E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.48047/ijprt/16.02.71

Research Article

Association Between Subclinical Hypothyroidism and Diabetic Nephropathy Among Patients With Type 2 Diabetes Mellitus: A Cross-Sectional Study

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Abstract

Background

Thyroid dysfunction is a common finding in patients with type 2 diabetes mellitus (T2DM), the most common anomaly being subclinical hypothyroidism (SCH). SCH may be implicated in the development and progression of diabetic microvascular complications, particularly diabetic nephropathy, emerging evidence suggests. However, data from South India are limited.

Objectives:

To evaluate the prevalence of SCH in patients with T2DM and its association with diabetic nephropathy.

Method

A hospital based cross sectional study was carried out among 114 patients with T2DM attending the out patient and in patient services of a tertiary care teaching hospital. Clinical evaluation, anthropometric measurements, glycemic assessment, thyroid function tests, urine microalbumin estimation, fundus examination and nerve conduction studies were done. SCH was defined as serum TSH >4 mIU/L with normal FT4 level. Statistical analysis was done using SPSS version 20.

Results

There were 42 (36.8%) participants with SCH among 114 participants. The mean age was similar in euthyroid and SCH groups (58.9±10 vs 60.53±9.15 years; p=0.405). The study population consisted of 58.8 % females. Diabetic nephropathy was found in 53 (46.5%) patients, of whom 39 (73.6%) had SCH. SCH was significantly associated with diabetic nephropathy (p<0.001). Higher HbA1c and urinary microalbumin were observed in SCH patients. SCH patients were more likely to have diabetic retinopathy and neuropathy; however, these associations did not reach statistical significance.

Conclusion

SCH is highly prevalent in patients with T2DM and is significantly associated with diabetic nephropathy. Routine thyroid screening could allow earlier recognition of high risk individuals and potentially better renal outcomes.

Keywords: Type 2 diabetes mellitus, subclinical hypothyroidism, diabetic nephropathy, microalbuminuria, thyroid stimulating hormone, microvascular complications.

Introduction

Diabetes mellitus is one of the most prevalent chronic metabolic disorders in the world and a major public health challenge. The International Diabetes Federation estimates that the global burden of diabetes is still rising, especially in low- and middle-income countries. India has been identified as one of the countries with the largest diabetic populations that has led to a huge increase in diabetes-related complications and healthcare costs [1].

Type 2 diabetes mellitus (T2DM) is a disease with insulin resistance, progressive β-cell dysfunction and chronic hyperglycemia. Chronic hyperglycemia results in widespread vascular damage and induces macro and microvascular complications. Diabetic nephropathy is among the microvascular complications that continue to be a major cause of chronic kidney disease and end stage renal disease globally [2].

Diabetic nephropathy arises from complex interactions of metabolic abnormalities, hemodynamic alterations, inflammatory mediators, oxidative stress and genetic susceptibility. Hyperglycemia causes glomerular hyperfiltration, mesangial expansion, thickening of the glomerular basement membrane and progressive albuminuria. Microalbuminuria is an early marker of diabetic nephropathy and a predictor of future renal and cardiovascular morbidity [3].

In recent years, the association between thyroid dysfunction and diabetes mellitus has been increasingly recognized. Thyroid hormones play an important role in glucose metabolism, lipid regulation, cardiovascular function and renal physiology. Changes in thyroid function can affect insulin sensitivity and metabolic homeostasis, and thus may impact diabetic outcomes [4].

Subclinical hypothyroidism (SCH) is defined biochemically by increased serum thyroid-stimulating hormone (TSH) concentrations with normal circulating free thyroxine (FT4) concentrations. Although often asymptomatic, SCH has been associated with endothelial dysfunction, dyslipidemia, insulin resistance, oxidative stress and cardiovascular disease [5].

