Assessment of hematological and immune parameters in patients with Thalassemia in Thi-Qar Province

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Assessment of hematological and immune parameters in patients with Thalassemia in Thi-Qar Province

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ABSTRACT

Background. Hemolytic anemia is caused by an imbalance in the production of hemoglobin chains, which results in thalassemia, a genetic disorder.

Objective: The purpose of this study was to assess the hematological, biochemical, and immunological parameters in beta-thalassemia patients in the province of Thi-Qar.

Methods. Thalassemia and Blood Diseases Center at Thi-Qar Province during the period from September 2023 to December 2023. The study included fifty patients, 38 matched healthy controls, and 41 patients with beta thalassemia major and 9 patients with beta thalassemia intermedia, ages ranging from 2 to 15 years.

Results. The present study revealed that thalassemia patients had significantly higher levels of immune parameters such as IL-23, and TGF-β1, while the level of INF-γ increased non-significantly in thalassemia patients compared to the control group.

Conclusions. Beta thalassemia causes anemia and may cause organ damage due to its diverse effects on hematological, biochemical and immunological parameters.

Keywords: β-thalassemia, TGF-β1, IL-23, Transferrin, INF-γ, hepatic enzymes, urea and creatinine

INTRODUCTION

Thalassemia is a genetic blood disease that is passed down from parents to their offspring, it affects how hemoglobin is formed in the children's blood, which results in severe anemia [1]. When Thomas Cooley described the syndrome of anemia, splenomegaly, and bone abnormalities among Italian offspring in 1925, thalassemia was first identified clinically [2]. Due to the disease's widespread prevalence in Mediterranean regions, it is also known as Mediterranean anemia. Point mutations in the globin gene are the primary cause of this disease, which is one of the most common disorders worldwide. About 1.67% of the population has thalassemia, which is spread throughout the Mediterranean coast, the Middle East, and Southeast Asia [3]. Thalassemia affects both males and females [4]. This condition has emerged as one of the most common genetic illnesses, greatly impairing public health in numerous parts of the globe [5]. Hemoglobin, the protein in red blood cells that carries oxygen, is either absent or produced in very small amounts in this condition. According to studies, the hemoglobin molecule is made up of two alpha and beta chains. The cause of this illness is a reduction in or absence of these chains' synthesis [6]. Depending on the type of globin chain that is impacted, thalassemia is classified into two types: beta-thalassemia and alpha-thalassemia [7,8]. People with thalassemia rely heavily on blood transfusions to prolong their lives. However, receiving blood transfusions repeatedly can have serious and varied side effects including hepatotoxicity from excessive iron deposition. Iron is stored as ferritin, which is highly harmful and can cause an imbalance in the organs' functions [9]. The thalassemia pathogenic factors include hemolysis, ineffective erythropoiesis, elevated iron absorption, and defects in erythrocytes and precursors of erythroid resulting from the first two factors. These defects are eliminated by the phagocytosis of

monocytes and macrophages, which undergo hyperplasia and hyperactivity, leading to defects in the phagocytosis of microorganisms [10]. Patients with β-thalassemia have various immune system disorders, such as cell-mediated immunity [11]. and functional, quantitative, and other immune system components [12]. These disorders involve an increase in immunoglobulin's, a weakened complement system, a decline in granulocyte phagocytosis, and opsonization [13].

MATERIAL AND METHODS

A total of 50 patients with beta-thalassemia ages ranging from 2-15 years, both genders attended to Thalassemia and Blood Disease Center in Thi-Qar Province in Iraq. The study also includes (38) a control group in Thi-Qar Province for the period between September 2023 until December 2023.

The patient provided 5 milliliters of venous blood, which was collected and stored in gel and EDTA. To make a complete blood picture, 1 milliliter of blood was combined with EDTA, the analyzer (Mindary/ Germany) was totally automated and used to estimate the hematological parameters. And the remaining 4 milliliter of the blood had been moved to a gel tube, which was centrifuged at 3000 rpm for 5 min to extract serum and complications have been field in an Eppendrof tube to prevent mistakes, make up for them, and keep the tube at -20°C until immunological parameters were measured. Biochemical parameters were carried out using a full-automatic clinical chemistry analyzer (Dirui, CS-T180). Immunological parameters usage in Sandwich-ELISA.

