

## Frequency of High Serum Ferritin Levels in Beta-Thalassemia Major Patients

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### ABSTRACT

**Aim:** To find out the frequency of high serum ferritin levels in cases of beta-thalassemia major.

**Methods:** This cross sectional study was conducted at Department of Pathology CMH Institute of Medical Sciences Bahawalpur from July 2019 to December 2019. A total of 67 cases of beta thalassemia major, having age 2-15 years either gender were included. ELISA kit was used to perform serum ferritin levels. Serum ferritin levels were labeled as high if > 1000ng/ml. The data was entered on a predesigned Performa along with demographic profile of all the patients.

**Results:** A total of 67 cases of beta thalassemia major were recruited for this study. Mean age was 7.27±3.55 years. Out of the 67 patients, 41(58.21%) were male and 26 (41.79%) were females with male to female ratio of 1.6:1. Mean duration of disease was 5.23±3.15 years. Mean blood transfusions/year was 12.89±4.34 transfusions/year. Mean serum ferritin levels were 2752.33 ± 945.41 ng/ml. High serum ferritin level was found in 58 (86.57%) cases, whereas there was no High serum ferritin level in 09 (13.43%) cases.

**Conclusion:** This study concluded that that frequency of high serum ferritin levels in beta-thalassemia major patients is very high. So, we recommend that there should be proper screening of serum ferritin levels in these particular patients for early and proper management of this disastrous complication by chelation therapy in order to reduce the morbidity and mortality of these particular patients.

**Keywords:** Thalassemia, iron overload, ferritin.

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### INTRODUCTION

Beta thalassemsias (MT) are a group of hemoglobin-inherited blood disorders, resulting in variable phenotypes from serious anemia to clinicamente-asymptomatic individuals, due to reduced or absent synthesis of hemoglobin beta chains<sup>1</sup>. The annual total occurrence is reported at 1 in 100,000 in the world for symptomatic persons<sup>2</sup>. There are three main forms defined: main thalassemia, moderate thalassemia and minor thalassemia<sup>3</sup>. Regular lifelong blood transfusions are needed for affected children. Intermediate beta thalassemia is less severe than major beta thalassemia and episodic transfusions of the blood may be required<sup>4</sup>.

Pakistan typically does not undergo a daily chelation therapy in hospitals with regular blood transfusions.<sup>5</sup>In fact, bone marrow transplantation is not usually available.<sup>6</sup> Prevention is therefore the cheapest and most effective way to deal with beta thalassemia in Pakistan<sup>7</sup>. Precautionary strategy in many regions such as Thailand, Italy, Saudi Arabia and Iran has changed the prevalence of beta thalassemia<sup>8-9</sup>. Such prevention measures involved carrier testing for households at high risk, pre-marital community monitoring, genetic counseling and reproductive diagnostics. Carrier testing is extremely important for preventive strategies. In several countries, carrier screening programs are implemented. In general, high-risk families are screened<sup>10</sup>.

While thalassemsics ' survival decreases gradually, the severity of iron-over-load complications rises.<sup>11</sup>Progressive iron overload is induced by ineffectual erythropoiesis, decreased gastrointestinal accumulation of iron, loss of physiological mechanisms for excreting excess iron and, particularly, multiple blood transfusions in beta-thalassaemia major patients<sup>12</sup>. As iron cargo is increasing, the capacity to bind or detoxify iron can be surpassed for serum transferrin, the main transport protein iron. The anti-transferrin-bound iron fraction in the plasma can then stimulate the development of free hydroxyl radicals, oxygen-related harm spreaders<sup>13</sup>.

Excess iron is extremely toxic to all cells of the body and can cause serious and irreversible organic damage, such as cirrhosis, diabetes, heart disease, and hypogonadism<sup>14</sup>. Serum ferritin, iron and TIBC levels may measure the iron load on the skin. Effective control of iron overload in thalassemia calls for both iron toxicity and unnecessary chelation results tracking.<sup>15</sup>The measurement of serum ferritin concentrations in beta-thalassemia-major is the most widely applied measure of iron overload. Mishra AK et al<sup>16</sup> in his study has found frequency of high serum ferritin levels in 87.4% patients of beta-thalassemia major patients.

Since there are a great number of patients with transfusion dependent thalassemia, this study would also be performed in beta-thalassemia patients, in our population, to determine the frequency of high serum ferritin levels. If this frequency is identified high, some practical recommendations for the early and proper iron over load management of these specific patients in our

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routine practice could be made to prevent iron overload complications which would lead to a decrease in disease and mortality in these patients.

