International Journal of Biomedical Research

ISSN: 0976-9633 (Online)
Journal DOI:10.7439/ijbr
CODEN:IJBRFA

Research Article

Epidemic of Dengue and Dengue Hemorrhagic Fever in Pakistan

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Abstract

Background: Dengue fever is a quickly emerging arboviral infection spread by *Aedes aegypti* mosquitoes with major public health consequences for millions of people around the world, particularly in rural South-East Asia and Asia-Pacific, according to the World Health Organization.

Objectives: To study the clinical presentations and laboratory findings of dengue and dengue hemorrhagic fever during the October to December 2011 outbreak in Islamabad / Rawalpindi, Pakistan.

Methods: We sampled 220 patients aged 14 years and above with confirmed dengue fever, presented in the outpatient and emergency department at Capital Development Hospital, Islamabad from October to December 2011. All patients were inlucded in the survery during a dengue outbreak in Islamabad and Rawalpindi area, and were studied for clinical and laboratory findings of dengue and dengue hemorrhagic fever. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS, Version 13.0).

Results: The most common symptoms were fever (100%), myalgia (100%), vomiting (86%), skin rash (53.7%), joint pain (20%), retro-orbital pain (18%), and headaches (13%). Moreover, in 10% of cases bleeding (epistaxis, melena and hematemesis) occurred. Routine laboratory findings were leucopenia (100%), thrombocytopenia (100%), proteinuria (96%), raised ALT (60%), AST (40%) and ECG changes (2.5%). The diagnosis was confirmed by ELISA detection of dengue virus immunoglobulin M antibodies.

Conclusion: High grade fever with myalgia, leucopenia and thrombocytopenia were characteristic features of dengue fever, and additionally, hemorrhagic manifestations indicated dengue hemorrhagic fever.

Keywords: Dengue fever, arbovirus, *aedes aegypti*, hemorrhagic fever, myalgia, joint pain, thrombocytopenia, leucopenia, proteinurea, immunoglobulin

1. Introduction

Dengue is an acute infectious disease of viral etiology. It is an ancient disease that has re-emerged in the past 20 years with an expanded geographic[1]. The world health organization (WHO) estimates that 50 million dengue infections occur each year, and that approximately 2.5 billion people live in dengue endemic countries. Pakistan has received a number of dengue fever outbreaks since 1992. [2]

Dengue virus belongs to the family Flaviviridae and has four serologically distinct serotypes (DEN-1, DEN-2, DEN-3, and DEN-4). These serotypes are distinguishable by complement-fixation and neutralization tests[3,4]. Infection with one serotype confers long-term immunity only to that serotype and therefore persons may be infected up to four times [5].

Dengue virus is transmitted by mosquitoes of the genus Aedes, such as Aedes aegypti and Aedes albopictus. Aedes aegypti is an efficient vector because it is highly susceptible to dengue virus, feeds preferentially on human blood, and is a daytime feeder[6]. After an infected mosquito has bitten a person, the virus replicates in regional lymph nodes and is disseminated through the lymphatic system and blood to other tissues. Replication in the reticuloendothelial system and skin results in viremia[7].

The incubation period ranges from 3 to 14 days, averaging 4 to 7 days. Infection with dengue virus of any of the four serotypes causes a spectrum of illness, ranging from no symptoms or mild fever, to severe and fatal hemorrhage, depending largely on the patient's age and immunologic condition[6].

The aim of the study was to assess the serological results and clinical presentation in patients with dengue and dengue hemorrhagic fever.

2. Materials and Methods

2.1 Overview

This study was conducted from October to December 2011 during an outbreak of dengue and dengue hemorrhagic fever in an outpatient medical department of Capital Development Hospital, Islamabad, Pakistan; which is a tertiary care hospital.

2.2 Data collection procedure

After getting permission from the relevant authorities of of Capital Development Hospital (Head of the Department of Medicine, Hospital Ethical Committee), the data collection phase was conducted from October to December 2011.

2.3 Data collection

By non probability convenient sampling, 220 patients with confirmed dengue and dengue hemorrhagic fever, aged 14 years and above were included in the study.

