University of Al-Qadisiyah

College of Pharmacy

Evaluation of Some Biochemical Changes Associated with Oral Iron Chelating Agents in β-Thalassemia major patients in Al-Diwaniyah province

By

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بِسْمِ اللهِ الرَّحْمنِ الرَّحِيم

(قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا
إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ)

صَدق اللهُ العَلي الْعَظِيمِ

سورةالبقرة (32)

Dedication

To my Mother

To my Father

To my brothers

To my sisters

Supervisor Certification

I certify that this research was carried under my supervision at the College of Pharmacy/ University of AL-Qadisiyah, as a partial fulfillment of the requirement for the B.Sc in Pharmacy.

Dr. Ghufran Mohammed Hussein

Supervisor

In review of the available recommendation, I forward the present research for debate by the examining committee.

Dr. Ghufran Mohammed Hussien

Head of Department of Clinical Laboratory Science

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Zahraa

Summary

The present study was designed to assess the serum ferritin level and to evaluate the effect of oral iron chelating agent on serum ferritin level. To achieve this aim, 62 of β-thalassemia major patients with ages range between (5-16) years are taken.

Determination types of hemoglobin by using hemoglobin electrophoresis, Serum ferritin concentration was estimated by an enzyme linked immunosorbant assay (ELISA) method.

Results indicated that significant decrease in serum ferritin concentration in β-thalassemia major patients group who used oral deferasirox for four, eight and twelfth month when compared with the same patients group before using the deferasirox. They also show non-significant changes in serum ferritin concentration among β-thalassemia major patients group who used oral deferasirox for four, eight and twelfth month.

In conclusion, treatment with oral iron chelation therapy, Deferasirox (DFX), in beta thalassemia major patients result in decrease in serum ferritin level reducing related iron overload complications.

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Chapter One

Introduction and Literature Review

1.1-Thalassemia

Thalassemia is an inherited impairment of hemoglobin production, in which there is partial or complete failure of synthesis of a specific type of globin chain, it results in excessive destruction of red blood cells, which leads to anemia [(1)].

Haemoglobin consists of globin chains attached to haem molecule, globin made up of four protein chains α, β, γ, and δ, arranged in matching pairs as α2β2, α2δ2, α2γ2. The hemoglobin type is determined by the combination of tetra-globin chains into: HbA (α2β2), HbA2 (α2δ2), and HbF (α2γ2) [(2)].

Normal adult blood contains three types of haemoglobin, the major component is HbA (α2β2), the minor haemoglobins are HbF (α2γ2), and HbA2 (α2δ2), fetal haemoglobin (HbF) constitutes the predominant haemoglobin during fetal life, while representing less than 1% in adult because HbA replace HbF shortly after birth [(3)].

Thalassemia is derived from the Greek word "*thalassa*" meaning "the sea" because the condition was first described in populations living near the Mediterranean Sea, first recognized in 1952 by Dr. Thomas B. Cooley [(4)].

1.2 -Classification

The classification of thalassemia according to the type of globin chain defect, the defect may affect either alpha or beta chain or may affect some combination for this type [(4)]. The two basic groups of thalassemia disorders are: alpha thalassemia and beta thalassemia, they are causing varying degrees of anemia, which can range from insignificant to life threatening [(1)].

1.2.1 -Alpha-thalassemia

These are usually caused by gene deletions. As there are normally four copies of the α-globin gene, the clinical severity can be classified according to the number

of genes that are missing or inactive. Loss of all four genes completely suppresses α-chain synthesis and because the α chain is essential in fetal as well as in adult haemoglobin this is incompatible with life and leads to death *in utero*, three α gene deletions leads to a moderately severe anemia with splenomegaly, while the α-thalassemia traits are caused by loss of one or two genes and are usually not associated with anemia [(2)].

1.2.2 -Beta-thalassemia

Beta-thalassemia is considered as the most common autosomal single gene disorder worldwide, in which the β globin chain synthesis is impaired, characterized by reduced or absent beta globin chain synthesis, resulting in reduced Hb in red blood cells (RBC), decreased RBC production and anemia [(1)].

The β-thalassemias are subdivided into the β^0, β^+ and β^{++} groups, to designate a complete, severe or mild defect in β-globin chain synthesis, respectively. β-thalassemia includes three main forms: Thalassemia Major, Thalassemia Intermedia, and Thalassemia Minor [(4)].

1.2.2.1 - Beta thalassemia minor

Beta-thalassemia minor, also called "β-thalassaemia carrier", "β-thalassaemia trait" or "heterozygous β-thalassaemia", it results from the inheritance of one defective gene for β-globin synthesis (heterozygous) of the thalassemia gene[(5)] .

In β-thalassemia trait, hemoglobin electrophoresis results in the neonatal period are normal, but by 1 year of age, hemoglobin A2 and/or F are elevated because of increased synthesis of δ- and/or γ-globin chains, respectively [(6)].

No treatment is necessary for β-thalassemia minor, carriers of thalassemia minor are usually clinically asymptomatic but sometimes have a mild anemia.

When both parents are carriers there is a 25% risk at each pregnancy of having children with homozygous thalassemia [7].

