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# Thyroid Dysfunction in Type 2 Diabetes Patients: A Study at the Diabetes Centre, Al-Gamhouria Modern General Hospital, Aden, Yemen

Nazeh Al-Abd[1,2*], Wafa Al-Aiashy[1], Abdulrahman Habtor[1], Abrar Aref[1], Ahmed Othman[1], Amal Awadh[1], Ayat Fuad[1], Bassam Ali[1], Eman Abdulrqeeb[1], Faiza Hassan[1], Khadiga Mohammed[1], Majed Naji[1], Nermeen Nasr[1], Rasha Mohammed[1], Rawan Abdulkarim Mohammed[1], Rawan Abdulkareem Ali[1], Raqya Anwer[1], Saleh Adel[1], Wahda Mohammed[1] and Zainab Khaled[1]

[1] *Department of Health Sciences, Faculty of Medicine and Health Sciences, University of Science and Technology, Aden, Yemen*
[2.] *Department of ParaClinic, Faculty of Medicine and Health Sciences, University of Aden, Aden, Yemen*

## ABSTRACT

**Background:** Patients with type 2 diabetes mellitus (T2DM) frequently have thyroid dysfunction, an endocrine condition that requires careful examination. **Objective:** The prevalence of thyroid dysfunction among 100 T2DM patients was explored in this cross-sectional study. **Method:** Thyroid function was assessed using levels of free thyroxine (FT4), free triiodothyronine (FT3), and thyroid-stimulating hormone (TSH). **Results:** The findings showed a 20% prevalence of thyroid dysfunction, with hypothyroidism accounting for 18%. Notably, patients with and without thyroid disease did not differ significantly in terms of age or gender. However, patients with thyroid dysfunction had noticeably higher TSH levels (p=0.001). **Conclusion:** These results underscore how crucial routine thyroid function testing is for T2DM patients to promote early detection and efficient treatment.

**Keywords:** Thyroid Dysfunction, Type 2 Diabetes Mellitus, Hypothyroidism, Hyperthyroidism, Thyroid Function Tests

**** Corresponding author address:*** *nazehali78@yahoo.com*

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## INTRODUCTION

Thyroid dysfunction and type 2 diabetes mellitus (T2DM) are two endocrine conditions that frequently coexist in individuals and have been associated with a multitude of health complications and challenges (1). T2DM is a chronic metabolic condition exemplified by impaired insulin sensitivity and secretion, ultimately leading to a rise in blood glucose levels (2). T2DM is thought to be the most common type of diabetes, accounting for 90–95% of all cases (3). Thyroid dysfunction encompasses various conditions, including hyperthyroidism, hypothyroidism, and thyroiditis, which affect the thyroid gland's ability to make essential hormones (4).

The thyroid gland plays an essential role in regulating metabolic activities, growth, and development through the production of thyroxine (T4) and triiodothyronine (T3) (5). Dysfunctions of the thyroid gland can manifest in various symptoms, including fatigue, weight changes, mood disturbances, and cardiovascular issues (6).

The coexistence of T2DM and thyroid dysfunction can significantly impact an individual's health and well-being, complicating clinical management and exacerbating symptoms and complications (7, 8). Although the relationship between these disorders is intricate and not yet fully elucidated, existing research indicates that individuals affected by one of these conditions are more likely to develop the other, suggesting a potential link between the two disorders (7, 8).

Several epidemiological studies have consistently shown that individuals with T2DM have a higher likelihood of developing thyroid disorders compared to the general population, suggesting a potential association between these two conditions (7, 8). Similarly, individuals with thyroid dysfunction are at increased risk of developing T2DM (17, 18). The underlying mechanisms linking the two conditions are not fully understood. However, factors such as insulin resistance, chronic inflammation, immune system interactions, hormonal interactions, and genetic predisposition may play a role in their combined pathophysiology (19, 20, 21).

The frequent co-occurrence of T2DM and thyroid dysfunction necessitates a proactive approach to screening and management. Healthcare providers should prioritize thyroid function testing in diabetic patients and vice versa. Early detection and treatment of both conditions can lead to improved clinical outcomes, enhanced quality of life, and better overall health (1). An integrated care model that simultaneously addresses both endocrine disorders is essential for optimal patient care.

It has proposed a reciprocal relationship between diabetes and thyroid function. Data from the Third National Health and Nutrition Examination Survey (NHANES III), large-scale cross-sectional research involving 17,353 US individuals, showed that 4.6% had hypothyroidism and 1.3% had hyperthyroidism (9). Additionally, the study showed that thyroid dysfunction and diabetes were significantly correlated, with a higher prevalence of thyroid abnormalities among diabetics (9).

