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A study of vitamin D concentration and some physiological variables among patients with beta thalassemia in Kirkuk city

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Abstract

The current study aimed to estimate vitamin D concentration and some physiological variables in patients with beta thalassemia. 150 subjects with thalassemia were taken from both Azadi Teaching Hospital and Al Jumhuri Hospital from November 2021 to April 2022. The experimental work was carried out in private laboratories in Kirkuk, Iraq. The volunteers in the current study were divided as follows: 50 healthy volunteers as a control group. 150 thalassemia patients as a second group. The results showed that the activity of liver enzymes showed a significant increase ($P < 0.05$) in thalassemia patients with beta thalassemia compared to the control group. the ferritin and D dimer concentrations showed a significant increase ($P < 0.05$) in patients compared to the control group. For oxidative stress, malondialdehyde (MDA) level showed a significant increase ($P < 0.05$) in patients compared to the control group. The glutathione (GSH), catalase and superoxide dismutase (SOD) concentration showed a significant decrease ($P < 0.05$) in the patients (0.284 ± 0.025) compared to the control group. the concentration of vitamin D showed a significant decrease ($P < 0.05$) in patients compared to the control group. It is concluded from the current study that there is a link between thalassemia and liver enzymes, and this indicates the direct effect of beta-thalassemia on the liver. On the other hand, it was found that both ferritin and D dimer can be considered as indicators for the detection of thalassemia. The results of the current study also showed that there is an association between vitamin D deficiency and beta thalassemia.

Keywords

Thalassemia, liver enzymes, ferritin, D dimer, oxidative stress.

Thalassemia is a group of disorders that result from impaired production of hemoglobin and defective red blood cells. For those who suffer from a severe form of thalassemia. Lifelong blood transfusion is the mainstay of treatment. Children with severe thalassemia usually do not live beyond five years. While chronic blood transfusions and comprehensive medical care had an average life expectancy of the fourth decade of life and more [1]. Complications directly related to transfusions include blood-borne infections, development of erythrocyte antibodies, late hemolytic reactions, and fever. The goal of blood transfusions is to keep the hemoglobin level at 9 to 10 g/dL. Blood is usually given every three to four weeks to reach this target hemoglobin level [2-3]. Thalassemia is an autosomal inherited condition characterized by either a deficiency or an absence of synthesis of one of the polypeptide chains (α or β) that make up the adult human hemoglobin molecule. Its clinical severity varies from major, intermedia, and minor, with different forms described based on the severity of the condition [4]. Usually, thalassemia major is not compatible with further uterine life. β-

thalassemia major occurs in infancy and requires lifelong transfusion therapy and bone marrow transplantation for successful control of the disease [5]. in Iraq; It is common among populations with higher α-chain production of β-globin chains, which divert the function of hemoglobin to toxic inclusion bodies causing peripheral erythrocyte hemolysis [6]. Thalassemia major is considered an important health problem in the province of Sulaymaniyah, where there are more than 600 cases registered in a population of more than 1.5 million people (Records of the Preventive Health Department - Sulaymaniyah) [7], as well as in the neighboring countries of Iraq such as Jordan. Bashir et al., [8] showed that the percentage of thalassemia major reached (3-3.5%), and in Lebanon it reached (1.7-3%) [9], and in Saudi Arabia it reached (3%) [10] and in Turkey (2.6-3.7%) [11]. People who are carriers of beta thalassemia minor are usually asymptomatic. Their hematologic criteria are predominantly hypochromic microcytic, anemia, elevated hemoglobin A2 level with normal or moderately elevated HBF level on Hb electrophoresis [12]. The prevalence of thalassemia minor in Baghdad was 4.4% as reported by Yahya in 1996. In the city of Mosul in northern Iraq, the prevalence of beta thalassemia minor was 8.8% as noted in 2009 by Khaleel et al., [13].

Materials & Methods

Samples collection

150 subjects with thalassemia were taken from both Azadi Teaching Hospital and Al Jumhuri Hospital from November 2021 to April 2022. The experimental work was carried out in private laboratories in Kirkuk, Iraq. The volunteers in the current study were divided as follows:

- 50 healthy volunteers as a control group.
- 150 thalassemia patients as a second group.

