

Evolution of some Biochemical and Hematological Parameters of Thalassemia Patients in Maysan Governorate, Iraq

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Abstract: Thalassemia is inherited anemia publicity that common in the world and especially in Mediterranean region, and the most important cause of mortality in patients. The study included (108) patients (males & females) with thalassemia in Amara city and (20) healthy individuals as a control group. All subjected to examination tests for assessment hematological parameters as well as liver functions tests. The results showed a significant increase ($p < 0.01$) in glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT), and Alkaline Phosphatase (ALP) in patients with thalassemia compared with healthy subjects, however, total bilirubin concentration (TSB) did not show significant difference. There are also a significant increases ($p < 0.01$) in White blood cells (WBC) and Platelets (PLT), While Red blood distribution width (RDW) in thalassemia patients compared with healthy subjects, Red blood cell (RBC), Mean cell volume (MCV), Mean corpuscular hemoglobin (MCH), Mean concentration of hemoglobin (MCHC), Hemoglobin (Hb) showed significant decrease ($P < 0.01$) in thalassemia patients compared with healthy subjects. In conclusion: liver enzymes GPT, GOT, and ALP were significantly higher in thalassemia patients, hematological parameters were contradictory when compared with healthy subjects.

Keywords: Thalassemia, Hematological, Biochemical, parameters, MCV

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Introduction

Thalassemia are the widespread human monogenic disease (Cappellini, *et al.*, 2018). Thalassemia have been distributed around the world, with significant frequencies in the Mediterranean region, Middle East and Arabian Peninsula to the Indian subcontinent, and South-eastern Asia, including Iraq (Weatherall, 2018). It is hereditary disorder where one of the subunits in the hemoglobin is decreased or absent (Cappellini, *et al.*, 2018), which causes a disruption in the biosynthesis of peptide chains in the hemoglobin, leading to a disturbance in shapes and functions of the red blood cells (Rija, 2016). This disease is caused by genetic mutations in the alpha or beta globin genes (Angastiniotis and Lobitz, 2019).

Thalassemia is classified into two types, depending on the type of affected chains. It may be thalassemia alpha or thalassemia beta. It is classified into subtypes depending on the location of the defect. The two pairs of genes that encode the alpha chains to chromosome 16, while the pair of genes that encoded the beta chains to chromosome 11. For this reason, thalassemia is a more common beta type for the lack of dominant genes (Rooks, *et al.*, 2012; Mettananda and Higgs, 2018).

The severity of the disease depends on the equilibrium of the production of alpha and beta chains, as the loss of this balance leads to the accumulation of alpha and beta chains within the red blood cell so that the hemoglobin becomes insoluble (Mettananda and Higgs, 2018), reversing the normal state in which hemoglobin is dissolved in red blood cells and that the continued manufacture of alpha chains and the absence of beta chains leads to the accumulation of the first is known as inclusion bodies that cause damage of plasma membrane of RBC may be happen in bone marrow, while, which is released from the bone marrow into the bloodstream, is abnormal and is filled with the bodies that contain severe anemia, these cells are removed when passing through the spleen and therefore the patient needs to transfer blood and notes increased absorption of iron from the bowel causing accumulation in the body which leads to the destruction of the liver and heart and pancreas (Origa, 2017).

At the southern regions of Iraq, the phenomenon of mating relatives is dominant especially in Maysan province where the center of inherited blood disorders still records new cases of thalassemia. So, the study aimed demonstrate the correlation between thalassemia and sociodemographic characters as well as the effect of thalassemia on blood and liver parameters.

1. Materials and Methods

The study was carried out in center in Maysan governorate during the period from November 2016 to April 2017 on patients with thalassemia who visit the Center of inherited blood diseases for the purpose of treatment and who have been confirmed to be infected with this disease through the tests conducted on them.

The study included (108) patients with thalassemia aged between (1-30) year and were divided into three age groups according to age: the first age group (1-10) year, the second age group (11-20) year third group (21-30) year.

Twenty blood samples were taken from healthy people from different locations in Amara city with gender and age matched with the patient for comparison purposes as a control group.

2. Questionnaire

The information was collected through the preparation of a questionnaire for the registration of the necessary information as the age, location, consanguineous of parents, number of infected persons, blood group, and rhesus factor

3.1 Biochemical parameters:

Measuring the enzyme (GPT) and (GOT): These enzymes were measured using bioMerieux kit - France. The colorimetric method, these were determined using Reitman and Frankel (1957).

