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Comparison of Thyroid Dysfunction in Patients with Controlled Versus Uncontrolled Diabetes Mellitus: A Comparative Cross-Sectional Study

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ABSTRACT

Thyroid dysfunction (TD) and type 2 diabetes mellitus (DM) are the two endocrine conditions most frequently encountered in clinical settings. **Objectives:** To compare the frequency of thyroid dysfunction in patients with controlled versus uncontrolled DM. **Methods:** This comparative cross-sectional study was conducted at the Pathology Department of Nishtar Hospital, Multan, from February to July 2025. Diabetic patients aged 30–70 years of both genders were enrolled in the study as uncontrolled diabetes (n=124) and controlled diabetes (n=124). Patients with pre-existing TD, on its treatment, or using medications known to alter thyroid function were excluded. Demographic details, including age, gender, duration of diabetes, and hypertension status, were recorded. TD was categorized into subclinical hypothyroidism, clinical hypothyroidism, subclinical hyperthyroidism, and hyperthyroidism. Descriptive statistics were run through SPSS version 23.0, and the Shapiro-Wilk test for normality. Chi-square test at 5% significance level was used for comparisons, with stratification done to control confounding. **Results:** Among 248 participants, the mean age was 49.2 ± 10.3 years. Males constituted 48% and 73.4% had hypertension. TD was found in 14.5% of diabetics, more common in uncontrolled (69.4%) than controlled diabetes (30.6%) (p=0.012). Most frequent type was subclinical hypothyroidism (6%), followed by hypo- and hyperthyroidism (3.2% each), and subclinical hyperthyroidism (2%). TD was high in uncontrolled diabetics ≥50 years, females, and hypertensive patients. **Conclusions:** Thyroid dysfunction was remarkably more common in persons with uncontrolled diabetes, particularly in older age, females, and hypertensives.

INTRODUCTION

Thyroid dysfunction (TD) and type 2 diabetes mellitus (DM) are the two most common endocrine conditions that endocrinologists encounter in their clinical work [1]. Because thyroxin and insulin both are important in controlling cellular metabolism, and one of them acts in a counter-regulatory way against the other, the link between thyroid impairment and DM is well established [2]. Along with the detrimental impact thyroid dysfunction has on glucose balance, numerous investigations have shown that TD is more prevalent in diabetic patients than in normal healthy individuals [3]. A study carried out in Karachi, Pakistan, revealed that 36.9% of persons with type 2 DM had thyroid abnormalities [4]. Thyroid hormones influence glucose metabolism in a variety of ways. It has long been known that hyperthyroidism contributes to poor glycemic control; in this condition, the half-life of insulin is shortened. This shorter half-life is most likely caused by a greater breakdown and increased production of insulin precursors that are physiologically inactive [5]. It has been demonstrated that both subclinical and clinical hypothyroid conditions are linked to elevated insulin resistance, even though hypothyroidism can result in a

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decreased rate of hepatic glucose synthesis [6]. Al-Rubaye et al. conducted a study on 500 cases with type 2 DM. Out of those, 364 patients (72.8%) had poor glycemic control. Thyroid dysfunction was diagnosed in 67/364 patients (18.4%) with uncontrolled DM and 9/136 (6.6%) patients with controlled DM. The frequency of subclinical hypothyroidism, primary hypothyroidism, subclinical hyperthyroidism, and clinical hyperthyroidism was 38.8%, 19.4%, 23.8% and 17.9% in uncontrolled DM cases versus 33.3%, 22.2%, 11.1%, and 33.3% in controlled DM cases, respectively [7]. Alo et al. included a total of sixty subjects in their study. Out of all, 30 patients were diabetic, both controlled and uncontrolled, and 30 were healthy individuals. Mean levels of serum TSH were markedly high (4.77 ± 3.12 vs. 2.52 ± 1.46), and mean serum FT4 level (10.64 ± 1.29 vs. 12.21 ± 2.21) was substantially lower in uncontrolled diabetic persons as compared to those who had controlled diabetes [8]. By knowing the relationship between the status of thyroid function and glycemic control, physicians would be more careful in the future to prevent thyroid dysfunction by maintaining good control of diabetes in their patients. Moreover, early screening will be helpful in timely diagnosis and appropriate treatment, thus positively affecting the health of diabetic patients.

Despite growing evidence linking thyroid dysfunction with type 2 diabetes mellitus, the relationship between thyroid abnormalities and glycemic control remains inconsistent across different populations. Most available studies either include heterogeneous diabetic groups or are conducted outside Pakistan, limiting their applicability to local clinical practice. Furthermore, regional data from Southern Punjab comparing thyroid dysfunction in controlled versus uncontrolled diabetes are scarce. Therefore, there is a need for context-specific evidence to clarify this association and guide screening strategies in high-risk diabetic patients. This study aims to determine the magnitude of TD and its types in patients presenting with controlled versus uncontrolled T2DM in our local setting.

