Clinical and laboratory profile of dengue fever cases in children less than 12 years in a tertiary care centre in rural Kerala

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Abstract
Objective: To study the clinical features and laboratory parameters of dengue fever cases in children, to classify the cases based on WHO 2012 guidelines and to assess the outcome of these cases.

Materials and Methods: This was a prospective observational study of 193 children less than 12 years diagnosed with dengue fever based on clinical and laboratory findings and confirmed by serological tests admitted in our institution between May to October 2017.

Results: The maximum number of cases were in the age group 6-12 years. The male: female ratio was 1.19:1. Percentage of severe dengue, dengue with warning signs and dengue without warning signs were 2.5%, 18.1% and 69.4% respectively. 68.5% had a total WBC count below 3999. 36.2% had a platelet count below 100000. The most common presenting symptom was fever with myalgia (68%).

Conclusion: Application of revised WHO classification helps in better stratification and management of patients admitted with dengue fever.

Keywords: Dengue fever, Children, Profile, WHO guidelines, Outcome.

Introduction
Dengue fever,1 also called break bone fever is a vector borne illness and is a fast emerging disease in various parts of the world. The disease flourishes in rural, suburban and urban poor areas in tropical and subtropical countries. The incidence of this disease has increased to more than 30 fold, with up to 100 million new cases occurring annually in the endemic areas. The life cycle of the infection involves Aedes Aegypti mosquitoes as the vector and humans as the main victim and source of infection. Dengue virus comprises of 4 groups – DEN-1,2,3,4 belonging to the flavivirusidae group. Asian serotypes DEN 22 and 3 are associated with severe disease. Recovery2 from infection gives immunity to that particular strain only. Sequelae infection increases the risk of severe dengue manifestations. Humoral,3,4 cellular and innate host responses are implicated in the progression of the illness. The most severe clinical syndrome may not correlate with the magnitude of viral load. Alteration in the endothelial micro vascular permeability and thrombo regulatory mechanisms lead to increased loss of plasma and proteins. The first reported Dengue like illness was in Chennai in 1780 whereas the first virologically proved illness occurred in Calcutta in 1963.5 Dengue fever is suspected when a patient from the endemic area or with travel to endemic area comes with high grade fever, malaise, myalgia, arthralgia, headache, retro orbital pain, abdominal pain, vomiting, rash or bleeding manifestations. The disease has a biphasic course. 10-20% patients can develop shock with haemorrhagic manifestations. The clinical spectrum can vary from asymptomatic to severe dengue. The three phases of the disease are febrile phase, critical phase and recovery phase. WHO in 1997 has categorised dengue as (1) undifferentiated dengue fever, (2) Dengue fever characterised by fever of 2-7 days duration along with myalgia, retro orbital pain, arthralgia, headache and rash (3) Dengue haemorrhagic fever with fever of 2-7 days duration, bleeding tendencies, thrombocytopenia (platelet count less than 1 lakh), hemo concentration (defined as 20% rise in hematocrit) and plasma leak (pleural effusion, ascitis, hypo proteinemia). WHO in 2009 has categorised dengue fever as dengue fever, dengue with warning signs and severe dengue fever. Warning signs2,6 are detected by close observation of the patient. The important warning signs are abdominal pain or tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeds, hepatomegaly more than 2 cm, fluid accumulation evidenced by increase in hematocrit with concomitant fall in platelet count. Severe manifestations include profound shock, bleeding and multi system involvement. Thrombocytopenia is attributed to the reduced megakaryocytopoiesis and compromised progenitor cell growth along with platelet depletion, dysfunction and defect, fibrinogen consumption, prolongation of PT/PTT, and vasculopathy. Expanded8 dengue syndrome involves unusual and severe involvement of the heart, kidney, liver and brain in association with dengue fever the present study aims at analysing the important presenting symptoms and laboratory parameters in these children and their outcome following the standard management according to WHO guidelines.

Materials and Methods
This study is a prospective longitudinal study comprising of all patients admitted with symptoms suggestive of Dengue fever like high grade fever, vomiting, abdominal pain, myalgia, rash, bleeding manifestations, shock and end organ failure whose blood tests are positive for dengue. Children with urinary tract infection, enteric
fever and meningitis were excluded. A meticulous history and physical examination was done at presentation and then daily till discharge. Vital signs monitoring and tourniquet tests were done daily. Complete blood counts and LFT was done in all patients initially. Haemoglobin, total count, platelet count, haematocrit were monitored serially. Those with clinical evidence of hepatomegaly or deranged liver enzymes underwent ultrasonography of abdomen and chest x ray to detect fluid collection. Patients were classified into three groups—dengue fever without warning signs, dengue fever with warning signs and severe dengue. Patients with severe dengue were admitted to the intensive care unit and managed with iv fluids, inotropes and blood component therapy depending on their condition. The symptoms, signs and lab parameters were entered to MS excel and analysed using SPSS 16 software. The different groups were compared using chi square test. The age wise distribution of cases in different categories, the male-female distribution of cases in different groups, distribution of lab abnormalities in different groups were studied.

