CORRELATION BETWEEN HYPOTHYROIDISM AND IRON DEFICIENCY ANEMIA IN FEMALE PATIENTS

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ABSTRACT

Iron deficiency anemia is a frequent clinical condition accompanying thyroid dysfunction including hypothyroidism, the hormones of Thyroid can be effect directly of blood formation especially red blood cells by enhancement erythropoietin production which that necessary for erythrocytes proliferation. In this study, 20 newly diagnosed hypothyroid women patients were investigated for levels of ferritin and hemoglobin (HB) and compared healthy controls. The levels of HB and ferritin were found to be significantly decreased in patients as compared to controls. Therefore iron deficiency anemia negatively influences hypothyroidism. Thus, assessment of ferritin (iron storage) and hemoglobin (HB) as a very important parameters useful in the diagnosis of iron deficiency anemia of hypothyroid patients.

KEYWORDS: hypothyroidism, iron deficiency anemia, serum ferritin, hemoglobin.

INTRODUCTION

Deficiency of thyroid hormone is central feature of the clinical syndrome termed as hypothyroidism, leading to generaly diminished of all metabolic processes.[1] Hypothyroidism is common, affecting 1% of general population and about 5% of individuals over age 60 years , which is marked by elevated thyroid stimulating hormone(TSH) levels and reduced thyroid hormones including triiodothyronine (T3) and thyroxin(T4).[2] Hypothyroidism can affect all organ systems, and its affecting dependent of the degree of hormone deficiency.[3] Ferritin is an iron storage protein found in all body organisms, serum ferritin levels become well marker of iron deficiency therefore it have been common useful in a diagnostic test for iron storage diseases especially iron deficiency anemia.[4,5,6] As well as it have been recorded for changing in patients with thyroid dysfunction.[7] An important notice is that anemia in
hypothyroidism is often not diagnosed because of a lower volume of plasma which causes a false high assessment of haemoglobin in blood. On the other hand, hypothyroidism may lead to low iron levels due to poor gut absorption as a result of decreased levels of digestive acids/ enzymes or due to associated autoimmune conditions like celiac disease. It may also be as a result of heavy mensuration seen in some female patients. Thus, hypothyroidism and iron deficiency cases are highly correlated and almost iron deficiency anemia may be on treatment with thyroxin if patient is iron deficient. Indeed, Iron also given to iron deficient women with decrease blood levels of thyroid hormones and may affect thyroid hormone in iron deficient adolescent Iranian girls. In fact the iron deficiency are more serious for women. The iron deficiency can be appearance when the iron store become diminished and decrease supply of iron to various tissues, and it leading to impair in almost metabolic rate. Martinez-Torres and co-workers reported 10% lower T3 levels in human subjects with moderate to severe iron deficiency anemia, also Beard and his co-workers showed that in iron deficiency anemic subjects, serum T3 and T4 levels were significantly decreased. Plasma ferritin is the best single test to iron deficiency and Low hemoglobin concentration is very important sign of anemia. Thyroid hormones also play an important role in hemoglobin production in adult and maturation of HB in fetus. Recently, studies carried out in human and animals have reported that iron deficiency can affect the thyroid hormone metabolism and peroxidase enzyme which is catalyzed initial steps of thyroid hormone synthesis is dependent on the iron. A priori studies revealed that iron, T4 and T3 levels in circulation were significantly decreased during conversion of thyroxine (T4) to triiodothyronine (T3). Therefore this study was projected to estimate levels Ferritin and HB in newly diagnosed patients of hypothyroidism thyroid and explain the correlation between hypothyroidism and iron deficiency anemia.

