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Original Research Article

Prevalence of Subclinical Hypothyroidism and Its Relationship with Glycemic Control and Microvascular Complications in Type 2 Diabetes Mellitus

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Conflict of interest: Nil

Abstract

Introduction: Subclinical hypothyroidism (SCH) is the most common thyroid disease in patients with type 2 diabetes mellitus (T2DM). There is growing evidence that SCH may adversely affect glycemic control and contribute to the development of diabetic microvascular complications. However, data from the Indian subcontinent are limited and inconsistent.

Objectives: To determine the prevalence of SCH in patients with T2DM and to assess its correlation with glycemic status and microvascular complications like diabetic nephropathy, diabetic retinopathy and diabetic neuropathy.

Methods: A cross-sectional study was conducted in a tertiary care teaching hospital among 114 adult patients with T2DM. Thyroid function tests, fasting blood glucose, postprandial blood glucose, glycated hemoglobin (HbA1c), urinary microalbumin estimation, fundus examination, nerve conduction studies were done. SCH was defined as elevated serum thyroid stimulating hormone (TSH) levels (>4 mIU/L) with normal free thyroxine (FT4) concentrations. Statistical analysis was carried out using SPSS version 20.

Results: Among 114 participants, 42 patients (36.8%) had SCH. Mean HbA1c was significantly higher in SCH group in comparison to euthyroid individuals (9.19±2.21% vs. 8.16±1.65%; p=0.005). Neuropathy was present in 15 (13.2%) participants, retinopathy in 30 (27.0%) and nephropathy in 53 (46.5%) . There was a finding of SCH in 8 patients with neuropathy (54%) and 15 patients with retinopathy, but these associations were not statistically significant. Conversely, diabetic nephropathy was significantly associated with SCH with 39 of 53 patients with nephropathy having SCH (p<0.001).

Conclusion: SCH is very common in T2DM patients and is associated with worse glycemic control and significantly increased burden of diabetic nephropathy. Routine screening of the thyroid may help to identify early those patients who are at increased risk for microvascular complications.

Keywords: Type 2 Diabetes Mellitus, Subclinical Hypothyroidism, HbA1c, Diabetic Nephropathy, Diabetic Retinopathy, And Diabetic Neuropathy.

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Introduction

T2DM is a prevalent chronic metabolic disease in the world. It is characterized by persistent hyperglycemia caused by insulin resistance and progressive dysfunction of pancreatic β-cells. T2DM has become a major global health challenge because of its association with cardiovascular disease, chronic kidney disease, blindness, neuropathy and premature mortality [1]. Microvascular complications are an important cause of morbidity in patients with diabetes mellitus. These complications are diabetic nephropathy, diabetic retinopathy, and diabetic neuropathy; all have great impact on quality of life and raise health care costs. Persistent hyperglycemia is noted as the main mechanism of microvascular damage through oxidative stress, advanced glycation end products, inflammatory cytokines, endothelial dysfunction, and altered

hemodynamics [2]. Thyroid hormones are important regulators of carbohydrate metabolism, lipid homeostasis, cardiovascular function, and renal physiology. Thyroid status changes can affect insulin sensitivity, hepatic glucose output, peripheral glucose utilization, and vascular integrity. Therefore, thyroid dysfunction has gained increasing attention as a possible etiopathogenesis of diabetic complications [3].

The most common thyroid disorder seen in diabetics is subclinical hypothyroidism (SCH). SCH is defined as an elevation of serum TSH concentrations with normal circulating FT4 concentrations and is frequently clinically asymptomatic. SCH is associated with dyslipidemia, insulin resistance, endothelial dysfunction, and increased cardiovascular risk [4], although many patients are asymptomatic. Several epidemiological studies have reported a higher prevalence of SCH in patients with T2DM than in the general population. Diabetes and thyroid dysfunction together form a complex metabolic environment that can impair glycemic control and hasten vascular injury [5].

There is increasing evidence that SCH may affect diabetic microvascular complications. High TSH levels have been associated with increased albuminuria, impaired renal function and diabetic nephropathy. Proposed mechanisms include decreased glomerular filtration rate, endothelial dysfunction, renin-angiotensin system activation, oxidative stress and increased insulin resistance [6].

Likewise, thyroid dysfunction has been investigated in relation to diabetic retinopathy and diabetic neuropathy. Some studies have indicated positive associations, but other studies could not show statistically significant associations, suggesting that more research is needed [7].

