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Thyroid dysfunction and autoimmunity in type 2 diabetes mellitus: A Sudanese perspective

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Abstract

Background: Autoimmune Thyroid Disease (AITD) is the most common thyroid condition that coexists with diabetes mellitus. Although Anti-Thyroid Peroxidase (anti-TPO) and Anti-Thyroglobulin (anti-TG) antibodies are important indicators of AITD, little is known about how they relate to Type 2 Diabetes Mellitus (T2DM) in Sudan. The frequency of these antibodies in hypothyroid T2DM patients in Nyala, South Darfur, was examined in this study.

Objective: To determine the presence of anti-TPO & anti-TG antibodies in hypothyroid T2DM patients and assess the prevalence of clinical and subclinical hypothyroidism.

Materials and methods: A cross-sectional study was conducted at Yashfeen Diagnostic Center (Nyala) from November 2016 to January 2017. Serum anti-TPO & anti-TG levels were measured via immunofluorescence in hypothyroid T2DM patients. Thyroid dysfunction was classified as clinical hypothyroidism (elevated TSH with low T4) or subclinical hypothyroidism (elevated TSH with standard T4)

Results: Of 200 T2DM patients aged 35–83, 18 (9%) had hypothyroidism, with 6 having overt hypothyroidism (3%) and 12 having subclinical hypothyroidism (6%). When compared to normal thyroid diabetic patients, biochemical analysis showed significantly higher TSH levels (mean 8.78 µIU/mL, P<0.0001) and lower T3 (0.77 ng/mL, P=0.007) and T4 (5.62 µg/dL, P=0.004) levels. Anti-TPO or anti-TG antibodies were detected in 61.1% of hypothyroid patients, as determined by thyroid autoantibody testing, with a significant female predominance (75% vs. 25%, P=0.022). The glycemic indices (fasting glucose and HbA1c) of the hypothyroid and euthyroid groups were comparable.

Conclusion: Among type 2 Sudanese patients with diabetes, thyroid dysfunction that presents as autoimmune hypothyroidism is pretty common. Women are more likely than men to experience this phenomenon. To aid in early detection, routine thyroid screening, including autoimmune detection, and customized treatment should be considered.

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Keywords: Sudan; Anti-TPO; Anti-TG; Hypothyroidism; Thyroid autoimmunity; and T2DM.

Introduction

T2 Diabetes Mellitus (T2DM) and thyroid dysfunction are two of the most prevalent endocrine disorders worldwide, and their coexistence has been increasingly recognized as a significant clinical challenge [1]. Epidemiological studies suggest that T2DM patients are at a higher risk of developing thyroid disorders compared to the general population, with hypothyroidism being the most common [2,3]. The interplay between these conditions is bidirectional: thyroid dysfunction exacerbates insulin resistance and glycemic variability, while chronic hyperglycemia may impair thyroid hormone synthesis and action [4,5].

Autoimmune Thyroid Disease (AITD), particularly Hashimoto's thyroiditis, is the leading cause of hypothyroidism in iodine-sufficient regions [6]. The presence of autoantibodies against thyroid peroxidase (anti-TPO) and thyroglobulin (anti-Tg) serves as a hallmark for AITD, with anti-TPO antibodies being detected in up to 90% of affected individuals [7]. Notably, AITD exhibits a strong female predominance, likely due to hormonal and genetic factors [8,9]. Emerging evidence suggests that chronic inflammation and immune dysregulation in Type 2 Diabetes Mellitus (T2DM) may further predispose patients to thyroid autoimmunity [10].

Notwithstanding these connections, both the diffusion and clinical relevance of thyroid autoimmunity in T2DM patients remain under-researched in sub-Saharan Africa, especially in Sudan. Limited data exist on the interplay between T2DM and AITD in this region, where genetic, environmental, and nutritional factors may influence disease patterns [11,12]. This research attempts to address this issue by examining the incidence of hypothyroidism and anti-TPO/anti-TG antibodies in T2DM patients in Nyala, South Darfur, Sudan. Our findings will provide critical insights into the need for routine thyroid screening in this high-risk population and contribute to the growing literature on diabetes-thyroid interactions in understudied populations.

Materials and methods

Study design

A hospital-based, cross-sectional study investigated thyroid dysfunction in patients with Type 2 Diabetes Mellitus (T2DM). The study adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for cross-sectional studies.

