Section: General Medicine

Original Research Article

STUDY OF PREVALENCE OF DIABETIC NEPHROPATHY IN PATIENTS WITH DIABETES MELLITUS WITH ASSOCIATED HYPOTHYROIDISM

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ABSTRACT

Background: Diabetic nephropathy (DN) is a major microvascular complication of type 2 diabetes mellitus (T2DM) and a leading cause of end-stage renal disease (ESRD). Emerging evidence suggests that hypothyroidism, which commonly coexists with T2DM, may independently contribute to the development and progression of diabetic nephropathy. However, the extent of this association remains underexplored. The objective is to estimate the prevalence of diabetic nephropathy among patients with T2DM and hypothyroidism, and to evaluate whether the severity and duration of hypothyroidism are associated with the presence and stage of nephropathy. **Materials and Methods:** This was a prospective, cross-sectional observational study conducted over one year (2015–2016) in the General Medicine OPD and Diabetic Clinic of R.G. Kar Medical College and Hospital, Kolkata. Ninety adult patients with T2DM and either overt or subclinical hypothyroidism were enrolled. Clinical and biochemical data including HbA1c, thyroid profile, lipid profile, urine ACR, and eGFR were recorded. Diabetic nephropathy was staged using KDIGO criteria. Statistical analyses included Mann–Whitney U test, chi-square test, discriminant function analysis, and Spearman's correlation. **Result:** Out of 90 patients, 47 (52%) had diabetic nephropathy. HbA1c, duration of diabetes, duration of hypothyroidism, systolic blood pressure, TSH, and total cholesterol were significantly higher in the DN group ($p < 0.05$). Discriminant analysis revealed HbA1c as the strongest predictor of nephropathy, followed by total cholesterol and TSH. A significant positive correlation was observed between TSH levels and the stage of CKD ($\rho = 0.369$, $p = 0.000$). **Conclusion:** Diabetic nephropathy is highly prevalent among T2DM patients with hypothyroidism. Elevated TSH and longer duration of hypothyroidism are independently associated with nephropathy severity, underscoring the need for routine thyroid screening in diabetic patients.

INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent chronic metabolic disorders globally, characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. It is associated with long-term damage to various organs, particularly the eyes, kidneys, nerves, heart, and blood vessels.[1] The International Diabetes Federation estimated that 463 million adults were living with diabetes in 2019, and this number is projected to rise to 700 million by 2045, with India contributing significantly to this global burden.[2]

Among the microvascular complications of diabetes, diabetic nephropathy (DN) is one of the most serious and is the leading cause of end-stage renal disease (ESRD) worldwide.[3] It is clinically characterized by persistent albuminuria, a progressive decline in glomerular filtration rate (GFR), and increased blood pressure. Approximately 20%–40% of patients with type 2 diabetes mellitus (T2DM) eventually develop diabetic nephropathy during their lifetime.[4]

Thyroid dysfunction is another common endocrine disorder, and its prevalence is significantly higher among individuals with T2DM compared to the general population.[5] Hypothyroidism—both subclinical and overt—is the most frequent form of thyroid dysfunction seen in diabetic patients.[6] The interplay between thyroid dysfunction and diabetes arises from shared autoimmune, metabolic, and

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hormonal pathways. Thyroid hormones influence glucose metabolism, insulin sensitivity, lipid profiles, and vascular tone—all of which are implicated in the pathogenesis of diabetic complications.[7,8]

Several studies have suggested that hypothyroidism may exacerbate the progression of DN by reducing cardiac output, increasing peripheral vascular resistance, and impairing renal hemodynamics, ultimately leading to reduced renal perfusion and filtration.[9,10] Subclinical hypothyroidism has also been associated with increased urinary albumin excretion and declining eGFR in diabetic individuals.[11]

Despite this plausible link, the association between hypothyroidism and diabetic nephropathy remains underexplored, especially in the Indian context. The present study aims to estimate the prevalence of diabetic nephropathy in patients with T2DM who also have hypothyroidism and to examine whether thyroid dysfunction contributes significantly to the severity of nephropathy.

