ISSN: 0067-2904

Antithyroid Peroxidase and Thyroid Hormones in a Sample of Iraqi Patients with Type 2 Diabetic Mellitus

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Received: 12/4/2022 Accepted: 3/7/2022 Published: 30/4/2023

Abstract

This study aims to investigate the relationship between thyroid peroxidase antibody (TPO) and thyroid function tests (TSH, T3 and T4) in patients with type 2 diabetes mellitus (T2DM). Ninety women and men, with ages ranging between 35-65 years and weighing 60-80 kgs, were selected for this study. They were classified into three groups: G1 included 15 healthy control group, G2 had15 patients with T2DM and G3 had 60 patients with T2DM and hypothyroidism. Blood samples were collected from each individual via vein puncture to assess thyroid hormone and TPO-Ab. The results showed highly significant ($p < 0.01$) increase in TSH level in the diabetic group with hypothyroidism when compared to the other groups. There was no significant difference between diabetic and control groups. T4 and T3 levels showed highly significant ($p<0.01$) decrease in the diabetic group with hypothyroidism when compared to the diabetic and healthy control groups. On the other hand, there was no significant difference between the diabetic and healthy control groups. The results showed highly significant ($p < 0.01$) increase in the TPO-AB level in diabetic group with hypothyroidism when compared with the diabetic and healthy control groups.

Keywords: T2DM, TSH, T4, T3, TPO-Ab.

بيروكسيداز مضاد الغدة الدرقية وهرمونات الغدة الدرقية في عينة من المرضى العراقيين المصابين بداء السكري من النوع الثاني

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الخلاصة

تهدف هذه الدراسة إلى التحقق من العلاقة بين اختبار الأجسام المضادة لبيروكسيداز الغدة الدرقية (TPO) واختبارات وظائف الغدة الدرقية (TSH، T3، T4) في مرضى السكري من النوع الثاني. شارك في هذه الدراسة تسعون من النساء والرجال الذين تراوحت أعمارهم بين (35–65) سنة واوزانهم (60–80) كغم. تم تصنيفهم إلى ثلاث مجموعات ؛ شملت G1 15مجموعة الاصحاء ، G2 وتضمنت 15 مريضًا مصابا بالسكري النوع الثاني، اما G3 فشملت (60 مريضًا يعانون من قصور الغدة الدرقية المصاحب لداء السكري

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من النوع الثاني). جمعت عينات الدم من كل فرد عن طريق سحب الدم من الوريد لتقدير هرمون الغدة الدرقية و TPO–Ab. أظهرت النتائج زيادة معنوية عالية ($p < 0.01$) في مستوى هرمون TSH في مرضى السكري مع مجموعة قصور الغدة الدرقية ، مقارنة بمجموعة مرضى السكر ومجموعة السيطرة. علاوة على ذلك لم يكن هناك فرق معنوي بين مجموعة مرضى السكر ومجموعة السيطرة. أظهر مستوى T4 و T3 انخفاضًا معنويًا عاليًا ($p < 0.01$) في مرضى السكري مع مجموعة قصور الغدة الدرقية عند مقارنتهم بمجموعة مرضى السكر ومجموعة الاصحاء. علاوة على ذلك ، لم يكن هناك فرق معنوي بين مجموعة مرضى السكر ومجموعة الاصحاء. أظهرت النتائج زيادة معنوية ($p < 0.01$) في مستوى TPO–AB في مرضى قصور الغدة الدرقية المصاحب للسكري بالمقارنة مع مجموعة مرضى السكر ومجموعة الاصحاء.

Introduction

Thyroid disorders are one of the most prevalent endocrine illnesses with an increasing prevalence as one ages. Subclinical thyroid disease is characterized by elevated blood thyroid stimulating hormone (TSH) but normal triiodothyronine (T3) and thyroxin (T4) levels. While those with clinical thyroid disease have elevated serum TSH, T3 and T4 levels requiring medication [1].

Hypothyroidism is a common endocrine condition caused by thyroid hormone deficiency or less commonly by reduced tissue function. Since all metabolically active cells require thyroid hormone, lacking them leads to a wide range of consequences like typical auto-immune disease [2].

Thyroid peroxidase (TPO) is required for thyroid hormone production and secretion. Additionally, it is a significant autoantigen in autoimmune thyroid disorders [3].

