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Original Article

# The Relationship between Thyroid Hormone Levels and Body Iron Status in Iranian Hypothyroidism Patients

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**A B S T R A C T**

**Backgrounds and Aims:** Thyroid hormones have a crucial physiological role to maintain balance of metabolism of body. Thyroid hormones have an important role in metabolism and proliferation of blood cells. Thyroid gland also has a vital influence on erythropoiesis by induction of erythropoietin secretion and proliferation of erythroid progenitors. In the present study, it was tried to evaluate the effect of hypothyroidism on hematological parameters and also body iron store.

**Materials and Methods:** The research population consisted of 90 subjects divided into two groups: 45 people with hypothyroidism and 45 age-matched healthy individuals. This study checked the amounts of total triiodothyronine (T3), total thyroxine (T4), thyroid stimulating hormone (TSH), and some iron status and hematological parameters.

**Results:** The mean TSH levels were significantly increased in hypothyroid patients compared to control group. On the other hand, the levels of T4 and total iron binding capacity, serum iron, ferritin, Hemoglobin, and Hematocrit were significantly lower in hypothyroid patients compared to control group ($p<0.05$). However, there was no significant difference in the mean of T3 between hypothyroidism and control.

**Conclusion:** Our data suggest that alterations in thyroid status change serum iron metabolism and hematological index. Hypothyroidism is often associated with anemia,depleted body iron store. As there is no significant clinical manifestation of hypothyroidism at earlier stages with anemia, it is advisable to routinely investigate it for early detection allowing its early management.

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## Introduction

Thyroid hormones are critical for normal growth of our body and are supposed as one of the very essential required hormonal factors in regulation of the basic metabolic rate of effective organs like liver, heart, kidney and brain [1]. Thyroid hormone performs a role in haemoglobin synthesis in adults and maturation of haemoglobin in fetus; and hypothyroidism leads to anemia via reducing the oxygenation process through disturbing hematopoietic process [2-4]. It is considered that thyroid hormones influence hematopoiesis through an increase in erythropoietin generation or hematopoietic factors by non erythroidcells. The actions of triiothyronine (T3), similar to the steroid hormones, are mediated through intracellular T3-receptor proteins which perform mainly to modulate transcription by binding to specific T3-response elements in effective genes [5, 6].

Iron deficiency could be defined as happening when the body's iron stores become exhausted and a restricted supply of iron to different tissues becomes apparent [7]. It also leads to depletion of iron-dependent intracellular enzymes participating in numerous metabolic pathways. Studies in animals and also humans demonstrate that iron deficiency with or without anemia impairs thyroid hormone metabolism [8]. Many studies advise that thyroid hormones might affect on erythropoiesis and serum ferritin levels should be confirmed together with iron and transferrin measurements in these cases [9]. Newly, it has been revealed that the serum amount of ferritin is elevated in hyperthyroidism and reduced in hypothyroidism, and also alterations in the serum levels reflect thyroid performance [10].

Hypothyroidism is a clinical disorder caused attributable to the decreased thyroid activity. It is characterized biochemically by a reduction in serum T3 and thyroxine (T4) levels that result in an increase in serum thyroid stimulating hormone (TSH) concentration [1, 11]. Hypothyroidism may cause different types of anemia through decreasing the oxygen metabolism. Microcytic anemia is usually characterized to mal-absorption of iron and loss of iron by menorrhagia;while, macrocytic anemia causes or persuades mal-absorption of vitamin B12, folate, pernicious anemia, and also inadequate nutrition. Anemia that normalizes due to T4 replacement, even in the presence of normal serum iron, vitamin, and folate is found in around 25% of hypothyroid patients [12].

Patients with hypothyroidism have a reduced erythrocyte mass because of decrease of plasma volume and might be undetectable by routine evaluation like hemoglobin concentration; whereas an elevated erythrocyte mass is identified in many hyperthyroid patients [13, 14]. Modification is connected with thyroid malfunctions in other hematological parameters like hemoglobin, mean corpuscular hemoglobin (MCH), hematocrit, mean corpuscular volume (MCV), white blood cell count, and platelet count. It is realized as well, but almost all adjustments return to normal if a euthyroid (normal) condition is acquired [15].

This study was taken to find out effect of hypothyroidism in body iron store in the form of Ferritin, as well as its effect on haematopoiesis by evaluating haemoglobin level and red cell indices.

