The Association Between Hypothyroidism and Anemia: a Clinical Study

Mitra Kazemi-Jahromi,1 Ali Shahriari-Ahmadi,1 Seyed-Hosein Samedanifard,1 Soraya Doostmohamadian,1 Esmat Abdolahpoor,2 Seyed Farshad Allameh3

Hematology-Oncology Department, Rasul Akram Hospital, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Dr. Ali Shahriari Ahmadi, MD; Hematologist-Oncologist
Hematology-Oncology Department, Rasul Akram Hospital
Niayesh St, Sattarkhan St, Tehran, Iran
Tel: +98 21 66515001
E-mail: shahriariahmadi@yahoo.com

Abstract
Introduction: Hypothyroidism is diagnosed by elevated thyroid stimulating hormone (TSH) and normal or decreased serum levels of T4 or T3, and is associated with a wide range of metabolic abnormalities, including anemia. This clinical study aimed to assess the improvement of anemia in patients with primary hypothyroidism following administration of levothyroxine in Iranian population.

Materials & Methods: The effect of levothyroxine in 70 patients with hypothyroidism was examined and the improvement of anemia in patients who had a poor or good response to levothyroxine was assessed during a 3 month follow-up.

Results: Three months after treatment, the levels of TSH in 64 patients with hypothyroidism (91.4%) significantly decreased to a normal limit (TSH< 2.5 IU/ml). Forty three out of 70 patients (61.4%) had a concurrent anemia. A significant difference was found in the levels of hematologic parameters between those who had a good response (TSH< 2.5 IU/ml) and those with poor responses to the treatment (TSH≥2.5 IU/ml) (p< 0.05).

Conclusions: Current study showed a high rate of association between anemia and hypothyroidism in Iranian population. Improvement in hypothyroidism and its associated anemia was observed in majority of patients (more than 90%), indicating a dual benefit for hypothyroidism treatment. Less than 10% of patients poorly responded to levothyroxine, with no clear reasons.

Keywords: Anemia, Hypothyroidism, Iran, Levothyroxine

Introduction
Hypothyroidism is a clinical syndrome resulting from deficiency of thyroid hormones, leading to generalized slowing of all metabolic processes.(1) Hypothyroidism in infants and children results in growth and mental development retardation.(2, 3) The prevalence of hypothyroidism has been shown to be varied from 2-5% depending on the study, increasing to 15% by age 75 years, with a higher incidence in females.(4) In iodine deficient areas such as India the incidence can reach as higher as 10-20 times more than non-iodine areas like U.S.A.(5-7)

Metabolic abnormalities associated with hypothyroidism include anemia, dilutional hyponatremia, hyperlipidemia, and reversible increase in creatinine.(8) The prevalence of anemia in patients with hypothyroidism has been shown to be 20-60% .(9) Thyroid hormones involve in hemoglobin synthesis in adults and maturation of hemoglobin in fetus (3, 10) and by affecting hematopoietic process, hypothyroidism results in anemia through slowing the oxygen metabolism.(11)

Hypocoagulopathies, hemorrhages, malabsorbtion of iron, vitamin B12 and folic acid, reduced erythropoietin and bone marrow hematopoietic cells hypoplasia are known as the reasons for anemia.(12)
Table- 1. Frequency of anemia in patients with hypothyroidism

<table>
<thead>
<tr>
<th>Anemia</th>
<th>Male (n= 11, 25.6%)</th>
<th>Female (n= 32, 74.4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcytic</td>
<td>1 (14.3%)</td>
<td>6 (85.7%)</td>
</tr>
<tr>
<td>Normocytic</td>
<td>10 (32.3%)</td>
<td>21 (67.7%)</td>
</tr>
<tr>
<td>Macrocytic</td>
<td>0 (0%)</td>
<td>5 (100%)</td>
</tr>
</tbody>
</table>

Table- 2. Hematological parameters in patients who had a good or poor response to treatment before and after administration of levothyroxine