Study population and setting

Participants: 200 consecutively recruited T2DM patients (both sexes) attending Yashfeen Diagnostic Center, Nyala City, Southern Darfur State, Sudan, during November 2016 to January 2017. In this study, individuals with normal thyroid function (euthyroid T2DM) constituted the baseline group for internal scrutiny. This group was essential in evaluating biochemical and immunological differences relative to patients diagnosed with overt or subclinical hypothyroidism. The study approach, which lacked a separate non-diabetic control group, was driven by our principal objective: to assess the proportion and features of thyroid dysfunction within the diabetic cohort.

Inclusion criteria: Adults (≥18 years old) who have been diagnosed with Type 2 Diabetes (T2DM) according to the American Diabetes Association's 2016 criteria. Diagnosis at least six months before enrollment.

Exclusion criteria: Acknowledged thyroid-related disorders include hypothyroidism, hyperthyroidism, and thyroiditis.

Chronicle of thyroidectomy and radioactive iodine treatment.

Gestation or severe medical condition (e.g., infection, recent surgical procedure).

Sample size and sampling technique

Based on the anticipated prevalence of thyroid dysfunction in T2DM (20%±5%, 95% CI), the sample size (n=200) was determined using OpenEpi, assuming a 10% non-response rate. To reduce selection bias, consecutive sampling was used.

Data and sample collection

Clinical data: Structured questionnaires were used to collect clinical data (diabetes duration and medication) and demographic data (age and sex).

Measurement and sampling of blood: Each participant had 5 mL of blood drawn after fasting overnight. Three milliliters were placed in lithium heparin tubes for the analysis of thyroid hormones (TSH, T3, and T4), anti-TPO, anti-TG, and blood glucose. Two milliliters were placed in K3EDTA tubes for the measurement of glycated hemoglobin. The plasma was stored at -20°C until analysis, which was performed within 24 hours after the samples were centrifuged for 10 minutes at 3000 rpm. Fasting blood glucose was assessed via the glucose oxidase–peroxidase method, while HbA1c was quantified through an enzymatic assay and represented as estimated average glucose using the formula eAG (mg/dL) = 28.7×HbA1c (%) − 46.7, both using the Mindray BS-240Pro chemistry analyzer (SN: BC7-2B005644, China). Thyroid function tests, comprising TSH, T3, and T4, were conducted on the TOSOH AIA-360 automated analyzer (SN: 2A192506, Japan) using competitive fluorescence enzyme immunoassay with daily internal quality control measures. Thyroid autoantibodies (anti-TPO and anti-TG) were identified by indirect immunofluorescence (Euroimmun AG, Germany), with positive established at titers of ≥ 1:40 for anti-TPO and ≥ 1:100 for anti-TG.

Statistical analyses

The data were analyzed with precision using both descriptive and inferential statistics (SPSS version 20, IBN, Chicago). Continuous variables exhibiting a normal distribution were represented as the mean ± Standard Deviation (SD), whereas frequencies and percentages denoted categorical variables. Comparisons between hypothyroid and normothyroid patients were conducted with exacting standards, using the independent samples t-test for continuous variables and the Chi-square test (or Fisher's exact test when applicable) for categorical data. To assess the relative risk of thyroid autoimmunity by gender, Odds Ratios (OR) with 95% CI were calculated. Statistical significance was defined as a P-value of less than 0.05.

Results

This cross-sectional study involved 200 patients with T2DM, comprising 66% females and 34% males, aged between 35 and 83 years (Figure 1). The duration of diabetes was 7.5±5.5 years. The findings highlighted how common thyroid dysfunction, especially hypothyroidism, was in this group and how it was classified. Of the subjects, 6 (3%) had hypothyroidism (95% CI: 1.4–6.4%), 12 (6%) had subclinical hypothyroidism (95% CI: 3.4–

10.2%), and 182 (91%) had normal thyroid function (Figure 2).

Thyroid function testing verified shows biochemical hypothyroidism. Individuals in this category exhibited significantly higher TSH levels (8.8 µIU/mL), alongside diminished T3 (0.77 ng/mL) and T4 (5.6 µg/dL) concentrations, in contrast to normal thyroid diabetic individuals (TSH=1.0 µIU/mL; T3 1.07 ng/mL; T4 7.6 µg/dL). Significant differences between hypothyroid patients and other people with type 2 diabetes were revealed by the significant and massively impactful hormonal changes. Thyroid-stimulating hormone (TSH) levels (P<0.0001) and lower levels of triiodothyronine (T3) (P<0.007) and thyroxine (T4) (P<0.004) are particularly noteworthy in these results. The detailed results are encapsulated in (Table 1). Thyroid dysfunction in this group, however, did not adversely affect overall glycemic control, as evidenced by the lack of significant differences in fasting blood glucose and HbA1c levels between the hypothyroid and euthyroid groups.