Measuring the enzyme (ALP): This enzyme was measured by France - kit bioMerieux and the basis of this method is based on the activity of this enzyme in the basal medium, this enzyme determined using Kind and King (1954)

Measuring the (TSB): TSB was measured using a spectrophotometer, by method of Burtis and Ashwood (1999)

3.2 Hematological parameters:

Blood parameters were measured by a complete blood count (CBC) test which gives a complete assessment of the number of blood cells: RBC, WBC, PLT, and Red Cell Indices include mean cell volume (MCV), mean corpuscular hemoglobin (MCH), mean concentration of hemoglobin (MCHC), red blood cell distribution width (RDW) and concentration of hemoglobin (Hb). Used the Cell-Dyn Ruby Hematology analyzer (Abbott, Germany).

3. Statistical analysis

All data were analyzed using SPSS version 20 package. Tests used in the current study included descriptive statistics, and ANOVA.

4.1 Results and discussion

Figure (1) illustrates thalassemia patients according to gender and age with highest percentage of thalassemia in the first age group (1-10 years). There is also increase in thalassemia occurrence in males of ages (11-20 years) and females aging between (1-10 and 21-30 years).

Since the genes responsible for the production of peptide chains involved in the hemoglobin are found on somatic chromosomes, there is no association between sex and disease (Waye, *et al.*, 2014). However, Khairallah, *et al.* (2018) mentioned that thalassemia was increased in patients aging between (1-10 years).

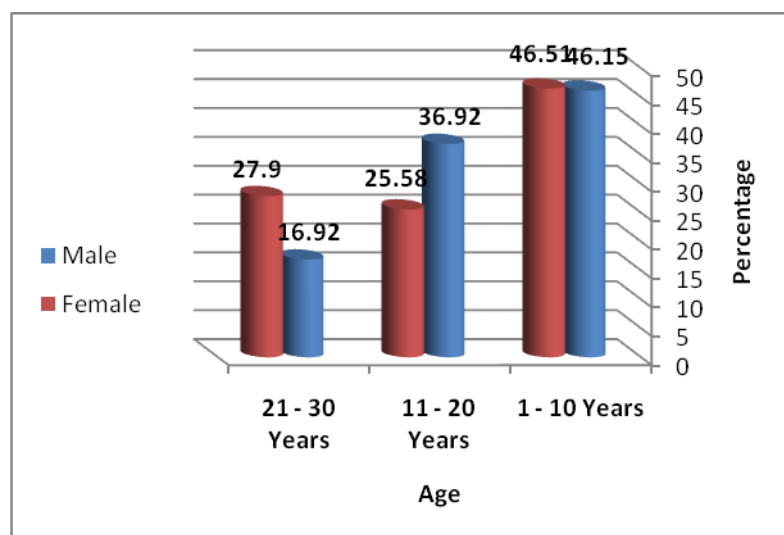


Figure 1: Percentages of thalassemia patients according to age and sex.

Results of table (1) showing the percentages of thalassemia according to the place of residence, relatedness of parents and family history. Thalassemia occur significantly in urban environment especially in patients who are born from relative parents. There is no significance association of thalassemia disease and family history of patients.

Table 1: Frequencies of Thalassemia According to Residence, Relatedness of Parents and Family History

Parameters		No.	%	P value
Residence	Urban	86	79.62	<0.001
	Rural	22	20.38	
Parents	Relative	97	89.81	<0.001
	Non-Relative	11	10.18	
Family History	Positive	50	46.3	0.44
	Negative	58	53.7	

The marriage of consanguineous is a big problem facing all Iraqi communities, the sons of uncles who make the disease continue from generation to generation in the event of disease in the family. This result showing that huge works are needed to stop marriage of relatives who are bearing or infected with thalassemia. The results of this study are consistent with the results of American Medical Association (2005).

Thalassemia was found to be dominant in patients of O and B blood groups with percent of (32.4 for both), on the other hand thalassemia was uncommon among patients of AB blood group as seen in table (2). This results are consistent with results of Al-Moussawi(2004),Khairallah, *et al.*(2018).

