Iodine status, thyroid function, thyroid volume and thyroid autoimmunity in patients with type 1 diabetes mellitus in an iodine-replete area

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Objective: To analyze the prevalence and clinical significance of thyroid autoimmunity, thyroid volume and iodine status in patients with type 1 diabetes mellitus compared with age and sex matched healthy controls, in an iodine-deficiency improved area.

Method: Fifty-eight patients with type 1 DM, 30 female and 28 male, who attended the pediatric endocrinology clinic of Karadeniz Technical University Hospital were included in the study. They were compared with 58 healthy children matched for sex and age. Routine thyroid function parameters, thyroid autoantibodies (TPOAb, TgAb and TRAb) and urinary iodine excretion were measured and thyroid volume was determined by ultrasonography (US).

Results: Twenty-six patients (44.8%) in diabetic patients and 20 subjects (34.5%) in the control group had thyroid autoantibody positivity. TPOAb and TgAb positivity were significantly high in diabetic patients (P=0.01 and P=0.032, respectively). Thyroid US revealed a thyroid volume of 6.6±3.5 ml (median 6.4 ml, range 1.1-17.2 ml) in the diabetic patients compared with 3.7±2 ml (median 3.1 ml, range 0.8-8.6 ml) in the control group (P=0.0001). Median urinary iodine levels of both groups were clearly above the threshold level for iodine deficiency, but 26 patients with type 1 DM (44.8%) and 16 controls (27.5%) had urinary iodine excretion below 100 µg/L, and 21 (36.2%) of diabetic patients and two subjects (3.4%) of the control group were consistent with severe iodine deficiency. No significant differences were noted in diabetic patients in terms of age, duration and metabolic control of the disease and thyroid volume when compared according to the autoantibody presence. Additionally, there were no significant differences between the iodine deficient and iodine sufficient diabetic patients in terms of age, sex, duration of disease, HbA1c, thyroid hormones and thyroid volumes. Thyroid autoimmunity was lower in patients with iodine deficiency (38.4% vs. 50%), but not statistically significant.

Conclusion: We found that type 1 DM patients had larger thyroid volume compared with healthy control groups, and a large portion of them had the markers of autoimmune thyroid disease and iodine deficiency. Surprisingly, we found that a large portion of the healthy children had TRAb positivity. We proposed that TRAb must be considered in community surveys or prevalence studies of autoimmune thyroid disorders in iodine-replete areas. Additionally, prospective longitudinal studies are needed to determine the clinical significance of TRAb positivity in diabetic patients.

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Introduction

Iodine deficiency was an important public health problem in Turkey. The total goiter prevalence was found as 30.5% and that of visible goiter in 6.7% nation-wide [1,2]. Goiter prevalence was increased up to 50% in some remote areas [3]. The prevalence of iodine deficiency in Black Sea coast was first recorded in a national survey in 1998. The survey reported a goiter rate between 22% and 64% in schoolchildren aged between 9-11 years, in various cities of the region; which indicated severe to moderate iodine deficiency [2,4].

The Health Ministry initiated a national program including standardization of iodized salt and its use nationwide in 1998, and legislation for mandatory iodization of household salt was passed in July 1999. After this program, a monitoring study on school age children had been completed by the end of the year 2002, by using urinary iodine concentration. It showed a significant improvement of iodine deficiency in Black-Sea region, and median urinary iodine concentrations were above the 100 µg/l in all cities of the region [5].

The etiology of autoimmune thyroiditis remains unclear. Predisposing genetic factors, increased age and sex seem to be evident. Environmental factors such as stress, infections, trauma, smoking, drugs and nutrition, especially an increased iodine supply, have been shown to be linked to autoimmune thyroiditis. Most of the epidemiological studies demonstrated an increased prevalence of autoimmune thyroid disease with the elimination of iodine deficiency. A marked rise in thyroid antibodies has been observed in iodine deficient geographic areas when iodine supplementation is introduced [6,7].

