims to determine demographic, clinical and laboratory profile along with disease outcome of all confirmed cases of dengue fever (DF) and dengue hemorrhagic fever (DHF) admitted in King Abdulaziz Hospital & Oncology Center, Jeddah, Saudi Arabia. We also want to highlight the significance of implementing a well targeted community based disease prevention program. **Methods:** All patients admitted from May 2004 till April 2005 with a suspected diagnosis of DF and DHF were followed. All cases confirmed by a positive serology (IgM alone or IgM and IgG) to dengue fever were studied in detail to determine age, gender, ethnicity, monthly distribution, clinical and laboratory profile. **Results:** A total of 80 patients were admitted with a suspected diagnosis of DF. Among these, 39 (48.75%) patients were confirmed by positive serology to have the disease. Male to female ratio was 3.3:1. Their ages ranged from 2 to 60 years with a mean of 27.6 ± 11.2. Twelve patients were Saudis, while the rest were non-Saudis coming from different countries in Asia, Africa and Middle East. Maximum number of patients (48.72%) was seen in the summer months of June, July and August. Commonest presentation was fever (100%), headache (48.72%), myalgias (66.7%) and vomiting (25.64%). Rash, hemorrhagic manifestations and positive tourniquet test were relatively uncommon. Only two patients fulfilled WHO criteria of DHF. Main hematological abnormalities were thrombocytopenia (79.49%) and leucopenia (48.72%). Significant elevation of PTT was observed in 25.64% of patients. Abnormal liver function tests with high transaminases were seen in about 66.7% of patients, whereas 33.33% of patients had significantly elevated creatine kinase. All patients improved clinically with improvement of chemical and hematological parameters. None of the patients died in this series. **Conclusion:** DF continues to be a significant health problem in Western region of Saudi Arabia. Large number of pilgrims coming from disease endemic areas all over the world facilitates the continued introduction of dengue virus with different strains. Fortunately there has been no serious outbreak of dengue fever in recent years. A sharp vigilance is required by concerned authorities to prevent and minimize any future outbreak. It is extremely important to implement and maintain an effective, sustainable and community based disease prevention program.

Key Words: Dengue fever, Dengue hemorrhagic Fever, Headache, Rash, Thrombocytopenia

INTRODUCTION

Dengue Fever is a mosquito-borne viral illness. It is caused by one of the four serotypes of dengue virus, belonging to the family Flaviviridae and predominantly transmitted by Aedes Egypti and few other members of Aedes species.[1] It has recently emerged as a major international health problem with an expanded geographic distribution and potential to cause major epidemics.[2] The disease is mainly found in the tropical and subtropical regions around the world, mainly affecting the urban population. The disease is now endemic in more than hundred countries in Africa, Mediterranean region, South America and South East Asia.[3, 4]

Dengue fever was initially reported form Jeddah in 2001.[5] Since then reports of sporadic cases continue to be published in national media.

King Abdulaziz Hospital & Oncology center is a large public hospital in Jeddah and provides a referral center for other ministry of health hospitals in western region of Saudi Arabia. A significant number of patients were referred to this hospital with suspected diagnosis of DF in early 2004. This study was undertaken to prospectively analyze the demographic, clinical and laboratory features of confirmed cases of DF and DHF admitted in King Abdulaziz Hospital & Oncology Center, Jeddah from May 2004 till April 2005.

MATERIAL AND METHODS

This prospective study was carried out on all cases of dengue fever and dengue hemorrhagic fever admitted in King Abdulaziz Hospital & Oncology center, Jeddah, Saudi Arabia from May 2004 till April 2005. The case definition was based on compatible clinical history and examination based on WHO criteria[6], confirmed by positive serology to dengue fever. A specially designed Proforma with three sections was used for data collection. Section A of the Performa included demographic details including age, gender, ethnicity, residence, occupation and recent travel outside the Kingdom. Section B inquired about

