Original Research Paper

Volume-9 | Issue-1 | January-2019 | PRINT ISSN - 2249-555X

Biochemistry

EVALUATION OF LIVER TRANSAMINASES IN PATIENTS WITH SICKLE CELL DISEASE

Dr. Sushma BJ Chandrakar MBBS, MD, FID, FCGP, Assistant Professor, Dept. of Biochemistry, CCMMC, Kachandur, Durg

Dr. Shrikant Chandrakar* MBBS, MD, FID, FCGP, Assistant Professor, Dept. of Biochemistry, CCMMC, Kachandur, Durg *Corresponding Author

ABSTRACT

Background: Sickle Cell Disease (SCD) is a life threatening autosomal recessive genetic disorder resulting from inheritance of abnormal genes from both parents. This disorder is prevalent in Central India along with other states like Maharashtra, Gujarat, Telangana, Odisha, Andhra Pradesh, Tamil Nadu and Kerala. SCD is frequently associated with liver disease resulting from multiple pathophysiological causes such as intrahepatic sinusoidal sickling, formation of gall stones (bilirubin stones), transfusion related hepatitis infections or excess iron deposition.

Methods: 80 diagnosed and HPLC confirmed cases of SCD along with 80 age and gender matched controls were involved in the study. In all the cases and controls 5mL of random blood sample was drawn for biochemical analysis (liver function tests) after taking consent from the patients.

Results: The serum total bilirubin, direct bilirubin, indirect bilirubin, aspartate transaminase (AST) and alanine transaminase (ALT) levels were significantly higher in SCD patients ($P<0.001$) than in controls.

Conclusion: SCD patients had elevation of Transaminases and remaining liver function parameters compared to age matched controls. It is advisable that liver function tests be interpreted with caution in these patients. SCD patients require serial monitoring of these parameters during their routine visits to the hospital.

KEYWORDS : Sickle Cell Disease, total bilirubin, direct bilirubin, indirect bilirubin, aspartate transaminase (AST) and alanine transaminase (ALT).

INTRODUCTION

Sickle Cell Disease (SCD) is a life threatening autosomal recessive genetic disorder resulting from inheritance of abnormal genes from both parents. It is a common hereditary hemoglobinpathy that occurs primarily in individuals of African Americans, Arabian and Indian descent. In India, this disorder is prevalent in Chhattisgarh, Madhya Pradesh, Maharashtra, Gujarat, Telangana, Odisha, Andhra Pradesh, Tamil Nadu and Kerala. In India hemoglobinopathies are responsible for the largest number of genetic disorders and hence are of great public importance [1,2].

Sickle Cell Disease (SCD) is the major health problem in Chhattisgarh Population. Recent statistical data reveals that, the prevalence of SCD among the screened population in Chhattisgarh is about 2.1% and sickle cell trait is 10% among the different tribes. Sickle Cell Disease is one of the most common monogenic disorder with an Autosomal Recessive inheritance, resulting from single gene mutation within the beta globin gene. The disease results from a single base A to T mutation in the triplet encoding the sixth residue of the β-globin chain, leading to a substitution of valine for glutamic acid resulting in abnormal hemoglobin S (HbS) [3,4]. James Herrick, was the first physician first to describe the characteristic sickle shaped red cells in a medical student from Grenada in 1910. Linus Pauling and his colleagues showed that sickle hemoglobin (HbS) had an altered electrophoretic mobility and they were the first to define it as a molecular disease in 1949. The primary pathophysiology is based on the polymerization of deoxy HbS with formation of long fibers within the RBCs causing a distorted sickle shape which eventually leads to increased hemolysis and vaso-occlusive crisis [5,6].

The term "sickle cell hepatopathy" has sometimes been used to reflect the overlapping causes of liver dysfunction in these patients and occurs more commonly in homozygous sickle cell anemia and to lesser extent in HbSC and HbS beta-thalassemia. Liver dysfunction due to various pathophysiological factors such as multiple blood transfusions associated with risk of hepatitis, excessive iron stores, intrahepatic sinusoidal sickling and bilirubin gallstones. Hence serial monitoring of liver function parameters is required in these patients to detect the liver dysfunction at the earliest and hence the treatment [7,8,9,10].

OBJECTIVE OF THE STUDY:

The present study aimed to evaluate liver function tests (total bilirubin, direct bilirubin, indirect bilirubin, ALT, AST, Total Protein and Albumin) in sickle cell disease subjects.

MATERIALS AND METHODS:

Source of Data: A cross-sectional study on Evaluation of liver transaminases in Sickle Cell Disease in Chhattisgarh Population was conducted in the patients aged 3-40 years who were regularly attending OPD (General Medicine and Pediatrics) were included in the study.

Inclusion Criteria: 80 proven cases of Sickle Cell Disease HbSS aged 3-40 years who were on regular follow-ups along with newly diagnosed cases of Sickle Cell Disease and 80 age and gender matched healthy controls were included in the study. All the patients suffering from Sickle Cell Disease was diagnosed and confirmed by High Performance Liquid Chromatography (HPLC), Hemoglobin Electrophoresis were included in the study.