The association between type 1 diabetes mellitus and autoimmune thyroid diseases has long been documented. Both are organ specific T-cell mediated disease, and have similar pathogenesis, which involves T-cell infiltration resulting in dysfunction of the target organ. Moreover, two immune regulatory genes, HLA and CTLA-4, contribute to the susceptibility to both diseases [8]. High prevalence of thyroid autoantibodies in children with type 1 diabetes mellitus has been found in many studies, and most of the antibody-positive diabetic patients were clinically and biochemically euthyroid [9-11]. However, iodine status of the diabetic patients was not considered in those studies.

Therefore, we aimed to analyze the prevalence and clinical significance of thyroid autoimmunity and iodine status in type 1 diabetic patients compared with age and sex matched healthy controls in Black Sea region, in an iodine-deficiency improved area. Furthermore, we wanted to evaluate their relationship with thyroid volume in diabetic patients.

Material and methods

Fifty-eight patients with type 1 DM, 30 female and 28 male, who attended the pediatric endocrinology clinic of Karadeniz Technical University Hospital were included into the study. The mean age of the patients and the duration of diabetes were 11.5±4 (range 1-18) years and 2.6 (range 0-11) years, respectively. Fifty-eight age and sex matched children, living in the same geographic area, were used as control group. The mean age of the control group was 11.2±4.1 (range 1-18) years (table I). None of the controls had an acute illness or a history of DM and thyroid disorders. None of them were receiving any drugs affecting thyroid functions or size.

A questionnaire was filled out about the date of birth, sex, height, weight, familial thyroid disorders and the consumption of iodized salt used at their homes. Then, sonographic thyroid volume measurement was performed by the same radiologist (P.K) in the supine position with hyperextended neck. The dimensions of both thyroid lobes were measured with a high resolution real-time ultrasonic

Table I
Clinical characteristics of the patients with type 1 diabetes mellitus and controls.

<table>
<thead>
<tr>
<th></th>
<th>Diabetics (n=58)</th>
<th>Controls (n=58)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD) (year)</td>
<td>11.5±4</td>
<td>11.2±4.1</td>
<td>0.915</td>
</tr>
<tr>
<td>BMI</td>
<td>18.6±3.6</td>
<td>17.3±2.8</td>
<td>0.061</td>
</tr>
<tr>
<td>Duration of the disease (range) (year)</td>
<td>2.6 (0-11)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>10.6±2.8</td>
<td>4.8±0.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Consumption of iodized salt (%)</td>
<td>41 (70.6)</td>
<td>48 (82.7)</td>
<td>0.187</td>
</tr>
</tbody>
</table>
scanner using a 7.5 MHz linear transducer (EUB 515 A, Hitachi). Longitudinal and transverse scans were performed allowing the measurement of the depth (D), the width (W) and the length (L) of each lobe. The volume of each lobe was calculated by the formula: 
\[ V (\text{ml}) = 0.479 \times D \times W \times L \ (\text{cm}) \]
The thyroid volume was the sum of the volumes of both lobes and the volume of the isthmus was not included. To define goiter, thyroid volumes measured by ultrasound for age and gender were compared with the reference thyroid volumes (percentile 97) defined previously [12].

After that, venous blood samples were taken for the determination of thyroid function variables, thyroid peroxidase antibodies (TPOAb), thyroglobulin antibodies (TGAb), thyroid stimulating hormone receptor antibodies (TRAb) and glycated haemoglobin (HbA1c) levels. Serum free thyroxine (FT4) (normal range 0.7-2.3 ng/ml), total thyroxine (TT4) (normal range 4.4-14 µg/dl), free triiodothyronine (FT3) (normal range 1.4-4.1 pg/ml), total triiodothyronine (TT3) (normal range 0.97-1.95 ng/ml) and thyroid stimulating hormone (TSH) (normal range 0.2-4.2 mIU/mL) concentrations were determined by chemiluminometric method. Serum TPOAb and serum TGAb were measured by chemiluminescent sequential immunometric method (Diagnostic Product Corporation, USA); values of ≥35 IU/mL and ≥115 IU/mL were considered positive, respectively. Serum TRAb (normal range <14 U/l) were studied using radioreceptor assay (RRA) method (R-CT-100-100 determinations, ZenTech s.a, Belgium). The following were considered guidelines for detection of thyroid dysfunction: normal (euthyroid), when total or free T4 and TSH were within the normal range; subclinical hypothyroidism, when total or free T4 were within the normal limits but TSH was >5 mIU/mL; hypothyroidism, when total T4 was <5 µIU/mL; hyperthyroidism, when total T4 was <1.4 µg/dl and TSH >5 mIU/mL; hyperthyroidism, when the serum TSH value was suppressed and below 0.2 mIU/mL in the presence of increased thyroid hormones[13]. Antibodies were considered positive if they were above the normal range mentioned above.

