Correlation of Serum Ferritin Levels with Creatinine, Sgot and Sgpt Levels in Thalassemia Major Patients

Fatwa Hasbi(✉) and Harpolia Cartika

Politeknik Kesehatan Kementerian Kesehatan Jakarta II, Jakarta, Indonesia
fatwa.hasbi.apt@gmail.com

Abstract. Thalassemia major patients receive regular blood transfusions every 2–5 weeks, to maintain pretransfusion hemoglobin levels above 9–10.5 g/dl. In patients with thalassemia major, continuous blood transfusion can cause iron overload by increased serum ferritin levels. Accumulated iron is toxic to many tissues causing dysfunction and failure of major organs, including the heart, kidneys, liver and endocrine glands (pituitary, thyroid, parathyroid, and pancreas). This study aims to determine the relationship between ferritin levels with creatinine, SGOT and SGPT in patients with thalassemia major. This research is observational with data collection using a cross-sectional method. The study population was 65 medical records of thalassemia major patients at Hermina Jatinegara Hospital, Indonesia, in 2019. The analytical method used is the Kruskal Wallis test and the Spearman correlation test. The results obtained were that the average levels of ferritin, creatinine, AST and ALT were 2952.23 ng/mL, 0.52 mg/dL, 32.37 /L and 32.33/L. The results of the Kruskal-Wallis test showed that the levels of ferritin and creatinine had a significant difference based on age (p 0.041 and p 0.049). The Spearman correlation test results showed a positive correlation between serum ferritin and SGPT (p 0.02) with a coefficient correlation of 0.289. There is no correlation between serum ferritin, SGOT and Creatinine (p 0.17 & p 0.73). Based on these results, serum ferritin levels have a weak correlation with SGPT levels and do not correlate with other parameters.

Keywords: Thalassemia · Ferritin · Creatinine · SGOT · SGPT

1 Introduction

Thalassemia is a disease that poses a global threat. Based on World Bank data, 7% of the world's population is a thalassemia trait carrier. About 300,000–500,000 newborns with severe hemoglobin disorders and 50,000 - 100,000 children die from thalassemia every year. As many as 80% of this amount comes from developing countries. Indonesia is one of the world's thalassemia belts, a country with a high frequency of thalassemia genes (carrier numbers) [1].

S. Februanti et al. (Eds.): MICon 2021, ASSEHR 708, pp. 1041–1049, 2023.
https://doi.org/10.2991/978-2-38476-022-0_116

Patients with thalassemia major must have regular blood transfusions every 2–5 weeks, to maintain pretransfusion hemoglobin levels above 9–10.5 g/dl [2, 3]. In patients with thalassemia major, continuous blood transfusion can cause iron overload, characterized by increased serum ferritin levels. Accumulated iron is toxic to many tissues causing dysfunction and failure of major organs, including the heart, kidneys, liver and endocrine glands (pituitary, thyroid, parathyroid, and pancreas) [3–5]. High iron levels also correlate with malondialdehyde levels in the body, which is a marker of oxidative stress, increasing the risk of damage to tissues in the body, including the kidneys and liver [5]. Data from the Jakarta Thalassemia Center showed the results of serological tests from 716 patients, 2% of patients infected with hepatitis B infection, 15% of patients infected with hepatitis C infection, and 5 patients infected with HIV infection [1]. Excess iron causes mitochondrial swelling and rupture of hepatocyte mitochondrial membranes, which results in liver cell death [6]. Excess iron in the liver often results in complications of diseases ranging from fibrosis cirrhosis to liver cancer [7]. SGOT and SGPT are enzymes found in the liver and used as liver function parameters. SGOT is not only found in the liver; SGOT is also found in the heart, liver, skeletal muscles, kidneys, brain, spleen, pancreas, and lungs.

In contrast to SGOT, SGPT is highest in the liver compared to other tissues. So that SGPT levels also need to be known to measure the function of the liver. SGOT and SGPT levels are also useful for diagnosing liver disease and hepatotoxic effects [8]. Abnormalities in the kidneys can be detected by checking the creatinine level in the blood [9]. Based on this, researchers are interested in conducting research on "Correlation of serum ferritin levels with SGOT, SGPT and creatinine levels in thalassemia major patients".

2 Research Method

2.1 Research Design

This study uses an observational research design with a cross-sectional approach.

Population
The research population is all thalassemia patients at Hermina Jatinegara Hospital 2019.

Sample
The sampling technique used the purposive sampling technique. The sample in this study were all populations that met the criteria in the study.