Anti-TPO antibodies are present in 90–95 percent of individuals with autoimmune thyroid disorders (AITD) and 10–15 percent in non-AITD patients. Anti-TPO antibodies from AITD patients have been shown to damage thyrocytes and impede enzymatic function. These antibodies are found in between 5-27% of general population. Their Anti-TPO-Ab values are greater than 40 IU/mL and are termed positive for TPO-Ab [4].

This study aims to investigate the relationship between thyroid peroxidase antibody (TPO) and thyroid function tests (TSH, T3 and T4) in patients with type 2 diabetes mellitus.

Materials and Method

Subjects

The current study took place in the Specialist Center for Endocrine and Diabetes Diseases/ Baghdad, between November 2021 and February 2022.90 individuals were selected and divided into three groups. The first group included 60 hypothyroidism patients with T2DM. The second group (positive control) consisted of 15 T2DM patients. While the third group had 15 healthy individuals (negative control). Hypothyroidism individuals were included in the current investigation with ages ranging from 30 to 64 years. Selected healthy adults served as the control group, consisting of subjects between the ages of 30 and 80 years.

Collection and Preparation of Blood Samples

Venous blood samples (5ml) obtained from all under study participants, were centrifuged for 10 minutes at 3000 rpm. The serum was collected and stored in the freezer (-20^{o} C) until it was used to determine biochemical and immunological parameters, according to the manufacturer's instructions. T3, T4 and TSH levels were measured using LDN (Germany) kits

as indications of thyroid function. ELISA kits from immuno lab CUSABIO (USA) were used to measure anti thyroid peroxidase (TPO-Ab).

Statistical Analysis

Statistical Analysis System- SAS (2012) program was used to detect the effects of study parameters. Analysis of Variation-ANOVA and L.S.D. test was used to compare the significance between means [5] at ($p<0.05$) and ($p<0.01$) [6].

Results and Discussion

As shown in Figure 1, there is a significant ($p \leq 0.01$) increase in the TSH level in the diabetic group with hypothyroidism as compared with negative and positive control groups. Furthermore, there is no significant difference between healthy negative and diabetic positive control groups. The TSH in diabetic with hypothyroidism was 8.63 ± 1.34 mIU/l. While it was 1.301 ± 0.27 mIU/l and 2.596 ± 0.28 mIU/l in negative and positive groups respectively. Hormones are normally lower when serum TSH is high because of negative feedback which agrees with a previous study [7].

TSH levels in T2DM were not significantly different from controls. The results of the present study agrees with previous studies that found out that diabetes influence on TRH, hyperglycemia detrimental effects on T3 and the lack of TSH response to TRH may all contribute to secondary hypothyroidism [8].

Serum TSH concentrations were higher in T2DM patients than in seemingly healthy controls and the difference was statistically significant [9]. Serum T3 and T4 levels were considerably lower in diabetes participants compared to non-diabetic subjects. Whereas TSH serum levels were significantly higher in diabetic subjects compared to non-diabetic people and come into agreement with this study [10].

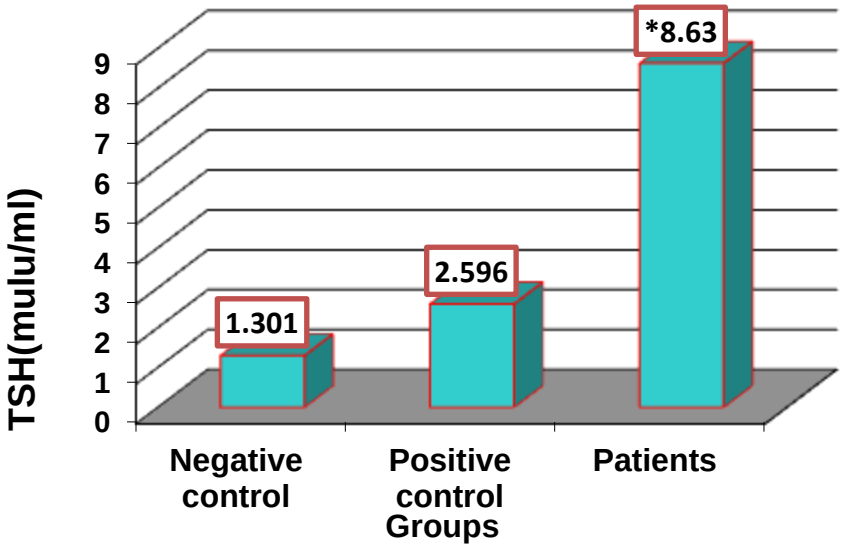

Figure 1: TSH levels in hypothyroid and control groups.

