ASSESSMENT OF LIVER FUNCTION IN SICKLE CELL DISEASE

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ABSTRACT

Background: The liver is one of the organs involved in the multi-organ failure that occurs in sickle cell disease, the pathophysiology of liver disease in this condition is complex because of the interrelated multifactorial causes.

Aim: The study was aimed at assessing the liver functions in steady state sickle cell disease patients.

Methods: Liver functions were assessed in 60 patients with sickle cell disease in the steady state and 50 control subjects. The transaminases, alkaline phosphatase and bilirubin were done by manual methods using semi auto analyzer for concentration readings.

Results: The mean values of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP) and Bilirubin (BIL) were 39.10±2.73, 28.53±2.77, 94.12±5.86U/I and 27.99±5.21µmol/l respectively. The corresponding values in controls were 20.66±1.01, 25.16±1.42, 68.00±2.89U/I and 2.55±0.27µmol/l. The AST, ALP and BIL values obtained in sickle cell disease patients were statistically significant when compared with controls while ALT values were not. Age and gender of the patients did not significantly affect the levels of these parameters with the exception of ALP which was significantly higher in the lower age groups.

Conclusion: Increased serum liver function tests except ALT which is not gender and age related were observed in sickle cell disease patients in the steady state and reflect the classic histologic features of Kupffer cell erythrophagocytosis and engorgement of sinusoids by aggregate of sickled red cells.

Key words: Liver enzymes, Transaminases, Sickle cell disease, Bilirubin

INTRODUCTION

Hepatic dysfunction is a commonly recognized complication of sickle cell disease due to multiple factors such as intra-hepatic sinusoidal sickling, bilirubin, gallstones, transfusion related hepatitis infections or excess iron deposition (Beutler, 1999 and Kakarala *et al.,* 2004). Clinical evidence of hepatic dysfunction in patients with sickle cell disease was explained by trapping of sickle cells during passage through the hepatic sinusoids which are engulfed by phagocytes causing hepatomegaly (Beutler, 1999). Hemolysis raises plasma levels of aspartate aminotransferase (AST), hepatocyte injury more accurately raises plasma alanine aminotransferase (ALT) levels (Benerjee *et al.,* 2001). Cholestasis or bone disease causes high levels of serum alkaline phosphatase (Brady *et al.,* 2001) while jaundice raises total serum bilirubin levels in patients with sickle cell disease.

Evidence of liver disease in sickle cell disease is obtained from abnormal biochemical tests with limitation in assessing postmortem liver biopsy specimen and biochemical tests often included only the liver enzymes.

Assessing the liver functions, its clinical relevance and understanding of the derangement of liver enzymes in sickle cell disease is unclear. Therefore, this study was undertaken to assess the pattern of liver function tests in sickle cell disease patients who are free of any acute illness and are in their steady state.

MATERIALS AND METHODS

The study included 60 patients, 25 males and 35 females aged between 15 to 51 years attending sickle cell clinic of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria. All patients included were in the steady state of the disease. Fifty (50) apparently healthy individuals including 32 males and 18 females aged between 19 to 42 years were selected randomly as controls. Informed consent was obtained from all subjects and those who decline to give consent were excluded. Ethical approval was gotten from the Ethics Committee on Use of Human Subjects for Research, ABUTH, Zaria.

A general examination was done on all patients including assessment of the conjunctiva for jaundice which was classified as mild, moderate or severe. Enlargement of the liver below the costal margin was classified as mild, moderate and massive if it is less than 5cm, less than 10cm and more than 10cm respectively. 5mls of blood samples were collected into lithium heparin container and the plasma used for liver function tests analysis. Laboratory data consisting serum transaminases were measured by Reitman and Frankel method, alkaline phosphatase by modified King Armstrong method and bilirubin by Malloy and Evelyn method using a Hitachi semi auto analyzer for concentration readings.

