Brief report

The rate of primary hypothyroidism in diabetic patients is greater than in the non-diabetic population. An observational study

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ABSTRACT

Background and objective: The aim of our study was to identify the rate of diabetic patients treated for hypothyroidism and compare them with a group without type 2 diabetes mellitus (T2DM).

Patients and methods: We reviewed the computerized clinical records of 5161 patients. We identified diabetic patients treated with L-thyroxine. We compared the prevalence of PH with those patients under treatment with levothyroxine without T2DM. We excluded patients with a thyroid neoplasia, thyroid surgery, panhypopituitarism, or surgical complications of multinodular goiter or a thyroid nodule. Subclinical hypothyroidism was not considered.

Results: We included 1848 adult patients with T2DM in the study group, 58% women and 42% men. For the control group, we included 3313 non-diabetic patients, 55% women and 45% men. The mean age in the study group was 52±7 years, and 47±4 years in the control group (p<.001). The rate of hypothyroidism in the study group was 5.7%, and in the control group 1.8% (odds ratio of 3.45; 95% confidence interval 2.51–4.79) (p<.001).

Conclusion: A strong association between T2DM and hypothyroidism was found. We recommend a thyroid profile in all patients with T2DM, similar to the recommendation in type 1 diabetes mellitus.

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La proporción de hipotiroidismo primario en pacientes diabéticos es mayor que la de pacientes no diabéticos. Estudio observacional

RESUMEN

Fundamento y objetivo: Nuestro objetivo fue determinar la proporción de pacientes con diabetes mellitus tipo 2 (DM2) con hipotiroidismo primario (HP) y compararlo con un grupo sin diabetes.

Pacientes y métodos: Se revisó una base electrónica que incluyó 5161 pacientes. Se identificaron los pacientes con DM2 tratados con levothyroxina. Se comparó con la prevalencia de HP en aquellos pacientes sin DM2. Se excluyeron enfermos con neoplasia o cirugía de tiroides, panhipopituitarismo o complicaciones quirúrgicas de bocio multinodular o nódulo tiroides.

Resultados: Se incluyeron 1848 pacientes adultos con DM2 en el grupo de estudio, 58% mujeres y 42% hombres. Para el grupo control se revisaron 3.313 individuos, 55% mujeres y 45% hombres. La edad media del grupo de estudio fue de 52±7 años, y 47±4 años en el grupo control (p<0.001). La tasa de hipotiroidismo en el grupo de estudio fue de 5.7% (n = 105) y en el grupo control 1.8% (n = 60) (odds ratio 3.45; intervalo de confianza del 95% 2.51-4.79) (p<0.001).

Conclusión: Existe una asociación significativa entre HP y DM2. Recomendamos el perfil tiroideo en todos los pacientes con DM2, similar a lo sugerido en la diabetes mellitus tipo 1.

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Background

In patients with type 1 diabetes mellitus (T1DM) a prevalence of Primary Hypothyroidism (PH) between 10% and 15% has been found. The presence of antithyroid antibodies is predictive of the

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onset of the disease even in subclinical hypothyroidism. On the other hand, the prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus (T2DM) is in the 10–31% range, being subclinical hypothyroidism the most common, which only progresses to clinical hypothyroidism at a low rate. Because of that concern, the utility of routine annual screening for thyroid dysfunction in those patients has been questioned by some authors while others recommend that it should be mandatory, especially if the population is over 50 years of age or has lipid disorders.

Over the last few years, multiple nontraditional risk factors for cardiovascular disease have been identified and these are related both with T2DM and PH, which is why the search for PH constitutes a priority in the overall assessment of this group of patients. Moreover subclinical hypothyroidism may be associated with increased risk of symptomatic hypoglycemia potentially resulting in deterioration of metabolic control.

Most guidelines do not recommend screening for PH in all type 2 diabetic patients at initial diagnosis, and there is no consensus regarding subsequent annual testing in euthyroid patients.

The aim of this study was to determine the rate of PH in patients with T2DM.

Methods

We developed a retrospective cross-sectional study examining the prevalence of PH among Mexican patients with T2DM in a private clinic in Monterrey, Nuevo León during 2009. The protocol was approved by the local ethics committee. We reviewed the patients electronic records as a search strategy. In order to report these results we followed the STROBE recommendations.

In our database, we identified patients with diagnostic criteria and treatment of T2DM and who were treated with L-thyroxine. For comparison, we defined a group of non-diabetic patients under treatment with L-thyroxine. PH was defined in all patients treated with thyroid hormone therapy. We excluded patients with thyroid neoplasia, panhypopituitarism, or surgical complications of multinodular goiter or a thyroid nodule. We extracted demographic and clinical information. We documented the presence of hypertension and dyslipidemia. Subclinical hypothyroidism was not considered.

The analysis was performed using SPSS version 19.0. For continuous variables we used Student’s t test, and the \( \chi^2 \) test was used to compare the rate of hypothyroidism in both groups. A \( p \) value <0.05 was considered significant. The association between T2DM and PH was quantified by OR and a 95% CI.

Results

We included 1848 adult patients with T2DM in the study group, 58% women and 42% men. For the control group 3313 adult patients from the non-diabetic population were analyzed, 55% women and 45% men. The mean age in the study group was 52 ± 7 years, and 47 ± 4 in the control group (\( p < 0.001 \)). In the study group 40% patients had hypertension and 32% dyslipidemia. In the control group 18% had hypertension and 12% dyslipidemia (\( p < 0.001 \)). The rate of PH in the study group was 47.7% (IC 95%, 4.72–6.83), and in the control group 1.8% (IC 95%, 1.41–2.32). When comparing the results the calculated OR for PH in diabetic patients was 3.45 (95% CI 2.51–4.79; \( p < 0.0001 \)) (Table 1).

