

# Research Letters

## *Chelation Therapy and Cardiac Status in Young Patients with Thalassemia Major*

Cardiac dysfunction is a frequent and important cause of morbidity and mortality in patients with thalassemia major.<sup>1-4</sup> The chelating drug desferoxamine (DFO) increases iron excretion in urine and reduces iron storage. Multiple studies<sup>5-7</sup> have shown that patient who are compliant with DFO therapy are less likely to suffer complications from iron overload, particularly cardiac dysfunction. Patients who begin treatment at a young age can be protected from the lethal complications of iron overload for at least two decades.<sup>8,9</sup>

We studied 67 patients with thalassemia major during a period of 1 year from March 1996 to February 1997. Ages ranged from 4 to 18 years (mean age  $12.3 \pm 3.7$  years); 34 were female and 33 male. Cardiac involvement (CI) was considered to be present if a patient had ECG abnormality or cardiomegaly on chest X-ray, and/or clinical presentation of cardiac failure or pericardial effusion. Three patients showed ECG abnormalities; six cases showed cardiomegaly without cardiac failure; seven had one episode of cardiac failure; and in one case cardiac failure was associated with pericardial effusion. A 16-year-old boy died with intractable cardiac failure. Overall 16 patients (24 per cent) showed some kind of CI and 51 (76%) were without CI. Comparing the two groups with each other, patients with CI were older ( $p < 0.001$ ), began DFO later ( $p < 0.001$ ), and had a lower shortening fraction ( $p < 0.05$ ). Ejection fraction was lower in patients with CI compared with those without CI ( $57.7 \pm 9.1$  vs.  $60.2 \pm 6.4$  per cent) but the difference was not significant. Seven patients with cardiac failure had both ejection fraction and shortening fraction lower than the 60 patients without cardiac failure, the differences being significant (both  $p < 0.05$ ). It seems that during the course of cardiac siderosis, shortening fraction decreased earlier than ejection fraction and ejection fraction decreased later when the clinical symptoms of cardiac failure appeared. Serum ferritin levels were higher in patients with CI compared to those without CI ( $3039.3 \pm 1421.1$  vs.  $2608.7 \pm 1163.5$  ng/ml), but the difference was not significant. Compliance with DFO therapy were relatively similar in both groups ( $5.2 \pm 0.9$  vs.  $5.4 \pm 0.8$  nights/week). A serum ferritin level of 1000 ng/ml and 6 nights/week of DFO injection are known as safe limits of concentration and compliance. In our study 65.6 per cent of patients had serum ferritin levels greater than 2000 ng/ml and 82 per cent of them reported 5 nights or more of DFO injection per week; 76 per cent of cases were without CI. Seventy-five per cent of patients with CI were 15 years of age or older. It seems that a ferritin concentration of 2000 ng/ml and 5 nights/week DFO injection may be safe in early childhood but the toxic

cumulative effect of iron overload will appear in older patients. More studies with an extended period of follow-up are needed to pursue these children after their second decade of life.

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## *Gall Bladder Wall Edema in Serology Proven Pediatric Dengue Hemorrhagic Fever: A Useful Diagnostic Finding which may Help in Prognostication*

In the dengue epidemic of 1997 in Delhi, two hospitalized children with serologically proven dengue infection exhibited gall bladder wall edema. A Medline search revealed three published studies showing gall bladder wall edema in association with dengue infection.<sup>1-3</sup> The studies did not utilize serological criteria but depended on clinical findings. We initiated this study to evaluate the incidence of gall bladder wall edema in serologically proven dengue infection in 1998.

The study was started in September 1998 when the first dengue cases of the year were reported in Delhi. All children presenting to the hospital who fulfilled the clinical criteria for the diagnosis of dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) were hospitalized during the period September to December.<sup>4,5</sup> All children admitted with fever had their white cell count measured as part of a routine baseline work-up. If there was associated thrombocytopenia (platelet count  $\leq 100\,000/\text{mm}^3$ ) or hemorrhagic manifestations or increased capillary permeability (ascites, pleural or other effusions) they were included in the study.

Blood testing for dengue serology was carried out at the National Institute of Communicable Diseases, Delhi. IgM hemagglutination antibody titers  $>1:160$  were interpreted as a positive result. Ultrasound of the abdomen was performed in all cases. The criterion of gall bladder wall edema was a thickening of  $>3\text{ mm}^2$ . The clinical and ultrasound findings were tabulated into two groups according to whether they were seropositive or seronegative.

