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Original Article

Correlation of Increased Serum Ferritin with SGOT, SGPT, and Albumin Levels in Children with β-Thalassemia Major

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Abstract:

Background: Routine transfusion in β-thalassemia major children will cause excess iron in organs, especially the liver, as illustrated by the serum ferritin value. Excess iron in the liver can cause disturbances in liver enzymes and liver function, which can be assessed using SGOT, SGPT, and albumin examination parameters. This study intends to assess the relationship between increased serum ferritin levels with SGOT, SGPT, and albumin levels in β-thalassemia major children.

Methods: This is an observational cross-sectional study which was conducted at the dr. Zainoel Abidin Hospital in Banda Aceh. Research subjects underwent examination of serum ferritin, SGOT, SGPT, and albumin.

Results: A total of 37 β-thalassemia major children between 1 until <18 years of age were included in this study. The mean serum ferritin, SGOT, SGPT and albumin levels in β-thalassemia major patients were 4596 ± 2750.07 ng/mL, 57.32 ± 44.20 U/L, 57.46 ± 54.77 U/L, and 4.34 ± 0.22 g/dL respectively. The correlation coefficient between ferritin levels and SGOT was 0.768 (p-value <0.05). While, the correlation coefficient between ferritin and SGPT levels was 0.708 (p-value < 0.05). On the other hand, the correlation value between ferritin and albumin levels was -0.114 (p-value > 0.05).

Conclusion: Increased serum ferritin levels in β-thalassemia major children are related to SGOT and SGPT levels. But there is no relationship between increased serum ferritin and albumin levels in β-thalassemia major children.

Keywords: β-thalassemia major, albumin, serum ferritin, SGOT, SGPT

Introduction

Thalassemia is a major global health problem, including in Indonesia.[1] This disease occurs due to a disproportion of globin chains production during the formation of red blood cells.[1,2] Excess of iron is a devastating consequence of blood transfusion in β-thalassemia major patients. This is also exacerbated by increased iron absorption in

β-thalassemia major patients.[3,4] Iron accumulation can be measured by determining serum ferritin levels because it best reflects the body's iron status.[4]
Liver is a storage place for iron and the only site of transferrin and ferritin synthesis, and hence the first organ to be affected.[5] Accumulation of hepatocyte damage begins after at least 10-20 routine transfusions or after one year of transfusion therapy in thalassemia patients.[6,7] Ferritin level of more than or equal to 1500 ng/mL indicates iron overload, which is significantly associated with liver injury.[4,8,9] Excessive accumulation of iron in β-thalassemia major patients will cause liver injury, thereby, triggering the release and increase of the transaminases enzyme such as serum glutamate oxaloacetate transferase (SGOT/AST) and serum glutamate pyruvate transferase (SGPT/ALT) in circulating blood.[10–12] SGPT, which has high sensitivity and specificity, is a more specific primary marker for liver injuries compared to SGOT.[11]

Another important test for liver function is albumin.[13] Injury to hepatocytes due to iron overload in the liver can cause a decrease in albumin production, which can be detected through blood tests.[14–16]

The purpose of this study was to assess the relationship of elevated serum ferritin and levels of SGOT, SGPT, and albumin in children with β-thalassemia major.

Methods

Thirty seven children with β-thalassemia major, aged one year until less than 18 years old, who was treated at the Children's Thalassemia Center at dr. Zainoel Abidin Hospital (RSUDZA) Banda Aceh in the period of February 2022 to March 2022 were recruited. They met the inclusion criteria and were willing to take part in the study. Inclusion criteria were as following: β-thalassemia major patients, aged more than 1 year to less than 18 years, serum ferritin levels more than 1500 ng/mL, β-thalassemia major children who received deferiprone as iron chelation medication, β-thalassemia major children who did not receive deferasirox as iron chelation medication for at least 3 months due to its hepatotoxicity that may interfere with the result of this study. Exclusion criteria were β-thalassemia major children who were infected by hepatitis B and C viruses and β-thalassemia major children who were taking deferasirox as iron chelation medication. Subjects were selected by consecutive sampling to obtain a sufficient number of subjects. Three millilitres of blood samples were taken for examination of albumin, serum ferritin, SGOT, and SGPT.

