ORIGINAL ARTICLE

Thyroid Dysfunction in Individuals with Type 2 Diabetes Mellitus and Its Relationship with Diabetic Nephropathy: A Hospital Based Cross-Sectional Study

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ABSTRACT

Introduction: People diagnosed with type 2 diabetes mellitus have a heightened susceptibility to thyroid-related issues. For these individuals, hypothyroidism can exacerbate microvascular complications like diabetic nephropathy, and the combination of diabetes and hypothyroidism significantly elevates the risk of cardiovascular problems. Conducting screenings for thyroid dysfunction in type 2 diabetic patients allows for the early identification and management of hypothyroidism. **Aims:** To evaluate how common thyroid dysfunction is among those with type 2 diabetes and to explore the possible relationship between thyroid issues and complications associated with diabetes like diabetic nephropathy. **Methods:** This study was a cross-sectional analysis conducted at the Department of biochemistry with collaboration to medicine of Nepalgunj medical college & teaching hospital, kohalpur, from June 2024 to May 2025. It included 400 outpatients with type 2 diabetes mellitus who had no previous history of thyroid disorders, chronic liver disease, or acute illnesses. All participants were evaluated for diabetic complications, such as nephropathy. Furthermore, thyroid function tests were performed on all participants using the chemiluminescence immunoassay technique. **Results:** The prevalence of thyroid dysfunction among individuals with type 2 diabetes mellitus was identified to be 34.5%. Hypothyroidism was identified in 28% of the participants, whereas 6.5% were diagnosed with hyperthyroidism. The occurrence of thyroid dysfunction was notably higher in women compared to men. Additionally, a significant relationship was established between thyroid dysfunction and diabetic complications, specifically nephropathy, within the study group ($P<0.05$). **Conclusion:** There is a statistically significant relationship between thyroid dysfunction and diabetic nephropathy, indicating that individuals with diabetes who also have thyroid dysfunction are at a higher risk of developing nephropathy.

***Keywords*:** Nephropathy, thyroid dysfunction, type 2 diabetes mellitus & Neuropathy

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INTRODUCTION

Patients with type 2 diabetes mellitus (T2DM) are more prone to developing thyroid disorders[1], particularly hypothyroidism, due to underlying insulin resistance. This coexisting condition can worsen diabetes-related complications, such as dyslipidemia, hypertension and cardiovascular diseases.[2] Timely detection and management of thyroid dysfunction in diabetic patients is essential to prevent the progression of diabetic related complications.[3] Screening for hypothyroidism is simple, requiring only a blood test, and can be routinely carried out in primary care settings. Early diagnosis and treatment may help stabilize blood glucose and lipid levels, improving overall outcomes. Subclinical hypothyroidism has been linked to an increased risk of diabetic nephropathy and cardiovascular problems in T2DM patients.[4,5] Furthermore, the coexistence of hypothyroidism and diabetes can exacerbate microvascular complications, including retinopathy and neuropathy, primarily due to lipid metabolism disturbances.[6] Recent studies have identified varying prevalence rates of diabetic

nephropathy, such as 13% in one study population[7], 16.6% in Enugu (Nigeria)[8] and 72.6% in Benin (Nigeria).[9] Interestingly, one of these studies found a significant association between thyroid dysfunction and diabetic nephropathy[7]; supporting previous findings that hypothyroidism may be a contributing risk factor.[10] Despite global research efforts, there remains a gap in data specific to Nepal, particularly in the mid-western region. To address this, the current study aims to assess the prevalence of thyroid dysfunction among T2DM patients in mid-western Nepal and explore its relationship with diabetic complications, especially nephropathy. This research seeks to provide localized insight that could support early intervention strategies in this population.

METHODS

This Hospital based cross-sectional study was carried out among patients with type 2 diabetes mellitus who visited the biochemistry laboratory at the Biochemistry Department of Nepalgunj Medical College and Teaching Hospital, located in Kohalpur, Banke, from June 2024 to May 2025. The research received approval from the Institutional Review Committee (IRC Ref. No. 10/081-082).