Objectives

- To determine the prevalence of diabetic nephropathy among patients with type 2 diabetes mellitus (T2DM) attending the Medicine OPD and Diabetic Clinic at R.G. Kar Medical College and Hospital.

MATERIALS AND METHODS

This study was designed as a prospective, non-randomized, non-interventional, cross-sectional observational study, conducted over a period of one year from 2023 to 2024. It was carried out in the General Medicine Outpatient Department (OPD) and Diabetic Clinic of R.G. Kar Medical College and Hospital, Kolkata, a tertiary care teaching hospital. The study population comprised adult patients aged above 18 years, who attended the Medicine OPD and Diabetic Clinic during the study period and met the predefined inclusion criteria. Eligible patients were consecutively enrolled after obtaining informed written consent.

Inclusion Criteria

- Patients diagnosed with type 2 diabetes mellitus (T2DM) as per ADA 2014 criteria:
  - Fasting plasma glucose (FPG) > 126 mg/dL
  - Postprandial glucose (2-hour) > 200 mg/dL
  - Random plasma glucose > 200 mg/dL with symptoms of hyperglycemia
  - HbA1c > 6.5%

Patients with hypothyroidism, categorized as:

  - Subclinical hypothyroidism: TSH 5–10 µIU/mL with normal FT4
  - Overt hypothyroidism: TSH >10 µIU/mL with low FT4
  - Poorly controlled hypothyroidism: On treatment, with TSH >5 µIU/mL

Exclusion Criteria

- Patients unwilling to give informed consent
- Pregnant women
- Patients with Type 1 DM
- Individuals with urinary tract infection, heart failure, severe sepsis
- Presence of other endocrinopathies (e.g., Polyglandular Autoimmune Syndrome)

Sample Size and Sampling

Based on pilot data indicating a 13% prevalence of diabetic nephropathy among diabetics with hypothyroidism, and using the formula:

$$n = \frac{Z^2 \cdot p \cdot q}{e^2} = \frac{(1.96)^2 \cdot 13 \cdot 87}{(7)^2} \approx 89$$

Methodology:

Data were collected using a predesigned and pretested proforma that included relevant clinical and biochemical information. Standard instruments such as a stethoscope, sphygmomanometer, and weighing scale were used for anthropometric and blood pressure measurements. All laboratory investigations were performed in the hospital's central laboratory using standardized procedures.

Prior to data collection, ethical clearance was obtained from the Institutional Ethics Committee and The West Bengal University of Health Sciences. Written informed consent was obtained from each participant using the approved consent form (Annexure-2). The diagnosis of type 2 diabetes mellitus (T2DM) and hypothyroidism was confirmed based on clinical evaluation and relevant laboratory investigations.

Each participant underwent a comprehensive history taking and physical examination, followed by the following laboratory tests: fasting plasma glucose (FPG), postprandial plasma glucose (PPPG), HbA1c, serum TSH, free T4, serum urea, serum creatinine, urine routine examination, urine albumin-creatinine ratio (ACR), and fasting lipid profile. The estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault formula to assess renal function.

RESULTS

After distribution of CKD cases in each age group, it showed only 1 case of CKD present in the 31-40 years age group and highest number of CKD cases was in age group of 61-70 years (18).

Table 1: Distribution of study subjects according to age (n= 90)

Age in years	No	Percentage
31 - 40	8	9
41 - 50	26	29
51 - 60	25	28
61 - 70	23	25

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71 - 80	8	9
Total	90	100

Table 2: Average duration of T2 DM in CKD and non CKD group

Status	Mean	SD	Mean Rank	Sum of Ranks	Mann-Whitney U	p Value
No CKD	4.28	4.22	33.69	1448.50	502.500	0.000
CKD	7.85	5.41	56.31	2646.50		

The difference in average duration of T2DM between patients with and without CKD was statistically significant (p Value < 0.05), i. e. average duration of DM was significantly higher among cases with CKD compared to those without CKD.

