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# Association of Liver and Kidney Dysfunction with Beta-Thalassemia Patients

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## Abstract

Beta-thalassemia is a category of hemoglobin synthesis disorders that are recessively autosomal. The most important cause of mortality and morbidity is these patients with thalassemic is organ failure related with shortened red cell life span, rapid iron turnover and tissue deposition of excess iron. The present study was carried out on a total of 50 thalassemic patients to evaluate liver function levels (GOT, GPT, ALP, TP, Alb) and kidney function such as (Urea, Uric acid and Creatinine). Seventy individuals of Iraqi adults were divided into two groups: 50 thalassemic patients (28 male and 22 female) (group 1) and 20 normal individuals (10 male and 10 female) as control (healthy group) (group 2). The results show a significant increase ($p \leq 0.01$) in (GOT, GPT and ALP) while also showed a significant decrease ($p \leq 0.01$) in T.p and Alb levels of thalassemia patients compared with control group. The mean values of Uera, Uric acid and Creatinine in thalassemic patients were (42.75 ± 3.37, 9.27 ± 0.63 and 1.31 ± 0.13) mg/dl respectively as compared with control group (22.25 ± 1.41, 4.90 ± 0.23 and 0.623 ± 0.04) mg/dl respectively. Also, the results showed the effect of duration of disease on (GOT and Urea) level in thalassemic patients ($p \leq 0.05$). Also, this study has no significant differences between male and female patients in all parameters study and also the effect of age on parameters was studied.

**Keywords:** B-thalassemia; Liver function; Renal dysfunction

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## Introduction

Beta-thalassemia is the most prevalent hereditary hemoglobin apathy worldwide. Thalassemia are classified into alpha (α) and beta (β) thalassemia according to the globin chain whose synthesis is adversely affected [1]. The excess of globin chain synthesis in thalassemia contributes to damage to red blood cells, leading to loss of red blood cells in the bone marrow and peripheral circulation (hemolysis) [2]. A sustained blood transfusion is the major therapy for these patients.

Iron can replace in various organs following blood transfusion, such as the liver, heart, endocrine and kidney [3]. Iron load can be ended to this organ dysfunction and mortality [4]. The liver is the main site of iron storage and the only site for transferrin and ferritin synthesis, free ferrous iron is highly toxic and is typically bound to the liver by protein. Unbound iron catalyzes the development of free radicals that have been involved in hepatotoxicity and lipid peroxidation [5]. Within the hepatocytes and reticulo-endothelial cells, the earliest location for iron deposition causes reversible liver damage resulting in fibrosis and thus liver cirrhosis [6,7]. However, cardio toxicity is life-threatening and the most severe complication of iron overload. Iron-chelating therapy is primarily responsible for doubling the life expectancy of patients with thalassemia, and has been shown to prevent liver and heart damage, inducing normal growth and sexual development in children with thalassemia, and raising the life span of children with thalassemia [8]. In patients with thalassemia, signs of kidney dysfunction such as increased renal blood flow, urine concentration defects, and renal tubular acidosis have been identified [9]. Toxicity of iron chelators (deferoxamine, deferiprone and deferasirox) can lead to glomerular dysfunction [10]. For many decades, the identification of renal involvement in thalassemia by conventional markers, such as blood urea nitrogen and serum creatinine, has remained unchanged [11]. Kidney injury in thalassemia increases with age and duration of blood transfusions [12]. In patients with B-thalassemia, little attention has been paid to the potential kidney damage, but recent studies indicate that the existence of various tubular and glomerular dysfunctions [13].

## Materials and Methods

The present study represents a case control study, conducted during the period from the September 2019 to the January 2020 at AL-karamah Teaching Hospital-Department of hereditary blood disorders. A total of 50 patients with thalassemia, 28 male their age range (17-27) year and 22 female their range (16-40) ear and 20 subjects as control (healthy group) (10 male+10 female) their age range (17-42) year and (17035) year respectively. All

individuals were having blood to measure serum liver enzyme tests such as Glutamate Oxaloacetate Transaminase (GOT), Glutamate Pyruvate Transaminase (GPT), Alkaline Phosphatase (ALP), Total Protein (T.P), Albumin (Alb) and reual function tests such as Urea, Uric acid and Creatinine 5 ml veuous bloods were obtained by using a disposable plastic syringe. The samples were centrifuge at 3000 rpm for 10 min to obtain serum samples. Part of clear serum was separated into sterile epindrof tube for measurement of GOT, GPT, ALP by enzymatic assay and total protein was determined by Biuret method, Albumin was determined by used chemical method. The separated serum was used to determine serum creatinine Jaffe Kinetic reaction [14]. Serum uric acid was determined by uricase method [15] and serum urea was determined by enzymatically method [16].