Statistical analysis:

Data were analyzed statistically using SPSS for windows release 16.0. Student t-test was used to test the difference between sickle cell patients in the steady state and the control group. Pearson's product moment correlation coefficient was used to determine if there was significant difference between pattern of liver function tests, gender and age. Statistical significance was set at P-values less than 0.05 ($P<0.05$).

Results and Discussion

The results of the present study are summarized in table I and II. Statistical significance ($P<0.05$) was observed in AST, ALP and BIL levels in sickle cell disease patients when compared with controls while ALT levels showed no statistical significance ($P>0.05$). These were in concordance with the reports of Cage, (2001) and Kotila *et al.,* (2005).

Table I: Serum Liver Function Tests in sickle cell patients and controls

	PATIENTS n=60	**CONTROLS n=50**	**T-VALUE**	**P-VALUE**
AST (U/l)	39.10 ± 2.73	20.66±0.01	6.0	<0.05
ALT (U/L)	28.53±2.77	25.16±1.42	1.0	>0.05
ALP (U/L)	94.12±5.86	68.00±2.89	3.8	<0.05
C.BIL (µmol/l)	9.93±1.95	0.99±0.14	4.2	<0.05
T.BIL (µmol/l)	27.99±5.21	2.55±0.27	4.9	<0.05

Values are mean ±SEM

Table II: Sex related distributions of serum liver function tests in patients with sickle cell disease

	MALES	FEMALES	T-VALUE	P-VALUE
	N=25	N=35		
AST (U/l)	38.43±4.34	39.60±3.56	0.2	>0.05
ALT (U/L)	26.96±4.36	29.66±0.41	0.5	>0.05
ALP (U/L)	99.72±10.72	80.83±5.62	1.5	>0.05
C.BIL (µmol/l)	10.64±3.16	9.41±2.50	0.3	>0.05
T.BIL (µmol/l)	29.19±8.14	27.13±6.88	0.2	>0.05

Values are mean±SEM

The results obtained from sickle cell patients were generally higher than those obtained from the control subjects. These findings agree with the reports of Ometa*et al.,* (1986), Roshkow and Sanders, (1990) and Hamatz*et al.,* (2000). Their findings suggest that the high concentrations of serum total bilirubin and its conjugated fraction observed in the sickle cell patients are expected and could be explained by certain clinical conditions prevalent among patients with sickle cell disease. These include viral hepatitis (Johnson *et al.,* 1985), intrahepatic cholestasis (Buchanean and glader, 1997), hepatic crisis (Davies and Brozovic, 1987) and hemolytic jaundice (West *et al.,* 1992). The observed high activities of serum alanine aminotransferase and aspartate aminotransferase in patients with sickle cell disease could be as a result of the presence of numerous sickle red blood cells in the lobular parenchyma of the liver (Shao and Orringer, 1995). The observed high activities of serum alkaline phosphatase in sickle cell patients could be attributed to both bone and liver complications usually associated with sickle cell anemia. The mechanism for this increase could be due to increased osteoblastic activity in bone infiltration (Brady *et al.,* 2001). This also agrees with the reports of Ojuawo *et al.,* (1994) and Soliman *et al.,* (2001) which suggest the increased alkaline phosphatase activities to be due to either cholestasis or vaso-occlusive crisis involving the bone.

No statistical significance was reported in sex and age related distributions of liver function tests in sickle cell patients by (yeomans *et al.,* 1990 and Kotila *et al.,* 2005). In this study ~~too~~, this appears true as values in males and females were similar. However, the observed high activities of serum ALP in the lower age group could be attributed to the rapid growth occurring in children and young adults (Brady *et al.,* 2001). This has also been reported by (Kotila*et al.,* 2005 and Omata*et al.,* 1986).

In conclusion, increased serum activities of AST, ALP, BIL level and normal activity of ALT which are not gender or age related were observed in sickle cell disease patients in the steady state. Marked increase in liver enzymes may be due to complications arising from management of the disease. Hence, liver function tests could serve as an adjunct to other conventional laboratory tests for this disease such as hemoglobin electrophoresis, sickling test and solubility test.

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