The prevalence of SCH in T2DM patients is significantly higher than that of the general population. In several studies, prevalence rates of 8% to 20% have been reported, suggesting a significant overlap between these endocrine disorders [6]. The coexistence of SCH and T2DM may have important clinical implications, since thyroid dysfunction may adversely affect glycaemic control and accelerate vascular complications.

Several mechanisms have been proposed for the association between SCH and diabetic nephropathy. Diminished thyroid hormone activity may impair renal blood flow and glomerular filtration rate. High TSH levels may cause endothelial dysfunction, oxidative stress and activation of inflammatory pathways leading to albuminuria and renal damage [7]. In addition, hypothyroid states have been associated with abnormalities of the renin-angiotensin system, dyslipidemia and increased insulin resistance that may accelerate the progression of nephropathy.

There is significant association between SCH and diabetic nephropathy, as shown in studies in China, Japan, Egypt and Taiwan [8–11]. Yet, some studies have shown inconsistent results, emphasizing the necessity for additional regional data [12].

The increasing burden of diabetes and the potential role of SCH as a modifiable risk factor makes understanding the relationship between SCH and diabetic nephropathy clinically relevant. Early recognition of SCH may allow for timely intervention and better renal outcomes.

The present study was conducted to determine the prevalence of subclinical hypothyroidism in T2DM patients and to find its association with diabetic nephropathy in South Indian population.

Materials and Methods

Study Design

Hospital-based cross-sectional observational study.

Study Setting

Department of General Medicine, Chamarajanagar Institute of Medical Sciences, Chamarajanagar, Karnataka

Study Duration

Eighteen months.

Study Population

A total of 114 patients with T2DM fulfilling the inclusion criteria were enrolled.

Inclusion Criteria

- Age >18 years.
- Diagnosed T2DM according to ADA criteria.
- Known T2DM receiving treatment.

Exclusion Criteria

- Known thyroid disorders.
- eGFR <60 mL/min/1.73m².
- Pregnancy.
- Hepatic dysfunction.
- Recent severe acute illness.
- Psychiatric illness.
- Use of medications affecting thyroid function.

Data Collection

The following assessments were performed:

- Demographic profile
- BMI measurement
- Blood pressure
- Fasting and postprandial glucose
- HbA1c
- Serum TSH
- Free T4
- Spot urine microalbumin
- Fundus examination
- Nerve conduction studies

Definition of SCH

TSH >4 mIU/L with normal FT4 levels.

Definition of Diabetic Nephropathy

Urinary microalbumin 20–200 mg/dL or greater.

Statistical Analysis

Data were analyzed using SPSS version 20. Continuous variables were expressed as mean ± SD and categorical variables as frequencies and percentages. Chi-square test and Pearson correlation analysis were applied. A p-value <0.05 was considered statistically significant

.**Results**

Table 1. Age Distribution of Study Population

Age Group (Years)	Euthyroid	SCH	Total (%)
≤40	0	2	2 (1.8)
41–50	9	6	15 (13.2)
51–60	31	17	48 (42.1)
61–70	22	11	33 (28.9)
71–80	8	6	14 (12.3)

>80	2	0	2 (1.8)
Total	72	42	114

Source: Thesis results section.

The majority of participants belonged to the 51–60-year age group, reflecting the typical age distribution of T2DM. SCH was observed across all age categories without a statistically significant age-related trend.

