e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(4); 705-709

Original Research Article

Relationship between Microalbuminuria and Free Thyroid Hormone and Thyroid Stimulating Hormone in Euthyroid Patients with Type 2 Diabetes Mellitus

Archana Bharti[1], Pritam Prakash[2], Sweta Kumari[3], Poonam Sinha[4]

[1]Assistant Professor, Department of Biochemistry, I.G.I.M.S., Patna, Bihar, India
[2]Additional Professor, Department of Biochemistry, I.G.I.M.S., Patna, Bihar, India
[3]Associate Professor, Department of Biochemistry, I.G.I.M.S., Patna, Bihar, India
[4]Senior Resident, Department of Biochemistry, I.G.I.M.S., Patna, Bihar, India

Received: 25-01-2024 / Revised: 23-02-2024 / Accepted: 25-03-2024
Corresponding Author: Dr. Poonam Sinha
Conflict of interest: Nil

Abstract:

Background: The study seek to investigate the potential relationship between Thyroid Stimulating Hormone (TSH) and Free Thyroxine (T4) levels with the presence of microalbuminuria in Euthyroid patients diagnosed with Type 2 Diabetes Mellitus (T2DM).

Methods: 500 participants with T2DM who were euthyroid were enlisted. Information was gathered on medical history, thyroid function tests, microalbuminuria, and demographic traits. Measurements of height, weight, blood pressure, and an assessment of diabetic complications were all part of the clinical examination. The laboratory testing included lipid profile, HbA1c, fasting blood glucose, thyroid function tests, microalbuminuria assessment, and renal function tests. SPSS version 16.0 was used for the statistical analysis, which included logistic regression analysis and descriptive statistics.

Results: Demographic analysis revealed a mean age of 56.7 ± 8.4 years, with 60% male participants. Participants with microalbuminuria displayed significantly higher TSH levels (3.5 ± 1.4 mIU/L) and lower Free T4 levels (1.0 ± 0.2 ng/dL) compared to those without microalbuminuria. Logistic regression analysis adjusted for confounding factors demonstrated independent associations between TSH and Free T4 levels with microalbuminuria. Elevated TSH levels were related with increased microalbuminuria risk (OR = 1.45, 95% CI = 1.20-1.75), while lower Free T4 levels correlated with higher microalbuminuria risk (OR = 0.62, 95% CI = 0.48-0.80).

Conclusion: The study suggests a significant association between thyroid function, specifically TSH and Free T4 levels, and microalbuminuria in Euthyroid patients with T2DM. Elevated TSH levels and lower Free T4 levels were independently related with elevated microalbuminuria risk, highlighting the potential role of thyroid hormones in the pathogenesis of diabetic kidney disease.

Recommendations: To clarify underlying mechanisms and investigate clinical implications, more research is necessary. Screening for thyroid dysfunction may be beneficial in the management of diabetic patients to mitigate the risk of microalbuminuria and diabetic kidney disease.

Keywords: Thyroid function, microalbuminuria, Type 2 Diabetes Mellitus, Euthyroid, cross-sectional study.

Introduction

Thyroid function, particularly the levels of thyroid hormones like free thyroxine (FT4) and thyroid-stimulating hormone (TSH), is crucial in managing health conditions such as Type 2 Diabetes Mellitus (T2DM). A growing body of research has explored the correlation between thyroid hormone levels and microalbuminuria in euthyroid patients with T2DM, revealing significant associations that could impact disease management and outcomes [1].

In euthyroid subjects with T2DM, several studies have identified a relationship between TSH and FT4 levels and the presence of microalbuminuria. One study highlighted that higher TSH levels and lower FT4 levels are often related with an elevated risk of developing microalbuminuria, suggesting a potential thyroid involvement in renal function in diabetic populations [2]. Further supporting this, another study found that alterations in FT3 and FT4 levels could serve as significant predictors for microvascular complications, including nephropathy in these patients [3].

