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Original Article

# Erythroferrone level in β-thalassemia patients

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## ABSTRACT

**Background**: β thalassemia patients have repeated blood transfusions those lead to iron overload, resulting in iron toxicity. In such cases Hepcidin results in excessive iron absorption. Iron accumulation in organs leads to several complications. Erythroferrone (ERFE) is a hormone that regulates iron metabolism through its actions on hepcidin.

**Objective:** we aimed to study the role of erythroferrone and its relationship with hepcidin in B-thalassemia patients (major –intermedia).

**Patient and Methods:** This Prospective case control study was conducted on 50 participants. 13 β thalassemia major (β- TM) patients (group Ia) and 12 β thalassemia intermedia (β- TI) patients (group Ib). In addition to, 25 healthy individuals included as control group (group II). Routine laboratory investigation, serum hepcidin, serum erythroferrone and iron markers were measured in all groups.

**Results**: In this study, there was significant increase in erythroferrone in group Ia and group Ib while hepcidin showed significant decrease in group Ia and group Ib when compared to a control group (group II) with P value <0.001 , There was significant increase in serum ferritin, total iron binding capacity (TIBC), Serum iron and transferrin saturation (TS) in group Ia and group Ib when compared to a control group (group II). There was negative significant correlation between hepcidin and RDW, significant positive correlation with MCH, MCV. There was negative significant correlation between ERFE and MCV, MCH.

**Conclusions**: Expression of ERFE is altered in multi transfused β thalassemia patients. Extended studies should be performed to assess its discriminative ability between β thalassemia major and minor.

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**Keywords**: Erythroferrone, hepcidin, thalassemia, transferrin saturation

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## INTRODUCTION

Thalassemia is a genetic disorder characterized by the production of defective hemoglobin. Hemoglobin consists of alpha and beta' chains' which are faulty in a patient with thalassemia and therefore the hemoglobin formed is dysfunctional. Thalassemic patient often sufferers from low Hemoglobin (HB) level and low HB quality [1]. The patient's body often keeps trying to generate both red blood cells and hemoglobin. Nevertheless, although hemoglobin has become with genetic defect in the body, the new hemoglobin created tends to cause more complications when abnormal hemoglobin overproduction occurs. Thalassemic people can be managed to the intensity of their illness. Although some mild cases of thalassemia may even go untreated and cause only minimal anemia and iron deficiency problems, other more severe types may lead to death. Regular blood transfusions are used in thalassemia cases [2].

The two predominant thalassemia classifications are alpha and beta thalassemia, which are then split in to more subtypes[3]. Beta thalassemia (β thalassemia) are variants of thalassemia triggered by decreased or absent hemoglobin beta chains that contribute to different results from severe anemia to clinically asymptomatic individuals. It is estimated that the average annual incidence is one in 100,000. Beta thalassemia is caused by chromosome 11 defects in the hemoglobin subunit Beta (HBB) gene inherited as autosomal recessive. The magnitude of the illness depends on the nature of the defect[4].

The incapacity of the body to create new beta chains leads to HbA underproduction. Overall HbA reductions available to fill red blood cells in turn lead to microcytic anemia. Lastly, microcytic anemia develops due to inadequate HBB protein for adequate red blood cell function [5] . Due to this factor, blood transfusions may be needed in the patient to compensate for blockages in the beta-chain. Repeated blood transfusions may lead to iron overload, which eventually leads to iron toxicity. This iron toxicity can cause several problems, including myocardial siderosis and heart failure, which can lead to death.[6]. In patients with β-thalassemia syndromes, pathologic iron-regulatory hormone hepcidin inhibition results in inadequate iron absorption that leads to oxidative damage and serious medical problems including liver , endocrine, renal and other systems [7]. Hepcidin, a 25-amino acid peptide hormone completely synthesized within the liver, is considered a key regulator for iron homeostasis and is stimulated by infection and inflammation [8]Hepcidin mediating regulatory effect through Ferroportin receptor (Fpn) on iron absorption from the intestine and recycling in MQ and RES. This activity effectively reduces free serum iron, promote production of ferritin [9].Hepcidin acts by attaching to ferroportin. The only established exporter of cellular iron that contributes to ferroportin degradation in lysosomes [10]. Erythroferrone is a glycoprotein hormone. It is a member of the C1q-tumor necrosis factor–related family of proteins, and function as the main hepcidin feedback negative regulator in cases with stress erythropoiesis such as cases of anemia with ineffective erythropoiesis [11]. Aim of the study to spotlight on role of erythroferrone and its relationship with hepcidin in B-thalassemia patients (major-intermedia).

