Prevalence of Hypothyroidism in Type 2 Diabetic Female Kurdish Subjects

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Abstract

Background: The incidence of thyroid disorders is more prevalent in type 1 diabetes compared to type 2 diabetes, due to associated autoimmune disorders. Physiological and biochemical interconnection between type 1 diabetes mellitus and autoimmune thyroid disease is now stimulating subject of study. Objectives: The objective was to assess the prevalence of thyroid dysfunction among type 2 diabetic Kurdish females and to explore the correlation between metabolic syndrome components and autoimmune thyroid abnormality. Materials and Methods: The study included 60 type 2 diabetic Kurdish females and 30 sex- and age-matched controls. All patients in the study were exposed to anthropometric characteristics, including HbA1c, lipid profile, serum uric acid, thyroid-stimulating hormone (TSH), free triiodothyronine, free thyroxine, anti-thyroid peroxidase (TPO), and anti-thyroglobulin (anti-Tg). Results: Primary hypothyroidism was found in 24 (40%) diabetic patients (5.67 ± 3.35 µIU/mL) versus three (10%) controls (1.76 ± 1.19 µIU/mL) (P < 0.001). Anti-TPO was found in 66.7% (367.21 ± 234.53) of diabetic patients versus 10% (31.78 ± 32.14) of controls (P > 0.001). Anti-Tg was found in 60% (499.98 ± 358.14) of diabetic patients versus 0 (53.27 ± 36.23) controls (P > 0.001). A significant positive relationship was estimated between both TPO antibodies and Tg antibodies and TSH (P = 0.05 and P = 0.001, respectively) in diabetic patients. Conclusion: Autoimmune thyroid disorder is more prevalent in Kurdish women with type 2 diabetes than nondiabetic women, and thus points to a role of autoimmunity in the pathogenesis of type 2 diabetes.

Keywords: Antithyroglobulin, anti-thyroid peroxidase, autoimmune thyroid dysfunction, stimulating hormone, type 1 diabetes mellitus
thyroid dysfunction will be increased, and higher incidence of thyroid disease has been reported in female compared to male and in diabetic patients compared to nondiabetics.⁴

Perros et al. published an overall incidence of 13.4% of thyroid diseases in diabetic patients, with the highest rate in type 1 DM (T1DM) females (31.4%) and lowest rate in T2DM males (6.9%). Thyroid disorders were pointed out to be more prevalent in individuals with T1DM compared to those with T2DM, due to the associated autoimmunity. Physiological and biochemical interconnections between T2DM and autoimmune thyroid disease are now an interesting field of research.⁵

There is no data on autoimmune thyroid diseases in T2D in Kurdish individuals; therefore, this study was performed to find out about autoimmune disease in T2D females.

Materials and Methods
A descriptive cross-sectional case–control study was performed at the Department of Internal Medicine, Layla Qasim diabetic center and outpatient Department of Endocrinology, Hawler Teaching Hospital, Erbil, Iraq. The study was approved by Ethical Review Committee of Diabetic Association of Hawler Medical University. It included 60 T2DM Kurdish females living in iodine-sufficient area without a previously known thyroid disease and 30 sex- and age-matched nondiabetic healthy controls (age range 30–58 years).

The patients were involved according to inclusion and exclusion criteria:

Inclusion and exclusion criteria
Inclusion criteria included female patients (Known case of T2DM), and the duration of DM ≥5 years. Exclusion criteria included the following: (1) patients taking drugs that influence the thyroid function, (2) postpartum women, (3) pregnancy, (4) known history of thyroid disease, and (5) unstable cardiac disease, renal impairment, liver cirrhosis, and malignancy.

An informed verbal consent was taken from each and every patient. All study participants were submitted to proper history taking, including duration of DM, current treatment, other comorbidities, and family history of DM and thyroid dysfunction.

Physical examination, including vital signs and general, head, neck, thyroid, extremities, chest, heart, abdominal, and neurological examination, was made. Anthropometric characteristics, including body mass index (calculated as weight in kilograms/height in square meters) and waist circumference, were made. The waist was measured at the midway point between the lowest rib plane and the iliac crest. A medical history including duration of diabetes, age, sex, present diabetes conditions, and medication records was obtained. Height and weight were measured, and body mass index was calculated.

Laboratory investigations
With all aseptic precautions, 5 ml venous blood was drawn from the anterior cubital vein in a disposal syringe and delivered in ethylenediaminetetraacetic acid tubes and mixed well.