## Materials and Methods

### Study of population

The study population consisted of 90 adults (aged 19-42 years) divided into two groups: hypothyroid patients who were not on thyroxin or antithyroid drugs at the time of sample collection (n=45), and healthy control subjects (n=45). All the patients and controls were recruited from Isfahan Imam Hossein hospital during February of 2014 to January of 2015. General healthy characteristics such as age, sex, history of disease and disorders, smoking status, alcohol consumption, and dietary habits were investigated by a self-administered questionnaire. Then subjects with a history of cardiovascular disorders, diabetes, hypertension, metabolic disorders, chronic liver or kidney disease, Smokers, antioxidants dietary, and other endocrine disorders were omitted from the study. The Ethics Committee of the Yazd Shahid Sadoughi University of Medical Sciences approved the study and informed consent was attained from all patients after explaining the aims and also protocol of the study.

### Blood collection

Venous Blood samples were collected by venous puncture, and Ethylenediaminetetraacetic acid plasma and sera were obtained by centrifugation and stored at -70°C until they were analyzed.

Serum iron and total iron binding capacity (TIBC) were analyzed by diruiautoanalyzer. Serum ferritin was analyzed on Roche Elecsys 2010. Hemoglobin and hematocrit were analyzed on Sysmex X-100.

### Hormonal analyses

The levels of serum TSH, total T3, and total T4 were measured using enzyme-linked immunosorbent assay (ELISA) methods (according to kits from Pishtaz Teb Co, Tehran, Iran.).

### Statistical Analysis

The results are expressed as means ± standard deviation (SD), of three repetitions. All data were subjected to Analysis of Variance (ANOVA) and significant differences ($p<0.05$) between the results were identified using Independent T-Test. SPSS version 16.0 was used for data analysis.

## Results

The mean age of hypothyroid patients was 35.18±6.63 years and of control subject was 30.71 ±۷.۲۰ years ($P<0.05$). The levels of TSH of hypothyroid patients show a significant increase in comparison to healthy control ($p<0.05$).Hypothyroid patients also had significantly lower levels of T4 ($p<0.05$). Moreover, there was no significant difference in the mean of T3 between hypothyroidism and controls (Table 1).

**Table 1.** Demographic and hormone features of patient and control subjects

| Parameter | | Control subjects | Hypothyroid patients |
|---|---|---|---|
| Age (years) | | 30.71± 7.20 | 35.18±6.63* |
| sex | Female | 35 | 35 |
| | Male | 10 | 10 |
| BMI (kg/m$^2$) | | 22.85±4.37 | 24.28±4.38 |
| T3 (nmol/L) | | 1.34±0.32 | 1.26±1.17 |
| T4 (nmol/L) | | 81.68±18.39 | 59.82±15.68* |
| TSH (µmol/L) | | 2.57±1.07 | 10.64±6.61* |

All values are presented as mean±SD
Hypothyroid patients compared with control subjects (*p<0.05)

Serum iron, ferritin, TIBC, hemoglobin and hematocrit were measured for studying the deleterious consequence of hypothyroidism on iron status. The results show a significant difference in the mean of these parameters between hypothyroidism and controls (Table 2).

**Table 2.** Parameters of iron status in hypothyroid patients and Control subjects

| Parameter | Control subjects | Hypothyroid patients |
|---|---|---|
| Iron (µg/dl) | 108 ± 21 | 88.2 ± 27* |
| Ferritin | 136.5 ± 31.5 | 54.6 ± 32* |
| TIBC (µg/dl) | 287.2 ± 36.6 | 271.6 ± 29.5* |
| Hemoglobin (g/dl) | 13.8 ± 1.1 | 13.1 ± 1.4* |
| Hematocrit (%) | 41.5 ± 7.2 | 39.8 ± 8.8* |

Values are given as mean±SD
Hypothyroid patients compared to control subjects (*p<0.05)

As shown in Figures 1 and 2, no significant correlations were seen between hemoglobin, hematocrit, iron and TIBC with either thyroid hormones or TSH. However, a week association was also seen between TSH levels and ferritin compare to other parameters.

