Prevalence of Thyroid Autoimmunity among Type 2 Diabetes Moroccan subjects: A Retrospective study

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SUMMARY

Type 2 diabetes (T2D) is a growing concern in the general Moroccan population and often associated with common endocrine disorders particularly thyroid dysfunction. The purpose of this study is to evaluate the prevalence of T2D and the thyroid autoimmunity (TDI) in Moroccan subjects.

A retrospective study was conducted between January 2012 and December 2018. We collected data from 52 diabetic patients and 71 non-diabetic subjects (controls). Thyroid stimulating hormone (TSH), free thyroxin (FT4), free triiodothyronine (FT3), thyroid peroxidase antibodies (TPOAb), and thyroglobulin antibodies (TGAb) levels were measured using Chemiluminescent microparticle immunoassay. Fasting blood glucose (FBG), triglyceride (TG), and total cholesterol (CT) concentrations were determined using dry chemistry method. Hemoglobin A1c (HbA1c) level was evaluated using high performance liquid chromatography principle.

Among 52 diabetic subjects, 23 (44.2.8%) were positives for thyroid antibodies. The TPOAb mean did not differ significantly between diabetic and control individuals (24.51 ± 8.22 vs. 13.27 ± 3.72, p=0.167). However, regarding the TgAb level a significant difference was observed in T2D (20.32 ± 4.94 vs. 8.51 ± 2.59, p = 0.004) compared to subjects without diabetes. Hypothyroidism was reported in 52 diabetic patients (44.23%) and (50.7%) in non-diabetic subjects.
The analysis of multiple logistic regressions indicated that high risk of TDI in diabetic patients was not related to diabetes, sex, age, or status of dyslipidemia.

Our data revealed no significant association between T2D and TDI disorders in Moroccan subjects. However, further studies on a large sample are needed to confirm these findings.

1. Introduction

Type 2 diabetes (T2D) is among the most common endocrine disorders worldwide (Faghilimnai, 2006). DM is characterized by hyperglycemia resulting as an impairment of insulin secretion and/or insulin resistance (Guariguata, 2014). The global prevalence of diabetes in adult increases from 1980 to 2014, the estimated number of people affected worldwide has quadrupled from 108 million to 422 million (NCD Risk Factor Collaboration, 2016). Preventing the effect of complications in at risk people of type 2 diabetes (T2D) will require lifestyle changes, healthy diet, regular physical activity, healthy weight, avoiding smoking, managing blood pressure and cholesterol levels (Zimmet P, 2001; Asif M, 2014).

Thyroid hormones (TH) are essential for normal development, growth, neural differentiation, and metabolic regulation in mammals (Cheng, 2010). Thyroid function has an important effect on the regulation of energy balance and metabolism (Bahj, 2005; Körhle, 2018). There is a large variability in the prevalence of thyroid dysfunction in the general population ranging from 6.6% to 13.4% (Silva, 2005; Umpierrez, 2003). In diabetic patients, the prevalence of thyroid dysfunction is higher and ranges from 10 to 24% (Umpierrez, 2003; Duntas, 2011). The link between thyroid autoimmunity (TDI), including raised thyroglobulin antibodies (TgAb) and thyroid peroxidase antibodies (TPOAb), and type 1 diabetes is more evident than in T2D (Umpierrez, 2003; Gonzales, 2007; Riley, 1981; Biondi, 2019).

During the last decade, many epidemiological studies have evaluated the connection between thyroid dysfunction and diabetes in different countries in order to assess the prevalence and clarify the underlying pathophysiology mechanism. Since the prevalence of TDI among the North Africa population is not being well described; we sought to determine in this study, for the first time, the prevalence of TDI in T2D Moroccan subjects.

2. Material and methods

2.1. Study population

A retrospective case-control study was carried out at Pasteur Institute of Morocco from January 2012 to December 2018. According to the American Diabetes Association, the inclusion criteria for cases were T2D patients aged ≥ 20 years (American Diabetes Association, 2005). We excluded pregnant women, users of drugs affecting thyroid function, subjects with known history of thyroid disease, thyroidectomy, treatment with radioactive iodine, and history of other serious diseases. All participants (diabetics and controls) in this study were of Moroccans living in the district of Grand Casablanca and the neighboring regions. The total population was 123 participants, aged 21 to 83 years, including 52 diabetic patients and 71 nondiabetic controls were included.

2.2. Explored biochemical parameters

Thyroid stimulating hormone (TSH), free thyroxin (FT4), free triiodothyronine (FT3), thyroid peroxidase antibodies...
(TPOAb), and thyroglobulin antibodies (TgAb) levels were measured by Chemiluminescent microparticle immunoassay (Abbott Laboratories, UK). Fasting blood glucose (FBG), triglyceride (TG), and total cholesterol (CT) levels were evaluated using dry chemistry methods (Ortho Clinical Diagnostics, Johnson & Johnson, Inc.). Hemoglobin A1c (HbA1c) level was measured using high performance liquid chromatography principle (Bio-Rad Laboratories, Hercules, CA). All measurements were done according to the manufacturer’s instructions.

