Original Article

Detection of enzymatic levels in patients with thalassemia in Dewanyah province

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Abstract

This study deals with the knowledge of the relationship and the negative impact of thalassemia disease on liver function. The study included 60 children with thalassemia in the age group (2-14) years, and the study included 20 children as a control group and in the same age group. The study included measuring liver function represented by measuring the activity of liver enzymes. The current study aimed to find the immune differences for people with thalassemia anemia in Al-Diwaniyah Governorate, where samples were collected from pathological analysis laboratories in Al-Diwaniyah hospitals. They were randomly selected with gender and age proportional to the group of patients, and patient groups and control groups were distributed as follows (31 males and 29 females) for patients and (10 males 10 females) for the control group. The current study examined the differences in the effect of sex on the average concentrations of components in the blood serum at a probability level of 5% in the serum of thalassemia patients. Liver enzymes were included in the study of GOT enzyme and were for ages 2-5 years (25.6±17.6), age 6-9 years (25.9±6.93), and age 10-14 years (28.5±8.61) without significant difference, and GPT enzyme also did not appear. Any significant difference between the age groups was determined for ages 2-5 years (14.2±21), ages 6-9 years (17.25±8.46), and ages 10-14 years (25.52±3.76). In the same study context, it was found that the glucose concentration was not significant for age groups, as it was 2-5 years old (123±5.94), 6-9 years old (120.6±4.43), and 10-14 years old (122.9±5.7), although it was significantly higher with the healthy control group.

Keywords: Thalassemia, Liver Enzymes, IL-6, Ferritin.

Introduction

Genetic disorders of human hemoglobin that fall within the gene disorder the single disorder gene is a common disorder affecting about 5% of the world's population who carries one or more mutations in the genes responsible for the synthesis of hemoglobin in the body (1). The most important hereditary blood disorders that affect the human body, because of two different types of protein, the alpha globin and beta globin, which bind with the hem pigment to form the complete molecule of hemoglobin, and any genetic defect that hinders the production of these proteins in the body sufficiently for one or both proteins will lead to The blood cells become unable to transport sufficient oxygen, resulting in anemia that occurs (2)Life is free and continues early childhood in. 2004) The reason for the occurrence of thalassemia is due to the reduction of its synthesis of one or more of the polypeptide chains of blood globin, which represents abnormal quantitative changes in the manufacture of hemoglobin, so it differs from hemoglobinopathies (which represent specific disorders). There can be several types of thalassemia and youngsters (alpha-thalassemia and beta-thalassemia, and among the most clinically important and common types), and by studying the distribution of thalassemia in the world It appears that in addition to the Mediterranean cities in which cases of thalassemia were recorded in the beginning, and the disease was named after her, It is noted that the disease is widespread in most parts of the world, including our Arab homeland, in addition to the continuous migration of some human societies from one region to another in the world, which helps in the spread of the disease (3). Governorates, where the most numbers were recorded in Baghdad, Basra, and Mosul, and the number of injuries was recorded in other governorates such as Najaf, Karbala, Diwaniyah, and others. And that these numbers are increasing annually

until the number in 2009(4) reached about 12000 patients, due to several different factors, the most important of which is the prevalence of consanguineous marriage, lack of health awareness, in addition to the lack of medical care and the provision of treatment supplies such as ex jade medicine, which is an alternative (5) pill for painful injections. Al-Dispferal, especially since most of the patients are from poor families who were unable to bear the costs of treatment (6).

Materials and working methods

1- The CBC Test

It consists of three main systems, a hydraulic system, an electrical system, and a pneumatic pressure system. As for the hydraulic system, a blood sample is taken, mixed with some chemicals, and analyzed into their basic components of red and white blood cells and platelets for the counting process. As for the electrical system, it analyzes and calculates the resulting signals from the counting process. In addition, there is a pneumatic pressure system, as there is an air pump with a constant pressure rate. The result of this test is printed from a printer containing tables and graphs of the results.