### Statistical analysis

The Statistical Analysis System-SAS (2012) program was used to detect the effect of differential factors on parameters studied. The T-test and the LSD test were used to compare the mean values of the parameters [17].

## Results and Discussion

As shown in **Table 1**, the mean values of GOT, GPT, AIP and albumin (AIb) in thalassemic patients were significantly higher ($P \leq 0.01$) than in the control group. The level of T.P was not significantly different between the patients and the healthy group, the mean value reached to 7.05 ± 0.08 g/dl in patients and it was reached to 10.09 ± 3.20 g/dl in healthy subjects.

The statistical results in **Table 2** show the effect of β-thalassemia disease on kidney function levels ($p \leq 0.01$). The findings suggest that the mean values of Urea, Uric acid and Creatinine were elevated in thalassemic patients to (42.75 ± 3.77, 9.27 ± 0.63, 1.51 ± 0.13) mg/dl respectively compared with healthy group (22.25 ± 1.41, 4.90 ± 0.23, 0.623 ± 0.04) mg/dl respectively.

As represented in **Table 3**, there was a significant rise in the mean value of GOT and urea levels in thalassemic patients in three duration of disease. The mean value of GOT reached to (42.25 ± 5.60, 63.42 ± 13.20 and 28.60 ± 0.51) mg/dl in (less 15, 15-25 and more than 25) years respectively while the mean value of Urea in three duration of disease were (43.37 ± 4.13, 30.57 ± 1.97, 56.8 ± 11.67) mg/dl. On the other hand, the mean values of (GPT, ALP, T.P, Alb, Uric acid and Creatinine) for the three durations of disease did not vary significantly.

In **Table 4** shows, there is no significant difference between male and female in the mean values of liver function and renal function levels in thalassemic patients.

The results illustrated, there is no effect of age on (GOT, GPT, ALP, T.P, Alb, uric acid and urea) concentrations in all β-thalassemic patients and there were no significant differences between them while there is effect of age on serum urea level, the mean value reached to (46.44 ± 5.17) mg/dl in (16-19) years and (31,72 ± 2.44) mg/dl in group in (20-24) years, while the mean value reached to (50.57 ± 9.13) mg/dl in (25-40) years ($P \leq 0.05$) **(Table 5)**.

Transfusions are the primary therapy for thalassemia but have significant cumulative risks. In **Table 6**, there were no effect of interval of blood transfusion on liver functions, Urea and Uric acid levels while there is effect of interval of blood transfusion on uric acid level, the mean value were reached to (10.44 ± 1.57, 12.33 ± 2.02, 7.90 ± 0.49) mg/dl in (14, 21, 30) day respectively ($P \leq 0.05$).

