Original Article

Ferritin Relationship with Clinical Changes Nutrient Elements, Vitamins D & C and Liver, Kidney Functions in β-Thalassemia Major Patients

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ABSTRACT

Objective: The current study was carried out to study ferritin levels and their effect on nutrient and Vitamins C&D levels in patient with beta thalassemia major.

Study Design: Case series study

Place and Duration of Study: This study was conducted at the Department of Biochemistry, Thalassemia Center for Genetic Blood Diseases in Thi Qar University, southern Iraq from November 2023 to April 2024.

Methods: Current study studied 48 cases of beta thalassemia major and 44 healthy as controls, aged range (8-22) years. Biochemical and hemotograte ferritin, calcium, potassium, iron, sodium, D and C vitamins. Enzymes were measured: alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, urea, creatinine and total Bilirubin levels.

Results: The study found highly statistically significant in ferritin (1624.81 µg/L) and a significant decrease in hemoglobin (Hb) levels (7.205 g/dL) vitamins D and C recorded 17.319 µg/L, 1.202mg/dl respectively, also a significant increase in AST (39.38 IU/L) , ALT (58.71 IU/L)and TSB (2.52 mg/dL), and a decrease in ALP(73.90IU/L) ,urea (27.01mg/dL) and Creatinine (0.80mg/dL), also calcium (3.03 mg/dL), (P > 0.05) and potassium (3.08mmol/L) and a significant increase in sodium (139.14 mmol/L) and iron (164.47µg/dL) in patients compared to healthy group.

Conclusion: The present study showed differences in ferritin, calcium, potassium, sodium, ions, and vitamins D and C content in the serum of beta thalassemia patients compared with the control group

Key Words: Nutrients, Ca, K, Na, Iron, Vitamins D & C.

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INTRODUCTION

β-Thalassemia major an inherited disease that is transmitted from parents to children through genes. It is a defect in biosynthesis of hemoglobin leads to inactive of erythropoiesis hence leads to severe anemia, β-Thalassemia is often diagnosed in the first six months of life. The newborn, and it may be fatal if the patient does not receive appropriate treatment[1]. Main cause of death is heart failure, because iron overload. The patient's symptoms of thalassemia appear on patient in first months of life because a defect and rapid breakdown of erythrocytes[2]. Symptoms of strong anemia are as follows: yellowing of skin color with pale, delayed growth, poor appetite, and infections.[3] As anemia continues, other pathological symptoms are observed, change in bone shape, especially the cheeks bones and face.[4] Regular blood transfusions and iron chelation therapy It led to a significant improvement in survival and quality of life in beta thalassemia patients dependent on blood transfusion, but it led to the emergence of multiple complications, including the kidneys Abnormalities and diseases of the liver and heart and deficiency of some important nutrients for the body[5]. A significant increase in low molecular weight proteinuria or decreased levels of some important nutrients and biochemical variables that are signs of other diseases.[6] The current study was carried out to determine effect of increasing ferritin levels in serum of patients with β- thalassemia major on enzymes, biochemical liver and kidney function parameters and some essential nutrients, sodium, potassium, and iron compared to healthy subjects Vitamin D is a fat-soluble vitamin found in many natural products. It can be synthesized in the body with the help of skin exposure

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to sunlight. Vitamin D is an essential factor for calcium metabolism[7]. Low levels of vitamin D in children and adolescents with beta-thalassemia cause multiple bone problems. Vitamin C, or ascorbic acid, is a water-soluble vitamin. Vitamin C easily reaches the body's tissues but is not stored well. .Vitamin C is a good antibacterial and antifungal, and is important antioxidant that can neutralize harmful free radicals.[8]

METHODS

48 patients with beta thalassemia 29 males and 19 females and 44 healthy people as a control group 22 males and 22 females. Referring to Thalassemia Center for Genetic Blood Diseases in Thi Qar province, southern Iraq, during from November 2023 to April 2024. Consent was provided by all Volunteers in study Diagnosis of disease was made on the basis of clinical features, Hb-electrophoresis, and frequent blood transfusion.