1. Inclusion criteria

   - Thalassemia patient medical record at Hermina Jatinegara Hospital.

2. Exclusion Criteria

   - The patient's medical record does not contain Ferritin, Creatinine, SGOT and SGPT data.

Variable

1. Dependent variable: SGOT and SGPT levels
2. Independent variable: Ferritin Level

2.2 Research Procedure

1. Data retrieval

Data were collected by looking at the patient's medical records. Samples that meet the requirements (inclusion and exclusion criteria) are recorded in the research form. The data needed include patient identification, disease history, physical examination data, laboratory examination data, diagnosis, therapy received by the patient, Ferritin levels, creatinine, SGOT and SGPT.

2. Processing and data analysis

Patient data that has been taken from medical records, nurse records and patient follow-up are then collected in data collection sheets. The data that has been collected above is then analyzed using the Kruskal Wallis test and the Spearman correlation test.

3 Results and Discussion

This research was conducted at Hermina Jatinegara Hospital, DKI Jakarta Province, Indonesia. The hospital was chosen because it has a special service unit for thalassemia. Data were taken based on the patient's medical records, including gender, age, serum ferritin levels, creatinine, SGPT and SGOT (Table 1).

The total medical records obtained in this study were 65 patients consisting of 29 men (44.6%) and 36 women (55.4%). Belhoul et al. (2013) reported that women had a statistically significant lower serum ferritin($P < 005$) compared to men. In addition, it is also mentioned that men have a significantly higher risk of heart disease than women [10, 11]. However, women have more anxiety and depression [12] (Table 2).

In the patient data table by age, there are more patients with children age than other age groups with 31 people (47.7%). Thalassemia is a hereditary disease, so it is possible to appear from an early age [13].

Table 3 shows the patients' mean serum ferritin, SGOT and SGPT levels. The patient's mean serum ferritin level was 2952.23 ng/mL. Guidelines recommend that

Table 1. Patient Data by Gender

No	Gender	Amount	Percent
1	Man	29	44.6%
2	Woman	36	55.4%
Total		65	100%

Table 2. Patient Data by Age

No	Age	Amount	Percent
1	Toddler (0–4 years)	7	10.8%
2	Children (5–11 years)	31	47.7%
3	Teenagers (12–25 years)	20	30.8%
4	Adult (26–45 years)	7	10.8%
Total		65	100%

Table 3. Average Ferritin, SGOT and SGPT levels

No	Parameter	Average Rate	Normal Level
1	Ferritin	2952.23 ng/mL	1000–2500 ng/mL
2	SGOT	32.37/L	4–35/L
3	SGPT	32.33/L	5–35/L
4	Creatinine	0.52 mg/dL	0.5–1.2 mg/dL

Table 4. Data on Ferritin, SGOT and SGPT Levels by Gender

No	Parameter	Average Levels by Gender (min - max)		Normal Level	Sig. (p)
		Man	Woman		
1	Ferritin	3209.8 ng/mL	2731.45 ng/mL	1000–2500 ng/mL	0.932
2	SGOT	26.25/L	38.16/L	5–35/L	0.310
3	SGPT	25.52/L	37.62/L	5–35/L	0.288
5	Creatinine	0.52 mg/dL	0.52 mg/dL	0.5–1.2 mg/dL	0.964

iron chelation should be initiated after the patient has received more than 10 units of blood or after achieving a serum ferritin level of >1,000 ng/mL. Patients undergoing iron chelation should receive periodic monitoring of serum ferritin [14–16]. Historically, a ferritin value of 1,000 ng/l equivalents to a LIC value of about 7 mg/g was used as a trigger to initiate chelation with desferrioxamine (DFO). However, DFO has a risk of side effects of over chelation when serum ferritin values are below 1000 ng/l [16]. Serum ferritin greater than 2000 ng/ml or LIC greater than 15 mg/g dry weight was associated with an increased risk of complications and death in the initial observational study. Ferritin should be measured at least every 3 months [17]. Further research is needed on the factors that influence the inadequate treatment. The average SGOT and SGPT values of patients are normal; this explains that the patient's liver is still functioning well on average. Creatinine values also show normal levels in the average patient (Table 4).