Urinary iodine concentration was measured in 24 h samples by Sandhell-Kolttkoff reaction. Urine was first digested with chloric acid in a heating block and iodine was determined by its catalytic reduction of ceric ammonium sulfate in the presence of arsenious acid. The mean urinary iodine excretion lower than 20 µg/L was accepted as severe, levels between 20-49.9 µg/L as moderate and levels between 50-99.9 µg/L as mild iodine deficiency[12].

Statistical analysis was carried out using the Statistical Package for Social Science. Results were expressed as mean, median, standard deviation and ranges. Student’s t-test and Mann-Whitney U-test were used to compare 2 groups. Chi-square test was used where appropriate. P<0.05 denoted a statistically significant difference.

The study was approved by the Karadeniz Technical University Ethical Committee and Informed consent forms were obtained from the families of all subjects recruited for the study.

Results

No significant differences were found between the groups according to age and BMI (table I). As expected, HbA1c levels were significantly higher in patients with type 1 DM (P=0.0001).

According to the questionnaire responses, 70.7% of the diabetics (41/58) and 82.7% of the control subjects (48/58) were consuming iodized salt (P=0.187), approximately for four years. Analysis of the urine samples showed that median urinary concentration of iodine in diabetics and control group was 134.2 µg/L and 154.7 µg/L, respectively (figure 1). The results revealed that median urinary iodine levels of both groups were clearly above the threshold level for iodine deficiency, but 26 patients with type 1 DM (44.8%) and 16 controls (27.5%) had urinary iodine excretion below 100 µg/L, and 21 (36.2%) of diabetic patients and two subjects (3.4%) of the control group were consistent with severe iodine deficiency (table II). There was no correlation between the urinary iodine and HbA1c in diabetic patients and controls (R=-0.15, P=0.23 and R=0.86, P=0.16, respectively).

Among the diabetics, 26 patients (44.8%) had thyroid autoantibodies, 12 had TPOAb, 10 had TGAb and 14 had TRAb (5 had both TPOAb and TGAb positivity, 1 had both TGAb and TRAb positivity, and in 2 patients all three autoantibodies were positive). The duration of the disease
was less than one year in 13 (50%) of 26 autoantibody positive diabetic patients. In the control group, 20 subjects (34.5%) had positive thyroid autoantibodies (18 had TRAb positivity, one had TPOAb positivity and two had both TGAb and TRAb positivity). TPOAb and TGAb positivity were significantly high in the diabetic patients (P=0.01 and P=0.032, respectively) (table II).