Exclusion of study: Patients with thyroid dysfunction, diabetes, kidney failure diseases, genetic diseases other than beta thalassemia major.

Sample Collection: Blood samples were collected early in the morning . Where 5 ml divided into two parts, whole blood for measured complete blood count. The other part is put in clean, dry test tubes for five minutes, then serum was separated at 4000 rpm, frozen serum is stored and frozen at temperature -80°C Determination of hemoglobin.by a Coulter LH 750 auto analyzer

Determination the ferritin

Determination Calcium, Sodium, Potassium, iron and D, C vitamin

Determination AST, ALT and TSB

Determination Serum Creatinine and Urea[9]

Statistical analysis: The statistical method ANOVA was used and Pearson correlation coefficients, p-value level of $p < 0.05$ and $p < 0.001$. Conduct statistical analysis using SPSS statistical program, version 23.0.3.

RESULTS

Demographic and clinical of Studied Groups: 92 volunteers in study, age range from 8 to 22 years, were divided into two groups: patients group, (48) and the healthy group (44) as control. Table 1.

Serum ferritin and hemoglobin levels: A highly statistically significant difference P≤0.01 in ferritin between patients (1624.81 µg/L) and control 59.29 a significant decrease at P≤0.01 hemoglobin (7.205 g/dL) in patients compared with (12.85 g/dL) control. Table 2.

Table No.1: β- thalassemia patients and controls

β- thalassemia (n = 48)	Controls (n = 44)	Parameter
Age (years): Mean ± SD	15.22727± 5.102867	14.0625± 5.051428
Sex (%): Male Female	22(50%) 22(50%)	29 (60.42%) 19 (39.58%)

S.D. standard deviation, n : number of subjects.

Table No.2: Ferritin and hemoglobin levels

Parameter Groups	Ferritin (µg/L) Mean ± SD	Hb (g/dL) Mean ± SD
Control (n=44)	12.85a±1.03	59.29 a±20.74
β- thalassemia (n=48)	7.205b±1.82	1624.81b±149.60

Hb: hemoglobin, (a , b) Means having different letters in the same column differed significantly (P≤0.01)

A negative correlation, between ferritin and Hb at β- thalassemia group with correlation coefficient, r= -0.06434. Figure No. 1.

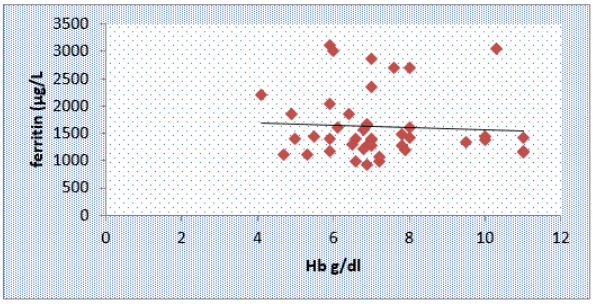

Figure No.1: Ferritin correlation with Hb

Serum Nutrients emements Levels: Increases statistically significant differences in Fe (109.77 µg/dL) and Na (139.14 mmol/L) levels, while decreases statistically significant in Ca (3.03 mg/dL) and K (3.08 mmol/L) at (P>0.05) and (P≤0.01) Comparison with control. Table 3.

Correlations between ferritin in patients with Ca (r= 0.169), a positive correlation, while ferritin with Na (r = 0.0288), a moderate positive correlation, also ferritin with K (r = -0.20695) its a moderate negative correlation and ferritin with Fe (r = -0.00091) a moderate positive correlation. Figure 2.

