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A study effect of Iron overload on Thyroid gland and other tissues in thalassemia patients in najaf city

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Abstract:

This study highlights the effects of iron overload on endocrine glands (Thyroid gland), kidney functions and liver functions in thalassemia patients in Najaf province in Iraq.

One hundred patients suffering from thalassemia were contributed in the current study. Their age range was 3-18 years old. Thirty apparently healthy person were nominated as "control group". Serum iron , liver functions test (AST,ALT,ALP,TSB) and Kidney functions test (Uera& Creatinine) were measured spectrophotometrically while Serum ferritin, was measured using ELISA, Thyroid hormones (T3 & T4) estimation by Using(I-Chroma instrument)

The results indicated significant increase ($p<0.05$) in iron , ferritin and TSB in patients in comparing with healthy control group while liver functions test (AST,ALT,ALP) and Kidney functions test (Uera& Creatinin) were no significant.

We conclude from this study that Thalassemia patients in Najaf city are exposed to the risk of overload and the risk of oxidation. . thalassmic patients are susceptible to tissue damage produced by "oxidative stress". There is no statistically significant correlation noticed between each serum AST,ALT,TSB, Uera and Creatinin with iron status The reason is that these patients continue treatment(Defroxamin) that reduces iron levels in their bodies.

Key words:*Thalassemia, Thyroid hormones, liver functions test and Kidney functions test.*

Introduction:

Mediterranean sea anemia(Thalassemia) is a genetic disease prevalent in most areas of the Middle East[1], especially Iraq, and this disease is a actual problem that began to increase widely. In 2010, the number of patients in Najaf province in Iraq was about 500 patients[2]. and the number increased to 1500 cases in 2018, according to information recorded in Al -Zahraa Teaching Hospital in Najaf province.

The treatment of this disease by blood transfusion to compensate for the deficiency of the amount of globin . continue the process of transfusion leads to increased levels of iron in the body, leading to the risk of injury and oxidation and deposition of iron in the endocrine, liver and kidney, The increase in iron levels leads to the formation of hydroxyl radicle according to the reaction of Fenton.Hydroxyl radical attacks unsaturated fats and has lipid peroxide [1],[2],[3]:

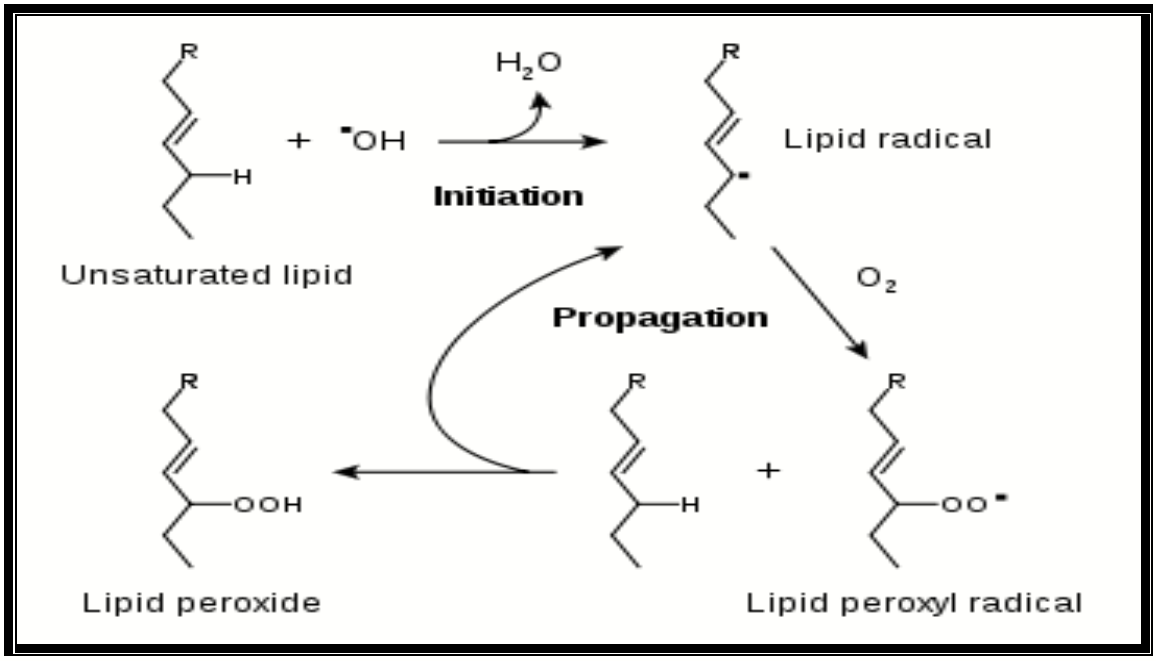

Figure (1) Mechanism of Lipid Oxidation[4]

Subjects and Methods

A-Patients: One hundred "Iraqi patients with β-thalassemia" were contributed in the thist study. Their age about "3-18 years old". These patients were recorded as "β-thalassemic patients in Thallassemia Unit at AL-Zahra'a Teaching Hospital in" Najaf city", Iraq. The diagnosis was established hemoglobin high-pressure liquid chromatography (HPLC) analysis".