Table 5. Data on Ferritin, SGOT and SGPT Levels by Age

No	Parameter	Average Levels by Age				Normal Level	Sig.
		Toddler (0–4 years)	Children (5–11 years)	Teenagers (12–25 years)	Adult (26–45 years)		
1	Ferritin	2113.37 ng/mL	2314.75 ng/mL	3894.73 ng/mL	4204.57 ng/mL	1000–2500 ng/mL	0.041
2	SGOT	35.53/L	27.94/L	27.37/L	60.91/L	5–35/L	0.062
3	SGPT	41.06/L	26.92/L	26.62/L	59.78/L	5–35/L	0.407
5	Creatinine	0.50 mg/dL	0.50 mg/dL	0.56 mg/dL	0.54 mg/dL	0.5–1.2 mg/dL	0.049

Serum ferritin levels of male and female thalassemia major patients did not have a significant difference (Sig. 0.932). This result is different from the study conducted by Jung et al. (2017), which examined serum ferritin levels in healthy adolescents; from this study, it was found that the average hemoglobin and serum ferritin levels were significantly higher in boys than in girls ($P < .001$): hemoglobin [18]. In addition, Li et al. (2014) also reported significantly higher mean serum ferritin levels in men compared to women (121.9 vs 51.0 ng/ml, $P < 0.001$), however, these data were obtained in patients with metabolic syndrome. Patients with metabolic syndrome have differences in the increase in waist circumference, blood pressure, fasting glucose, triglycerides between men and women, whereas in thalassemia patients, there is no difference in these factors. The results also showed no significant difference in the SGOT, SGPT and Creatinine values of thalassemia patients based on gender ($p < 0.05$) [19].

Based on Table 5, it is known that serum ferritin levels have a significant difference based on age (Sig. 0.041). The higher the age, the serum ferritin level will increase. The World Health Organization (2011) explains that serum ferritin concentrations are high at birth, increase during the first two months of life, and then fall during infancy. At the age of about one year, concentration begins to rise again and increases until adulthood [20]. Mussalam et al. (2014), in their research, reported that the higher the age, the morbidity of thalassemia patients would increase due to high levels of iron in the blood [21].

Creatinine values also significantly differed based on age (p 0.049). Age can affect the value of serum creatinine and glomerular filtration rate (GFR). Serum creatinine concentrations continue to increase with age; in women from 40 years of age and 60 years for men, at the age interval of 20 to 94 years [22]. The rate of GFR is also known to decrease with age. This indicates a decrease in kidney function with age [23–26] Differences in SGOT and SGPT levels in thalassemia patients based on age in Table 5 did not show significant results (Sig. 0.062 & 0.407). However, the greatest SGOT and SGPT values were found in adults compared to others. This is because the liver function can decline with age [21]. Schmucker (2005) reported that changes in liver volume with age could explain these age-related changes in liver function, shifts in the expression of various proteins, a lower inflammatory response to oxidative stress, decreased hepatobiliary function and increased fibrosis [27]. In addition, McPherson et al. (2016) reported a natural age-related decline in serum SGPT (while SGOT levels remained stable) [28] (Table 7).

Table 6 shows the relationship between serum ferritin levels and creatinine, SGOT and SGPT. Tests were carried out using the Spearman test to determine the significance

Table 6. Relationship of serum ferritin levels to SGOT and SGPT (Spearman's test)

No.	Variable	Ferritin	
		Sig. (2-tailed)	Correlation Coefficient
1.	SGOT	0.17	0.176
2.	SGPT	0.02	0.289
4.	Creatinine	0.739	-0.044

Table 7. Strength of the relationship between variables (Spearman test)

Coefficient	Relationship strength
0.00	No connection
0.01–0.09	Relationships are meaningless
0.10–0.29	Weak relationship
0.3–0.49	Moderate relationship
0.5–0.69	Strong relationship
0.70–0.89	Very strong relationship
>0.90	Close to perfect relationship

and strength of the relationship between variables. The test results showed that serum ferritin levels did not significantly correlate with creatinine levels (Sig. 0.73), so ferritin levels did not affect kidney function. While the SGPT level has a significance value of 0.02 and a positive correlation coefficient value of 2.89, serum ferritin levels have a significant relationship with the strength of a weak relationship and are in the same direction as serum SGPT levels (Table 6). These results follow the research of Parvin F et al. (2016), which reported a significant positive correlation ($r = 0.259$; $p = 0.006$) between serum ferritin and ALT [29].