Thyroid dysfunction has been extensively documented in individuals with diabetes (DM) worldwide. Nevertheless, there have been limited studies on this association in Yemen. This research aims to identify the prevalence of thyroid dysfunction among T2DM patients; thereby, the results of the current study will contribute to expanding the existing knowledge base on diabetes and thyroid dysfunction in Yemen, particularly in Aden Governorate. This study will provide valuable insights into the prevalence of thyroid dysfunction among individuals with T2DM.

Understanding the types and prevalence of thyroid dysfunction in T2DM patients is crucial for several reasons. Firstly, thyroid disorders can exacerbate diabetes complications and affect the management of diabetes. Secondly, identifying the prevalence and nature of thyroid dysfunction in T2DM patients can lead to better screening and management strategies, improving patient outcomes. Lastly, this study can provide insights into the need for routine thyroid function tests in diabetic care, which could enhance prompt detection of thyroid-related issues in diabetic patients. The findings are expected to contribute valuable insights to the field of diabetes management and endocrinology.

## METHODOLOGY

### Study Design and Period of the Study

The prevalence of thyroid dysfunction among individuals with T2DM was investigated through an analytical cross-sectional institution-based study.

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This study was conducted over four months, from October 2023 to January 2024.

**Study Area**
The study was conducted at the Diabetes Center at Al-Gamhouria Modern General Hospital in Aden Governorate, Yemen.

**Study Population**
The study sample comprised adults with a confirmed diagnosis of T2DM who regularly visited the diabetes center for treatment.

**Study Subjects**
Eligible participants were adults (≥18 years) residing in Aden Governorate with a confirmed T2DM diagnosis for a minimum of a year. Inclusion criteria included T2DM diagnosis, willingness to provide informed consent, availability during data collection, and age ≥18. Exclusion criteria comprised type 1 diabetes, age <18, thyroid disorders, medications affecting thyroid function, pregnancy, breastfeeding, and specific medications (amiodarone, propranolol, levothyroxine, antithyroid drugs, corticosteroids, and oral contraceptives).

**Sample Size Calculation**
Two-tailed α will be used with a p-value = 0.05 at a 95% confidence interval (CI), so Zα = 1.96, at 80% power, for all variables. The sample size was computed based on the prevalence rates of patients with T2DM in Yemen, which is approximately 4% among adults aged 20 to 79, according to IDF and data from 2020 (22). p = 4.0 %; then q = 96.0 %, degree of precision = 5 %. Using the following formula (10).
Thus, the sample size was 59. In addition, inflation of the sample size by 10% is done to preserve sample size when there is missing data or errors. So, the minimum sample size was n = 65. = 59

**Data Collection**
A structured questionnaire was used to gather demographic and medical history data, which included demographic information and medical history. Clinical measurements such as weight and height were recorded. Blood samples were obtained for laboratory analysis of fasting blood sugar (FBS), glycated hemoglobin (HBA1C), and thyroid function.

**Blood Collection**
A 5-milliliter (5 ml) venous blood sample was obtained through venipuncture and transferred into a gel tube, where it was permitted to clot, after which it was centrifuged for 5 minutes at 3000 rpm. The resulting serum, separated from the clotted blood, was carefully transferred into labeled vials or Eppendorf tubes for further analysis.
Tube using a micropipette and kept at -20° C until required use. Laboratory analysis was conducted at the National Center of Public Health Laboratories in Aden, Yemen. The laboratory tests included thyroid function tests, which included free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH). These tests were performed using the Cobas e 411 analyzer, which utilizes electrochemiluminescence immunoassay (ECLIA) technology, following the manufacturer's instructions.

**CLASSIFICATION OF THYROID DYSFUNCTION BASED ON THYROID FUNCTION TESTS**
Thyroid function test reference ranges based on the national center of public health laboratories Aden's set reference:

- Thyroid-Stimulating Hormone (TSH): 0.27–4.2 mU/ml
- Free Triiodothyronine (FT3): 1.8–4.6 pg/dl
- Free Thyroxine (FT4): 0.9–1.7 ng/dl

Thyroid dysfunction is classified based on thyroid function test results, as described in previous literature (11-17). The classification is as follows:

**Hypothyroid Disorders**
**Subclinical Hypothyroidism:** Characterized by elevated TSH levels with FT3 and FT4 levels falling within the reference range
**Primary Hypothyroidism:** This is defined by elevated TSH levels with normal or reduced FT3 and FT4 levels.
**Secondary Hypothyroidism:** Marked by decreased TSH, FT3, and FT4 levels, indicative of pituitary or hypothalamic dysfunction.