These patients were treated by "blood transfusion". Serum CRP "C-reactive protein has been estimated and has been given a negative result (CRP<6mg/L), this means that high ferritin does not return to inflammation [1]. The this study disqualified the patients with apparent "diabetes mellitus, infection and inflammation, heart diseases, and patients from non-Arabic ethnic group". B-Controls: 30 apparently healthy person were nominated as "control group". Their age were similar to that of patients.

Measurements: Blood samples were collected from persons in the morning in plain tubes and the serum separated by centrifugation after clotting. Serum levels of iron were estimated using Ferrozine colorimetric method [5], The ferritin quantitative kit based on a solid phase enzyme-linked immunosorbent assay (ELISA) was supplied by Monobind® Inc. USA [2].

T3 and T4 estimated by ichroma™ T3,T4 respectively**,** the test uses a competitive immunodetection technique , the objective material in the taster attached to the "fluorescence (FL)-labeled detection antibody", to produce the complex . This complex was laden to transfer onto the nitrocellulose matrix, where the "covalent couple of T3 or T4 and bovine serum albumin (BSA) was immobilized on a test strip, and interferes with the binding of target material and FL-labeled antibody If the more

target material exists in blood, the less detection antibody is accumulated, resulting in the less fluorescence signal" [6].

Liver Function tests estimated spectrophotometry, Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) by (Randox kit)[7],while alkaline Phosphatase(ALP) by (Biosystem kit)[8].

Kidney Function test estimated spectrophotometry ,Urea by (Linear kit)[8],while Creatinine by (Biolabo kit)[9].

Results and discussions: The Clinical parameters parameters in thalassemia patients and controls groups as shown in the table(1).

Table(1) The Clinical parameters parameters in thalassemic patients and healthy sets .

Item	Patients Mean± SD	Controls Mean± SD	P. Value
Age	9.35±5.82	9.53±4.62	0.87
Hb	7.83±1.42	11.52 ±1.66	3.37 E-14
PCV	26.5±4.25	37.57±4.98	3.37 E-14
GOT	39.27±29.5	32.3±15.55	0.1461234
GPT	38.1±52.41	30.37±14.25	0.289
ALP	151.9± 144.5	124.5±8.055	0.1487
TSB	1.68±0.71	0.547±0.178	3.894 E-18
Urea	31.55±8.68	33.67±8.479	0.27 14566
Creatinine	0.75±0.258	0.66 ±0.237	0.104
Ferritin	2278.61± 1760.99	129.3±49.879	2.01 E-13
Iron	609.1±332.43	80.47±33.99	4.76E-18
T3ng\ml	1.41±0.358	1.45± 0.33	0.518
T4nmol\l	93.56±10.96	95.169±11.14	0.5196

The results in Table (1) appearances decrease ($p<0.05$) in hemoglobin concentration and PCV in patients comparison with the healthy group.. This result is like with the other study [10].Clinical data approve that Low hemoglobin levels may be associated with decreased the amount of RBC.[2]

In other hand These results are probable in thalassemia which is a irregular of "hemolytic anemia" , "PCV" and hemoglobin decreases. Unbalanced hemoglobin variants characterize a unusual etiology of native hemolytic anemia finding of deranged hemoglobin alternates in kids with abnormal forms of hemolytic anemia, mainly those suffering from beta-thalassemia trait[11].These finding are in accordance with the results of other studies [12]found significant decrease in PCV and Hb% level in value in thalassemia paitents in comparison with controls[12]. The results in Table (1) show a high significant increase ($p<0.05$) in serum iron concentration in thalassemia patients as compared with the control group. These results show iron excess in thalassemia patients due to repeated transfusion and fast hemolysis. Prolonged transfusion therapy lead to iron overload that cause a extensive range of complications due to cardiac , hepatic and endocrine system injury [13]. In

iron excess state, the iron which is originally kept as "ferritin", is placed in tissues as haemosiderin and this is noxious to tissue, lead to oxidative stress [1].
The human body is unable to excrete iron out of the body so the iron level in the body increases with repetitive blood transfusions leading to iron overload [14]. The accumulation of unbounded iron leads to free radical synthesis based on the reaction of Fenton, which causes the risk of oxidation to the body organs [2].
Result of serum ferritin in thalassemia patients than controls explain in figure (1).