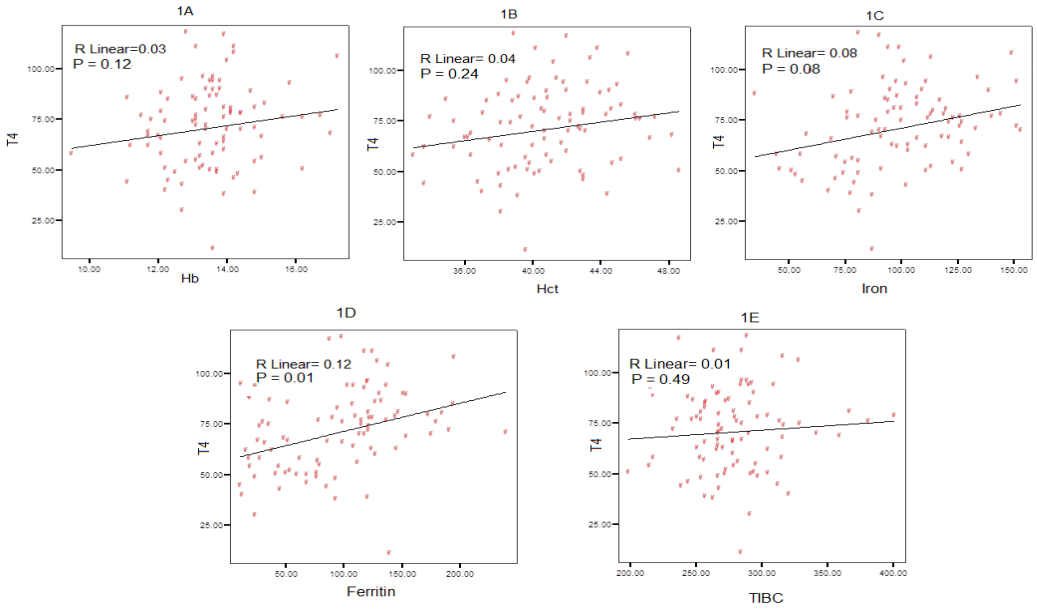


**Fig.1.** Associations between markers of thyroid malfunction and/or body iron parameters in individuals with hypothyroidisms (n=45) 1A: Hemoglobin and T4; 1B: Hematocrit and T4; 1C: Serum iron and T4; 1D: Ferritin and T4; 1E: Total iron binding capacity (TIBC) and T4

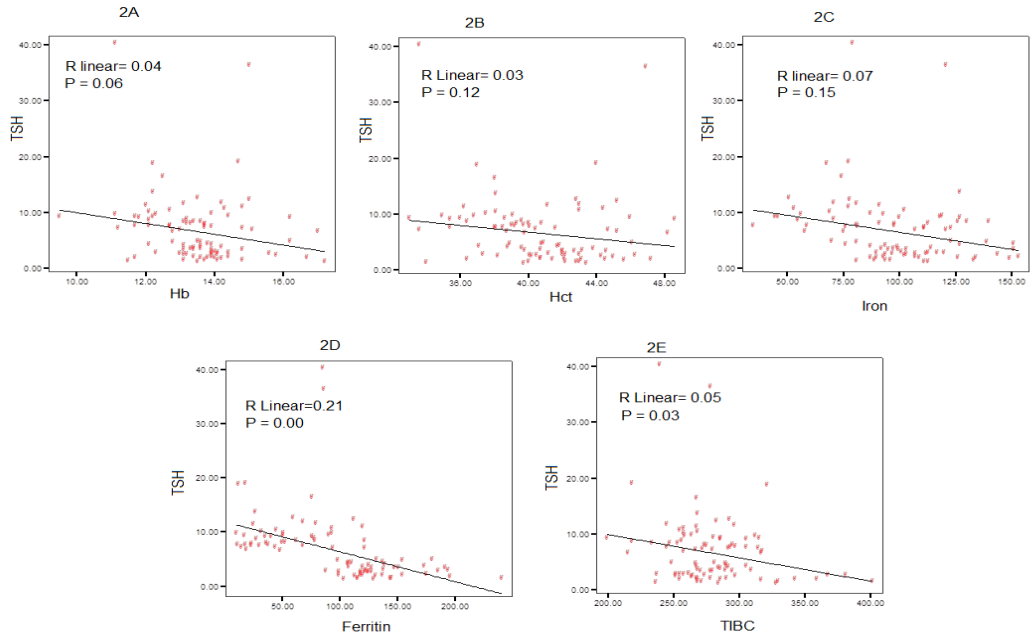


**Fig.2.** Associations between markers of thyroid malfunction and/or body iron parameters in individuals with hypothyroidisms (n=45) 2A: Hemoglobin and TSH; 2B: Hematocrit and TSH; 2C: Serum iron and TSH; 2D: Ferritin and TSH; 2E: Total iron binding capacity and TSH.