The purpose of this study was to evaluate the Liver function and renal function concentrations in thalassemic patients in Iraq. Via the actual mechanism, B- thalassemia is not clear that patients with beta-thalassemia major are vulnerable to metabolic problems with multiple organ dysfunctions, B-thalassemia is known to be linked to anemia and iron overload, organ failure is the most significant cause of iron deposition mortality and morbidity in patients with beta thalassemia. Our results revealed a significant increase in serum GOT and GPT levels in patients compared to controls, this result is agreement with Mansi, et al. [18], who reported the increased level of GOT and GPT in B-thalassemic patients. The increased in GOT and GPT levels indicate that patients with B-thalassemia are increased risk of heart and liver dysfunction [19]. Serum transaminases were elevated in (66%) of transfused patients with B-thalassemia major [20]. Hepatic damage secondary to hemosiderosis which lead to an increased serum GOT, GPT and they increase in both females and males [21]. Khaled, et al. [22], were found higher levels of Liver enzymes in patients treated by deferoxamine, but the difference was significant in serum GPT Level .The present study showed high levels of ALP, GOT, GPT in patients, these findings are in line with the work of Bashir, et al. [23]. As part of care, affected children require daily blood transfusion, excessive red cell transfusion contributes to iron overload and increased iron level deposited in different parts of the body such as heart, hepatic and kidney tissues [24]. Total protein is considered total protein is considered as the most abundant compounds in serum. Abnormal of T.P and Alb Levels are indicators of Liver malfunction [19]. Awadallah, et al. [25], were reported no association of T.P and Alb with B-thalassemia patients. Also renal dysfunction may occur in B-thalassemia asymptomatic patients and sometimes kidney injury happens before the manifestation of any other complications [26]. Renal dysfunction is a side effect of blood transfusion in patients suffering from B-thalassemia major [27]. The increasing level of urea and creatinine in thalassemic patients may be due to higher deposition of iron in their kidneys, shortened life span of red cells and excess iron that causes functional and physiological abnormalities in thalassemia patients in different organ systems [28]. Renal involvement is a rare complication of beta thalassemia. Both tubular and glomerular dysfunction might occur in these patients [29]. Jalali, et al. [12], study demonstrated that renal dysfunction in thalassemia major patients can be increase by acceleration of age, increased frequency of blood transfusion and hyper calciuria. Serum level of creatinine was higher in patients in comparison to control, this was in agreement with other studies, they reported impairment in classical kidney functions (Creatinine, Albumin and Glomerular filtration rate) [18,30]. Helin, et al. [31], found a positive correlation between age and serum creatinine in patients with B-thalassemia major.

| Parameters | Control (n=20) | Patients (n=40) | P value | T-Test |
|---|---|---|---|---|
| GOT (U/L) | 22.8 ± 1.57 | 44.47 ± 4.75 | ≤ 0.01 | 13.06** |
| GPT (U/L) | 20.0 ± 1.05 | 39.52 ± 3.26 | ≤ 0.01 | 8.94** |
| ALP (U/L) | 108.70 ± 4.28 | 164.56 ± 14.71 | ≤ 0.01 | 40.24** |
| T.P (g/dl) | 10.09 ± 3.20 | 7.05 ± 0.08 | NS | 4.76 |
| Alb (g/dl) | 4.11 ± 0.09 | 4.68 ± 0.01 | ≤ 0.01 | 0.315** |
| Results are expressed as Mean+SE (Standard Error) | | | | |

**Table 1:** Mean values of serum GOT, GPT, ALP, T.P and Alb in -thalassemic patients.

| Parameters | Control (n=20) | Patients (n=40) | P value | T-Test |
|---|---|---|---|---|
| Urea (mg/dl) | 22.25 ± 1.41 | 42.73 ± 3.37 | ≤ 0.01 | 9.35** |
| Uric acid (mg/dl) | 4.90 ± 0.23 | 9.27 ± 0.63 | ≤ 0.01 | 1.75** |
| Creatinine (mg/dl) | 0.623 ± 0.04 | 1.51 ± 0.13 | ≤ 0.01 | 0.362** |
| Results are expressed as Mean ± SE (Standard Error) | | | | |

**Table 2:** Comparison of parameters between thalassemic patients and control group.

| Parameters | Duration of disease (year) | | | LSD value |
|---|---|---|---|---|
| | Less than 15 | 15-25 | More than 25 | |
| GOT (U/L) | 42.25 ± 5.60 | 63.42 ± 13.20 | 28.60 ± 0.51 | 30.03* |
| GPT(U/L) | 36.0 ± 3.84 | 46.85 ± 9.18 | 39.0 ± 7.25 | 21.47 NS |
| ALP(U/L) | 183.87 ± 19.57 | 128.71 ± 23.73 | 122.0 ± 22.97 | 87.43 NS |
| T.P(g/dl) | 7.04 ± 0.01 | 7.12 ± 0.15 | 7.04 ± 0.24 | 0-5222 NS |
| Alb(g/dl) | 4.75 ± 0.14 | 4.54 ± 0.12 | 4.54 ± 0.16 | 0.651 NS |
| Urea(mg/dl) | 43.37 ± 4.13 | 30.57 ± 1.97 | 56.80 ± 11.67 | 20.75* |
| Uric acid (mg/dl) | 9.00 ± 0.75 | 9.71 ± 1.54 | 10.00 ± 2.16 | 3.68 NS |
| Creatinine (mg/dl) | 1.61 ± 0.15 | 1.24 ± 0.26 | 1.40 ± 0.47 | 0.825 NS |
| P ≤ 0.05)*, NS: Non-Significant | | | | |

