

Relationship between Serum Thyrotropin and Urine Albumin Excretion in Euthyroid Subjects with Diabetes

¹Rajeev Ranjan Kumar, Ex Senior Resident, Department of Medicine, All India Institute of Medical Sciences, Patna, Bihar, India

²Jyoti Prakash, Professor & HOD, Department of Medicine, All India Institute of Medical Sciences, Patna, Bihar, India

Corresponding author: Jyoti Prakash, Professor & HOD, Department of Medicine, All India Institute of Medical Sciences, Patna, Bihar, India

Abstract

Increased urine albumin excretion (UAE) is a typical sign of diabetic nephropathy. This study examined UAE and serum thyrotropin (TSH) levels in euthyroid diabetics. Even after controlling for age, gender, BMI, blood pressure, duration of diabetes, HbA1c, and lipid profile, serum TSH levels were positively correlated with UAE in a cross-sectional analysis of 200 euthyroid patients with type 1 and type 2 diabetes. The connection was strongest among type 2 diabetics. These data imply that serum TSH levels, even within the normal range, may contribute to diabetic kidney disease pathogenesis and highlight the need for future research to understand this association and its therapeutic consequences.

Keywords: Diabetic nephropathy, Thyrotropin, Urine albumin excretion, Euthyroid.

Introduction

In the context of chronic metabolic disorders, diabetes mellitus is distinguished by the presence of high blood glucose levels, which can give rise to a range of microvascular consequences, such as diabetic nephropathy [1,2]. The primary cause of end-stage renal disease is diabetic nephropathy, which is commonly characterized by elevated urine albumin excretion (UAE), serving as an early indication of renal impairment [3,4]. It is essential to identify the elements that contribute to higher urinary uric acid levels in diabetic individuals to prevent the advancement of renal disease [5]. Thyrotropin, or thyroid-stimulating hormone (TSH), is a hormone synthesized by the pituitary gland that controls thyroid activity and is essential for

preserving equilibrium in metabolism [6]. While thyroid diseases are principally linked to TSH levels, current research indicates that TSH may also influence metabolic processes outside thyroid function, especially in individuals with diabetes [7]. In euthyroid individuals, who have normal thyroid function, thyroid-stimulating hormone (TSH) levels persist within the normal range and may be linked to metabolic alterations in the body, such as renal function [8].

An investigation into the correlation between serum thyrotropin levels and urine albumin excretion in euthyroid individuals with diabetes may offer valuable understanding of the underlying mechanisms of diabetic nephropathy and maybe reveal new biomarkers for the early identification and treatment of kidney disease in diabetic patients. The objective of this study is to examine the correlation between serum TSH levels and UAE in euthyroid diabetic patients in order to gain a deeper understanding of the potential interaction and contribution of these variables to the advancement of renal problems in diabetes.

Methodology

Diabetes patients at a tertiary care hospital's endocrine clinic were studied in this cross-sectional study. We included euthyroid adults 18 and older with type 1 or 2 diabetes. Normal serum thyrotropin (TSH) and free thyroxine (FT4) values confirmed euthyroid condition. Patients with thyroid problems, thyroid medicines, or acute or chronic renal failure unrelated to diabetes were excluded from the study.

Data Collection

Patient records and interviews included demographics, medical history, and medications. Weight, height, and BMI were measured. After 5 minutes of rest, a typical sphygmomanometer assessed blood pressure.

Laboratory Measurements

All participants gave fasting blood samples for TSH, FT4, glucose, HbA1c, creatinine, and lipid profile. TSH and FT4 were measured by chemiluminescent immunoassay. Urine albumin and creatinine were measured. Urine albumin excretion (UAE) was measured by measuring

the spot urine albumin-to-creatinine ratio (ACR). Clinical guidelines defined UAE as normal, microalbuminuria, and macroalbuminuria.

Statistical Analysis

Analytics were done with statistical software. Continuous variables were provided as mean \pm SD or median with IQR, whereas categorical variables were presented as frequencies and percentages. The relationship between blood TSH levels and urine albumin excretion was examined using Pearson or Spearman correlation coefficients, depending on data normality. Multiple linear regression was used to control for age, gender, BMI, blood pressure, diabetes duration, HbA1c, and lipid profile. A p-value under 0.05 was significant.

Results

The study included 200 euthyroid diabetic patients: 110 men (55%) and 90 women (45%). Individuals had a mean age of 54.2 ± 10.3 years and a median duration of diabetes of 8.5 years (IQR: 4-12 years). The participants had a mean BMI of 28.1 ± 4.5 kg/m². 65% of patients had type 2 diabetes, while 35% had type 1. All patients were diagnosed with euthyroid disease due to their normal blood TSH levels (2.3 ± 0.8 mIU/L) and free T4 (FT4) levels (1.3 ± 0.2 ng/dL). The average HbA1c level was $8.1\% \pm 1.5\%$, indicating poor glycaemic management in most individuals. The median albumin-to-creatinine ratio (ACR) was 30 mg/g, with an IQR of 12-55 mg/g.

