Prevalence and predictors of thyroid dysfunction amongst patients with Type 2 diabetes mellitus in Pakistan

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Abstract

Introduction: Diabetes and thyroid disorders are the two most common disorders amongst endocrine diseases. Uncontrolled diabetes mellitus (DM) may disturb thyroid metabolism by disturbing the levels of thyroid hormones in the plasma. This study was undertaken to determine the prevalence and thyroid dysfunction in type 2 diabetic population presenting in a public sector tertiary care teaching hospital. Materials and Methods: This descriptive cross-sectional study was conducted in Civil Hospital Karachi (CHK) in the department of medicine from October 01, 2018, to March 31, 2019. The study population consisted of 317 patients diagnosed with DM type 2 based on American Diabetes Association (ADA) criteria. Patients with fasting blood sugar ≥ 126 mg/dL, or HbA1c >6.5 (%), and 2 h postprandial blood glucose levels >200 mg/dL were included. After a minimum of 8 h of fasting, plasma samples of patients were collected and sent for fasting blood glucose, HbA1c, FT3, FT4, and thyroid-stimulating hormone (TSH). Descriptive statistics were calculated. Post-stratification Chi-squared test was applied, and a P value of ≤ 0.05 was considered significant. Results: Among all enrolled DM type 2 patients, 207 (65.3%) were male with a mean age of 46.54 ± 8.72 years. Mean fasting blood sugar (FBS), random blood sugar (RBS), and HbA1c were 212.76 ± 26.91 (mg/dL), 328.89 ± 52.89 (mg/dL), and 9.43 ± 2.47 (%), respectively. The mean duration of DM was 7.81 ± 3.15 years. Mean FT3, FT4, and TSH were 113.13 ± 44.40 (ng/dL), 7.63 ± 3.11 (mg/dL) and 2.64 ± 2.57 (µIU/mL), respectively. In the present study, 55 (17.4%) patients had subclinical hypothyroidism, 27 (8.5%) had hypothyroidism, 19 (6.0%) had hyperthyroidism, and 16 (5.0%) had subclinical hyperthyroidism. Significant association of thyroid dysfunction was established with age group, female gender, and family history of thyroid dysfunction (P<0.001). Conclusion: The prevalence of thyroid dysfunction is higher among patients with type 2 diabetes mellitus (T2DM), in which hypothyroidism was the most common dysfunction with more prevalence among female patients.

Keywords: FT3, FT4, hyperthyroidism, hypothyroidism, thyroid dysfunction, TSH, type II diabetes mellitus

Introduction

Diabetes mellitus (DM) is the most common endocrine disorder caused by the dysfunction of pancreatic β cells.[1] In 2019, it was reported that globally 463 million adults (age 20–79 years) were living with diabetes, 79% of whom were living in low- and
According to the American Diabetes Association (ADA), additional 374 million people are at risk for developing type 2 diabetes mellitus (T2DM).\[11\]

Thyroid dysfunction is ranked as the second most common endocrine disorder.\[10\] In the USA, 4.6% of the population were diagnosed with hypothyroidism, and 1.3% had hyperthyroidism, whereas these figures were 3.05% and 0.75% in Europe, respectively.\[11\]

It has been documented that diabetic patients are more susceptible to developing thyroid dysfunction, and many clinical trials have been conducted across the globe to understand the link between them.\[10\] Several studies have reported the prevalence of thyroid dysfunction among patients with DM to be varying from 4% to 35%.\[8-10\] Recent studies have reported insulin resistance as a major factor in disrupting thyroid hormone functions and causing hypothyroidism in T2DM patients.\[10\] It does this by modifying thyroid-stimulating hormone (TSH) released from the hypothalamus or affecting peripheral tissue conversion of tetraiodothyronine (T4) to triiodothyronine (T3).\[18,19\]

In subclinical hypothyroidism, the declining rate of insulin-induced glucose transport is thought to be due to the disrupted gene transcription of glucose type 2 receptor (GLUT-2), leading to insulin resistance.\[10\] A study conducted by Elgazar et al\[18\] showed a greater incidence of thyroid dysfunction among patients with higher HbA1c levels. Thyroid dysfunction has also been associated with increased levels of serum cholesterol and triglycerides, which amplify the risk of cardiovascular disorders in diabetic patients.\[10,13\]

Although various studies have been conducted showing the link of thyroid dysfunction to DM, data from Pakistan are lacking in this regard. In this study, we aim to assess the incidence of thyroid disorders in the diabetic population with relation to age and gender in the Pakistani population, which would prompt primary care physicians to take necessary measures for public health awareness among the masses.