1.2.2.2-Thalassemia intermedia

Nearly 10% of thalassemia patients have thalassemia intermedia (TI). Genetically, this group may have tow β globin (homozygous) carrying a thalassemia mutation at least one of which is mild [4].

They have a moderate hemolytic anemia, maintaining Hb levels >7 g/dL without transfusion support. The use of transfusions is what clinically divides the categories of TI from TM. When their transfusion requirements reach > 8 units per year, they are reclassified as TM [8].

TI patients' clinical presentation typically occurs at 2-4 years of age, later than TM patients, and symptoms can include anemia, hyperbilirubinemia, and hepato splenomegaly. These patients generally present with better growth development, and sexual maturation than TM patients, and they typically live longer before dying of complications of chronic anemia with pulmonary hypertension, iron-induced cardiac disease, or liver failure [9].

1.2.2.3-β-thalassemia major

Variably referred to as "Cooley's Anaemia", this is the most severe form of beta thalassemia in which there is complete lack of beta protein in the hemoglobin, which causes a life-threatening anemia that requires regular blood transfusions and extensive ongoing medical care. These extensive, lifelong blood transfusions lead to iron overload which must be treated with chelation therapy to prevent early death from organ failure [7].

Iron overload is derived not only from blood transfusion and increased gastro-intestinal absorption but also from ineffective erythropoiesis and constant

hemolysis start to appear such as liver cirrhosis, endocrine dysfunction, and pulmonary defect [10].

1.3-Epidemiology

People of Mediterranean, Middle Eastern, African, and Southeast Asian descent are at higher risk of carrying the genes for thalassemia [1]. Thalassemia has been a burden on the healthcare systems of many countries in region of Transcaucasia, Central Asia, and the Indian subcontinent. Due to the migration of people from these regions, thalassemia populations have become a public health concern even in North America [11].

Thalassemia affects men and women equally and occurs in approximately 4.4 of every 10,000 live births. It has also been estimated that, worldwide, 9 million thalassemia carrier women become pregnant annually and 1.33 million pregnancies are at risk for a thalassemia major condition [12].

1.4 -Etiology

More than 200 mutations have been so far reported; the large majority are point mutations (single base changes), small deletions or insertions, in functionally important regions of the beta globin gene. Deletions of the beta globin gene are uncommon [8]. Mutations are characterized as (β^o) if they prevent any formation of β chains; they are characterized as (β^+) if they allow some β chain formation to occur [4].

1.5 -Pathophysiology

In thalassemia major no or only a very small amount β chains are produced, preventing the synthesis of normal adult haemoglobin and severely damaging the red blood cells' capacity to transport oxygen [7].

The child's body reacts by continuing to make fetal haemoglobin HbF. However, it cannot make a sufficient quantity to meet the needs of the child's growing body and replace the oxygen transporting functions of adult haemoglobin HbA [13].

As the body continues to produce normal amounts of α-chains but insufficient, β chains for them to pair up with, the excess α-chains begin to accumulate. These excess α-chains interfere with the body's production of red blood cells, reducing production by up to 95%. With few mature red blood cells in the blood, the body develops severe anemia [14].

The body tries to compensate for the impaired maturation process by accelerating the space for red blood cell production in the bone marrow. The liver and the spleen, which do not normally produce red blood cells, are also activated [8]. As a result of this extreme activity, the bone marrow cavities expand and the liver and spleen are enlarged. The blood volume increases and, as a consequence, the heart is under great pressure [4]. As shown in figure (1-1)