Thyroid US revealed a thyroid volume of 6.6±3.5 ml (median 6.4 ml, range 1.1-17.2 ml) in the diabetic group compared with 3.7±2 ml (median 3.1 ml, range 0.8-8.6 ml) in the control group (P=0.0001) (table II, figure 2). Thyroid volume was significantly correlated with age (R=0.676, P=0.001), duration of DM (R=0.320, P=0.014) and BMI (R=0.649, P=0.001) in diabetic patients, but not correlated with TSH, thyroid hormones and urinary iodine excretion. HbA1c was negatively correlated (but not significant) with thyroid volume in patients with type 1 DM. When compared with the upper limits of reference thyroid volumes by US, goiter was found in 6 patients (10.3%) (3 male, 3 female) with type 1 DM, and in 3 (5.1%) subjects (1 male, 2 female) in control group. Additionally, an anechogenic nodule (size 9×6×4 mm) suggestive of cystic degeneration was found in a patient with type 1 DM. There was no significant difference in thyroid volumes when diabetic patients were divided into subgroups according to the presence of thyroid antibody; thyroid volume was 7.1±3.9 in autoantibody positive patients and 6.2±3.1 in autoantibody negative patients (P=0.342). However, goiter prevalence was higher among the patients with autoantibody positivity. After excluding the diabetic patients with thyroid dysfunction and thyroid autoimmunity and iodine deficiency (n=15), thyroid volume was significantly difference compared to control group without thyroid dysfunction, thyroid autoimmunity and iodine deficiency (n=27), 6.02±3.7 versus 3.2±1.9 (P=0.007).

Six patients (10.4%) with type 1 DM and two subjects (3.5%) from the control group were identified to have subclinical hypothyroidism (TSH>5 mIU/ML, normal T4). All other diabetic patients and controls were clinically and biochemically euthyroid. There was no significant difference in the prevalence of thyroid dysfunction between diabetics and controls (P=0.271), but there was a significant difference in thyroid hormones (T3, T4, FT3). There was a significant inverse correlation between T3 levels and HbA1c in diabetic patients (R=-0.35, P=0.006).

When diabetic patients were divided into two groups according to the presence of thyroid autoantibodies, there were no significant differences between the groups in age, sex, BMI, duration of diabetes, HbA1c, TSH, thyroid dysfunction, urinary iodine excretion and iodine deficiency (table III). Additionally, there was no significant difference between the only TRAb positive patients (n=11) and with thyroid autoantibody negative patients (n=32) in terms of

Table II
Thyroid hormones, urinary iodine levels, thyroid autoimmunity and thyroid volumes in patients with type 1 DM and control group.

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=58)</th>
<th>Controls (n=58)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (mIU/mL)</td>
<td>2.1±1</td>
<td>2.1±1</td>
<td>0.149</td>
</tr>
<tr>
<td>T3 (ng/ml)</td>
<td>1.2±0.4</td>
<td>1.6±0.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>T4 (µg/dl)</td>
<td>7.6±2.1</td>
<td>9.5±1.9</td>
<td>0.003</td>
</tr>
<tr>
<td>FT3 (pg/ml)</td>
<td>2.9±0.7</td>
<td>3.6±0.8</td>
<td>0.030</td>
</tr>
<tr>
<td>FT4 (ng/ml)</td>
<td>1.3±0.3</td>
<td>1.7±1</td>
<td>0.295</td>
</tr>
<tr>
<td>Subclinical hypothyroidism (%)</td>
<td>6 (10.4)</td>
<td>2 (3.5)</td>
<td>0.271</td>
</tr>
<tr>
<td>Autoantibody positivity (%)</td>
<td>26 (44.8)</td>
<td>20 (34.5)</td>
<td>0.342</td>
</tr>
<tr>
<td>TPOAb positivity (%)</td>
<td>12 (20.6)</td>
<td>2 (3.4)</td>
<td>0.010</td>
</tr>
<tr>
<td>TGAb positivity (%)</td>
<td>10 (17.2)</td>
<td>2 (3.4)</td>
<td>0.032</td>
</tr>
<tr>
<td>TRAb positivity (%)</td>
<td>14 (24.1)</td>
<td>18 (32.7)</td>
<td>0.533</td>
</tr>
<tr>
<td>Thyroid volume (ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>6.4</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>6.6±3.5</td>
<td>3.7±2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Range</td>
<td>1.1-17.2</td>
<td>0.8-8.6</td>
<td></td>
</tr>
<tr>
<td>Urinary iodine (µg/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>134.2</td>
<td>154.7</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>124.7±109.8</td>
<td>152.6±73.5</td>
<td>0.181</td>
</tr>
<tr>
<td>Range</td>
<td>1-356.4</td>
<td>16.2-409.3</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>32 (55.1)</td>
<td>42 (72.4)</td>
<td>0.082</td>
</tr>
<tr>
<td>Severe iodine deficiency</td>
<td>21 (36.2)</td>
<td>2 (3.4)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Moderate iodine deficiency</td>
<td>1 (1.7)</td>
<td>2 (3.4)</td>
<td>0.99</td>
</tr>
<tr>
<td>Mild iodine deficiency</td>
<td>4 (6.8)</td>
<td>12 (20.6)</td>
<td>0.059</td>
</tr>
</tbody>
</table>