details of clinical profile and examination. Section C recorded information on various parameters of blood count, coagulation profile and basic chemistry including creatine kinase and lactate dehydrogenase. Details of chest X-ray and other imaging tests were also recorded. Sera from all suspected cases were tested in the Central Laboratory of Jeddah for anti-dengue immunoglobulin (IgM and IgG) by Enzyme Linked Immunoassay (ELISA). Patients were confirmed to have DF or DHF, if IgM alone or both IgM and IgG were positive. These patients were prospectively followed for clinical and laboratory profile. All patients had complete septic screening including blood, urine and stool culture and the blood film was checked for malarial parasites in both thick and thin films. All the data was entered using a d-Base program and was electronically analyzed using SPSS version 7.5 software.[7]

RESULTS

Demographic Features: During the study period, 80 patients were admitted with suspected diagnosis of DF. Out of these, 39 (48.75%) were found to have positive serology (IgM or IgM and IgG) to dengue virus by ELISA. Among these 39 patients with confirmed diagnosis, 30 were males while the rest were females giving a male to female ratio of 3.3:1. Their ages ranged from 2 years to 60 years with a mean age of 27.6 ± 11.2 years. The age distribution is shown in Table 1. Twelve patients were Saudis, while the rest were non-Saudis coming from other Middle Eastern Countries, Africa and Asia .

Seasonal Distribution: The frequency of cases varied in different months (Table 2). Most of the cases (48.72%) were seen in the summer months of June, July and August.

Clinical Profile: Various clinical features are summarized in Table 3. Fever was the most common clinical presentation, occurring in all patients on presentation. There was no specific pattern of fever and height of fever ranged from 38 C to 40 C. Other common clinical features were headache (48.72%), myalgia (66.7%), vomiting (25.64%) and diarrhea (20.51%). A maculopapular and erythematous rash was seen in 6 (20.51%) patients.

Two patients fulfilled the WHO criteria[6] of dengue hemorrhagic fever, presenting with various combinations of fever, rash, gastrointestinal bleeding, gingival bleeding and homodynamic instability. Tourniquet test was positive in both of these patients. Both these patients also had severe thrombocytopenia (Platelet Count < 20,000 / mm3) and markedly prolonged partial thromboplastin time.

Hematological and Chemical Profile: The most common hematological abnormalities were thrombocytopenia and leukopenia (Table 4). Platelet count below 50,000 /cumm was seen in 23 (58.97%) patients. Nineteen (48.72%) patients had total white cell count below 4000/ cumm. A raise hematocrit of more than 20% was seen in 10 (25.64%) patients. Partial Thromboplastin time (PTT) was significantly prolonged in 10 (25.64%) patients, whereas prothrombin time was normal in all patients.

Liver enzymes, both Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) were significantly elevated in 26 (66.7%) patients. Only 5 patients (12.82%) had mild hyperbilirubinemia. Creatine Kinase (CK) of more than 175 U/L was seen in 13 (33.33%) patients. Septic screening with blood, urine, sputum and stool culture was negative in all patients. Similarly thick and thin blood film for malarial parasite was reported as negative in each patient.

Table-1: Age Distribution of Patients with Dengue Fever (n = 39)

Age Groups (Years)	Number of Cases (%)
0-10	3 (7.7)
11-20	6 (15.4)
21-30	15 (38.46)
31-40	10 (25.64)
41-50	3 (7.7)
> 50	2 (5.13)
Total	**39**

Table-2:Seasonal Distribution of Patients with Dengue Fever (n = 39)

Month	Number of Cases (%)
May 2004	3 (7.7)
June 2004	8 (20.51)
July 2004	6 (15.38)
August 2004	5 (12.82)
September 2004	2 (5.13)
October 2004	2 (5.13)
November 2004	2 (5.13)
December 2004	2 (5.13)
January 2005	2 (5.13)
February 2005	2 (5.13)
March 2005	3 (7.7)
April 2005	2 (5.13)

Course of the Illness: All patients were treated symptomatically with intravenous fluids and analgesics. Two patients with platelet count of < 20,000 /cumm required platelet transfusion. Patients with CK > 1000 U/L were given sodium bicarbonate infusion for urinary alkalinization. The duration of stay in the hospital varied from 4 to 23 days with average of 7.3 days. All patients improved symptomatically and had significant improvement of biochemical and hematological parameters (Table 5)

and were discharged home in a stable condition. None of the patient died in our series.

