

## Clinical spectrum during dengue haemorrhagic fever epidemics in Tirupur (India)

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Dengue is an acute viral disease caused by any of four dengue virus serotypes (DEN 1–4). A small proportion of infected persons may develop the severe form of disease, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). All over 99% of the cases of viral haemorrhagic fever reported worldwide are related to DHF<sup>1</sup>. Dengue fever (DF) has great variability of clinical features, which depends on many factors such as person, place and time<sup>2–3</sup>. It may be confused clinically with other infections, viz. influenza, measles, typhoid, leptospirosis and any non-specific viral syndromes<sup>4</sup>.

Tirupur town in Tamil Nadu is a leading foreign exchange earning centre in India. It has a residential population of about 0.35 million living in an area of about 27.2 km<sup>2</sup>. Water scarcity occurs frequently and the local residents of Tirupur are storing water for at least seven days in order to manage their daily needs, which leads to high breeding of *Aedes aegypti* (Diptera: Culicidae). DF is not endemic in Tirupur. Number of suspected dengue cases were reported periodically in the past three years but no case was diagnosed serologically. In July 2005, a case of DHF identified in Tirupur, a major epidemic ensued, moving briskly through a number of sub-urbans.

We surveyed four areas in Tirupur where the suspected dengue outbreak occurred. Case records of all the notified cases admitted to the hospitals including Government and private hospitals in the region were collected. The demographic data consisting of age, gender, locality, patient complaints, clinical examination in detail and laboratory data (blood, urine, chest X-ray and USG) were collected. Patients admitted with a provisional diagnosis of dengue or suspected dengue were followed up throughout their hospital stay. A detailed history of the patients was collected and a thorough clinical examination was carried out. Blood specimens were collected for CBC, LFT and dengue confirmation. Daily physical examination by paediatrician and CBC findings were recorded.

The cases were classified as ‘probable’ on the basis of

clinical findings. Clinical diagnosis was made based on the WHO 1997 case definition criteria for DF/DHF/DSS. Classification of definite cases required laboratory investigations and virus isolation. The study was carried out after getting informed consent from the parents or guardians. Statistical analysis was carried out by using SPSS version 11.5.

A total of 152 patients clinically diagnosed as probable dengue fever were identified during this outbreak. The mean age of the patients was 23.5 yr (1 to 48). The mean duration of symptoms prior to admission was three days. About 22 (14.4%) were aged <1 yr, 37 (24.4%)

Table 1. Clinical findings during Tirupur epidemic of dengue

Symptoms	No. of cases	Percentage
Fever	148	97.4
Retro-orbital pain/puffiness	95	62.5
Vomiting	82	53.9
Headache	88	57.9
Myalgia	86	56.6
Arthralgia	86	56.6
Rash	82	21.1
Tourniquet test	43	53.9
Petechiae, ecchymosis, purpura	44	28.9
Haematemesis	26	17.1
Rapid weak pulse	31	20.4
Narrow pulse pressure	29	19.1
Hypotension	57	37.5
Cold, clammy skin	39	25.7
Pain abdomen	36	23.7
Pruritis	36	23.7
Giddiness	25	16.4
Spleen/liver enlargement	48	31.6
Platelet count*	71	46.7
WBC count*	72	47.4
Hb/PCV*	73	48
LFT*	55	36.2
Chest X-ray*	25	16.4
Ultrasound abdomen*	25	16.4
Fully recovered	148	97.4

\*Abnormal findings.

were under 5 yr, 69 (45.39%) were in the age group of 6–15 yr and 24 (15.8%) were >16 yr old. The mean duration of hospital stay was found to be 4.5 (range 1–15) days. Males (90/152) remained most affected than females (62/152).

An admission diagnosis of dengue fever was made in 34 cases and viral illness in remaining cases. Other admission diagnoses included chest infection or asthma (five cases), gastroenteritis (two cases), encephalopathy (two cases), enteric fever (two cases), and urinary tract infection (one case). The symptoms recorded in the hospitalized patients are given in Table 1. Fever was documented in most cases. About 52% had a maximum temperature of 40°C and 47% had a maximum temperature of 38°C. Patients who did not have fever at the time of admission had been symptomatic 2–7 days prior to admission and it was likely that they mostly had been febrile during that period.

Headache, retro-orbital pain and musculoskeletal pain were documented in 57.9% (children <5 yr were omitted because they were unable to express their symptoms). Rash was noticed only in 53.9%. GI symptoms like nausea, vomiting (53.9%) and pain in abdomen in 23.7% was noticed. There were 71 cases with low platelet count as per WHO criteria for DHF/DSS. Patients who did not satisfy all criteria for diagnosis of DHF, but had positive serology were classified as DF. There were 46 cases that fulfilled all the four WHO criteria for DHF/DSS.