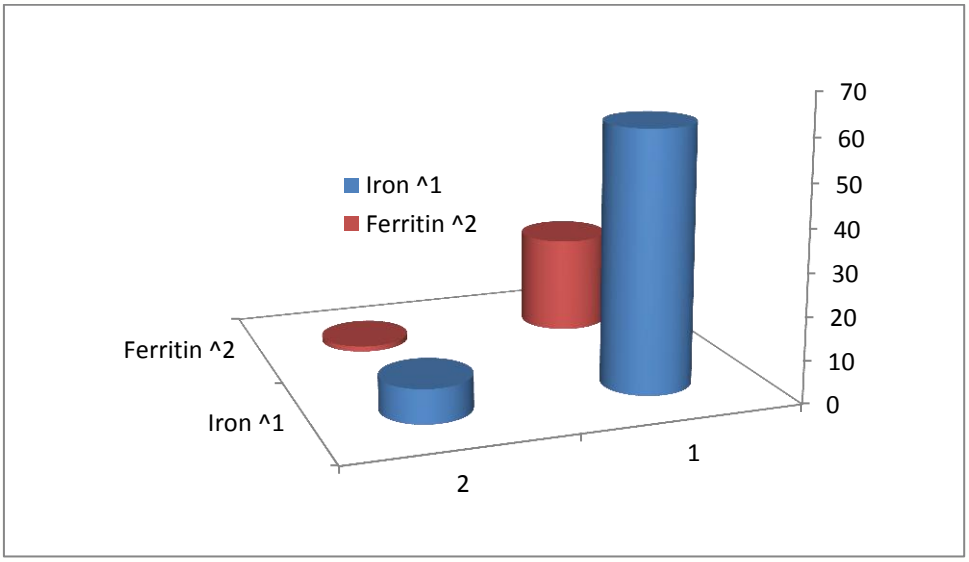

Figure (1): Clinical parameters (Iron and ferritin) in thalassemia patients and controls groups

These results presented a significantly high ferritin level in thalassemia patients in comparison with the healthy group. these results indicate iron overload in the patients group due to the fact that ferritin is used as a marker for iron overload disorders, such as "hemochromatosis" and "hemosiderosis". The signs and symptoms of high ferritin levels include weariness, lethargy, pain in the abdomen, deficiency of sex energy and several heart problems [15].
Result of serum thyroid function (T3, T4) in thalassemia patients than controls explain in table (1) and in figure (2):

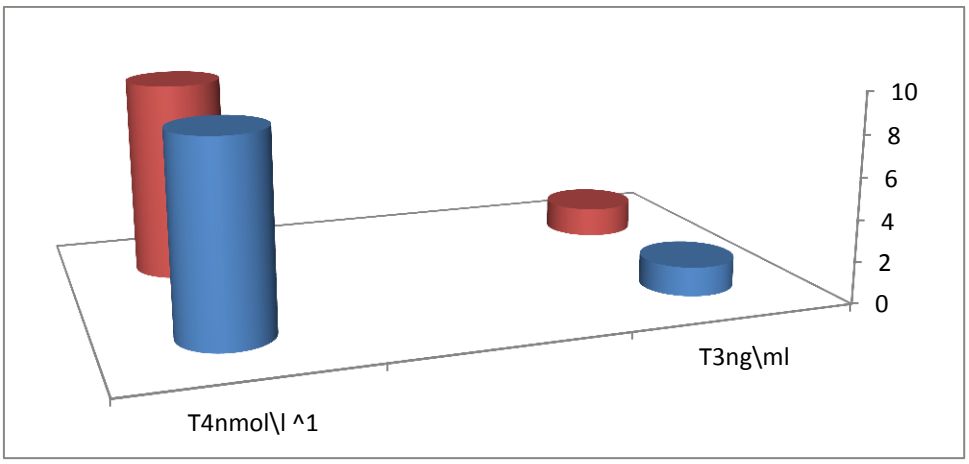

Figure (2): Clinical parameters (T3 and T4) in thalassemia patients and controls groups

thyroid function tests (T3, T4) were near to healthy values. This study included thalassemia patients aged 3 to 18 years and signs of hypothyroidism were evident after the second decade of age, so the outcome was normal[16]

There is no significant difference between patients and control group for both urea and creatinine as indicated in figure(3).