Results
193 children were diagnosed to have dengue fever in the study period.

![Sex distribution](image1)

**Fig. 1: The male to female distribution**

The male- female ratio was 1.19:1.

![Age distribution](image2)

**Fig. 2: The age wise distribution**

10 cases (5.2%) occurred in children less than 1 year, 60 cases (31.1%) in 1-5 years and 123 cases (63.7%) in 6-12 years age group. Maximum cases were in the age group 6 to 12 years. Maximum number of cases were residing in semi urban area with proximity to rubber plantations. More cases of severe dengue were seen in the 6-12 years age group. More cases of dengue with warning signs were seen in the age group 6-12 years.

Dengue without warning signs was also seen more in the age group 6-12 years.

High grade fever was the most common presenting symptom (100%). Fever less than 5 days was the presenting symptom in 120 patients. (62.3%). Fever more than 5 days was the presenting symptom in 73 patients (37.8%). Fatigue and malaise was present in 83%. Vomiting was present in 56.6% of patients. Abdominal pain was present in 61%. Headache was present in 36% of patients. Myalgia was present in 23%. Seizures were noted in 3 patients, but were febrile seizures with normal CSF study. Bleeding manifestations were noted mostly in the form of petechiae and gum bleeds. Positive tourniquet test was seen in 54 patients (27.9%). 9.9% patients had crepitations and wheeze requiring bronchodilators and antibiotics.

### Table 1: Showing the important lab parameters and the percentage of patients with abnormality in these parameters

| Parameter | Frequency | Percent |
|-----------|-----------|---------|
| PLC< 20000 | 3 | 1.6% |
| PLC 20000 - 49999 | 17 | 8.8% |
| PLC 50000 - 99999 | 51 | 26.4% |
| PLC100000 - 149999 | 74 | 38.3% |
| PLC>= 150000 | 48 | 24.9% |
| Total | 193 | 100.0% |

| TC | Frequency | Percent |
|---|-----------|---------|
| <= 1500 | 3 | 1.6% |
| 1501-2499 | 48 | 24.9% |
| 2500-3999 | 81 | 42.0% |
| >= 4000 | 61 | 31.6% |
| Total | 193 | 100.0% |

| PCV | Frequency | Percent |
|---|-----------|---------|
| > 45% | 2 | 1.0% |
| 40% - 45% | 63 | 32.6% |
| 35% - 39% | 113 | 58.5% |
| < 35% | 15 | 7.8% |
| Total | 193 | 100.0% |

| Hb | Frequency | Percent |
|---|-----------|---------|
| 8 - 9.9 g/dl | 3 | 1.6% |
| 10 - 12 g/dl | 125 | 64.8% |
| > 12 g/dl | 65 | 33.7% |
| Total | 193 | 100.0% |

| LFT Abnormality | Frequency | Percent |
|---|-----------|---------|
| Present | 85 | 44.0% |
| Absent | 108 | 56.0% |
| Total | 193 | 100.0% |
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Fig. 3: Figure showing the distribution of wbc counts

Fig. 4: Percentage of NS1 positivity

Fig. 5: The percentage of IgM/IgG positivity

Table 2: Table showing the distribution of dengue fever cases

| Diagnosis                  | Frequency | Percentage |
|----------------------------|-----------|------------|
| Dengue fever               | 134       | 69.4       |
| Dengue with warning signs  | 35        | 18.1       |
| Severe dengue              | 24        | 12.4       |
| Total                      | 193       | 100        |
Dengue NS1 was positive in 76.7%. IgM was positive in 30.6%. 69.4% of cases were dengue fever without warning signs, 18.1% were dengue with warning signs and 12.4% were severe dengue. LFT abnormality was present in 44% of cases. Main USG findings obtained were hepatomegaly, ascitis, pleural effusion and gall bladder thickening. Of the 85 patients with LFT abnormality, 5 were below 1 year of age, 20 were between one to five years and 60 were between six to twelve years. USG abnormality was present in 25.9% patients. Of the 50 patients with USG abnormality, 39 were between 6-12 years. 37 patients with LFT abnormality had no USG abnormality. Thrombocytopenia was present in 71 patients(37%) of cases. 36.8% had platelet below 1 lakh.26.4% had platelet between 50000 to 99999. 8.8% had platelet between 20000 TO 49999. 1.6% had platelet below 20000. Lowest PLC was 16000 in 1 patient. Highest value was 290000 in 1 patient. Most frequent value was 120000 in 17 patients. Mean platelet count was 113933 with standard deviation of .976.