Headache and musculoskeletal pain and gastrointestinal symptoms, especially nausea, were very common. The presence or absence of other symptoms was recorded in less than half of the case records. The presence of altered taste, ocular pain and pruritis were reported very common. Bleeding of any severity was noted in 19 patients. Complications that were ascribed to dengue infection including 'dehydration' were noticed in 20 patients. Treatment with intravenous fluids was often commenced as a consequence of nausea.

Rash was described as being particularly severe in 29 patients, which appeared more in the extremities with florid petechiae, frank haemorrhage and/or intense pruritis. Bleeding was listed as a complication in 19 patients. Amongst these patients, bleeding varied in severity from gum bleeding to haematemesis, haematuria or melena.

There were 46 cases that fulfilled the WHO criteria for DHF<sup>5</sup> and 42 cases occurred in the children with haematemesis and melena. The serological profile was that of a primary dengue infection. Four young males showed with a serological profile of secondary dengue infection. Chest X-ray and ultrasonography done only in hospitalized cases and 25 (26.8%) of them showed positive findings.

In all, 11 patients had measurements of hepatic transaminases and 45% of these patients had levels, which exceeded the laboratory normal range for aspartate transaminase (AST) (NR <40 U/L). Alanine transaminase (ALT) (NR <45 U/L) and  $\gamma$ -glutamyltransferase (GGT) (NR <50 U/L) were elevated. AST was elevated in all of the patients and three patients had AST levels that exceeded 1000 U/L. Urine analysis results were recorded in 137 of the patients and blood was detected in 5%<sup>6</sup>.

A total of 66 patients had probable primary dengue and 34 probable secondary dengue virus infections. The hospitalized patients with secondary infections were older and less likely to have a rash associated with their illness. The duration of stay in hospital ( $p >0.05$ ) and other manifestations of illness, including the incidence of haemorrhagic phenomena and dual infection were very high in the hospitalized group. Four children (three female and one male) all <5 yr were reported to be died due to the haemorrhagic complications. This may be due to the delay in hospital admission, diagnosis, consequence of inadequate care and treatment.

Severe clinical manifestations with a high hospitalization rate characterized DENV-3 epidemics in Tirupur, south India. Previous epidemics were not reported but silent transmission of dengue virus was reported in 1998<sup>7</sup> with much lower hospitalization rates. Particular features of the epidemic included a very high incidence of gastrointestinal manifestations, and a high incidence of unusually severe rash, in those patients who were hospitalized. Mostly in other cases the clinical features were typical for dengue fever. The apparently low reported rates of altered taste and pruritis are possibly a reflection on the retrospective nature of the study. Many of doctors in the hospital were unfamiliar with the clinical features of dengue fever and did not enquire routinely about the presence of symptoms such as taste perversion and skin itch. A large number of dengue cases were misdiagnosed based on clinical findings since the symptoms are consistent with other diseases.

Forty-two cases of DHF were documented in children. The serological profile in this case was consistent with a primary dengue infection. Four cases of DHF identified in young males, the serological profile in this case was secondary dengue infection<sup>8–10</sup>. Overlapping in major clinical features among DF and DHF is obscuring the severity of this epidemic, it emphasized the need for simple classification which is acceptable to all the regions.

The AST was elevated more often than the ALT, which is a pattern that has been observed previously. Hepatic disorders, in conjunction with bleeding and thrombocytopenia, have been proposed as an indicator

of severe disease<sup>11</sup>. Several patients had a clinical picture dominated by their probable sub clinical hepatitis.

From our experience we could conclude that the circulation of DENV-3 is responsible for the recent DHF with low mortality. High morbidity of population and urbanization leads to circulation of multiple dengue serotypes<sup>12-13</sup> and development of severe DHF among paediatrics in Tirupur. The mortality rate is low in the present epidemic; it may increase in subsequent epidemics. Four children who died had DSS and delayed in hospital admission. It emphasized that the children with high fever should seek hospital treatment without any delay. Health education regarding manifestations of DF is important during epidemics. Results of the serological and virological studies of this episode have been published elsewhere<sup>14</sup>.

To conclude, this study shows that DF is expanding wings with its severe manifestations, early treatment can reduce the morbidity and mortality during epidemics. Early detection and case management practices have been noted as critical factors for survival. Yet well-targeted operational research in these areas is rare. Population-based epidemiological studies with clear operational objectives should be launched as concerted efforts at regional levels. Health education and training of district level health personnel regarding manifestations of DHF is important during epidemics, which will help in early case detection and treatment.

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