## MATERIALS AND METHODS

This Prospective case-control study was conducted on 50 cases. their age ranged between 20 to33 years old they were 24 males and 26 females, scheduled for measurement of erythroferrone and hepcidin in B-thalassemia patients after approval of Al-Azhar Faculty of Medicine for girls Ethics Committee and a written informed consent from all participants in this research. A code number for each patient was used, symbols to the name and address that were kept in a special file.

Exclusion criteria were blood transfusion in the past 4 weeks, diabetes, obesity, current pregnancy, participation in any experimental drug trials and underlying chronic inflammatory disorder. Exclusion β-thalassemia minor cases as were not subjected for blood transfusion so do not lead to iron overloading. Exclusion children cases as they were newly diagnosed and were not subjected for excess blood transfusion that lead to iron overloading.

Subjects were allocated into two groups, 25 patients in each. Group I (patient group): 25 β-thalassemia patients. They were selected then classified into group-Ia and group-Ib. Group-Ia was 13 adult β-TM patients and Group-Ib was 12 adult β-TI patients. Group II (control group): there were 25 healthy age and sex-matched subjects were selected and included in our study. For each patient, medical and surgical history was evaluated including demographic data, family history of thalassemia ,age of onset of the disease, disease duration, age of start of blood transfusion, frequency of blood transfusion ,history of splenectomy, or liver diseases, type of therapy received, including chelation therapy (type, dose, age of start and compliance). Clinical examination was performed for Vital signs, anthropometric measures, signs of thalassemic feature and abdominal examination for hepatosplenomegaly. Routine laboratory investigations were assessed including complete blood picture, measuring Iron profile (serum iron, ferritin, transferrin saturation and TIBC). Serum hepcidin and erythroferrone levels were measured in all cases and control. From each subject 6ml venous blood sample was withdrawn and divided into 2 specimens:

- Four ml blood was added to plan tube and left to clot in water bath (37C°) for 30 min, then centrifuged at 2000 rpm for 15 minutes. Then the serum collected and divided into 2 aliquots. One for measuring serum iron and ferritin and. The second aliquot was stored at –20C° for subsequent measuring of serum Hepcidin &Erythroferrone.
- Two ml of blood was added to EDTA tube for measuring CBC.

Hepcidin and erythroferrone were measured in serum samples with Enzyme Immunoassay (ELISA) using DRG Kit (kit was supplied by DRG Inc., USA, EIA 2395) for measurement of Hepcidin and ERFE in serum of all patients and controls. On ELISA system (Reader A3 1851& Washer 909) from das (Italy).

**Statistical analysis**

The collected data was revised, coded, tabulated and organized using SPSS v25 (IBM, USA). Shapiro-Wilks test was used to test the normality of our data and all our data were normally distributed so non-parametric data can expressed as numerical data. Numerical variables were presented as mean and standard deviation (SD) and compared utilizing unpaired Student's t- test. Categorical variables were presented as frequency and percentage (%) and were compared utilizing the chi-square test. Pearson's rho coefficient of correlation (r) was used to calculate the degree of correlation between 2 variables. The p-value was considered significant if it was $< 0.05$.

## RESULTS

The present study was conducted on 50 persons, 25 of them were β-thalassemia then classified into group-Ia their mean age ± SD was24.2 ± 2.5 (range 21 - 29 years), and group-Ib. their age was 26.2 ± 3.8 (range 20 - 33 years). They were 10 males (40%) and 15 females (60%)). In addition to 25 apparently healthy individuals as control group of matched age and gender, their mean age ± SD was 26 ± 4(range 25 - 35 years). They were 12 males (48%) and 13 females (52%) (Table 1). There was significant increase in erythroferrone in G Ia and G Ib when compared to a