Table-3: Clinical Manifestations of Patients with Dengue Fever (n = 39)

Symptoms and Signs	Number of Cases (%)
Fever	39 (100)
Headache	19 (48.72)
Myalgias	26 (66.7)
Vomiting	10 (25.64)
Diarrhea	8 (20.51)
Rash	8 (20.51)
Gingival bleeding	2 (5.13)
Gastrointestinal bleeding	2 (5.13)
Positive tourniquet test	2 (5.13)
Jaundice	2 (5.13)
Drowsiness	1 (2.56)
Hepatosplenomegaly	1 (2.56)

Table-4: Profile of Abnormal Laboratory Investigations in Patients with Dengue Fever

Investigation	Number of Cases (%)
Hematocrit ≥ 20% of normal	10 (25.64)
Platelet count > 100,000 mm^3	8 (20.51)
Platelet count 50000 – 100000 mm^3	8 (20.51)
Platelet count < 50,000 mm3	23 (58.97)
White Blood Cells count < $4x10^3$ / mm^3	19 (48.72)
Total Bilirubin > 17 micromol / L	5 (12.82)
Aspartate Aminotransferase (AST) > 40 U/L	26 (66.7)
Alanine Aminotransferase (ALT) > 40 U/L	26 (66.7)
Creatine Kinase (CK) > 175 U/L	13 (33.33)
Lactate dehydrogenase (LDH) > 200Uu/L	8 (20.51)
Partial thromboplastin time (PTT) > 2-fold *versus* controls	10 (25.64)

DISCUSSION

Dengue viruses, belonging to the genus Flavivirus of the family Flaviviridae has antigenically four distinct serotypes, called DEN-1, DEN-2, DEN-3 and DEN-4. The virus is transmitted to the humane beings by the bite of infected Aedes Egyptii mosquito and few other members of Aedes species.[1] Dengue virus causes a broad spectrum of illness ranging from mild undifferentiated fever to classical dengue fever, as well as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Each serotype of the virus produces specific life-long immunity, but provides only short term cross immunity.[8] It is thought that these hetrologus antibodies from previous infections act as non-neutralizing antibodies in any subsequent infection with a different serotype of the virus and form new complexes with the new infecting serotype. These complexes can cause the antibody dependant enhancement of heterotypic secondary dengue infection.[9]

Table-5: Progress of Laboratory Abnormalities in Patients with Dengue Fever during the Course of Illness

Laboratory Finding	Day 1 of Admission No. of Cases (%)	Day 3 of Admission No. of Cases (%)	On Discharge No. of Cases (%)
Platelets > 100,000 / mm^3	8 (20.51)	8 (20.51)	24 (61.54)
Platelets 50,000 – 100,000 / mm^3	8 (20.61)	13 (33.33)	11 (28.20)
Platelets < 50,000 / mm^3	23 (58.97)	18 (46.15)	4 (10.26)
White Cell count > $4x10^3$ / mm^3	19 (48.72)	15 (38.46)	36 (92.31)
White Cell count < $4x10^3$ / mm^3	20 (51.28)	24 (61.54)	3 (7.70)
Hematocrit ≥ 20% of normal	10 (25.64)	5 (12.82)	0
Creatine Kinase > 175 U/L	13 (33.33)	6 (15.38)	0
High Partial Thromboplastin time (PTT) ≥ 2-fold verses normal	10 (25.64)	10 (25.64)	0

Epidemics of dengue has been reported from Arabian Peninsula in late nineteenth century affecting many major cities like Aden, Jeddah, Makkah and Madinah .[10] In 1984, a case of dengue hemorrhagic fever was reported from Yemen.[11] Dengue fever virus was first isolated in Jeddah in 1994 from a fatal case of DHF.[5] Since that time, all medical personnel in the area were alerted and a surveillance system was established by the ministry of health. From 1994 - 1999, a total of 207 cases of dengue fever, confirmed by serological methods were reported from a private hospital in Jeddah.[5] Since then, sporadic cases continue to be reported from Jeddah and Makkah regions in the local media. However, there has no report of a serious outbreak in the region.