The connection between these thyroid parameters and kidney health is hypothesized to stem from the thyroid hormones' effects on renal and vascular endothelial function, which are crucial in maintaining renal integrity and function. Additional

research has shown that in a study involving euthyroid patients, higher serum TSH levels were related with higher prevalence of microalbuminuria, suggesting that even within the normal range, variations in TSH levels can influence renal outcomes [4].

Monitoring and potentially managing thyroid hormone levels could be a strategic component of comprehensive care in euthyroid patients with T2DM, especially those at risk or already showing signs of microalbuminuria. These findings underscore the need for further research to explore the underlying mechanisms and to confirm the clinical benefits of monitoring thyroid function in this patient population. This could ultimately lead to more targeted therapies that address not only glycemic control but also the broader endocrine interactions within the body, enhancing the quality of care for patients with T2DM.

The purpose of the study was to look into any possible correlation between microalbuminuria and levels of free T4 and TSH in euthyroid patients who had been diagnosed with T2DM.

Methodology

Study Design: A cross-sectional design.

Study Setting: The study was conducted at the Department of Biochemistry, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India. The study duration spanned from October 2022 to October 2023.

Participants: A total of 500 participants were involved for the study.

Inclusion Criteria:

1. diagnosed with T2DM.

2. categorized as Euthyroid based on thyroid function tests.

3. Age ≥ 18 years.

Exclusion Criteria:

1. with a history of thyroid disorders or on thyroid medication.

2. with acute or chronic kidney disease.

3. Pregnant or lactating women.

4. with any acute illness or infection.

Bias: Efforts were made to minimize bias by ensuring strict adherence to the inclusion and exclusion criteria, and by employing standardized procedures for data collection and analysis.

Variables: Variables included TSH levels, free T4 levels, presence of microalbuminuria.

Data Collection: Data on demographic characteristics, medical history, thyroid function tests, and presence of microalbuminuria were collected through face-to-face interviews, medical records review, and laboratory investigations.

Clinical Examination:

- Height and weight measurement to calculate body mass index (BMI).

- Blood pressure measurement.

- Assessment of diabetic complications, including neuropathy, retinopathy, and peripheral vascular disease.

- Assessment of thyroid gland for any palpable abnormalities.

Laboratory Measurements:

Thyroid Function Tests:

- Thyroid Stimulating Hormone (TSH) levels: Serum samples were collected and analyzed using chemiluminescence immunoassay (CLIA).

- Free Thyroxine (T4) levels: Serum samples were collected and analyzed using ELISA or CLIA.

Assessment of Microalbuminuria:

- Urine samples were collected and analyzed for albumin concentration using quantitative methods such as immunoturbidimetry.

- Microalbuminuria was defined as urinary albumin excretion rate of 30-300 mg/24 hours or albumin-to-creatinine ratio (ACR) of 30-300 mg/g.

Other Laboratory Measurements:

- Fasting blood glucose levels: Serum glucose levels were measured using hexokinase methods.

- Glycated Hemoglobin (HbA1c) levels: Blood samples were collected and analyzed using high-performance liquid chromatography (HPLC) or immunoassay methods.

- Lipid profile: Enzymatic techniques were used to quantify serum lipid levels, including triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol.

- Renal function tests: Serum creatinine levels were measured using kinetic Jaffe's method or enzymatic methods, and estimated glomerular filtration rate (eGFR) was calculated using appropriate formulas.

Test for Thyroid Function: Thyroid function tests included the measurement of TSH and Free T4 levels in serum samples. TSH levels were assessed using CLIA, while Free T4 levels were measured using similar methods. These tests were performed to determine the thyroid status of participants and to confirm euthyroidism.

Statistical Analysis: Statistical analysis was performed using SPSS version 16.0. The association between TSH, Free T4 levels, and microalbuminuria was analyzed using appropriate statistical tests, including regression analysis, with significance set at $p < 0.05$.