A significant positive connection ($r = 0.35$, $p < 0.001$) was seen between blood TSH levels and urine albumin excretion (UAE) as evaluated by ACR. These findings suggest that diabetics with normal thyroid function had higher serum TSH levels and higher UAE. After controlling for potential confounding factors such age, gender, BMI, blood pressure, diabetes duration, HbA1c, and lipid profile, the multivariable regression analysis showed a significant correlation between serum TSH levels and UAE ($\beta = 0.27$, $p = 0.002$). We also found that blood TSH levels are independently connected to higher UAE in euthyroid diabetics, even after controlling for other risk factors.

A deeper analysis showed a greater association between serum TSH levels and UAE in type 2 diabetic patients compared to type 1 patients ($r = 0.41$, $p < 0.001$ vs. $r = 0.21$, $p = 0.045$). Patients with microalbuminuria or macroalbuminuria exhibited significantly higher serum TSH levels than those with normal albumin outflow (2.7 ± 0.9 mIU/L vs. 1.9 ± 0.6 mIU/L, $p < 0.001$). This study found a strong association between blood TSH and urine albumin excretion in euthyroid diabetics. This relationship was unrelated to other risk variables for diabetic nephropathy, suggesting TSH may be involved in its development. This linkage highlights the need for greater research into its processes and clinical effects.

Variable	Overall (n = 200)	Type 1 Diabetes (n = 70)	Type 2 Diabetes (n = 130)
Age (years)	54.2 \pm 10.3	48.7 \pm 9.2	57.5 \pm 8.4
Gender (Male, n [%])	110 (55%)	30 (42.9%)	80 (61.5%)
BMI (kg/m ²)	28.1 \pm 4.5	27.4 \pm 4.0	28.5 \pm 4.7
Duration of Diabetes (years)	8.5 (4-12)	12 (7-15)	6 (3-10)
HbA1c (%)	8.1 \pm 1.5	8.4 \pm 1.3	7.9 \pm 1.6
Serum TSH (mIU/L)	2.3 \pm 0.8	2.1 \pm 0.7	2.5 \pm 0.9
Free T4 (ng/dL)	1.3 \pm 0.2	1.4 \pm 0.2	1.3 \pm 0.2
ACR (mg/g)	30 (12-55)	22 (10-45)	38 (18-65)
Correlation (TSH vs. UAE, r)	0.35 ($p < 0.001$)	0.21 ($p = 0.045$)	0.41 ($p < 0.001$)

Table Notes: • Age, BMI, HbA1c, Serum TSH, and Free T4 are shown as mean \pm SD.

• Diabetes and ACR durations are shown as median with IQR.

• The Pearson correlation coefficients (r) between blood TSH levels and urine albumin excretion (UAE) are shown, with matching p-values indicating statistical significance.

This table shows the demographic, clinical, and biochemical features of research participants and the correlations between blood TSH levels and UAE in type 1 and type 2 diabetics.

Discussion

This study examined the relationship between serum thyrotropin (TSH) and urine albumin excretion (UAE) in euthyroid diabetes. Our results show a strong association between serum

TSH levels and UAE, suggesting that even those with adequate thyroid function have higher UAE [9]. This link remained significant after controlling for age, gender, BMI, blood pressure, diabetes duration, HbA1c, and lipid profile, which affect kidney function [10]. This implies that TSH may cause diabetic nephropathy independently. The connection between thyroid-stimulating hormone (TSH) and uric acid (UAE) is stronger in type 2 diabetics than in type 1 [11]. This may be due to differences in the pathophysiological processes that cause renal impairment in type 1 and type 2 diabetes, or to insulin resistance and its effects on thyroid function and renal health. These findings support previous research linking thyroid function to kidney health, even at normal thyroid levels. TSH may affect kidney function in diabetics by directly manipulating renal hemodynamics, glomerular filtration, or inflammation [12,13].

Our study adds to the growing body of evidence linking thyroid hormones, particularly TSH, to diabetic kidney damage [14]. Due to the rising prevalence of diabetes and its complications, understanding renal impairment's causes is crucial to developing better preventative and treatment methods [15]. Even with normal thyroid function, diabetic patients may benefit from regular thyroid function testing, particularly TSH levels, to identify those at risk of nephropathy. However, this study has limitations. We cannot prove a causal link between UAE exposure and TSH levels due to the cross-sectional methodology [16]. A longitudinal study is needed to validate these findings and investigate relevant explanations. The study sample was small and largely consisted of patients from one tertiary care hospital, limiting its usefulness. Future research should involve larger and more diverse individuals to confirm these findings and investigate the clinical effects of TSH levels in diabetic renal disease treatment [17,18]. Our investigation found that diabetic patients with normal thyroid function have a significant association between blood TSH levels and urine albumin excretion. This suggests that TSH may contribute significantly to diabetic nephropathy. The results highlight the need for greater research to understand the processes and assess the feasibility of monitoring TSH levels in diabetics to detect and treat kidney issues early [19,20].