## Discussion

Thyroid gland as the greatest and the most vital endocrine gland of human body with the secretion of two hormones, T3 and T4, has a main role in metabolism of cells and bodily organs. Thyroid gland also has a critical effect on erythropoiesis by induction of erythropoietin production and also proliferation of erythroid progenitors [16, 17]. On the other hand, several studies showed a relationship between body iron status (indulging iron metabolism, ferritin, and serum iron) and thyroid hormones function [18-20]. The most typical thyroid dysfunctions, hypothyroidism, and hyperthyroidism influence body iron status, blood cells and cause anemia with various severities. Blood indices such as MCV, MCHC, and hemoglobin also may modify during thyroid dysfunction [15]. Thus, this study aimed to evaluate effects of thypothyroidism on body iron status and red blood cells indices.

Our results show a significant decrease in the levels of hemoglobin and hematocrit in hypothyroidism patient compared to control group. Dorgalaleh et al., (2012) revealed that red blood cell, hemoglobin and hematocrit in patients with hypothyroidism were significantly lower than healthy groups; whereas these parameters were increased in hyperthyroidism [18]. In other study of Geetha and Srikrishnain (2012), hematologic parameters were compared in hypothyroidism patients and normal individuals and revealed that hemoglobin and hematocrit did not show any significant differences in comparison to euthyroid status. However, these parameters were statistically different between patients with hypothyroidism and control group in our study [19].

In this study, the mean TIBC, ferritin, and serum iron level in hypothyroidic patients were significantly lower than those of healthy individuals. A number of groups have reported a relationship between T3 ranges and ferritin expression. In previous studies, hypothyroidism created by thyroidectomy was associated with enhanced rat hepatic ferritin content, that was found to be due to post-transcriptional adjustments in the ferritin synthetic rate. Administration of T3 to hypothyroid individuals generates a significant increasing amount of the serum ferritin [20, 21]. More recently, however, and in contrast, hyperthyroid rats with elevated T3 and T4 levels were found to have an increased liver ferritin protein synthesis rate [22, 23]. Our findings of decreased serum iron and ferritin levels and levels in hypothyroidism may be regarded as an indicator of decreased iron turn over in accordance with diminished erythropoiesis.

Records from many groups are special interests in which T3 was demonstrated to positively improve serum ferritin measurements in humans, like the alterations reported in the rat [24]. Increased serum ferritin levels were realized in hyperthyroid individuals, and levels reduced significantly after antithyroid treatment with normalization of T3 levels [25–28].

Moreover, administration of T3 to hypothyroid individuals generated a significant improve in the serum ferritin level [29-30]. Although the result of the T3-induced increases in the serum ferritin amount in humans is undiscovered, improved synthesis of ferritin in the liver may be an essential factor. These links between T3 and the regulation of ferritin expression recommend that a positive correlation exists between the levels of T4/T3 and ferritin in the serum [30].

Animal and human studies show that thyroid hormones stimulate red cell production. The erythrocyte life span remains normal in hypothyroidism, and there is hypo proliferative erythropoiesis, too [31]. There have been some ideas which try to explain how thyroid hormones stimulate erythropoiesis. Improved metabolic rate and its related increase in oxygen requirement have been the main justifications. The proposed mediator was erythropoietin. Consistent with this suggestion, Cinemre et al. (2009) found elevated hemoglobin, hematocrit and erythropoietin levels after levothyroxine therapy in subclinical hypothyroid patients [32].

One study has reported sideropenia to be a general finding in women with subclinical hypothyroidism and recommends consistently determining ferritin levels in such patients [33]. Another study disclosed no change in haemoglobin or haematocrit amounts upon restoration of euthyroidism in women with subclinical hypothyroidism [34].

These identical adjustments suggest that stimulation of erythropoiesis by thyroid hormones is not the only mechanism, but thyroid hormones influenced on iron metabolism are also needed Erythropoietin resistance in the presence of hypothyroidism, and even subclinical hypothyroidism are usually disclosed in chronic renal failure. Moreover, this resistance is resolved by managing hypothyroidism. These studies obstacle the erythropoietin hypothesis as exogenous human erythropoietin alone are unable to correct anemia in hypothyroid, chronic renal failure patients. Hence, it appears reasonable to summarize that thyroid hormones affect on erythropoiesis in various ways including stimulating iron involvement into erythrocytes, improving iron absorption, and functioning as a switch between proliferation or differentiation of erythroid progenitors by an inhibitory impact or even by acting on its receptors [32, 35].

## Conclusion

In conclusion, our data suggest that alterations in thyroid status change serum iron metabolism and hematological index. Hypothyroidism is often associated with anemia, and depleted body iron store. As there is no significant clinical manifestation of hypothyroidism at earlier stages with anemia it is advisable to routinely investigate it for early detection allowing its early management.

## Conflict of Interest

The authors declare no conflict of interest in this study.

## Acknowledgement

There is no acknowledgement to declare.

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