Result

Table 1: Demographic features of study population

Characteristic	Mean ± SD / n (%)
Age (years)	56.7 ± 8.4
Gender	
- Male	300 (60%)
- Female	200 (40%)
Duration of Diabetes	7.2 ± 3.5 years
BMI (kg/m²)	28.4 ± 4.2

The study involved a total of 500 patients diagnosed with T2DM, aiming to investigate the correlation among thyroid function and microalbuminuria in Euthyroid individuals. Demographic analysis revealed a mean age of 56.7 ± 8.4 years, with a predominance of male participants (60%). The average period of diabetes was 7.2 ± 3.5 years, and the average BMI stood at 28.4 ± 4.2 kg/m², reflecting a typical profile of diabetic patients in the study population.

Table 2: Thyroid Function Parameters and Microalbuminuria

Parameter	Microalbuminuria Present	Microalbuminuria Absent	p-value
TSH (mIU/L)	3.5 ± 1.4	2.6 ± 1.1	<0.001
Free T4 (ng/dL)	1.0 ± 0.2	1.3 ± 0.3	<0.001

Thyroid function assessment indicated a mean TSH level of 2.8 ± 1.2 mIU/L and a mean Free T4 level of 1.2 ± 0.3 ng/dL. Notably, 30% of participants exhibited microalbuminuria. Upon comparing participants with and without microalbuminuria, significant differences emerged. Those with microalbuminuria displayed higher mean TSH levels (3.5 ± 1.4 mIU/L vs. 2.6 ± 1.1 mIU/L, $p < 0.001$) and lower mean Free T4 levels (1.0 ± 0.2 ng/dL vs. 1.3 ± 0.3 ng/dL, $p < 0.001$).

Table 3: Logistic Regression Analysis for Relationship Between Thyroid Function and Microalbuminuria

Parameter	Odds Ratio (OR)	95% CI	p-value
TSH	1.45	1.20-1.75	<0.001
Free T4	0.62	0.48-0.80	<0.001

Regression analysis, adjusted for age, gender, diabetes duration, and BMI, elucidated independent associations between thyroid function parameters and microalbuminuria. Elevated TSH levels were linked with a heightened risk of microalbuminuria (OR = 1.45, 95% CI = 1.20-1.75, $p < 0.001$), while lower Free T4 levels correlated with increased microalbuminuria risk (OR = 0.62, 95% CI = 0.48-0.80, $p < 0.001$), underlining the potential influence of thyroid hormones on diabetic kidney disease pathogenesis.

Table 4: Clinical and Laboratory Parameters in Participants with and without Microalbuminuria

Parameter	Microalbuminuria Present	Microalbuminuria Absent	p-value
Fasting Blood Glucose (mg/dL)	156.4 ± 32.1	130.2 ± 25.6	<0.001
HbA1c (%)	8.2 ± 1.1	7.5 ± 0.9	<0.05

Further examination of clinical and laboratory parameters unveiled additional insights. Participants with microalbuminuria exhibited significantly increased fasting blood glucose levels (156.4 ± 32.1 mg/dL vs. 130.2 ± 25.6 mg/dL, $p < 0.001$) and HbA1c levels (8.2 ± 1.1% vs. 7.5 ± 0.9%, $p < 0.05$) compared to those without microalbuminuria. However, lipid profile parameters and renal function tests did not vary significantly between the two groups.

Discussion

The study investigated the relationship between thyroid function, specifically TSH and Free T4 levels, and microalbuminuria in Euthyroid individuals with T2DM. Demographic analysis of the study population, consisting of 500 participants, revealed a typical profile of diabetic patients, with an average age of 56.7 years, a male predominance (60%), an average duration of diabetes of 7.2 years, and an average BMI of 28.4 kg/m².

Thyroid function assessment demonstrated a mean TSH level of 2.8 mIU/L and a mean Free T4 level of 1.2 ng/dL. Notably, 30% of participants exhibited microalbuminuria. Comparison between participants with and without microalbuminuria revealed significant differences. Those with microalbuminuria showed higher mean TSH levels (3.5 mIU/L vs. 2.6 mIU/L) and lower mean Free T4 levels (1.0 ng/dL vs. 1.3 ng/dL), indicating a potential association between thyroid function and microalbuminuria.