Leucopenia with total count below 4000 was seen in 132 patients. (63.4%). Lowest TC was 1200 in 1 patient. Highest value was 18000 in 1 patient. Most frequent value was 2400. Haemoglobin less than 12 was seen in 128 patients (66.4%). Mean total wbc count was 3834 with standard deviation of .793

Lowest Hb was 8.8 in 1 patient. Highest value was 15.8gm/dl in 1 patient.

Most frequent value was 12 in 40 patients. Hematocrit more than 40 was seen in 65 patients. (33.6%) Lowest value of PCV was 26 seen in 1 patient. Highest value was 49, seen in 1 patient. Most frequent value was 38, seen in 43 patients Mean PCV was 38 with standard deviation of .612. LFT abnormality was present in 85 patients (44%).

The patients were treated with monitoring of pulse rate, respiratory rate, urine output charting, monitoring for fluid overload, liver span measurement, checking for basal crepitations, JVP, bleeding manifestations. Dengue without warning signs were treated with symptomatic management with paracetamol and oral fluids 3ml/ kg/hour. Patients with vomiting and unable to take oral feeds were given iv fluids for short period which was promptly stopped once oral feeding was established. Patients with shock were managed with iv crystalloids and inotropes. Platelet transfusion was given in 3 patients who had platelet count below 20000 and in 2 patients with platelet count between 20000 to 50000 with gum bleeds. There was no mortality in these cases.

Discussion
In this study male to female ratio is 1.19:1. Males accounted for 54.4% and females accounted for 45.6% of cases. In a study done by Jimmy Antony et al, 60.7% were males and 39.29% were females. Study done by Eong et al in Singapore showed greater number of adult males affected compared to adult females. Ruel Perez et al in their study showed that males are more affected. Study from Cambodia, Malaysia, Sri Lanka also showed increased preponderance in males probably due to the outdoor work and play habits thereby being more exposed to mosquito bite. This same trend is noted in children also although the difference is much less. Maximum number of cases (63.7%) were noted in the age group 6-12 years. This is similar to the study by Bhaswati et al where maximum number of cases were in the age group 11-30 years with males outnumbering females. The most common age group was school going children (42%) and adolescents (36%). In study done by Srinivasa et al, headache was the most common presenting symptom. Fever with myalgia was the most common presenting symptom in our study where as in the study done by T.D Thal et al, abdominal pain, vomiting, retroorbital pain, and abdominal distension were seen commonly. Mittal et al found that fever with headache and abdominal pain were the commonest presenting symptom. Fever with myalgia was predominantly seen in a previous study done by Ahammad et al. Rashes and positive tourniquet test were seen in 12.7% and 7.8% of cases in the study done by Ferede et al in Ethiopia. Positive tourniquet test was seen in 54 patients (27.9%) in this study which is similar to other south Asian studies where as in the study done by Subhankar et al, in the majority of the patients, tourniquet test was found to be negative The most consistent finding was hepatomegaly, which was similar to many other studies done by Joshi et al. Seizures were noted in 3 patients, but were febrile seizures with normal CSF study. Study done by Subhankar Mishra et al showed that two patients in the severe dengue group had convulsion. Among the various clinical findings hypotension, pleural effusion, and respiratory distress were notable and were analogous to other studies. Leukopenia was seen, which was the earliest haematological abnormality which made us suspect dengue fever similar to study by Vaughan et al. According to the study done by Ferede et al, the most common hematological finding observed was thrombocytopenia (platelet count < 140,000/cumm) in 59.8% followed by anemia (hemoglobin level < 11.5 g/dl) in 44.1% and leucopenia (total leukocyte count < 4,000/cumm) in 26.5% of the cases. Hematocrit > 44% were noted in 9.8% of the cases. Neutrophil < 1500 was seen in 15.7% and lymphocyte > 2900 in 2% of the cases were noticed. In our study, leucopenia was the most common abnormality with 63.4% having a total count below 4000. Platelet count less than one lakh was found in 37% patients and hematocrit more than 40 was found in 33.6%. Hemoglobin less than 12% was found in 63.4% of children probably owing o the high incidence of nutritional anaemia in our area. Study done by Jhabhar et al showed leucopenia (WBC < 4,000/mm2) and hemoconcentration (Hct > 20% of expected for age and sex) in 38% and 5.26% of the cases, respectively. According to the study done by Subhankar Mishra et al, elevation in aspartate transaminase (SGOT) was found in 47.42% and thrombocytopenia in 27.5% and the correlation between hepatomegaly and elevated SGOT was significant and case fatality rate (CFR) was 1.03%. Severe cases accounted for one tenth of the cases according to the study by Subhareeon et al. There was less mortality in the present study group, whereas mortality rate was high.
in earlier previous studies. This could be due to better facilities, increased awareness among the general public regarding dengue fever and early seeking of medical care. Case fatality rate (CFR) of the SEAR countries in 2006 was less than 1%. India, Indonesia, Bhutan, and Nepal still have case fatality rates above 1% as per studies by Seneviratna et al. There was no mortality in this study.

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