

Extremely High Serum Ferritin Levels Associated With Abnormal Liver Function In Multi-Transfused Patients With Beta Thalassemia Major In Myanmar

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Citation

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Abstract

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Our goal was to determine the etiology of abnormal liver function in multi-transfused patients with beta thalassemia major in Myanmar. Beta thalassemia major (β TM) is a transfusion dependent inherited haematological disorder, exposing affected patients to a variety of transfusion related complications. Liver injury in β TM patients due to transfusions can be attributable to hepatitis viruses or iron overload (1-4).

Selection of subjects and inclusion and exclusion criteria: We conducted a hospital based, cross-sectional study of β TM patients among the tertiary hospitals in Yangon, Myanmar between May 2006 and December 2006. β TM patients who had received over 20 units of blood were enrolled in the study. Patients with less than 20 units of blood transfusions, and those taking alcohol, herbal or traditional medicine, or drugs that can affect liver enzymes were excluded from our study.

History and physical examinations and lab studies were carried out after consent was obtained. Blood samples were sent to the Department of Medical Research (Lower Myanmar) for serum ferritin, liver enzymes (serum ALT & AST), HBs Ag and anti HCV Ab. Serum ferritin was measured by a detection kit (ACCU TEST Ferritin (Bio – Cyber Co. Shizuoka, Japan). Hepatitis B (HBV) and hepatitis C (HCV) were tested by one step strip style immunoassay in serum and confirmed by ELISA. Serum ALT and AST were measured by a Colorimetric end-point method.

A total of 36 patients, 16 male and 20 female, participated in our study. Mean age was 10.4 years and ranged from 4 to 17 years. Elevated ALT and AST were noted in 11 (30.6%) and 14 (38.9%) respectively. Only two of the study population (5.6%) had clinical features of chronic liver disease. None of the patients had hepatitis B infection. Eight patients (22.2%) were positive for hepatitis C virus, but only 5 patients with hepatitis C had abnormal liver function tests.

A previous study carried out prior to 2000 in Myanmar found that 39% of multi-transfused subjects with thalassemia major were positive for hepatitis C (5). The incidence of hepatitis C was reported to be 0.96% in a study of donors in Myanmar from November 2005 to June 2007 (6).

Table 1

Relationship between blood transfusion characteristics, serum ferritin level and serum ALT among β TM patients

Variables	ALT > 30 U/L	ALT ≤ 30 U/L	P value
	Mean ± SD	Mean ± SD	
Age (in months)	123.3 ± 39.1	162.2 ± 45.7	0.844
Age of 1 st transfusion (in months)	22.8 ± 17.8	40.7 ± 30.3	0.035*
Total unit of blood transfusion	87.6 ± 74.6	66.4 ± 53.4	0.424
Serum Ferritin (ng/ml)	19264 ± 30497	3909 ± 4318	0.013*

T-test analyses were carried out. * Significance differences.

High ALT level was significantly associated with the age of first blood transfusion (P=0.035) and serum ferritin level (P=0.013).

Abnormal liver function appeared to be related to the high

ferritin levels and the age when transfusions were initiated, but liver function was not related to the age of the patients or the total amount of transfusion (Table 1).

The mean serum ferritin levels in patients with abnormal liver function tests was 19,264 ng/ml while subjects with normal liver function tests had mean ferritin levels of 3,909 ng/ml. Extremely high serum ferritin levels have been previously reported in multi-transfused patients with thalassemia major and in Stills disease (7,8). The basis for these high ferritin levels is not understood.

Ferritin levels in hemochromatosis rarely exceed 3000 ng/ml. Patients with hemochromatosis with ferritin levels of 1,000 ng/ml are likely to have cirrhosis. Standard care in United States would be to do liver biopsy and to initiate iron chelation.

In our study, only 16 patients received iron chelation, whereas the rest had no treatment mainly due to financial constraints and limited support. Among those treated with iron chelation therapy, two received subcutaneous desferrioxamine via infusion pump, the rest were given combined therapy of oral deferiprone and intravenous desferrioxamine. Currently, routine screening for serum ferritin levels and transfusion related infections like hepatitis B, C and HIV are done to all beta thalassemia major patients in Myanmar. Assessment of liver function, ultrasound abdomen and echocardiogram to detect complications of iron overload are performed in selected patients.

CONCLUSION

The study suggests that iron overload in multi-transfused

patients with thalassemia major is responsible for liver dysfunction. The limitation of our study is the small number of patients, but we intend to continue studying this problem in Myanmar. Nevertheless, our study confirms that serum ferritin levels can be extremely high in multi-transfused patients with thalassemia major.

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