control group while hepcidin show significant decrease in G Ia G Ib when compared to a control group (P value <0.001). They showed a non-significant change in erythroferrone and hepcidin between GIa and GIb (P value =0.071, 0.06 respectively) (Figure 1 and 2). There was significant increase in serum ferritin, TIBC, Serum iron and TS in G Ia and G Ib when compared to a control group (P value <0.001), showed highly significant increase in serum ferritin, TIBC, Serum iron and TS in G Ia when compared to G Ib (P value <0.001)([Table (4)). Also, there was highly significant decrease of HB, MCV, MCHC in group Ia, Ib (P value <0.001) while RDW showed highly significant increase when compared to a control group (P value <0.001). Platelet and WBCs counts showed non-significant difference (Table 2 and 3). There was negative significant correlation between hepcidin and RDW, significant positive correlation with MCH, MCV. However, there was no correlation between other parameters (HB, WBC, ferritin, TS, TIBC, Iron, and Erythroferrone) (Table 5). There was negative significant correlation between erythroferrone and MCV, MCH, significant positive correlation with ferritin, transferrin saturation, serum iron, RDW and platelet. However, there was no correlation between other parameters (HB, MCHC, WBC, TIBC, and Hepcidin) (Table 6).

**Table (1): Comparison of age and sex between G-I a, G Ib and, GII**

| | Group Ia (n =13) | Group Ib (n = 12) | Group II (n = 25) | P value |
|---|---|---|---|---|
| **Age** | | | | |
| Mean ± SD<br>Range | 24.2 ± 2.5<br>21– 29 | 26.2 ± 3.8<br>20-33 | 26 ± 4<br>25-35 | 0.105 |
| **Sex** | | | | |
| Male<br>Female | 5 (38.46 %)<br>8 (61.54 %) | 5 (41.66 %)<br>7 (58.34 %) | 12(48%)<br>13 (52%) | 0.351 |

**Table (2): Comparison of complete blood count parameters between G Ia and G II**

| | Group Ia (n = 13) | Group II (n = 25) | P value |
|---|---|---|---|
| **Hb** | | | |
| Mean ± SD<br>Range | 6.99 ± 1.21<br>4 –8 | 14.15 ± 1.42<br>12.1– 17.4 | 0.001* |
| **MCV** | | | |
| Mean ± SD<br>Range | 67.74 ± 10<br>42.8 – 81.7 | 76.3 ± 6.41<br>60 – 86.4 | 0.001* |
| **MCH** | | | |
| Mean ± SD<br>Range | 22.78 ± 3.3<br>15.9 – 30.5 | 27.69 ± 2.52<br>20.8 – 31.3 | 0.001* |
| **MCHC** | | | |
| Mean ± SD<br>Range | 33.98 ± 8.06<br>30.1 – 61.5 | 36.21 ± 0.91<br>33.4 – 38.6 | <0.001* |
| **RDW** | | | |
| Mean ± SD<br>Range | 28.3 ± 5.7<br>19 – 38.2 | 15.7 ± 2.4<br>5.5 – 13.5 | 0.001* |
| **Platelets** | | | |
| Mean ± SD<br>Range | 278.8 ± 84.8<br>149000 – 430000 | 226.04 ± 79.5<br>95000 – 472000 | 0.245 |
| **WBC** | | | |
| Mean ± SD<br>Range | 9.15± 3.06<br>4100 – 13310 | 8.21± 2.2<br>4400 – 13430 | 0.056 |

*significant as P value <0.05, Hb: hemoglobin, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, MCH: mean corpuscular hemoglobin, RDW: red cell distribution width, WBC: white blood cell.