There is an association between the gene responsible for the production of globulin on the chromosome 16 and the genes responsible for the type of antigen on the red blood cell membrane responsible for the blood group (Lucarelli *et al.* 1997). Higher prevalence of blood group B in the thalassemia patients than group A could be due to chance only or possibly that people with group B are more prone to develop thalassemia, a suggestion which need to be studied in a wider and more generalized (Abdul –Karim, *et al.*,2005), and may be explained by the sensitivities of these groups and readiness to become infected, and may be due to the spread of these groups among the local population should be attention and blood test for children of those born in families infected with the disease and early detection of the disease.

Table (2):Percentages of Thalassemia patients according to Blood Groups

Blood groups		Number	%	Total
A	A+	27	25	31(28.7%)
	A-	4	3.7	
B	B+	31	28.7	35(32.4%)
	B-	4	3.7	
AB	AB+	5	4.62	7(6.48%)
	AB-	2	1.85	
O	O+	29	26.85	35(32.4)
	O-	6	5.56	

Accordingly, liver functions tests results (seen in table 3) showed a significant increase ($P < 0.01$) in the concentration of GPT in patients (22.5 ± 15.54 U/L) compared to healthy (15.97 ± 5.31 U/L). Also GOT was significantly increased ($P < 0.01$) in patients (24.51 ± 17.69 U/L) compared with healthy subjects (15.29 ± 6.22 U/L), and the concentration of ALP was significantly higher in patients (117.46 ± 54.89 U/L) than in healthy subjects (75.43 ± 23 U/L). No significant differences in total bilirubin concentration between thalassemia patients (1.41 ± 1.31 mg/dl) and healthy subjects (1.03 ± 1.02 mg / dl).

The difference in the concentration of transportable enzymes compared to healthy individuals may be due to excessive breakage of red blood cells or because of the need to synthesis peptide chains through the effectiveness of these enzymes in the transmission of amine groups in amino acids (Al-Khashli and Al-Shawi, 2013). Both GPT and GOT are common in many tissues of the human body (Bushra *et al.*, 2013a). The GOT enzyme is more effective than the GPT enzyme. It is more common in the tissue of the heart, liver, skeletal muscles and kidneys. The liver contains large amounts of GPT and other tissues such as kidney, heart and skeletal muscles contain abundant amounts of this enzyme. The reasons for the increase of the effectiveness of this enzymes from the normal level of healthy may be due to the amounts of iron in the serum of patients, which are deposited in these organs, resulting in the breakdown of fat of some cells of this organs (Piga, 2004; Ellis, 2010).

As for the enzyme alkaline phosphatase (ALP), the results showed a significant increase in the activity of this enzyme compared with the healthy that the reason may be due to the fact that the activity of this enzyme comes from liver and bone tissue and since patients with thalassemia suffer from the destroyed of these tissues, This enzyme leaks to the circulatory system and then increases the effectiveness of this enzyme (Samir *et al.*, 2012; Bushra *et al.* 2013b). There may be a reason why these results can be interpreted as the type of stress that is given to these patients. The presence of large amounts of iron in thalassemia patients will lead to the formation of the root of hydroxyl through a reaction is known Fenton reaction. This free root is one of the freest radicals in the cell, so we see it attacking all the vital molecules, such as fat, proteins and DNA, leading to cell death and other effects (Fateme *et al.*, 2011).

There was a significant decrease in patients, possibly due to the deterioration of hemoglobin and accumulation of bilirubin in the body, also the difference in total bilirubin concentration between patients and healthy may be due to blood transfusions.

Table (3): Concentration of (GOT, GPT, ALP, and TSB) in thalassemia patients and control group

Enzymes	GPT (U/L)	GOT(U/L)	ALP(U/L)	TSB (mg / dl).
Patients	22.5±15.54	24.51±17.69	117.46 ±54.89	1.41±1.31
Control	15.97±5.31	15.29±6.22	75.43±23	1.03±1.02
P value	0.0001**	0.0001**	0.0001**	0.253

** refer to significant difference at ($p < 0.001$)

There are significant variations in the hematological parameters between thalassemia patients and healthy subjects. Table (4) reveals the changes in blood cells number (WBC, RBC, PLT), RBC indexes (MCV, MCH,

MCHC, RDW), and hemoglobin concentration (Hb). In addition, WBC count increases significantly ($p < 0.01$) in patients ($18.77 \pm 13.74 \times 10^3/\text{UI}$) compared to control individuals ($7.77 \pm 1.55 \times 10^3/\text{UI}$), this could be due to general disease conditions and hyperactivities of immunity system for patients receiving blood continually from various donors which is evident through the spread of fever immediately after transfusion, and may be due to break high percentage of red blood cells inside and outside bone marrow that stimulates the secretion of erythropoietin hormone from the kidney leading to the stimulation of the bone marrow to increase formation of red and white blood cells (Goodnough, *et al.*, 2005; Ponticelli, *et al.*, 2010). Also, the infection with thalassemia causes increasing of monocytes which broken the malformed red cells (Ganong, 1997), our result is consistent with results of Shanthi, *et al.* (2013), Abeid (2014).