Methodology

Study design and location
The study design of the research was analytical cross-sectional conducted in the department of medicine, Civil Hospital Karachi (CHK), Pakistan from October 01, 2018, to March 31, 2019.

Sample size
The sample size was calculated through the OpenEpi software, the prevalence of thyroid disorders was 29%\[13\] among T2DM patients, the margin of error was 5%, and confidence interval of 95%, then at least \( n = 317 \) participants were required.

Patient selection
In this study, 317 diabetic patients were selected, who were attending the out-patient department (OPD), with non-probability, consecutive sampling technique, who fulfilled the selection criteria. Patients of age between 35 and 65 years of having fasting blood sugar of \( \geq 126 \text{ mg/dL} \) at two or more occasions, or HbA1c >6.5%, or 2 h glucose levels >200 mg/dL were enrolled in the study as per the selection criteria. All study participants were diagnosed cases of T2DM for a minimum of 2 years duration and were taking oral hypoglycemic agents, insulin, or both.

Informed consent was taken from each patient for participating in the study. Patients with any history of thyroid disorders or those who had undergone any thyroid surgery were not included in the study. Those patients who were taking any medication affecting glycemic status such as steroids for any disease, for any duration, diagnosed case of type-1 DM, critically ill patients, and those taking medication affecting thyroid function were not enrolled.

Ethical approval
The research evaluation unit (REU) committee approved the research synopsis with REU No. 34,936, College of Physicians & Surgeons Pakistan (CPSP).

Data collection and statistical analysis
Information regarding age, gender, and clinical history of diabetes was documented on a pre-approved proforma. Venous samples of participants were collected after a minimum of 8 h fasting for measurement of fasting blood glucose levels, HbA1c, FT3, FT4, and TSH levels in plasma.

Statistical analysis of composed data was performed via Statistical Package SPSS (version 20.0). Frequency and percentage were computed for categorical variables such as the occurrence of hyperthyroidism, hypothyroidism, subclinical hyperthyroidism, and subclinical hypothyroidism and gender. Mean and standard deviations (SD) were calculated for numeric variables such as age and duration of T2DM. Effect modifiers such as age, gender, duration of diabetes mellitus, and family history of thyroid dysfunction were controlled through stratification. Post-stratification Chi-squared test was applied among different strata to calculate any significant differences, and \( \leq 0.05 \) was considered significant as \( P \) value.

Results
Out of the sample population of 317 T2DM patients, 207 (65.3%) were males and 110 (34.7%) were females. Overall, 37% of participants had thyroid dysfunction. The mean age was 46.54 ± 8.72 years. The mean duration of diabetes was 6.80 ± 2.62 years. Mean fasting blood sugar, random blood sugar, and HbA1c were 212.76 ± 26.91 (mg/dL), 328.89 ± 5.89 (mg/dL), and 9.43 ± 2.47 (%), respectively [Table 1]. The mean duration of DM was 7.81 ± 3.15 years. Mean FT3, FT4 and TSH were 113.13 ± 44.40 (mg/dL), 7.63 ± 3.11 (mg/dL), and 2.64 ± 2.57 (µIU/mL), respectively. In the sample population, 15 (4.7%) reported a family history of thyroid dysfunction, whereas these figures were 3.05% and 0.75% in Europe, respectively.
whereas 302 (95.3%) answered negatively in response to this question.

In the present study, 200 (63.1%) patients had normal thyroid function, 55 (17.4%) patients had subclinical hypothyroidism, 27 (8.5%) had hypothyroidism, 19 (6.0%) had hyperthyroidism, and 16 (5.0%) had subclinical hyperthyroidism as shown in Figure 1.

The results showed a significant association of clinical hypothyroidism with age, 16 (51.9%) were females ($P \leq 0.001$), as shown in Table 3.

Discussion

The coexistence of DM and thyroid disorders is a well-established fact. These conditions are two of the most common endocrine diseases that clinicians come across in clinical practice. In this study, we have assessed the incidence of thyroid dysfunction in T2DM patients and their relation to gender and age in the Pakistani population.

In our study, the overall prevalence of thyroid dysfunction in T2DM patients was slightly higher, that is, 37% compared to 29%, 31%, and 35% reported in different studies. The slightly higher rate can be attributed to the differences in ethnicity and the dietary pattern of the region.

