THE 2003 OUTBREAK OF DENGUE FEVER IN DELHI, INDIA

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Abstract. Dengue fever (DF) and Dengue hemorrhagic fever (DHF) are widespread in Southeast Asia. An outbreak of DF/DHF in Delhi in 2003 started during September, reached its peak in October - November, and lasted until early December. This study describes the clinical and laboratory data of the 185 cases of DF/DHF admitted to Lok Nayak Hospital, New Delhi. The mean age of the patients was 26±10 years. Fever was present in all the cases with an average duration of fever being 4.5±1.2 days with headache (61.6%), backache, (57.8%), vomiting (50.8%) and abdominal pain (21%) being the other presenting complaints. Hemorrhagic manifestations in the form of a positive tourniquet test (21%), gum bleeding and epistaxis (40%), hematemesis (22%), skin rashes (20%) and melena (14%) were also observed. Hepatomegaly and splenomegaly were observed in 10% and 5% of cases, respectively. Laboratory investigations revealed thrombocytopenia (with a platelet count of < 100,000 /μl) in about 61.39% of cases, Leukopenia (WBC <3,000/mm^2) and hemoconcentration (Hct >20% of expected for age and sex) were found in 68% and 52% of the cases, respectively. The mortality rate was 2.7%.Despite widespread measures taken to control outbreaks of DF, it caused major outbreaks. More stringent measures in the form of vector control, improved sanitation and health education are needed to decrease morbidity, mortality and health care costs caused by a preventable disease.

INTRODUCTION

In recent years, DF has become a major international public concern particularly in tropical and subtropical regions, affecting urban and suburban areas. Currently, DF and DHF are endemic to Southeast Asia, the Western Pacific and the Carribean. Since the first recorded outbreak of DF in India in 1812 (Jatanasen and Thongcharoen, 1993), recurrent outbreaks have been reported in India, despite measures taken to prevent and control it. Over the past 10-15 years, next to diarrheal diseases and acute respiratory infections, dengue has become a leading cause of hospitalization and death among children in the Southeast Asia region (Park, 2000). The increase of DF and DHF is due to uncontrolled population growth and urbanization without appropriate water management, global spread of dengue via trade and travel, and to erosion of vector control programs. This is a case-series study of the outbreak of DF and DHF in Delhi during 2003.

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MATERIALS AND METHODS

Lok Nayak Hospital, a large Goverment. funded institution, situated in the heart of New Delhi, draws patients from all over Delhi and neighboring states. In the dengue outbreak of 2003, a number of suspected cases of DF/DHF were admitted to this hospital. This paper is the description of these cases after review of the medical records of the 185 patients with DF/DHF.

The criteria for diagnosing DF were: 1. sudden onset continuous fever; 2.Two or more of the following: severe headache, retro-orbital pain, severe myalgia/arthralgia/back pain, hemorrhagic manifestations, or Leucopenia; 3. A high index of suspicion based on the population and location; 4. Absence of convincing evidence for any other febrile illness. The diagnosis of DHF was given when the criteria for DF were present and one or more of the following hemorrhagic

manifestations were present: 1. Positive tourniquet test; 2. Petechaie / ecchymosis / purpura; 3. Mucosal bleeding (epistaxis, gum bleeding); 4. Hematemesis, melena, hematuria, PV bleeding; or 5. Thrombocytopenia with platelets <100,000/mm^3; and any evidence of plasma leakage due to increased capillary permeability manifested by one or more of the following: 1.A ≥20% higher hematocrit for age or sex; 2. A ≥20% drop in hematocrit following treatment with fluids compared to baseline; 3. pleural effusion/ ascites/hypoprotinemia.

In each patient, a detailed history was taken and clinical examination was preformed on admission and during subsequent days of stay in the hospital. In each patient a platelet count was performed daily. Platelet function and platelet antibody tests were not carried out due to lack of resources. Hematocrit, serum biochemistry, CXR, and urine examinations were also performed in most of the patients. A serological diagnosis of DF was also carried out in almost all of the patients by the ELISA method for IgM and IgG antibodies against dengue virus. No virological studies or virus isolations were attempted. The clinical profiles and laboratory data were analyzed and are presented in the subsequent sections.

RESULTS

Of the 185 patients, 139 were males and 46 were females. The mean age was 26±10 years. The majority of the patients were residents of Delhi, barring a few who hailed from neighboring states. The age and sex distribution of the patients are summarized in Table 1.