**Table (3): Comparison of complete blood count parameters between G Ib and G II**

| | Group Ib (n = 13) | Group II (n = 25) | P value |
|---|---|---|---|
| **Hb** | | | |
| Mean ± SD<br>Range | 7.72 ± 0.7<br>5.9– 10 | 14.51 ± 1.42<br>12.1– 17.4 | 0.001* |
| **MCV** | | | |
| Mean ± SD<br>Range | 66.93 ± 6.7<br>52.5– 77 | 76.3 ± 6.41<br>60 – 86.4 | 0.001* |
| **MCH** | | | |
| Mean ± SD<br>Range | 20.1 ±2.3<br>15.9 – 23.6 | 27.69 ± 2.52<br>20.8 – 31.3 | 0.001* |
| **MCHC** | | | |
| Mean ± SD<br>Range | 30.03± 1.5<br>27.9 – 33.1 | 36.21 ± 0.91<br>33.4 – 38.6 | 0.001* |
| **RDW** | | | |
| Mean ± SD<br>Range | 29.7 ± 5.04<br>21.2 – 37.5 | 15.7 ± 2.4<br>5.5 – 13.5 | 0.001* |
| **Platelets** | | | |
| Mean ± SD<br>Range | 226.04 ± 79.5<br>122000 – 429000 | 226.04 ± 79.5<br>95000 – 472000 | 0.245 |
| **WBC** | | | |
| Mean ± SD<br>Range | 8.21± 2.25<br>4400 – 13410 | 8.21± 2.2<br>4400 – 13430 | 0.056 |

*significant as P value <0.05, Hb: hemoglobin, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, MCH: mean corpuscular hemoglobin, RDW: red cell distribution width, WBC: white blood cell.