**Hyperthyroid Disorders**
**Subclinical Hyperthyroidism:** This is identified by suppressed TSH levels with FT3 and FT4 levels within the normal range.

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**Primary Hyperthyroidism:** Marked by suppressed TSH levels with normal or elevated FT3 and FT4 levels.
**Overt Hyperthyroidism:** Diagnosed when TSH levels are suppressed, accompanied by higher FT3 and/or FT4 levels.
**Generalized Hyperthyroidism:** Characterized by suppressed TSH levels and elevated FT3 and FT4 levels.

**Euthyroid and Non-Thyroidal Conditions**
Euthyroid Sick Syndrome (Non-Thyroidal Illness Syndrome): Defined by normal or suppressed TSH levels with decreased FT3 and/or FT4 levels, often observed in critically ill patients.
**Euthyroid State:** TSH, FT3, and FT4 levels lie within the typical range, indicating normal thyroid function. This classification provides a systematic approach for diagnosing thyroid dysfunction, facilitating appropriate clinical management.

## RESULTS

This study enrolled 100 diabetic patients who participated voluntarily. The cohort comprised 49 males (49.0%) and 51 females (51.0%), with ages spanning 18 to 72 years. Participants were categorized into four age groups: ≤ 40 years, 41-50 years, 51-60 years, and ≥ 60 years. The mean age (±Standard Deviation (SD)) of the study population was 52.59±10.9 years, and the dominant age group was 51-60 years old (40.0 %), followed by the 41-50 years old, which accounted for 29.0 %. Educationally, 36 % held a diploma or higher qualification, and 28 % had a primary level of education. Among the respondents, the majority were married (80%), 8% were widows, 7% were single, and 5% were divorced. In terms of professional class, 48% were in professional roles, 17 % were not currently working, and 31 % were housewives. The mean DM duration for the entire cohort was 12.21 ± 7.8 years. The duration of the disease was reported to be less than 5 years for 22 individuals, between 5 and 10 years for 30 individuals, and greater than 10 years for 48 individuals. The demographic profile of participants is outlined in Table 1.

**Table 1:** Demographic Profile of Participants (n=100)

| Characteristic | Frequency (100) | Percentage (%) |
|---|---|---|
| **Level of education** | | |
| Illiteracy | 11 | 11.0 |
| Primary school | 28 | 28.0 |
| secondary school | 25 | 25.0 |
| Diploma and above | 36 | 36.0 |
| **Marital Status** | | |
| Married | 80 | 80.0 |
| Single | 7 | 7.0 |
| Divorce | 5 | 5.0 |
| Widow | 8 | 8.0 |
| **Professional class** | | |
| Working | 48 | 48 |
| Student | 4 | 4 |
| Not currently employed | 17 | 17 |
| Housewife | 31 | 31 |
| **Duration of Diabetes (years) (mean ±SD)** | 12.21 ± 7.8 years | |
| <5 | 22 | 22 |
| 5-10 | 30 | 30 |
| >10 | 48 | 48 |

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**Prevalence of Thyroid Dysfunction**

Out of 100 assessed patients, 20 (20%) had thyroid dysfunction, as illustrated in Figure 1. Hypothyroidism was the most common diagnosis, affecting 18% of patients, followed by hyperthyroidism, which affected 2%.