In addition, there was a significant ($p \leq 0.01$) decrease in T3 concentration in diabetes patients with hypothyroidism as compared with the negative and positive control groups. Furthermore, there was no significant ($p < 0.01$) difference between the healthy negative and diabetic positive control groups. The T3 concentration in diabetes patients with hypothyroidism was 82.04 ±6.64 ng/dl. While it was 149.40 ± 9.45 ng/dl and 132.70 ±9.01

ng/dl in negative and positive groups respectively. These findings can be explained by the fact that most hypothyroidism patients have disorders of glucose and insulin metabolism, including defective insulin secretion in response to glucose, hyperinsulinemia, altered peripheral glucose disposal and insulin resistance [11].

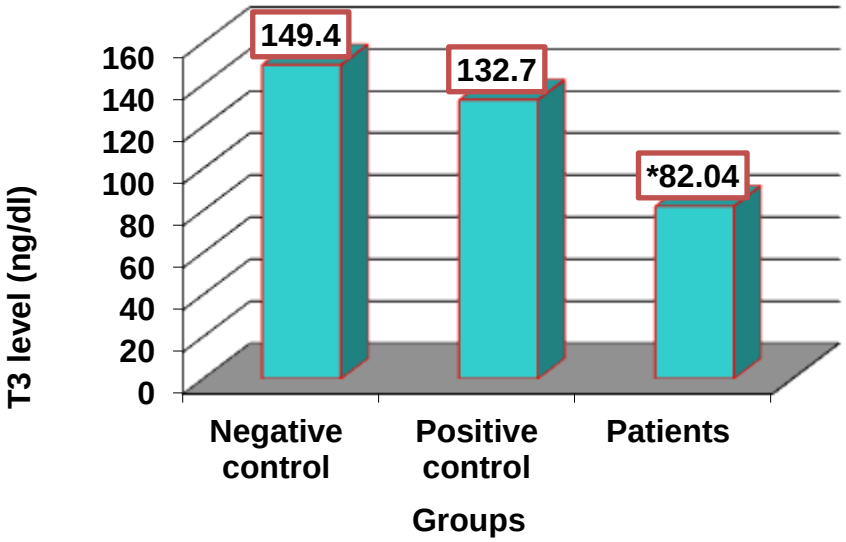

Figure 2: T3 level in hypothyroid and control groups.

Further, there was a significant ($p \leq 0.01$) decrease in T4 level mean in diabetic patients with hypothyroidism as compared with the negative and positive control groups. Furthermore, there was no significant ($p > 0.01$) difference between the healthy negative and diabetic positive control groups. The T4 level mean in diabetics with hypothyroidism was 5.34 ±0.61 µg/dl. While it was 11.23 ±0.29 µg/dl and 9.67 ±0.68 µg/dl in negative and positive groups respectively (Figure 3).

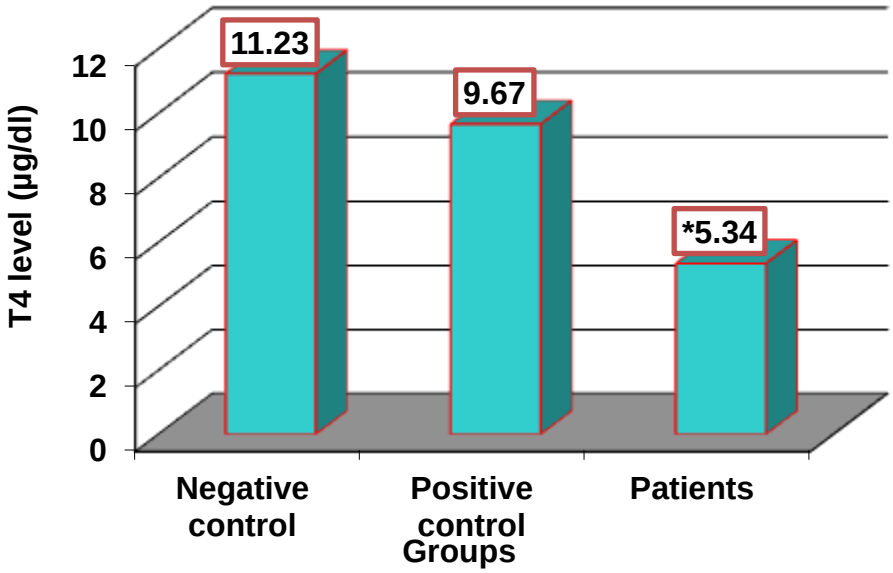

Figure 3: T4 level hormone in hypothyroid and control groups.

