

## A Comparative Study of Liver Function and Lipid Profile between Minor and Major Thalassemia Patient

Assal Ghazi Alshammary<sup>1</sup> \*, Luma Qasim Ali<sup>2</sup>  and Rusul A.A. Alshammary<sup>1</sup> 

<sup>1</sup>Mustansiriya University, College of Science, Department of Microbiology, Iraq-Baghdad.

<sup>2</sup>Mustansiriya University, College of Science, Department of biology, Iraq-Baghdad.

\*Corresponding Author: Assal Ghazi Alshammary

DOI: <https://doi.org/10.55145/ajbms.2026.05.02.013>

Received 13 September 2026; Accepted 20 July 2026; Available online August 2026

**ABSTRACT:** It is thought that only patients with major thalassemia need to be under healthy control compared to minor. Therefore, the purpose of this study is to compare the liver status complications of small thalassemia with those of major thalassemia. Therefore, 84 patients with thalassemia were randomly selected; 56 with major and 28 with minor. After the blood samples were obtained, the levels of ferritin, liver enzymes, and lipid profiles were measured. The findings demonstrated that whereas ALP levels did not differ considerably, major thalassemia had significantly higher ALT and AST levels than minor thalassemia. All the patients with major and minor had abnormal higher ALP, 45% of major had elevated AST and 30% of the major had abnormal ALT than normal range. BilD, BilT, LDH and HDL levels were found to be significantly elevated in the major group compared to the minor group, whereas cholesterol and trig levels were significantly greater. The BilD levels in 90% of the major compared to 40% of the minor were increase than normal range. As conclusion, there were abnormality in the ALP and some lipid profile of minor thalassemia. Therefore, the patients with minor thalassemia could be under risk of liver disorder so they need to be under control and to find the exact reason of this disorder need more researches.



**Keywords:** Major Thalassemia, Minor Thalassemia, Liver Function, Lipid Profile

### 1. INTRODUCTION

Thalassemia is a genetic blood condition. The Greek words thalassa, which means Mediterranean Sea, and anemia are combined to form thalassemia [1]. The two kinds,  $\alpha$ -thalassemia and  $\beta$ -thalassemia, are characterized by inadequate synthesis of the hemoglobin molecule's globin chain. The most clinically dangerous cases are homozygous  $\beta$ -thalassemia, while  $\alpha$ -thalassemia homozygotes are frequently deadly in utero [2].

Reduced beta globin chain synthesis causes beta-thalassemia, which is characterized by decreased hemoglobin [Hb] levels in red blood cells [RBC], decreased RBC output, and anemia [3]. Beta-thalassemia comes in three different forms: major, intermedia, and minor [4]. Clinical manifestations of thalassemia major often appear between the ages of 6 and 24 months. Affected infants suffer from pallor and fail to thrive. Along with frequent episodes of fever and significant abdominal expansion from spleen and liver enlargement, feeding issues, diarrhea, and irritability may also arise. If a regular blood transfusion program is developed that maintains a minimum Hb concentration of 9.5 to 10.5 g/dL, growth and development are typically normal for 10 to 12 years. Patients who have been transfused may exhibit iron overload symptoms such as failure or delay in sexual development and growth retardation [5]. Individuals with thalassemia intermedia are asymptomatic until adulthood, with mild anemia causing several difficulties. Beta-thalassemia Minors are normally asymptomatic; however, they might have mild anemia [6].

The liver is an important organ in the human body that is in charge of many activities including metabolism, immunity, digestion, detoxification, and the storage of vitamins, all of which are controlled by liver enzymes. Alkaline phosphatase [ALP], aspartate transaminase [AST], and alanine transaminase [ALT] are liver enzymes that aid in accelerating bodily chemical reactions. The production of bile and substances that support blood coagulation, the

digestion of food and toxins, and infection resistance are examples of these chemical processes [7]. Enzymes [typically ALT, AST, or ALK] are released into the bloodstream in abnormally high concentrations when the liver is injured [8].