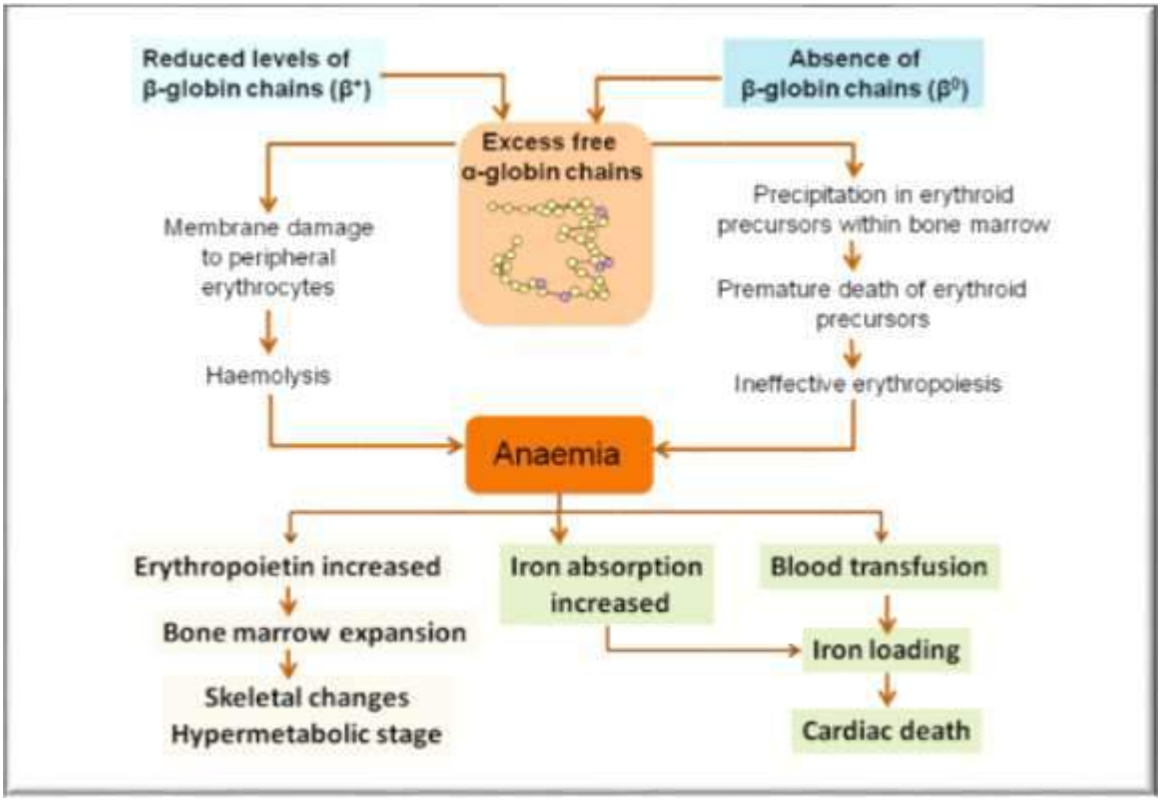

Figure (1-1): pathophysiology of beta thalassemia major

1.6 -Clinical features

Affected infants usually are born healthy, having only hemoglobin F detected on electrophoresis in the neonatal period. Symptoms usually develop in the second six months after birth, when the transition in hemoglobin predominance from F to A should occur [(2)]. Generally, the clinical features of TM include: [(4)]

1. Severe anaemia becomes apparent at 3 – 6 months after birth.
2. Enlargement of the liver and spleen occurs as a result of excessive red cell destruction, extramedullary haemopoiesis and because of iron overload, the large spleen increases blood requirements by increasing red cell destruction and pooling, and by causing expansion of the plasma volume.
3. Expansion of bones caused by intense marrow hyperplasia which causes bones to widen. This can result in abnormal bone structure, especially in the face and

skull. Bone marrow expansion also makes bones thin and brittle, increasing the risk of broken bones.

4 Infections, can occur for a variety of reasons: [2]

a. In infancy, without adequate transfusion, the anaemic child is prone to bacterial infections.
b. Pneumococcal, *Haemophilus* and meningococcal infections are likely if splenectomy has been carried out and prophylactic penicillin is not taken.
c. *Klebsiella* and fungal infections may cause severe gastroenteritis due to deferoxamine.
d. hepatitis C, hepatitis B, or Human immunodeficiency virus (HIV) by transfusion of viruses by blood transfusion may occur.

1.7-Diagnosis

1.7.1-Compelete Blood Count (CBC)

Complete blood count, a primary screening for thalassemia, MCV and MCH are the most important indicies, i.e., when individuals who have hypochromic microcytosis with MCV<80 fL and MCH< 27 pg should be investigated further [15].

1.7.2-Peripheral Blood Film

Affected individuals show RBC morphologic changes, the number of erythroblasts is related to the degree of anemia and is markedly increased after splenectomy. There is a severe hypochromic microcytic anaemia, raised reticulocyte percentage with normoblasts, target cells and basophilic stippling in the blood film [2].

1.7.3-Hemoglubine electrophoresis

Electrophoresis identifies the amount and type of Hb present. The Hb pattern in beta-thalassemia varies according to beta-thalassemia type. In $beta^0$ thalassemia, HbA is absent and HbF constitutes the 92-95% of the total Hb, while in $beta^+$ thalassemia HbA levels are between 10 and 30% and HbF between 70-90%[6]. Hb electrophoresis and HPLC also detect other hemoglobinopathies that may interact with beta-thalassemia [8].

1.7.4- Serum ferritin

Ferritin is the iron storage protein serves to store iron in a non-toxic form, to deposit it in a safe form, and to transport it to areas where it is required [16].
Ferritin level in serum directly relates to the amount of iron stored in the body, which is important for red blood cell production. If ferritin is high, there is iron in excess. Ferritin is also used as a marker for iron overload disorders [10].

1.8-Treatment

1.8.1-Regular blood transfusion

A decision to initiate regular transfusions in patients with beta thalassemia may be difficult and should be based on the presence and severity of the symptoms and signs of anemia, including failure of growth and development [17].

Blood transfusions prevent complications of anemia. Also allowances of normal or near normal growth and development, and extension of patients' life spans [18]. Multiple blood transfusions cause also iron overload, while repetitive blood transfusions increase the risk of transmission of viruses with immunosuppressive properties, such as cytomegalovirus, Ebstein-Barr virus and hepatitis C[19].

Blood transfusion is need every 2-5 weeks to maintain pre-transfusion Hb level above 10 g/dl as life saving for patients [20]. The volume of transfusion is usually 10-15 ml/kg and should be monitored occasionally for assessment of the rate of fall in Hb level between transfusion [21].