Figure 1. Age Distribution of Participants

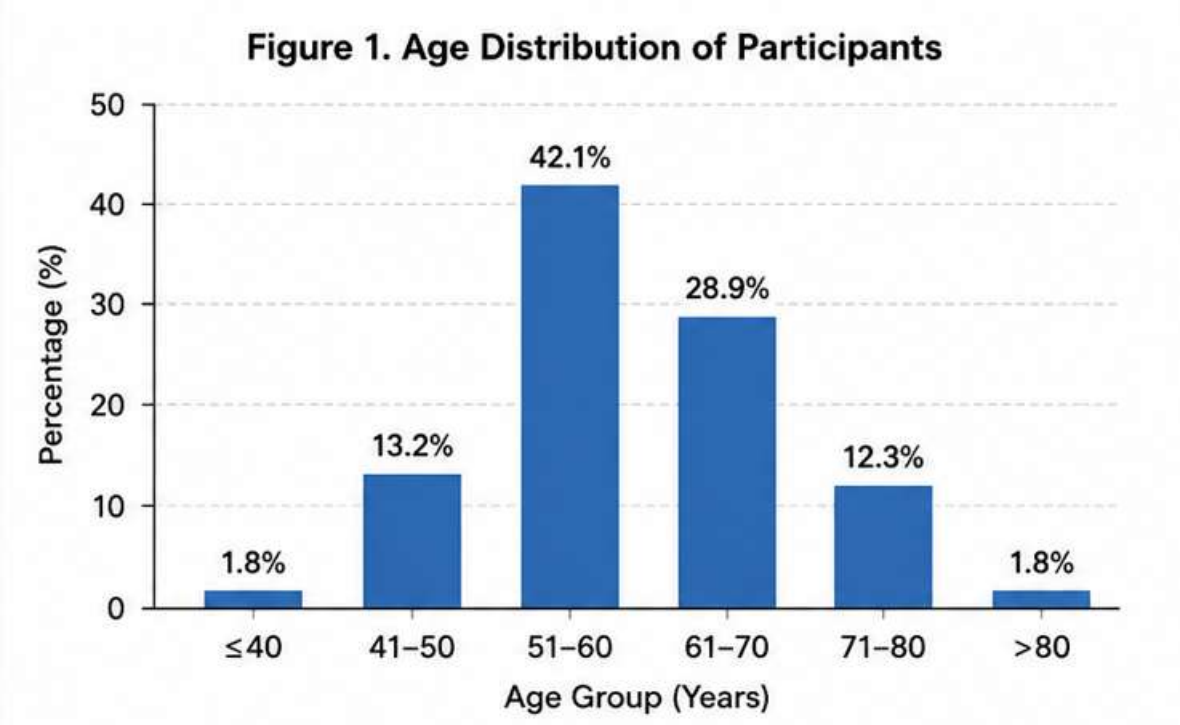


Table 2. Gender Distribution and SCH

Gender	Euthyroid	SCH	Total (%)
Female	42	25	67 (58.8)
Male	30	17	47 (41.2)
Total	72	42	114

p = 0.901.

Females constituted the majority of the study population. However, the occurrence of SCH did not differ significantly between genders, suggesting that diabetes-related factors may play a greater role than sex-related factors in SCH development.

Table 3. Prevalence of Microvascular Complications

Complication	Number	Percentage
Neuropathy	15	13.2
Retinopathy	30	27.0

Nephropathy	53	46.5

Diabetic nephropathy emerged as the most common microvascular complication. Nearly half of all participants demonstrated evidence of renal involvement, highlighting the substantial burden of kidney disease among T2DM patients.

Table 4. Prevalence of SCH

Thyroid Status	Number	Percentage
Euthyroid	72	63.2
SCH	42	36.8

More than one-third of the participants had SCH. This prevalence is considerably higher than that reported in the general population, reinforcing the strong association between thyroid dysfunction and T2DM.