Collection of blood samples

Blood samples were collected by well-trained nurses from each patient. 5 ml of venous blood samples were obtained from each person and divided into 1 ml in an EDTA tube and 4 ml in a normal tube. Tubes were left normal for a short time to allow blood to clot, then clear serum samples were obtained by centrifugation at 4,000 rpm for 10 minutes. The separated serum was placed into five regular tubes, tightly closed and stored at −20 °C until the time of analysis. Frozen serum samples were thawed at 4−8 °C and then mixed by shaking at room temperature before use. The activity of liver enzymes, concentrations of ferritin, D dimer, vitamin D, MDA, GSH, SOD and catalase were calculated by using ELISA.

Statistical analysis

Statistic evaluation Means and SE were used to express the results. using one-way analysis of variance to statistically analyze the data, ANOVA was used to analyze the data and find differences between the groups before and after the treatment. SPSS (SPSS 2003, SPSS Inc.) was used to analyze the data, and P 0.05 was considered statistically significant.

Results & Discussion

Liver enzymes

Table (1) shows significant differences ($P < 0.05$) in the activity of liver enzymes in thalassemia patients compared to the control group, where ALT levels showed a significant increase ($P < 0.05$) in thalassemia patients (65.36 ± 8.51) compared to the control group (23.06). ± 6.41). On the other hand, a significant increase ($P < 0.05$) was found in the AST levels of thalassemia patients (54.26 ± 8.56) compared to the control group (24.43 ± 4.28). ALP levels showed a significant increase ($P < 0.05$) in the patients (87.9 ± 6.29) compared to the control group (52.3 ± 8.51).

Table (1): shows the levels of liver enzymes in the study groups

Groups Parameters	Control	Patients	P-Value
ALP U/L	23.06+6.41	65.36+8.51	0.03
AST U/L	24.43+4.28	54.26+8.56	0.048
ALP U/L	52.3+8.51	87.9+6.29	0.041

The mean serum ferritin level was significantly higher in thalassemia patients with elevated ALT or elevated AST compared with patients with normal levels. Moreover, the mean levels of ALT and AST were significantly higher in patients with elevated ferritin than with normal ferritin. These results are consistent with other previous studies by Ameli et al. [14], Ruhl et al. [15] who reported that an abnormal ALT level is associated with elevated ferritin. These results are consistent with the studies of Abdallaet al.,[16] in Jordan that there is a significant correlation between serum ALT levels ($R = 0.315$) and AST levels ($R = 0.291$) and serum ferritin levels in thalassemia patients compared to the control group.

A similar study conducted by Company et al.,[17] in Kurdistan on 40 patients with beta thalassemia major showed that mean SGOT levels were 50 ± 27.8 units/L ($p = 0.2$). Another study conducted on 104 patients with thalassemia showed

a significant correlation between the level of iron as indicated by transferrin saturation or serum ferritin levels and levels of SGOT and SGPT. Abnormal liver function is represented by elevated levels of SGOT, SGPT, and serum alkaline phosphatase, which is observed more frequently in patients with iron overload than in patients with low iron [18].

Ferritin and D dimer

Table (2) shows the concentration of ferritin in thalassemia patients, where the ferritin concentration showed a significant increase ($P < 0.05$) in patients (794.52 ± 67.13) compared to the control group (124.08 ± 22.57). The concentration of D-dimer showed a significant increase ($P < 0.05$) in the patients (329.57 ± 45.04) compared to the control group (174.19 ± 32.67).

Table (2): shows the levels of ferritin and D dimer in the study groups

Groups Parameters	Control	Patients	P-Value
Ferritin ng/ml	124.08±22.57	794.52 ±67.13	0.0001
D dimer ng/ml	174.19 ±32.67	329.57 ±45.04	0.02

The findings of the present study on ferritin levels are consistent with Pootrakul et al. [19], who found that serum ferritin levels in thalassemia patients were higher than normal. The same finding was found by Mishra and Tiwari [20], who found that serum ferritin levels in thalassemia patients in India were higher than those in a control group. Easa[21] conducted a study on seventy patients with thalassemia, including thalassemia major and thalassemia intermediate, at the time of their attendance at the Thalassemia Center in Karbala Teaching Hospital. The result was also a high ferritin level for all thalassemia patients in that study. The result is iron deficiency anemia. These results came in the current study in agreement with Hallberget al.,[22] who determined the concentration of ferritin in the blood of 203 women aged 38 years. They concluded that the serum ferritin value is the best predictor of iron deficiency and noted that the threshold was similar to that derived from previous population surveys and clinical case studies. Also, the study of Zanellaet al.,[23] showed similar results to the results of the current study. They examined the sensitivity and predictive value of serum ferritin concentration to identify iron deficiency. The overall sensitivity and diagnostic specificity were 82% and 95% for serum ferritin, respectively. However, the sensitivity was more than 80% for ferritin in cases of severe anemia, and in the absence of anemia, the sensitivity to ferritin decreased to 70%. In a systematic review of the diagnostic value of different laboratory tests for diagnosing iron deficiency, it was concluded that serum ferritin was the most powerful test for simple iron deficiency in both the population and hospital patients. The results of the current study showed that compared with the control group, the concentrations of D-dimer in the serum were significantly increased. These results are consistent with research conducted in Egypt [24] and Iraq [25].