Statistical Analysis

Statistical analysis was done using SPSS version 26 (Statistical Package of Social Science), ANOVA test was used to determine significant differences at p. value <0.05 and <0.01.

RESULTS

The present results showed that the thalassemia patients' Hb level, HCT percentage, RBC count, neutrophil percentage and MCV were all significantly decreased in them than in the control group, while thalassemia patients' WBC lymphocyte percentage, MCHC, and PLT count elevated significantly compared to the control group, also, noted the MCH not scored significant difference at p< 0.05 as in Table 1.

Table 1: Evaluation of hematological parameters in patients with thalassemia and comparison with the control group

Hematological Parameters	Patients No. 50	Control No. 38	p. value
	Mean ± SD		
HCT	21.5 ± 3.70	38.2 ± 4.76	< 0.001[s]
RBC	2.82 ± 0.50	4.62 ± 0.68	< 0.001[s]
WBC	11.2 ± 3.04	9.23 ± 2.16	< 0.001[s]

NUE	47.2 ± 9.21	68.4 ± 17.3	< 0.001[s]
LYM	38.8 ± 8.48	27.6 ± 8.20	< 0.001[s]
MCV	76.5 ± 6.37	83.0 ± 7.78	< 0.001[s]
MCH	27.0 ± 2.10	26.5 ± 2.93	0.354[ns]
MCHC	35.4 ± 1.65	31.9 ± 1.01	< 0.001[s]
PLT	335.4 ± 108.5	261.8 ± 67.70	< 0.001[s]

*non-significant (ns), significant (s)

The present results showed in Table 2 that the level of IL-23 and TGF-β1 increased significantly in thalassemia patients than in the control group, while the level of INF-γ increased non-significantly in thalassemia patients than in the control group.

Table 2: Assessment of immune parameters in patients with thalassemia and comparison with the control group

Immune Parameters	Patients No. 50	Control No. 38	p. value
	Mean ± SD		
IL-23	26.5 ± 7.60	21.7 ± 6.60	0.002 [s]
TGF-B_1	15.6 ± 4.65	9.44 ± 2.82	< 0.001[s]
INF-γ	22.0 ± 6.45	20.2 ± 6.18	0.182 [ns]

*non-significant (ns), significant (s)

The current findings demonstrated as shown in Table 3, the levels of the hepatic enzymes ALT and AST were significantly higher in thalassemia patients compared to the control group, but the level of ALP was non-significantly higher in thalassemia patients compared to the control group.

Table 3: Evaluation of the liver enzyme parameters in individuals with thalassemia and comparison with the control group

Parameters	Patients No. 50	Control No. 38	p. value
	Mean ± SD		
ALT	30.5 ± 9.47	16.2 ± 4.43	< 0.001[s]
AST	42.4 ± 10.4	35.4 ± 10.4	< 0.001[s]
ALP	144.4 ± 38.6	141.4 ± 40.3	0.772 [ns]

*non-significant (ns), significant (s)

The present results showed that the level of blood urea, serum creatinine, transferrin and

ferritin were increased significantly in thalassemia patients than in the control group as in Table 4.

Table 4: Evaluation of RFT, ferritin and transferrin in thalassemia patients and comparison with the control group

Parameters	Patients No. 50	Control No. 38	p. value
	Mean ± SD		
B. urea	31.5 ± 7.23	22.6 ± 6.63	< 0.001[s]
S. creatinine	1.17 ± 0.09	0.58 ± 0.19	< 0.001[s]
Ferritin	2160.0 ± 659.5	38.56 ± 11.38	< 0.001[s]
Transferrin	4.88 ± 1.59	2.87 ± 0.81	< 0.001[s]

*non-significant (ns), significant (s)