Sample Collection and Analysis: A general examination was done on all the subjects before blood samples were taken for hematological and biochemical analysis. The general examination included assessing conjunctiva for jaundice and palpation of liver for hepatomegaly. 5 mL of whole blood sample was collected into plain tube for biochemical analysis (Liver function tests: Total Bilirubin, Indirect Bilirubin, Alanine Transaminase, Aspartate Transaminase, Total Protein and Albumin). These parameters are estimated in Automated Biochemistry Analyzer MISPA nano.

Statistical Analysis: Students t-test was used to compare means of variables between sickle cell disease patients and controls. P value <0.05 was considered as statistically significant.

Depending upon the serum levels of Alanine amino transferase & Aspartate amino transferase the hepatic involvement is graded into 4 different grades: [Table no-1].

Table No 1: Evaluation of hepatic involvement as four grades

Grade 1	Normal levels of aminotransferase
Grade 2	Elevated levels of aminotransferase with increase in levels of atleast one of the enzymes
Grade 3	Elevated levels of aminotransferase with increase in levels of atleast one of the enzymes to > 3times of its reference values
Grade 4	Acute hepatitis with aminotransferase levels increased to atleast 10 times their normal values.

RESULTS

A Total of 80 sickle cell disease subjects and 80 age and gender matched controls were studied. Of the 80 sickle cell disease subjects 48

were males and 32 were females and among 80 controls 44 were males and 36 were females. The mean age in sickle cell disease subjects was 25.214.8, while that of 23.716.3 in controls. All the sickle cell disease subjects were hemoglobin SS homozygous, while all the controls were hemoglobin AA.

Table 1: Shows the comparison of liver function tests between sickle cell disease subjects and controls

	Sickle Cell Disease Subjects	Controls	p Value
Total Bilirubin (mg/dL)	4.55 2.13	0.72 0.23	<0.001
Direct Bilirubin (mg/dL)	1.65 0.76	0.23 0.06	<0.001
Indirect Bilirubin (mg/dL)	2.89 1.80	0.49 0.17	<0.001
ALT (U/L)	56.95 39.5	25.95 14.5	<0.001
AST (U/L)	79.58 46.1	29.58 12.1	<0.001
Total Protein (gm/dL)	6.65 0.76	6.5 0.76	NS
Albumin (gm/dL)	3.56 0.78	3.59 0.72	NS

From the table 1: it is evident that the total bilirubin, direct bilirubin, indirect bilirubin, ALT and AST levels were significantly elevated in Sickle Cell Disease patients compared to controls. There was no significant difference in the levels of total protein and albumin levels between sickle cell disease patients and controls.

Table 2: Shows Evaluation of ALT and AST in patients with Sickle Cell Disease

	ALT & AST Levels	ALT	AST
Grade A	Normal levels	44 (55%)	24 (30%)
Grade B	1-3 times elevation	32 (40%)	45 (56.2%)
Grade C	>3-10 times elevation	4 (5%)	11 (13.7%)
Grade D	(>10 times elevation)	0 (0%)	0 (0%)

From table 2: It is evident that 55% of the SCD patients had normal ALT levels, and it was increased to 1-3 times, >3-10 times in 40% and 5% of the SCD patients respectively and none of them had more than 10 times rise. AST was normal in 30% of the SCD patients and was raised to 1-3 times and >1-3 times in 45% and 11% respectively and none of them had greater than 10 times. It is also evident that AST is elevated in more number of SCD patients compared to ALT elevation.

DISCUSSION

In the present study, we found elevated levels of liver transaminases and bilirubin levels (total, direct and indirect) in sickle cell disease patients as compared to controls. The clinical spectrum of liver dysfunction in SCD patients varies from mild to severe and resulting in sickle crisis with marked hyperbilirubinemia and liver failure [2]. Several factors play a significant role in liver disease such as ischemia (vaso-occlusion), multiple transfusion related infections (hepatitis), excess of iron deposition due to multiple transfusions and gallstone disease (bilirubin stones) [11].

Bilirubin is a degradation product of hemoglobin metabolism, mainly produced in the liver. Hyperbilirubinemia (increased bilirubin levels) can be seen in pre-hepatic (hemolytic), hepatic or post hepatic (obstructive) phases. In sickle cell disease, there is liver dysfunction and hemolysis hence we find elevated bilirubin levels. In this study, we found elevated total bilirubin levels, direct and indirect bilirubin levels (indirect bilirubin levels are more elevated compared to direct bilirubin levels. This similar finding was also seen in the previous studies [12,13].

AST levels were elevated in 56% of the total sickle cell disease subjects as compared to control groups and 46% of them had normal levels. ALT levels were elevated in 45% of the sickle cell disease patients as compared to control groups and 55% of them had normal levels. Taiwo Koitla et al reported that 50% of their study subjects had elevated AST levels and 50% of them had normal levels [14]. Similarly, Ahmad M et al found that all the three cases of SCD had elevated AST and ALT levels. [15]. Hemolysis and liver dysfunction in sickle cell disease patients elevates ALT and AST levels, which makes a useful test for detecting liver damage [16].