2- Iron Test

Where blood samples were taken for children with thalassemia, for which a CBC test was performed Iron analyzer for children with thalassemia anemia in the ferritin test, the concentration of ferritin in the serum is checked, and ferritin is the largest iron store in the body. The cause of the anemia can be diagnosed. A low level of ferritin generally indicates iron loss due to bleeding or due to low iron consumption

3- Liver Enzymes Test

Which is represented as follows, (Got. Got. Glue)) Then the samples on which the CBC and iron tests and the analysis of liver enzymes were conducted were taken to the Centrifuged device for the purpose of separating the samples and taking the serum in order to use the serum resulting from the separation of samples in the ELISA device using Inter cyclin 6 Liver enzymes test It is a test for the level of one of the liver enzymes called aspartate aminotransferase (AST). It is a protein that helps with protein metabolism. This enzyme is found in various internal organs of the body (particularly the liver and heart). An injury to one of these organs causes it to leak into the blood and raise its level

Statistical analysis

Data were analyzed using the statistical package for social science (SPSS). The computer software package SPSS 15.0 was used in the analysis. For quantitative variables, mean, standard deviation, minimum, and maximum (as measures of variability) were presented. Frequency and percentages were presented for the qualitative variable. ANOVA, Independent T, Mann-Whit, and Kruskal Wallis tests were used to estimate differences in quantitative variables. Chi-square and there were used to estimate differences in qualitative variables. Spearman’s rank correlation test was used to determine the relationship between different numerical variables. For all tests, probability values (P) of less than 0.05 were regarded as statistically significant.

Results

Thalassemia is one of the diseases that lead to a genetic blood disorder that leads to a lower percentage of hemoglobin in the body than the normal rate because the hemoglobin in red blood cells is responsible for carrying oxygen. The severity of thalassemia varies between patients to mild, moderate, and severe, and as a result, its impact on patients and how to deal with it in terms of treatment and food varies. Therefore, during this study, several factors were identified that were studied to know their impact on patients, including the comprehensive blood picture, oxidation indicators, and the level of Interleukin-6 (Interleukin-6).) and the patients' of gender and age on hematological parameters and their comparison with the control group. During this study, a hundred samples were collected from donors, and they were divided into two groups, fifty patients

with thalassemia and fifty control groups. Healthy people who do not show any side effects of the disease or other.

Count (CBC) Test

The current study included the examination of 50 blood samples for thalassemia compared to the examination of 50 blood samples from the healthy group. The current results showed at the probability level (0.05%) that the average white blood cell count did not show any significant difference on the probability ratio P>0.05, and the average white blood cell count was P>0.05. White blood in thalassemia patients (7.78 ± 2.67) compared to the control group, which was (7.06 ± 1.36), although it was high compared to the control group, it did not show any significant difference and this study agrees with other studies that showed a clear increase in blood cells (7).(8).It was noted that the rate of red blood cells in the group of thalassemia patients was (3.17 ± 0.44) and that of the healthy group was (4.56 ± 0.54), and a significant difference was found in the average number of red blood cells in the patients, and this was confirmed by other studies (9)(10)It was noted that the rate of red blood cells in the group of thalassemia patients was (3.17 ± 0.44) and that of the healthy group was (4.56 ± 0.54), and a significant difference was found in the average number of red blood cells in the patients, and this was confirmed by other studies (11) Where it was found that there is a significant and significant decrease in the number of red blood cells, some of which are significantly distorted, meaning that these cells cannot perform their functional work and transfer oxygen appropriately and according to the severity of the disease, whether it is severe, moderate or low in symptoms. In addition, it was found that there was a significant increase in blood platelets in the group of thalassemia patients (384.6±157.8) and significantly compared with the healthy control group (288.2±71.1) in the study. This is in agreement with the studies of researchers that have shown that thalassemia patients usually have continuous clotting in their blood. Therefore, the deficiency that occurs as a result of this clot must be filled and compensated by continuous differentiation of bone cells (12). Also in this study, the average hemoglobin was determined in thalassemia patients (7.91 ± 1.05) and it was significantly lower than the healthy control group (13.83 ± 1.11) and this decrease is normal due to the decrease in the number of red blood cells in thalassemia patients, which was confirmed by other studies (13) due to the fact that hemoglobin in the blood is one of the main components of red blood cells, which suffers from a significant deficiency due to thalassemia, which in turn leads to It is also lacking. As shown in Table No. (1) below. Through the foregoing, it was found that the current study agrees with many studies on the effect of the disease on the blood picture of thalassemia patients compared to the healthy control group, which confirms a significant decrease in red blood cells, platelets and hemoglobin, but it has been proven that there is a clear rise in white blood cells in patients. This may be due to the exposure of Thalassemia patients to secondary diseases, which may stimulate the production of a greater number of immune cells to confront the seriousness of diseases. Table (1) This table shows the total number and average of the major blood components.