1.8.2-Iron chelating agent

Iron-chelating compounds that bind the element and promote its excretion in urine and bile are essential to the treatment of transfusion iron overload in patients with thalassemia [22]. The goal of chelation is to maintain safe level of iron among patients who have increased iron loading from transfusion therapy. Chelators prevent excess iron accumulation in organs [23].

Deferasirox

- **Mechanism of action:** Deferasirox is an orally active chelator that is selective for iron (as Fe^{3+}). It is a tridentate ligand that binds iron with high affinity in a 2:1 ratio [25].

- **Pharmacokinetics:** Deferasirox is absorbed following oral administration with median times to maximum plasma concentration (tmax) of about 1.5-4 hours. The absolute bioavailability (AUC) of deferasirox tablets for oral suspension is 70% compared to an intravenous dose. Deferasirox is highly (~99%) protein bound almost exclusively to serum albumin. Glucuronidation, with subsequent biliary excretion, is the main metabolic pathway for deferasirox. Deconjugation of glucuronides in the intestine and subsequent reabsorption (enterohepatic recycling) is likely to occur. Deferasirox and its metabolites are primarily excreted in the faeces (84% of the dose). Renal excretion of deferasirox and its metabolites is minimal (8% of the dose, 6% as hydroxylated deferasirox) [26].

- **Dosage:** Recommended initial daily dose is 20 mg/kg body weight while, maximum daily dose is 40 mg/kg body weight, 50% starting dose reduction in moderate hepatic impairment. Monthly monitoring of serum ferritin for assessing patient's response to therapy. In patients not adequately controlled with doses of 30 mg/kg, doses of up to 40 mg/kg may be considered. In patients whose serum ferritin level has reached the target (usually between 500 and 1000 microgram/L), dose reductions in steps of 5 to 10 mg/kg should be considered to maintain serum ferritin levels within the target range. Deferasirox should be interrupted if serum ferritin falls consistently below 500 micrograms/L. Deferasirox must be taken once daily on an empty stomach at least 30 minutes before food. Deferasirox tablets to be dispersed in water or apple or orange juice [24].

- **Side effect:** Common or very common side effect include fatal gastro-intestinal haemorrhage, gastro-intestinal disturbances, gastrointestinal ulceration, headache, proteinuria and pruritus rash [27].

1.8.3-Stem cell transplantation

Haemopoitic stem cell transplantation is the conventional curative option for thalassemia patients. This therapy infuses the thalassemic patients with stem cell harvested from compatible donor. If engraftment occurs, these normal stem cells will then re-populate the recipient's marrow and proliferate to produce normal red blood cell. If the treatment is successful, the patient is no longer transfusion dependent [28].

Aims of the study

The main objectives of the present study can be summarized as follows:

1. To assess the serum ferritin level.

2. To evaluate the effect of oral iron chelating agent on serum ferritin level.

Chapter Two

Materials and Methods

2.1-Materials

2.1.1-Subjects

The study included group of β-thalassemia major. All samples were collected from July2016 till February 2017. The work was carried out in the Laboratory of AL-Diwaniyah pediatrics hospital.

2.1.1.1- Patient Group

The study was performed on 62 patients with β-thalassemia major (26 male and 36 female). The patient ages ranged between 5 years to 16 years. Patients were diagnosed by specialist pediatric physicians. They were selected from specialty unit for thalassemia.

2.1.2-Chemicals

Chemicals and kits used in this study were tabulated in Table 2-1.

Table 2-1: Chemicals and Kits Used

No.	Chemicals and Kits	Origin
1	The D-10 Dual Program kit	BIO-RAD (USA)
2	Mini VIDAS kit	Biomerieux (France)

2.1.3-Apparatus and Equipments

Apparatus and equipments used in this study were tabulated in Table 2-2.

Table 2-2: Apparatus and Equipments Used

No.	Apparatus and Equipments	Origin
1	Disposable syringes (5 mL)	Medical jet (Syria)
2	Plan tube	Plastilab (China)
3	EDTA tube	Plastilab (China)
4	Hb electrophoresis	BIO-RAD (USA)
5	Spectrophotometer	Apel (Japan)
6	Mini VIDAS instruments	Biomerieux (France)
7	Micropipette tips (different size) (10 µl) (10-100 µL) (100-200 µL)	Promega (USA)
8	Micropipettes (different size) (10, 20, 100, 200, 1000 µL	Watson Nexty (Japan)

2.2-Methods

2.2.1-Determination different types of hemoglobin (Diagnosis)

Measure and identify the different types of hemoglobin by using hemoglobin electrophoresis (BIO-RAD **D-10 Dual Program**).

Principle:

The D-10 Dual Program is based on chromatographic separation of the analytes by ion exchange high performance liquid chromatography (HPLC). The samples are automatically diluted on the D-10 and injected into the analytical cartridge.

The D-10 delivers a programmed buffer gradient of increasing ionic strength to the cartridge, where the hemoglobins are separated based on their ionic interactions with the cartridge material.

The separated hemoglobins then pass through the flow cell of the filter photometer, where changes in the absorbance at 415 nm are measured. The D-10 software performs reduction of raw data collected from each analysis [29][30].