Oxidative and antioxidant parameters

Table (3) shows some blood changes in thalassemia patients, where MDA level showed a significant increase ($P < 0.05$) in patients (2.175 ± 0.073) compared to the control group (1.495 ± 0.085). The glutathione concentration showed a significant decrease ($P < 0.05$) in the patients (0.284 ± 0.025) compared to the control group (0.457 ± 0.018). On the other hand, it was found that the concentration of catalase showed a significant decrease ($P < 0.05$) in patients (0.649 ± 0.032) compared to the control group (1.381 ± 0.051). The results also showed that the SOD concentration showed a significant increase ($P < 0.05$) in the patients (0.795 ± 0.034) compared to the control group (0.618 ± 0.021).

Table (3): shows the levels of liver enzymes in the study groups

Groups Parameters	Control	Patients	P-Value
MDAnmol / ml	1.495 ± 0.085	2.175 ± 0.073	0.0001
GSHnmol / ml	0.457 ± 0.018	0.284 ± 0.025	0.001
CATnmol / ml	1.381 ± 0.051	0.649 ± 0.032	0.0001
SODnmol / ml	0.618 ± 0.021	0.795 ± 0.034	0.002

Patients with thalassemia are more likely to have increased oxidative stress as evidenced by an increased MDA level in part due to the presence of iron in the form of heme released from excess globin chains and the deposition of excess iron in various tissues. Therefore, MDA may be a useful test for persistence of membrane damage in patients with iron overload. Oxidative stress seen in thalassemia patients is related to premature cell removal and anemia [26], as well as iron overload in these patients which generates reactive oxygen species (ROS) and peroxidative tissue injury [27], ensuring that MDA levels are increased. ROS generation is an invariant cellular event in respiring cells. Its production can be dramatically amplified in response to a variety of pathophysiological conditions. The release of hemoglobin during hemolysis and subsequent therapeutic transport in some cases leads to

a systemic overload of iron that increases ROS production [28] leading to oxidative damage to lipids and proteins of cellular membranes [29]. Increased levels of MDA indicate an increase in hyperoxicity, which leads to increased oxidative stress in patients with thalassemia. Excess iron in thalassemia patients stimulates fat oxidation processes. Thalassemia endogenous blood cells generally respond to oxidative stress by reacting with hydrogen peroxide to form a hydroxyl radical that breaks down small cellular molecules [30].

Vitamin D

Table (4) shows the concentration of vitamin D in thalassemia patients, where the concentration of vitamin D showed a significant decrease ($P < 0.05$) in patients (13.72 ± 4.12) compared to the control group (34.42 ± 9.05).

Table (4): shows the concentration of vitamin D in the study groups

Groups Parameters	Control	Patients	P-Value
Vit. D (ng/ml)	34.42± 9.05	13.72 ± 4.12	0.001

In table (4), the results indicated a significant decrease ($P<0.05$) in the concentration of vitamin D among thalassemia patients compared to the control group. Some studies have indicated that vitamin D deficiency is due to disturbances in the synthesis of 25-hydroxyvitamin D in the liver due to iron overload [31]. Other mechanisms include low intake, weak absorption, or reduced skin production [32]. As we know that the liver is the main site for the synthesis of hydroxyl in Vitamin D, it is possible that the excessive amount of iron in the liver may have directed to the deficiency of Vitamin D which suggests that the excessive amount of iron in the liver may affect the metabolism of Vitamin D [33].

Conclusions

It is concluded from the current study that there is a link between thalassemia and liver enzymes, and this indicates the direct effect of beta-thalassemia on the liver. On the other hand, it was found that both ferritin and D dimer can be considered as indicators for the detection of thalassemia. The results of the current study also showed that there is an association between vitamin D deficiency and beta thalassemia.

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