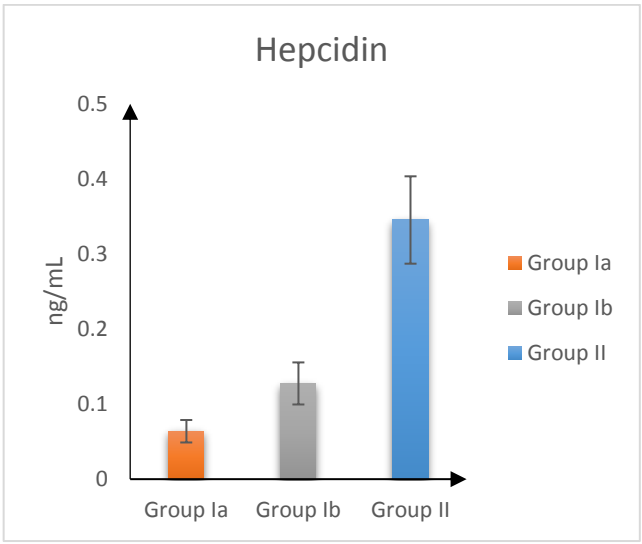


**Figure 1: Comparing GIa vs. G Ib vs GII as regard Hepcidin level**

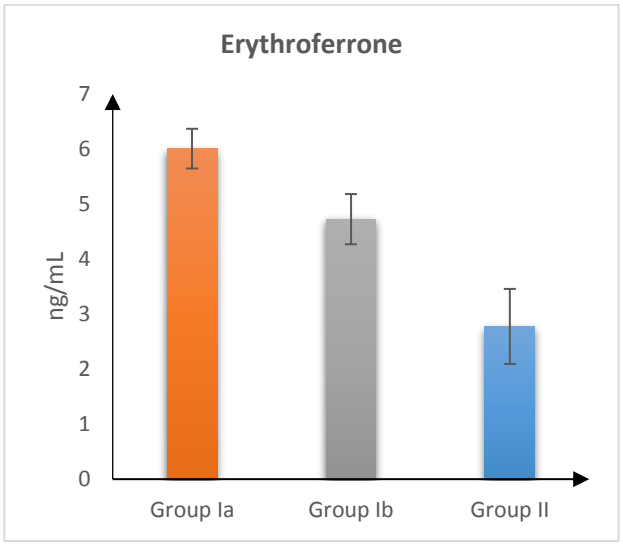


**Figure 2: Comparing GIa vs. G Ib vs GII as regard Erythroferrone level**

**Table (4): Comparison of iron profile between the studied groups**

| | Group Ia (n = 13) | Group II (n = 25) | P value |
|---|---|---|---|
| **Serum Iron** | | | |
| Mean ± SD<br>Range | 320± 22.8<br>280 – 350 | 80 ± 7.6<br>60 – 100 | 0.001* |
| **Total Iron Binding Capacity** | | | |
| Mean ± SD<br>Range | 400 ± 15.7<br>380 – 430 | 300 ± 13.2<br>270 – 330 | 0.001* |
| **Ferritin** | | | |
| Mean ± SD<br>Range | 3311.5± 615.8<br>2120 – 4151 | 44.12 ± 12.07<br>25 – 69 | 0.001* |
| **Transferrin saturation** | | | |
| Mean ± SD<br>Range | 79.6 ± 6.8<br>66– 88 | 25.4 ± 3.3<br>20 – 31 | 0.001* |
| | **Group Ib (n = 12)** | **Group II (n = 25)** | **P value** |
| **Serum Iron** | | | |
| Mean ± SD<br>Range | 260± 12.4<br>240 – 290 | 80 ± 7.6<br>60 – 100 | 0.001* |
| **Total Iron Binding Capacity** | | | |
| Mean ± SD<br>Range | 370 ± 9.7<br>340 – 390 | 300 ± 13.2<br>270 – 330 | 0.001* |
| **Ferritin** | | | |
| Mean ± SD<br>Range | 1520± 404.2<br>890 – 2100 | 44.12 ± 12.07<br>25 – 69 | 0.001* |
| **Transferrin saturation** | | | |
| Mean ± SD<br>Range | 70.7 ± 4.5<br>61– 78 | 25.4 ± 3.3<br>20 – 31 | 0.001* |
| | **Group Ia (n = 13)** | **Group Ib (n = 12)** | **P value** |
| **Serum Iron** | | | |
| Mean ± SD<br>Range | 320± 22.8<br>280 – 350 | 260± 12.4<br>240 – 290 | 0.001* |
| **Total Iron Binding Capacity** | | | |
| Mean ± SD<br>Range | 400 ± 15.7<br>380 – 430 | 370 ± 9.7<br>340 – 390 | 0.001* |
| **Ferritin** | | | |
| Mean ± SD<br>Range | 3311.5± 615.8<br>2120 – 4151 | 1520± 404.2<br>890 – 2100 | 0.001* |
| **Transferrin saturation** | | | |
| Mean ± SD<br>Range | 79.6 ± 6.8<br>66– 88 | 70.7 ± 4.5<br>61– 78 | 0.001* |

*significant as P value <0.05

**Table (5): Correlations of hepcidin with other parameters in patients**

| Parameters | Coefficient of correlation (r **) | P value |
|---|---|---|
| **Hb** | 0.0907 | 0.213 |
| **MCV** | 0.472 | 0.001* |
| **MCH** | 0.609 | 0.001* |
| **MCHC** | 0.330 | 0.022* |
| **RDW** | -0.792 | 0.001* |
| **WBC** | -0.238 | 0.103 |
| **Platelets** | -0.391 | 0.006* |
| **Ferritin** | -0.0903 | 0.728 |
| **Transferrin saturation** | -0.124 | 0.634 |
| **TIBC** | 0.087 | 0.312 |
| **Serum Iron** | 0.062 | 0.113 |
| **Erythroferrone** | -0.032 | 0.543 |

** Pearson's rho coefficient of correlation, *significant as P value <0.05, Hb: hemoglobin, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, MCH: mean corpuscular hemoglobin, RDW: red cell distribution width, WBC: white blood cell, TIBC: total iron binding capacity.

**Table (6): Correlations of erythroferrone with Other Parameters in patients.**

| Parameters | Coefficient of correlation (r **) | P value |
|---|---|---|
| **Hb** | 0.056 | 0.117 |
| **MCV** | -0.455 | 0.001* |
| **MCH** | -0.567 | 0.001* |
| **MCHC** | -0.247 | 0.092 |
| **RDW** | 0.72 | 0.001* |
| **WBC** | 0.229 | 0.118 |
| **Platelets** | 0.405 | 0.004* |
| **Ferritin** | 0.915 | 0.001* |
| **Transferrin saturation** | 0.933 | 0.001* |
| **TIBC** | 0.105 | 0.543 |
| **Serum Iron** | 0.522 | 0.001* |
| **Hepcidin** | -0.032 | 0.543 |

** Pearson's rho coefficient of correlation, *significant as P value <0.05, Hb: hemoglobin, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, MCH: mean corpuscular hemoglobin, RDW: red cell distribution width, WBC: white blood cell, TIBC: total iron binding capacity.