The minimum sample size was estimated at 358 participants, derived from the previously documented prevalence of thyroid dysfunction in diabetic patients, which was 36.84%.[11] This calculation was done with a desired absolute precision of 5% and a significance level of 5%. A convenience sampling approach was adopted to select diabetic patients from the outpatient department of medicine. Patients were excluded from the study if they had acute illness, chronic liver disease,a history of other diseases, hyperlipidemia, were pregnant, had hypertension, were undergoing corticosteroid treatment, or were on medications that could affect thyroid function. Diabetes mellitus diagnoses adhered to the criteria established by the American Diabetes Association (ADA).[12]

Data collected from each patient included demographic details (age and sex), anthropometric measurements (height, weight, BMI), as well as blood pressure readings (systolic and diastolic), duration of diabetes, family history of diabetes and thyroid conditions, and lifestyle factors such as alcohol use and smoking habits. Body Mass Index (BMI) was calculated by dividing weight (in kg) by the square of height (in meters). Participants with a BMI between 25 and 29.9 kg/m² were categorized as overweight, while those exceeding 30 kg/m² were classified as obese. Blood pressure was recorded using a digital sphygmomanometer, with values above 140/90 mm Hg indicating hypertension. A venous blood sample of 5 mL was collected from each participant following an overnight fast for biochemical evaluation. Analysis of fasting serum samples included measuring serum thyroid stimulating hormone (TSH), free triiodothyronine (free T3), and free thyroxine (free T4) via chemiluminescent immunoassay technology (using ADVIA Centaur XP from Siemens Healthcare Global, USA). The normal reference ranges for TSH, free T3, and free T4 were established as 0.35-4.5 mIU/L, 2.3- 4.2 pg/mL, and 0.89-1.76 ng/dL, respectively. Subclinical hypothyroidism was defined as TSH levels between 5-10 mIU/L with normal free T3 and T4, whereas overt hypothyroidism was indicated by TSH levels above 10 mIU/L accompanied by low free T3 and T4. Subclinical hyperthyroidism was characterized by low TSH with normal free T3 and T4, while overt hyperthyroidism was identified by low TSH and elevated free T4 levels. Blood glucose levels were assessed in the laboratory using the glucose oxidase-peroxidase method, whereas, 2 mL of EDTA blood sample was taken for estimation of glycosylated hemoglobin (HbA1c)level in blood through high-performance liquid chromatography (Bio Rad Laboratories, USA).

Diabetic nephropathy was diagnosed based on measurement of estimated globular filtration rate (eGFR) and the presence of albuminuria, with microalbuminuria defined as urinary albumin excretion between 30 and 300 mg/day, and macroalbuminuria as excretion exceeding 300 mg/day. Microalbuminuria levels were evaluated using the nephelometry technique (Mispa i3) at the biochemistry laboratory.The 2009 CKD-EPI creatinine equation for estimating glomerular filtration rate (GFR) is:

eGFR = 141 × min (Scr/k, 1)a × max(Scr/k, 1)-1.209 × 0.993Age × 1.018 [if female] × 1.159 [if Black].

Where,

- eGFR: Estimated GFR in mL/min/1.73 m².
- Scr: Serum creatinine level in mg/dL.
- k: A constant that varies based on sex (0.7 for females, 0.9 for males).
- a: A constant that varies based on sex (-0.329 for females, -0.411 for males).
- Min(Sc/k, 1): The minimum value between (Sc/k) and 1.
- Max(Scr/k, 1): The maximum value between (Scr/k) and 1.
- Age: Patient's age in years.
- 1.018: A modifier applied if the patient is female.

1.159: A modifier applied if the patient is Black

Statistical analysis:

Continuous variables, including age, duration of diabetes, BMI, and HbA1c, were reported as means with standard deviations (SD). Categorical variables, such as the prevalence of thyroid dysfunction, hypertension, obesity, and diabetic complications, were expressed as percentages and analyzed using the Chi-square test (χ^2). All statistical analyses were performed at a 5% significance level, with p-values lower than 0.05 considered statistically significant.