The data were collected from the outpatient and emergency department of medicine at the Capital Development Hospital in Islamabad, Pakistan. Verbal consent was taken from all the patients after explaining the nature and purpose of the study at the beginning of the study. All patients were treated by the same phycisians to minimize bias. Patients with dengue and dengue hemorrhagic fever were identified and detailed history was taken for diagnosis and for fulfillment of the required selection criteria.

2.4 Tools

Using structured proforma information was collected. Information regarding the baseline characteristics of patients were collected first. Their age and sex were noted. Using vigorous and strict criteria, only patients with confirmed dengue and dengue hemorrhagic fever were selected. Patients' detailed medical histories were taken regarding symptoms such as fever, headaches, retro-orbital pain, myalgia, arthalgia, sore throat, scarlatiniform/maculopapular rash, vomiting, epigastric pain, cough, shortness of breath and hemorrhagic manifestations.

Detailed examinations of respiratory, cardiac, gastrointestinal tract and the central nervous system were performed for pleural effusion, myocarditis, hepatosplenomegaly, ascities and coma, respectively. Dermatological examination was also done for skin rashes. Blood pressure, temperature, pulse rate, and respiratory rate were noted.

Other investigations performed included complete blood analysis, urine routine examination, liver function test, chest x-ray, and electrocardiography to look for dengue associated abnormalities. Dengue fever was confirmed by using the standardized Elisa method.

2.5 Data analysis procedure

The statistical package for the social sciences (SPSS, version 13.0, Chicago, IL) was used to enter and analyze the data in the form of tables and graphs. Mean values, frequencies, and percentages were calculated.

2.6 Exclusion criteria

Patients having malaria, typhoid fever, pyrexia of unknown origin, pulmonary tuberculosis, acute viral hepatitis (A, B, E), autoimmune diseases, chronic liver diseases, connective tissue disorder and idiopathic thrombocytopenia were excluded from the study.

3. Results

We analyzed the clinical characteristics of 220 confirmed cases of dengue and dengue hemorrhagic fever. We found that the case rate peaked in the month of November, and that the male-to-female ratio was 1.2:1. The mean age was 29 years (range: 14 years to 80 years). The highest incidence occurred between ages 14 years to 35 years (68%). The most common symptoms were fever and myalgia in all cases (100%). Fever was between 37.8C - 40.6C; 18% were having a fever of 37.8C (100F); 29.5% had 38.3C (101F); 13.6% had 38.9C (102F); 31.8% had a faver of 40C (104F); 4.5% had 39.4 (103F) and 2.27% cases had a fever of 40.6C (105F). Bleeding manifestations occurred in 10% of patients, with the least common clinical feature being a productive cough, which was seen only in 0.9 % cases, as listed in Table 1.

The most common laboratory findings were leucopenia and thrombocytopenia; and the least common finding was bilateral pleural effusion, as listed in Table 2.

The mean of total leukocyte count, platelets count, ALT & AST were $2.5X10^9$/L, $60X10^9$/L, 72u/l, 64u/l, respectively. The means and ranges of different investigations in dengue fever are listed in Table 3.

Table 1. Clinical features of 220 Dengue patients

CLINICAL FEATURES	NO. OF PATIENTS (%)
Fever	220 (100%)
Myalgia	220 (100%)
Skin rash	118 (53.7%)
Vomiting	190 (86%)
Retrorbital pain	40 (18%)
Joint pain	44 (20%)
Headache	30 (15%)
Bleeding	22 (10%)
Sore throat	10 (4%)
Dry cough	10 (4%)
Productive cough	2 (0.9%)

Table 2. Laboratory investigations of 220 Dengue patients

INVESTIGATION	NO. OF PATIENTS (%)
LEUCOPENIA	220 (100%)
THROMBOCYTOPENIA	220 (100%)
PROTEINURIA	212 (96%)
ALT	133 (60%)
AST	110 (40%)
ECG CHANGES	5 (2.27%)
BILATERAL EFFUSIONS	1 (0.45%)
DENGUE SEROLOGY IGM	220 (100%)