An alarming 18 (9%) of the 200 T2DM patients had hypothyroidism. In addition to a standard biochemical thyroid profile, all 18 patients underwent testing for thyroid autoantibodies, including anti-TPO and anti-TG. The group's overall autoantibody positivity rate was 11 out of 18, or 61.1% (95% CI: 35.7%-82.7%). The autoantibody results revealed the presence of specific antibodies in the hypothyroid patients. Notably, eight patients (44.4%) tested positive for anti-TPO antibodies, and three patients (16.7%) tested positive for anti-TG antibodies (Figure 3). Conversely, negative anti-TPO and anti-TG represent 7(38.9%).

A significant gender disparity was noted. In males with hypothyroidism, 25% (2 cases) tested positive for anti-TPO, while in females, 75% (6 cases) tested positive, and 37.5% (3 cases) tested positive for anti-TG. This difference was statistically significant (P<0.022) with an odds ratio of roughly 1.89, showing that hypothyroid women with T2DM were nearly twice as likely as males to exhibit autoimmune thyroid signs.

Discussion

The prevalence of thyroid dysfunction, specifically hypothyroidism, was evaluated in this cross-sectional study. Sixty-six percent of the population was female, and the average duration of diabetes was 7.5±5.5 years. The majority of subjects (91%) had normal thyroid function, while 3% had hypothyroidism and 6% had subclinical hypothyroidism. These results not only support the existing body of knowledge in this area but also align with other studies that have shown a higher prevalence of thyroid dysfunction in diabetic populations, particularly in women [13,14].

This study indicates a significant prevalence of thyroid autoimmunity in Sudanese patients with T2DM and thyroid dysfunction, with 61.1% exhibiting anti-TPO or anti-TG positivity. This finding is consistent with those from Greece [15]. From Ghana, where 14.4% of T2DM patients exhibited thyroid autoimmunity, which significantly surpasses the rates in non-diabetic controls, the prevalence of autoantibodies in African T2DM populations appears elevated, especially in conjunction with thyroid dysfunction [16].

The positivity rate of our autoantibodies corresponds with previous findings from Middle Eastern and North African populations, which reported a prevalence of anti-TPO-only at 15–20% and anti-TG-only at 8-9% [17]. The variability probably indicates disparities in assay sensitivity, patient demographics, and underlying causes.

Table 1: Biochemical and hormone values among the thyroid dysfunction T2DM.

Parameter	Hypothyroidism (Mean±SD) (n=18)	Other T2DM Patients (Mean ± SD) (n=182)	P-value
Fasting Blood Glucose mg/dL	181.12±42.95	200.25±59.35	0.369
HbA1C %	7.73±2.97	7.69±1.87	0.945
TSH µUI/mL	8.78±3.06	1.02±0.75	0.000
T3 ng/mL	0.77±0.166	1.07±0.31	0.007
T4 µg/dL	5.62±1.66	7.56±1.84	0.004

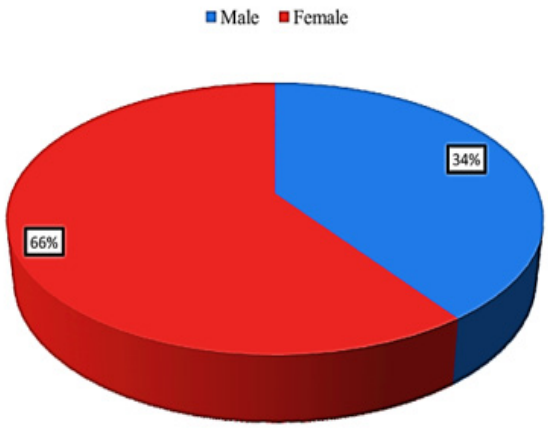

Figure 1: Gender distribution among T2DM patients.

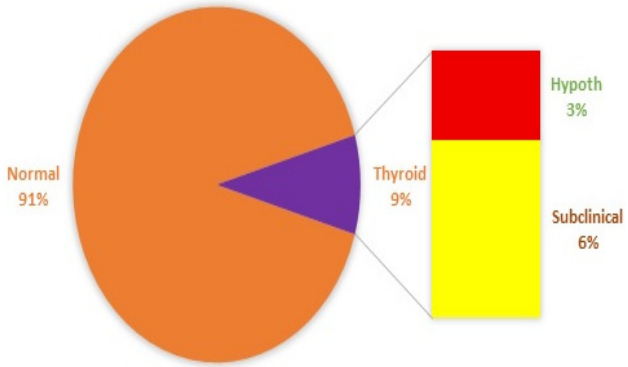

Figure 2: Prevalence and classification of thyroid dysfunction in T2DM.