Figure 2. Prevalence of SCH

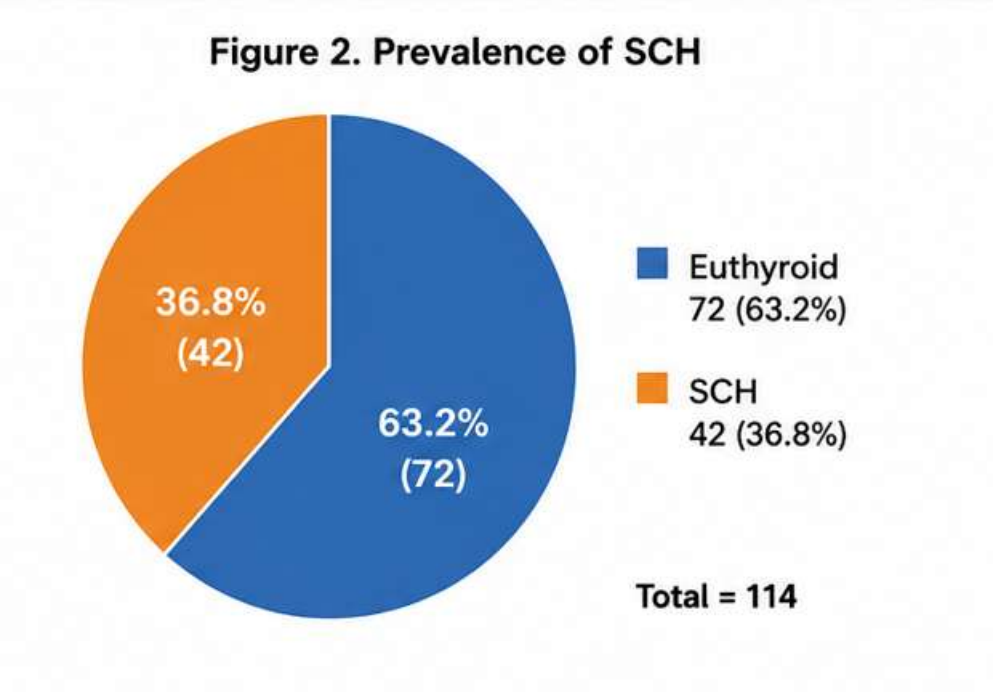


Table 5. Association Between SCH and Diabetic Nephropathy

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

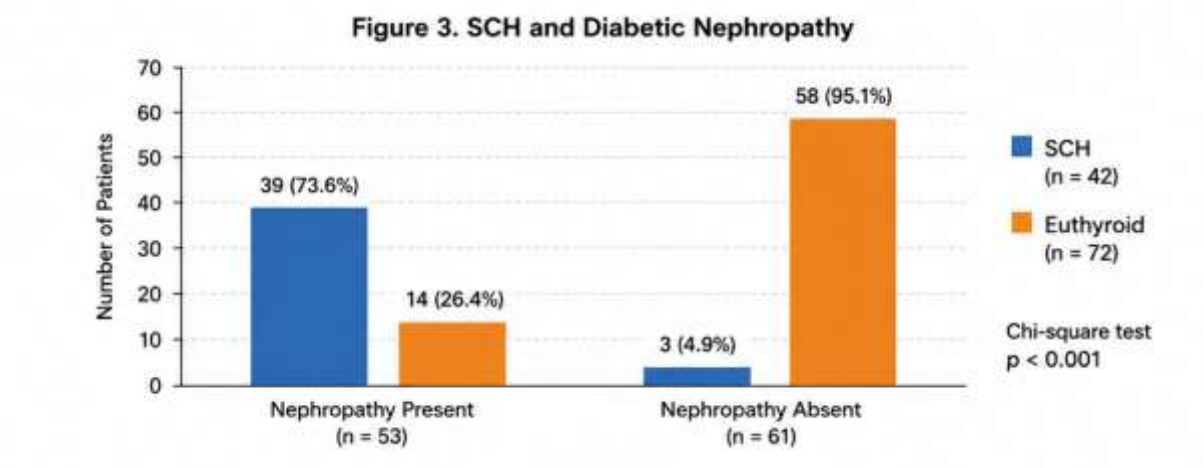
$p < 0.001$

Among patients with nephropathy, 73.6% had SCH, compared with only 4.9% among those without nephropathy. This striking difference demonstrates a strong association between thyroid dysfunction and renal involvement in T2DM.

Clinical Correlation

Microalbuminuria represents early renal endothelial injury. Elevated TSH levels may aggravate endothelial dysfunction, oxidative stress, and renal hemodynamic disturbances, thereby accelerating nephropathy development.

