Acute Liver Failure in Dengue Present Some Peculiar Features

Sir,

Acute liver failure (ALF) in Indian subcontinent is primarily caused by hepatotropic viruses such as hepatitis A, B and E virus.¹ Liver dysfunction is a well-known feature of dengue; often demonstrated by mild-to-moderate elevation of serum transaminases, however, ALF is generally uncommon.² Because of endemicity of dengue in the tropical world, the absolute number of ALF caused by dengue virus may be considerable. However, data on dengue-ALF is still scant, and most of the published studies on ALF have not included this particular aetiology. In our tertiary care centre, 183 patients of dengue were admitted between July 2015 and December 2015. Among them, 156

patients had evidence of hepatitis and 5 patients fulfilled the criteria for ALF. Though the diagnosis of dengue was confirmed in all patients, serological tests were also done to rule out viral hepatitis A, B, C and E. The baseline characteristics, laboratory parameters and outcome of dengue-ALF patients are summarized in Table 1. The median interval from onset of fever to ALF was 5 (4–6) days. The majority (80%) of the patients were male. Icterus-encephalopathy interval was <7 days in all patients suggesting a uniform hyper-acute liver failure. All patients had massive elevation of transaminases levels at presentation, with median aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels being 13,282 IU/L and 3167 IU/L, respectively. The level of AST was greater than ALT in all patients. At presentation, none of the ALF patients had hypotension. Severe thrombocytopenia was

Table 1 Baseline Characteristics, Laboratory Parameters and Outcome of Dengue ALF Patients.

Parameters ^a	Total N = 05	Died patients N = 04	Survived patient N = 01
Age, median (range) (years)	35 (19–58)	45 (32–58)	19
Male:female	04:01	03:01	01:00
Bilirubin, median (range) (mg/dl)	3.4 (2.4–9.02)	3.9(3.0–9.02)	2.41
Aspartate transaminase (AST), median (range) (IU/L)	13,282 (1612–45,176)	23,641 (6858–45,176)	1612
Alanine transaminase (ALT), median (range) (IU/L)	3167 (598–12,260)	5256 (2347–12,260)	898
AST/ALT ratio > 1	05 (100%)	04 (100%)	01 (100%)
Albumin, mean ± SD (g/dl)	3.0 ± 0.3	3.0 ± 0.1	3.0
Sodium, mean ± SD (meq/dl)	136 ± 6.0	137 ± 6.9	133
Potassium, mean ± SD (meq/dl)	5.3 ± 0.7	5.3 ± 0.1	5.2
Serum creatinine, median (range) (mg/dl)	1.9 (1.3–3.1)	2.3 (1.8–3.1)	1.3
Hemoglobin, mean ± SD (g/dl)	12.7 ± 1.7	12.7 ± 1.7	14
Packed cell volume mean ± SD	40.8 ± 5.4	40.5 ± 6.2	42
Total leukocyte count, median (range)/mm ³	8480 (3090–27,310)	15,705 (3090–27,310)	7900
Platelet count, median (range)/mm ³	30000 (5000–40,000)	20,000 (5000–39,000)	40,000
International normalized ratio, median (range)	3.5 (1.7–5.5)	4.3 (2.6–5.5)	2.1
Outcome, n (%)			
Died	04 (80%)	–	
Survived	01 (20%)		

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase.

^aNormally distributed continuous variables are expressed as mean (SD) and the continuous variables with skewed distribution were expressed as median (range). Categorical data are presented as proportions.

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noted in all patients. Four of 5 (80%) dengue-ALF patients died. All patients who died had developed multi-organ dysfunction (MOD) pre-terminally. Compared to patients who died, the one who survived was younger, and had lesser degree of transaminase elevation and preserved renal function.

The proportion of patients with dengue hepatitis progressing to ALF was 3.2% (05/156), which was on the higher side of the risk of ALF in patients with viral hepatitis (0.2–4%).³ All dengue-ALF patients had unusually high transaminitis and hyper-acute presentation, suggesting the rapidity of this catastrophic insult to liver. Previous studies have revealed that the severity of hepatitis is associated with high mortality in dengue patients.⁴ Contrary to what is seen in ALF due to other viruses, AST elevation was higher than ALT in all dengue-ALF. This may be due to release of AST from extrahepatic sources. The damaged skeletal muscles may be an important source of AST in such patients.^{5–7} Other laboratory abnormalities peculiar dengue-ALF were presence of significant thrombocytopenia and raised packed cell volume (Table 1). The mechanism by which the dengue virus causes ALF is not well understood. Studies have found dengue virus antigen in the hepatocytes and kupffer cells, and have suggested a role of cellular apoptosis in the pathogenesis.^{8,9} The histological changes include massive hepatic necrosis and a nonspecific pauci-cellular acute hepatitis.⁸ Apart from direct viral injury, there can be other reasons for hepatitis in dengue patients such as dysregulated immune response, ischemic/hypoxic injury secondary to hepatic sinusoidal congestion and/or shock, and toxicity of drugs like paracetamol. We found a high mortality rate (80%) among dengue-ALF patients. Paradoxically, one study has reported 100% survival rate among dengue-ALF patients with standard medical therapy.¹⁰ However, stringent criteria were not used to define ALF in that series as the median prothrombin time prolongation was only 4.8 s. Because both dengue fever and ALF can independently lead to MOD, it would be difficult to establish clearly the individual role of each factor. However, because severe liver dysfunction preceded the onset of MOD in dengue-ALF patients, it might have contributed substantially to the mortality. In conclusions, our study found several peculiar features in ALF caused by dengue virus such as uniform hyper-acute presentation, massive transaminase elevation, AST levels greater than ALT, severe thrombocytopenia, and high mortality.

SOURCE OF SUPPORT

None.

CONFLICTS OF INTEREST

The authors have none to declare.

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