Red blood cells (RBC) decreased significantly ($p < 0.01$) in patients ($4.61 \pm 3.70 \times 10^6/\text{uL}$) compared to healthy individuals ($4.87 \pm 0.32 \times 10^6/\text{uL}$), this may be due to the genetic mutations in genes responsible for the synthesis of protein chains of hemoglobin which lead to disorder in the biosynthesis of the globin chains and loss of balance in the manufacture of hemoglobin (Waye, *et al.*, 2014). This may also affect the number and shape and size of red blood cells during their formation stages in the bone marrow as a result, the red blood cells are small size and therefore they do not hold the same volume occupied by normal red blood cells (Weatherall, and Clegg, 2001; Rija, 2016), moreover, the red blood cells that enter into the circulatory system may be engulfed inside the spleen by Kupffer cells that phagocytose abnormal and aged RBCs (Kutlar, 1992). This result shows agreement with results of Shanthi, *et al.* (2013), Abeid (2014), Rija (2016).

The platelets number (PLT) was significantly higher ($p < 0.01$) in thalassemia patients ($236.88 \pm 16.96 \times 10^3 / \text{uL}$) compared to healthy subjects ($224.36 \pm 43.73 \times 10^3 / \text{uL}$), the possible causes of increase platelet counts among these patients, growth and development of marrow mononuclear cells to generate colony forming unit-megakaryocytes (CFU-Meg) consist with Archararit, *et al.* (2017).

Our results showing a significant decrease ($P < 0.01$) in all of MCV, MCH, MCHC in patients ($69.20 \pm 15.81 \text{ fL}$, $22.43 \pm 8.07 \text{ pg}$, $30.73 \pm 8.71 \text{ gm / dl}$, respectively) compared with healthy subjects ($84.8 \pm 1.74 \text{ fL}$, $27.69 \pm 0.66 \text{ pg}$, $32.63 \pm 0.63 \text{ mg / dl}$, respectively), while RDW had a significant increase in patients ($29.64 \pm 15.19\%$) compared with healthy subjects ($13.72 \pm 0.72\%$). Same results also reported by Abeid (2014).

The concentration of hemoglobin in patients was significantly lower ($P < 0.01$) in thalassemia patients ($8.95 \pm 2.88 \text{ gm / dl}$) when compared with control group ($13.58 \pm 0.86 \text{ gm / dl}$), this can be explained by genetic defect in synthesis globin chains leading to the lack or low production of hemoglobin (Bennet and Plum, 1996) as a result, most patients have moderate to severe anemia (Rathod *et al.*, 2007; Voskaridou *et al.*, 2011). This result is consistent with results of studies Shanthi, *et al.*, (2013), Abeid (2014).

Table (4): Hematological parameters in thalassemia patients and control group.

Parameters	WBC	RBC	PLT	MCV	MCH	MCHC	RDW	Hb
patients	18.77 ± 13.74	4.61 ± 3.70	236.88 ± 16.96	69.20 ± 15.81	22.43 ± 8.07	30.73 ± 8.71	29.64 ± 15.19	8.95 ± 2.88
Control	7.77 ± 1.55	4.87 ± 0.32	224.36 ± 43.73	84.8 ± 1.74	27.69 ± 0.66	32.63 ± 0.63	13.72 ± 0.72	13.58 ± 0.86
P value	0.000**	0.000**	0.000**	0.000**	0.000**	0.000**	0.000**	0.000**

** . The mean difference is significant at the 0.01 level

4. Conclusion

The present study showed deteriorated biochemical and hematological statuses of thalassemia patients. This may be due to red blood cell degeneration, frequent iron overload transfer, hepatitis, renal dysfunction and chronic hemolytic anemia. This study explains the necessity of fortify efforts for organized assessment and follow-up of thalassemia patients with pressure to use the iron treatment, which can it is very recommended to develop or modify administration the protocols thus progress their clinical image as the stem cell culture is not possible in our country.

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