**Table 3:** Effect of duration of disease on liver function and renal function levels in thalassemic patients.

| Parameters | Sex | T-Test | 42.25 ± 5.60 |
|---|---|---|---|
| | Male | Female | |
| GOT (U/L) | 50.5 ± 8.45 | 40.05 ± 25 | 19.89 NS |
| GPT (U/L) | 37.50 ± 4.31 | 39.35 ± 4.84 | 12.44 NS |
| ALP (U/L) | 194.50 ± 27.36 | 140.60 ± 13.29 | 57.92NS |
| T.P (g/dl) | 7.16 ± 0.13 | 6.97± 0.09 | 0.345 NS |
| Alb (g/dl) | 4.51 ± 0.06 | 4.81 ± 0.17 | 0.431 NS |
| Urea (mg/dl) | 41.75 ± 5.67 | 43.55 ± 4.16 | 13.74 NS |
| Uric acid (mg/dl) | 9.93 ± 0.96 | 8.75 ± 0.85 | 2.44 NS |
| Creatinine (mg/dl) | 1.58 ± 0.19 | 1.45 ± 0.18 | 0.547 NS |
| NS: Non Significant | | | |

**Table 4:** Effect of sex on parameters study.

| Parameters | Age groups(year) | | | LSD value |
|---|---|---|---|---|
| | 16-19 year | 20-24 year | 25-40 year | |
| GOT (U/L) | 40.44 ± 5.87 | 52.18 ± 10.27 | 42.71 ± 11.35 | 26.04 NS |
| GPT (U/L) | 36.61 ± 4.99 | 37.54 ± 4.01 | 45.00 ± 9.26 | 18.62 NS |
| ALP (U/L) | 189.33 ± 23.41 | 154.72 ± 24.02 | 116.28 ± 17.62 | 73.84 NS |
| T. Protein (g/dl) | 7.03 ± 0.12 | 7.14 ± 0.11 | 6.98 ± 0.17 | 0.452 Ns |
| Alb (g/dl) | 4.68 ± 0.08 | 4.80 ± 0.30 | 4.47 ± 0.14 | 0.564 NS |
| Urea (mg/dl) | 46.44 ± 5.17 | 31.72 ± 2.44 | 50.57 ± 9.13 | 18.003* |
| Uric acid (mg/dl) | 8.33 ± 0.75 | 10.09 ± 1.28 | 10.43 ± 1.70 | 3.19 NS |
| Creatinine (mg/dl) | 1.47 ± 0.17 | 1.76 ± 0.24 | 1.21 ± 0.34 | 0.716 NS |
| (P ≤ 0.05) *, NS: Non-Significant | | | | |

**Table 5:** Study the effect of age on Liver and renal function Levels in B-thalassemic patients.

| Parameters | Interval of blood transfusion | | | |
|---|---|---|---|---|
| | 14 day | 21 day | 30 day | LSD value |
| GOT (U/L) | 51.33 ± 12.24 | 43.67 ± 14.29 | 41.76 ± 5.12 | 27.62 NS |
| GPT (U/L) | 37.67 ± 7.27 | 40.50 ± 5.24 | 38.33 ± 4.56 | 19.75 NS |
| T. Protein (g/dl) | 7.07 ± 0.13 | 7.03 ± 0.16 | 7.05 ± 0.12 | 0.48 NS |
| Alb (g/dl) | 4.73 ± 0.37 | 4.75 ± 0.13 | 4.63 ± 0.08 | 0.599 NS |
| Urea (mg/dl) | 40.78 ± 6.09 | 40.67 ± 9.08 | 44.19 ± 4.65 | 19.09 NS |
| Uric acid (mg/dl) | 10.44 ± 1.57 | 12.33 ± 2.02 | 7.90 ± 0.49 | 3.39* |
| Creatinine (mg/dl) | 1.73 ± 0.28 | 1.58 ± 0.34 | 1.39 ± 0.16 | 0.759 NS |
| (P ≤ 0.05)* , NS: Non Significant | | | | |

**Table 6:** Effect of interval of blood transfusion on parameters study.

## Conclusion

This research aimed to evaluate liver and renal function in patients with β- thalassemia. The increased in AST and AlP levels indicate that patients with β- thalassemia are in increased risk of heart and liver dysfunction and renal dysfunctions are common findings in B-thalassemia patients and no effect of sex on various parameters.

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