RESULTS

The study involved a total of 400 participants, with their primary characteristics summarized in Table I. On average, the individuals had been living with diabetes for 14.3 years

(±6.75), and their mean glycosylated hemoglobin (HbA1c) level was recorded at 9.64% (±2.01). The research indicated that 34.5% of the participants (138 individuals) experienced thyroid dysfunction. Figure 1 illustrates the results of the thyroid function tests, revealing that the majority of participants (65.5%) had normal levels of TSH, free T3, and free T4. Subclinical hypothyroidism and overt hypothyroidism were found in 16% and 12% of participants, respectively, while subclinical hyperthyroidism and overt hyperthyroidism were present in 3.5% and 3% of individuals respectively.

Table II presents detailed information regarding participant demographics, including age, family history of diabetes, duration of diabetes, glycemic control, and gender distribution. The largest proportion of diabetic patients was found in the 41 to 70-year age range. Additionally, the table outlines the prevalence of thyroid dysfunction in relation to various factors, showing that women exhibited a higher incidence of both hypothyroidism and hyperthyroidism compared to men. Hypothyroidism was particularly prevalent among those with diabetes for longer than five years, whereas hyperthyroidism was more frequently observed in individuals with diabetes for more than ten years. The analysis revealed statistically significant relationship between thyroid dysfunction and several factors: age ($p<0.001$), gender ($p<0.001$), duration of diabetes ($p<0.001$), family history of diabetes ($p<0.001$), and glycemic control ($p<0.001$). Furthermore, Table II indicates a statistically significant relationship between thyroid dysfunction and diabetic complications, particularly diabetic nephropathy ($p<0.05$), within the population of participants with Type 2 diabetes.

Characteristics		Mean±SD/n (%)
Age(years)		55.07±13.08
Gender	Female	229 (57.20 %)
	Male	171 (42.80 %)
Duration of Diabetes mellitus (years)		14.30±6.75
Body mass index (BMI) (kg/m^2)		27.79 ± 3.16
Fasting blood glucose (FBG) (mg/dl)		182.41±74.96
Postprandial Blood glucose (PPBG) (mg/dl)		293.79± 104.89
Glycated hemoglobin(HbA1c) %		9.64±2.01
Total no. of people with thyroid dysfunction		138 (34.50%)
Thyroid function test	FT3(pg/ml)	2.90±0.88
	FT4(ng/dl)	1.17±0.34
	TSH(µIU/ml)	7.92±7.71
Family history of DM	Yes	175 (43.80%)
	No	225 (56.20%)
History of alcoholism	Yes	207 (51.80%)
	No	193 (48.20%)
History of smoking	Yes	165 (41.20%)
	No	235 (58.80 %)

Table I: Demographic and clinical characteristics of study population (n=400)

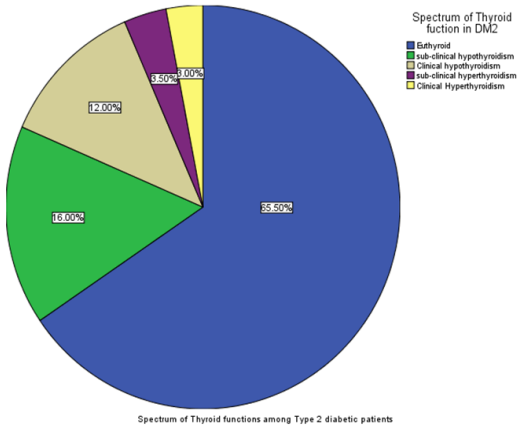

Figure1: Spectrum of Thyroid functions among Type 2 diabetic patients

Thyroid function Characteristics		Spectrum of thyroid function (N=400) Euthyroid (n=262, 65.5%)	Hyper-thyroidism (n=26, 6.50%)	Hypo-thyroidism (n=112, 28.0%)	P-value
Age group (years)	21-30	16 (6.10 %)	0	0	
	31-40	40 (15.30%)	0	4 (3.60 %)	
	41-50	61 (23.30%)	0	23 (20.50)	
	51-60	83 (31.70%)	12 (46.20%)	57 (50.90%)	

