Clinical Profile of Dengue Infection in Immune-compromised Children

Review of records of children admitted with dengue infection was carried out to compare clinical and laboratory parameters, course of illness, and outcome between immune-compromised and immune-competent patients. Statistically significant differences were found in days to platelet recovery (P=0.03), hepatic dysfunction (P= 0.04), and higher requirement of fluid (P= 0.01) in immune-compromised group.

Keywords: Immunodeficiency; Outcome; Arboviril.

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The complex interplay of immunity with dengue virus is not well understood and is an area of active research. The immune-compromised host provides a model to understand the role of immunity in dengue infection pathogenesis.

This retrospective study aimed to assess the clinical features and outcome of dengue in immune-compromised children less than 12 years of age as compared to immune-competent children. The case records of children admitted with dengue at a tertiary centre from July to November 2013 were reviewed. Cases were grouped into immune-compromised patients (those on cancer chemotherapy with primary disease in remission or on steroids (>2 mg/kg/day for >2 weeks), and premorbidly normal patients. Data were collected for clinical features of dengue at presentation, underlying illness, severity, laboratory parameters and course of the disease and recovery. Cases were classified as Dengue fever, Dengue fever with or without warning sign, and Severe dengue as per the WHO 2009 guidelines. Dengue was diagnosed on the basis of NS1 antigen positivity and/or Dengue-specific IgM positivity on the rapid test (Dengue day 1 kit, J Mitra, New Delhi). Cases were managed as per the 2009 WHO guidelines [1].

We identified 58 children who were hospitalized with dengue infection during the study period. Sixteen patients (all immunocompetent) who were admitted with confirmed dengue infection during the same period were not included in the study. Of the 42 children included in the study (cases and consecutive control in 1:1 ratio), twenty-one patients were immune-compromised at onset of dengue and 21 were premorbidly normal. Details of clinical features, laboratory parameters and outcome in two groups are shown in ***Table* I**.

TABLE I DISEASE CHRACTERISTICS OF DENGUE IN IMMUNE-COMPETENT AND IMMUNE-COMPROMISED CHILDREN

Characteristics	*Immune-compromised (n=21)*	*Immune-competent (n=21)*
*Fever duration, d	4.3 (1.71)	4.76 (1.62)
Presenting symptoms		
Rash	7 (33.3)	7 (33.3)
Pain abdomen	6 (28.6)	9 (42.9)
Vomiting	8 (38.1)	9 (42.9)
Myalgia	10 (47.6)	5 (23.8)
Joint pain	5 (23.8)	3 (14.3)
^Headache	11 (52.4)	3 (14.3)
Retro orbital pain	6 (28.6)	8 (38.1)
Facial puffiness	8 (38.1)	4 (19.0)
Bleeding	6 (28.6)	4 (19.0)
Dengue with warning signs	18 (85.7)	19 (90.1)
Severe dengue	3 (14.3)	2 (95.2)
$^{\$\#}$Intravenous fluid > 5mL/kg/h	17 (80.1)	6 (28.6)
Intravenous fluid (>48 h)	9 (42.9)	3 (14.3)
Platelets <20000/ µL	9 (42.9)	3 (14.3)
$^{\#}$Raised transaminases	18 (85.7)	10 (47.6)
$^{*\#}$Time to platelet recovery (d)	10 (4.1)	3 (2.1)
^Pancytopenia	8 (38.1)	0
Pleural Effusion	8 (38.1)	6 (28.6)
Free fluid/gall bladder edema	7 (33.3)	8 (38.1)
NS1 antigen positive	17 (80.1)	14 (66.7)
Dengue IgM positive	4 (19.0)	7 (33.3)
Encephalopathy	1 (4.8)	0
Myocarditis	1 (4.8)	0
Internal bleeds	3 (14.3)	0
Secondary infections	3 (14.3)	2 (9.5)
Mortality	2 (9.5)	0
*Hospital stay, d	4.4 (1.4)	3.1 (1.1)
Mortality	2 (9.5)	0

*Figures are n (%), *mean (SD); $^{\#}P<0.05$; $^{\wedge}P<0.01$; $^{\$}$in the first 6 hr of presentation.*

Proportions were compared by the chi-square test or Fisher's exact test. Quantitative variables were compared by nonparametric Mann Whitney test and Freidman and Wilcoxon test. A P value of less than 0.05 was considered to indicate statistical significance.

There was no statistically significant difference in age and sex of the two groups. The immune compromised group had headache as a symptom more often than the control group (P=0.01). Statistically significant differences were found in hepatic dysfunction in form of raised transaminases, days to platelet recovery (documented rise in platelet count form baseline by at least 20000/µL and above 50000/µL twice), and higher requirement of fluid in immune-compromised **(*Table* I**). The duration of stay was higher in immune-compromised compared to immune-competent group. Six patients in immune-compromised group with hematological malignancy with severe thrombocytopenia and two immune-competent patients with mucosal bleeding (in presence of severe thrombocytopenia) received platelet transfusion. Colloid was required during fluid resuscitation in only 5 patients (3 in immune compromised and 2 in immune-competent).

Sharma, *et al*. [2] in a series of five patients with hematological disease reported no difference in clinical outcome of patient compared to normal population. Ramzan, *et al*. [3] reported similar observation of lower day 1 platelet in their case series on dengue fever as a cause of febrile neutropenia in children with acute lymphoblastic leukemia [4]. Duration of illness in normal population is reported as 4-7 days [4]. Visuthranukul, *et al*. [5] in a case report of dengue in a stem cell transplant recipient, also observed prolonged duration of illness in immune compromised. Principles of treatment and prevention remain the same as in immune-competent individuals.

This study shows a trend towards greater severity and complications of dengue in immune-compromised children. A similar study on larger population including estimation of viral load and immunological response estimation will help in understanding the complex interplay of dengue infection and immunity.

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Incidentally Detected Elevated Liver Enzymes: From Liver to Muscle

We describe 8 children – with incidentally detected isolated elevation of liver enzymes aspartate aminotansferase and alanine aminotransferase – who were extensively evaluated for hepatic causes before finally being diagnosed to have muscular dystrophy. Serum creatinine phosphokinase levels, if performed early during the work-up, may help in diagnosis of muscle disease and avoid unnecessary investigations for liver disease.

Keywords: *Anicteric hepatitis, Creatinine phosphokinase, Muscular dystrophy.*

Elevated levels of serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) usually indicates hepatocyte injury. However, due to their widespread distribution in the body, serum levels of these enzymes can be elevated in other conditions as well [1,2]. Muscle disorders like muscular dystrophies, inflammatory myopathies and metabolic myopathies can lead to elevated blood levels of creatine phosphokinase (CPK), lactate dehydrogenase (LDH), ALT and AST [1] .

Over a period of 6 years, eight boys with a median (range) age of 4.5 (0.5,13) year were referred to us for evaluation of persistently abnormal liver function test (LFT). Abnormal LFTs were detected incidentally and the