The data obtained were recorded and then processed through the statistical product and service solution (SPSS) version 26.0. Numerical data were presented in the form of mean (SD) if the distribution of data was normal or median (range) if the distribution of data was not normally distributed. We used the Shapiro Wilk to test for

the normality due to the number of subjects were under 50. Categorical data were presented in the form of frequency and percentage. Correlation between liver function tests (SGOT, SGPT, albumin) and serum ferritin was evaluated by using the Spearman correlation test. The strength of the relationship was expressed in r value, with a p-value of < 0.05 considered as significant.

Results

This study was conducted from February to March 2022 on pediatric patients with β-thalassemia major aged less than 18 years who came for treatment at the Children's Thalassemia Center at RSUDZA Banda Aceh. The total sample obtained during the study were 37 patients and had exceeded the minimum sample size for this research.

Table 1. The basic characteristics of the research sample

Variables	Frequency	Percentage (%)
Sex		
Male	17	45.9
Female	20	54.1
Age		
1 - 5 years old	8	21.6
5 - 18 years old	29	78.4
Nutritional Status		
Mild malnutrition	7	18.9
Good nutrition	30	811

This study involved 37 samples of β-thalassemia major patients consisting of 20 (54.1%) female patients and the rest were male patients (45.9%). When viewed by age group, it is known that more than 78% of the total patients are aged between 5 to 18 years. Meanwhile, there were only 8 patients aged 1 to 5 years old (21.6%) of the total patient sample. Most patients (81.1%) involved in this study had good nutritional status (**Table 1**).

The lowest value of ferritin levels in the patients in this study was 1715 ng/mL and the highest was 12450 ng/mL. This study found that the average (±SD) serum levels of SGOT and SGPT in β-thalassemia major patients involved in this study were 57.32 U/L (±44.20 U/L) and 57.46 U/L (±54.77 U/L), respectively. Furthermore, the average value (±SD) of albumin levels in the study patients was 4.34 g/dL (± 0.22 g/dL) (**Table 2**).

Table 2. Description of serum levels in patients with β-thalassemia major

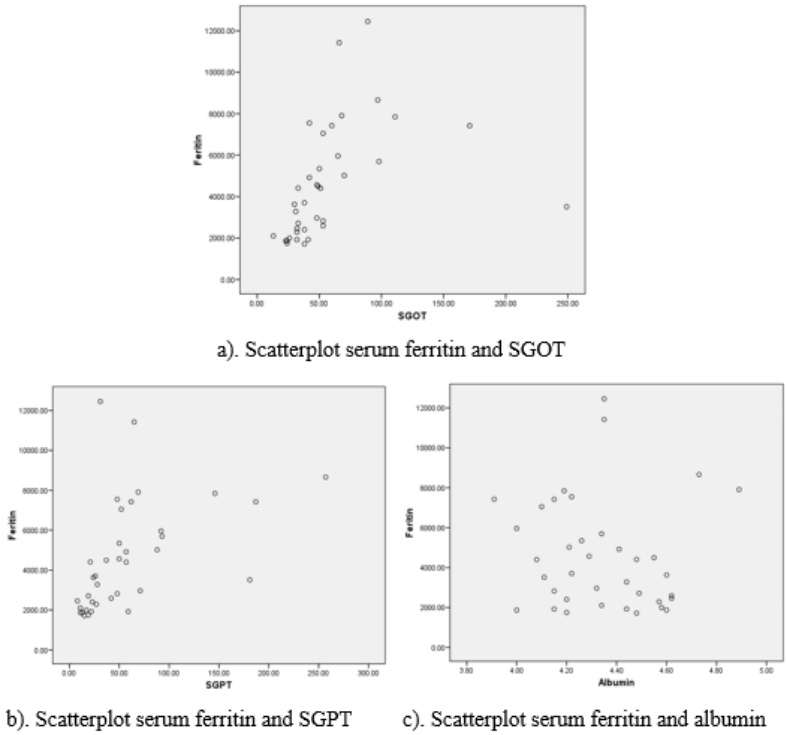
Value	Serum Level			
	Ferritin (ng/mL)	**SGOT/AST (U/L)**	**SGPT/ALT (U/L)**	**Albumin (g/dL)**
Minimum	1715.00	13.00	8.00	3.91
Median	3702.00	48.00	48.00	4.34
Mean	4596.00	57.32	57.46	4.34
Standard deviation	2750.07	44.20	54.77	0.22
Maximum	12450.00	249.00	257.00	4.89