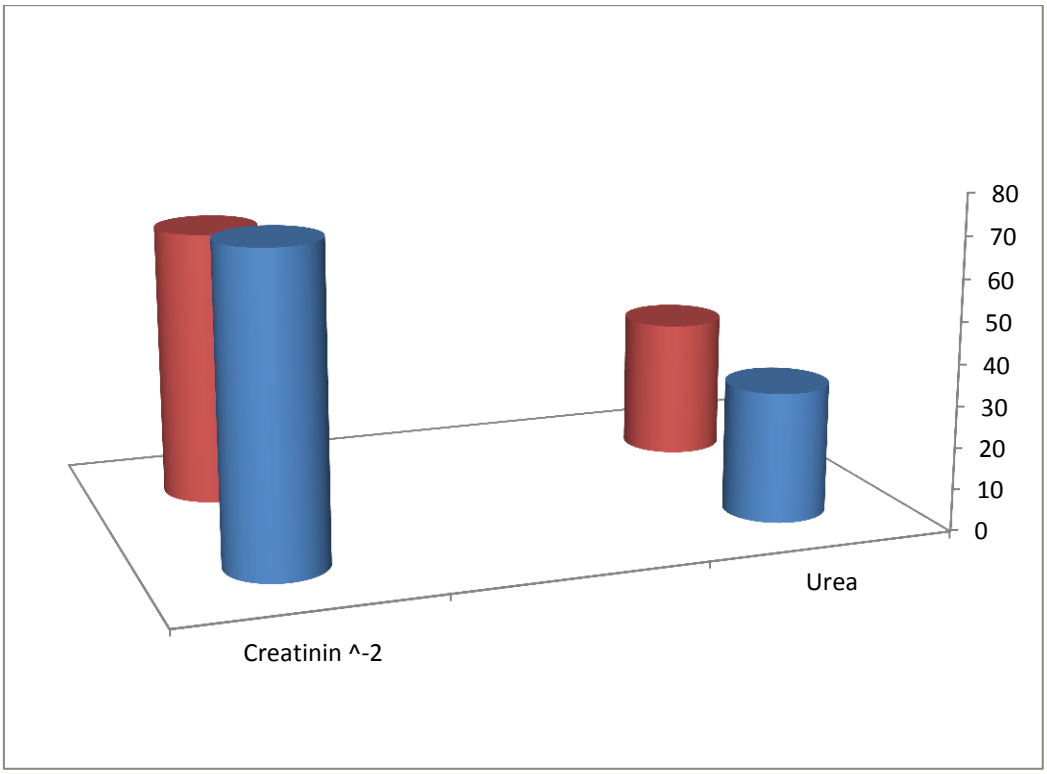

Figure (3): Clinical parameters (Urea and Creatinin) in thalassemia patients and controls groups

This is due to continuous follow-up of patients and adherence to treatment as mentioned in their files.

These results are not consistent with some studies that mention the high level of urea and creatinine in patients with thalassemia compared to healthy people[17].

As for liver function, the study showed no significant difference between control group and patients except (TSB), as shown in the figure (4).

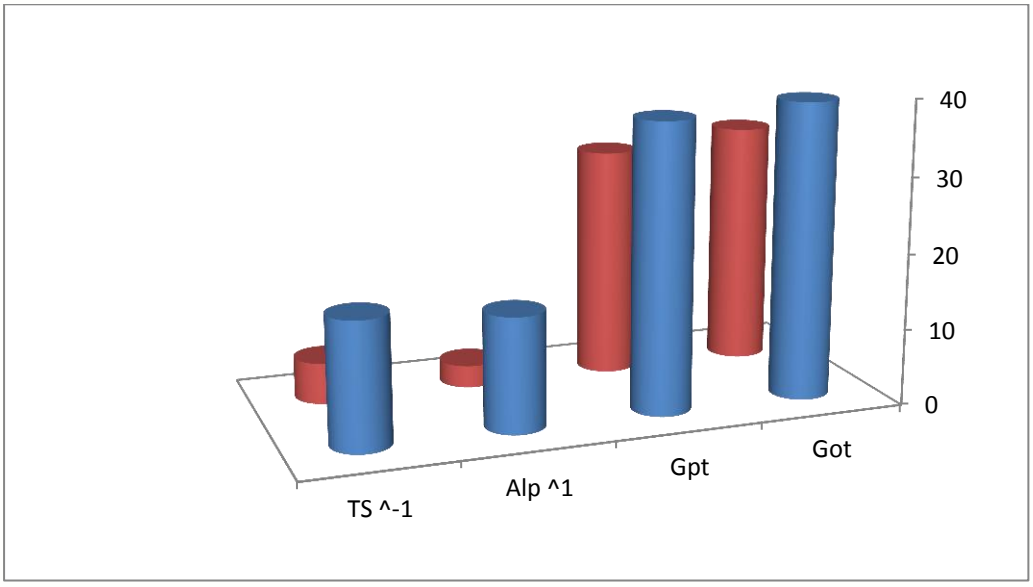

Figure (4): Liver Function Test in thalassemia patients and controls groups

This results proved that the use of chelating agent and the continuous follow-up of patients to remove excess iron leads to the preservation of the integrity of liver cells from damage and the risk of oxidation and thus remain concentrations of liver enzymes within the normal level, this result is consistent with another study[18]
In the other hand this study disagrrement with some other studies that show increased concentrations of liver enzymes in patients with thalassemia due to the effect of excess iron that causes liver tissue damage [19].

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