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Good response (Mean± SD, n= 64)</th>
<th>Poor response (Mean± SD, n= 6)</th>
<th>p-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb, g/dL</td>
<td>11.5± 1.3</td>
<td>10.5± 0.52</td>
<td>0.001</td>
<td>0.06</td>
</tr>
<tr>
<td>HCT, %</td>
<td>34.8± 2.7</td>
<td>33.4± 2.6</td>
<td>0.001</td>
<td>0.34</td>
</tr>
<tr>
<td>MCH, pg</td>
<td>24.09± 3.1</td>
<td>21.9± 3.2</td>
<td>0.001</td>
<td>0.48</td>
</tr>
<tr>
<td>MCHC, g/dL</td>
<td>33.04± 1.72</td>
<td>31.4± 2.2</td>
<td>0.001</td>
<td>0.15</td>
</tr>
<tr>
<td>MCV, fL</td>
<td>82.5± 4.2</td>
<td>80.1± 3.06</td>
<td>0.001</td>
<td>0.80</td>
</tr>
<tr>
<td>PLT, ×10^9/mL</td>
<td>254± 620</td>
<td>239± 110</td>
<td>0.001</td>
<td>0.90</td>
</tr>
<tr>
<td>RBC, ×10^12/L</td>
<td>4.2± 0.78</td>
<td>4.1± 0.49</td>
<td>0.001</td>
<td>0.48</td>
</tr>
<tr>
<td>WBC, ×10^3/mm³</td>
<td>6.3±1.565</td>
<td>6.3±0.8</td>
<td>0.060</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*The parameters that had a significant difference between the two groups.

AT: After treatment with levothyroxine; BT: Before treatment with levothyroxine; Hb: Hemoglobin; HCT: Hematocrit; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; MCV: Mean corpuscular volume; PLT: Platelet; RBC: Red blood cells; WBC: White blood cells.

Table- 3. Hematological parameters in the patient who had a good or poor response to levothyroxine administration

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Mean ± SD after treatment in patients with good response (n = 64)</th>
<th>Poor response (n = 6)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb, g/dL</td>
<td>13.4± 1.1</td>
<td>11.3± 1.1</td>
<td>0.030</td>
</tr>
<tr>
<td>HCT, %</td>
<td>37.7± 4.5</td>
<td>34.9± 2.7</td>
<td>0.040</td>
</tr>
<tr>
<td>MCH, pg</td>
<td>28.5± 2.9</td>
<td>24.1± 3.4</td>
<td>0.001</td>
</tr>
<tr>
<td>MCHC, g/dL</td>
<td>35.9± 1.3</td>
<td>30.7± 2.7</td>
<td>0.003</td>
</tr>
<tr>
<td>MCV, fL</td>
<td>84.1± 3.9</td>
<td>80.3± 2.3</td>
<td>0.020</td>
</tr>
<tr>
<td>PLT, ×10^9/mL</td>
<td>235± 814</td>
<td>244± 68</td>
<td>0.700</td>
</tr>
<tr>
<td>RBC, ×10^12/L</td>
<td>4.7± 0.88</td>
<td>4.41± 0.58</td>
<td>0.400</td>
</tr>
<tr>
<td>WBC, ×10^3/mm³</td>
<td>6.2± 1.3</td>
<td>6.0± 0.6</td>
<td>0.650</td>
</tr>
</tbody>
</table>

*, the parameters that had a significant difference between the two groups.

Hb: Hemoglobin; HCT: Hematocrit; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; MCV: Mean corpuscular volume; PLT: Platelet; RBC: Red blood cells; WBC: White blood cells.

Autoimmune reactions are the most common causes of hypothyroidisms than non-autoimmune type and it has been shown that the increased frequency of chronic anemia in patients with autoimmune thyroid disease (ATD) can be caused by concurrent autoimmune gastrointestinal diseases.(13) This study aimed to assess the prevalence of anemia associated with hypothyroidism and the effect of current hypothyroidism treatment in reducing frequency of anemia in Iranian population, which can provide further insight to better understanding of disease management and epidemiology.