Figure 2
Thyroid volumes of the diabetic patients and the controls. Note that the diabetic patients have larger thyroid volume compared to controls (P=0.0001). The black lines indicate the median values of the groups.
Table III
Clinical characteristics of diabetic patients with and without thyroid autoantibody.

<table>
<thead>
<tr>
<th></th>
<th>Thyroid autoantibody (+) (n=26)</th>
<th>Thyroid autoantibody (-) (n=32)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>11.4±4</td>
<td>11.7±4.1</td>
<td>0.821</td>
</tr>
<tr>
<td>Number of female patients (%)</td>
<td>11 (42.3)</td>
<td>19 (59.3)</td>
<td>0.303</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>2.7±3.2</td>
<td>2.5±3</td>
<td>0.962</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>10.5±2.8</td>
<td>10.7±2.9</td>
<td>0.727</td>
</tr>
<tr>
<td>Urinary iodine (µg/L) (mean±SD)</td>
<td>132.7±109</td>
<td>118.3±111.8</td>
<td>0.595</td>
</tr>
<tr>
<td>Number of patients with iodine deficiency (%)</td>
<td>10 (38.4)</td>
<td>16 (50)</td>
<td>0.539</td>
</tr>
<tr>
<td>TSH (mIU/mL)</td>
<td>3.1±3.5</td>
<td>3±1.6</td>
<td>0.162</td>
</tr>
<tr>
<td>Number of patients with thyroid dysfunction</td>
<td>4 (15.3)</td>
<td>2 (6.2)</td>
<td>0.392</td>
</tr>
<tr>
<td>Thyroid volume (ml)</td>
<td>7.1±3.9</td>
<td>6.2±3.1</td>
<td>0.342</td>
</tr>
<tr>
<td>Number of patients with goiter</td>
<td>6 (23)</td>
<td>0</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Table IV
Clinical characteristics of the patients with and without iodine deficiency.

<table>
<thead>
<tr>
<th></th>
<th>Normal iodine levels (n=32)</th>
<th>Decreased iodine levels (n=26)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>11.1±4.3</td>
<td>9.5±5</td>
<td>0.378</td>
</tr>
<tr>
<td>Number of female patients (%)</td>
<td>16 (50)</td>
<td>12 (46.1)</td>
<td>0.978</td>
</tr>
<tr>
<td>Duration of diabetes (year)</td>
<td>2.8±3.1</td>
<td>2.7±3.1</td>
<td>0.500</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>10.5±2.6</td>
<td>10.8±3.1</td>
<td>0.689</td>
</tr>
<tr>
<td>T3 (ng/ml)</td>
<td>1.2±0.2</td>
<td>1.3±0.5</td>
<td>0.774</td>
</tr>
<tr>
<td>T4 (µg/dl)</td>
<td>6.8±2.5</td>
<td>7.9±1.9</td>
<td>0.097</td>
</tr>
<tr>
<td>TSH (mIU/mL)</td>
<td>2.8±1.6</td>
<td>3.3±3.5</td>
<td>0.390</td>
</tr>
<tr>
<td>Thyroid dysfunction (%)</td>
<td>3 (9.3)</td>
<td>3 (11.5)</td>
<td>0.999</td>
</tr>
<tr>
<td>Thyroid volume (ml)</td>
<td>6.8±3.9</td>
<td>6.3±2.9</td>
<td>0.641</td>
</tr>
<tr>
<td>Number of patients with goiter (%)</td>
<td>5 (15.6)</td>
<td>1 (3.8)</td>
<td>0.209</td>
</tr>
<tr>
<td>Thyroid autoantibody (%)</td>
<td>16 (50)</td>
<td>10 (38.4)</td>
<td>0.539</td>
</tr>
</tbody>
</table>