Reagents:

Reagents	Composition	
1. Elution Buffer 1	Bis-Tris/Phosphate buffer, pH 6 sodium azide	200 ml <0.05%
2. Elution Buffer 2	Bis-Tris/Phosphate buffer, pH 6.7 sodium azide	1000 ml <0.05%
3. Wash/Diluent Solution	deionized water sodium azide	1600 Ml <0.05%
4. Analytical Cartridge	One cation exchange cartridge (4.0 mm ID x 30 mm)	
5. C.Calibrator/Diluent Set, Hb A2/F/A1c	Calibrator Level 1 Lyophilized human red blood cell hemolysate with gentamicin, tobramycin, and EDTA as preservatives. Calibrator Level 2	

	Lyophilized human red blood cell hemolysate with gentamicin, tobramycin, and EDTA as preservatives. Calibrator Diluent Deionized H2O 100 mL sodium azide <0.05%
6. ample Vials	Two packs 1.5 ml each
7. Floppy Diskette	specific D-10 Dual Program Parameter information
8. Whole Blood Primer	Four vials of lyophilized human red blood cell hemolysate with gentamicin, tobramycin, and EDTA as preservatives.
9. Thermal Paper	Box of 10 rolls

Sample preparation

- Sample volume collected: 2.0 mL.
- Type of specimens used: Whole Blood.
- Store: at 4C, in EDTA tube.

Procedure:

1.Allow sample tubes to reach room temperature (15-30°C) before performing the assay.

2. Load the sample tubes into the D-10 sample racks so that the barcodes will be facing the back of the instrument.

3. started up the analyzer from SLEEP, Press the START UP button to begin this process, which will take approximately five minutes. A "Daily Report" will print out at the completion of start-up.

4. Insert the rack into the slot on the right side of the analyzer. Patient/QC IDs will appear on the screen after they have been scanned by the barcode reader.

5.Press the START button to begin the analysis. Press YES when asked if you are sure you want to start the run. One full rack often samples will take approximately 65 minutes to complete (6.5 minutes per sample).

6.The rack can only be ejected when the instrument returns to STANDBY, at which time a subsequent rack for analysis can be loaded in the same manner

Calculation

The D -10 software performs reduction of raw data collected from each analysis. Two-level calibration is used for quantitation of the HbA2/F/A1c values. A sample report and a chromatogram are generated for each sample.

2.2.2-Determination of Serum Ferritin Concentration

Principle:

The assay principle combines a one-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA).

The Solid Phase Receptacle (SPR®) serves as the solid phase as well as the pipetting device for the assay. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips. All of the assay steps are performed automatically by the instrument, the reaction medium is cycled in and out of the SPR several times. During the final detection step, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out the SPR.

The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-MethyI-umbelliferone) the fluorescence of which is

measured at 450 nm. The intensity of the fluorescence proportional to the concentration of antigens present in the sample.

At the end of the assay, the results are automatically calculated by the instrument in relation to the calibration curve stored in memory, and then printed out [31][32].

Reagents:

60 FER Strips	STR	Ready-to-use
60 FER SPRs 2X30	SPR	Ready-to-use
FER CONTROL 1X2 ml (liquid)	C1	Ready-to-use
Calibrator 1x2 ml (liquid)	S1	Ready-to-use
FER dilution buffer 1x25 ml (liquid)	R1	Ready-to-use

Sample preparation:

- Sample volume collected: 2.0 mL.
- Type of specimens used: serum.

Procedure

1. Only remove the required reagents from the refrigerator and allow them to come to room temperature for at least 30 minutes
2. Use one "FER" strip and one "FER" SPR for each sample, control or calibrator to be tested.

3. The test is identified by the "FER" code on the instrument. The calibrator must be identified by" S1", and tested in duplicate. If the control needs to be tested. it should be identified by "C1".
4. For this test, the calibrator, control, and sample test portion is 100 µl
5. insert the "FER" spRs and "FER" strips into the instrument. Check to make sure the color labels with the assay code on the SPRs and the Reagent strips match.
6. Initiate the assay as directed in the User's Manual. All the assay steps are performed automatically by the instrument.
7. The assay will be completed within approximately 30 min. after the assay is completed remove the SPRs and strips from the instrument.

2.3. Statistical Analysis

The results were expressed as mean ± SD. Student's t-test was used for the evaluation of data. P-value of < 0.05 was considered to be statistically significant.

Chapter Three

Results and Discussion

3.1-General Characteristics of β-Thalassemia Major Patients Group

The general characteristics of the β-thalassemia major patients was shown in Table (3-1).

Table (3-1): General Characteristics of β-Thalassemia Major Patients Group

Characteristics	
Number	62
Sex Male/Female	26/36
HbA_2 %	7.09±6.57
HbF %	82.57±19.94
Duration of treatment (year)	1 year

3.1.1-Age

The distributions of age among the β-thalassemia major patients groupis demonstrated in Figure (3-1).