The prevalence and clinical importance of SCH varies widely between populations, due to ethnic, genetic, environmental and nutritional influences. Data on SCH and diabetic microvascular complications from India are limited and, in particular, from South India.

Thus, the present study was undertaken to determine the prevalence of SCH in patients with T2DM and to evaluate its relationship with glycemic control and microvascular complications.

Objectives

Primary Objective: To determine the prevalence of subclinical hypothyroidism among patients with type 2 diabetes mellitus.

Secondary Objectives

1. To evaluate glycemic status in patients with and without SCH.
2. To assess the relationship between SCH and diabetic nephropathy.
3. To evaluate the association between SCH and diabetic retinopathy.
4. To determine the relationship between SCH and diabetic neuropathy.
5. To compare demographic and clinical characteristics between SCH and euthyroid diabetic patients.

Materials and Methods

Study Design: Hospital-based cross-sectional observational study.

Study Setting: Department of General Medicine, Chamarajanagar Institute of Medical Sciences, Chamarajanagar, Karnataka, India.

Study Duration: Eighteen months.

Study Population: A total of 114 adult patients diagnosed with T2DM were included in the study after fulfilling the eligibility criteria.

Inclusion Criteria

- Patients aged more than 18 years.
- Diagnosed T2DM according to ADA criteria.
- Known cases of T2DM receiving treatment.
- HbA1c ≥6.5%, fasting plasma glucose ≥126 mg/dL, postprandial plasma glucose ≥200 mg/dL, or random plasma glucose ≥200 mg/dL with classical symptoms.

Exclusion Criteria

- Known thyroid disease.
- eGFR <60 mL/min/1.73m².
- Pregnancy.
- Hepatic dysfunction.
- Psychiatric illness.
- Recent severe illness or ICU admission.
- Use of medications interfering with thyroid function.

Data Collection

All participants underwent:

1. Detailed clinical evaluation.
2. Anthropometric assessment including BMI.
3. Fasting and postprandial blood glucose estimation.
4. HbA1c measurement.
5. Thyroid function testing (TSH and FT4).
6. Spot urinary microalbumin estimation.
7. Dilated fundus examination.
8. Nerve conduction studies.
9. Serum creatinine estimation.

Definition of SCH: SCH was defined as serum TSH >4 mIU/L with normal FT4 levels.

Assessment of Microvascular Complications

Diabetic Nephropathy: Urinary microalbumin concentration between 20–200 mg/min or higher was considered indicative of nephropathy.

Diabetic Retinopathy: Diagnosis was established by ophthalmological fundus examination.

Diabetic Neuropathy: Peripheral neuropathy was assessed using nerve conduction studies.

Statistical Analysis: Data were analyzed using SPSS version 20. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. Chi-square testing and Pearson correlation analysis were employed where appropriate. A p-value <0.05 was considered statistically significant.

Results

A total of 114 patients with type 2 diabetes mellitus who fulfilled the inclusion criteria were enrolled in the study. The prevalence of subclinical hypothyroidism (SCH) was evaluated, and its relationship with glycemic control and diabetic microvascular complications was assessed.

Table 1: Age Distribution of Study Participants

Age Group (Years)	Number	Percentage (%)
≤40	2	1.8
41–50	15	13.2
51–60	48	42.1
61–70	33	28.9
71–80	14	12.3
>80	2	1.8
Total	**114**	**100**

The majority of participants belonged to the 51–60-year age group (42.1%), followed by the 61–70-year age group (28.9%). The mean age was 58.9±10 years in the euthyroid group and 60.53±9.15 years in the SCH group. Age was not significantly associated with SCH.

Table 2: Gender Distribution and SCH

Gender	Euthyroid	SCH	Total
Male	30	17	47
Female	42	25	67
Total	72	42	114

p = 0.901

Females constituted 58.8% of the study population, whereas males accounted for 41.2%. SCH was observed in both sexes without a statistically significant difference. This finding suggests that gender did not independently influence SCH prevalence in this diabetic cohort.

Table 3: Glycemic Parameters and SCH

Parameter	Euthyroid	SCH	p-value
FBS (mg/dL)	172.18 ± 57.96	177.48 ± 58.45	0.640
PPBS (mg/dL)	243.03 ± 67.93	255.71 ± 77.93	0.364
HbA1c (%)	8.16 ± 1.65	9.19 ± 2.21	0.005

Patients with SCH demonstrated higher fasting glucose, postprandial glucose, and HbA1c values compared with euthyroid patients. The difference in HbA1c was statistically significant, indicating poorer long-term glycemic control among SCH patients.