In our series, eighty patients were admitted with suspected diagnosis of dengue fever. Among these, 39 patients (48.75 %) were confirmed to have the disease by the presence of IgM alone or IgM and IgG antibodies against dengue fever. A second sample for viral serology could not be taken in majority of patients due to various reasons. It is possible that some of the cases might have been missed. Majority of patients (76.92%) in our series were males. This is probably because the males are

more at risk of being exposed to mosquito bites due to occupational and recreational activities. Commonest age group involved were young adults varying from 20 to 40 years of age. There were very few children and no infant was affected in our series. This is contrary to most other reported studies from India, Sri Lanka and Thailand.[12-14] In fact in many countries, it is mainly a pediatric health problem. Most of the patients were admitted in the summer months of June, July and August. The reason for this are not entirely clear as Jeddah and surrounding areas have mainly dry and hot climate without much rainfall. One explanation may be increased travel of people during this period due to annual vacation of the children. In countries with abundant rainfall, the peak incidence is usually seen in the autumn months after monsoon season.[13]

Fever, headache, myalgia and vomiting are the most frequent symptoms, as has been observed in other studies.[12,15] Rash, hemorrhagic manifestations and positive tourniquet test were relatively infrequent in our study. Low proportion of positive tourniquet test in our patients may be due to dark skin color in some of our patients.[16] Only two patients fulfilled WHO criteria for DHF, mainly presenting with fever, petecheaii, gingival bleeding, hematemesis and melena.[6] Both patients were transfused with platelets, fresh frozen plasma and packed cells. These patients recovered completely, although fatalities have been reported elsewhere in this region.[5]

The most significant laboratory abnormality seen in our patients was thrombocytopenia, as observed in other studies.[17,18] This is thought to be due to depression of bone marrow observed in acute stage of dengue virus infection. Other explanations are direct infection of the megakaryocytes by virus leading to increased destruction of the platelets or the presence of antibodies directed against the platelets.[19] Coagulopathy is also frequent in most patients with dengue fever. In our study, prolongation of PTT was quite common, whereas PT was normal in all patients, as reported in other studies.[14,15] Disseminated Intravascular Coagulation (DIC) which is common in DF and DHF may account for prolonged PTT. The other important laboratory abnormality was raised liver enzymes seen in about 67% of our patients.[20] An interesting observation in our study is that co-infection with malaria and dengue was not seen. We did not have the facility for typing the dengue virus, although previous studies have confirmed the presence of three different serotypes in this region.[5]

To conclude, this study confirms the endemic occurrence of dengue fever in this region. Jeddah is a transit place for millions of pilgrims coming from all over the world to visit Islamic Holy places in Makkah and Madinah. This provides an ideal opportunity for introduction and exchanges of various infectious diseases including dengue fever among pilgrims and residents. It is extremely important that all concerned agencies should be on high alert to take all possible measures to prevent the spread of this potentially serious disease. Unfortunately it is not easy to control the spread of dengue fever. Effective disease prevention program should include vector control by chemical, biological or environmental measures. Purpose of the control is to reduce the vector density below which epidemic disease activity will not occur.[21] Any disease prevention program should also include education of medical community and the general population to reduce the impact of the epidemics. We should focus our efforts on sustainable community based environmental control rather than eradication.[22] In Jeddah and Makkah with high pilgrim traffic all year around, we need to promote dengue as a priority among health officials and other public administrators and also encourage active community participation for effective disease control.

Acknowledgement

We wish to thank Mrs. Salwa Al-Kholy, Infection control co-coordinator, for her assistance in date collection.

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