METHODS

This comparative cross-sectional study was performed at the Department of Chemical Pathology, Nishtar Hospital, Multan, from 1st February 2025 to 31st July 2025 after approval from the institutional ethics review committee (ERC no: 1553/NMU). Patients 30 - 70 years of age, either male or female gender and diabetic for ≥5 years were approached. All patients underwent HbA1c% measurement from a single laboratory. Diabetic patients with HbA1c ≥ 7% were taken as uncontrolled diabetes, and <7% as controlled diabetes. A total of 124 controlled and 124 uncontrolled diabetes patients were enrolled through non-probability consecutive sampling in the study after informed consent. Based on history and medical record reviews, patients with thyroid dysfunction before the onset of diabetes mellitus, already on treatment for thyroid dysfunction and using medications like amiodarone, nitroprusside, sulfonylurea, thalidomide, interleukin, lithium, perchlorate, and interferon-alpha treatment were excluded. Patient characteristics like age, gender, duration of diabetes, and hypertension were recorded. All the patients underwent venous blood sampling aseptically for the assessment of thyroid functions (TSH, T3, and T4) measured by chemiluminescence immunoassay (CLIA). Thyroid dysfunction was labelled if any of the following abnormality was identified on thyroid profile; subclinical hypothyroidism: serum TSH values >4.2 mU/L and normal free T3 (210-440pg/dl) and free T4 levels (0.8-2.7ng/dl), hypothyroidism: if free T4 is low (ng/dl) <0.8 and serum TSH level is high (21 - 54yrs - >4.2 mU/L, 55 - 87 yrs - >8.9mU/L), subclinical hyperthyroid: serum TSH values <0.4 mU/l in 21-54 years and <0.5 mU/l in 55-87 years, normal free T3 and free T4 levels and hyperthyroidism as high free T3 (>440pg/dl), free T4 (>2.7 ng/dl) and low TSH (<0.4 mU/l in 21-54 years and <0.5 mU/l in 55-87 years). A minimum sample size of 248 (124 uncontrolled and 124 controlled diabetes) was calculated through Open Epi online software using formula for comparative cross-sectional study [9]: $n = (Z\alpha/2 + Z1-\beta)2\ \bar{p}\bar{q}(r+1) / r\ (p1 - p2)2$, assuming thyroid dysfunction of 6.6% in uncontrolled diabetics, 18.4% in controlled diabetics at 80% power and 95% confidence interval [7]. SPSS version 25.0 was used for data analysis. The Shapiro-Wilk test was used for normality assessment. Mean and standard deviation are presented for quantitative data like age and duration of diabetes. Numerical data between the groups was compared through an independent sample t-test. Frequency and percentages for categorical data like gender, hypertension, thyroid dysfunction, and type of thyroid dysfunction. Thyroid dysfunction between the uncontrolled and controlled diabetics was compared through a chi-square test at 5% significance level and 95% confidence level. Confounding was controlled through stratification on demographic factors. The p-value<0.05 was considered significant for all comparisons. The study followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for a cross-sectional study [10].

RESULTS

The mean age of the participants was 49.2 ± 10.3 years, and 133 (53.6%) were <50 years old. There were 129 (48%) male and 129 (52%) female participants. Hypertension was identified in 182 (73.4%) of the participants. The mean duration of diabetes mellitus was 9.0 ± 3.1 years, and in 158 (63.7%) of participant's duration of diabetes was <10 years. The demographic characteristics were comparable between uncontrolled and controlled diabetics (Table 1).

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Table 1: Characteristics of Patients with Diabetes Mellitus (n=248)

Characteristics	All (n=248)	Uncontrolled Diabetes (n= 124)	Controlled Diabetes (n= 124)	p-Value*
Age				
Year	49.2 ± 10.3	48.3 ± 10.9	50.2 ± 9.5	0.152
<50-Years	133 (53.6%)	73 (54.9%)	60 (45.1%)	0.098
≥50-Years	115 (46.4%)	51 (44.3%)	64 (55.7%)	
Gender				
Male	119 (48%)	61 (51.3%)	58 (48.7%)	0.703
Female	129 (52%)	63 (48.8%)	66 (51.2%)	
Hypertension				
Yes	182 (73.4%)	91 (50%)	91 (50%)	1.00
Diabetes				
Duration	9.0 ± 3.1	9.4 ± 3.6	8.7 ± 2.6	0.083
<10-Years	158 (63.7%)	75 (47.5%)	83 (52.5%)	0.291
≥10-Years	90 (26.6%)	49 (54.4%)	41 (45.6%)	