The liver contains approximately one-third of the body's stored iron [ferritin and haemosiderin] [8]. The effectiveness and prognosis of chelation treatments have been predicted using hepatic iron reserves, which are closely linked to the cumulative transfusion iron burden [9]. Many researchers investigated the influence of iron overload in major thalassemia on liver status and discovered that it produces fibrosis, cirrhosis, and liver failure, suggesting a connection between the emergence of iron-induced hepatotoxicity and hepatic iron levels [8]. On the other hand, as our knowledge, there is no research about the minor complications especially on the liver. Thus, this work aimed to investigate the minor thalassemia complications in the liver status and compare them with the major thalassemia

## 2. MATERIAL AND METHODS

84 thalassemia patients participated in this study that were randomly selected from visitor of Ibn Al-Balady Hospital [Hereditary Blood Disorder Center] in Bagdad, Iraq; 56 with major thalassemia and 28 with minor thalassemia. The age of participates was about 10-32 years. The biochemical analysis was conducted in Imam Ali Hospital. The Blood Samples [about 5ml] were collected from all participates by the venous puncture in a gel tubes. To separate the serum, these tubes were centrifuged for five minutes at 3000 rpm.

Simple tubes were used to collect the serum samples, which were then kept in a freezer at -20°C until they were used to measure the amounts of:

1. Ferritin by Fluorescence immunochromatographic method using Finecare™ Kit and instrument from Wondfo Company/ China country

2. Alkaline phosphatase [ALP], This employs the phosphatase substrate p-nitrophenyl phosphate [pNPP] in accordance with the Abnova Company kit/Taiwan, Alanine aminotransferase [ALT] by using Activity Assay according to Gen Way Biotech company kit/USA and Aspartate aminotransferase [AST] according to the Abnova Company kit/Taiwan, employing p-nitrophenyl phosphate [pNPP] as a phosphatase substrate.

3. Lipid profiles by enzymatic colorimetric method including; total cholesterol [TC] using biolabo company kit/France, HDL [high-density lipoprotein] and triglycerides [TG] using linear chemical company kit / Spain.

Results were given as mean± SD or percentage for the case frequency. Data were analyzed using one-way analysis of variance [ANOVA] and either Fisher's test or t-test for multiple comparison using Statview version 5.0. Regressions were also examined using CANOVA with Statview version 5.0. Differences were considered significant when  $p < 0.05$ .

## 3. RESULT

Table [1] summarizes the patients with minor and major thalassemia characteristic features. The mean age of major thalassemia was significantly higher than the minor [ $20.5 \pm 1.4$  and  $14.0 \pm 0.89$  years, respectively]. Moreover, the percentage of the major thalassemia removed their spleen was significantly higher than the minor [23% and 14%, respectively]. In addition, the men percentage was significantly higher than the women in the major thalassemia [69% and 23%, respectively] which is opposite in the minor where the women percentage was significantly higher than the men [71% and 29%, respectively].

**Table 1. - The characterized features of major and minor thalassemia**

| The features          |         | Major Th. | Minor Th. | P-Value |
|-----------------------|---------|-----------|-----------|---------|
| Age [Years] [mean±SE] |         | 20.5±1.4  | 14.0±0.89 | 0.0006  |
| Spleen removal %      |         | 23%       | 14%       | <0.0001 |
| Gender %              | Male    | 69%       | 29%       | <0.0001 |
|                       | Female  | 23%       | 71%       | <0.0001 |
|                       | P-Value | <0.0001   | <0.0001   |         |

Figure [1] shows the value of ferritin in the patients. It was significantly increase in the major thalassemia compared to minor, which is abnormal higher in the major but within the normal value [24-336 ng/ml] in the minor.