Discussion

In this study, we found that the median urinary iodine concentration was 154.7 µg/L and the frequency of goiter detected by ultrasound was 5% in the healthy control group, indicating the improvement of iodine deficiency in our region. Similar results were observed in a previous study, which was held by National Coordinating Committee for IDD in this region, in 2003 [5]. In diabetic patients, median urinary iodine concentration was found as 134.2 µg/L, which is above the threshold limit for the iodine deficiency defined by WHO [12]. However, approximately 45% of our diabetic patients had iodine deficiency and 10% of the patients had goiter detected by ultrasound. It suggests that iodine deficiency is still a problem in diabetic patients.

Our study confirms that patients with type 1 DM have higher prevalence of positive thyroid autoantibodies (44.8%) than healthy controls (34.5%), but without significant difference (P=0.342). Both our diabetic patients and healthy control subjects had higher prevalence of thyroid autoantibodies when compared with the previous studies [9-11,14,15]. Explanation for this high prevalence of thyroid autoantibodies in our study can be due to use of TRAb along with TPOAb and TgAb for the screening of thyroid autoimmunity. TPOAb is the most sensitive assay for detecting autoimmune thyroid disease, and it is the first abnormality to appear in the course of developing hypothyroidism secondary to Hashimoto’s thyroiditis [10,16,17]. TgAb is another sensitive assay for the detecting autoimmune thyroid disease especially in iodine deficient areas, and it is commonly correlated with TPOAb [10,18]. TRAb is generally used for the confirmation of the diagnosis of autoimmune thyrotoxicosis [19]. The clinical significance of TPOAb and TgAb positivity in diabetic patients has been well documented in many studies. The prevalence of thyroid antibodies (TPOAb, TgAb) showed a wide range between 8-44% due to ethnic variations and difference of the iodine status of the study populations. They are more common in girls with diabetes during the second decade of life and commonly associated with subclinical hypothyroidism [9-11,15]. As in our study, these autoantibodies may be also present at the time of diagnosis [20,21]. Prevalence of TRAb positivity and its clinical significance in diabetic patients have not been studied previously. We found that 24% of the cases had TRAb positivity, and no significant differences were found in terms of age, sex, duration of diabetes, HbA1c, TSH, thyroid dysfunction, urinary iodine excretion and iodine deficiency (data not shown).

Table IV shows the characteristics of the diabetic patients with and without thyroid autoantibody. There were no significant differences between the iodine deficient patients and iodine sufficient patients in terms of age, sex, duration of disease, HbA1c, thyroid hormones and thyroid volumes. Thyroid autoimmunity was lower in patients with iodine deficiency (38.4% vs. 50%), but the difference was not statistically significant.

Type 1 diabetes mellitus and thyroid
control group with similar anthropometry; and they pro-
diabetic patients compared to age and sex matched healthy
position variables especially fat-free mass is different in
process towards islet cells can also cause alterations in thy-
gland may be involved in diabetic patients without any
ntitity and iodine deficiency in diabetic patients, but in agree-
gen in the previous study, thyroid volumes of the diabetic
patients without thyroid dysfunction, thyroid autoimmu-
ity and iodine deficiency were increased compared to
healthy control group [22]. This indicates that thyroid
gland may be involved in diabetic patients without any
apparent thyroid dysfunction, thyroid autoantibody and
thyroid autoimmunity and iodine deficiency. It suggests that ongoing autoimmune
process towards islet cells can also cause alterations in thy-
roid glands without any clinical or biochemical signs of
thyroid disease. Gomez et al. [22] showed that body com-
position variables especially fat-free mass is different in
 diabetic patients compared to age and sex matched healthy
control group with similar anthropometry; and they prop-
ated fat-free mass is the main determinant of thyroid vol-
ume in different populations. Confirming the previous
studies, we found that thyroid volume is primarily depend-
ent on age, BMI, and without any relation with thyroid
hormones and urinary iodine excretion in diabetic patients
[10,22]. In this study, thyroid dysfunction was present in six
patients with type 1 DM (10.4%). The prevalence of thy-
roid dysfunction is in agreement with some studies on type
1 DM patients, but lower than the others, which demon-
strated 13.4% and 20% prevalence rate of thyroid dysfunc-
tion [23,24]. Moreover, all the cases with thyroid
dysfunction were subclinical hypothyroidism. Addition-
ally, we found that there was a significant inverse corre-
lation between T3 levels and HbA1c in diabetic patients
suggesting that patients with poor metabolic control tend
to be more common to hypothyroidism.

