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# CORRELATION OF THE LIVER FUNCTION TEST WITH PHYSICAL STATUS OF LIVER IN THE PATIENTS WITH HEMOGLOBINOPATHY-CROSS SECTIONAL STUDY

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**Abstract:**

**Introduction:** Hemoglobinopathies are one of the commonest genetic disorders worldwide. They include Thalassemia and abnormal variant hemoglobin such as Hemoglobin S, D, E etc. it is estimated that 7% of the world population carry an abnormal hemoglobin gene. In Hemoglobinopathies recurrent ischemic insults with parenchymal necrosis can result in hepatic fibrosis, chronic liver disease, and cirrhosis. Overall physical status of liver is assessed by liver function test.

**Material & Methods:** Hospital based cross sectional study was conducted involving patients under 18 years of age registered for treatment of haemoglobinathies in the Department of Pediatrics, of Rajendra Institute of Medical Sciences, Ranchi during June 2021 to June 2022. Data was collected by using pretested & predesigned questionnaire. Detailed history of all study participants was taken followed by through clinical examination and laboratory investigation.

**Result:** AST, ALT & ALP levels are significantly higher in patients with fibrosis, male participants affected more compared to female participants and proportion of patients with fibrosis was significantly higher with no. of blood transfusion.

**Conclusion:** Overall positive correlation was observed between increasing stage of fibrosis and level of liver enzymes.

**Keywords:** Hemoglobinopathy, Liver Function Test.

## Introduction:

Hemoglobinopathies are one of the commonest genetic disorders worldwide. They include Thalassemia and abnormal variant hemoglobin such as Hemoglobin S, D, E etc. it is estimated that 7% of the world population carry an abnormal hemoglobin gene, while about 3 lakh to 5 lakh children are born annually with significant hemoglobin disorders. They consist of two major groups – Thalassemia and Sickle cell syndromes. Being an important cause of morbidity and mortality, they impose a heavy burden on families and the health sector in our country. India has the largest number of children with Thalassemia major in the world – about 1 to 1.5 lakhs and almost 42 million carriers of ß (beta) thalassemia trait. About 10,000 -15,000 babies with thalassemia major are born every

year[1]. Sickle cell disease affects many communities in certain regions, such as central India and States of Gujarat, Maharashtra and Kerala. The carrier frequency of the Sickle cell gene varies from 1 to 35 % and hence there are a huge number of people with Sickle cell disease[2,3,4,5,6].
Sickle cell disease (SCD) or homozygous sickle cell anemia is the most common inherited disorders of erythrocytes, characterized by the presence of pathogenic hemoglobin S(HBS). HbS polymerizes in deoxygenated conditions, precipitating changes in the red cell membrane and dehydration of red cells leading to formation of sickle cells[7]. Recurrent ischemic insults with parenchymal necrosis can result in hepatic fibrosis, chronic liver disease, and cirrhosis[8]. Overall physical status of liver is assessed by liver function test. With this background present study was planned to measure correlation between liver function test of the patient and physical status of liver in the study population.

**Material & Methods:**
Hospital based cross sectional study was conducted involving patients under 18 years of age registered for treatment of haemoglobinathies in the Department of Pediatrics, of Rajendra Institute of Medical Sciences, Ranchi during June 2021 to June 2022.
Data was collected by using pretested & predesigned questionnaire. Detailed history of all study participants was taken followed by through clinical examination and laboratory investigation.
Sample size: Average 100 patients were registered for the treatment of hemoglobinopathies in one year. Among these 50 percent receive more than 20 transfusions. Considering this 50 patients receiving more than 20 transfusions were included in the study.

**Inclusion criteria:**
All hemoglobinopathies patients under 18 years of age and those who give informed consent for the study.

**Exclusion Criteria:**
1. Patients with any other liver pathology such as:-
2. Hepatitis B (hepatitis B surface antigen [HBsAg] positive),
3. Hepatitis C (anti–hepatitis C virus [HCV] positive),
4. Human immunodeficiency virus (enzyme-linked immunosorbent assay [ELISA] positive),
5. Wilson‟s disease (ceruloplasmin <20 mg/dL and 24-hour urinary copper >100 mg),
6. Autoimmune hepatitis (positive for serum anti-nuclear antibody [ANA],
7. Anti–smooth muscle antibody [ASMA].

Purpose of the study was explained to the study participants and their parents. Only after written consent of parents, study participants were enrolled in the study. Institutional ethics committee permission was taken prior to beginning of the study. Confidentiality of the information was ensured.

**Methodology and Laboratory Investigations:** Detailed history regarding duration and number of blood transfusions, history of drug intake, any other past illnesses was taken. The patient has to undergo Fibro scan study of liver a non-invasive method, liver function test (AST,ALT& ALP) and serum ferritin will be done in all the patients.

**Collection of samples** Sterile venipunctures were used to take blood samples. After centrifuging samples for ALT, AST, ALP, and ferritin for 20 min at a speed of 2000–3000 rpm, the samples were stored at −80 C until testing. Prior to giving packed red blood cell transfusions, all samples were collected. Abbott Architect ci4100 analyzer was used to measure LFT and serum ferritin.