## DISCUSSION

The β-thalassemia is considered as the most widespread chronic hemolytic anemia with the highest incidence of occurrence of carriers. [12]iron excess is the leading cause of morbidity and mortality in β-thalassemia-dependent transfusion patients. Because the body has no excretion system, uncontrolled iron load causes damage to several organs through excess iron loading in cells and macrophages [13]. Many studies and research showed that Optimal chelation therapy reduces long-term follow-up morbidity and mortality risk. These can be achieved by appropriate iron overload evaluations, iron toxicity and optimal follow-up on effective iron chelation medication consequences.[14]. Erythroferrone (ERFE) is a glycol-protein hormone which acts as an erythropoietin (EPO) responsive 'erythroid regulator' element. [15].

Our results according RBCs indices and Hb pattern assay in line with (Ezzat et al., 2016)[16] study concluded that β-Thalassemia patients had reduced Hb levels (mean 8.4 g/dl) when compared to control groups(mean 11.3 g/dl). Also Aboul-Enein et al., 2015 [17], study declared that β-TM patients had reduced Hb levels (<7 g/dl) when compared to control groups Hb levels (> 13 g/dl).

Regarding pre-transfusion iron overload parameters in the present study, we declared that serum ferritin levels were increased in β- TM patients and TI patients (mean was 3311 ng/ml, 1520 ng/ml) respectively when compared to normal controls (mean was 44 ng/ml). Similar to our results Pratummo et al [18]who studied serum ferritin levels which were markedly increased in β-thalassemia patients when compared to normal controls. Also Kaddah et al, [19] concluded that pre-transfusion serum ferritin mean was significantly increased in the β- TM group when compared to β- TI.

Our results regarding TS% were increased in β- TM patients and TI patients (mean was79.6 % and 70.7 %) respectively when compared to normal controls (mean was25.4 %). Same previous findings were also

reported by Mohapatro et al [20], who studied TS% and iron overload effects in β-Thalassemia patients and reported a significant increase in TS% (mean was 73.98 %).

Regarding pre-transfusion serum hepcidin levels in the present study, there was maximum decrease in β-thalassemia patients (group Ia, Ib) (mean was 0.06 ng. /ml,0.12 ng. /ml) when compared to normal controls (group II) (mean was 0.36 ng. /ml). similar to our study, studies by Haghpanah et al and Aboul-Enein et al [17, 21] on β-TM patients, those declared that the peripheral expression of hepcidin messenger RNA (mRNA) was downregulated among their β-thalassemia patients compared to healthy controls. On the other hand, Jawad [22] who studied hepcidin regulation in poly-transfused β-TM patients, declared that the pre-transfusion serum hepcidin mean was almost similar in their β-TM patients and normal controls explanation of controversy that the serum hepcidin levels were similar in both, thalassemic patients and controls, because these patients were on chelation therapy.

In our study, pre-transfusion ERFE levels showed a marked increase in β-thalassemia patients (group Ia, Ib) (mean was 6.0,4.7 ng. /ml) when compared to our controls (group II) (mean was 2.7 ng. /ml). Similar results were found in studies by Jiang et al [23] on β-thalassemia mice. They showed that ERFE was rapidly increased in mice under Phenylhydrazine induced hemolytic anemia

We found that ERFE level showed significant positive correlation with ferritin, the estimated TS%, RDW, Plat and Statistically significant negative correlation with MCV, MCH but there was no correlation between Erythroferrone and Hepcidin, WBC, MCHC, Hb.Concerning the relation between ERFE and the degree of total iron burden, Kautz et al [15] mice studies show that ERFE plays an important role in hepcidin suppression and erythropoietic regeneration after a short hemorrhage or an acute hemolytic attack because Hepcidin suppression occurs by increased erythropoietic activity underlies the development of iron overload in inherited anemias with ineffective erythropoiesis. Comparing serum erythroferrone levels to different patients showed no correlations to hepcidin. But it was demonstrable that those with low serum ERFE had higher hepcidin than those with high serum ERFE. Similar results were found in study done by Kautz et al.[15] and another study by Latour et al [24] . As regards ERFE relation with iron regulation and metabolism, a study by Pasricha et al [25]in human patients with chronic kidney disease on hemodialysis, showed that ERFE correlated inversely with hepcidin. they concluded that ERFE is involved in iron metabolism by suppressing the elevated hepcidin levels. In contrast with our results, studies by Jiang et al [23] showed that the expression of ERFE occurred early in mice under both acute and chronic induced hemolysis. ERFE in their study did not correlate with serum iron as it was normal early and only started to significantly elevate late with chronic hemolysis.

