THE 1996 OUTBREAK OF DENGUE HEMORRHAGIC FEVER IN DELHI, INDIA

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Abstract. A major outbreak of dengue hemorrhagic fever (DHF) affected more than 10,000 people in Delhi and neighboring areas in 1996. The outbreak started in September, peaked in October to November and lasted till early December. The clinical and laboratory data of 515 adult patients admitted to Lok Nayak Hospital, New Delhi were reviewed. Fever (100%), myalgias and malaise (96%), abdominal pain (10.2%) and vomiting (8.7%) were the prominent presenting features. Hemorrhagic manifestations were seen in all patients- a positive tourniquet test (21.2%), scattered petechial rash (23.07%), confluent rash (2.7%), epistaxis (38.4%), gum bleeds (28.06%) and hematemesis (22.86%) being the major bleeding manifestations. Hepatomegaly was observed in 96% of the patients. Laboratory investigations revealed thrombocytopenia, hemoconcentration and leukopenia. Serological confirmation with a microcapture ELISA technic was done in 143/515 patients. The mortality rate was 6.6% and, multiple bleeding manifestations, severe thrombocytopenia, hypoproteinemia and dengue shock syndrome (DSS) were associated with a higher mortality.

INTRODUCTION

Dengue fever (DF) and dengue hemorrhagic fever (DHF) are widespread in Southeast Asia, the Western Pacific and the Carribean. The first recorded outbreak of DF in India was in 1812 (Jatanasen and Thongcharoen, 1993). Sporadic outbreaks of DF have been reported on a regular basis since then. DHF was first reported in India in Calcutta in 1964 (Sarkar, 1967). Minor outbreaks of DF have been recorded 4 times over the past 4 decades in Delhi. A major outbreak of DHF affected more than 10,000 people in Delhi and neighboring areas in September - December 1996. This communication describes the clinical and laboratory data of 515 adult patients with DHF.

MATERIALS AND METHODS

Lok Nayak Hospital, situated in the heart of New Delhi, is a large government-funded hospital, drawing patients from all over Delhi and from the adjoining states of North India. One thousand and six patients-515 adults and 491 children-were admitted

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with DHF in Lok Nayak Hospital. We reviewed the case records of the 515 adults with DHF, and their clinical and laboratory data were analysed and are presented in the subsequent sections.

RESULTS

Five hundred and fifteen (515) adults, 376 males and 139 females, with mean age 25.6 ± 10.3 years (range 12-75 years) were admitted with DHF. Most of the cases were from the eastern parts of Delhi and a few cases were hailing from the adjoining states of Uttar Pradesh and Haryana. The age and sex distribution of the patients is summarized in Table 1.

Clinical features

All the patients presented with a prodromal illness of fever, myalgia and generalized body aches. The fever was of a high grade, associated with chills and rigors and was self-limiting in nature. The average duration of fever was 4.8 ± 1.32 days and almost all patients became afebrile prior to the development of the hemorrhagic manifestations.

Myalgia in 96%, abdominal pain 10.2% and vomiting in 8.7% patients were the other presenting features. Diarrhea / constipation was observed in less than 1% of patients.

Table 1

Age - sex distribution of the cases.

Age groups (in years)	Male	Female
12-20	103 (5)	27 (3)
20-30	178 (8)	55 (3)
30-40	47 (4)	26 (3)
40-50	15 (4)	10 (1)
50-60	8 (2)	8 (1)
60-70	1 (-)	2 (-)
> 70	1 (-)	- (-)
Total	376	139

Figures mentioned within ( ) are those of the cases that died.

Hemorrhagic manifestations were universal. Myriad hemorrhagic manifestations were seen - varying from only a positive tourniquet test to multiple, widespread bleeding manifestations. Hepatomegaly was observed in 96% of the patients. The clinical data are summarized in Tables 2, 3. According to the WHO criteria (WHO Technical Advisory Committee, 1980), the patients were categorized into:

Grade I	34/515
Grade II	452/515
Grade III and IV	29/515

Table 2

Clinical manifestations of the cases.

Finding	Percentage of cases
Fever - duration	
2-4 days	15.8
5-7 days	60.9
> 7 days	23.3
Myalgias	96.0
Abdominal pain	10.2
Vomiting	8.7
Diarrhea / Constipation	< 1
Hepatomegaly	96
Pleural effusion	< 1

Table 3

Hemorrhagic manifestations.

Manifestation	% of cases
Positive tourniquet test	21.2
Petechial rash	
Scattered	23.07
Confluent	2.7
Epistaxis	38.4
Gum bleeds	28.06
Hematemesis	22.86
Hematochezia	8.73
Hemoptysis	6.65
Hematuria	2.7
Subconjunctival hemorrhages	< 1

Laboratory data

Estimation of total leukocyte counts (TLC) revealed leukopenia (TLC< 3,000/mm^3) in 95.6% patients. The average TLC was 2,460 cells/mm^3 and transformed lymphocytes were observed on the peripheral blood film in many cases. Hemoconcentration, reflected by a rise in the hematocrit (average $51.2 \pm 7.6\%$) was documented in all patients. Thrombocytopenia was observed in all patients. The observed platelet counts were ranging from 50,000 to 1 Lac/mm^3 (61.9%), 20,000-50,000/mm^3 (30.1%)and< 20,000/mm^3 (8.0%) in the patients. A transient elevation of serum transaminases (ALT and AST, less than thrice the normal limit), was observed in 8% of patients.