Age group (years)	61-70	21 (8.0%)	8 (30.80%)	23 (20.50%)	<0.001
	71-80	35 (13.40)	0	5 (4.50%)	
	>80	6	6 (23.10%)	0	
Gender	Female	127 (48.5%)	15 (57.7 %)	87 (77.7%)	<0.001
	Male	135 (51.5%)	11 (42.3%)	25 (22.3 %)	
Family history of DM	Yes	87 (33.20%)	11 (42.30)	77 (68.80%)	<0.001
	No	175 (66.8 %)	15 (57.7%)	35 (31.20%)	
Duration of diabetes years	< 1	18 (6.90%)	0	7 (6.9%)	<0.001
	1-5	60 (22.90)	0	12 (10.70%)	
	5-10	63 (24%)	12 (46.20%)	49 (43.8%)	
	>10	121 (46.2%)	14 (53.80%)	44 (39.3%)	
(HbA1c %)	6.5-7.0	24 (9.20)	0	0	<0.001
	7.10-8.0	56 (21.40)	0	8 (7.10%)	
	8.1-9.0	48 (18.30)	6 (23.1%)	28 (25 %)	
	>9	134 (51.1%)	20 (76.9%)	76 (67.9%)	
Nephropathy	Yes	31 (11.8%)	16 (61.6%)	37 (33%)	<0.001
	No	231 (88.2%)	10 (38.5%)	75 (67%)	

Table II: Relationship of Thyroid dysfunction with age, gender, duration of diabetes, glycemic status, Diabetic nephropathy and family history of thyroid disease in study participants (n=400)

DISCUSSION

The coexistence of diabetes mellitus (DM) and thyroid disorders is a well-recognized phenomenon. Both of these are among the most prevalent endocrine conditions encountered in clinical practice. Insulin resistance, a common feature in T2DM patients, is significantly implicated in the development of thyroid dysfunction. This dysfunction may manifest as hypothyroidism or hyperthyroidism, with subclinical hypothyroidism also prevalent among diabetic patients, potentially leading to complications such as retinopathy, neuropathy, and cardiovascular disease.[13] Our findings revealed a prevalence of thyroid dysfunction in 34.5% of T2DM patients, which is notably higher than the prevalence rates reported in several other studies (ranging from 23.6% to 37%).[11,14,15,16,17,18] This variation may be attributed to regional disparities in ethnicity and dietary practices.[19,20] Among the thyroid disorders identified, subclinical hypothyroidism was the most common at 16%, followed by clinical hypothyroidism (12%), clinical hyperthyroidism (3%), and subclinical hyperthyroidism (3.5%). These results are consistent with studies conducted in Nepal, India, and Bangladesh[11, 14,18,21,22], indicating the necessity for routine screening of T2DM patients for concurrent thyroid dysfunction, given its significant impact on glycemic control and overall diabetes management.[23]

Our study found significant statistical relationship between thyroid dysfunction and factors such as age (p<0.001), gender (p<0.001), duration of diabetes (p<0.001), family history of diabetes (p<0.001), and glycemic control (p<0.001). According to Ogbonna et al, females with T2DM have a 3.8 times greater risk of developing thyroid dysfunction compared to males.[7] This is believed to be due to the influence of estrogen on thyroid follicular cells and thyroxine-binding globulin (TBG).[24] Our study supports this finding, as the significant relationship of thyroid disorders was higher among diabetic females (P < 0.001) as compared to male, which is consistent with previous research.[7,14, 15, 25] Bassyouni et al (2010) reported a higher prevalence of thyroid dysfunction in older individuals with type 2 diabetes. Similarly, our study found an increase in thyroid dysfunction with age up to 70 years, after which it decreased, a pattern that aligns with the findings of Sahu Sulagna et al in their research.[26]