In conclusion, we found that type 1 DM patients had
larger thyroid volume compared with healthy control
groups, and a large portion of them had the markers of
autoimmune thyroid disease and iodine deficiency. Sur-
prisingly, we found that a large portion of the healthy chil-
ren had TRAb positivity without any predisposition
disease for Graves’ disease except iodine supplementation.
Therefore, we proposed that TRAb must be considered in
community surveys or prevalence studies of autoimmune
thyroid disorders in iodine-replete areas. Furthermore,
prospective longitudinal studies are needed to determine
the clinical significance of TRAb positivity in diabetic

of diabetes, HbA1c levels, thyroid hormones, thyroid vol-
ume and urinary iodine levels between TRAb positive and
negative cases. Since DR3 antigen is found commonly in
both Graves’ disease and diabetic patients, high prevalence of
TRAb positivity is an expected finding in diabetic patients.

It is difficult to compare our thyroid volume results
with previous studies due to differences in age distribution,
iodine status and high thyroid autoimmunity. We found
increased thyroid volumes in diabetic patients compared to
age and sex matched healthy control group. This may
attributed to higher prevalence of both thyroid autoimmu-
ity and iodine deficiency in diabetic patients, but in agree-
ment with a previous study, thyroid volumes of the diabetic
patients without thyroid dysfunction, thyroid autoimmu-
nity and iodine deficiency were increased compared to
healthy control group [22]. This indicates that thyroid
gland may be involved in diabetic patients without any
apparent thyroid dysfunction, thyroid autoantibody and
iodine deficiency. It suggests that ongoing autoimmune
process towards islet cells can also cause alterations in thy-
roid glands without any clinical or biochemical signs of
thyroid disease. Gomez et al. [22] showed that body com-
position variables especially fat-free mass is different in
 diabetic patients compared to age and sex matched healthy
control group with similar anthropometry; and they prop-
ated fat-free mass is the main determinant of thyroid vol-
ume in different populations. Confirming the previous
studies, we found that thyroid volume is primarily depend-
ent on age, BMI, and without any relation with thyroid
hormones and urinary iodine excretion in diabetic patients
[10,22]. In this study, thyroid dysfunction was present in six
patients with type 1 DM (10.4%). The prevalence of thy-
roid dysfunction is in agreement with some studies on type
1 DM patients, but lower than the others, which demon-
strated 13.4% and 20% prevalence rate of thyroid dysfunc-
tion [23,24]. Moreover, all the cases with thyroid
dysfunction were subclinical hypothyroidism. Addition-
ally, we found that there was a significant inverse corre-
lation between T3 levels and HbA1c in diabetic patients
suggesting that patients with poor metabolic control tend
to be more common to hypothyroidism.

In conclusion, we found that type 1 DM patients had
larger thyroid volume compared with healthy control
groups, and a large portion of them had the markers of
autoimmune thyroid disease and iodine deficiency. Sur-
prisingly, we found that a large portion of the healthy chil-
ren had TRAb positivity without any predisposition
disease for Graves’ disease except iodine supplementation.
Therefore, we proposed that TRAb must be considered in
community surveys or prevalence studies of autoimmune
thyroid disorders in iodine-replete areas. Furthermore,
prospective longitudinal studies are needed to determine
the clinical significance of TRAb positivity in diabetic

References