Materials & Methods

Patients: In a clinical trial, 70 patients with clinical and laboratory signs of hypothyroidism admitted in Endocrine clinic of Rasul Akram Hospital from March 2006 to March 2009 were selected. Patients with a normal range of ferritin, vitamin B12 and reticulocyte count that had no known diseases and did not take drugs affecting hematopoiesis and thyroid functions were considered eligible for this study. The levels of TSH, T3, T4 were measured to determined the hypothyroidism. Blood parameters, including red blood cells (RBC) and white blood cells (WBC) count, hemoglobin (Hb) concentration, mean corpuscular hemoglobin concentration (MCHC), mean corpuscular haemoglobin (MCH) and mean corpuscular volume (MCV), platelets (PLT), hematocrit (HCT), levels were measured, peripheral blood morphology and reticular cell count, including platelets (PLT), hematocrit (HCT), hemoglobin were assessed before and 3 months after treatment with levothyroxine. Other common causes of anemia, including iron deficiency and megaloblastic anemia were ruled out.

On the basis of hematological criteria, patients were categorised into non-anemic patients, patient with macrocytic anemia, patients with normochromic-normocytic anemia, and patients with hypochromic-
The anemia in patients with hypothyroidism varies between 20 and 65%, and in this current study, it was found to be 61% (43 out of 70). A good correlation between hypothyroidism and anemia in Iran. Anemia was classified and the frequency of microcytic and normocytic anemia was determined (Table 1). Three months after thyroid hormone administration, 64 patients (86.6%) did not show a significant change in WBC and PLT values. No significant increase was observed in WBC and PLT values. No significant response to treatment after 3 months. The significant differences between the levels of blood parameters were noted in Table 2. The significant differences between the two groups after 3 months are also summarized in Table 3.

In conclusion, this study showed that hypothyroidism is highly prevalent in women, and proper treatment of hypothyroidism can obviate treatment of concurrent anemia.

An autoimmune thyroiditis is the most common cause of hypothyroidism. Thyroid antibodies are increased and not diagnosed. Autoimmune hyperthyroidism is the most common cause of hypothyroidism. Thyroid antibodies are increased, and not diagnosed. Autoimmune hyperthyroidism is the most common cause of hypothyroidism. Thyroid antibodies are increased, and not diagnosed.

In the current study, 85.7% of women were anemic. The greater percentage of patients with increased risk of bleeding and hematologic parameters, including MCV, MCHC, HCT, and HB, significantly increased compared to pre-treatment values. Patients with thyroid hormone treatment showed significant response to treatment, with improvement in mean values of MCV, HCT, and HB.

The results from the current study showed that 64 out of 70 patients (91.4%) had a significant improvement in mean values of MCV, HCT, and HB after treatment with thyroid hormone. Over 3% of patients had positive antithyroid antibodies and only 19% were euthyroid. It is suggested that an autoimmunedriven hypothyroidism.

Statistical analysis: Quantitative variables were statistically analyzed using independent t-test and Mann-Whitney U test for the means and differences between two groups. Qualitative variables were assessed using Chi-square test and Fisher test (SPSS version 16) and differences with p-values less than 0.05 were considered significant. Data are expressed as mean ± standard deviation (SD).

Levodopa was administered according to the protocol described previously (15, 16). The protocol for treatment of hypothyroidism:


case of pregnancy, decreased fertility rate, increased infant mortality, and its associated symptoms. This study was approved by institutional ethics committee and the patient's information was kept confidential.

While little is known about the frequency of hypothyroidism and its associated symptoms, the results from this study showed that 64 out of 70 patients (91.4%) had a significant improvement in mean values of MCV, HCT, and HB after treatment with thyroid hormone. Over 3% of patients had positive antithyroid antibodies and only 19% were euthyroid. It is suggested that an autoimmunedriven hypothyroidism.
anemia, with an emphasis on using more efficient therapeutic replacements or options for those patients who had a poor response to the levothyroxine therapy.

Acknowledgements
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References