2.3. Clinical classification criteria

DM was defined as FBG ≥ 126 mg/dL (7 mmol/L), HbA1c ≥ 6.5% (American Diabetes Association, 2005). Hyperlipidemia was defined as TG ≥ 150 mg/dL (1.7 mmol/L), CT ≥ 200 mg/dL (5.6 mmol/L) (National Cholesterol Education Program (NCEP), 2002). Both hypothyroidism and TDI was defined as positive in agreement with the reference range suggested by the manufacturer (TSH us ≥ 4 UI/L, FT4 ≤ 0.70 ng/dl, FT3 ≤ 1.71 pg/mL, TPOAb ≥ 5.6 U/L and TgAb ≥ 4 U/L).

2.4. Statistical analysis

The comparison between the means was carried out by Student’s t test. Categorical variables were compared using the chi-square test. To adjust the effect of confounding factors, logistic regression models were performed to identify independent predictors of TDI. Data was analyzed using Graph Pad Prism 7 software (San Diego, USA). A p-value less than 0.05 was considered significant.

3. Results

The demographic characteristics of the study population, composed of 123 participants, including 52 patients with T2D and 71 non-diabetic controls, are presented in Table I. There was no difference in terms of age (53.54 ± 1.43 vs 52.66 ± 1.72) or gender (84.6 vs 73.2, p = 0.710) between the two groups of participants.

The distribution of positive TDI cases among diabetic subjects was about 1.5 times lower than in controls. Of 52 diabetic patients, 22 (42.3%) were tested positive for antibodies against TPOAb, TgAb, and both. While, 36 (50.7%) positives TDIs were detected in the non-diabetic controls.

Table I. Demographic and clinical characteristics of study population (M, mean ; SEM, standard error of the mean.; HbA1c, hemoglobin A1c; FBG, fasting blood glucose; CT, cholesterol; TG, triglyceride; TSH, thyroid stimulating hormone; FT4, free thyroxin; FT3, free triiodothyronine; TPOAb, thyroid peroxidase antibodies; Tg Ab, thyroglobulin antibodies ; TDI, Thyroid autoimmunity).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Diabetic n= 52</th>
<th>Controls n= 71</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (M± SEM)</td>
<td>53.54 ± 1.43</td>
<td>52.66 ± 1.72</td>
<td>0.710</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>44(84.6)</td>
<td>52 (73.2)</td>
<td>0.132</td>
</tr>
<tr>
<td>HbA1c, n (%)</td>
<td>7.93 ± 0.19</td>
<td>5.70 ± 0.09</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FBG, mg/mL (M± SEM)</td>
<td>146.50 ± 5.68</td>
<td>91.85 ± 1.67</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CT, mg/dL (M± SEM)</td>
<td>167.1 ± 8.33</td>
<td>160.70 ± 5.85</td>
<td>0.527</td>
</tr>
<tr>
<td>TG, mg/dL (M± SEM)</td>
<td>137.8 ± 12.97</td>
<td>112.60 ± 8.19</td>
<td>0.091</td>
</tr>
<tr>
<td>TSH, µU/mL (M± SEM)</td>
<td>1.57 ± 0.17</td>
<td>1.45 ± 0.12</td>
<td>0.553</td>
</tr>
<tr>
<td>FT4, ng/dl (M± SEM)</td>
<td>0.98 ± 0.02</td>
<td>1.04±0.04</td>
<td>0.234</td>
</tr>
<tr>
<td>FT3, pg/mL [range]</td>
<td>2.2 [2.06-2.72]</td>
<td>2.66 [2.55-2.76]</td>
<td>0.267</td>
</tr>
<tr>
<td>Hypothyroidism, n (%)</td>
<td>23(44.23)</td>
<td>36(50.7)</td>
<td>0.478</td>
</tr>
<tr>
<td>TPOAb, U/L (M± SEM)</td>
<td>24.51 ± 8.22</td>
<td>13.27 ± 3.72</td>
<td>0.167</td>
</tr>
<tr>
<td>Tg Ab, U/L (M± SEM)</td>
<td>8.51 ± 2.59</td>
<td>20.32 ± 4.94</td>
<td>0.004</td>
</tr>
<tr>
<td>TDI, n (%)</td>
<td>22(42.30)</td>
<td>34(47.8)</td>
<td>0.539</td>
</tr>
</tbody>
</table>
No significant differences were observed in mean TPOAb levels between diabetic subjects and controls (24.51 ± 8.22 vs 13.27 ±3.72, p=0.167). However, mean TgAb showed significantly higher titers in T2D patients compared to controls (20.32 ± 4.94 vs 8.51 ± 2.59, p = 0.004).