Table No.3: Nutrient elements levels

Parameter Groups	Ca (mg/dL) Mean ± SD	Na (mmol/L) Mean ± SD	K (mmol/L) Mean ± SD	Fe (µg/dL) Mean ± SD
Control (n=44)	6.63^{a}±2.09	130.74^{a}±6.74	4.144^{a}±1.00	109.77^{a}±11.25
β- thalassemia (n=48)	3.031^{b}±1.02	139.14^{b}±7.60	3.08^{c}±1.21	164.476^{b} ± 21.7

Fe: iron, **Ca:** calcium **Na:** sodium, **K:** potassium, **SD** standard deviation , **n** umber of the subjects

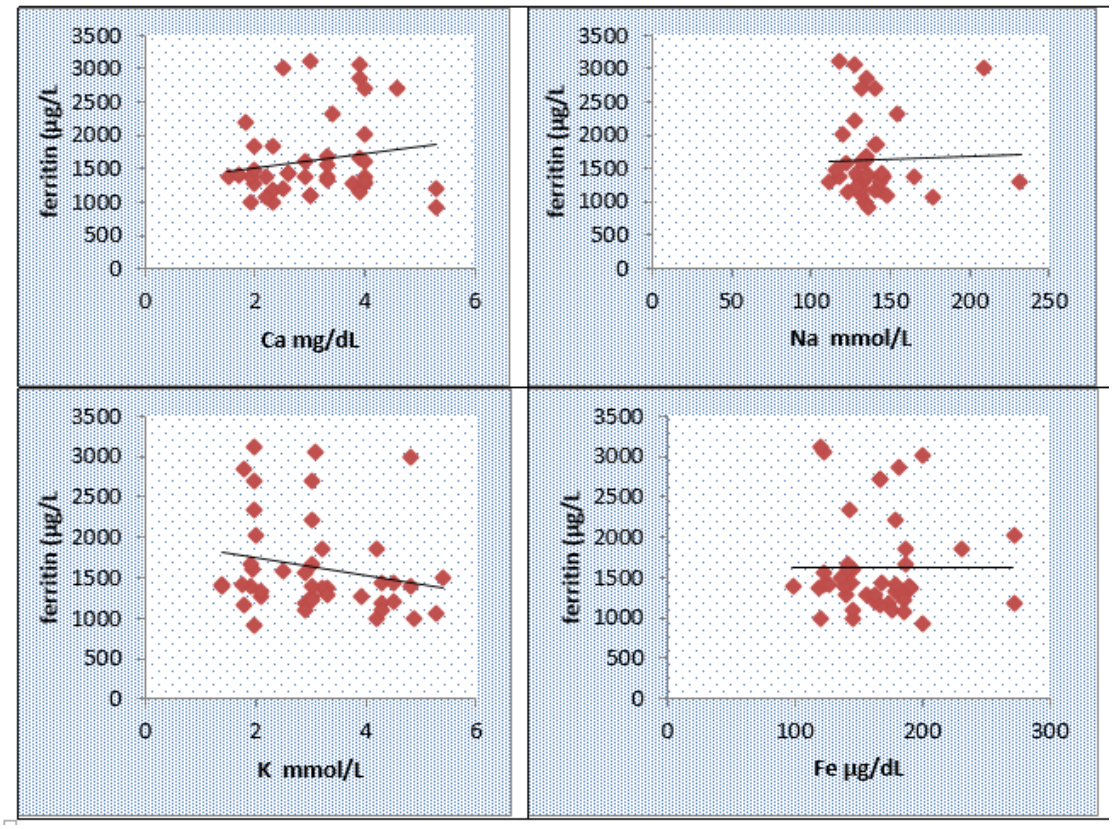

Figure No.2: Ferritin correlation with Ca,Na, K and Fe.