Clinical features

A prodromal phase of fever was universal in the patients. Fever was high grade, associated with chills and rigors and was self limiting in nature. The average duration of fever was 4.5±1.20 days. Headache, backache and vomiting were common complaints. Loss of consciousness and abdominal symptoms were rarely observed. Hemorrhagic manifestations in the form of rashes, hematemesis, melena, petechaie, purpura, conjunctival congestion, gum bleeding and epistaxis were also noted in a fair proportion of cases, gum bleeding and epistaxis being the most common manifestation seen in 40% of the cases. The clinical data are summarized in Tables 2 and 3.

Table 1
Age-sex distribution of the cases.

Age in years	Number of Males	Number of Females
12-19	46	12
20-29	56	18
30-39	20	10
40-49	9	3
50-59	6	2
60-69	2	1
Total	139	46

Table 2
Clinical manifestations of the cases.

Clinical features	Number (%) of cases
Fever	185 (100)
Headache	114(61.6)
Back ache	107(57.8)
Vomiting	94(50.8)
Abdominal pain	39(21)
Hepatomagaly	20 (10.8)
Splenomegaly	10 (5.4)
Icterus	8 (4.3)
Ascites	2 (1.08)
Pleural effusion	2(1.08)
Loss of consciousness	3 (1.6)

Table 3
Hemorrhagic manifestations.

Manifestation	Number(%) of patients
Rash	37 (20)
Hematemesis	41 (22.2)
Melena	26 (14)
Bleeding from other sites (Gum bleeding, epistaxis)	74 (40)
Petechaie	22 (11.9)
Purpura	8 (4.3)
Conjuctival congestion	16 (8.6)
Positive tourniquet test	39 (21)

Table 4
Clinical profiles of the expired patients.

Total number (males/females)	5 (2/3)
Mean age	23 years
Mean hematocrit	64%
Mean platelet count	66,000/mm^3
Average number of bleeding sites	2.5
Mean systolic blood pressure upon presentation	80 mm Hg

Laboratory data

Estimation of WBC count revealed leukopenia (WBC <3,000 cells mm^3) in 68% of cases. The average WBC count was 6380. A rise in hematocrit (Hct >20% of the expected hematocrit for age and sex) was observed in 52% of the cases. Thrombocytopenia (with a platelet count <100,000/μl) was found in about 61.39% of cases. A transient elevation of SGOT and SGPT (>2 times) was found in 16% of cases. Deranged renal function (BUN >45 mg% and serum creatinine > 1.5 mg%) was observed in 10 of the 185 (5.4%) cases.

Outcomes

Of the 185 cases analyzed, 5 died (case fatality rate = 2.7%). The remaining patients recovered using supportive therapy with crystalloid, colloid, blood transfusion, or platelet transfusions. Of the 5 deaths, 2 were males and 3 were females with similar prodromal symptoms, but with more severe hemorrhagic manifestations, ≥2 bleeding sitess and 4 out of 5 having platelet counts <40,000. No statistical analysis of the clinical profiles of the expired patients was possible due to the small number (5) of dead patients. The clinical parameters of the expired patients are shown in Table 4.

DISCUSSION

Of all the arthropod-borne viral diseases, dengue fever is the most common. It is endemic in more than 100 countries and 40% the world's population is at risk for this disease (Park, 2000). All 4 types of dengue viruses have been isolated from the affected Indian population. Cyclical epidemics of dengue are becoming more frequent. In New Delhi and adjoining areas, outbreaks of DF and DHF were reported in 1967, 1970, 1982 (World Health Organization, 1993), 1988 (Srivastava *et al*, 1990), and 1996 (Anuradha *et al*, 1998). The outbreak in 1996 was the largest one to occur in Delhi (Anuradha *et al*, 1998), following which vigorous steps were taken to prevent and control DF/DHF.

Most of the patients in the present outbreak were young adults (mean age = 26±10yrs). A similar trend was also noted in a previous outbreak of dengue fever in Delhi in 1996 (Anuradha, Singh, Rizvi, *et al*, 1998) and in Singapore (Goh, 1995; Chan *et al*, 1977). This may be due to the fact that adults infected with one strain are not immune to the other strains of DF. In Singapore, where vector control measures had been carried out since 1973, the mean age group with the most common occurrence, has increased from 14 yrs in 1973 to 28 in 1994. Increased mortality has also occurred in young adults (Goh, 1995).

The average duration of prodromal fever was 4.5±1.2 days. erythematous morbilliform macular or maculopapular rash was found in 20% of the cases. This percentage is lower than that previously reported (36.7%) in a DF outbreak in Delhi in 1996 (Sharma *et al*, 1998) and in Vishakhapatnam (Krishnamurthy *et* al, 1965). In a series of hemorrhagic fever cases from Calcutta, 40% of the patients. Had a diffuse erythematous flush (Aikat *et al*, 1964).