Hgb	platelets	RBC	WBC	the group
13.83±1.11	288.2±71.1	4.56±0.54	7.06±1.36	the control
7.91±1.05	384.6±157.8	3.17±0.44	7.78±2.67	The patients
0*	0.012*	0*	0.175	p. value

***There are significant differences at the 5% probability level**

Results the ferritin test results in the blood serum of thalassemia patients and the control Ferritin is a general protein secreted inside cells and stores iron and releases it in a regular manner because it is the main protein for storing iron inside cells, which keeps iron in a soluble and non-toxic form, it acts as a buffer against iron deficiency and iron overload, ferritin is found in most tissues as a cytosolic protein, but amounts of Small of it is excreted in the serum where it acts as an iron transporter (14).In addition, plasma ferritin is also an indirect indicator of the total amount of iron stored in the body; Therefore, during this study, the amounts of ferritin in the serum of thalassemia patients were determined compared with the control group. The results showed that the average concentration of ferritin in thalassemia patients was very high (2894.7 ± 2578) with a clear significant difference compared to the healthy control group (1292.8 ± 1567) which agrees is remarkably consistent with the lack of red blood cells in thalassemia patients due to disturbances during their development

in the bone marrow from the mother stem cells producing them. As can be seen in Table (2) below. It is worth noting that these results were recorded by many researchers (15) (16) who found that there A significant and significant increase in the concentration of ferritin in thalassemia patients, and this may be due to the breakdown of many red blood cells due to the presence of some incompletely differentiated cells during the stages of their formation, which leads to the release of large amounts of soluble iron in the form of ferritin in the patient stints. thalassemia Table No. (2) shows the average ferritin concentration in Thalassemia patients compared to the healthy control.

Ferritin	the group
1292.8±1567	the control
2894.7±2578	The patients
0.004*	p. value

***There are significant differences at the 5% probability level.**

The results of the examination of oxidation indicators in the blood serum of thalassemia patients and the study of the control included the determination of oxidative stress in thalassemia patients in comparison with the control group at a probability ratio of P>0.05. It included the enzyme (GOT) aspartate transaminase (AST) or aspartate aminotransferase, also (Asp AT/ASAT/AAT) or (serum) glutamic. oxaloacetic transaminase(SGOT) It an important enzyme in amino acid metabolism and is secreted in various places in the liver, heart, skeletal muscles, kidneys, brain, red blood, cells, and The bile sac and its examination is very important to determine the vitality of the liver in the blood serum (17). Therefore, the level of this enzyme was studied in Thalassemia patients, where it was observed that it was significantly elevated. Significant and significant (27.37 ± 14.08) in patients compared to the healthy control group (13.85 ± 3.45) and this study agreed with other studies (18) It was confirmed that the level of this enzyme was significantly increased in the serum of thalassemia patients. As in Table No. (3). Also, the average concentration of serum glutamic pyruvic transaminase (GPT) or alanine transaminase (ALT) was determined in the serum of thalassemia patients (21.62 ± 17.1). This is what other researchers observed, as they confirmed the results of our current study and that thalassemia has a clear effect in raising the concentration of this enzyme in patients' blood serum (19) The current study also showed that the average concentration of glucose (Glue) in the serum of thalassemia patients is very high (122.2 ± 5.47) compared to the healthy control group (76.8 ± 6.57). In the identification of thalassemia and the possibility of Very high (122.2 ± 5.47) compared to the healthy control group (76.8 ± 6, these results confirm that the clear significant increase of these enzymes in the blood serum of thalassemia patients is a clear indicator in determining thalassemia disease and the possibility of diagnosing it for those who suffer from high levels of these enzymes. As in Table No. (3). There are many researchers who have proven these results from our study (20), where they found that thalassemia causes a process of glucose intolerance that occurs as a result of a lack of insulin production in thalassemia patients, which regulates Levels of glucose in the blood, which reduces glucose storage in the muscles, liver and adipose tissue, and thus leads to a higher concentration patient's serum.

