International Journal of Basic and Applied Medical Sciences ISSN: 2277-2103 (Online)
An Open Access, Online International Journal Available at http://www.cibtech.org/jms.htm
2014 Vol. 4 (3) September-December, pp. 74-76/Warade and Pandey
Research Article

SICKLE CELL HEPATOPATHY DUE TO MULTIPLE TRANSFUSION

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ABSTRACT
There are studies suggesting that the main causes of liver injury in SCD patients are due to factors other than intrahepatic sickling, which was considered to be reversible, such as viral hepatitis or transfusional iron overload. In this study, we have investigated abnormalities of hepatic biochemical markers in SCD due to multiple blood transfusions. Serum enzyme (ALP, ALT, and AST) and bilirubin parameters are significantly increased in subjects those who have received multiple transfusions. Multiple transfusions are one of the reasons to be considered in case of liver dysfunction in sickle cell disease patients.

Keywords: *Iron Overload, Hepatic Abnormality, Hemosiderosis, Sinusoidal Sickling*

INTRODUCTION
Sickle cell anemia is an inherited blood disorder characterized primarily by chronic anemia and periodic episodes of pain. The underlying problem involves hemoglobin, a component of red blood cells. The liver can be affected by a number of complications due to the disease itself and its treatment (Banerjee *et al.*, 2001; Berry *et al.*, 2007; Ebert *et al.*, 2010).
In addition to the vascular complications from the sickling process, patients with SCD have often received multiple transfusions, placing them at risk for viral hepatitis, iron overload, and (combined with the effects of chronic hemolysis) the development of pigment gallstones, all of which may contribute to the development of liver disease.
The term "sickle cell hepatopathy" has sometimes been used to reflect the overlapping causes of liver dysfunction in these patients. Sickle cell hepatopathy occurs predominantly in patients with homozygous sickle cell anemia. There are other studies suggesting that the main causes of liver injury in SCD patients are due to factors other than intrahepatic sickling, which was considered to be reversible, such as viral hepatitis or transfusional iron overload (Rosenblate *et al.*, 1970; Omata *et al.*, 1986). In this study, we have investigated abnormalities of hepatic biochemical markers in SCD due to multiple blood transfusions.

MATERIALS AND METHODS
The present study was carried out during the period of December 2007 - September 2009 in the Department of Biochemistry, Indira Gandhi Government Medical College, Nagpur. The study protocol was approved by the Institutional Ethical Committee. To evaluate biochemically, the patients with sickle cell disease (n=100) from medicine and pediatrics wards/OPD were included in the study. An informed written consent was obtained from all the study subjects who were enrolled in the study. Detailed history was obtained from the study subject. Study subjects were divided according to number of blood transfusion they have received.
The estimation of biochemical parameters such as AST, ALT, ALP and bilirubin in serum was done by Transasia Erba XL 300 fully automated analyzer with dedicated reagents.
Statistical Analysis: All values were reported as mean ± SD. The unpaired two tailed Student's t test was used to assess the significance of the difference in the values in the sickle cell disease subjects and in healthy controls.
The differences were considered as statistically significant at a probability value, $P < 0.05$. All statistical analyses were performed by using statistical software Graph Pad Prism.

RESULTS AND DISCUSSION

Results

The results obtained after estimating liver parameters in subjects those with received blood transfusion are tabulated. It is found that the subjects who have received more than 10 blood transfusions have significantly higher levels of liver enzyme than those who have received less than 5 transfusions.

Discussion

Here the abnormal liver function test in our study is thought to be due to staining of hepatocyte and kupffer cell with hemosiderin. Repeated transfusion has caused increase in iron stores of the body which has cause injury to hepatic cells. The iron overload is may be the chief cause of hepatic dysfunction in this study. The possibility of viral hepatitis due to HBV, HCV and CMV infection is theoretically ruled out as all of the licence blood banks issuing blood and its components have mandatory screening of HBV, HCV, and CMV. Also the cases which were investigated for this viral marker were negative. Emel *et al.,* (2005) tried to evaluate the frequency of hepatic dysfunction and etiological factors in 48 patients with sickle cell disease.

Table 1: Serum Parameters Value in Patients with Multiple Transfuion

	>10 Blood transfusion	**5-10 Blood Transfusioon**	**< 5 Blood Transfusion**	**P value**
Sr.ALP(IU/L)	189.8±11.03	112.4±8.69	62.63±6.8	<0.001(HS)
Sr.ALT(IU/L)	89.73±11.07	58.85±5.2	29.54±4.84	<0.001(HS)
Sr.AST(IU/L)	84.11±10.18	60.56±4.8	29.02±6.77	<0.001(HS)
Sr. Bilirubin (T)	3.56± 0.91	2.10± 0.5	1.78± 0.45	<0.001(HS)

Table 2: Number of Blood Transfusion Received by Study Subjects

No. Of Blood Transfusion	**No. Of Subjects**
00	15
01	22
02	17
03	12
04	08
05	05
06	05
07	06
08	07
09	02
10	01

The most significant contributory finding was the presence of hemosiderosis in histological examination of liver specimens. The data of their study suggest that chronic liver injury in patients with sickle cell disease seems to be a multifactorial phenomenon depending mostly on overlapping factors such as iron overload and viral damage rather than primary disease itself (Gürkan *et al.,* 2005).

Fabiola *et al.,* (2007) evaluated the incidence and etiology of chronic liver abnormalities in 70 living patients with sickle cell disease. They found that in patients with sickle cell disease, chronic liver abnormalities are frequent and seem to be a multifactorial phenomenon, depending on overlapping factors such as cholelithiasis, viral damage, iron overload and also the primary disease itself (Traina *et al.,* 2007). There are other studies suggesting that the main causes of liver injury in SCD patients are due to factors other than intrahepatic sickling, such as viral hepatitis or transfusional iron overload (Rosenblate *et al.,* 1970; Omata *et al.,* 1986).

Hepatic injury due to transfusional iron overload and staining of hepatocytes and Kupffer cell with iron leading to hepatic iron overload due to repeated blood transfusion may be a possible reason for hepatic dysfunction in those patients who have received multiple blood transfusions.

The risk of hepatitis B and C infections has been related to the number of blood units transfused. Hepatic dysfunction is a commonly recognized complication of sickle cell disease (SCD) due to multiple factors such as intrahepatic sinusoidal sickling, bilirubin gallstones, transfusion-related hepatitis infections or excess iron deposition (Choi *et al.,* 2008; Chumakov, 2007). Recent studies have indicated that chronic HCV infection and iron overload place sickle cell patients at risk for significant liver disease and that the HCV antibody positivity is directly related to the number of transfusions given (Hassan *et al.,* 2003; Hassan *et al.,* 2003).

Conclusion

Serum enzyme (ALP, ALT, and AST) and bilirubin parameters are significantly increased in subjects those who have received multiple transfusions. The liver function of the patients was significantly compromised as compared to controls. Multiple transfusions are one of the reasons to be considered in case of liver dysfunction in sickle cell disease patients.

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