**OPERATIONAL DEFINITIONS**

- **Beta Thalassemia Major:** presence of all of the following was deemed as positive;
  - Hemoglobin level <7.0g/dl.
  - Hypochromic Microcytic anemia, poikilocytic RBCs, Target cells, Basophilic Stippling, Tear Drop cells and Nucleated RBCs on peripheral blood smear.
  - On Hemoglobin electrophoresis, Hb A < 3.5% and Hb F > 70%.
  - Require packed red cells every month to maintain Hb> 8.0g/dl.
- **High serum ferritin levels:** Serum ferritin levels > 1000ng/ml was considered as positive.

**MATERIAL AND METHODS**

This cross sectional study was conducted at Department of Pathology CMH Institute of Medical Sciences Bahawalpur from July 2019 to December 2019. A total of 67 cases of beta thalassemia major as per operational definition, having age 20-14 years either male or female with duration of disease greater than 1 years and with history of H/o >10 pints of blood transfused were selected. Hemoglobinopathies other than beta thalassemia major, patients already taking chelating therapy, having not exact history of blood transfusion pints, patients with chronic liver disease or chronic liver failure which were assessed by taking history and medical record of the patients were excluded from the study.

Approval from ethical committee was taken before commencement of study.Consent was taken from patients or their attendants.Total 5ml venous blood sample was taken and allowed to clot. After separating serum, it was stored at -20°C.ELISA kit was used to perform serum ferritin levels.Serum ferritin levels were labeled as high if > 1000ng/ml. The data was entered on a predesigned Performa along with demographic profile of all the patients.

Data was analyzed by using SPSS version 18.Age, serum ferritin level, duration of disease and number of blood transfusion were presented as mean and SD.

Gender, socioeconomic status (poor/middle/upper) and high serum ferritin levels (yes/no) were presented as frequencies and percentages. Chi-square test was used to detect the association of high serum ferritin level with different variables and P-value ≤0.05 was considered assignificant.

**RESULTS**

In present study age range was 2-14 years and mean age was 7.27 ± 3.55 years.Mean duration of disease was 5.23 ± 3.15 years. Mean blood transfusions/year was 12.89 ± 4.34 transfusions/year. Mean serum ferritin levels were 2752.33 ± 945.41 ng/ml.

Out of 67 patients, serum ferritin level was found high in 58 (86.57%) patients.(Fig. 1)

Age range in this study was 2-14 years.Two equal age group groups (2-8 years and 9-14 years) were made.Age group 2-8 years and age group 9-14 years were consisted on 41 (61.19%) patients and 26 (38.81%)

patients respectively.High serum ferritin level was found in 35 (85.37%) patients and 23 (88.46%) patients respectively in age group 2-8 years and age group 9-14 years. Association of high serum ferritin level with age groups was not statistically significant with p value 0.717 (Table 1). Male patients were 41(61.19%) and female patients were 26 (38.81%).Serum ferritin level was found high in 34(82.93%) male patients and in 24(92.31%) female patients. Association of high serum ferritin level with gender was not significant with p value 0.273 (Table 2).

Patients were divided into groups according to duration of thalassemia i.e. ≤5 years group and >5 years group. Total 37(55.22%) patients belonged to ≤5 years duration of disease group and 30(44.78%) patients belonged to >5 years duration of disease group. Serum ferritin level was found high in 31(83.78%) patients and 27(90%) patients respectively in ≤5 years group and >5 years group. No association of high serum ferritin level with duration of disease was found with p value 0.458.(Table 3)Patients were divided into two equal groups according to blood transfusion/year i.e. ≤12 transfusion/year group and >12 transfusion/year. Total 29(43.28%) patients belonged to ≤12 group and 38(56.72%) patients belonged to >12 years group. High serum ferritin level was found in 24 (82.76%) patients and 34(89.47%) patients respectively. But the difference was not statistically significant with p value 0.425 (Table 4).Total 21(31.34%) patients belonged to poor families, followed by 30(44.78%) patients to middle family and 16(23.88%) patients belonged to high class. High serum ferritin level was noted in 18 (85.71%) patients, 28 (93.33%) patients and 12 (75.0%) patients respectively in poor, middle and high income group. But association of high serum ferritin level with socio-economic status was not statistically significant with p value 0.219 (Table 5).

Figure 1: frequency of high serum ferritin level

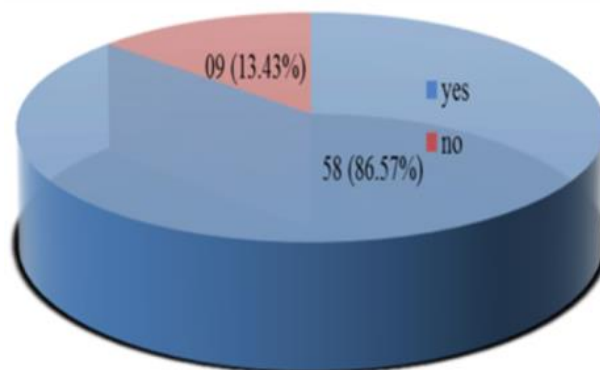


Table 1: Association of high serum ferritin level with age groups.

