Abstract

Beta-thalassemia probably is the most common single gene disorder causing a major genetic health problem in the world. People of Mediterranean, Middle Eastern, African, and Southeast Asian descent are at higher risk of carrying the genes for thalassaemia. Endocrine complications in Thalassaemia Major Patients with multi-transfused Thalassaemia Major develop severe endocrine complications. The aim of the study is to determine the relation between serum circulating ferritin and thyroid gland function in Thalassemic patients. Patients & methods: A cross sectional study was conducted on β-thalassaemia major patients whom attended the thalassaemia center in Tikrit Teaching Hospital (TTH) from beginning of January to the mid of June 2014. Fifty six β- thalassemia major female patients aged 10 to 16 were participated in the study. Thirty nine female subjects apparently healthy, with no family history of hereditary blood disease attendants to out-patient pediatric clinic, who were assessed by a pediatrician, all control healthy subjects aged 10 to 16 years. Body weight & height and serum ferritin, serum TSH, T3, & T4 were measured. Results: There was a highly significant increase in serum circulating ferritin concentration in female thalassemic patients as compare with control subjects. Also, there is significant increase in serum Thyroid stimulating hormone (TSH) concentration in female thalassemic patients. However, there is significant reduction in serum T3 and T4 concentrations in female thalassemic patients as compare with female control subjects. Conclusion; Thalassemic female patients had a lower T3 & T4 as compare with normal healthy female control subjects of same age.

Key words: Body weight, serum ferritin, T3, T4, & TSH, and Thalassemic female patients

Introduction

Thalassemia has been classified by the world health organization as a major public health problem (1). It occurs throughout the world and regarded as one of the major health problems in endemic regions as the, Middle East, North Africa, Mediterranean countries and Asia, (2,3). Beta-thalassemia probably is the most common single gene disorder causing a major genetic health problem for
hemoglobinopathies throughout the world (4,5).

The clinical manifestations are seen within the first three to six months after birth and are characterized by severe anemia because the decreasing levels of fetal hemoglobin (HbF) cannot be replaced by normal adult hemoglobin, (6).

Endocrine complications in Thalassaemia Major Patients with multi-transfused Thalassaemia Major develop severe endocrine complications. Iron overload due to multiple transfusions is the main cause of such complications. Iron accumulates in many tissues such as liver, heart and endocrine glands (7,8).

Thyroid gland produce two distinct hormones, triiodothyronine (T3) and thyroxin (T4). These hormones are responsible for raising the level of activity in the systems essential for exercise performance, (9,10,11).

Iron overload is a consequence of frequent blood transfusion, which is the most important treatment modality for thalassaemia major (12).

The aim of the study is to determine the relation between iron overload and thyroid function in Thalassemic patients.

**Patients & Methods**

A cross sectional study was conducted on β-thalassaemia major patients whom attended the thalassaemia center in Tikrit Teaching Hospital (TTH) in Tikrit from March 2014 to the mid of June 2014. Fifty six β- thalassemia major female patients aged 10 to 16 were participated in the study. Thirty nine female subjects apparently healthy, with no family history of hereditary blood disease attendants to out-patient pediatric clinic, who were assessed by a pediatrician, all control healthy subjects aged 10 to 16 years.

Body weight was measured to the nearest 100 gram & body height was measured to the nearest centimeter (CM).

The circulating ferritin concentrations in the serum of all subjects included in this study were determined quantitatively by a microplate immunoenzymometric assay by using a kit supplied from...
Study of Thyroid gland function and serum circulating ferritin in Beta- thalassemia Major female patients in Tikrit city

(Monobind, USA) and measured by ELISA (9).

Thyroid stimulating hormone (TSH), T3 & T4 for Females were measured, (10-11).

**Results**

There is a high significant decrease in body weight & height of female thalassemic patients as compare with female counterpart of control subjects of same age.

Moreover, there is a high significant decrease in body mass index (P≤0.01) in female patients (18.825 ± 2.8 kg/m2) as compare with BMI of female control subjects (23.61 ± 3.6 kg/m2), as shown in (table -1).