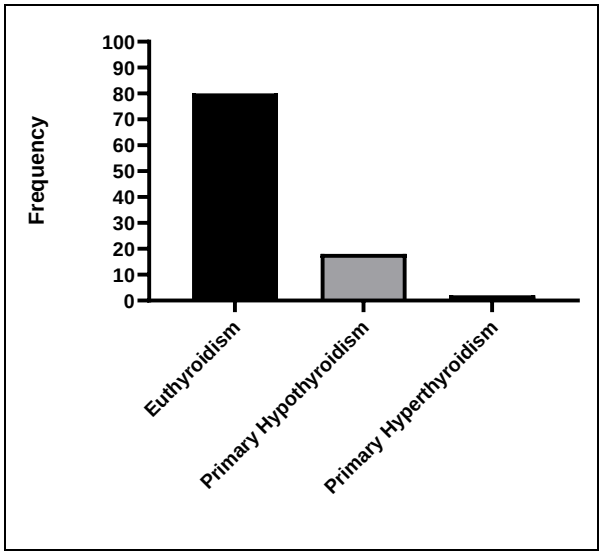


**Figure 1:** Seroprevalence of HBV and HCV among HD patients

Table 2 presents the demographic characteristics of patients with thyroid dysfunction. The population was evenly distributed between males (50%) and females (50%), with a mean age of 53.11 years (SD: 12.71; range: 35-70 years). The mean duration of diabetes was 10.89 years (SD: 6.07 years). Age distribution among patients with thyroid dysfunction revealed that 10% were ≤40 years, 30% were 41-50 years old, 40% were 51–60 years old, and 20% were ≥60 years old. This age distribution did not, however, differ substantially from that of patients who were euthyroid (p=0.99). Notably, hypothyroidism affected an equal number of males and females (9 each), while hyperthyroidism affected 1 female and 1 male. The mean age and duration of diabetes for patients with hyperthyroidism were 55 years and 10 years, respectively.

**Table 2**: Demographic Variables of Thyroid Dysfunctions

| **Variables** | **Primary Hypothyroidism** | **Primary hyperthyroidism** |
|---|---|---|
| Age | 53.11±12.71 | 55±0.00 |
| Gender | | |
| Male | 9 | 1 |
| Female | 9 | 1 |
| Duration of Diabetics | 10.89±6.07 | 10.00±0.00 |
| Family history of thyroid dysfunction | 4 | 0 |
| Family history of diabetic | 1 | 2 |

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Among the 20 patients with thyroid dysfunction, the age distribution was as follows: 10% (n=2) were ≤40 years, 30% (n=6) were 41-50 years, 40% (n=8) were 51-60 years, and 20% (n=4) were ≥60 years. The age distribution of the study population was comparable to that of patients with normal thyroid function (p=0.99) (Table 3).

**Table 3:** Thyroid Profile According to Age Group

| Age group (yrs) | Thyroid dysfunction | | | $\bar{X}$ | p-value |
|---|---|---|---|---|---|
| | Yes | No | Total | | |
| ≤40 | 2 | 9 | 11 | 0.33 | **0.99** |
| 41-50 | 6 | 23 | 29 | | |
| 51-60 | 8 | 32 | 40 | | |
| > 60 | 4 | 16 | 20 | | |

**Table 4**: Clinical Profiles of T2DM Patients with/without Thyroid Dysfunction

| Characteristics of T2DM | Diabetic subjects without thyroid dysfunction (n=80) | Diabetic subjects with thyroid dysfunction (n=18) | $\bar{X}$ | P-VALUE |
|---|---|---|---|---|
| Age (years) | 52.41±10.76 | 53.3± 12.03 | 42.0 | **0.26** |
| **Gender** | | | | |
| Male | 41 | 10 | 0.92 | **0.56** |
| Female | 39 | 10 | | |
| Duration of diabetes (years) | 12.56± 8.22 | 10.80± 5.74 | 21.26 | **0.51** |
| **Family history (1st degree of relative) of thyroid disorder** | | | | |
| Yes | 13 | 4 | 0.69 | **0.46** |
| No | 67 | 16 | | |
| BMI (kg/m2) | 28.01± 4.73 | 27.09± 5.80 | 100 | **0.18** |
| **Smoking Status** | | | | |
| Non-smoker | 63 | 16 | 0.90 | **0.59** |
| Smoker | 17 | 4 | | |
| **Chewing Khat** | | | | |
| Yes | 38 | 7 | 0.31 | **0.23** |
| No | 42 | 13 | | |
| **Comorbidities** | | | | |
| Cardiac diseases | 1 | 0 | 1.21 | **0.753** |
| Renal disease | 1 | 0 | | |
| Asthma | 2 | 1 | | |
| Liver disease | 0 | 1 | | |

The mean age of patients with type T2DM and thyroid dysfunction was 53.3 ± 12.03 years, compared to 52.41 ± 10.76 years for euthyroid patients. Yet, this variation did not exhibit a significant difference (p = 0.26). Gender distribution was similar between the two groups, with no statistically significant difference detected (p = 0.56). Specifically, 19.6% of males and 20.4% of females had thyroid dysfunction, while 80.4% of males and 79.6% of females had normal thyroid function.

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## DISCUSSION

Two of the most common endocrine conditions impacting people globally are diabetes mellitus and thyroid problems (18). The interconnectedness of both conditions lies in their effects on cellular metabolism (19). Insulin and thyroid hormones are crucial regulators of the body's metabolism and energy production (20). An excess or deficit of either hormone can disrupt these processes, leading to functional derangements in cellular metabolism.