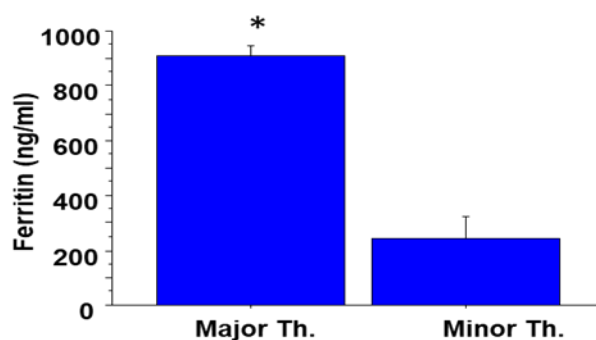


**FIGURE 1. - Ferritin level in major and minor thalassemia**

In table [2] determined liver enzymes in the patients. Major thalassemia patients had noticeably increased ALT and AST levels [ $29.23 \pm 0.74$  and  $32.85 \pm 2.60$  U/L, respectively] compared to minor [ $6.43 \pm 0.26$  and  $25.67 \pm 1.13$  U/L, respectively] while there were no significant variations in ALP levels between major and minor thalassemia. Although both means of ALT and AST were within the normal range, about 45% of the major thalassemia patients have abnormal higher level of the AST and 30% have significantly increase ALT level compared to minor thalassemia who have only normal levels of ALT and AST. On the other hand, ALP levels in both major and minor thalassemia were abnormal higher according to the normal range.

**Table 2. - Liver enzymes levels in the major and minor thalassemia**

| Groups       | ALT [U/L ]         | AST [U/L ]         | ALP [U/L ]         |
|--------------|--------------------|--------------------|--------------------|
| Major Th.    | $29.23 \pm 0.74^*$ | $32.85 \pm 2.60^*$ | $163.15 \pm 12.21$ |
| Minor Th.    | $6.43 \pm 0.26$    | $25.67 \pm 1.13$   | $172.43 \pm 12.18$ |
| P-Value      | <0.0001            | 0.024              | 0.598              |
| Normal Value | 4-36               | 8-33               | 44-147             |

In table [3] determined lipid profile in the patients. BilD, BilT, cholesterol and trig levels were significantly higher in the major thalassemia [ $0.64 \pm 0.04$ ,  $1.97 \pm 0.16$ ,  $110.5 \pm 3.2$  and  $133.6 \pm 12.8$  mg/dl, respectively] compared to minor [ $0.26 \pm 0.03$ ,  $0.66 \pm 0.08$ ,  $148.3 \pm 8.02$  and  $92.57 \pm 9.31$  mg/dl, respectively]. While LDH and HDL levels were significantly elevated in the minor thalassemia [ $180.4 \pm 14.6$  U/L and  $44.57 \pm 2.3$  mg/dl, respectively] compared to major thalassemia [ $112.7 \pm 14.2$  U/L and  $22.39 \pm 1.31$  mg/dl, respectively]. Chol, LDH and HDL levels were within the normal range in both major and minor thalassemia while the BilD levels in 90% of the major thalassemia compared to 40% of the minor thalassemia were increase than the normal value. Although both means of BilT and Trig were abnormal higher than the normal range in the major, only 80% of them have abnormal higher level of the BilT and 70% have abnormal higher Trig.

**Table 3. - Lipid profile levels in the major and minor thalassemia**

| Groups    | BilD [mg/dl ]     | BilT [mg/dl ]     | Chol [mg/dl ]     | LDH [U/L ]         | Trig [mg/dl ]      | HDL [mg/dl ]      |
|-----------|-------------------|-------------------|-------------------|--------------------|--------------------|-------------------|
| Major Th. | $0.64 \pm 0.04^*$ | $1.97 \pm 0.16^*$ | $110.5 \pm 3.2$   | $112.7 \pm 14.2$   | $133.6 \pm 12.8^*$ | $22.39 \pm 1.31$  |
| Minor Th. | $0.26 \pm 0.03$   | $0.66 \pm 0.08$   | $148.3 \pm 8.0^*$ | $180.4 \pm 14.6^*$ | $92.57 \pm 9.31$   | $44.57 \pm 2.3^*$ |
| P-Value   | <0.0001           | <0.0001           | <0.0001           | 0.002              | 0.017              | <0.0001           |
| Normal V. | 0-0.3             | 1-1.2             | <200              | 105-333            | <150               | 35-65             |

Table [4] shows the correlation of all studied biochemical parameters with the spleen removal, age and gender. The patient who underwent splenectomy represented by the number 2 and whose was not removed represented by the number 1. As well as, the woman represented by number 2 and the man represented by number 1. Only BilD, Trig and Ferritin have significant positive correlation with spleen removal while with age, there was significant positive correlation with the BilD, BilT, Trig and ferritin and negative correlation with ALP and HDL. Additionally, there was significant positive correlation of Chol, LDH and HDL and negative correlation of BilD with the gender.