DISCUSSION

The results of Table (1) showed a significant decrease at a p<0.05 in the Hb concentration, HCT percentage, average cell volume, and number of red blood cells in thalassemia patients compared with the control group. The reason is due to the decrease in beta globin chains in the hemoglobin molecules, as red blood cells are characterized by the presence of Excess of unbound globin protein in cell membranes and susceptible to phagocytic cells in the bone marrow when they are in structural changes of hemoglobin molecules. According to Gaaib and Ali [14], these cells can recognize and harm abnormal cells, which in turn stimulates the process of erythropoiesis, leading to the comprehensive destruction of red blood cells. These results are consistent with previous studies conducted by Bazvand *et al*. [15]; Kareem *et al*. [16], which showed that macrophages in the spleen work to destroy senescent and abnormal cells, giving the abnormal red blood cells a short lifespan and a tendency to self-degradation. The low percentage of HCT can be explained by the fact that HCT is mainly affected by the size and number of RBCs, hemodilution and hemoconcentration. Thalassemia patients had elevated platelet counts, which may have been caused by splenectomy in some cases [17]. Depending on this study's conclusions it was revealed that patients with βT exhibited an elevated white blood cell count compared to the control group. This increase was attributed to heightened levels of cytokines, like interleukin-3 (IL-3) which stimulate precursor cells in the bone marrow to develop into blood cells [18]. The level of IL-3 increased significantly in children with homozygous βT patients, which is consistent with earlier research by [16,19,20]. Furthermore, compared to the control group, the mean neutrophil value for the patients significantly decreased. Which may be caused by humeral and cellular dysfunction caused by iron overload as well as impaired neutrophil chemotactic activity from transfusion overload [21]. It is thought that interleukin 23 (IL-23) linked to the disease pathophysiology, especially the inflammatory response, is increased in children who have thalassemia. According to Korta *et al*. [22], the pro-inflammatory cytokine is thought that it contributes to the patients' increased immunological activity. The activation of the system triggers the

body's response potentially causing a drop in red blood cell production and leading to bone marrow failure. It is believed that IL-23 is found in levels in children with thalassemia and this may be associated with disease's pathogenesis particularly its inflammatory response. This pro-inflammatory cytokine is thought to contribute to the patients' heightened immune responses. Patients with thalassemia have elevated transferrin levels for two main reasons: first, erythropoiesis is increased red blood cells with thalassemia have a shorter lifespan which causes them to be destroyed too soon. Inducing the synthesis of transferrin results in elevated levels of the protein because it is necessary for the transfer of iron during erythropoiesis. In βT where beta-globin chain synthesis is somewhat reduced [23]. Patients with thalassemia often experience secondary iron overload because of frequent blood transfusions. Elevated IFN-γ levels in children with thalassemia are associated with the disease's immunological pathogenesis, specifically, T cell-mediated immune responses. According to Abuga *et al*. [24], the cytokine IFN-γ has a role in regulating the immune response and has been related to several autoimmune and inflammatory diseases [24]. Children diagnosed with thalassemia are believed to have TGF-β1 levels because of changes in the bone marrow that lead to fibrosis. According to Al-Hindy *et al*. [25], TGF-β1 a cytokine recognized for regulating responses, cell differentiation and growth is known for its effectiveness. The rise in levels could be linked to the activity of osteoblasts in thalassemia and consequent restructuring of bone. Elevated production of TGF-β1 may stem from prolonged inflammation and inadequate erythropoiesis in the bone marrow eventually causing changes and sclerosis in the marrow [26]. Increased ferritin levels and elevated liver enzymes levels (ALT, AST, and ALP) are linked; however, this connection relies on the iron overload that thalassemia patients experience due to blood transfusions [27,28]. Based on the findings of the study it was observed that patients with β thalassemia had elevated levels of serum ferritin due to blood transfusions. Since ferritin plays a role in managing iron levels the commonly employed method to assess iron overload in β thalassemia patients is by measuring their serum ferritin levels. The increased serum ferritin in the current study agreed with previous studies obtained by [29,30]. Renal dysfunction can develop in persons with βT [31]. Among individuals with βT, renal dysfunction is a side effect of blood transfusion [32]. Thalassemia individuals may have elevated iron deposition in their kidneys and reduced red cell lifespans, all contributing factors to their elevated urea and creatinine levels [33]. Renal function is commonly evaluated by measuring levels of creatinine and plasma urea [34]. Patients' serum creatinine levels were greater than those of the control groups, which agreed with findings from prior studies that showed impairment of three classical kidney functions (albumin, creatinine, and glomerular filtration rate) [35].

CONCLUSION

According to these results, thalassemia has a complex effect on immunological, hematological, and renal function, requiring multimodal approaches to care.

Conflict of interesting

None

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