*t-test for numerical and chi-square test for categorical comparison

Thyroid dysfunction was diagnosed in 36 (14.5%) diabetic patients. Prevalence of TD was significantly more frequent in uncontrolled diabetics compared to controlled diabetics (69.4% vs. 30.6%). Subclinical hypothyroid was diagnosed in 15 (6%), hypo- and hyperthyroid in 5 each (3.2%), and subclinical hyperthyroid in 5 (2%) of diabetic patients. Types of thyroid dysfunction were comparable in uncontrolled and controlled diabetics (p-value >0.050) (Table 2).

Table 2: Thyroid dysfunction in Patients with Diabetes Mellitus (n=248)

Characteristics	All (n=248)	Uncontrolled Diabetes (n=124)	Controlled Diabetes (n=124)	p-Value*
Thyroid Dysfunction				
Yes	36 (14.5%)	25 (69.4%)	11 (30.6%)	0.012¥
No	212 (85.5%)	99 (46.7%)	113 (53.3%)	
Type of Thyroid Dysfunction				
Hypothyroid	08 (3.2%)	5 (62.5%)	3 (37.5%)	0.882
Subclinical Hypothyroid	15 (6.0%)	11 (73.3%)	4 (26.7%)	
Hyperthyroid	08 (3.2%)	5 (62.5%)	3 (37.5%)	
Subclinical Hyperthyroid	05 (2.0%)	4 (80%)	1 (20%)	

* chi-square test (Fisher's exact test where cell count <5), ¥ statistically significant

Thyroid dysfunction was significantly higher in uncontrolled diabetics ≥50 years in contrast to controlled diabetics (65.6% vs. 34.4%, p-value<0.004). Similarly, in uncontrolled diabetics, TD was significantly high in females (70% vs. 30%, p-value <0.039) and in hypertensive patients (69.4% vs. 30.6%, p-value<0.009) compared to controlled diabetics (Table 3).

Table 3: Factors Associated with Thyroid Dysfunction in Diabetic Patients (n=248)

Associated Factors		Thyroid Dysfunction	Uncontrolled Diabetes (n=124)	Controlled Diabetes (n=124)	p-Value*
Age	<50-Years	Yes	4 (100%)	0 (0.0%)	0.127
		No	69 (53.5%)	60 (46.5%)	
	≥50-Years	Yes	21 (65.6%)	11 (34.4%)	0.004¥
		No	30 (36.1%)	53 (63.9%)	
Gender	Male	Yes	11 (68.8%)	5 (31.3%)	0.132
		No	50 (48.5%)	53 (51.5%)	
	Female	Yes	14 (70%)	6 (30%)	0.039¥
		No	49 (45%)	60 (55%)	
Diabetes Duration	<10-Year	Yes	3 (100%)	0 (0.0%)	0.105
		No	72 (46.5%)	83 (53.5%)	
	≥10-Year	Yes	22 (66.7%)	11 (33.3%)	0.076
		No	27 (47.4%)	30 (52.6%)	
Hypertension	Yes	Yes	25 (69.4%)	11 (30.6%)	0.009¥
		No	66 (45.2%)	80 (54.8%)	
	No	Yes	–	–	–
		No	33 (50%)	33 (50%)	

* chi-square test (Fisher's exact test where cell count < 5), ¥ statistically significant

DISCUSSION

In this study, we observed that TD was frequently common in diabetic patients. Frequency of TD was more commonly seen in patients with uncontrolled diabetes, in contrast to controlled diabetes. The most common dysfunction was subclinical hypothyroidism, followed by hypo- and hyperthyroidism and subclinical hyperthyroidism. Al-Rubaye *et al.* reported in their study that the frequency of thyroid impairment was 18.4% in patients with uncontrolled diabetes and 7.6% of all type 2 diabetics [7]. Díez *et al.* documented that the overall magnitude of TD was 13.4% in diabetic cases. It was low in Type 2 diabetes men (7%) and greatest in Type 1 diabetic women (31.4%). Subclinical hypothyroidism (4.8%), hypothyroidism (0.9%), hyperthyroidism (0.5%), and subclinical hyperthyroidism (0.5%) were the most frequently diagnosed conditions [11]. Our findings are very close to these observations. Ghimire *et al.* observed that thyroid problems were seen in 27.9% of patients with type-2 DM. Subclinical hypothyroidism was the most prevalent thyroid condition, affecting 14.71% of persons [12]. In a meta-analysis, Hadgu *et al.* included 38 studies. Thyroid dysfunction was present in 20.24% of cases. Subclinical hyperthyroidism, hypothyroidism, hypothyroidism, and subclinical hypothyroidism were shown to have respective pooled prevalences of 11.87%, 7.75%, 2.49%, and 2.51% [13]. Since most of the individuals were previously diagnosed with thyroid dysfunction before their inclusion in the study, the discrepancy can be explained by the disparities in health systems and the referral of complex cases to diabetes clinics in tertiary care