Different results were reported by Patel SA et al. (2018) in terms of the relationship between serum ferritin and SGOT; they conducted a study of 70 subjects with criteria aged 2 to 14 years, had undergone > 5 blood transfusions and had received oral chelation therapy for more than one year. The results SGOT and SGPT levels had a statistically significant correlation with serum ferritin exceeding 2000 ng/ml (Pearson correlation coefficient $r = + 0.62$) [30]. In addition, Al-Moshary M et al. (2020) reported that 138 subjects with an age range of 2–23 years had an average serum ferritin level of 3278.64 ng/ml, and an increase in serum ferritin levels was positively correlated with SGOT and SGPT levels in the body [31]. The difference in the relationship between ferritin and SGOT in our study may be due to using more diverse subjects in terms of age. Iron overload and elevated liver enzymes are common findings in beta-thalassemia major patients suggesting an increased risk of liver dysfunction. The impaired liver function begins when the serum ferritin level is above 1000 ng/ml. Therefore, liver function should be monitored carefully in patients with thalassemia major [30].

4 Conclusion

Based on the results and discussion, it can be concluded that:

1. The patient's mean serum ferritin level was high at 2952.23 ng/mL. There was a significant difference in ferritin levels based on age (Sig. 0.02).
2. Serum ferritin levels, SGOT and SGPT did not have a significant difference based on gender (Sig. > 0.05)
3. Serum ferritin levels had a significant difference based on age (Sig. 0.041)
4. Serum ferritin levels did not significantly correlate with SGOT levels (Sig. > 0.05). In contrast, SGPT levels have a significant relationship with serum ferritin (Sig. 0.02) with a positive correlation coefficient of 2.89 (strength of weak relationship).

Acknowledgments. This work is supported by Research Program supported by Poltekkes Kemenkes Jakarta II.

References

1. Kemenkes RI. Keputusan Menteri Kesehatan Republik Indonesia Nomor Hk.01.07/Menkes/1/2018 Tentang Pedoman Nasional Pelayanan Kedokteran Tata Laksana Thalasemia [Internet]. Kementerian Kesehatan Republik Indonesia. Jakarta; 2018. Available from: http://hukor.kemkes.go.id/uploads/produk_hukum/KMK_No._HK_.01_.07-MENKES-1-2018_ttg_Pedoman_Nasional_Pelayanan_Kedokteran_Tata_Laksana_Thalasemia_.pdf
2. Maria Domenica Cappellini, Alan Cohen, John Porter, Ali Taher VV. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT) 3rd Edition. Thalassaemia International Federation. 2014.
3. Sewwandi Karunaratna AMD, Ranasingha JS, Mudiyanse RM. Iron overload in beta thalassemia major patients. Int J Blood Transfus Immunohematol. 2017; 7:33.
4. Rasool M, Malik A, Jabbar U, Begum I, Qazi MH, Asif M, et al. Effect of iron overload on renal functions and oxidative stress in beta thalassemia patients. Saudi Med J. 2016; 37(11): 1239–42.
5. Shander A, Cappellini MD, Goodnough LT. Iron overload and toxicity: The hidden risk of multiple blood transfusions. Vox Sang. 2009; 97(3): 185–97.
6. Kew MC. Hepatic iron overload and hepatocellular carcinoma. Cancer Lett [Internet]. 2009; 286(1): 38–43. Available from: https://doi.org/10.1016/j.canlet.2008.11.001
7. Chen MJ, Peng SSF, Lu MY, Yang YL, Jou ST, Chang HH, et al. Effect of iron overload on impaired fertility in male patients with transfusion-dependent beta-thalassemia. Pediatr Res [Internet]. 2018; 83(3): 655–61. Available from: https://doi.org/10.1038/pr.2017.296
8. Mehta K. Oxidative Stress in Iron Toxicity of the Liver [Internet]. The Liver. Elsevier Inc.; 2018. 43–54 p. Available from: https://doi.org/10.1016/B978-0-12-803951-9/00004-5
9. Eschbach JW, Adamson JW. Iron overload in renal failure patients: Changes since the introduction of erythropoietin therapy. Kidney Int Suppl. 1999; 55(69): 35–43.
10. Borgna-Pignatti C, Cappellini MD, De Stefano P, Del Vecchio GC, Forni GL, Gamberini MR, et al. Survival and complications in thalassemia. Ann N Y Acad Sci. 2005; 1054: 40–7.