Figure 3. SCH and Diabetic Nephropathy



Discussion

This study aimed to investigate the prevalence of subclinical hypothyroidism (SCH) and its relationship with diabetic nephropathy in patients with T2DM. The results revealed a high prevalence of SCH and a strong association of SCH with diabetic nephropathy in this cohort. The original thesis dataset included SCH in 36.8% of patients and diabetic nephropathy in 46.5%. There was a highly significant association between SCH and diabetic nephropathy.

The mean age of the participants was around 59 – 61 years and most of them were in the age group of 51 – 60 years. The age distribution is similar to the previous studies evaluating thyroid dysfunction in T2DM, where the majority of the population was middle aged and elderly [6,8,9]. Although the prevalence of SCH generally increases with age in the general population, age was not significantly associated with SCH in this study, as reported by Kim et al. [12].

The study population was comprised of 58.8% female participants. Thyroid disorders are more common in women mainly because of autoimmune susceptibility and hormonal effects [4,5]. However, in the present study, there was no significant association between gender and SCH. Palma et al. [6] have reported similar observations suggesting that diabetes-related metabolic disturbances may contribute substantially to thyroid dysfunction irrespective of sex.

A key finding of this study was the high prevalence of SCH (36.8%). This prevalence is greater than that reported in many international studies. In Chinese patients with T2DM, Chen et al. reported a prevalence of 8.8%, whereas Furukawa et al. reported SCH in 17% of Japanese diabetic patients [8,9]. Mansournia et al. reported a prevalence of 19.1% among Egyptian patients with T2DM [10]. The higher prevalence observed in the present study might be attributed to variations in ethnicity,glycemic control, duration of diabetes,iodine status,environmental factors and study methodology.

Almost half of the study participants had diabetic nephropathy. Diabetic kidney disease is one of the most serious microvascular complications of diabetes and a leading cause of chronic kidney disease and end-stage renal disease worldwide [2,3]. The pathogenesis involves glomerular hyperfiltration due to chronic hyperglycemia, mesangial expansion, oxidative stress, inflammatory activation and progressive albuminuria [2,3].

The main finding of this study was the strong association between SCH and diabetic nephropathy. A significant proportion of nephropathy patients had SCH and this association was statistically highly significant. Our results are consistent with those of Chen et

al, who showed that higher TSH levels were independently associated with diabetic nephropathy in Chinese patients with T2DM [8]. Similarly, Furukawa et al. reported significantly higher urinary albumin-creatinine ratio in diabetic patients with SCH, and serum TSH levels were independently associated with albuminuria [9].

Moreover, the present results are in agreement with the study of Mansournia et al. who reported that SCH significantly increased the risk of diabetic nephropathy and other vascular complications in Egyptian subjects with T2DM [10]. Similarly, Tseng et al. reported that diabetic patients with SCH had a significantly higher albuminuria and increased risk of nephropathy compared with euthyroid individuals [11]. Collectively, these results suggest a possible independent association of SCH with renal involvement in diabetes.

Several mechanisms could explain the association of SCH with diabetic nephropathy. Thyroid hormones play a key role in the regulation of renal blood flow, glomerular filtration rate, sodium balance and endothelial function [7]. Decreased thyroid hormone activity in SCH may lead to endothelial dysfunction, increased systemic vascular resistance, and renal perfusion impairment [7]. Endothelial dysfunction has been identified as an important contributor to the development and progression of diabetic nephropathy [7].

Insulin resistance is another potential mechanism. Previous studies have shown the association of SCH with increased insulin resistance which can worsen the hyperglycemia and lead to microvascular injury [5,7]. In addition, in hypothyroid states oxidative stress and chronic low-grade inflammation are increased, favouring glomerular damage and albumin leakage [2,7]. These pathophysiological processes add biological plausibility to the observed association.