MATERIAL AND METHODS
In this study, five milliliters of blood sample that was collected from twenty women (at mean age 35±15) was conducted on newly clinical and laboratory diagnosed patients of hypothyroidism and twenty cyclic women as a healthy control group. The diagnosis was based on detailed history and thyroid hormone analysis to determine the hypothyroidism and blood measurement including hemoglobin concentration and ferritin also was determined. All the patients and controls were subjected to routine biochemical investigations, so the pregnant or lactating females and also those with any associated chronic diseases or on drugs/ supplements which may affecting hematopoiesis and thyroid functions were excluded from
the study. Serum was separated and stored at -20°C for estimation of hemoglobin (HB), ferritin and thyroid hormones. The Total T3 (TT3) ,Total T4 (TT4) and ferritin (FER) were determined in human serum by each of VIDAS® T3 kit, VIDAS® T4 kit and VIDAS FER kit (all these kits distributed by bioMerieux SA 376 Chemin de l’Orme 69280 Marcy-l’Etoile - France) using the ELFA technique (Enzyme Linked Fluorescent Assay), thyroid stimulating hormone (TSH) was measured by using the VIDAS® TSH assay which is intended for use on the instruments of the VIDAS family (Vitek® Immuno Diagnostic Assay system) as an automated quantities enzyme-linked fluorescent immunoassay (ELFA) for the determination of human thyroid stimulating hormone (TSH) concentration in human serum that is intended for use as an aid in the diagnosis of thyroid disorders (distributed by bioMerieux,Inc.100 Rodolphe Street Durham, North Carolina 27712-USA). Hemoglobin was measured in patient and control group by using Auto Hematology Analyzer (Diagon® Ltd D-Cell 60).

The data were analyzed by Graph pad prism software (version 5). Statistical significance level was considered P < 0.05. Frequency, percentage, one-way ANOVA, and Pearson correlation test were used.

RESULTS
In this study twenty females patients at mean age 35±15 were compared with homologue healthy control. All different correlation of the levels of T3(nmol/l), T4 (nmol/l), TSH (mlu/ml), ferritin (ng/ml) and HB% (g/dl) between patients and control groups have shown in the table and the results were calculated using Tukey’s Multiple Comparison Test.

Table: 1. Comparison of thyroid hormones with HB and ferritin in hypothyroid patients and healthy controls (p< 0.05).

<table>
<thead>
<tr>
<th>Tukey's Multiple Comparison Test</th>
<th>Mean Diff.</th>
<th>q</th>
<th>Significant? P &lt; 0.05?</th>
<th>95% CI of diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH vs T4</td>
<td>-40.66</td>
<td>3.790</td>
<td>No</td>
<td>-89.59 to 8.259</td>
</tr>
<tr>
<td>TSH vs T3</td>
<td>17.92</td>
<td>1.670</td>
<td>No</td>
<td>-31.00 to 66.85</td>
</tr>
<tr>
<td>TSH vs Ferritin</td>
<td>-55.30</td>
<td>5.154</td>
<td>No</td>
<td>-104.2 to -6.375</td>
</tr>
<tr>
<td>TSH vs HB%</td>
<td>8.598</td>
<td>0.8013</td>
<td>Yes</td>
<td>-40.33 to 57.52</td>
</tr>
<tr>
<td>TSH vs TSHCo</td>
<td>17.63</td>
<td>1.342</td>
<td>No</td>
<td>-42.28 to 77.55</td>
</tr>
<tr>
<td>T4 vs T3</td>
<td>58.59</td>
<td>5.460</td>
<td>Yes</td>
<td>9.664 to 107.5</td>
</tr>
<tr>
<td>T4 vs HB%</td>
<td>49.26</td>
<td>4.591</td>
<td>Yes</td>
<td>0.3389 to 98.18</td>
</tr>
<tr>
<td>T4 vs T4Co</td>
<td>-15.44</td>
<td>1.175</td>
<td>No</td>
<td>-75.36 to 44.47</td>
</tr>
<tr>
<td>T3 vs Ferritin</td>
<td>-73.22</td>
<td>6.824</td>
<td>Yes</td>
<td>-122.1 to -24.30</td>
</tr>
<tr>
<td>T3 vs HB%</td>
<td>-9.326</td>
<td>0.8691</td>
<td>No</td>
<td>-58.25 to 39.60</td>
</tr>
<tr>
<td>T3 vs T3Co</td>
<td>-0.5115</td>
<td>0.03892</td>
<td>No</td>
<td>-60.43 to 59.41</td>
</tr>
<tr>
<td>Ferritin vs HB%</td>
<td>63.90</td>
<td>5.955</td>
<td>Yes</td>
<td>14.97 to 112.8</td>
</tr>
</tbody>
</table>
Concerning to Ferritin was shown a negatively correlated ($r = -0.186$, $p=0.9114$) with T3 (Figure 1), while a positively correlated with T4 ($r = 0.2572$, $p=0.8615$) and TSH ($r = 0.2463$, $p=0.6442$) (Figure 2,3) with a significant difference between Ferritin and T3,TSH and control (Table 1). Regarding to HB was also positively correlated T3,T4, TSH ($r = 0.1029$, $p=0.9114$), ($r = 0.2260$, $p=0.657$), ($r = 0.1833$, $p=0.6442$) respectively (Figure 4,5,6) while a significant difference between HB and T4 and control (Table 1).