Given the complex interplay between diabetes mellitus and thyroid diseases, individuals with one endocrinopathy may be at higher risk of developing the other (21). Accurate diagnosis and effective management of these conditions are essential for mitigating complications and enhancing overall health outcomes (23). Effective management of these conditions requires close monitoring of blood sugar and thyroid hormone levels and strict adherence to prescribed medications and lifestyle recommendations (24).

Notably, approximately 20% of individuals with T2DM exhibit thyroid dysfunction. Specifically, 18% had primary hypothyroidism, and 2 % had hyperthyroidism. These findings highlight the significant prevalence of thyroid dysfunction among type 2 diabetic patients and the potential impact on their overall health. This finding is in line with other research, such as a study in Sanaa that found a comparable rate of thyroid dysfunction among T2DM patients at about 20% (25).

The current study's finding of thyroid dysfunction prevalence exceeds that reported by Akbar et al. (16% in Saudi T2DM patients) (26) and Perros et al. (13.4% in T2DM patients), suggesting a higher prevalence in our study population (27); Other studies reported the prevalence of thyroid dysfunctions was 16 % (28-30) in their subjects. In contrast, other studies have reported higher prevalence rates. For instance, a study carried out in the ASIR region of Saudi Arabia (31) revealed a prevalence rate of 49.8%; in Egypt, the prevalence was 29% (32). Disparities in prevalence rates can be explained by variations in study populations, diagnostic criteria, and geographical settings, suggesting that the concurrence of type 2 diabetes and thyroid dysfunction is a frequent occurrence (33, 34).

Previously, it was reported that there is a bidirectional relationship between diabetes and thyroid dysfunction, with each condition potentially influencing the development and progression of the other (35, 36).

A current study has shown that there is a high prevalence of thyroid dysfunction among patients with type 2 diabetes, with hypothyroidism (18%) being the most common thyroid disorder in this population, indicating a significant burden of this condition among individuals with diabetes. This finding is consistent with previous research that has also reported a high prevalence of hypothyroidism among diabetes patients. Similarly, in another study conducted in Saudi Arabia, 17.6 % of patients were diagnosed with hypothyroidism (37), and 18.7% of them had hypothyroidism (38). In contrast, our findings exceeded those reported in a Scottish study, which detected a 13.4% prevalence of hypothyroidism among type 1 and type 2 diabetic patients (27). Similarly, a Jordanian study found a lower prevalence of 12.5% among T2DM patients (39). However, case-control research carried out in Jordan revealed that T2DM patients had a noticeably greater prevalence of thyroid problems (26.7%) than non-diabetic controls (13.7%), with subclinical hypothyroidism being the most common type (40).

The precise mechanisms linking hypothyroidism and type 2 diabetes are not fully understood, but research suggests that thyroid hormones exert a significant influence on glucose metabolic pathways and insulin sensitivity (41, 42). In susceptible individuals, thyroid dysfunction can precipitate alterations in insulin sensitivity and glucose metabolism, potentially increasing the risk of developing diabetes (41-44).

The high mean HbA1c levels observed in T2DM patients with and without concomitant thyroid dysfunction indicate poor glycemic control, consistent with earlier research (45, 46). Notably, 88% of T2DM patients failed to achieve the desired glycemic goal. This suboptimal glycemic control may be attributed to various factors, including inadequate diet, poor medication adherence, financial constraints, and disruptions in healthcare delivery, exacerbated by war-related drug supply shortages and electricity outages (46, 47).

Effective management of T2DM patients and thyroid dysfunction requires healthcare providers to

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consider the intricate relationship between these conditions (24, 48). Thyroid disorders can exacerbate T2DM, and diabetes can, in turn, aggravate thyroid dysfunction. Consequently, failing to identify suboptimal thyroid hormone levels in diabetic patients and insulin resistance in both conditions can compromise patient outcomes and hinder effective management (49).

The distribution of patients with thyroid dysfunction across different age groups suggests a demographic trend where the majority of patients tend to cluster within the age of 41-60 years, with fewer patients in the younger (up to 40 years) and older (61 years or more) age groups.