Serolgical tests

Serological tests for the diagnosis of dengue virus (1,2,3 and 4) infection were perfomed in 143 patients. Tests for both IgM (143 patients) and IgG (44) antibodies were done with a microcapture ELISA Technic (Genelabs Diagnostics Singapore Dengue IgM / IgG blot) and development of color over the "spot" constituted a positive test. A primary infection was indicated by an IgM response only whereas presence of both IgM and IgG antibodies constituted a secondary response. All samples tested for IgG were also IgM positive, indicating a prior exposure to dengue virus infection in all cases . The tests had a 63.6% sensitivity.

Virus isolation

Sera collected from patients, were sent to the National Institute of Communicable Diseases (Delhi) and National Institute of Virology, Pune for virus isolation. DEN-2 was later isolated as the strain responsible for the outbreak (personal communication, NICD).

Outcome

Of the 515 cases of DHF, 34 died. The others made an uneventful recovery and most of these patients required only supportive therapy. Among the 34 deaths, 9 had Grade II DHF and 25 had Grade IV DHF. DSS-25, disseminated intravascular coagulation - 9; intracranial bleeding 3 and acute renal failure - 1 were the causes of death. Clinical data of the 34 deaths are summarized in Table 4.

Table 4

Clinical data of the 34 deaths.

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* Total number   34
Male : female ratio   2.1 : 1
Prodromal symptoms - similar to others
Hemorrhagic manifestations
    * More severe
    * ≥3 Bleeding sites - 25/34
Clinical grade of disease
    25/34 - Gr IV DHF
    9/34   - Gr II DHF
Platelet count (/ mm^3)
    > 30,000 - 19/34
    20-30,000 - 7/34
    < 20,000 - 8/34
Hypoalbuminemia (S.albumin < 3.0 g/dl) - 60%

DISCUSSION

Outbreaks of DF and DHF have been reported from India on a regular basis. All 4 types of dengue viruses have been isolated from the affected Indian population, though DEN-1 and DEN-2 are known to be more widespread (Smithburn et al, 1954). In New Delhi and neighboring areas, outbreaks of DF and DHF have been reported in 1967, 1970, 1982 (Mohan Rao et al, 1982) and 1988 (Srivastava et al,

1990). Endemicity of the virus in Delhi and adjoining areas has been well established. This outbreak, from September to December 1996, was the largest one to occur in Delhi.

Delhi, which faced the major brunt of the outbreak, is the capital city of India. The eastern and south eastern parts of Delhi are heavily populous areas with overcrowding in the face of poor- town planning. Abundant mosquito breeding sites like water - coolers, metal receptacles, rubber tires and other water storage tanks are present all over Delhi. Most outbreaks of dengue virus infection have been reported in the rainy or cool-dry seasons. September to October marks the end of the monsoon and beginning of winter over Delhi and adjoining areas of north India. So, an ideal climatic condition, a large susceptible population, abundant mosquito breeding sites provided the backdrop for this outbreak.

The classical symptoms of an acute febrile illness and hemorrhagic manifestations were observed in all patients. The average duration of fever was 4.8 ± 1.32 days and almost all patients were afebrile at the time of onset of hemorrhagic phenomena.

A positive Hess test was found in only 21.2% of patients. This clinical sign has been reported to occur in upto 84% of the patients in the previous reports (Nimmannitya et al, 1969). The darker color of Indian skins may have accounted for this sign being missed in many patients. Another distinctive feature of this outbreak was the high incidence of mucosal bleeds - observed in more than 60% of patients.

Most of these mucosal bleeds, however were minor, requiring only supportive therapy. Hepatomegaly was present in 96% of patients. No cases of encephalitis were recorded.

Leukopenia occured in 95.6% patients and the lowest observed leukocyte count was 1,000 cells/ mm^3. Thrombocytopenia and hemoconcentration were universal and were more pronounced in patients with Grades III and IV DHF.

Bleeding manifestations were severe, multiple and widespread in a few patients with Grade II DHF and in all those who died. Nearly 74% of these had 3 or more bleeding sites and 50% had a significant upper gastrointestinal bleed. Hypotension, shock and hypoalbuminemia were the markers of a poor prognosis.

Serological detection of dengue virus infection

was done in a limited number of patients only, as the kits for detection of anti-dengue antibodies was available well ofter the outbreak set in. Also, in many patients who presented with clearcut symptoms and signs of DHF with thrombocytopenia, serological tests were not performed.

Conventional serological testing for dengue virus infection includes technics like hemagglutination inhibition and neutralization. These tests however are lengthy, and cumbersome, and cause a delay in the diagnosis. Rapid assay systems for the detection of anti-dengue antibodies IgG/IgM have been developed recently and have shown good results. These include hemadsorption - immunosorbent technic (Gunasekaran et al, 1986) and dengue blot assay (Fang et al, 1992). These technics offer simple and faster results and, obviate the need to examine convalescent sera, which is of importance in the interpretation of the results of the conventional tests. The dengue blot assay used in the present study also offered quick results. These serological tests can only confirm the presence of dengue virus infection. Strain dentification is not possible, and virus isolation technics are required for it.

Rapid viral isolation technics have been recently developed using the polymerase chain reaction (Morita et al, 1994). Rapid detection times (within 3 hours) and accurate results, greatly facilitate the diagnosis of dengue virus strains.

The 1996 DHF outbreak highlighted the following points. Dengue virus is endemic in Delhi and neigboring areas and that provided the ideal combination of a susceptible population, abundant mosquito - breeding areas, slackened anti-mosquito measures and lack of public awareness, dengue virus infections can recur at any time. Strengthening of vector - control measures, emphasizing the need to dispose off artificial water collections, improvements in sanitation and active involvement of the media in spreading anti-dengue measures have curtailed the occurrence of a repeat outbreak in 1997. However, these measures will need to be carried on with the same enthusiasm in the future to prevent further large scale outbreaks.

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