Also, there is significant increase in serum Thyroid stimulating hormone (TSH) concentration (P≤0.01) in female thalassemic patients (4.412 ± 0.21 µIU/ml) as compare with female control subjects (3.22 ± 1.23).

However, there is highly significant reduction in serum T4 concentration (P≤0.01) in female thalassemic patients (0.533 ± 0.225 µg/dl) as compare with female control subjects (6.667 ± 0.71 µg/dl).

Furthermore, there is significant reduction in serum T3 concentration in female thalassemic patients (1.034 ± 0.381 ng/ml) as compare with female control subjects (1.195 ± 0.29 ng/ml).

Table (3) Show the mean & standard deviation of packed cell volume & hemoglobin, white blood count, serum ferritin between female patients and female controls:

Regarding packed cell volume (PCV): there is a high significant reduction (p≤0.01) in female thalassemic patients (27.93 ± 1.23 L/L) as compare with female control subjects (38.83 ± 2.03 L/L).

Moreover, regarding hemoglobin (Hb): there is a highly significant reduction (p≤0.01) in Hb of female thalassemic patients (8.27 ± 0.41 gm/dl) as compare with female control subjects (13.72 ± 0.68 gm/dl).

Also, there is a highly significant increase in white blood cell count (9753 ± 734 cell/cm3) as compare with normal healthy control female subjects of same age (5841 ± 982 cell/cm3).

Moreover, there is a high significant increase (p≤ 0.01) in serum ferritin
Discussion

In the present study, there is highly significant reduction in serum T4 concentration in female thalassemic patients as compare with female control subjects. Furthermore, there is significant reduction in serum T3 concentration in female thalassemic patients as compare with female control subjects. Also, there is significant increase in serum Thyroid stimulating hormone concentration in female thalassemic patients as compare with female control subjects.

The abnormal thyroid function found in the presented patients was the isolated elevation of TSH, which was consistent with the diagnosis of compensated hypothyroidism, the most common thyroid dysfunction in all previous reports, (12-13).

Thyroid dysfunction in β-thalassemic patients has been reported in various prevalence, ranging from a low prevalence of 0-12% (14).

Previous study have stated that impaired thyroid function is present in a considerable proportion of transfusion-dependent beta-thalassemia patients with associated iron overload, (15).

Impaired thyroid function is frequent among present thalassaemia major patients and this necessitates regular follow up and early commencement of chelation therapy to prevent such complication, (17).

Previous study was done in Irbil –Iraq, it was found that the mean levels of thyroid hormones; T3 and T4 were significantly lower (P<0.001) among thalassaemia patients, while the mean TSH level was higher (P ≤0.003) compared to the control group, (18). Also, in the same study, nineteen patients (24.3%) had hypothyroidism, of these, 2 patients (2.5%) had overt hypothyroidism (low T4, and high TSH) and 17 patients (21.8%) had subclinical hypothyroidism (normal T4 and high TSH). They were heavily iron overloaded (mean S. Ferritin = 5250 ng/ml).

The incidence of overt and subclinical hypothyroidism in b-
thalassemia was reported to be relatively high especially in patients with long standing B-thalassemia, (19).

In the present study, there is a significant reduction in PCV and hemoglobin (Hb) of female thalassemic patients as compare with female control subjects.

Other factors like hypoxia due to persistent anemia and perfusion defect, also contribute to the derangement. Hypothalamic pituitary axis, thyroid, para-thyroid, adrenal, pancreas, gonads, all show hypoactivity, (16).

Previous study found that the mean T4 of cases (7.36 ± 1.61 μg/dL) was significantly lower (p<0.001) than that of controls (9.30 ± 2.15 μg/dL). The mean TSH level was significantly higher (p<0.01) in cases (3.56 ± 1.49 μg/dL) as compared to controls (2.31 ± 2.74 μg/dL), (20).

In the present study, there is a highly significant increase in white blood cell count (9753 ± 734 cell/cm3) as compare with normal healthy control female subjects of same age (5841 ± 982 cell/cm3).