Clinical Correlation: Elevated HbA1c among SCH patients suggests increased insulin resistance and impaired glucose utilization. Thyroid hormones influence glucose transport, hepatic gluconeogenesis, and insulin sensitivity. Even mild thyroid dysfunction may therefore worsen diabetic control and contribute to vascular complications.

Table 4: Prevalence of Microvascular Complications

Complication	Number	Percentage (%)
Neuropathy	15	13.2
Retinopathy	30	27.0
Nephropathy	53	46.5

Diabetic nephropathy was the most frequent microvascular complication, affecting nearly half of the study population. Retinopathy was observed in approximately one-fourth of patients, while neuropathy affected 13.2%.

Table 5. Prevalence of Subclinical Hypothyroidism

Thyroid Status	Number	Percentage (%)
Euthyroid	72	63.2
SCH	42	36.8
Total	114	100

More than one-third of diabetic patients had SCH. This prevalence is considerably higher than that reported in the general population and indicates a strong overlap between thyroid dysfunction and T2DM.

Table 6. SCH and Diabetic Neuropathy

Neuropathy	SCH	Euthyroid	Total
Present	8	7	15
Absent	34	65	99
Total	42	72	114

p = 0.700

Among patients with neuropathy, 54% had SCH. Although SCH was numerically more common among patients with neuropathy, the association was not statistically significant.

Clinical Correlation: Hypothyroidism has been implicated in nerve dysfunction through altered metabolism and reduced nerve conduction velocity. The lack of significance in the present study may reflect limited sample size and warrants further investigation.

Table 7: SCH and Diabetic Retinopathy

Retinopathy	SCH	Euthyroid	Total
Present	15	15	30
Absent	27	57	84
Total	42	72	114

p = 0.383

Fifteen patients with retinopathy had SCH. Although the prevalence of retinopathy appeared higher among SCH patients, statistical significance was not achieved.

Clinical Correlation: Microvascular retinal injury is strongly influenced by glycemic control and duration of diabetes. Thyroid dysfunction may contribute indirectly through endothelial dysfunction, but larger studies are required to establish causality.

Table 8: SCH and Diabetic Nephropathy

Nephropathy	SCH	Euthyroid	Total
Present	39	14	53
Absent	3	58	61
Total	42	72	114

p < 0.001

A highly significant association was observed between SCH and diabetic nephropathy. Nearly three-fourths of patients with nephropathy had SCH, whereas only a small proportion of patients without nephropathy had SCH.

Clinical Correlation: The findings strongly suggest that SCH may contribute to renal injury in diabetes through endothelial dysfunction, oxidative stress, activation of inflammatory pathways, and alterations in renal hemodynamics.

Discussion

Objective: To determine the prevalence of subclinical hypothyroidism (SCH) and its association with glycemic control and diabetic microvascular complications in patients with type 2 diabetes mellitus (T2DM). The findings revealed high prevalence of SCH and a significant association between SCH, poor glycemic control and diabetic nephropathy.

Forty-two (36.8%) of 114 patients had SCH. This prevalence is much higher than that reported in the general population where SCH affects about 4–10% of adults [1,2]. Previous studies reported prevalence rates in diabetic populations ranging from 8.7% to 19.1% [3–6]. The higher prevalence reported in the present study could be attributed to ethnic variations, referral bias of tertiary care hospitals, differences in glycemic status and

different diagnostic criteria used in different studies.

The relationship between diabetes mellitus and thyroid dysfunction is complicated and goes in both directions. Thyroid hormones affect glucose metabolism via effects on hepatic gluconeogenesis, intestinal glucose absorption, insulin secretion and peripheral glucose utilization [7]. On the other hand, chronic hyperglycemia may change function of hypothalamic-pituitary-thyroid axis and thyroid hormone metabolism [8]. Thyroid dysfunction is therefore more common in diabetic patients than in the general population.

The most important finding of the present study was the significant association between SCH and poor glycemic control. Patients with SCH had significantly higher HbA1c levels than euthyroid patients (9.19±2.21% vs. 8.16±1.65%, p=0.005). Furukawa et al. reported similar findings with significantly higher HbA1c levels in diabetic patients with SCH [9]. Increased insulin resistance, impaired glucose disposal, and decreased activity of glucose transporter associated with hypothyroid states may explain elevated HbA1c in SCH [10]. Thyroid hormone deficiency may also impact negatively on pancreatic beta cell function and insulin sensitivity and, in turn, impair long-term glycemic control [11].