**Table 4. - Correlation of spleen removal, age and gender with the Ferritin, liver enzymes and lipid profile**

|                   | Spleen removal      | Age [age ]           | Gender                |
|-------------------|---------------------|----------------------|-----------------------|
| ALP [U/L ]        | P= 0.34, R=0.14     | ↓ P=0.009, R=0.37    | P=0.61, R=0.07        |
| ALT [U/L ]        | P=0.63, R=0.07      | P=0.23, R=0.17       | P=0.076, R=0.26       |
| AST [U/L ]        | P = 0.86, R=0.03    | P = 0.26, R=0.17     | P=0.17, R=0.2         |
| BilD [mg/dl ]     | ↑ P = 0.03, R=0.32  | ↑P<0.0001, R=0.58    | ↓ P=0.012, R=0.37     |
| BilT [mg/dl ]     | P=0.42, R=0.12      | ↑ P=0.0001, R=0.52   | P= 0.14, R=0.22       |
| Chol [mg/dl ]     | P = 0.51, R=0.1     | P=0.32, R=0.15       | ↑P<0.0001, R=0.54     |
| Trig [mg/dl ]     | ↑ P=0.002, R = 0.44 | ↑P<0.0001, R=0.7     | P=0.56, R=0.09        |
| LDH [U/L ]        | P=0.38, R=0.13      | P=0.29, R=0.17       | ↑P= 0.0002, R = 0.52  |
| HDL [mg/dl ]      | P=0.34, R=0.14      | ↓ P = 0.0003, R=0.51 | ↑ P = 0.003, R = 0.42 |
| Ferritin [ng/ml ] | ↑ P = 0.006, R=0.4  | ↑ P = 0.0004, R=0.5  | P = 0.24, R = 0.17    |

Table [5] demonstrates the relationship between the lipid profile and all liver enzymes, as well as the relationship between ferritin and the liver enzymes. While only trig and HDL have a significant positive link with AST, HDL and AST have a large negative correlation., ALT is significantly positively correlated with ferritin, BilT, and Trig and significantly negatively correlated with HDL. However, ALP has only significant negative correlation with trig. On the other hand, ferritin has significant positive correlation with ALT, AST, BilD, BilT and Trig and negative correlation with Chol and HDL.

**Table 5. - Correlations of liver enzymes with lipid profile and ferritin with liver enzymes and lipid profile**

|               | ALP [U/L ]              | ALT [U/L ]             | AST [U/L ]             | Ferritin [ng/ml ]     |
|---------------|-------------------------|------------------------|------------------------|-----------------------|
| BilD [mg/dl ] | P=0.82<br>R=0.032       | P=0.12<br>R=0.23       | P=0.49<br>R=0.10       | ↑P<0.0001<br>R=0.6    |
| BilT [mg/dl ] | P=0.41<br>R=0.12        | ↑ P=0.0008<br>R=0.4    | P=0.58<br>R=0.08       | ↑P<0.0001<br>R=0.6    |
| Chol [mg/dl ] | P = 0.22<br>R = 0.18    | P = 0.19<br>R = 0.19   | P = 0.76<br>R = 0.045  | ↓P<0.0001<br>R = 0.5  |
| Trig [mg/dl ] | ↓P = 0.0002<br>R = 0.52 | ↑P = 0.005<br>R = 0.41 | ↑P = 0.014<br>R = 0.36 | ↑P= 0.0005<br>R = 0.4 |
| LDH [U/L ]    | P=0.14<br>R=0.22        | P=0.93<br>R=0.03       | P=0.57<br>R=0.26       | P=0.27<br>R=0.16      |
| HDL [mg/dl ]  | P=0.49<br>R=0.1         | ↓ P=0.015<br>R=0.36    | ↓ P=0.009<br>R=0.37    | ↓P<0.0001<br>R = 0.7  |

|                      |                  |                     |                      |
|----------------------|------------------|---------------------|----------------------|
| Ferritin<br>[ng/ml ] | P=0.42<br>R=0.12 | ↑ P=0.0004<br>R=0.4 | ↑ P=0.023<br>R= 0.33 |
|----------------------|------------------|---------------------|----------------------|