Also, we found that hepcidin level showed significant negative correlation with RDW and Statistically significant positive correlation with MCV, MCH but there was no correlation between ERFE, ferritin, TS% and Hepcidin. Very similar to ours, Haghpanah et al [21] found that in TM patients, there were non-significant correlations between pre-transfusion serum hepcidin and both ferritin levels and Hb%.Similar findings were also reported by Aboul-Enein et al [17]. In disagreement with ours, a study by Kaddah et al [19] in β-TM patients concluded that serum hepcidin levels correlate positively with serum ferritin that claimed due to small sample size in his study

## CONCLUSION

Expression of ERFE is altered in multi transfused β thalassemia patients. Extended studies should be performed to assess its discriminative ability between β thalassemia major and minor. Accordingly, we recommend careful selection of patient at time of diagnosis before blood transfusion to evaluate hepcidin level and S. erythroferrone as a benchmark for patients' body iron status.

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**Conflict of Interest:** The authors declared there is no **Conflict** of interest to be declared

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# الملخص العربي

## مستوي الاريثروفيرون في مرضى أنيميا البحر المتوسط

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**ملخص البحث**

**الخلفية:** مرضي انيميا البحر المتوسط يحتاجون الي نقل دم بصوره متكررة مما يؤدي الي زياده نسبه الحديد في الجسم مما يزيد من اثاره الجانبية .الهيبسيدين يتواجد مع زيادة امتصاص الحديد بالجسم .تراكم الحديد داخل اعضاء الجسم يؤدي الي مضاعفات عديده. هرمون الاريثروفيرون يساعد علي تنظيم التمثيل الغذائي للحديد بتأثيره علي الهيبسيدين.

**الهدف** :القاء الضوء علي الاريثروفيرون وعلاقته بالهيبسيدين وتأثيره علي انيميا البحر المتوسط (العظمي والمتوسطة).

**الطرق :** أجريت هذه الدراسة في مستشفيات جامعة الازهر في قسم الباثولوجي الاكلينيكي والهدف من الدراسة بحثي علمي. ان الدراسة تتكون من 50 شخص تم وضعهم في مجموعتين. المجموعة الاولي :تحتوي علي 25 مريض من نوع البيتا من انيميا البحر المتوسط العظمى، حيث ان 13 مريض منهم كانوا أنيميا البحر المتوسط العظمي و ال 12 مريض الاخرين كانوا انيميا البحر المتوسط المتوسطة. المجموعة الثانية: تحتوي علي 25 شخصا سليما. تم سحب عينات دم من افراد كلا المجموعتين لعمل التحاليل المعملية التالية: صورة دم كاملة وقياس مستوي الهيبسيدين ومستوي الاريثروفيرون .

**النتائج:** كان هناك زياده ملحوظه في نسبه الاريثروفيرون في المجموعة الاولي .بينما كان هناك نقص ملحوظ في نسبه الهيبسيدين في المجموعة الاولي مقاربه بالمجموعة الثانية .كان هناك ايضا زياده في نسبه الفيريتين والنسبة الكلية المحملة من الحديد و نسبه الحديد ونسبه إشباع الترانسفرين في المجموعة الاولي مقارنه بالمجموعة الثانية .وكان هناك علاقه سلبيه ملحوظه بين الهيبسيدين و فحص تعداد الدّم .وكان هناك علاقه سلبيه بين الاريثروفيرون ومتوسط حجم كرات الدم وكذا متوسط الهيموجلوبين في كرات الدم.

**الاستنتاجات:** ان الاريثروفيرون يتغير في مرضي انيميا البحر المتوسط مع تعدد مرات نقل الدم.

**الكلمات المفتاحية:** الاريثروفيرون، الهيبسيدين، انيميا البحر المتوسط، نسبه اشباع الترانسفيرين.

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