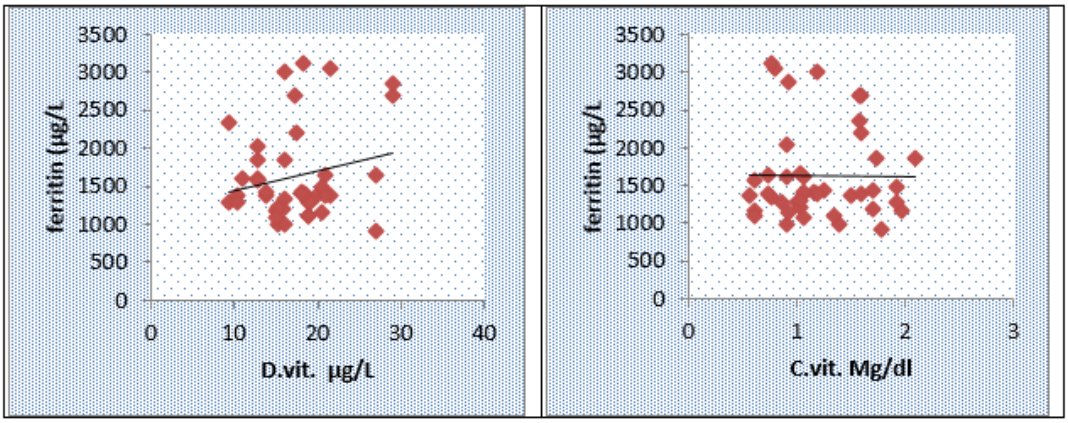

Figure No.3: Ferritin correlation with Ca,Na, K and Fe

Vitamin D, with an average of 17.319µg/L. and vitamin C 1.202 mg/dL in patients compared to controls. see table 4.

Correlation between ferritin in patients with Vit.D a positive correlation (r= **0.2112)**, while ferritin with Vit.C. a negative correlation (r = - 0.0028). Figure 3.

Table No.4: D.vit and C.vit levels

Parameter Groups	**D.vit (µg/L) Mean ± SD**	**C.vit (mg/dL) Mean ± SD**
Control (n=44)	33.82[a]±6.49	1.81 [a]±0.51
β- thalassemia (n=48)	17.31905 [b]±4.74	1.202[c]±0.46

Serum Liver Function parameters Levels: Increases significant of AST, ALT and TSB at (P< 0.01) and high decreases significant of ALP at (P< 0.01) in β- thalassemia patients compared with control. Table 5.

Correlations between ferritin in patients with AST (r= 0.057), a positive correlation , while ferritin with ALT (r = 0.0153), a weaken negative correlation , ferritin with ALP (r = -0.1707) its a moderate negative correlation and ferritin with TSB (r = 0.232631) a weaken negative correlation. the Figure 4.

Table No.5: Kidney Function parameter levels

Parameter Groups	AST (IU/L) Mean ± SD	ALT (IU/L) Mean ± SD	ALP (IU/L) Mean ± SD	TSB(mg/dL) Mean ± SD
Control (n=44)	25.94[a]±8.60	24.86[a]±10.04	90.83[a]±49.83	0.724[a]±0.45
β- thalassemia (n=48)	39.38[b] ± 15.57	58.71[b]±32.67	73.90[b]±27.10	2.52[b]± 1.313

ALT: Alanine transaminase, **ALP:** Alkaline phosphatase, **AST:** Aspartate transaminase, **TSB** : Total Serum Bilirubin