Table (3)

Glue	GPT	GOT	the group
76.8±6.57	15.7±4.16	13.85±3.45	the control
122.2±5.47	21.62±17.1	27.37±14.08	The patients
0*	0.044*	0*	P value

* There are significant differences at the 5% probability level.

34- Results of testing the level of interleukin-6 (IL-6) in the blood serum of thalassemia patients and controlsInterleukin-6 (IL-6) is one of the interleukins that are highly effective before any inflammatory or anti-inflammatory process, so its concentration varies according to the pathological condition. Significantly high (112.6 ± 29.2) in the g of thalassemia patients compared with the concentration of interleukin-6 in the healthy

control group (41.8 ± 15.7), which showed a low concentration, as in table (4) below. Interleukin IL-6 is one of the immune modulators that respond before inflammation and is considered an anti-inflammatory, and it was found to be significantly elevated in other studies that agreed with our study, and it was very high (21) in thalassemia history and this is an indication of its elevation in thalassemia patients. Table (4) shows the rate of interleukin-6 (IL-6) in the blood serum of thalassemia patients and control.

IL-6	the group
41.8±15.7	the control
112.6±29.2	The patients
0*	P value

* There are significant differences at the 5% probability level.

35- Studying the effect of sex on the blood picture of thalassemia patients and healthy controls. Although many studies have confirmed that the male gender is more susceptible to thalassemia compared to the female gender, the differences between the sexes at the level of studying the blood picture in terms of components are almost close and not large (22).Therefore, the current study dealt with the differences in the effect of sex on the average concentrations of components in the blood serum at a probability level of 5% in the serum of thalassemia patients, and the results did not show any significant difference between the parameters that were measured in comparison between males and females, except for hemoglobin, which was high with a significant difference in males (8.54±0.89) compared to females (7.47±1.04), possibly due to the menstrual cycle In females, during which females lose blood regularly, which is absent in males. As in Table (5).It was also noted that most of the criteria included in this study were high in males compared to females, but all of them did not show any significant difference, as the current results showed that the white blood cells in males were (7.92 ± 2.88) and close to the rate of blood cells in females, which was At a rate of (7.62 ± 2.47), while the rate of red blood cells in males was (3.21 ± 0.42) and in females, it was at a rate of (3.13 ± 0.47), and it was also noted that there was a significant increase in the rate of ferritin concentration (Ferritin). It was also noted that there was a significant increase in the mean ferritin concentration in the blood of females (3079.8 ± 3111.1) compared to the serum of males (2743.3 ± 811.2), while the platelets in males were at a rate of (422.7 ± 174.9) and in females, they were at a rate of (422.7 ± 174.9) (338.05 ± 123.1) and these results are somewhat in agreement with other studies, which showed a clear significant difference between females and males, where it was found that the number of white blood cells, red blood cells, hemoglobin, and ferritin were high with a significant difference, but our current study did not show a significant difference (23)Whatever the case, the platelet count was elevated in males in Thalassemia patients compared to females, and this study did not agree with other studies that showed an increase in platelets in females compared to males. , (24) There are other studies that did not identify any significant differences between the sexes in the size of platelets for thalassemia patients(25). A s for the average concentration of Glutamic-oxaloacetic transaminase (GOT) in males, it was higher than females at an average of (28.18 ± 18.33) compared to the serum of females with a concentration of (26.38 ± 6.15), in addition, it was found that the mean concentration of alanine aminotransferase (GPT) was slightly higher in males with an average of (22.72 ± 21.09) compared to its concentration in the serum of females (20.27 ± 10.8), however, the current study revealed that the increase in the level of the two enzymes between the sexes was with a non-significant difference in this, and this is what was found by many studies in this regard, which confirmed that the change did not There is a significant difference with the effect of gender (26) and that the rise in these two enzymes is due to Thalassemia disease and there is no effect of sex on their concentration in the blood serum of patients Also, the level of glucose concentration was measured at a rate of (123.04 ± 4.55) slightly high compared to its average concentration in the blood serum of females (121.2 ± 6.42), but no significant difference was shown and this study agreed with other studies that did not show any significant differences on the basis of sex Among patients despite the increase in glucose in the serum of thalassemia patients compared with healthy controls (27).In addition to the above, the level of the IL-6 immunoglobulin concentration level was determined in the blood of males, which was slightly elevated at a rate of (115.4 ± 28.05) compared to the average of its concentration in females at an average of (109.2 ± 31.06) without any significant difference between them. There are studies that showed that the immune system IL-6 is significantly elevated in the serum of patients with thalassemia with a clear significant difference from the