**Statistical Analysis:**
Data collected during the study compiled in Microsoft excel version 2019 and further analysis done using SPSS 25.0 software. Categorical data was expressed in proportion, and percentage and numerical will be expressed in mean and standard deviations (SD). P-value less than 0.05 considered as significant.

**Result:**
A total of 52 beta-thalassemia major patients with a mean age of 8.47 ± 3.48 years were enrolled in this study.

**Table No.1: Distribution of study participants as per Demographic details**

| Characteristics | Values |
|---|---|
| Age | 8.47 ± 3.48 |
| Gender | |
| Male | 38 (73.1%) |
| Female | 14 (26.9%) |
| Disease | |
| Beta Thalassemia Major | 47 (90.4%) |
| Sickle cell anemia | 05 (9.6%) |

A total of 52 beta-thalassemia major and Sickle cell anemia patients with a mean age of 8.47 ± 3.48 years were enrolled in the study. Out of total study participants 38 (73.1) were male and 14 (26.9) were females.

**Table No.2: Comparison of study participants with and without fibrosis of liver**

| Parameters | No Fibrosis | Fibrosis | Value |
|---|---|---|---|
| Age (mean±SD) | 5.9±3.6 | 9.8±2.5 | <0.05 |
| Gender | | | |
| Male | 11(61.1%) | 27(79.4%) | |
| Female | 7(38.9%) | 7(20.6%) | |
| AST | 70±21 | 99±24 | |
| ALT | 74±22 | 120±40.3 | |
| ALP | 203±118 | 305±116 | |
| No. of blood transfusion | 43±19 | 126±51 | |
| Serum Ferritin | 1663±414 | 2823±901 | |

It was observed that AST, ALT & ALP levels are significantly higher in patients with fibrosis, male participants affected more compared to female participants, proportion of patients with fibrosis was significantly higher with no. of blood transfusion 126±51 and serum ferritin level 2823±901.

**Table No.3: Distribution of study participants as per blood transfusion and mean of median stiffness**

| Range of blood transfusion | Mean of median stiffness |
|---|---|
| 21-100 | 6.75 |
| 101-150 | 15.05 |
| 151-250 | 17.93 |

It was observed that as number of transfusion increases there is an increase in the severity of liver fibrosis suggesting that there is a strong positive correlation between the number of blood transfusions and median stiffness of liver.

**Table 4: Mean level of AST, ALT & ALP in respective stage of fibrosis**

| Stage of Fibrosis | Mean& SD | AST (U/L) | ALT (U/L) | ALP (U/L) |
|---|---|---|---|---|
| F0 & 1 | Mean | 70.78 | 74.06 | 203.17 |
| | SD | 21.17 | 22.75 | 118.76 |
| F2 | Mean | 85.67 | 93.44 | 237.11 |
| | SD | 16.09 | 25.23 | 104.75 |
| F3 | Mean | 86.42 | 105.58 | 297.92 |
| | SD | 14.32 | 25.11 | 108.73 |
| F4 | Mean | 120.69 | 152.92 | 359.08 |
| | SD | 20.51 | 39.36 | 111.76 |

It was observed that with increase in fibrosis of liver level of AST, ALT and ALP also increased.