Table 3: Average duration of hypothyroidism in CKD and non CKD group

Status	Mean	SD	Mean Rank	Sum of Ranks	Mann-Whitney U	p Value
No CKD	6.35	4.314	35.50	1526.50	580.500	0.000
CKD	10.70	5.834	54.65	2568.50		

The difference in average duration of hypothyroidism between patients with and without CKD was statistically significant (p Value < 0.05), i. e. average duration of hypothyroidism was significantly higher among cases with CKD compared to those without CKD.

Table 4: Average HbA1C in CKD and non CKD group

Status	Mean	SD	Mean Rank	Sum of Ranks	Mann-Whitney U	p Value
No CKD	7.93	1.316	30.07	1293.00	347.000	0.000
CKD	9.85	1.806	59.62	2802.00		

The difference in average HbA1Cbetween patients with and without CKD was statistically significant (p Value < 0.05), i. e. average HbA1C was significantly higher among cases with CKD compared to those without CKD.

Table 5: Average SBP among CKD and non CKD group

Status	Mean	SD	Mean Rank	Sum of Ranks	Mann-Whitney U	p Value
No CKD	157.67	14.77	39.41	1694.50	748.500	0.000
CKD	164.47	14.86	51.07	2400.50		

The difference in average SBP between the patients with and without CKD was statistically significant (p Value < 0.05), i. e. average SBP was significantly higher among cases with CKD compared to those without CKD.

Table 6: Average DBP among CKD and non CKD group

Status	Mean	SD	Mean Rank	Sum of Ranks	Mann-Whitney U	p Value
No CKD	71.23	10.583	42.55	1829.50	883.500	0.283
CKD	73.19	10.856	48.20	2265.50		

Difference in average DBP among patients in both group was not statistically significant (p > 0.05).

Table 7: Distribution of average TSH value among cases with and without CKD

Status	Mean	SD	Mean Rank	Sum of Ranks	Mann-Whitney U	p Value
No CKD	4.58	2.76	35.58	1530.00	584.000	0.001
CKD	7.28	5.25	54.57	2565.00		

The difference in average TSH value between the patients with and without CKD was statistically significant (p Value < 0.05), i.e. average TSH was significantly higher among cases with CKD compared to those without CKD.

Table 8: Distribution of patients with or without CKD according to their status of smoking

Status of smoking	Status of CKD		Total
	No CKD n=43 (47.8%)	CKD n=47 (52.2%)	
Without smoking (n =67)	35 (52.2%)	32 (47.8%)	67 (100%)
With smoking (n=23)	8 (34.8%)	15 (65.2%)	23 (100%)
Total	43 (47.8%)	47 (52.2%)	90 (100%)

X2= 2.091; df = 1; p = 0.148

Difference in proportion of smokers among patients in both the group was not statistically significant (p> 0.05).

Table 9: Distribution of average lipid profile in the form of total cholesterol among patients with and without CKD

Status	Mean	SD	t	df	p
No CKD	201.47	22.627	-2.248	88	0.027
CKD	212.40	23.441			

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The difference in average total cholesterol between patients with and without CKD was statistically significant (p Value < 0.05), i. e. average total cholesterol was significantly higher among cases with CKD compared to those without CKD.

Table 10: Distribution of average LDL among patients with and without CKD

Status	Mean	SD	t	df	p
No CKD	23.280	23.280	-1.706	88	0.091
CKD	21.018	21.018			

The difference in average LDL between patients with and without CKD was not statistically significant (p Value > 0.05).

Table 12: Ranking of Predictor Variables Based on Standardized Canonical Discriminant Function Coefficients

Rank	Predictor variables	Function coefficient
1	HbA1C	0.736
2	Total Cholesterol	0.466
3	TSH	0.326
4	Duration of Hypothyroidism	0.176
5	SBP	0.130
6	Duration of T2DM	0.086

Table 13: Correlation between TSH and Stages of CKD

Spearman's rho correlation co efficient*	0.369
p Value	0.000

* TSH level of Stage IIIa and IV CKDdid not show normal distribution pattern, so Spearman's rho correlation coefficient was applied.

TSH level and different stages of CKD showed a statistically significant (p<0.05) positive correlation.