The current study also showed that patients with SCH had poor glycemic control as indicated by a significantly higher level of HbA1c. Similar results were found in previous studies, where thyroid dysfunction had a negative impact on glucose metabolism and insulin sensitivity [4,5]. Poor glycemic control is a major determinant of diabetic nephropathy itself. Therefore, SCH may indirectly impair renal outcome through deterioration of glycemic status.

Diabetic retinopathy and neuropathy were more frequent in patients with SCH, but these correlations were not statistically significant. Similar findings have been reported in some studies showing that SCH was more associated with nephropathy than with other microvascular complications [8–11]. In contrast, Kim et al. found that SCH was more closely associated with diabetic retinopathy than nephropathy in Korean patients with T2DM [12]. Discrepancies may be attributed to variations in sample size, ethnicity, study design and diagnostic criteria .

The present study's findings have important clinical implications. Contemporary guidelines for management of diabetes underscore screening for microvascular complications and do not uniformly include routine testing of thyroid function. The strong association between SCH and diabetic nephropathy suggests that screening for thyroid dysfunction may help to identify diabetic individuals at increased risk for renal complications. Early diagnosis and treatment of SCH may have the potential to improve metabolic control and to reduce progression of nephropathy, although prospective intervention studies are needed to confirm this hypothesis [4,5].

This study has a number of strengths. Thyroid function and diabetic microvascular complications were comprehensively evaluated. However, some limitations must be acknowledged. The cross-sectional design precludes the establishment of a causal relationship. The study was conducted at a single tertiary-care center and the relatively small sample size limits generalizability. Longitudinal multicenter studies are needed to determine whether SCH directly contributes to the progression of nephropathy and whether treatment of SCH alters renal outcomes.

Conclusions Overall, the results contribute to the growing evidence that SCH is highly prevalent in patients with T2DM and is significantly associated with diabetic nephropathy. The results are consistent with several international studies and suggest that

SCH may be an important and potentially modifiable risk factor for diabetic kidney disease [8–11].

Conclusion

More than one-third of type 2 diabetes mellitus patients had subclinical hypothyroidism. Diabetic nephropathy was very common and affected nearly half of the study population. A significant association was observed between SCH and diabetic nephropathy. The burden of renal involvement was significantly higher in SCH patients than in euthyroid subjects.

Routine screening for thyroid dysfunction in patients with T2DM may help to identify early those individuals with increased risk for nephropathy. More prospective studies are needed to see if treatment of SCH can improve renal outcomes and reduce diabetes related complications.

References

1. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care. 2021;44(Suppl 1):S1-S232.
2. Alicic RZ, Rooney MT, Tuttle KR. Diabetic kidney disease. Clin J Am Soc Nephrol. 2017;12(12):2032-45.
3. Tuttle KR, Bakris GL, Bilous RW, et al. Diabetic kidney disease. Diabetes Care. 2014;37(10):2864-83.
4. Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. Lancet. 2017;390:1550-62.
5. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2008;29:76-131.
6. Palma CC, Pavesi M, Nogueira VG, et al. Prevalence of thyroid dysfunction in patients with diabetes mellitus. Diabetol Metab Syndr. 2013;5:58.
7. Iglesias P, Diez JJ. Thyroid dysfunction and kidney disease. Eur J Endocrinol. 2009;160:503-15.
8. Chen HS, Wu TE, Jap TS, et al. Subclinical hypothyroidism and diabetic nephropathy. Diabetes Care. 2007;30:1182-4.
9. Furukawa K, Yamashita H, Nakamura K, et al. Thyroid function and albuminuria in T2DM. Endocr J. 2014;61:1011-8.
10. Mansournia N, Riyahi S, Tofangchiha S, et al. Association between SCH and diabetic nephropathy. J Diabetes Metab Disord. 2017;16:43.
11. Tseng FY, Lin WY, Lin CC, et al. SCH and microvascular complications in diabetes. Diabet Med. 2015;32:113-20.
12. Kim BY, Kim CH, Jung CH, et al. Subclinical hypothyroidism and diabetic complications. Endocr J. 2011;58:1067-72.