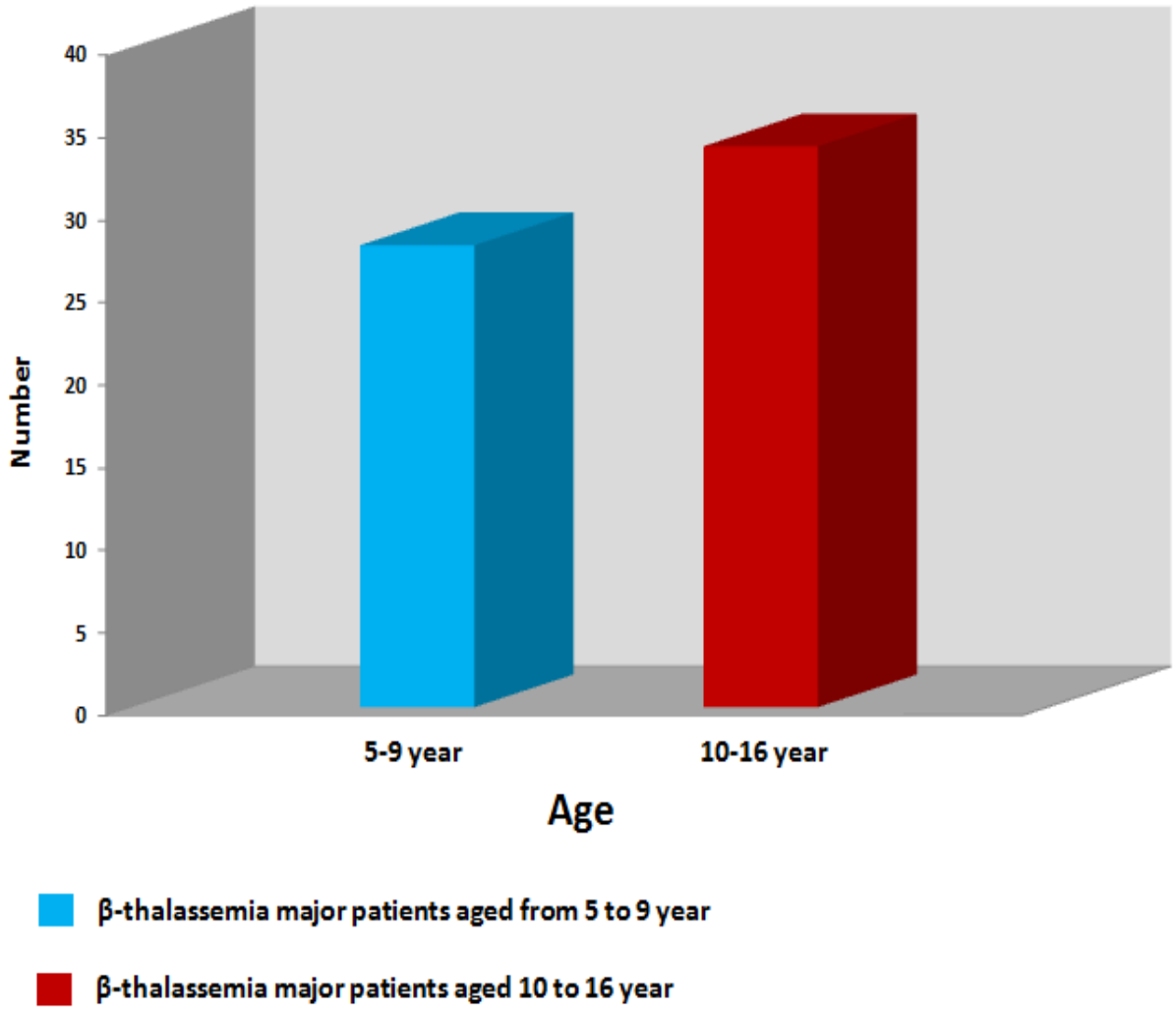

Figure (3-1): Age Distribution of β-Thalassemia Major Patients Group

3.1.2-Gender

The distributions of gender among the β-thalassemia major patientsgroupis demonstrated in Figure (3-2).