serum of healthy people, but there is no significant difference between the serum of patients with thalassemia in males and females, and this is what was revealed by our current study, which confirmed these studies and the findings (28).

Table No. (5) shows the level of study indicators by gender in patients

P Values	sex		pointer
	female	male	
0.729	7.62±2.47	7.92±2.88	WBC
0.591	3.13±0.47	3.21±0.42	RBC
0.092	338.05±123.1	422.7±174.9	platelets
0.001*	7.47±1.04	8.54±0.89	Hgb
0.687	3079.8±3111.1	2743.3±811.2	Ferritin
0.694	26.38±6.15	28.18±18.33	**GOT**
0.658	20.27±10.8	22.72±21.09	**GPT**
0.316	121.2±6.42	123.04±4.55	**Glue**
0.512	109.2±31.06	115.4±28.05	**IL-6**

***There are significant differences at the 5% probability level.**

36- Studying the effect of age on the blood picture in thalassemia patients and healthy controls. During this study, the same previous parameters were studied in the blood serum of thalassemia patients at different ages. The study included ages according to the following age periods, namely, the period 2-5 years, the period 6-9 years, and the period 10-14 years. The results for the different age periods of the blood serum of thalassemia patients showed that there is a difference in the concentrations among them, but there is no significant difference between them as shown in Table (6). Where it was found that the average concentration of white blood cells in the serum of Thalassemia patients was for the age of 2-5 years (10.16 ± 2.6), the age of 6-9 years (7.79 ± 1.98) and the age of 10-14 years (7.26 ± 3.63), meaning that it is close and there is no significant difference, as the concentration of red blood cells was for age 2-5 years (3.38±0.4), age 6-9 years (3.28±0.45) and age 10-14 years (3.07±0.5). Also, there was no significant difference, but platelet concentration It was for the age of 2-5 years (379.4±192.5), the age of 6-9 years (352.4±103.4), and the age of 10-14 years (402.5±67.03). Thalassemia was different between ages as it was 2-5 years old (8.24±1.03), 6-9 years old (7.95±1.38) and 10-14 years old (8.08±0.63) without any significant difference. Note that there are many studies conducted at different ages on the blood of thalassemia patients (29) and these studies proved that our current results and that there is a high Noticeable in the number of white and red blood cells, hemoglobin, serum and platelets, as a result of the disturbance of the bone cells that produce these cells to fill the deficiency in the body due to lack of oxygen or immunity and thus produce numbers that do not fill the deficiency of these elements and components in the blood, which did not show any significant difference With the age difference there are differences according to the severity of the disease and secondary diseases resulting with the disease that affect other factors in the body. It was also noted that the ferritin concentration was without significant difference between the age groups, as it was found for ages 2-5 years (2926.07 ± 2734), age 6-9 years (1850.5 ± 1668), and age 10-14 years (3432.8 ± 3329) in addition to the above It was found that the concentration of interleukin IL-6 for different age groups without any significant difference was for age 2-5 years (112.6±35.07), age 6-9 years (112.2±19.9) and age 10-14 years (112.9±21.7), and these results were In agreement with several studies (30) which were related to ferritin and IL-6 levels that were very high in serum of patients with Thalassemia compared to healthy controls, however, there were no significant differences, depending on the patients, and this shows that there is no relationship between age and the high level of ferritin and interleukin IL-6 in the patient's serum. If there is a difference, it is necessary to study other factors accompanying the disease. As for the liver enzymes, the study included GOT enzyme, and it was for the age of 2-5 years (25.6 ± 17.6), the age of 6-9 years (25.9 ± 6.93), and age of 10-14 years (28.5 ± 8.61) without a significant difference, and the GPT enzyme did not appear. The other, any significant difference between the age groups was determined for ages 2-5 years (14.2±21), age 6-9 years (17.25±8.46), and age 10-14 years (25.52±3.76). These results agreed with many studies (31) Which showed that these enzymes are elevated in the blood serum of all Thalassemia patients of all ages as a result of the disease, and this confirms the