Diabetic nephropathy was the most common microvascular complication in this study (46.5%). Importantly, a strong association was observed between SCH and diabetic nephropathy (p<0.001) with 39 out of 53 nephropathy patients having SCH. The findings are in line with previous studies by Yasuda et al., Chen et al., and Furukawa et al., who found a higher prevalence of albuminuria and nephropathy in diabetic patients with SCH [3,5,9].

Several explanations are possible for the observed association. Thyroid hormones are important for the maintenance of renal blood flow, glomerular filtration rate (GFR), sodium homeostasis and endothelial integrity [12]. SCH has been linked to reduced GFR, elevated systemic vascular resistance, activation of the renin-angiotensin-aldosterone system and endothelial dysfunction [13,14]. Endothelial dysfunction is a critical pathogenic event in diabetic nephropathy, causing increased glomerular permeability and albuminuria [15].

In addition, SCH has been associated with increased oxidative stress and chronic low-grade inflammation [16]. The increased levels of reactive oxygen species could lead to an increased mesangial expansion, glomerular basement membrane thickening and podocyte damage which could contribute to the progression of diabetic kidney disease [17]. In addition, SCH is associated with insulin resistance and abnormalities in coagulation and fibrinolysis that may further contribute to renal vascular injury [18,19].

SCH was present in 54% of the neuropathy patients in the present study, although the association between SCH and diabetic neuropathy was not statistically significant. Similar observations have been made by several investigators [20]. However, Allam et al. showed that SCH was associated with an increased severity of diabetic peripheral neuropathy and suggested that thyroid dysfunction may affect nerve conduction and axonal function [21]. The lack of significance in the present study may be due to the relatively small number of cases of neuropathy.

Similarly, no significant association was found between SCH and diabetic retinopathy. Retinopathy was present in 15 of the 30 SCH patients, but no statistical significance was found. The results are in line with those reported by Chen et al. [5]. However, Kim et al. [6] reported a much higher prevalence of severe diabetic retinopathy in patients with SCH. These differences may be due to variation in ethnicity, retinopathy grading systems, duration of diabetes and sample size.

In this study, SCH was not significantly related to age, gender, BMI or duration of diabetes. Similar results have been reported by other investigators [6,9]. The mean BMI and duration of diabetes were higher in SCH patients but the differences were not significant. This suggests that thyroid dysfunction may contribute independently to diabetic complications, irrespective of classical demographic risk factors.

The present findings have important clinical implications. SCH is often asymptomatic and thus frequently missed in routine diabetic care [22]. However, the positive association between SCH and diabetic nephropathy in this study suggests that screening for thyroid function might be useful to identify a subgroup of diabetic patients at higher risk of developing renal complications. Early diagnosis and treatment of SCH might lead to better metabolic control and delay the progression of diabetic kidney disease [23].

The study's strengths include a comprehensive assessment of thyroid function and all major diabetic microvascular complications using standardized methods.

However, there are some limitations that need to be recognized. Because the study was cross-sectional, a causal relationship cannot be established. The sample size was somewhat modest and the study was conducted at a single tertiary-care center that may limit generalizability. Moreover, thyroid function and urinary microalbumin levels were

measured only once, and severity grading of nephropathy and neuropathy was not done [24].

In conclusion, the results suggest that SCH is prevalent in T2DM patients and is strongly associated with poor glycemic control and diabetic nephropathy. Hence routine screening for thyroid dysfunction may be indicated in diabetic patients especially in patients having evidence of renal involvement. Future prospective longitudinal studies are needed to determine whether treatment of SCH can reduce the incidence and progression of diabetic nephropathy.

Conclusion

Subclinical hypothyroidism is common in patients with type 2 diabetes mellitus. Patients with SCH have markedly worse glycemic control and a much higher prevalence of diabetic nephropathy.

Neuropathy and retinopathy were found to be more common in SCH patients but the associations were not significant statistically. Routine screening for thyroid dysfunction may be useful in early identification of high risk diabetic patients and may provide a window of opportunity for targeted interventions to prevent progression of renal complications.

Strengths

- Comprehensive assessment of all major diabetic microvascular complications.
- Standardized biochemical evaluation.
- Inclusion of thyroid and glycemic parameters.
- Real-world tertiary care population.

Limitations

- Cross-sectional study design.
- Single-center study.
- Relatively small sample size.
- Single-point measurement of thyroid and urine microalbumin levels.
- Lack of severity grading for neuropathy and nephropathy.

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