Bleeding from various sites was found in 135 of 185 patients (72%). A similar percentage of patients with bleeding manifestations was found in the 1996 outbreak (70 of 98) (Sharma *et al*, 1998). The causes of bleeding in DF are not well established, but could be due to thrombocytopenia, consumption coagulopathy, capillary fragility or platelet dysfunction. Although thrombocytopenia was a constant finding, no correlation could be established between the platelet count and bleeding manifestations, indicating that other features, such as a disturbance in platelet function and capillary fragility, contribute to the bleeding diatheses. Since no platelet function tests or coagulation profiles were done, the exact cause can not be elucidated. Gum bleeding and epistaxis were the most common bleeding manifestations (40%)

followed by hematemesis (22%) and a positive tourniquet test (21%). The figures reported in the 1996 outbreak of DF (Sharma *et al*, 1998) were 32.6% for epistaxis, 22.4% for hematemesis and 26.5% for melena.

Hepatomegaly and splenomegaly were found in 10% and 5% of the cases, respectively, while the figures for the same manifestations were 20.4% and 8.2% in the 1996 outbreak (Sharma *et al*, 1998) and 22.2% and 9.3% in a report from Calcutta (Aikat *et al*,1964), respectively. SGOT and SGPT were also elevated in 16% of cases (16 of 100) which could be due to virus induced damage of the hepatocytes, shock, hypotension or associated liver disease. One pregnant female who presented with a deranged liver function test with bleeding and thrombocytopenia was initially diagnosed with HELLP syndrome and later proved to have dengue fever on serological testing and recovered without sequelae to the mother or fetus.

Renal dysfunction was observed in 5.4% of cases. Renal syndromes have been described with various hemorrhagic fevers, and hemorrhagic fever virus-induced changes in hemostasis and vascular biology have been proposed as a potential mechanism (Chen and Cosgriff, 2000).

Impaired consciousness was found in 3 of the 185 patients (1.6%) In the 1996 outbreak, 5 of the 98 (5.7%) (Sharma *et al*, 1998) had impaired onsciousness. A possible cause could be metabolic, disseminated intravascular coagulation, hepatic encephalopathy or gross edema of brain leading to encephalopathy (Nimmannitya *et al*,1987). In a study from Thailand, altered sensorium has been reported, but no evidence of encephalitis was found on autopsy of the patient (Nimmannitya *et al*,1987), Articles published elsewhere have shown that in some cases, a breakdown of the blood-brain barrier in the CNS can occur (Ramos *et al*, 1998; Cunha *et al*,1999). A report, (Lum *et al*, 1996) effectively supported the hypothesis of the occurrence of true encephalitis caused by dengue viruses. In another report (Ramos, Sanchez, Pando *et al*, 1998) antigen was detected by immunohistochemistry and DEN-4 RNA was found in neurons, astrocytes, microglia and endothelial cells.

Dengue specific IgM antibody was found in 120 of the 171 patients. (70.2%) tested. The sensitivity of this test depends on the duration of the prodromal illness. In a previous study (Sharma *et al*, 1998), 23 of the 27 patients. Tested for IgM Mu antibodies were positive. All the positive samples had a duration of fever of five or more days. The four negative samples had a duration of fever of 5-6 days and may not have seroconverted by this time. A study (Hayes and Gubler, 1992) using Mu capture ELISA in patients with confirmed DF showed that 96% of 76 blood samples drawn between 7th and 20th day after the onset of fever were positive. In a study in Thailand (Innis *et al*, 1989) the sensitivity of this test was found to be 97% in convalescent samples.

Five of the 185 patients died. These patients had lower hemoglobins and more bleeding sites. They also presented in shock and had higher hematocrits than the survivors (Table 4).

Despite increasing awareness among people regarding DF, through educating them about preventive and control measures via mass media, we have not been able to control DF. The result was another outbreak of dengue in 2003. Reasons for this may be due to overcrowding, abundant mosquito breeding sites, such as water coolers, metal receptacles, rubber tires, and water storage tanks, and changing lifestyles.

Ideal climatic conditions (rainy, cool dry season during September and October), a large, susceptible population, and abundant mosquito breeding sites, provided the backdrop for this outbreak. All the three factors of epidemiological triad, agent (dengue virus), host (susceptible population since no vaccine is available) and environment (abundant mosquito breeding sites) operated in combination to initiate the disease process in man, which ultimately led to the emergence of an outbreak.

It is time to open our eyes, help strengthen vector control measures, dispose off artificial water collections, improve sanitation, and involve the media in spreading anti-dengue measures on a large scale to curtail the occurrence of repeat outbreaks in the future.

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