disturbance of the liver function. In the same context of the study, it was found that the glucose concentration was not significant for the age groups, as it was for the age of 2-5 years (123 ± 5.94), the age of 6-9 years (120.6 ± 4.43) and the age of 10-14 years (122.9 ± 5.7), although it was Significantly higher with the healthy control group, and there are other studies (32)(33) I have reached the same results as the current study, and perhaps the reason is that thalassemia prevents the production of insulin quantities and thus it is difficult to store it, which leads to an increase in its concentration in the blood serum of patients, which proves that thalassemia causes a clear defect in the function of the pancreas as well and not by the effect of the age factor of patients.

Table (6) shows the level of study indicators by age in

P Values	The age			pointer
	10-14	6-9	2-5	
0.089	**7.26±3.63**	**7.79±1.98**	**10.16±2.6**	**WBC**
0.209	**3.07±0.5**	**3.28±0.45**	**3.38±0.4**	**RBC**
0.681	**402.5±67.03**	**352.4±103.4**	**379.4±192.5**	**Plates**
0.880	**8.08±0.63**	**7.95±1.38**	**8.24±1.03**	**Hgb**
0.231	**3432.8±3329**	**1850.5±1668**	**2926.07±2734**	**Ferritin**
0.842	**28.5±8.61**	**25.9±6.93**	**25.6±17.6**	**GOT**
0.237	**25.52±3.76**	**17.25±8.46**	**14.2±21**	**GPT**
0.499	**122.9±5.7**	**120.6±4.43**	**123±5.94**	**Glu**
0.998	**112.9±21.7**	**112.2±19.9**	**112.6±35.07**	**IL-6**

References

1- Ansari, S. H., Baghersalimi, A., Azarkeivan, A., Nozomi, M., & Rad, A. H. (2014). Quality of life in patients with thalassemia major. Iranian Journal of pediatric hematology and oncology, 4(2), 57

2- Adekile, A.D.& Hader, M.Z. (1996). Genetic epidemiology of sickle cell anemia and Alfa/beta Thalassemia in Kuwait. J K med Asso; 28:104-110.

3- Afifi, A.M. (1985). National plan for the management of thalassemia major hypertransfusion intensive desferroxia mine therapy in Egypt. In: Ed by M Aksoy. GFB Braidwood. Hypertransfusion and Iron chelation in thalassemia. Berni Hans Huber Publication: 19 – 29.

4- Barth, E.; Malorgio, C.& Tamarop. (2000). Allogenic bone marrow transplantation in hematologic disorders of childhood: New tendons and controversies. Haematologica;85(11): 2-8.