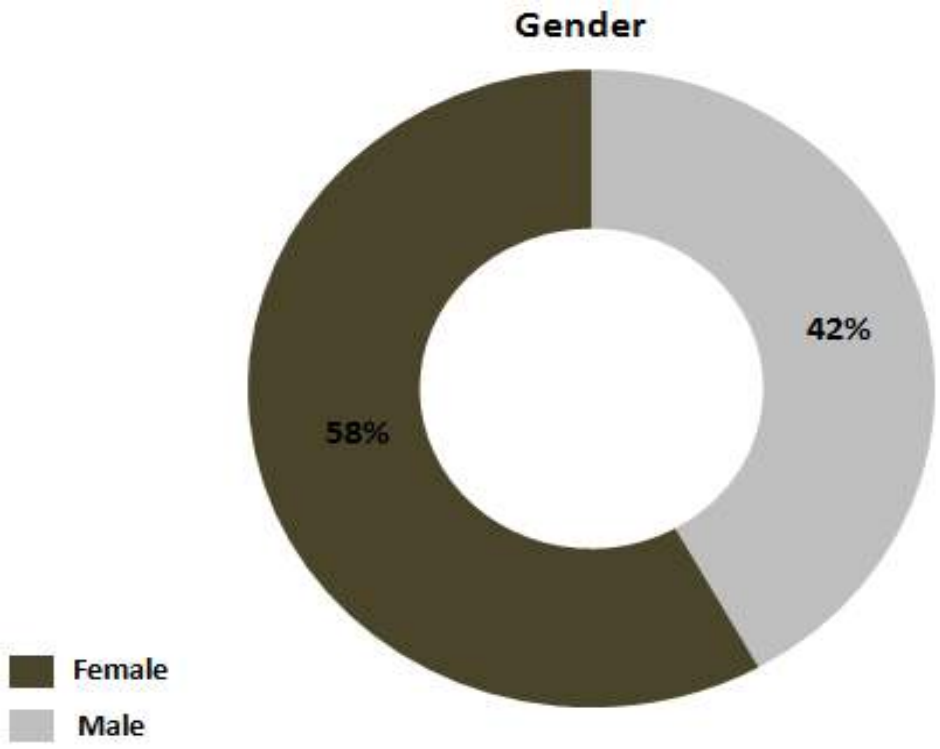

Figure (3-2): Gender Distribution of β-Thalassemia Major Patients Group

3.2-Levels of Serum Ferritin of β-Thalassemia Major Patients Group

The results of present study show significant decrease ($p<0.05$) in serum ferritin concentration in β-thalassemia major patients group who used oral deferasirox for four, eight and twelfth month when compared with the same patients group before using the deferasirox as show in figure (3-3). They also show non-significant changes ($p>0.05$) in serum ferritin concentration among β-thalassemia major patients group who used oral deferasirox for four, eight and twelfth month as show in figure (3-3).

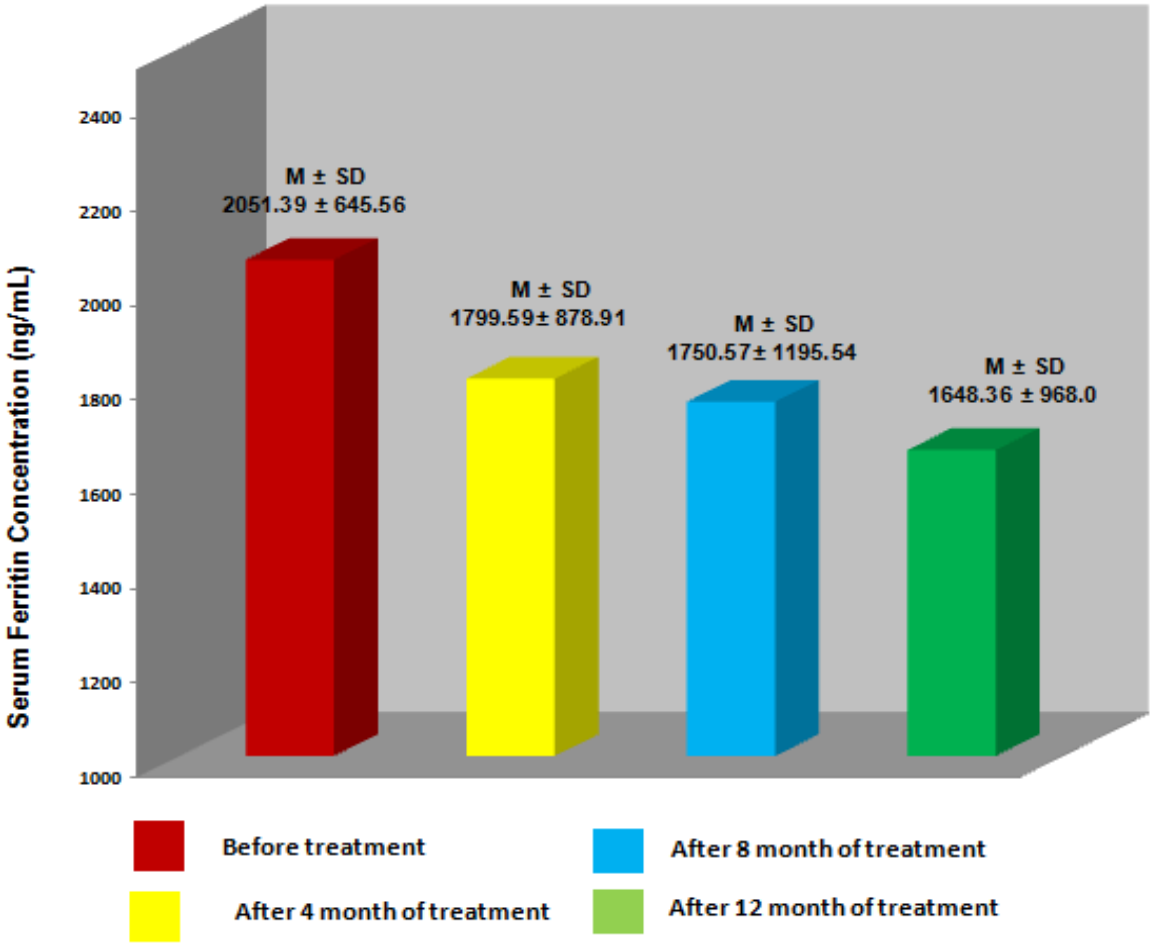

Figure (3-3): Serum Ferritin Concentration inβ-Thalassemia Major Patients Group

The present study show increase in serum ferritin concentration (increase in serum iron concentration) and decrease in serum hemoglobin concentration. The main causes of iron overload are ineffective erythropoiesis and blood transfusion. The patients have severe anemia due to ineffective erythropoiesis [33, 34].