11. Belhoul KM, Bakir ML, Kadhim AM, Dewedar HES, Eldin MS, Alkhaja FA. Prevalence of iron overload complications among patients with β-thalassemia major treated at Dubai Thalassemia Centre. Ann Saudi Med. 2013; 33(1): 18–21.
12. Seyedifar M, Dorkoosh FA, Hamidieh AA, Naderi M, Karami H, Karimi M, et al. Health-related quality of life and health utility values in beta thalassemia major patients receiving different types of iron chelators in Iran. Int J Hematol Stem Cell Res. 2016; 10(4): 224–31.
13. Fibach E, Rachmilewitz EA. Pathophysiology and treatment of patients with beta-thalassemia - an update. F1000Research. 2017; 6(0).
14. Rujito L. Buku Referensi Talasemia: Genetik Dasar dan Penanganan Terkini. 2020.
15. Angelucci E, Barosi G, Camaschella C, Cappellini MD, Cazzola M, Galanello R, et al. Italian Society of Hematology practice guidelines for the management of iron overload in thalassemia major and related disorders. Haematologica. 2008; 93(5): 741–52.
16. Musallam KM, Angastiniotis M, Eleftheriou A, Porter JB. Cross-talk between available guidelines for the management of patients with beta-thalassemia major. Acta Haematol. 2013; 130(2): 64–73.
17. Tubman VN, Fung EB, Vogiatzi M, Thompson AA, Rogers ZR, Neufeld EJ, et al. Guidelines for the Standard Monitoring of Patients With Thalassemia. J Pediatr Hematol Oncol. 2015; 37(3): e162–9.
18. Jung DW, Park JH, Kim DH, Choi M, Kim S, Kim H, et al. Association between serum ferritin and hemoglobin levels and bone health in Korean adolescents. Med (United States). 2017; 96(51).
19. Andreani M, Radio FC, Testi M, De Bernardo C, Troiano M, Majore S, et al. Association of hepcidin promoter c.-582 A > G variant and iron overload in thalassemia major. Haematologica. 2009; 94(9): 1293–6.
20. Who. Serum ferritin concentrations for the assessment of iron status and iron deficiency in populations. Vitamin and Mineral Nutrition Information System. Who [Internet]. 2011; 1–5. Available from: http://www.who.int/vmnis/indicators/serum_ferritin.pdf
21. Musallam KM, Cappellini MD, Daar S, Karimi M, El-Beshlawy A, Graziadei G, et al. Serum ferritin level and morbidity risk in transfusion-independent patients with β-thalassemia intermedia: The orient study. Vol. 99, Haematologica. 2014. p. e218–21.
22. Michael M, Tiao JY, Semmens JB, Masarsi JRL. Aging Population: Relevance To Vascular Surgery. 2002; 10(5): 445–51.
23. Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW. The effect of age on creatinine clearance in men: a cross sectional and longitudinal study. Journals Gerontol. 1976; 31(2): 155–63.
24. Verhave JC, Fesler P, Ribstein J, Du Cailar G, Mimran A. Estimation of renal function in subjects with normal serum creatinine levels: Influence of age and body mass index. Am J Kidney Dis. 2005; 46(2): 233–41.
25. Hallan SI, Matsushita K, Sang Y, Mahmoodi BK, Black C, Ishani A, et al. Age and association of kidney measures with mortality and end-stage renal disease. JAMA - J Am Med Assoc. 2012; 308(22): 2349–60.
26. Cohen E, Nardi Y, Krause I, Goldberg E, Milo G, Garty M, et al. A longitudinal assessment of the natural rate of decline in renal function with age. J Nephrol. 2014; 27(6): 635–41.
27. Schmucker DL. Age-related changes in liver structure and function: Implications for disease? Exp Gerontol. 2005; 40(8–9): 650–9.
28. McPherson S, Hardy T, Dufour JF, Petta S, Romero-Gomez M, Allison M, et al. Age as a Confounding Factor for the Accurate Non-Invasive Diagnosis of Advanced NAFLD Fibrosis. Am J Gastroenterol. 2017; 112(5): 740–51.
29. Parvin F, Naznin B, Chowdhury TT, Imran AA, Nahar ML, Hossain SA. An Association of Serum ferritin and SGPT Level in Transfusion dependent Thalassaemia major Patients-A Cross Sectional Study. North Int Med Coll J. 2017; 8(1): 170–3.

30. Patel S, Siddiqui A, Kareem I. A Correlative Study Of Serum Bilirubin and Liver Enzymes with Serum Ferritin in Beta Thalassaemia Major. IOSR J Dent Med Sci [Internet]. 2018; 17(1): 62–7. Available from: www.iosrjournals.org
31. Al-Moshary M, Imtiaz N, Al-Mussaed E, Khan A, Ahmad S, Albqami S. Clinical and Biochemical Assessment of Liver Function Test and Its Correlation with Serum Ferritin Levels in Transfusion-dependent Thalassemia Patients. Cureus. 2020; 12(4).