5- Bhardwaj, U.; Zhang, Y. H.& MacCabe, E. R. (2003). Neonatal hemoglobinopathy screening: Molecular genetic technologies. Mol Gent Metab.;80:129-137.

6. Crocker, John & Paul, G. Murray. (2003). Molecular Biology in cellular pathology. Birmingham, UK.

7- Davies, SC.; Cronin, E.; Gill, M.; Greengross, P.; Herman, M. & Normand, C. (2000). Screening for 1 sickle 1 cell disease and thalassemia: a systematic review with supplementary research. Health Technol Assesstls-Source1; 4: 1-99.

8- Dod, C.; Krishnamoorthy, R.; lamb, J. & Rochette, J. (1992). Rapid analysis of – alfa 3.7 thalassemia and alfa-alfa-alfaanti 3.7 triplications by enzymatic amplification analysis. BrJ Haematol; 82:11-105. Resources 50

9- Eastman, J.W.; Wong, R.; Liao, C. & Morales, D. (1996). Automated HPLC Screening of newborns for sickle cell anemia and other hemoglobin opathies . Clin Chem.; 42:704-710.

10- Eleftheriou, A. (2003). About thalassemia. TIF publications, Nicosia, Cyprus.

11-Advani, R., S. Sorenson, E. Shinar, W. Land, E. Rachmilewitz and S. Schrier (1992).
"Characterization and comparison of the red blood cell membrane damage in severe human alpha-and beta-thalassemia."Aggeli, C., C. Antoniades, C. Cosma, C. Chrysohoou, D.

12-Tousoulis, V. Ladis, M. Karageorga, C. Pitsavos and C. Stefanadis (2005). "Endothelial dysfunction and inflammatory process in transfusion-dependent patients with beta-thalassemia major." International journal of cardiology 105(1): 80-84.

13-Akhtar, M. S., F. Qaw, J. F. Borgio, W. Albuali, A. Suliman, Z. Nasserullah, S. Al-Jarrash and A. Al-Ali (2013). "Spectrum of α-thalassemia mutations in transfusion-dependent β-thalassemia patients from the Eastern Province of Saudi Arabia." Hemoglobin 37(1): 65-73.

14-Al-Nood, H. (2011). "Thalassemia and glucose-6-phosphate dehydrogenase deficiency in sickle-cell disorder patients in Tazi, Yemen/Thalassemia et deficit glucose-6-phosphate dehydrogenase chez des patients attaints de drepanocytes' à Tazi (Yemen)." Eastern Mediterranean Health Journal 17(5): 404.

15-Allen, A., C. Fisher, A. Premawardhena, T. Peto, S. Allen, M. Arambepola, V. Thayalsutha, N. Olivier and D. Weather all (2010). "Adaptation to anemia in hemoglobin E-β thalassemia." Blood, The Journal of the American Society of Hematology 116(24): 5368-5370.

16-Bazvand, F., S. Shams, M. B. Esfahan, L. Koochakzadeh, M. Monajemzadeh, M.-T. H. Ashtiani and N. Rezaei (2011). "Total antioxidant status in patients with major β-thalassemia." Iranian Journal of Pediatrics 21(2): 159.

17-Beutler, E. and C. West (2005). "Hematologic differences between African-Americans and whites: the roles of iron deficiency and α-thalassemia on hemoglobin levels and mean corpuscular volume." Blood 106(2): 740-745.

18-Cappellini, M. D., I. Motta, K. M. Musallam and A. T. Taher (2010). "Redefining thalassemia as a hypercoagulable state." Annals of the New York Academy of Sciences 1202(1): 231-236.