The iron overload can generate reactive oxygen species and promote oxidative damage to cells and the excess of iron accumulate in several organs including liver, pituitary gland, pancreas and heart [35].

The reactive oxygen species can cause damage in several tissue, mainly in the endothelial tissue [36]. Lipids and lipoproteins also affected by reactive oxygen species. The oxidative modification theory of atherosclerosis predicts the oxidation of protein and lipid in the vascular wall. Further, oxidative stress characterized by oxidized LDL [37].

Modified or oxidized LDL is scavenged by macrophages through the scavenger receptors that present in cell surface, that is leads to foam cell formation. The deposition and infiltration of foam cells in the arterial wall are the initiating steps in the development of atheromatous plaque [38].

Iron chelation therapy is lifelong requirement for thalassemic patients who were transfusion dependent, deferasirox (DFX) was generally well tolerated oral iron chelation therapy over the long term that has proven effective in reducing serum ferritin and tissue iron concentration levels [39].

Deferasirox is an orally administered once daily iron chelator, it is a tridentate iron chelators that mobilize tissue iron, requiring two molecules of drug to form a soluble stable complex with iron that are then excreted in feces [40].

DFX in β-thalassemia major patients result in decrease in serum ferritin and tissue iron level result in reducing related iron overload complications. DFX decrease free radical formation, lipid peroxidation, oxidative stress, inflammation and tissues damage, it removes iron from the heart, also reduce progressive nature of endocrine dysfunction (diabetes mellitus, adrenal insufficiency, hypothyroidism, osteoporosis, hypoparathyroidism and hypogonadism) in β-thalassemia major patients. As DFX decrease lipid peroxidation this results in reduce liver injury and necrosis [(41)].

This study shows significant decrease in serum ferritin concentration in β-thalassemia major patients group who used oral deferasirox when compared with the same patients group before using the deferasirox, the current results are in agreement with the result of Rageb M. et al. [(42)] study in which the serum ferritin concentration was significantly decreased in β-thalassemia major patients group who used oral deferasirox when compared with the same patients group before using the deferasirox.

Conclusions

1. There are a significant decrease in serum ferritin concentration in β-thalassemia major patients group who used oral deferasirox for four, eight and twelfth month when compared with the same patients group before using deferasirox.

2. Treatment with oral iron chelation therapy (deferasirox) in beta thalassemia major patients will result in redaction in serum ferritin level and reducing related iron overload complications.

3. Non-significant changes occur in serum ferritin concentration among β-thalassemia major patients group who used oral deferasirox for four, eight and twelfth months.

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الخلاصة

الدراسة الحالية صممت لتقييم مستوى الفيريتين في مصل الدم و تقييم تاثير خالبات الحديد عن طريق الفم على مستوى الفيريتين في المصل , لتحقيق هذا الهدف ,تم اخذ 62 من مرضى فقر دم البحر الابيض المتوسط نوع بيتا الكبرى وباعمار تتراوح بين(5-16) سنة .

لقد تم قياس نوع الهيموغلوبين باستخدام الترحيل الكهربائي لخضاب الدم وقياس تركيز الفيريتين في المصل باستخدام جهاز (ميني فايداس).

اشارت النتائج الى انخفاض كبير في مستوى الفيريتين في المصل في مجموعة مرضى فقر دم البحر الابيض المتوسط نوع بيتا الكبرى الذين استخدموا (الديفرازيروكس) عن طريق الفم لمدة أربعة وثمانية واثنا عشر شهرا بالمقارنة مع نفس المجموعة من المرضى قبل استخدام(الديفرازيروكس). وتبين أيضا تغيرات غير كبيرة في تركيز الفيريتين في المصل بين مجموعة مرضى فقر دم البحر الابيض المتوسط نوع بيتا الكبرى الذين استخدموا (الديفرازيروكس) عن طريق الفم لمدة أربعة وثمانية واثنا عشر شهرا.

يستنتج من ذلك ان , العلاج بخالبات الحديد عن طريق الفم (الديفرازيروكس) في مرض فقر دم البحر الابيض المتوسط نوع بيتا الكبرى يؤدي الى نقصان مستوى الفيريتين في المصل ويحد من مضاعفات الحديد الزائد المتعلقة به.

بِسْمِ اللهِ الرَّحْمنِ الرَّحِيم

(قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا
إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ)

صَدق اللهُ العَلي الْعَظِيمِ

سورةالبقرة (32)

جامعة القادسية
كلية الصيدلة

تقييم بعض التغيرات البيوكيميائية المرتبطة بخالبات الحديد عن طريق الفم لمرضى فقر دم البحر الابيض المتوسط نوع بيتا الكبرى في محافظة الديوانية

زهراء عبد الرضا حسين

زهراء كاظم وادي

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د.غفران محمد حسين

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