In our study, we found subclinical hypothyroidism (17.4%) to be the most common thyroid disorder associated with DM, followed by hypothyroidism (5.0%), hyperthyroidism (6.0%), and subclinical hyperthyroidism (6.0%), which is in concordance to the studies conducted in India and Bangladesh. The higher rate of subclinical disease in the diabetic population deems it necessary to screen the patients presenting with T2DM because concomitant thyroid disorder can have a major impact on the glycemic levels and the overall management of the diabetic patient.

According to Ogbonna et al., females with T2DM have a 3.8 times greater chance of developing thyroid dysfunction as compared to males. This can be ascribed to the effect

![Figure 1: Distribution of thyroid function among type 2 diabetic patients](image-url)
the estrogen hormone has on the thyroid follicular cells and thyroxine-binding globulin (TBG).\cite{21} Our results are consistent with these findings as the prevalence of all four types of thyroid disorders was higher among diabetic females ($P \leq 0.001$) than their male counterparts, this is also in line with the other studies conducted in the past.\cite{11,22,23}

The incidence of clinical hypothyroidism, hyperthyroidism, and subclinical hyperthyroidism in the diabetic population was significantly associated with age as the majority of the cases were reported in the (56–65) age range ($P \leq 0.001$) and follows the same trend as the study of Khassawneh et al.,\cite{24} in which the prevalence of thyroid dysfunction in the diabetic population significantly increased with the increasing age. However, a unique finding in our study was that a higher proportion of cases of subclinical hypothyroidism were reported in the younger population, approximately 74.5% in the (35–45) age range.

Hyperthyroidism increases metabolism in the body and leads to early processing and elimination of insulin from the body.\cite{25} Hypothyroidism, on the one hand, slows down the metabolic rate and on the other hand, is associated with insulin sensitivity, both of these factors can contribute to hypoglycemia.\cite{26,27} Dose adjustment for insulin is needed when a diabetic patient concomitantly suffers from both endocrinopathies.

Based on our research findings, we recommend regular screening of the diabetic population for underlying thyroid disorders, especially for older adults and females presenting with diabetes, to ensure early detection of thyroid disorder and better glycemic control to prevent complications in the long run with poorly controlled diabetes. With respect to primary care physicians, the challenges of obesity and unhealthy lifestyle practices prompt the role of primary care physicians in incorporating healthy lifestyles by promoting awareness and supporting ideas of those healthy practices in diabetes and thyroid disorders.

### Study Limitations

The present study is a non-randomized, observational study and is thus limited by patient selection bias. This study was a single hospital-based study with small sample size; therefore, the results might not be generalizable to larger populations. Although family history is a confounding factor, the number of patients with a positive family history was minimal.

### Conclusion

The prevalence of thyroid dysfunction is higher among patients with T2DM, in which hypothyroidism was more prevalent in females than males. Age more than 40 years, family history of diabetes and thyroid dysfunction, female gender were also significant risk factors.

### Take home messages

Our study reported the frequency of thyroid disorders within the diabetic population. Certain unhealthy lifestyle changes causing sedentary habits prompt primary care physicians to have a role to play in preventing unhealthy lifestyles by promoting awareness and supporting healthy practices including physical activity and a balanced diet in these diabetic individuals with thyroid discrepancies.

### Ethical approval statement

Ethical approval was taken in this study from the institutional review board of Dow University Hospital, and consent to participants was taken from all respondents.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.
Conflicts of interest

There are no conflicts of interest.