Table 3. Range of investigations of Dengue patients

Investigation	Range	Mean
Total leukocyte count	1.5 to 3.3×10^9/L	2.5×10^9/L
Platelet count	3 to 140×10^9/L	$60x10^9$/L
Alanine aminotransferase (ALT)	44 to 209 u/l	72 u/l
Aspartate aminotransferase (AST)	44 to 110 u/l	54 u/l

4. Discussion

Dengue and dengue hemorrhagic fever is notorious for its outbreaks especially in Southeast Asia, and is the leading cause of death in this region[8]. In this study, we studied an outbreak of Dengue and dengue hemorrhagic fever cases, presented in Capital Development Hospital, Islamabad, Pakistan. We here found that the majority of patients were male. Similarly, in a previous study, males represented 67.9% of all patients [9]. A similar study showed that Dengue mainly affected adults 20-49 years of age[10]. And a third study moreover revealed that the proportion of dengue cases were the highest among adults aged 20 to 29 years[11]. In our study, we observed the highest incidence in patients aged 14 to 35.

Expert consensus groups have suggested that dengue is a single entity with different clinical presentations, and that infected patients present with a range of clinical symptoms that vary according to the severity of disease, and age[12]. Some studies showed that fever and myalgia were the first presenting

symptoms, with other important symptoms being vomiting, rashes, headaches, retro-orbital pain, joint pain, sore throats, and coughing[4,13]. Our study showed similar clinical manifestations in cases of dengue fever. Furthermore, pretibial petechia, gastrointestinal bleeding and hemoptysis were the most common manifestations of dengue hemorrhagic fever in one study [14], and our study again showed similar results.

The diagnosis of dengue is typically made clinically, on the basis of reported symptoms and physical examination[15]. Early disease can be difficult to differentiate from other viral infections[16], and accordingly, we ruled out all other bacterial and viral infections before making a diagnosis of dengue fever.

A probable diagnosis is based on the findings of fever of 2-7 days plus at least two of the following: headache, retro-orbital pain, myalgia/arthalgia, nausea, vomiting, rash, low white blood cell count, and hemorrhagic manifestations (petechie and positive tourniquet test). The earliest laboratory findings are low white blood cell count, low platelet count, moderately elevated levels of alanine aminotransferase, aspartate aminotransferease (AST and ALT). In severe disease, plasma leakage results in hemoconcentration and hypoalbuminemia, which can lead to pleural effusion or ascites[16-18]. In our study one patient presented with severe features of disease in the form of bilateral pleural effusion.

The diagnosis of dengue fever may be confirmed by microbiological laboratory testing[19]. It can be done by virus isolation in cell cultures, nucleic acid detection by PCR, viral antigen detection by non-structural protein (NS1), or by specific antibodies (IgG and IgM)[20]. PCR and viral antigen detection are more accurate in the first seven days[16]. Serological IgG and IgM appear late in the blood and are very important diagnostic tool. IgM is produced after 5–7 days, with the highest levels of IgM being detected following a primary infection, and becoming undetectable 30–90 days after a primary infection. After a primary infection, IgG appearing in the blood indicates an old infection [21].

In our study, confirmation of dengue virus infection was achieved through isolation of virus from blood or serum, demonstration of dengue-specific IgM antibody in serum and a fourfold rise in dengue-specific antibody titers; no patient had IgG in the serum. Most of the patients in this study were poor and were unable to afford expensive tests, such as PCR & NS1. None of the patients included in the study died from the dengue virus infection.

5. Conclusions & Recommendations

In conclusion, a high level of suspicion is needed to diagnose dengue fever in patients presenting with high grade fever, myalgia, leucopenia and thrombocytopenia, and who are residents of endemic areas of mosquitoes (*Aedes Aegypti , Aedes Albopictus*).

Dengue infection can involve any organ of the body. Major factors responsible for epidemic outbreaks are inadequate water supply, substandard housing, poor sanitation systems, deterioration of mosquito control programs, and the poor health systems; all which are frequently observed in rural areas of Pakistan and other developing countries. There is currently no vaccine available for Dengue fever, but we can largely prevent the disease spreading by protecting ourselves from the bites of the mosquitos that transmits it, and early diagnoses together with successful disease management can help to prevent severe complications.

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