19-Çavdar, A. O. and A. Arcasoy (1971). "The incidence of β-thalassemia and abnormal hemoglobins in Turkey." Acta haematologica 45(5): 312-318.
20-Chaichompoo, P., P. Kumya, L. Khowawisetsut, W. Chiangjong, S. Chaiyarit, N. Pongsakul, N. Sirithanaratanakul, S. Fucharoen, V. Thongboonkerd and K. Pattanapanyasat (2012). "Characterizations and proteome analysis of platelet-free plasma-derived microparticles in β-thalassemia/hemoglobin E patients." Journal of proteomics 76: 239-250.
21-Chakraborty, D. and M. Bhattacharyya (2001). "Antioxidant defense status of red blood cells of patients with β-thalassemia and Eβ-thalassemia." Clinica chimica acta 305(1-2): 123-129.
22-Chen, S., A. Eldor, G. Barshtein, S. Zhang, A. Goldfarb, E. Rachmilewitz and S. Yedgar (1996). "Enhanced aggregability of red blood cells of beta-thalassemia major patients." American Journal of Physiology-Heart and Circulatory Physiology 270(6): H1951-H1956.
23-Chern, J. P., K.-H. Lin, M.-Y. Lu, D.-T. Lin, K.-S. Lin, J.-D. Chen and C.-C. Fu (2001). "Abnormal glucose tolerance in transfusion-dependent β-thalassemic patients." Diabetes care 24(5): 850-854.
24-Chuncharunee, S., N. Archararit, P. Hathirat, U. Udomsubpayakul and V. Atichartakarn (1997). "Levels of serum interleukin-6 and tumor necrosis factor in postsplenectomized thalassemia patients." Journal of the Medical Association of Thailand= Chotmaihet Thangphaet 80: S86-91.
25-Dleikh, F. S., A. J. Al-Aaraji, R. Mohin, M. J. Mousa, H. A.-A. M. Al-Hindy and B. A. Al-Ka'abi (2020). "Possible cause-and-effect linkage of transforming growth factor-beta1 and platelets derived growth factor-AB with delayed anthropometric parameters in adolescent patients with Cooley's anemia: Cases vis control research strategy." EurAsian Journal of BioSciences 14(1).
26-Eldor, A., Y. Krausz, H. Atlan, D. Snyder, A. Goldfarb, E. Hy-Am, E. Rachmilewitz, H. Kotze and A. D. P. Heyns (1989). "Platelet survival in patients with beta-thalassemia." American journal of hematology 32(2): 94-99.
27-Forman, D. and S. Parker (1980). "The measurement and interpretation of serum ferritin." Annals of Clinical & Laboratory Science 10(4): 345-350.
Galanello, R. and R. Origa (2010). "Beta-thalassemia." Orphanet journal of rare diseases 5(1): 1-15.
28-Garner, C., T. Tatu, J. Reittie, T. Littlewood, J. Darley, S. Cervino, M. Farrall, P. Kelly, T. Spector and S. Thein (2000). "Genetic influences on F cells and other hematologic variables: a twin heritability study." Blood, The Journal of the American Society of Hematology 95(1): 342-346.
29-Ghergherehchi, R. and A. Habibzadeh (2015). "Insulin resistance and β cell function in patients with β-thalassemia major." Hemoglobin 39(1): 69-73.
30-Harteveld, C. L. and D. R. Higgs (2010). "α-thalassemia." Orphaned journal of rare diseases 5(1): 1-21.
31- Hashemi, A., R. Ghilian, M. Golestan, G. M. Akhavan, Z. Zare and M. A. Dehghani (2011). "The study of growth in thalassemic patients and its correlation with serum ferritin level."
32-Heris, H. K., B. Nejati, K. Rezazadeh, H. Sate, R. Dolatkhah, Z. Ghoreishi and A. Esfahani (2021). "Evaluation of iron overload by cardiac and liver T2* in β-thalassemia: Correlation with serum ferritin, heart function and liver enzymes." Journal of cardiovascular and thoracic research 13(1): 54.
33- JWAID, S. H. and A. M. GATA (2020). "Comparison study of major thalassemia, thalassemia Intermedia of Iraqi patients and control groups for the effectiveness of liver enzymes." Medico-legal update 20(1): 1181-1184.
jyA YILMAZ, B. A. and E. Demiralp (2001). "Increased plasma levels of interleukin-6 and interleukin-8 in ß-thalassaemia major." Haematology 31(3): 237–244.