#### 4. DISSCUSION

Our results found that in the major thalassemia, age range was  $20.5 \pm 1.4$  years, which is agreed with the Prakash, 2012 [10], was significantly higher than it in the minor which was  $14.0 \pm 0.89$  years. The results of minor thalassemia could not compare it to the reference since we did not find research studied it. Thalassemia major is usually suspected in infants under two years old who have severe microcytic anemia, mild jaundice, and hepatosplenomegaly. Thalassemia mild appears later in life and has less clinical signs [11]. Therefore, the different between the age of major and minor could be because the patients with major thalassemia need to still under controlled by the doctors because its complications but the minor does not need it.

However, in the major, 69% from the patients were males compared to 29% females which were totally different than the minor where was only 23% males compared to 71% female. These findings corresponded with those of Nigam et al., 2020 [12], who discovered the same changes but considered them insignificant.

When hypersplenism raises blood transfusion requirements and hinders proper management of body iron with chelating treatment, splenectomy and ferritin raising levels are advised in the transfusion-dependent patient [13]. In contrast to those with thalassemia major, Because they either have little anemia or no anemia at all, people with thalassemia minor typically do not require blood transfusions [14]. These evidences could explain the increasing of the major thalassemia undergo splenectomy and the ferritin levels compared to minor and the positive correlation of ferritin with age and case frequency of splenectomy.

The liver is the only organ that produces ferritin and transferrin and is the primary organ for storing iron. Free ferrous iron is highly toxic since iron is normally protein-bound in the liver. Free radicals are produced by unbound iron, which has been linked to lipid peroxidation and hepatotoxicity [15]. The liver is the first location where iron builds up and is often the cause of illness in people with transfusion-associated thalassemia. Hepatocytes and reticuloendothelial cells both experience iron overload. Those with extra iron produce more free radicals due to the Fenton reaction. These free radicals damage and degrade tissue when they build up in the heart, liver, and other organs. [16]. Serum ferritin concentration is frequently used to evaluate iron overload in individuals with  $\beta$ -thalassemia because to the favorable correlation between iron levels and ferritin [17]. As it explaining above the ferritin levels increase in the major thalassemia, which explain the increase of case frequency, have abnormal results of liver enzymes.

In the current investigation, we discovered higher levels of ALT, AST, and ALP, as well as a positive correlation of ALT and AST with the ferritin level. Thus, the results of this study are in line with those of other research projects carried out by De Sanctis et al [18]. Although the suggested component of activity has been illustrated by a number of analysts, the optimal method is yet unknown. Seng Suk et al discovered that liver functions in  $\beta$ -thalassemia patients were three to four times higher than in healthy people [19]. In transfusion-dependent -thalassemia major, iron accumulation is related with increased oxidative stress, lipid peroxidation, and liver cell damage. Jensen et al. also discovered that when the iron level of the liver increases, so do serum transaminases and hepatic fibrosis [20]. The observed elevation of ALP in thalassemia minor patients, despite maintaining normal ferritin levels, suggested a mechanism independent of direct iron overload toxicity. Instead, this elevation is likely attributed to altered bone metabolism associated with hemoglobinopathies. In thalassemia minor, mild ineffective erythropoiesis-even if clinically silent-can drive compensatory bone marrow expansion and subsequent osteoclast activation [21].

The lipid profiles of patients with major and mild thalassemia were examined in this study. While triglyceride levels were high and cholesterol, HDL cholesterol, and LDL cholesterol were low, major patients with often transfused thalassemia had greater serum ferritin levels than minor patients. Serum ferritin and liver enzymes were negatively correlated with total cholesterol, HDL, and LDL, but they were positively correlated with serum triglycerides. Therefore, it seems that a variety of factors, such as iron overload [high ferritin levels], liver damage, and hormone instability, affect these people's lipid patterns. Mild erythroid hyperplasia also increases LDL clearance by bone marrow. The major causes of low plasma cholesterol levels include accelerated erythropoiesis, enhanced LDL absorption by macrophages, and reticuloendothelial system histiocytosis. Hepatic injury and iron excess produce low total cholesterol. Because these alterations are indicators of lipid peroxidation, the cause of the occurrence was investigated [22]. According to Papanastasiou et al., thalassemia patients had significantly lower levels of total, HDL, and LDL cholesterol than controls, but significantly greater levels of triglycerides. A positive correlation between age and triglyceride levels was discovered [23,33]. Kaltwassen et al. reported that triglyceride levels rose as ferritin levels rose and that oxidative LDL-C antibodies and patient age were positively correlated with triglyceride levels [24,32]. In a research done in Jordan in 2008, Kamal et al discovered significantly lower cholesterol, HDL, and LDL levels when compared to controls [25]. Louis et al. discovered a comparable reduction in total cholesterol [26,34]. Patne et al found that lipid abnormalities are more common in thalassemia children than in controls in their study [27,31]. Inati et al. found that patients with  $\beta$ -Thalassemia major have a different lipid profile during a study conducted in Lebanon.