Using the above criteria 15 patients were admitted in the pediatric ward with the presumed diagnosis of dengue infection, out of whom 10 were seropositive and five were seronegative. All patients had fever and thrombocytopenia on admission. Ultrasound of the abdomen showed gall bladder wall edema, ascites and right pleural effusion in seven of 10 seropositive cases (Fig. 1). The above findings were seen in four of seven cases with DHF and three of three with DSS. The

finding of gall bladder wall edema was seen in only one of the five seronegative cases.

The three previously published studies that looked at gall bladder wall edema in dengue have used clinical criteria only.<sup>1-3</sup> Our study also used the clinical criteria for recruitment of cases, but the findings were analysed in two separate groups according to the seropositivity of the children.

Evidence of gall bladder edema was present in all three cases of DSS. Four of the seven cases of DHF had gall bladder wall edema. This suggests that this may be a candidate marker of severity of dengue infection and impending shock syndrome. This is supported by the findings of Setiawan, *et al.*<sup>2</sup>

The presence of gall bladder wall edema in one of our seronegative cases underlines the fact that this is not pathognomonic of dengue infection and can occur in other conditions also. The entry criteria of this study required the presence of fever and thrombocytopenia. Thus we looked at cases of DHF but we would not have picked up cases of dengue infection without thrombocytopenia. A study during an epidemic, looking for dengue serology in all children with fever, together with ultrasonographic findings is called for.

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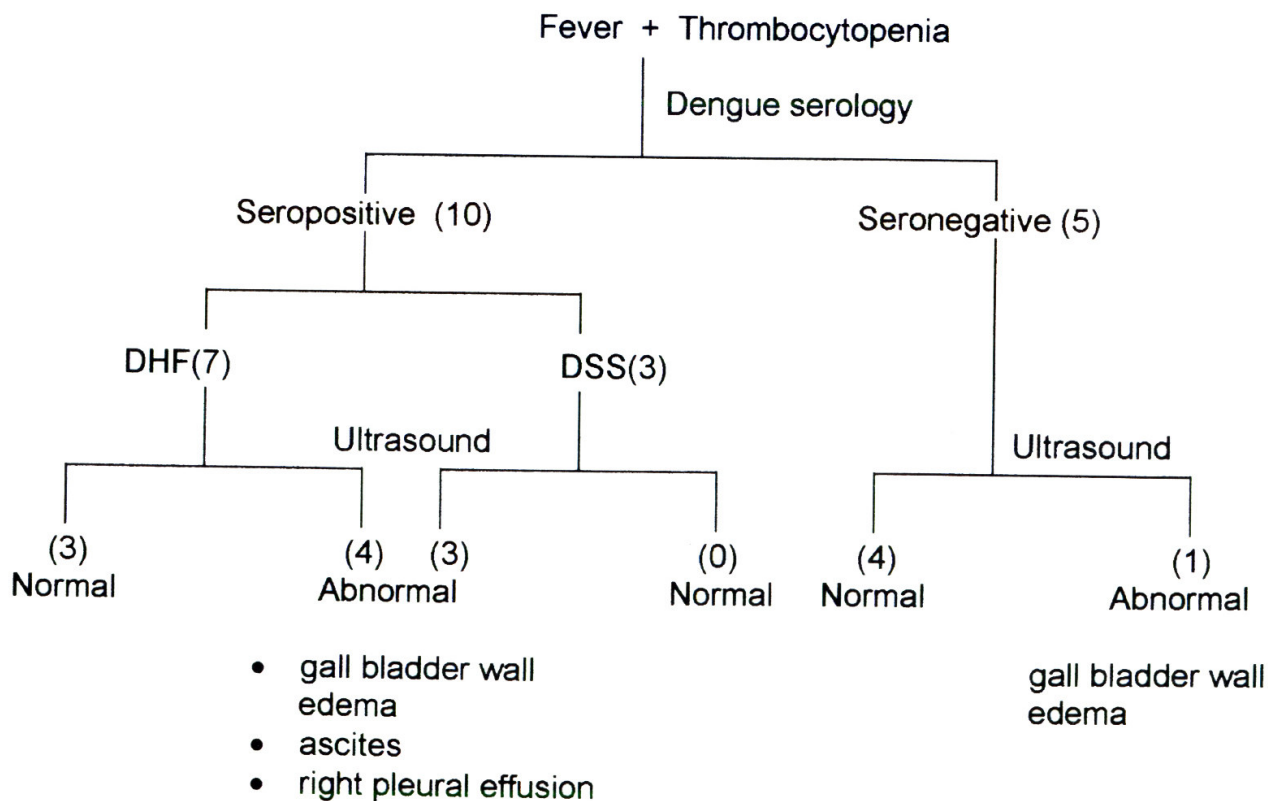


FIG. 1. Ultrasound abdomen examination of the study group.