Elevated HbA1c levels, indicative of poor blood sugar control, have been strongly linked to the development of chronic complications in diabetes mellitus (DM).[27,28] This study found a significant relationship between thyroid dysfunction and glycemic control. Specifically, individuals with type 2 DM and higher HbA1c levels were more prone to thyroid dysfunction compared to those maintaining good glycemic control (HbA1c < 7.0%). This pattern is consistent with findings from Ogbonna SU and Ezeani IU.[7] The potential cause may lie in the detrimental effects of prolonged hyperglycemia on the hypothalamo-pituitary axis, which can disrupt or eliminate the nocturnal peak of thyroid-stimulating hormone (TSH).[29] Previous researches have also categorized both clinical and subclinical hypothyroidism as insulin-resistant conditions. For instance, Bazrafshan et al[30] identified a significant correlation between HbA1c and TSH levels, aligning with our study's results. Similarly, Ardekani et al[31] observed that HbA1c levels were significantly elevated in diabetic patients with thyroid disorders, which corresponds with our findings. Chronic hyperglycemia further inhibits the conversion of thyroxine (T4) to triiodothyronine (T3) by reducing the activity of thyroxine deiodinase.[23] Schlienger et al[32] also reported that poor glycemic

control (with HbA1c levels ≥ 12%) is associated with a condition known as "low T3 syndrome," resulting from impaired T4 to T3 conversion. This study identified a significant relationship between thyroid dysfunction and the duration of diabetes. This finding aligns with the research by Ogbonna SU and Ezeani IU.[7] It suggests that a longer duration of diabetes could increase the risk of developing thyroid dysfunction, potentially due to the adverse effects of prolonged hyperglycemia, which impairs the conversion of T4 to T3, contributing to thyroid dysfunction. This observation is consistent with the results of Telwani et al[33], who reported a higher prevalence of thyroid disorders in individuals with diabetes lasting five years or more, compared to those with a shorter duration (75.9% vs. 24.1%). However, a study by Diez et al found no significant link between the presence of thyroid dysfunction and the duration of diabetes. [34]

In addition to insulin resistance, autoimmunity can also play a role in the development of thyroid dysfunction in type 2 diabetes mellitus. A study by Radaideh AR et al[35] revealed that 12.5% of diabetic patients had thyroid disease, with 8.3% of those with thyroid dysfunction testing positive for antibodies against thyroid peroxidase. This suggests that screening for asymptomatic thyroid dysfunction may be valuable in identifying thyroid disease in diabetic patients.

Hypothyroidism is believed to be linked to an increased risk of nephropathy and cardiovascular disease in diabetic patients. This was demonstrated in a study by Chen HS et al[4], which found that subclinical hypothyroidism was a risk factor for both nephropathy and cardiovascular disease in type 2 diabetes patients. Our studies showed significant relationship between thyroid dysfunction and nephropathy in Type 2 diabetic patients. In this study, 21% of patients with type 2 diabetes mellitus (DM) were found to have diabetic nephropathy. This is higher than the 16.6% prevalence reported by Ulasi et al in Enugu, Nigeria [8] and the 13% observed by Ogbonna and Ezeani in Nigeria[7], but significantly lowers than the 72.6% prevalence reported by Onovughakpo-Sakpa et al in Benin, Nigeria.[9] This study found a significant relationship between diabetic nephropathy and thyroid dysfunction ($p<0.05$), indicating that patients with diabetic nephropathy are more likely to experience thyroid dysfunction compared to those without nephropathy. This result aligns with the findings of several other studies[4,36,37] but contrasts with the various studies[18,38] which found no such association between diabetic nephropathy and thyroid dysfunction in type 2 diabetes patients. Thyroid dysfunction is frequently observed in patients with type 2 diabetes, especially among those with long-duration diabetes, poor blood sugar control, older age, and women. Effectively managing thyroid dysfunction in these patients may help reduce overall morbidity and prevent the worsening of diabetic complications, such as nephropathy.

LIMITATIONS

This study does not explore the underlying mechanisms linking thyroid dysfunction to nephropathy, such as the potential roles of inflammation or oxidative stress, which may limit the understanding of the pathophysiological connection between these conditions.

CONCLUSION

In this study, the prevalence of thyroid dysfunction among patients with type 2 diabetes mellitus was 34.5%, with hypothyroidism occurring more frequently than hyperthyroidism. A significant correlation was observed between thyroid dysfunction and the presence of diabetic complications, particularly nephropathy, in the study population.

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