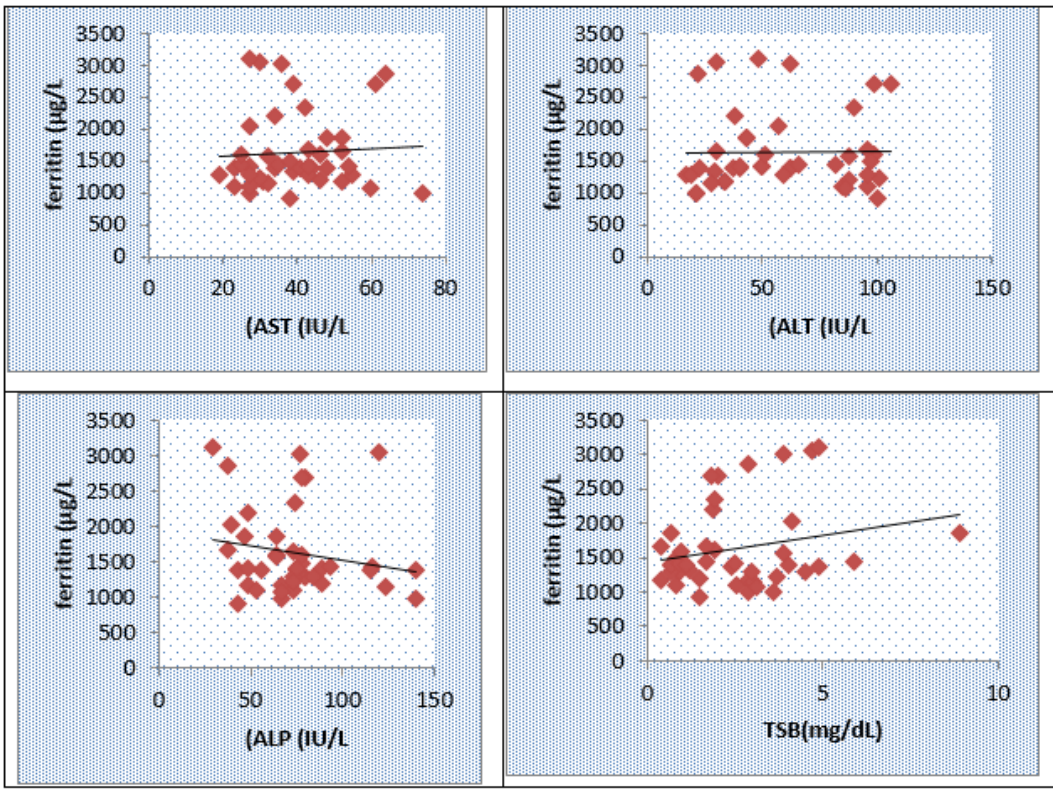

Figure No.4: Ferritin correlation with AST, ALT, ALP and TSB

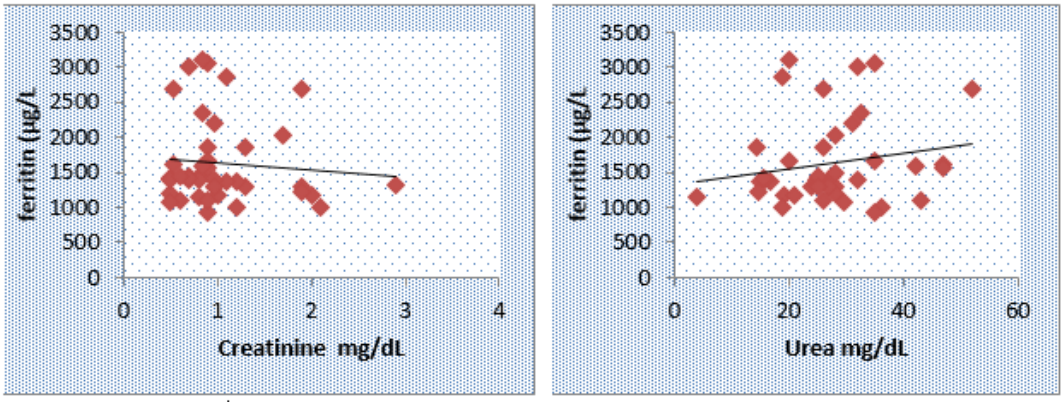

Figure No.5: Ferritin correlation with Creatinine and Urea

Serum kidney Function parameters Levels: A statistically significant increase at (P< 0.01) of creatinine (27.01 mg/dL), while no significant differences at (P< 0.01) in urea (0.80 mg/dL) in β- thalassemia patient compared with control. Table 6. Correlations between ferritin in patients with Urea r=0.179617,while ferritin with Creatinnine (-0.08805). Figure 5.

Table No.6: Urea and Creatinine

Parameter Groups	Urea (mg/dL) Mean ± SD	Creatinine (mg/dL) Mean ± SD
Control (n=44)	12.01[a]±3.83	0.67[a]±0.23
β- thalassemia (n=48)	27.01[b] ± 13.19	0.80[a]±0.17