AST and ALT are widely distributed throughout the body, and participate in gluconeogenesis by catalysing the transfer of amino groups from aspartate and alanine to -ketoglutaric acid to form oxaloacetate and pyruvate, respectively as well as glutamate. AST is found primarily in the heart, liver, skeletal muscle, red cells and kidney, whereas ALT is found mainly in the liver and kidney with lesser amounts in the heart and skeletal muscles [17,18].

In the present study, we observed that the AST levels were more elevated compared to ALT levels, this is mainly linked to hemolytic tendency in sickle cell disease. There is also evidence that vaso-occlusive crisis is associated with intensification of hemolysis, which again results in elevated levels of bilirubin. The disproportionately stronger correlation with AST than with ALT is consistent with higher concentrations of AST than ALT in red blood cells, which are released during intravascular hemolysis [19,20,21]. There was no significant differences in the total protein and albumin levels in sickle cell disease patients and controls. In some studies they have reported increased levels of total protein levels in sickle cell disease patients compared to controls. Similarly some other studies have reported decreased levels of serum total protein levels in sickle cell disease patients.

CONCLUSION

SCD patients had elevation of Transaminases and remaining liver function parameters compared to age matched controls. It is advisable that liver function tests be interpreted with caution in these patients. SCD patients require serial monitoring of these parameters during their routine visits to the hospital.

ACKNOWLEDGMENTS

The authors are grateful to technical team at the Clinical Analyses Laboratory of the Department of Biochemistry, CCM Medical College for their assistance in the biochemical analyses. My special thanks to our colleagues, hospital management, my parents, Miss Madhurya, Dr. B V Maruthi Prasad who was source of inspiration to me for my research work.

DISCLOSURE

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest.

REFERENCES

1. Kar BC. Sickle cell disease in India. J Assoc Physicians India. 1991;39:954-60. 6.
2. Mohanty D, Mukherjee MB. Sickle cell disease in India. Curr. Opin Hematol. 2002;9:117-22.
3. Sapna T, Ravindra S, Sharada NR. Incidence of Thalassemia and Sickle Cell Disease in Chhattisgarh, Central India: Using Hardy-Weinberg Equations. J Mol Genetic Med 2015; 9:1-5
4. Roshan B C, Malay B, Mukherjee, Snehal M, Kanjaksha G. Sickle cell disease in tribal populations in India. Indian J Med Res 2015; 141:509-15
5. Stuart MJ, Nagel RL. Sickle cell disease. Lancet 2004; 364:1343-60
6. Rees DC, Williams TM, Gladwin MT. Sickle cell disease. Lancet 2010; 376:2018-31
7. Kakarala S, Lindberg M. Safety of liver biopsy in acute sickle hepatic crisis. Conn Med. 2004;68(5):277-9.
8. Beutler E. The sickle cell diseases and related disorders. In: Beutler E, Lichtman MA, Coller BS, Kipps TJ, Seligsohn U, eds. Williams Hematology. New York: McGraw Hill. 1999;581-605.
9. Rosenblate HJ, Eisenstein R, Holmes AW. The liver in sickle cell anemia. A clinical-pathologic study. Arch Pathol. 1970;90(3):235-45.
10. Omata M, Johnson CS, Tong M, et al. Pathological spectrum of liver diseases in sickle cell disease. Dig Dis Sci 1986;3(3): 247-56.
11. Benerjee S, Owen C, Chopra S. Sickle cell hepatopathy. Hepatology 2001;33(5):1021-28
12. Hargrove MD. Marked increase in serum bilirubin in sickle cell anemia. A report of 6 patients. Am J Dig Dis. 1970;15(5):437-42
13. Isichef UP. Serum protein profile in sickle cell disease. J Clin Pathol. 1979;32:117-21
14. Kotila T et al. Liver Dysfunction in steady state sickle cell disease. Ann Hepatol 2005;4(4):261-63
15. Al-Suleiman AM, Bu-Sobaih J. Acute fulminant cholestatic jaundice in sickle cell disease; Ann Saudi Med 2006;26(2):138-40
16. Nsaiah K et al. Pattern of AST and ALT changes in relation to hemolysis in sickle cell disease. Clin Med Insight Blood Disord. 2011;4:1-9
17. Pratt DS, Kaplan MM. Evaluation of abnormal liver-enzymes results in asymptomatic patients. New Engl J Med. 2000;342:1266–71.
18. Kato GJ, McGowan V, Machado RF, et al. Lactate dehydrogenase as a biomarker of haemolysis-associated nitric oxide resistance, priapism, leg ulceration, pulmonary hypertension and death in patients with sickle cell disease. Blood. 2006;107:2279–85.
19. Neely CL, Wajima T, Kraus AP, Digg LW, Barreras L. Lactic acid dehydro- genase activity and plasma hemoglobin elevation in sickle cell disease. Am J Clin Pathol. 1969;52:167–9.
20. Ballas SK, Macolina MJ. Hyperhemolysis during the evolution of uncom- plicated acute painful patients with sickle cell anemia. Transfusion. 2006; 46:105–10.
21. Sonntago O. Haemolysis as an interference factor in clinical chemistry. J Clin Chem Clin Biochem. 1986;24:127–39.