This suggests that middle-aged to older adults with type 2 diabetes are more vulnerable to experiencing thyroid issues, which can be ascribed to the cumulative effects of aging and long-term diabetes. The lower prevalence in younger patients (up to 40 years) might be due to fewer years of exposure to diabetic complications or a naturally lower incidence of thyroid dysfunction in younger adults; similarly, the low prevalence of older patients (61 years and above) might reflect either a lower incidence of thyroid dysfunction in these age groups or a lower representation of these groups in the study. However, the 61-years-and-above group has a 20% prevalence, which, while still significant, is lower than the 51-60 age group. There are no significant statistical differences in the prevalence of thyroid dysfunction among different age groups in the current study, which suggests that age may not be a significant risk factor for the condition among type 2 diabetic patients in study subjects.

Interestingly, a subset of studies has identified a peak disease prevalence within the 60-69 age range (50). This could be influenced by factors such as population demographics, research methodologies, survivorship bias, or sample size constraints.

The study's findings indicate that thyroid dysfunction affects males and females with type 2 diabetes at a comparable rate, with no significant sex-based difference in prevalence. This equal prevalence suggests that gender does not play a significant role in the likelihood of developing thyroid dysfunction in the context of type 2 diabetes. It indicates that the risk is distributed equally among male and female diabetic patients, which could be useful in guiding gender-neutral screening and management strategies.

This is noteworthy, as some studies suggest that women are generally at higher risk for thyroid diseases; one study reported that prevalence was higher in females compared to males with statistically significant differences (30). However, in the context of type 2 diabetes, this gender disparity does not appear to exist. This discrepancy could be attributed to the specific characteristics of the T2DM patient sample, underlying health conditions, or other factors that may influence the relationship between type 2 diabetes and thyroid dysfunction.

This study identified a statistically significant correlation between thyroid dysfunction and elevated TSH levels among diabetes patients. Notably, patients with thyroid dysfunction exhibited higher TSH levels compared to those with euthyroid status. This finding is consistent with the existing literature, which has established a strong link between TSH levels and thyroid dysfunction in diabetes patients (1). Furthermore, a meta-analysis reported that high baseline TSH levels were associated with a 17% increased risk of developing T2DM (35).

TSH may contribute to hyperglycemia through various mechanisms, including stimulation of leptin secretion (51, 52), enhancement of hepatic glucose production (53), pancreatic β cell impairment, and suppression of insulin production and secretion (54). A longitudinal study (55) involving a large cohort of euthyroid individuals without diabetes (n = 17,061) over 6 years revealed that each 1 mIU/L increase in serum TSH levels significantly elevated the risk of developing type 2 diabetes (55). This suggests a reciprocal relationship between thyroid hormones and blood glucose, where each has a profound impact on the other (40).

The current study did not show significant differences in terms of age, gender, FT3, FT4, and FBS between euthyroid and those with thyroid dysfunction. This disagrees with some previous studies that have found associations between thyroid dysfunction and factors such as age and gender in diabetes patients (56).

Notably, our study did not find a significant correlation between thyroid dysfunction and the duration of diabetes, which is consistent with previous research (30, 40, 57). However, some

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studies suggest that a longer duration of diabetes (>10 years) could upsurge the likelihood risk of developing hypothyroidism in diabetic patients (58), highlighting the need for further investigation into this potential association.

However, the current study has numerous inherent limitations. The cross-sectional design restricts the ability to deduce causality, highlighting the need for longitudinal investigations to explicate the temporal association between thyroid dysfunction and diabetes. Furthermore, the modest sample size of 100 patients may not accurately represent the broader T2DM population and could have restricted our ability to identify statistically significant differences, underscoring the need for larger-scale studies to confirm these findings. Moreover, the absence of anti-thyroid peroxidase (anti-TPO) antibody measurements limits the understanding of autoimmune thyroid dysfunction, representing a notable knowledge gap.

The study's findings may not be generalizable to the broader T2DM population in Aden and Yemen, given its restriction to patients from a single diabetic center. Additionally, the investigation did not control for potential confounding variables, such as medication usage, which could have influenced the findings. Furthermore, thyroid function is subject to temporal fluctuations, and a single measurement may not reliably capture a patient's characteristic thyroid profile. Serial measurements over time would provide a more wide-ranging and accurate evaluation of thyroid condition.

## CONCLUSION

Thyroid dysfunction, with a notable prevalence of hypothyroidism, is a significant comorbidity among patients with T2DM. The study's results underscore the necessity of routine thyroid function screening in T2DM patients, which can inform evidence-based clinical decision-making and ultimately enhance patient outcomes. As an exploratory investigation, this study provides foundational data that can be leveraged to justify and inform the design of larger, more comprehensive research endeavors in the future.

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## Conflict of Interest

The authors declare that no conflict of interest.

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