Age (years)	High serum ferritin levels		Total (%)	p-value
	Yes (%)	No (%)		
2-8	35 (85.37%)	06 (14.63%)	41 (61.19%)	0.717
9-14	23 (88.46%)	03 (11.54%)	26 (38.81%)	
Total	58 (86.57%)	9 (13.43%)	67	

Table 2: Association of high serum ferritin level with gender.

Gender	High serum ferritin levels		Total (%)	p-value
	Yes (%)	No (%)		
Male	34 (82.93%)	07 (17.07%)	41 (61.19%)	0.273
Female	24 (92.31%)	02 (7.69%)	26 (38.81%)	
Total	58 (86.57%)	9 (13.43%)	67	

Table 3: Association of high serum ferritin level with duration of disease.

Duration of disease	High serum ferritin levels		Total (%)	p-value
	Yes (%)	No (%)		
≤5 years	31 (83.78%)	06 (16.22%)	37 (55.22%)	0.458
>5 years	27 (90.0%)	03 (10.0%)	30 (44.78%)	
Total	58 (86.57%)	9 (13.43%)	67	

Table 4: Association of high serum ferritin level with number of blood transfusion/year.

Blood transfusion/year	High serum ferritin levels		Total (%)	p-value
	Yes (%)	No (%)		
≤12	24 (82.76%)	05 (17.24%)	29 (43.28%)	0.425
>12	34 (89.47%)	04 (10.53%)	38 (56.72%)	
Total	58 (86.57%)	9 (13.43%)	67	

Table 5: Association of high serum ferritin level with socioeconomic status.

Socioeconomic status	High serum ferritin levels		Total (%)	p-value
	Yes (%)	No (%)		
Poor	18 (85.71%)	03 (14.29%)	21 (31.34%)	0.219
Middle	28 (93.33%)	02 (6.67%)	30 (44.78%)	
High	12 (75.0%)	04 (25.0%)	16 (23.88%)	
Total	58 (86.57%)	9 (13.43%)	67	

**DISCUSSION**

Objective of present study was to determine the frequency of high serum ferritin levels in beta-thalassemia major patients. Age range was 2-14 years and mean age was 7.27 ± 3.55 years. Majority of the patients 41 (61.19%) were between 2 to 8 years of age. Out of the 67 patients, 41 (58.21%) were male and 26 (41.79%) were females with male to female ratio of 1.6:1. High serum ferritin level was found in 58 (86.57%) cases, whereas there was no High serum ferritin level in 09 (13.43%) cases. In one study by Mishra AK et al<sup>10</sup>, total 72 patients were selected, male patients were 56.9% and female patients were 43%. In same study, total 44.4% patients found with higher serum ferritin level.

Total 94.4% patients, 4.4% patients and 1.1 patients had severe, moderate and mild grade serum ferritin levels respectively. Sever grade was defined as <2500 µg/L, moderate defined as 1000-2500 µg/L and mild defined as (<1000 µg/L.<sup>17</sup>

In one study by Ikram et al, total 75 patients of Beta thalassaemia major were selected and serum ferritin level was assessed. Male patients were 48 and female patients were 27. Mean serum ferritin level was 3390±135.6 ng/ml. In 2.67% patients, serum ferritin level was <1000 ng/ml. Total 21.34% patients found with serum ferritin level from 1000 to 2500 ng/ml and 76% had serum ferritin level >2500 ng/ml.<sup>18</sup> Cunningham et al mean serum ferritin level was 1696 ng/ml in cases of beta thalassemia.<sup>19</sup> In Indian study by Choudhry et al mean serum ferritin level was 6723 ng/ml<sup>20</sup> In a study, a total of 135 patients were recruited with age range 7-30 years. Males were 51% and females were 49%.

Statistically insignificant difference of mean serum ferritin level between male and female patients was noted with p value 0.366.<sup>21</sup> Ali et al reported that their most of patients found with high serum ferritin level.<sup>22</sup>

**CONCLUSION**

This study concluded that that frequency of high serum ferritin levels in beta-thalassemia major patients is very high. So, we recommend that there should be proper screening of serum ferritin levels in these particular patients

for early and proper management of this disastrous complication by chelation therapy in order to reduce the morbidity and mortality of these particular patients.

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