Conclusion

This study found a substantial connection between blood thyrotropin (TSH) levels and urine albumin excretion (UAE) in euthyroid diabetics, suggesting that even normal TSH levels

increase kidney injury risk. These data suggest that TSH may independently contribute to diabetic nephropathy, emphasizing the relevance of thyroid function in diabetes care. Longitudinal studies are needed to validate these findings and investigate how TSH affects kidney health in diabetics, which could improve early detection and prevention measures.

References

1. American Diabetes Association. Standards of medical care in diabetes—2020 abridged for primary care providers. *Clin Diabetes*. 2020;38(1):10–38.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int*. 2020;98(4S):S1–115.
3. Dinneen SF, Gerstein HC. The association of microalbuminuria and mortality in non-insulin-dependent diabetes mellitus: A systematic overview of the literature. *Arch Intern Med*. 1997;157(13):1413–1418.
4. Rodacki M, Maia AL, Ward LS, Graf H. Serum TSH levels in type 2 diabetes patients with normal thyroid function: A potential risk marker for nephropathy? *Braz J Med Biol Res*. 2006;39(3):349–355.
5. Brenta G, Danzi S, Klein I. Potential therapeutic applications of thyroid hormone analogs. *Nat Clin Pract Endocrinol Metab*. 2007;3(9):632–640.
6. Cooper DS, Biondi B. Subclinical thyroid disease. *Lancet*. 2012;379(9821):1142–1154.
7. Ittermann T, Khattak RM, Nauck M, Cordova CM, Volzke H. Shift of the TSH reference range with improved iodine supply in Northeast Germany. *Eur J Endocrinol*. 2015;172(3):273–280.
8. Duntas LH, Brenta G. The effect of thyroid disorders on lipid levels and metabolism. *Med Clin North Am*. 2012;96(2):269–281.
9. Ito S, Taniyama M, Omori K, Hiraiwa T, Ueki I, Sudo T, et al. Metabolic impact of plasma adiponectin in subclinical hypothyroidism. *Endocr J*. 2009;56(6):927–934.

10. Singh P, Kalra S. Thyroid disorders and diabetes mellitus: Double trouble. *J Pak Med Assoc.* 2016;66(12):1613–1617.
11. Kim BY, Won JC, Lee JH, Kim HK, Park JH, Ha KH, et al. Serum TSH level in type 2 diabetic patients is related to fasting and postprandial triglyceride levels but not to other cardiovascular risk factors. *Diabetes Care.* 2010;33(3):566–568.
12. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. *Endocr Rev.* 2008;29(1):76–131.
13. Jublanc C, Beaussier H, Bruckert E, Chadarevian R, Giral P, Turpin G. Sequential relationship between thyroid hormones, insulin sensitivity, and insulin secretion in euthyroid males. *Metabolism.* 2007;56(11):1487–1491.
14. Chubb SA, Davis WA, Davis TM. Interactions among thyroid function, insulin sensitivity, and serum lipid concentrations: The Fremantle Diabetes Study. *J Clin Endocrinol Metab.* 2005;90(9):5317–5320.
15. González Rodríguez S, De Marco S, Madrid E, Soto A, Sánchez I, Macías RM, et al. Risk factors associated with chronic kidney disease in patients with type 2 diabetes. *Kidney Blood Press Res.* 2019;44(6):1212–1226.
16. Maratou E, Hadjidakis DJ, Kollias A, Tsegka K, Peppas M, Alevizaki M, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. *Eur J Endocrinol.* 2009;160(5):785–790.
17. Duntas LH. Thyroid disease and lipids. *Thyroid.* 2002;12(4):287–293.
18. Chubb SA, Davis WA, Inman Z, Davis TM. Prevalence and progression of chronic kidney disease in women with type 1 diabetes: The Fremantle Diabetes Study. *Diabet Med.* 2014;31(10):1165–1171.
19. Chen HS, Wu TE, Jap TS, Lu RA, Wang ML, Chen RL, et al. Subclinical hypothyroidism is a risk factor for nephropathy and cardiovascular diseases in type 2 diabetic patients. *Diabet Med.* 2007;24(12):1336–1344.

20. Zhang Y, Chang Y, Ryu S, Cho J, Lee WY, Rhee EJ, et al. Thyroid hormones and mortality risk in euthyroid individuals: The Kangbuk Samsung Health Study. *J Clin Endocrinol Metab.* 2014;99(7):2467–2476.