The following laboratory investigations were performed: serum lipid profile (cholesterol [high- and low-density lipoprotein] and triglycerides) and serum uric acid using enzymatic assay (Boehringer, Mannheim, Germany); HbA1c using a kit supplied by Crystal Chem, Downers Grove, IL, USA; thyroid-hormone profile, including thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4), measured by enzyme-linked immunosorbent assay (DRG International, Springfield, NJ, USA);⁶ antithyroid antibodies, including anti-thyroid peroxidase (TPO) and antithyroglobulin (anti-Tg), measured by enzyme-linked immunosorbent assay (Orgentec Diagnostika GmbH, Mainz, Germany).

Statistical analysis
Statistical analysis was performed using SPSS (IBM, Armonk, NY, USA) version 22 and Microsoft Excel 2007. Results are expressed as means and standard deviation for quantitative data and as frequency (count) and relative frequency (percentage) for categorical data. Comparisons were done using unpaired t-tests. For comparison of categorical data, Chi-square tests were performed. Correlation was assessed by Pearson’ correlation coefficient. P < 0.05 was considered statistically significant.

Results
Table 1 shows comparability between DM patients (60) and controls (30) on clinical and anthropometric measures. There were statistically significant differences between the two groups in weight, body mass index, waist circumference, and systolic blood pressure.

Table 2 shows comparability between 60 diabetic patients and 30 controls on all laboratory data. There were highly statistically significant differences between the two groups in HbA1c, cholesterol (high- and low-density lipoprotein), uric acid, FT3, FT4, TSH, anti-TPO, and anti-Tg.

Table 3 shows that among euthyroid diabetic patients (34), 9 (25.0%) had both antibodies negative, 7 (19.44%) had only anti-TPO positive, 6 (16.66%) had only anti-Tg positive, and

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient Mean±SD</th>
<th>Control Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.6±7.78</td>
<td>40±8.04</td>
<td>0.051</td>
</tr>
<tr>
<td>Duration (years)</td>
<td>8.5±5.4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>152.5±5.32</td>
<td>154.3±6.2</td>
<td>0.212</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>86.5±13.12</td>
<td>75.0±13.42</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>34.06±5.2</td>
<td>29.1±11.43</td>
<td>0.001</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>109.8±11.23</td>
<td>97.9±11.78</td>
<td>0.001</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>125.2±20.30</td>
<td>110±16.8</td>
<td>0.005</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>73.45±16.77</td>
<td>71.39±11.65</td>
<td>0.70</td>
</tr>
</tbody>
</table>

SD: Standard deviation; BMI: Body mass index; BP: Blood pressure.
The prevalence of autoimmune thyroid disease among T1DM is high.\textsuperscript{[9]} However, thyroid dysfunction in T2DM is a less investigated field. Since normal thyroid function is mandatory to conduct energy metabolism, abnormal thyroid function may have adverse effects on blood glucose control in diabetes. The previous study has explored the effect of hypothyroidism on T2DM complication such as nephropathy and cardiovascular events; therefore, diabetic patients need to be screened for thyroid dysfunction.\textsuperscript{[10]}

In this study, primary hypothyroidism was found in 24 (40%) diabetic patients (5.67 ± 3.35 μIU/mL) versus 3 (10%) controls (1.76 ± 1.9 μIU/mL) ($P < 0.001$). Our results agree with other studies showing a high prevalence of hypothyroidism of 12.5%–32.4% in T2DM.\textsuperscript{[3,11]}

Among hypothyroid patients, a total of 24, 21 (87.5%) showed overt hypothyroidism, while only 3 (12.0%) showed subclinical hypothyroidism. In reverse, prior research has shown subclinical hypothyroidism as the most prevalent thyroid dysfunction in DM.\textsuperscript{[12,13]}

The present study revealed no significant correlation between HbA1c and TSH level or thyroid antibodies in diabetic patients, in accordance with the reports of.\textsuperscript{[14]} However, Billic-Komarica et al.\textsuperscript{[15]} found a significant positive correlation between TPO-Ab antibodies and HbA1c and TSH.

Type 1 diabetes has confirmed interconnection with autoimmune thyroid disorders through a common genetic inheritance.\textsuperscript{[16]} It has been reported that the positivity to TPO-Ab antibodies in euthyroid patients with type 1 diabetes predicts the progression to eventual hypothyroidism,\textsuperscript{[17]} whereas a few studies were conducted to evaluate thyroid autoimmunity in type 2 diabetic patients.\textsuperscript{[18]}

In this study, anti-TPO was found in 66.7% (367.21 ± 234.53) of diabetic patients versus 0 (53.27 ± 36.23) controls ($P > 0.001$). Anti-Tg was found in 60% (499.98 ± 358.14) of diabetic patients versus 0 (5.67 ± 3.35) controls ($P < 0.001$). Our results agree with other studies showing a high prevalence of antithyroid autoimmunity in type 2 diabetic patients.\textsuperscript{[19,20]}