![Figure 1](image1.png)  
**Figure: 1.** Scatter diagram showing correlation between Ferritin and T3 ($r = -0.186$, $p=0.9114$).

![Figure 2](image2.png)  
**Figure: 2.** Scatter diagram showing correlation between Ferritin and T4 ($r = 0.2572$, $p=0.8615$).
Figure: 3. Scatter diagram showing correlation between Ferritin and TSH ($r=0.2463$, $p=0.6442$).

Figure: 4. Scatter diagram showing correlation between HB and T3 ($r=0.1029$, $p=0.9114$).

Figure 5. Scatter diagram showing correlation between HB and T4 ($r=0.2260$, $p=0.657$).
DISCUSSION

The alteration in iron metabolism has been conceded as very active pathological markers in patients with anemia, and ferritin plays an important role in iron storage, so for this reason has become the broad indicator of iron. Meanwhile, hypothyroidism will cause anemia due to affect blood cells. In this study, the levels of ferritin and HB were recorded to low in female patients with hypothyroidism as compared to healthy controls. These results are agreed with other studies which revealed that iron deficiency may be associated with low levels of thyroid hormones. In reproductive age, female with hypothyroidism is highly percentage of female thyroid disease population because of increase estrogen which has an anti-thyroid action. Indeed, the patients with hypothyroid there are decreased in the number and proliferative activity of erythroid cells in the marrow by reduce in plasma erythropoietin levels and then the decrease oxygen supplement of the tissues leading to slowly metabolic rate in hypothyroidism due to reduce the diffusion of oxygen to tissues in deficiency of thyroid hormones leads to anemia. so that a significant negative correlation between TSH and Hb was observed leading to occur iron deficiency may both be a cause and an effect of hypothyroidism.

Furthermore, the patients with hypothyroid have been extreme reactive free radicals that casing oxidative stress. Therefore, increased oxidative stress has been reported in hypothyroidism and iron as a metal ion plays an important role in this mechanism for generation of reactive oxygen species in addition with some antioxidant properties of...
iron. On the other hand, the results of this study were recorded increasing of the levels of TSH in female patients with hypothyroidism beside reduced of levels of HB as compared to healthy controls. this was agreed with Beard et al. which was found in the study that T3 and T4 levels were significantly decrease, TSH levels were significantly higher in anemic women, and they have determined that T3 levels have been increased by treatment with iron.\(^{(33)}\) Which that will leading to pathological markers in patients hypothyroidism. Furthermore, there was reported that hemoglobin concentration is significantly lower both in patients with increased and decreased thyrotropin (TSH), if compared to euthyroid women.\(^{(34)}\) This may be an additional reason for decrease in ferritin levels which exhibits antioxidant properties in these patients. The expression of gene for ferritin has also been reported to be induced by T3 hormone.\(^{(35)}\) other studies have recorded decrease total T4 and T3 in addition to the converting of T4 to T3 also reduced and TSH has increased.\(^{(36)}\) In addition, Hess et al. have suggested that iron is an important part of the thyroid hormone function in the body cells and lack of it can lead to poor of thyroid hormone leading to deficient metabolic activity of hypothyroid even in presence of normal FT3 levels casing produce a thyroxine resistance and prevent T3 to T4 conversion by reducing the stimulate heme–containing thyroid peroxidase activity for thyroid hormone synthesis and then reducing thyroid hormone levels.\(^{(37)}\) A marked increase in ferritin can lead to an elevation of serum iron.\(^{(38)}\) Therefore, in our study it was seen that TSH levels which was significantly higher than control group and the negative correlation for TSH with ferritin (iron storage) and HB due to decrease the production of erythropoietin by bone marrow by the decrease of thyroxin level leading to increase TSH levels. This will accepted with other studies in this field which recorded thyroxin administration has been reported to increase erythropoietin levels and improve erythropoiesis, thus may used as marker of iron deficiency.\(^{(39)}\) as our results were statistically a high significant correlation of TSH with ferritin that has been accepted by some authors.\(^{(40)}\) At end we can concluded from this study that hypothyroidism is largely related with iron deficiency anemia, especially in women. So that from the extremely possible that thyroid function might be impaired with more severe iron deficiency and anemia with conversely.

REFERENCES