Based on thyroid function status, hypothyroidism was less common in patients with T2D than in the control group (44.23% vs 50.7%, respectively), no significant difference was observed between TSH levels in diabetic and nondiabetic subjects (1.57 ± 0.17 vs 1.45 ± 0.12, p = 0.553). FT4 and FT3 concentrations were in the normal range in all study participants.

Multiple logistic regressions analyses are shown in Table II. These results showed that the risk of increased TDI in diabetic patients was not related to diabetic status (OR=1.31; 95% CI: 0.63-2.71 p=0.462), gender female (OR= 1.56; 95% CI: 0.71-3.42, p=0.267), gender male (OR= 1.86; 95%CI: 0.28-12.31, p=0.650), in the < 50 years of age (OR= 0.63; 95% CI: 0.15-2.59, p=0.716), in more than 50 years old (OR= 1.80; 95%CI: 0.75 –4.33,p=1.0) or dyslipidemia (OR=1.20; 95%CI: 0.19 -7.44, p=0.196).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Odds ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Status</td>
<td>1.31 [0.63 - 2.71]</td>
<td>0.462</td>
<td></td>
</tr>
<tr>
<td>Gender Female</td>
<td>1.56 [0.71 - 3.42]</td>
<td>0.267</td>
<td></td>
</tr>
<tr>
<td>Gender Male</td>
<td>1.86 [0.28 -12.31]</td>
<td>0.650</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 50</td>
<td>0.63 [0.15 - 2.59]</td>
<td>0.716</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 50</td>
<td>1.80 [0.75 -4.33]</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.20 [0.19 – 7.44]</td>
<td>0.196</td>
<td></td>
</tr>
</tbody>
</table>

4. Discussion

In the present study we observed a lack of association between T2D and TDI in Moroccan subjects. This result is consistent with similar studies showing no significant difference between T2D patients and healthy controls concerning TDI condition (Radaideh AR, 2004; Ortega-Gonzalez C, 2000). Furthermore, in this study we found a higher prevalence of TDI in both diabetic patients (42.3%) and non-diabetic subjects (50.7%) which differ from other studies already described in the literature showing a prevalence of TDI in T2D patients ranging between 10% and 43% (Akbar, 2006; Yasmin, 2006; Sarfo-kantanka, 2017). The difference in the results described above could be attributed to different methods of laboratory testing used in the assessment of TDI. The prevalence of these autoantibodies has been shown to increase with the sensitivity of the test. In this study, the level of thyroid hormones and antibodies was determined using a more sensitive and accurate automated method. These conflicting results indicated that the interpretation of studies on the frequency of thyroid disorders should take into account the study design, duration of diabetes, genetic specifications and environmental factors, iodine intake, gender, and age (Lang, 2004; Gunasekara, 2011). Moreover, this study was based on data collected retrospectively from ambulatory patients of the medical diagnostic laboratory; this condition makes the characteristics of the patients quite different from those in the general population.
Hypothyroidism is very often the result of autoimmune thyroiditis or insufficient iodine intake in the diet. In our investigation, we observed no significant difference between T2D and hypothyroidism rates. This result is in agreement with previous reports (Radaideh, 2004; Akbar 2006). Given the circumstances, we suspect a probable protective effect of oral hypoglycemic against hypothyroidism in our sample. In many studies, authors suggested that the use of metformin may explain the lower TSH level in patients with T2D (Joffe, 2014; Capelli, 2009).

The mechanism by which the metformin affects the TSH levels is still unclear. Capelli et al. hypothesize that metformin treatment may enhance the inhibitor modulation of TH on central secretion. Another explanation attributes the abnormal TH levels in diabetes might be due to the presence of a TH binding inhibitor (Suzuki, 1994) or the antagonistic effect of insulin and TH on metabolism of carbohydrates, proteins and lipids (Dias, 1995).

In the other hand, we found no significant effect of confounding on TDI profile when analyzing various components (diabetes, age, gender, and lipid status). Whereas, a previous study suggested that TDI are generally associated with female gender and dyslipidemia (Safro-Kantanka, 2017) due to the role of estrogen as an immunomodulatory (Lang, 2004).

Given that the design of the study is retrospective, some limitations should be recognized. First, selection bias may have occurred in the current study because we have collected data of subjects visiting our outpatient institution for routine health check-ups. Second, sample size, missing information on physical examination and medical history could be considered as other limitations.

5. Conclusion

To our knowledge, this the first case-control study to address the relationship between TDI and T2D in North Africa indicating a relatively high distribution but not significant TDI abnormalities in Moroccan subjects with T2D. These results emphasize the need of systematic screening of TDI as part of the management of T2D disease.

Conflicts of Interest

The authors declare that they have no competing interest.

References


• American Diabetes Association (2005), "Diagnosis and classification of diabetes mellitus" Diabetes Care, Vol. 28 pp 37-42.