However, other studies showed that the prevalence of antithyroid

### Table 2: Comparison between patients and controls on laboratory data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patient</td>
<td>Control</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.64±2.24</td>
<td>3.98±1.32</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>242.95±439</td>
<td>164.35±33.07</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>42.23±9.12</td>
<td>52.32±6.45</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>168.03±47.8</td>
<td>94.09±41.2</td>
</tr>
<tr>
<td>Tg (mg/dl)</td>
<td>121.4±13.5</td>
<td>109.45±18.18</td>
</tr>
<tr>
<td>UA (mg/dl)</td>
<td>5.68±1.48</td>
<td>4.23±1.01</td>
</tr>
<tr>
<td>FT3 (pg/ml)</td>
<td>1.07±0.72</td>
<td>3.04±0.53</td>
</tr>
<tr>
<td>FT4 (ng/dL)</td>
<td>0.75±0.42</td>
<td>1.1±0.39</td>
</tr>
<tr>
<td>TSH (µU/ml)</td>
<td>148.03±47.8</td>
<td>164.35±33.07</td>
</tr>
<tr>
<td>Anti-Tg (IU/ML)</td>
<td>499.98±358.14</td>
<td>53.27±36.23</td>
</tr>
<tr>
<td>Anti-TPO (IU/ML)</td>
<td>367.21±234.53</td>
<td>31.78±32.14</td>
</tr>
</tbody>
</table>

TSH: Thyroid-stimulating hormone, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Thyroglobulin, FT3: Free triiodothyronine, FT4: Free thyroxine, TPO: Thyroid peroxidase, HbA1c: Hemoglobin, SD: Standard deviation

### Table 3: Thyroid antibodies in patients and controls

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Patients</th>
<th>Control</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>14 (38.88)</td>
<td>14 (58.33)</td>
<td></td>
</tr>
<tr>
<td>Hypothyroid</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>9 (25.0)</td>
<td>3 (12.5)</td>
<td></td>
</tr>
<tr>
<td>Hypothyroid</td>
<td>24 (88.8)</td>
<td>3 (100)</td>
<td></td>
</tr>
<tr>
<td>Only TPO positive</td>
<td>7 (19.44)</td>
<td>5 (20.8)</td>
<td></td>
</tr>
<tr>
<td>Hypothyroid</td>
<td>3 (11.11)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Only Tg positive</td>
<td>6 (16.66)</td>
<td>2 (8.3)</td>
<td></td>
</tr>
<tr>
<td>Hypothyroid</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

TG: Thyroglobulin, TPO: Thyroid peroxidase

14 (38.88%) had both antibodies positive. Among controls that showed hypothyroidism, 3 (100%) had both antibodies negative. Among those who had no hypothyroidism (24), 3 (11.11%) had positive anti-TPO.

Among diabetic patients, who showed hypothyroidism (24), 3 (12.5%) had negative antibodies, 5 (20.8%) had only anti-TPO positive, 2 (8.3%) had only anti-Tg positive, and 14 (58.33%) had both antibodies positive. Among hypothyroid patients, a total of 24, 21 (87.5%) patients showed overt hypothyroidism, while only 3 (12%) showed subclinical hypothyroidism.

Correlations between both thyroid antibodies and all clinical and biochemical parameters in diabetic patients were significantly positive between TSH and anti-Tg ($P = 0.001$), as shown in Figure 1, and TSH and anti-TPO ($P = 0.05$), as shown in Figure 2.

**DISCUSSION**

The prevalence of autoimmune thyroid disease among T1DM is high.\textsuperscript{[9]} However, thyroid dysfunction in T2DM is a less investigated field. Since normal thyroid function is mandatory to conduct energy metabolism, abnormal thyroid function may have adverse effects on blood glucose control in diabetes. The previous study has explored the effect of hypothyroidism on T2DM complication such as nephropathy and cardiovascular events; therefore, diabetic patients need to be screened for thyroid dysfunction.\textsuperscript{[10]}

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**Figure 1:** Correlation between antithyroglobulin and thyroid-stimulating hormone
Correlation between thyroid dysfunction and different parameters of metabolic syndrome could not be found in diabetic patients. On the other hand, higher TSH levels have been documented in patients with metabolic syndrome compared to a nonmetabolic syndrome group, indicating that subclinical hypothyroidism may be a risk factor for metabolic syndrome. This suggests that thyroid dysfunction may increase cardiovascular disease risk in diabetic patients through interconnections with dyslipidemia, insulin resistance, and vascular endothelial dysfunction.[23]

**Conclusion**

Hypothyroidism was found to be more common in Kurdish women with T2DM compared to controls. The significant positive correlation between both antithyroid antibodies and serum TSH in T2DM patients suggests that thyroid dysfunction in women with T2DM is due to an autoimmune-mediated pathogenetic mechanism, thus declaring the role of autoimmunity in the pathogenesis of T2DM.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**