DISCUSSION

Diabetes mellitus is one of the most prevalent endocrine disorders worldwide, and its burden continues to rise due to sedentary lifestyles, urbanization, and dietary transitions. Among its many complications, diabetic nephropathy (DN) remains a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD).[3] In this study, we observed a 52% prevalence of DN among T2DM patients with hypothyroidism, a figure notably higher than the 30% reported in the CURES 45 study by Unnikrishnan et al,[12] and 42.5% in the study by Abdulhakeem et al.[13] This elevated prevalence may be explained by the setting of a tertiary care hospital, where patients often present with more advanced disease, or may reflect a specific regional burden that merits further investigation.

The demographic profile of the study population showed that 62% were female, which is comparable with findings from the American National Diabetes Study (1995), which also reported a female preponderance.[14] The mean age of the study population was 55.3 years, with most patients (82%) falling in the 41–70 years range. This age distribution aligns with findings from the CDC (2012) and studies by Venkatachalam et al,[15] which also noted earlier onset of T2DM in Asian populations.

A key focus of this study was to examine the association of hypothyroidism with diabetic nephropathy, adjusted for traditional risk factors such as glycemic control, blood pressure, duration of diabetes, lipid profile, and smoking. Our results revealed that patients with DN had significantly higher mean duration of diabetes (7.85 years vs. 4.28 years), a finding consistent with literature indicating that disease duration is a major determinant of nephropathy.[16,17] Similarly, the duration of hypothyroidism was significantly longer in the DN group (10.7 years vs. 6.35 years), supporting the hypothesis that long-standing untreated or sub-optimally treated thyroid dysfunction contributes to renal damage.[18]

Glycemic control, assessed by HbA1c, was markedly worse in the CKD group (mean: 9.85%) compared to the non-CKD group (7.93%), and this difference was statistically significant (p<0.001). This reinforces the role of hyperglycemia in glomerular injury and is consistent with previous studies such as those by Sanjeev Kumar et al.[19] Poor glycemic control leads to increased advanced glycation end-products (AGEs), oxidative stress, and endothelial dysfunction, which in turn accelerate the progression of nephropathy.

Systolic blood pressure (SBP) was also significantly elevated in patients with DN (164.47 mmHg vs. 157.67 mmHg), again confirming its role as a major risk factor for renal impairment. However, diastolic blood pressure (DBP) did not show a significant difference, possibly due to a relatively lower average DBP in this cohort or the limited sample size. This is in contrast to findings by David J. Leehey et al,[20] who reported DBP as a strong independent predictor of DN progression.

A critical finding of our study was the role of thyroid dysfunction. The mean TSH level was significantly higher in patients with nephropathy (7.28 µIU/mL vs. 4.58 µIU/mL), suggesting a direct or indirect influence of hypothyroidism on renal function. The pathophysiological mechanisms may include

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decreased cardiac output, increased peripheral vascular resistance, reduced renal blood flow, and impaired glomerular filtration.[21,22] Furthermore, hypothyroidism may alter lipid metabolism and endothelial function, thereby exacerbating diabetic microangiopathy.

In support of this, our discriminant function analysis ranked HbA1c as the strongest predictor of DN (coefficient: 0.736), followed by total cholesterol (0.466) and TSH (0.326). Interestingly, TSH and duration of hypothyroidism ranked higher than SBP and duration of diabetes, highlighting the potential under-recognized impact of thyroid dysfunction on kidney health in diabetic patients.

Finally, a significant positive correlation was observed between TSH levels and stages of nephropathy (Spearman's $\rho = 0.369$; $p = 0.000$), suggesting that increasing TSH levels are associated with more advanced stages of CKD. This finding aligns with the large cohort study published in Nephrology Dialysis Transplantation, which found that lower eGFR was significantly associated with higher TSH values and an increased risk of hypothyroidism.[23]

CONCLUSION

Diabetic nephropathy was found in over half of the T2DM patients with hypothyroidism in this study. Poor glycemic control, prolonged diabetes, and elevated TSH levels were significantly associated with nephropathy. Notably, hypothyroidism emerged as an independent risk factor, with TSH showing a positive correlation with CKD stage. These findings highlight the importance of routine thyroid screening in diabetic patients to aid in early detection and prevention of kidney complications.

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