Thyroid function appeared to be affected by DM in two main ways. Firstly, at the level of the hypothalamus where TSH is managedand secondly at the level of peripheral tissues where T4 is turned into T3 [12]. Besides that thyroid hormones (THs) are key regulators of

differentiation, proliferation and metabolism. Indeed, TH is essential for virtually all tissues to function normally, with significant implications for oxygen consumption and metabolic rate [13].

Regarding anti-TPO-Ab, there was a significant ($p \leq 0.01$) increase in anti-TPO-Ab consideration in diabetics with hypothyroidism as compared with the negative and positive control groups. Furthermore, there was no significant ($p > 0.01$) difference between healthy negative and diabetic positive control groups. The anti-TPO-Ab level mean in diabetics with hypothyroidism was 0.223 ± 0.01 ng/ml. While it was 0.156 ± 0.01 ng/ml and 0.150 ± 0.02 ng/ml in both negative and positive groups respectively. As compared with the finding of their investigation, not all the patients were positive for the TPO-Ab which agreed with a previous study where TPO-Ab was found in 8% of the participants with thyroid dysfunction. This shows that TPO-Ab testing might detect thyroid dysfunction in type 2 diabetics. TPO-Ab positivity was found in 21.1% of euthyroid individuals. It revealed that if antibodies had been utilized as a sole diagnostic tool in this investigation, we would have overlooked 16.8% of people with thyroid dysfunction but with negative antibodies [14].

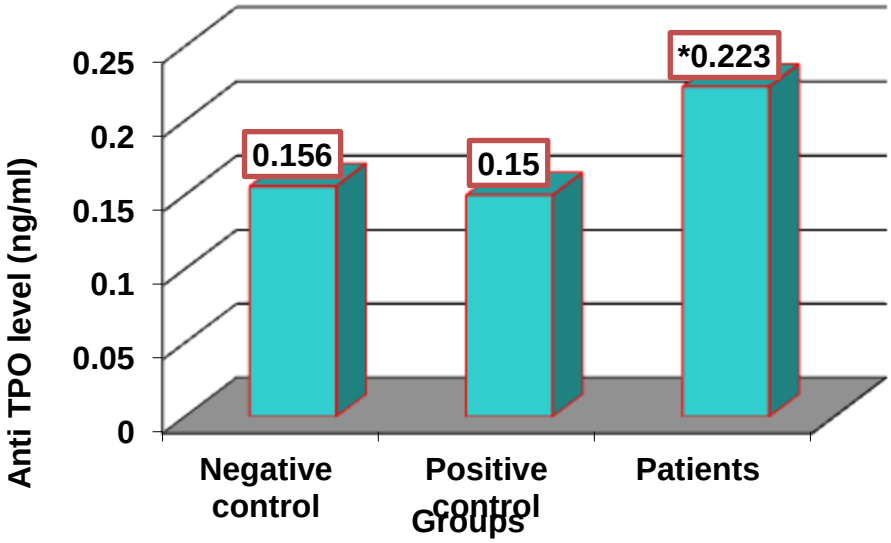

Figure 4: Anti TPO-Ab level in hypothyroid and control groups.

The results of the present study agree when compared with another study that found out that the mean serum anti-TPO antibodies also increased among T2DM patients as compared to control group, showing statistical significance between these groups [15].

The results of the present study also agree with other studies in diabetes that concluded that aberrant thyroid hormone levels may be caused by the presence of a thyroid hormone-binding inhibitor, an inhibitor of T4 to T3 conversion, a dysfunctional HPT axis or due to the effects of poorly managed diabetes on thyroid hormone concentrations [16].

The specific reason for higher occurrence of autoimmune thyroid disease in those with type 2 diabetes is still not known. This condition is thought to be caused by genetic and environmental factors, as well as infections and psychological stress. A probable relationship between T2DM and autoimmunity has been suggested. It is hypothesized that IR occurs when -cells and other immune cells respond to self-antigens by producing cytokines. Obese mice have been shown to have an accumulation of -cells in their visceral fat. Self-antigens

produced as a result of this process may provoke an autoimmune reaction, which in turn increases -cell death [17].

Conclusion

Thyroid hormones levels in diabetic group are normal which explains that not necessarily all diabetics have thyroid disorders. There is an increase in TPO-AB level in diabetic patients group with hypothyroidism. Some patients with thyroid disorders may develop diabetes mellitus in the future or vice versa.

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