**Figure No.1: Mean level of AST, ALT & ALP in respective stage of fibrosis**

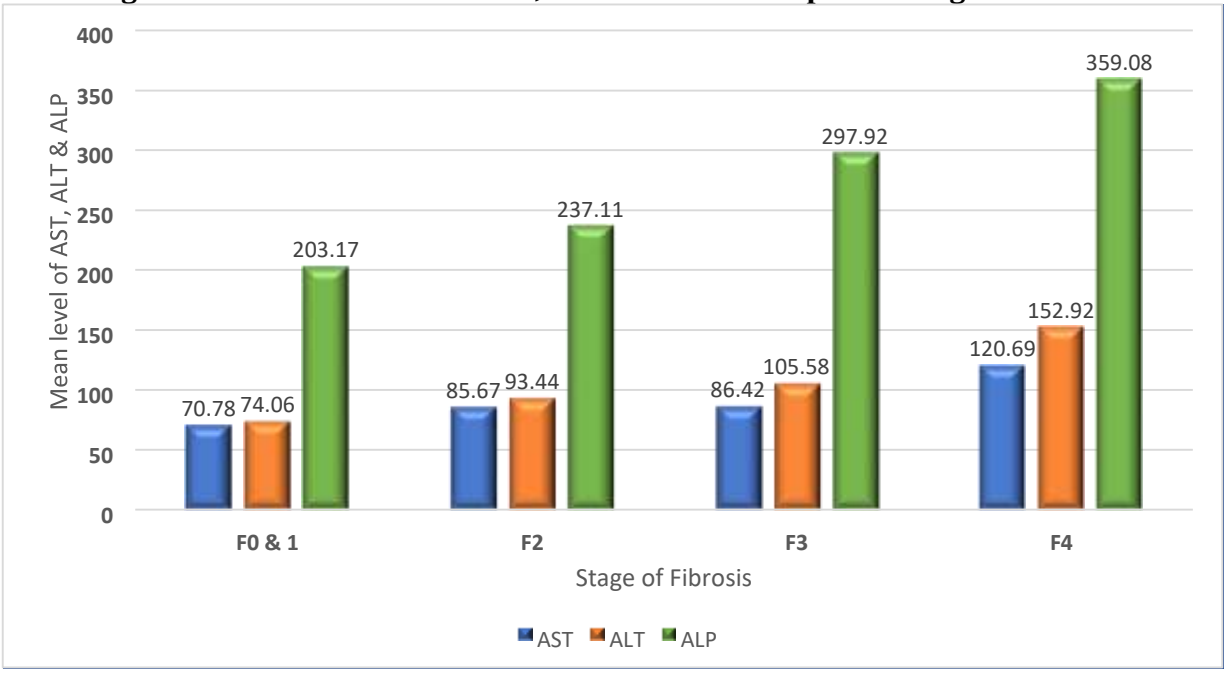
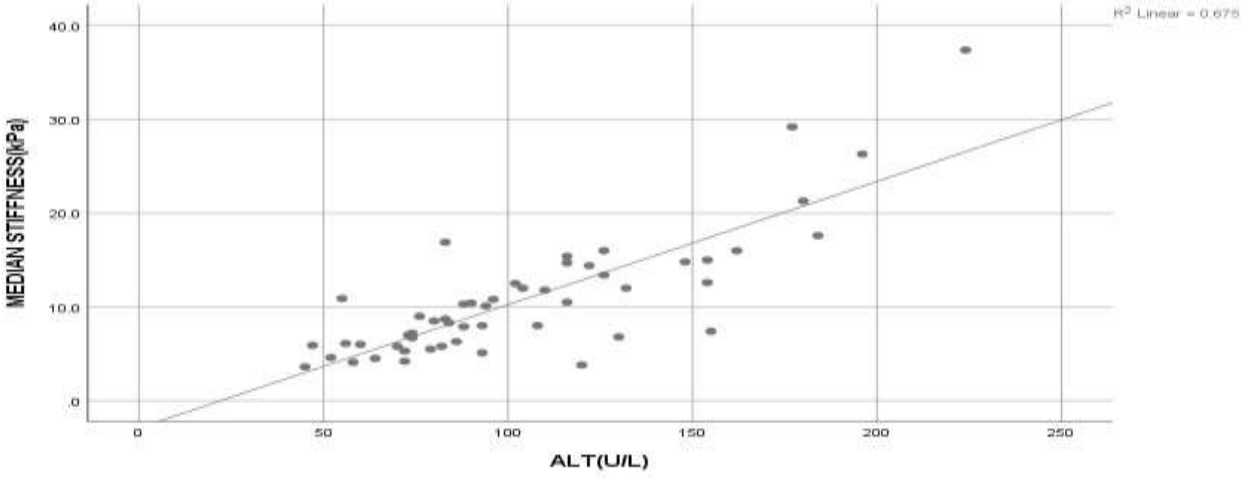



**Figure No.2: Correlation between median stiffness and ALT**



**Discussion:**

Present study aimed to find correlation between median stiffness of liver and liver function test in pediatric patients suffering from hemoglobinopathy. Patients of current series had a high rate of fibrosis/cirrhosis; thirty-four of them (65%) were deemed to have significant fibrosis (F2, F3, F4). Al-Khabori et al[9](2019) reported significant fibrosis in 60% of patients. In the present study rise in the level of AST, ALT & ALP was seen as the fibrosis progresses. Giovanna Ferraioli et al[10](2016) has found the similar correlation.

In the present study AST, ALT & ALP showed some progressive increase and was statistically significant in advanced liver disease. According to Ahmed et al[11](2018), scar tissue caused by fibrosis can obstruct or restrict blood flow within the liver, this can starve and ultimately kill healthy liver cells, leading to the formation of more scar tissue, which impairs liver function and allows enzymes from damaged tissue to leak.

Present study revealed that, as number of transfusion increases there is an increase in the severity of liver fibrosis suggesting that there is a strong positive correlation between the number of blood transfusions and median stiffness of liver further it is seen that those patients who underwent more than 100 blood transfusion has developed severe fibrosis. Similar result was seen in the study by Remacha et al[12](2013), the quantity of blood transfusions has a direct correlation with transfusion iron excess. Additionally, Tari et al.[13] (2018) reported that receiving numerous blood transfusions might lead to iron excess, which further disrupts metabolism and damages tissue and organs.

**Conclusion:**

Hepatic fibrosis is a common complication in patients with Hemoglobinopathies following repeated blood transfusion, there is a need to identify these changes early in patients in order to prevent or delay complications. One of the method to identify early defects in hepatic pathology is to estimate liver enzymes and other biochemical parameters including serum ferritin. Overall there is positive correlation between stages of liver fibrosis and increase in level of liver enzymes.

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