Triglyceride [TG ] levels are neither statistically different nor greater in thalassemia patients compared to normal controls, although serum levels of total cholesterol [TC ] and low-density lipoprotein cholesterol [LDL ] are lower [28,29 ]. Our findings support earlier authors' theory that serum iron and triglycerides are both implicated in the development of LDL cholesterol oxidation. In the present study, we discovered a strong positive association between serum ferritin and triglycerides, which are indicative of a disordered lipid profile linked to inadequate chelation and abnormal iron, overload [22,30 ].

## 5. CONCLUSION

The study findings demonstrated severe biochemical dysfunctions in patients with Thalassemia Major, primarily driven by excessive iron accumulation and elevated ferritin levels. Concurrently, despite maintaining ferritin levels within the normal range, patients with Thalassemia Minor also exhibited notable functional abnormalities, including elevated Alkaline Phosphatase (ALP) levels alongside marked alterations in lipid profiles. Specifically, 40% of Thalassemia Minor patients showed abnormal elevations in direct bilirubin (BILD), 30% in total bilirubin (BILT), and 20% in triglyceride levels, pointing toward underlying hepatic stress and early metabolic disturbances that warrant clinical attention. Consequently, these results strongly refute the widespread misconception that individuals carrying the Thalassemia Minor trait are completely healthy and do not require long-term medical follow-up. Given the clear risks posed to liver function and systemic metabolic homeostasis, routine medical monitoring and regular diagnostic evaluations are highly recommended for this patient population, alongside a pressing need for further research to clarify the precise pathophysiological mechanisms driving these systemic alterations.

## Funding

None

## ACKNOWLEDGEMENT

The authors express their gratitude to Mustansiriyah University in Baghdad, Iraq [<https://uomustansiriyah.edu.iq/>].

## CONFLICTS OF INTEREST

The authors declare no conflict of interest

## REFERENCES.

- [1] D. C. Sharma, A. Arya, P. Kishor, P. Woike, and J. Bindal, "Overview on thalassemias: A review article," *Medico Research Chronicles*, vol. 4, no. 4, pp. 325–337, 2017.
- [2] M. Angastiniotis and S. Lobitz, "Thalassemias: An overview," *International Journal of Neonatal Screening*, vol. 5, no. 1, Art. no. 16, Mar. 2019.
- [3] B. Modell and M. Darlison, "Global epidemiology of haemoglobin disorders and derived service indicators," *Bull. World Health Organ.*, vol. 86, no. 6, pp. 480–487, 2008.
- [4] R. Galanello and R. Origa, "Beta-thalassemia," *Orphanet J. Rare Dis.*, vol. 5, no. 1, pp. 1–15, 2010.
- [5] C. Borgna-Pignatti and R. Galanello, "Thalassemias and related disorders: Quantitative disorders of hemoglobin synthesis," in *Wintrobe's Clinical Hematology*, vol. 42, 2004, pp. 1319–1365.
- [6] A. Essopos, D. Farmakis, S. Deftereos, M. Tsironi, S. Tassiopoulos, I. Moyssakis, and M. Karagiorga, "Thalassemia heart disease: A comparative evaluation of thalassemia major and thalassemia intermedia," *Chest*, vol. 127, no. 5, pp. 1523–1530, 2005.
- [7] H. Altıparmak, Ş. Kaba, and M. Yuvalı, "Evaluation of HCV infection laboratory test results using machine learning methods," in *Proc. Int. Conf. Theory Appl. Soft Comput., Comput. Words Perceptions*, Cham, Switzerland: Springer, 2019, pp. 261–269.
- [8] M. Cappellini, A. Cohen, A. Eleftheriou, A. Piga, J. Porter, and A. Taher, *Guidelines for the Clinical Management of Thalassemia*, 3rd ed. Nicosia, Cyprus: Thalassemia International Federation, 2014.
- [9] J. C. Wood, C. Enriquez, N. Ghugre, J. M. Tyzka, S. Carson, M. D. Nelson, and T. D. Coates, "MRI R2 and R2\* mapping accurately estimates hepatic iron concentration in transfusion-dependent thalassemia and sickle cell disease patients," *Blood*, vol. 106, no. 4, pp. 1460–1465, 2005.
- [10] A. Prakash and R. Aggarwal, "Thalassemia major in adults: Short stature, hyperpigmentation, inadequate chelation, and transfusion-transmitted infections are key features," *N. Am. J. Med. Sci.*, vol. 4, no. 3, pp. 141–144, 2012.