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facilities. Similar to our results, according to Al-Rubaye *et al.* hypothyroidism was present in 58.2% of uncontrolled individuals, and subclinical hypothyroidism was seen in around two-thirds of these patients (26 patients, 38.81% of patients with thyroid dysfunction and poor glycaemic control) [7]. Similar results were also shown by Akbar *et al.* and Palma *et al.* [14, 15]. In a meta-analysis published by Han *et al.* showed that the frequency of subclinical hypothyroidism ranged between 4.69% and 18.86% regardless of whether the patients had poor or good glycemic control. In this study, the frequency of subclinical hypothyroidism was 7.14% of those with uncontrolled diabetes mellitus [16]. A case-control study, which found that HbA1c levels above 7% are a significant risk factor for thyroid dysfunction, with adjusted odds ratio (OR) of 2.553 (95% CI: 1.472–4.429; p=0.001), further supports the link between thyroid dysfunction and poor glycaemic management [17]. It has been demonstrated by researchers that the thyroid hormone controls the pancreas and glucose metabolism, and DM may alter thyroid function. For instance, it has been discovered that diabetes lowers the "TSH to thyrotropin-releasing hormone response," which results in hypothyroidism and lower T3 levels [18]. Numerous studies have also demonstrated that this pathophysiological association is mimicked by a variety of intricately linked hormonal, genetic, and biochemical problems. For instance, the primary target for modifying insulin sensitivity control and thyroid hormone feedback associated with hunger and energy utilization is the "5′ adenosine monophosphate-activated protein kinase" (AMPK) [19, 20]. Furthermore, the main cause of diabetes mellitus associated with thyroid problems is autoimmune. Additionally, some genetic changes, such as a mutation in GLUT4 [21], have also been related to thyroid issues and type 2 DM. Concordant with our study, age above 50 years was a significant predictor of thyroid dysfunction, with adjusted odds ratio (OR) of 3.89 (95% CI: 2.15–7.05; p<0.001), in a case-control study that enrolled 998 persons with type 2 DM [15]. This implies that the interaction between thyroid function and glycaemic management may worsen with age. According to the same study, thyroid dysfunction was more likely to be seen in women (OR 1.75; 95% CI: 1.12–2.74; p=0.013) [17]. Furthermore, a Saudi Arabian study reported that female type 2 DM patients, especially those with hypertension, had a higher prevalence of thyroid dysfunction [22]. These results highlight how crucial it is to evaluate TD in diabetic persons while taking gender and concomitant diseases like hypertension into account. The strengths of our study were that it was a case-control design, which effectively allowed comparison between controlled and uncontrolled diabetics, highlighting the association of TD with glycemic control. The study differentiated between subclinical and clinical forms of both hypo- and hyperthyroidism, adding granularity and clinical relevance to the findings.

This study has certain limitations, including its single-center cross-sectional design, which restricts causal inference and broader generalizability. Thyroid autoantibodies were not assessed, limiting differentiation between autoimmune and non-autoimmune thyroid dysfunction. Additionally, the absence of longitudinal follow-up prevents evaluation of the long-term impact of thyroid abnormalities on glycemic control and diabetic complications. Future multicenter prospective studies with larger sample sizes and comprehensive thyroid profiling are warranted to better elucidate the bidirectional relationship and inform cost-effective screening policies.

CONCLUSIONS

Thyroid dysfunction is more prevalent in individuals with uncontrolled diabetes, especially in patients who are over 50, female, or have high blood pressure. The significance of routine thyroid function monitoring in high-risk diabetes groups is highlighted by these findings. The findings highlight the importance of considering routine thyroid screening in patients with poorly controlled diabetes, especially women and those over 50 years of age, to enable earlier detection and timely management. The necessity for integrated care approaches in diabetes management is further supported by the possibility that early detection and treatment of thyroid abnormalities may improve glycaemic control and lower the risk of complications.

Authors' Contribution

Conceptualization: KQ
Methodology: KQ, MAA, MT, JN, SS, FF
Formal analysis: MT, JN
Writing and Drafting: KQ, MAA, FF
Review and Editing: KQ, MAA, FF, MT, JN

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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