Discussion

T2DM and PH are the two most common endocrine disorders. The total prevalence of DM is increasing and is projected to rise to 366 million worldwide in 2030, affecting 4.4% of all age groups. It is a prevalent, costly condition associated with substantial morbidity and mortality. Hypothyroidism is most frequently induced by an autoimmune process. Data on the global prevalence is subject to considerable variations due to different definitions of the conditions, particularly of subclinical thyroid dysfunction, and due to the design of the studies, selecting from population or defined patient groups. Reducing these factors and improving quality of life for diabetic patients is a critical public health objective.

In our study we found differences in the prevalence of PH in the general population compared with the one found in patients with T2DM, an association that increases the risk of cardiovascular disease, which is the leading cause of death in patients with T2DM.

These findings are consistent with those previously reported by Whitehead et al. who found a greater prevalence of this association. DM and thyroid disease appear to be closely linked. A recent meta-analysis of all available data in 10,920 patients with DM revealed a mean frequency of thyroid disease of 11%. The data in T1DM did not differ from those in T2DM but the prevalence on females was consistently more than twofold than in males.

Autoimmune thyroid disease is the most common autoimmune disorder associated with diabetes, occurring in 17–30% of patients with type 1 diabetes. The presence of thyroid autoantibodies is predictive of thyroid dysfunction. Recently, thyroid dysfunction was reported in 12.3% of Greek diabetic patients and 16% of Saudi diabetic patients. In Jordan, a study reported that thyroid dysfunction was present in 12.5% of type 2 diabetic patients. Thyroid disorders were found to be more common in subjects with type 1 diabetes compared to those with type 2 diabetes.

Subclinical hypothyroidism was not considered, since the treatment is still debated. A Cochrane analysis of randomized clinical trials found that levothyroxine therapy had no effect on morbidity or quality of life; despite this, we accept the general recommendations outlined in a recent publication.

Current clinical guideline recommendations are inconsistent in the detection of PH in patients with T2DM. The American Diabetes Association recommends an annual evaluation of TSH in all patients with type 1 diabetes, in those with dyslipidemia, and in women aged over 50 years, similar to that recommended by the American Association of Physicians. The American Association of Clinical Endocrinologists recommends screening for thyroid function in all adults over 35 years, with monitoring every 5 years or sooner if there is a high index of suspicion. Based on this information the United States Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend universal screening in these patients (grade 1 recommendation).

Diverse studies support a biologically plausible role for hypothyroidism increasing the risk of atherosclerotic cardiovascular diseases, which include a reduction in intravascular volume, increased peripheral vascular resistance, decreased cardiac contractility and oxygen consumption, via increases in circulating levels of highly atherogenic low-density lipoprotein (LDL) cholesterol particles, induction of diastolic hypertension, altered coagulability, and direct effects on vascular smooth muscle.

**Table 1**

<table>
<thead>
<tr>
<th>Demographic characteristics.</th>
<th>Group 1</th>
<th>Group 2</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52 ± 7</td>
<td>47 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>1071 (58)/&lt;br&gt;777 (42)</td>
<td>1822 (55)/&lt;br&gt;1491 (45)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>739 (40)&lt;br&gt;596 (18)</td>
<td>398 (12)&lt;br&gt;398 (12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>591 (32)</td>
<td>398 (12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary Hypothyroidism</td>
<td>105 (5.7)&lt;br&gt;60 (1.8)</td>
<td>60 (1.8)&lt;br&gt;60 (1.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Group 1 = patients with type 2 diabetes mellitus. Group 2 = patients without type 2 diabetes mellitus.
Furthermore, some evidence suggests that hypothyroidism may exacerbate the cardiovascular risk associated with cigarette smoking and insulin resistance.\(^3\)

T2DM is an independent risk factor for atherosclerotic cardiovascular disease, in which diverse factors contribute to its pathogenesis, including endothelial dysfunction with activation of protein kinase C, overexpression of growth factors and/or cytokines, oxidative stress, hyperglycemia, hyperlipidemia, hyperinsulinemia or hyperproinsulinemia as well as other changes in the coagulation and fibrinolysis process.\(^3,6\)

The benefit of early identification of both diseases has a significant impact on improving cardiovascular function, blood pressure, and lipid profile, thereby reducing long-term cardiovascular risk and improving quality of life for persons with diabetes.\(^3,10\)

The strength of our study is significant and the sample was obtained from an outpatient clinic, unlike other publications that usually perform studies in secondary or tertiary level clinics. An important limitation in our design is that the information was obtained through an electronic database in which there is no access to other demographic variables and metabolic control and could cause a bias in the information. Despite the current guidelines for the diagnosis and treatment of DM, thyroid disease, and co-morbidities as hypertension and hyperlipidemia, the therapeutic decisions can have an individual variability, as well as the fact that there was a significant difference between the age, co-morbidities in both groups, and we do not have information on serum levels of thyroid autoantibodies.

Additional studies will be needed to determine how frequently thyroid function should be tested in the follow-up of these patients based on the incidence rates. In our study PH is more prevalent in patients with T2DM than in the general population. We recommend the thyroid profile as a routine test in all patients with T2DM in the initial diagnosis and follow up.

Conflicts of interest

The authors declare that they have no conflicts of interest

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