A high increase in white blood cells and associated with a high concentrations of plasma ferritin and labile cell iron which are considered responsible in the formation of free radicals and the production of reactive oxygen species (ROS) may lead to cell and organ damage (23-24).
From the present result & previous findings, these findings reinforce the importance of the regular follow up of patients with b-thalassaemia major and thalassaemia intermedia for early detection and management of associated complications. In this way, the future prevalence of endocrine abnormalities can be lessened, (19-20).

High prevalence of hypothyroidism among thalassemic patients signifies the importance of regular screening for evaluation of endocrine function in these patients; especially when short stature is present, (25, 27).

However, as a result of hyper transfusion therapy and increased longevity, iron tissue toxicity has become more common, and contributes significantly to morbidity in these patients due to damage of several organs & endocrine glands by Iron overload, (28).

The present study concluded the followings;-

Thalassemic female patients had a higher significant increase in serum Thyroid stimulating hormone (TSH) concentration as compare with female control subjects. However, female thalassssemic patients had a lower T3 & T4 as compare with normal healthy female control subjects of same age.

The present study recommends the followings;

1-Assessment of pituitary hormone especially growth hormone by carry out hormonal test for both genders as a routine follow up of thalassssemic patients.

2- Assessment of certain hormones concentration is necessary for the follow up of the thalassemic patients especially during puberty.

References

4. Thein SL. Genetic insights in to the clinical diversity of beta
Study of Thyroid gland function and serum circulating ferritin in Beta- thalassemia Major female patients in Tikrit city

15. Al-Hader A, Bashir N, Hasan Z, Khatib S. Thyroid function in children with beta-thalassemia

Tikrit Medical Journal 2016;21(2):144-153
Study of Thyroid gland function and serum circulating ferritin in Beta- thalassemia Major female patients in Tikrit city


Study of Thyroid gland function and serum circulating ferritin in Beta-thalassemia Major female patients in Tikrit city

**Study of Thyroid gland function and serum circulating ferritin in Beta- thalassemia Major female patients in Tikrit city**

Table 1 The mean & standard deviation (SD) of age, body weight, height & BMI.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control (39)</th>
<th>Patients (56)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>13.91 ± 1.01</td>
<td>14.54 ± 1.58</td>
<td>NS</td>
</tr>
<tr>
<td>Body weight (Kg)</td>
<td>51.42 ± 8.12</td>
<td>34.32 ± 6.21</td>
<td>0.001</td>
</tr>
<tr>
<td>Height (Cm)</td>
<td>147.14 ± 8.4</td>
<td>135.53 ± 6.9</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.61 ± 3.6</td>
<td>18.825 ± 2.8</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 2 Show the mean & standard deviation (SD) of serum TSH, T3 & T4 in female patients and control subjects.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (µIU/ml)</td>
<td>3.22 ± 1.23</td>
<td>4.412 ± 0.21</td>
<td>0.05</td>
</tr>
<tr>
<td>T3 (ng/ml)</td>
<td>1.195 ± 0.29</td>
<td>1.034 ± 0.381</td>
<td>0.05</td>
</tr>
<tr>
<td>T4 (µg/dl)</td>
<td>6.667 ± 0.71</td>
<td>0.533 ± 0.225</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 3-The mean & standard deviation (SD) of PCV, hemoglobin, & white blood cells.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control (39)</th>
<th>Patients (56)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV (L/L)</td>
<td>38.83 ± 2.03</td>
<td>27.93 ± 1.23</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemoglobin (gm/dl)</td>
<td>13.72 ± 0.68</td>
<td>8.27 ± 0.41</td>
<td>0.01</td>
</tr>
<tr>
<td>WBCs (Cell/Cm³)</td>
<td>5841 ± 982</td>
<td>9753 ± 734</td>
<td>0.01</td>
</tr>
<tr>
<td>Ferritin (ng/ml)</td>
<td>53.54 ± 7.93</td>
<td>3513.6 ± 1412.2</td>
<td>0.01</td>
</tr>
</tbody>
</table>