- [11] M. Porcu, N. Landis, S. Salis, M. Corda, P. Orru, E. Serra, B. Usai, G. Matta, and R. Galanello, "Effects of combined deferiprone and desferrioxamine iron chelating therapy in beta-thalassemia major end-stage heart failure," *Eur. J. Heart Fail.*, vol. 9, no. 3, pp. 320–322, 2007.
- [12] N. Nigam, R. Kushwaha, G. Yadav, P. K. Singh, N. Gupta, B. Singh, et al., "A demographic prevalence of  $\beta$ -thalassemia carrier and other hemoglobinopathies in adolescent of Tharu population," *J. Family Med. Prim. Care*, vol. 9, no. 8, pp. 4305–4310, 2020.
- [13] H. A. Saleh, Y. M. Alkhateep, and A. N. Mohammed, "Role of splenectomy in thalassemic patients," *Menoufia Med. J.*, vol. 31, no. 1, pp. 118–125, 2018.
- [14] D. Langhi Jr., E. M. A. Ubiali, J. F. C. Marques Jr., M. D. A. Verissimo, S. R. Loggetto, A. Silvino, and W. M. Bernardo, "Guidelines on beta-thalassemia major—regular blood transfusion therapy: Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular: Project guidelines: Associação Médica Brasileira—2016," *Rev. Bras. Hematol. Hemoter.*, vol. 38, no. 4, pp. 341–345, 2016.
- [15] M. Al-Moshary, N. Imtiaz, E. Al-Mussaied, A. Khan, S. Ahmad, S. Albqami, and S. N. Albqami, "Clinical and biochemical assessment of liver function test and its correlation with serum ferritin levels in transfusion-dependent thalassemia patients," *Cureus*, vol. 12, no. 3, Art. no. e7574, Mar. 2020, doi: 10.7759/cureus.7574.
- [16] L. D. S. Onde, I. D. F. Estevao, M. I. P. Rocha, S. Percário, D. R. S. Souza, M. A. D. Pinhel, and C. R. Bonini-Domingos, "Oxidative stress and antioxidant status in beta-thalassemia heterozygotes," *Rev. Bras. Hematol. Hemoter.*, vol. 35, no. 6, pp. 409–413, 2013.
- [17] J. B. Porter, M. Evangelini, and A. El-Beshlawy, "The challenges of adherence and persistence with iron chelation therapy," *Int. J. Hematol.*, vol. 94, no. 5, pp. 453–460, 2011.
- [18] V. De Sanctis, A. Eleftheriou, and C. Malaventura, "Prevalence of endocrine complications and short stature in patients with thalassaemia major: A multicenter study by the Thalassaemia International Federation [TIF]," *Pediatr. Endocrinol. Rev.*, vol. 2, Suppl. 2, pp. 249–255, Dec. 2004.
- [19] C. Sengsuk, O. Tangvarasittichai, P. Chantanaskulwong, A. Pimanprom, S. Wantaneeyawong, A. Choowet, and S. Tangvarasittichai, "Association of iron overload with oxidative stress, hepatic damage and dyslipidemia in transfusion-dependent  $\beta$ -thalassemia/HbE patients," *Indian J. Clin. Biochem.*, vol. 29, no. 3, pp. 298–305, 2014.
- [20] P. D. Jensen, F. T. Jensen, T. Christensen, J. L. Nielsen, and J. Ellegaard, "Relationship between hepatocellular injury and transfusional iron overload prior to and during iron chelation with desferrioxamine: A study in adult patients with acquired anemias," *Blood*, vol. 101, no. 1, pp. 91–96, 2003.
- [21] N. Skordis and M. Toumba, "Bone disease in thalassaemia major: Recent advances in pathogenesis and clinical aspects," *Pediatr. Endocrinol. Rev.*, vol. 8, no. 3, pp. 300–306, Mar. 2011.