The strong immunologic profile (autoantibody positive) in our group highlights the autoimmune etiology of hypothyroidism in diabetic populations, aligning with the pathophysiology of Hashimoto's thyroiditis, where anti-TPO and anti-TG are frequently involved [18-20]. The predominance of females, although not explicitly defined in this context, is well-established in autoimmune thyroid illness.

The reported biochemical profiles, elevated TSH with suppressed T3 and T4, are indicative of overt autoimmune hypothyroidism and support the high prevalence of antibody positivity. Similar patterns have been observed worldwide [21].

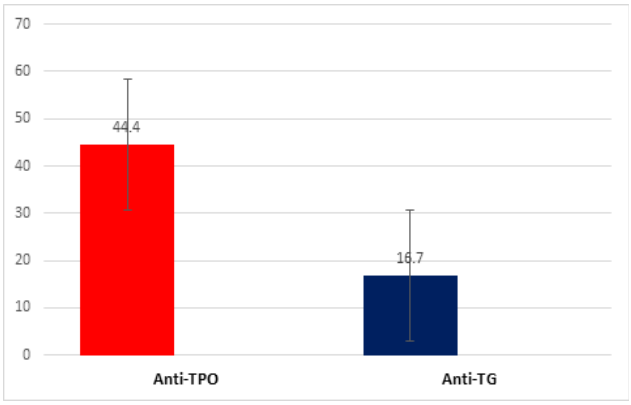

Figure 3: Frequency of thyroid autoantibodies among the hypothyroidism group.

Notably, glycemic control exhibited no significant differences between the thyroid dysfunction and euthyroid subgroups. This reflects discoveries that, although thyroid health can affect metabolism, the interaction with glycemic indicators is intricate and may be contingent upon the length and compensatory state of thyroid failure. A recent meta-analysis assessed the overall incidence of thyroid dysfunction in T2DM at nearly 20%, with elevated rates observed in Africa and Asia. With a pooled prevalence of approximately 11.9%, subclinical hypothyroidism was the most common type, which is especially concerning [22]. Although the sample size is small and context-specific, the prevalence of thyroid autoimmunity in our subgroup of patients with clinically diagnosed hypothyroidism reflects these trends.

The prevalence of positive TPO (75%) and TG (100%) autoantibodies was higher in females than in males, indicating a significant gender gap. This is consistent with epidemiological evidence that women are disproportionately affected by autoimmune thyroid disorders [23,24]. The higher odds ratios (1.89 and 2.33, respectively) and the statistical significance of these results ($P<0.022$ for TPO and $P<0.002$ for TG) highlight the vulnerability of women to thyroid autoimmunity. These findings underscore the urgent need for gender-specific approaches that could greatly improve patient outcomes and have significant implications for the diagnosis and treatment of autoimmune diseases.

Although a number of limitations must be noted, this study offers important insights into the prevalence and features of thyroid dysfunction in patients with type 2 diabetes. Further longitudinal research is required because the cross-sectional methodology limits our ability to establish causal links between thyroid dysfunction and type 2 diabetes. The results may not be as broadly applicable to male populations due to the small sample size and high prevalence of females. Third, the results of a single-center study could be impacted by selection bias, highlighting the need for multi-center research to increase external validity. Given that diet, lifestyle, and comorbidities (such as iodine intake, smoking, obesity, or cardiovascular disease) are known to impact thyroid function, the lack of information on these factors is a significant disadvantage. Variability in autoantibody testing procedures and cutoff values may contribute to inconsistent results. Ultimately, the study did not characterize regional or ethnic variation, which could have an impact on the prevalence of thyroid issues. These restrictions highlight the pressing need for further research in this area.

Conclusion

This study emphasizes the significant prevalence of thyroid dysfunction, especially hypothyroidism, in patients with T2DM, with a marked inclination towards female individuals. The notable biochemical differences in TSH, T3, and T4 levels indicate the necessity for routine thyroid screening in individuals with diabetes. The elevated prevalence of thyroid autoantibodies, particularly in women, suggests a potential autoimmune origin, requiring specific diagnostic and treatment strategies. To improve patient care methods, future research should investigate the molecular relationships between Type 2 Diabetes Mellitus (T2DM), autoimmunity, and thyroid dysfunction, considering the strong statistical correlations that have been observed.

Ethical considerations: The Faculty of Medical Laboratory Sciences Ethical Committee at Alneelain University gave its approval. Every participant provided written informed consent. According to the Helsinki Declaration (2013), confidentiality is upheld.

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