The coefficient correlation between ferritin levels with SGOT and SGPT is positive, while the correlation between ferritin levels with albumin is negative. The correlation coefficient between ferritin levels and SGOT was 0.768 with a p-value below 0.05. Furthermore, the correlation coefficient between ferritin and SGPT levels was 0.708 with the test p-value also smaller than 0.05. Meanwhile, the correlation value between ferritin and albumin levels is only -0.114 with a p-value of 0.503. Thus, it can be concluded that ferritin levels only have a significant relationship with SGOT and SGPT levels. The relationship between ferritin and albumin levels was not statistically significant as indicated by the p-value greater than 0.05 from the test. **(Table 3)**

Table 3. The relationship between ferritin levels with SGOT, SGPT, and albumin

Variables	**Correlation coefficient (r value)**	**p-value**
Feritin - SGOT	0.768	<0.001
Feritin - SGPT	0.708	<0.001
Feritin - Albumin	-0.114	0.503

The increase in ferritin levels will raise the SGOT and SGPT values. Likewise, the lower ferritin levels will also be followed by a decrease in SGOT and SGPT values. While the increase or decrease in serum ferritin will not affect albumin levels in β-thalassemia major patients involved in this study. This trend can also be seen through the scatterplot between ferritin levels and the other three levels in **Figure 1**.



a). Scatterplot serum ferritin and SGOT

b). Scatterplot serum ferritin and SGPT

c). Scatterplot serum ferritin and albumin

Figure 1. Scatterplot between ferritin levels with SGOT, SGPT, and albumin.

Discussion

This study involved 37 samples obtained from primary data collected from February to March 2022 at the Thalassemia Center, RSUDZA Banda Aceh. Characteristics of subjects based on age showed that patients above 5 years old were more likely to have more than 1500 ng/mL serum ferritin level (78.4%) than those of 1 to 5 years old (21.6%). This is in line with a research by Riaz et al. in which stated that increased serum ferritin levels have a significant association with increased age in β-thalassemia major children who received routine transfusions.[17]

The correlation coefficient between serum ferritin levels to SGOT and SGPT levels is positive, indicating an increase in serum ferritin levels will be followed by an increase in SGOT and SGPT levels. The correlation coefficient between ferritin levels and SGOT was 0.768 with a p-value below 0.05. Furthermore, the correlation coefficient between ferritin and SGPT levels was 0.708 with p-value also lower than 0.05. This shows that serum ferritin levels have a significant relationship with SGOT and SGPT levels. According to Mohammad et al., thalassemia patients experienced a significant increase in SGOT, SGPT and bilirubin levels compared to control subjects.[18] Research conducted by Asif et al. in children with thalassemia who received repeated transfusions also demonstrated a positive correlation between serum SGPT (Pearson Correlation 0.097; p = 0.181), serum SGOT (Pearson Correlation 0.045; p = 0.335) and serum ALP (Pearson Correlation 0.036; p = 0.364) compared to serum ferritin

levels.[3] Research by Saral et al. reported that iron overload due to repeated blood transfusion in children with thalassemia resulted in abnormal organ function tests, which was reflected by variations in the liver and renal function test parameters.[16] A significant positive correlation was found between serum ferritin and SGPT levels in both boys and girls with thalassemia ($p<0.05$).[18]

This study results were in accordance with a research conducted by Al-Moshary et al., which indicated a positive correlation among serum ferritin levels and liver enzymes. It was illustrated by an escalation in serum ferritin levels parallel with elevation in levels of SGOT, SGPT, and alkaline phosphatase (ALP).[19] Another study by Haris et al. concluded that serum ferritin levels and serum SGOT and SGPT levels have a statistically significant relationship ($p < 0.05$) with correlation coefficients of 0.31 and 0.55, respectively. SGOT and SGPT levels increased along with the increase in serum ferritin levels, with levels above 3000 ng/ml of serum ferritin levels will result in a sharp increase in SGOT and SGPT values.[20]

In this study, we demonstrated that the relationship between ferritin levels and albumin was not statistically significant, with a p-value greater than 0.05. The correlation value between ferritin and albumin levels was only -0.114 with a p-value of 0.503. This finding is similiar to the research conducted by Sharma et al., in which study in children with β-thalassemia showed no relationship between increased levels of serum ferritin and serum albumin ($r = 0.01714$).[21]

Conclusion

Based on data analysis and discussion, increased serum ferritin is in relationship with SGOT and SGPT levels in β-thalassemia major children. Normal range of albumin levels found in β-thalassemia major children, even in the presence of elevated serum ferritin.

Conflict of Interest

None declared.

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