- [22] R. Suman, A. Sanadhya, P. Meena, J. Singh, R. Jain, and S. Meena, "Lipid profile in children of  $\beta$ -thalassemia major and their correlation with serum ferritin," *Int. J. Contemp. Pediatr.*, vol. 4, no. 2, pp. 543–547, 2017.
- [23] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, "Executive summary of the third report of the National Cholesterol Education Program [NCEP] expert panel on detection, evaluation, and treatment of high blood cholesterol in adults [Adult Treatment Panel III]," *JAMA*, vol. 285, no. 19, pp. 2486–2497, 2001, doi: 10.1001/jama.285.19.2486.
- [24] J. P. Kaltwasser and R. Gottschalk, "Erythropoietin and iron," *Kidney Int. Suppl.*, vol. 55, no. 69, pp. S49–S56, 1999.
- [25] K. M. Mansi and T. A. Aburjai, "Lipid profile in Jordanian children with  $\beta$ -thalassemia major," *UHOD—Uluslararası Hematoloji-Onkoloji Dergisi*, vol. 18, no. 2, pp. 93–98, 2008.
- [26] L. C. Low, "Growth of children with  $\beta$ -thalassemia major," *Indian J. Pediatr.*, vol. 72, no. 2, pp. 159–164, 2005.
- [27] A. B. Patne, P. J. Hisalkar, and S. B. Gaikwad, "Lipid abnormalities in patients of beta thalassaemia major," *Int. J. Pharm. Pharm. Sci.*, vol. 2, no. 2, pp. 106–112, 2012.
- [28] A. Inati, M. A. Noureldine, A. Mansour, and H. A. Abbas, "Endocrine and bone complications in  $\beta$ -thalassemia intermedia: Current understanding and treatment," *BioMed Res. Int.*, vol. 2015, Art. no. 813090, 2015, doi: 10.1155/2015/813090.
- [29] S. S. Martin et al., "2024 AHA/ACC guideline on the management of blood cholesterol: A report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines," *Circulation*, vol. 149, no. 12, pp. e750–e812, 2024.
- [30] S. Babar et al., "Erythroferrone in focus: Emerging perspectives in iron metabolism and hematopathologies," *Blood Science*, vol. 6, no. 4, Art. no. e00198, 2024.
- [31] H. K. Jabbar, M. K. Hassan, and L. M. Al-Naama, "Lipids profile in children and adolescents with  $\beta$ -thalassemia major," *Hematology, Transfusion and Cell Therapy*, vol. 45, no. 4, pp. 467–472, 2023, doi: 10.1016/j.htct.2022.09.1277.
- [32] N. A. Soliman et al., "Growth patterns and risk factors of growth retardation in children and adolescents with transfusion-dependent  $\beta$ -thalassemia," *Pediatric Hematology and Oncology*, vol. 41, no. 2, pp. 115–128, 2024.

- [33] H. C. Shekar et al., "Lipid profile and atherogenic indices in children with transfusion-dependent beta-thalassemia: A comparative study," *European Journal of Cardiovascular Medicine*, vol. 15, no. 1, pp. 42–49, 2025.
- [34] R. T. Hamza, A. Habeb, E. Charmandari, et al., "International consensus guideline on the diagnosis and management of endocrine complications of  $\beta$  and  $\alpha$  thalassemia in children and adolescents," *Hormone Research in Paediatrics*, vol. 97, no. 5, pp. 412–430, 2024.