References

1. IDF Diabetes Atlas 9th edition 2019. Diabetesatlas.org. 2021. Available from: https://www.diabetesatlas.org/. [Last accessed on 2021 May 28].
2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2018. 2021.
3. Singh G, Gupta V, Sharma AK, Gupta N, editors. Evaluation of Thyroid Dysfunction Among Type 2 Diabetic Punjabi Population. 2011.
4. GarmendiaMadariaga A, Santos Palacios S, Guillén-Grima F, Golofré JC. The incidence and prevalence of thyroid dysfunction in Europe: A meta-analysis. J Clin Endocrinol Metab 2014;99:923-31.
5. Pickup J. Textbook of Diabetes. Malden, Mass.: Blackwell Science; 2003.
6. Subekti I, Pramono LA, Dewiasty E, Harbuwono DS. Thyroid dysfunction in Type 2 diabetes mellitus patients. Acta Med Indones 2017;49:314-23.
7. Jain G, Marwaha TS, Khurana A, Dhoat PS. Prevalence of thyroid disorders in patients of type 2 diabetes mellitus. J Indian Acad Clin Med 2016;17:12-5.
8. Bhusal K, Pokhrel P, Simkhada R. Thyroid dysfunction among patients with diabetes mellitus in Kathmandu. J CollMed SciNepal 2018;14:206‑8.
9. Vikhe VB, Kanitkar SA, Tamakuwala KK, Gaikwad AN, Kalyan M, Agarwal RR. Thyroid dysfunction in patients with type 2 diabetes mellitus at tertiary care centre. Natl JMed Res 2013;3:377-80.
10. Duntas L, Orgiazzi J, Brabant G. The interface between thyroid and diabetes mellitus. Clin Endocrinol 2011;75:1-9.
11. Elgazar E, Esheba N, Shalaby S, Mohamed W. Thyroid dysfunction prevalence and relation to glycemic control in patients with Type 2 diabetes mellitus. Diabetes MetabSyndr2019;13:2513-7.
12. Kadiyala R, Peter R, Okosiemme O. Thyroid dysfunction in patients with diabetes: Clinical implications and screening strategies. IntJ ClinPract 2010;64:1130-9.
13. Bjoro T, Holmen J, Kruger O, Midtghjell K, Hunstad K, Schreiner T, et al. Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trøndelag (HUNT). Eur J Endocrinol 2000;143:639-47.
14. Hage M, Zantout M, Azar S. Thyroid disorders and diabetes mellitus. J Thyroid Res2011;2011:1-7.
15. Naz N, Rizvi SK, Sadiq Z. Assessment of thyroid hormone levels and thyroid disorders: A case study from Gujranwala, Pakistan. Pak J Pharm Sci 2017;30:1245-9.
16. Jugati A, Biradar MS. Thyroid dysfunction in patients with Type 2 diabetes mellitus in a tertiary care centre of North Karnataka. Med Innov2018;7:28-30.
17. Kamrul-Hasan A, Akter F, Selim S, Asaduzzaman M, Rahman M, Chanda P, et al. Thyroid function and autoantibody status in Bangladeshi patients with type 2 diabetes mellitus. Thyroid ResPract2018;15:132.
18. Elmenshawi IM, Alotaibi SS, Alazmi AS, Alazmi AM, Alruwaili FR, Alazmi MM, et al. Prevalence of thyroid dysfunction in diabetic patients. J DiabetesMetabDisord Control2017;4:55-60.
19. Hollowell J, Staehling N, Flanders W, Hannon W, Gunter E, Spencer C, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National health and nutrition examination survey (NHANES III). J Clin EndocrinolMetab 2002;87:489-99.
20. Papazafiropoulou A, Sotropoulos A, Kokolaki A, Kardara M, Stamataki P, Pappas S. Prevalence of thyroid dysfunction among greek type 2 diabetic patients attending an outpatient clinic. J Clin Med Res 2010;2:75-8.
21. Aljabri KS, Bokhari SA, Alshareef MA, Khan PM, Mallosho AM, AbuElsaoud HM, et al. The prevalence of hypothyroidism in patients with Type 2 diabetes mellitus in Saudi community based hospital a retrospective single centre study. Arch Diabetes Obes 2019;2.doi: 10.32474/ADO.2019.02.000126.
22. Ogbonna S, Ezeani I. Risk factors of thyroid dysfunction in patients with Type 2 diabetes mellitus. Front Endocrinol2019;10:440.
23. Ahmed AA, Mohamed SB, Elmadi SA, Abdorabo AA, Ismail IM, Ismail AM. Assessment of thyroid dysfunctions in type 2 diabetes mellitus patients in Surman, Western-Libya. Int J Clin Exp Med Sci 2017;3:1-4.
24. Khasawneh A, Al-Mistarehi A, Zein Alaabdin A, Khasawneh L, AlQuran T, Kheirallah K, et al. Prevalence and predictors of thyroid dysfunction among Type 2 diabetic patients: Acase-control study. Int J Gen Med 2020;13:803-16.
25. Mitrou P, Raptis S, Dimitriadis G. Insulin action in hyperthyroidism: Afocus on muscle and adipose tissue. Endocr Rev 2010;31:663-79.
26. Why Thyroid Disease and Diabetes May Occur Together. Verywell Health. 2021. Available from: https://www.verywellhealth.com/thyroid-disease-and-diabetes-3289616. [Last accessed on 2021 May 30].
27. Kalra S, Sahay R, Unnikrishnan A. The hypoglycemic side of hypothyroidism. Indian J EndocrinolMetab 2014;18:1-3.