DISCUSSION

Beta thalassemia is one of the most common genetic diseases in world general and special of Asia. Thalassemia is a disease the formation of dysfunctional red blood cells. The presence of these abnormal erythrocytes stimulates increased iron absorption from small intestine, causing an increase blood iron levels[10]. Iron metabolism, showed thalassemia carriers have a higher levels of iron and ferritin compared to healthy people. thalassemia patients with H63D mutations. Many clinical studies have confirmed low hemoglobin concentration are accompanied a decrease in number of red blood cells and a decrease in values of their specific indicators (MCV, MCH, HCT)[11]. The current study found an increase, iron and ferritin levels in serum beta- thalassemia patients, this results consistent with many other studies. High ferritin content is directly related to accumulation of reactive iron in tissues with beta thalassemia patients. Iron overload leads to another pathological mechanism causes oxidative damage to red blood cell membranes, which is called the second disease.[12] Thalassemia is also accompanied by metabolic dysregulation. Lack of oxygen in cells ,cell damage and all physiological changes lead to ineffective erythropoiesis, hemolysis and anemia. Patients with thalassemia depend on blood transfusion and bone marrow ,transplantation for their survival[13]. A significant increase in sodium (Na), and iron, (Fe) in the studied group, and decrease of calcium (Ca) and potassium the results showed a slight, non-significant increase in Na conc. in beta-thalassemia, patients compared with control group. at ($P > 0.05$). These results are similar to the results of some previous studies[14]. Also decrease in potassium may be because they suffer from hemolysis of erythrocytes, (R.B.C). It occurs in blood has been stored for time periods and is transfused to patient because potassium tends to leak from stored blood. High sodium level in the beta thalassemia group caused damage renal tubules by excess iron levels[15]. Most scientific explanations point to the most important causes of these diseases, which are associated with toxic effects of iron overload associated with blood transfusion[16]. Results are consistent with other studies Dhale et al and Al-Rubae[17] there are several factors cause low concentrations of vitamin D in the serum of beta-thalassemia patients. The most important of these are malnutrition, insufficient exposure to sunlight, bone disorders and liver dysfunction.[18] Some studies have also confirmed that dysfunction of some endocrine glands that affect metabolism in the body, such as the thyroid, causes a deficiency in vitamin D levels. 19 Vitamin C is essential for maintaining, along with vitamin E, an essential role in the antioxidant activity in the body .Vitamin D and calcium are major factors in bone metabolism and play an important role in bone growth and maintenance. Previous studies have shown that patients with β-thalassemia suffer from a significant decrease in vitamin D levels due to excessive iron absorption, which leads to a significant decrease in calcium absorption. Vitamin D deficiency is considered a major cause of bone disease in patients with β-TM and thus anemia and skeletal dysfunction. a significant increase in ALT, AST and decrease ALP and increase in TSB, results are consistent, with studies conducted Navadia et. al.[19] This is due to secondary injury to liver cells and the occurrence of fusion with hepatocytes to deposit iron in the liver. High levels of AST and ALT and low levels of ALP in thalassemia shows muscle and liver dysfunction, studies on kidney health in thalassemia patients have been enhanced. Previous studies confirmed the presence of renal disease in 1.8% of TDT patients and classified renal dysfunction as the fourth most common cause of morbidity. Beta thalassemia, the most serious risk of which is high iron levels due to regular blood transfusion, leads to iron deposition in renal microtubules, glomeruli, and interstitium, leading to renal atrophy, glomerulosclerosis, and interstitial fibrosis[20]. Also, hypoxia and chronic severe anemia lead to an increase in the generation of free radicals of the type ROS, RNS, and the occurrence of oxidative stress, the main cause of many diseases in the body, including tubular cell dysfunction. In addition, iron chelate toxicity can lead to glomerular dysfunction.[21]

CONCLUSION

Current study were conclude increased ferritin in beta thalassemia patients have indirect influence on levels of serum calcium potassium, sodium, ion content, Vitamins D, C, liver enzymes and kidney function parameters.

Significant decrease in values of necessary nutrients in body leaded complications and disorder in kidney and liver with thalassemia patients.

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Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Jamal Harbi Hussein Alsaadi
Drafting or Revising Critically:	Jamal Harbi Hussein Alsaadi
Final Approval of version:	All the above author
Agreement to accountable for all aspects of work:	All the above author

Conflict of Interest: The study has no conflict of interest to declare by any author.

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