Further analysis using logistic regression, adjusted for relevant factors such as age, gender, diabetes duration, and BMI, confirmed independent associations between thyroid function parameters and microalbuminuria. Elevated TSH levels were correlated with an elevated risk of microalbuminuria, while lower Free T4 levels were linked with a higher risk of microalbuminuria. These findings suggest a potential role of thyroid hormones in the pathogenesis of diabetic kidney disease.

Additionally, examination of clinical and laboratory parameters revealed that participants with microalbuminuria had significantly higher fasting blood glucose levels and HbA1c levels compared to those without microalbuminuria. However, lipid profile parameters and renal function tests did not show significant variations between the two groups, suggesting that the correlation between thyroid function and microalbuminuria may not be confounded by these factors.

The findings underscore the significant correlation between thyroid function and microalbuminuria in Euthyroid individuals with T2DM. Higher TSH levels and lower Free T4 levels were identified as independent risk factors for microalbuminuria, suggesting potential implications for the management and understanding of diabetic kidney disease.

The relation between thyroid function and microalbuminuria in euthyroid patients with T2DM has been studied extensively, with significant findings indicating that even within the euthyroid range, thyroid hormone levels can have important clinical implications.In a well-known study, Wang et al. (2019) investigated the connection between euthyroid T2DM patients' thyroid hormone levels and diabetic nephropathy. Their cross-sectional investigation revealed, with statistical significance ($P<0.05$), that patients with diabetic nephropathy had lower serum levels of FT3 and FT4 and higher serum TSH levels than those without nephropathy. Both FT3 and FT4 levels were inversely connected with diabetic nephropathy, according to odds ratios adjusted for traditional risk variables (FT3 per-SD increase: OR 0.606 [95% CI, 0.481–0.762], $P<0.001$; FT4 per-SD increase: OR 0.944 [95% CI, 0.894–0.998], $P=0.040$). On the other hand, a positive correlation was found between the presence of diabetic nephropathy and serum TSH levels (per-SD increase: OR 1.179 [95% CI, 1.033–1.346], $P=0.015$) [5].

Hu et al. (2022) further expanded on these findings by examining the incidence of different microvascular complications and their relationship with thyroid hormones. Their study found significant odds ratios for FT3 and FT4 in the development of microangiopathies, including diabetic nephropathy (DN) and other conditions, highlighting the negative association of FT3 and FT4 with these complications and the positive association of TSH with diabetic peripheral neuropathy (DPN) [6].

In a similar vein, El-Eshmawy et al. (2013) examined the role of subclinical hypothyroidism in microalbuminuria among prediabetic Egyptian adults. Their findings suggested that subclinical hypothyroidism was significantly related with a higher prevalence of microalbuminuria, independent of confounding variables such as insulin resistance and lipid profiles ($\beta=2.59$; $P=0.01$). This study underscored the potential benefits of screening and treating subclinical hypothyroidism to prevent microalbuminuria in prediabetic populations [7].

Aljabri et al. (2019) found that in a Saudi community hospital, euthyroid T2DM patients with severely elevated albuminuria had significantly higher TSH and lower FT4 levels compared to those with normal or moderately increased albuminuria ($P=0.02$ for TSH; $P=0.045$ for FT4). This study provided further evidence supporting the correlation between thyroid function and renal outcomes in diabetic patients [8].

Conclusion

The study provides evidence for an independent relation between thyroid function, specifically TSH and Free T4 levels, and microalbuminuria in Euthyroid individuals with T2DM. These findings highlight the potential importance of thyroid hormones in the development and progression of diabetic kidney disease and may have implications for its management and treatment strategies.

Limitations: The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: To clarify underlying mechanisms and investigate clinical implications, more research is necessary. Screening for thyroid dysfunction may be beneficial in the management of diabetic patients to mitigate the risk of microalbuminuria and diabetic kidney disease.

Acknowledgement: We are thankful to the patients; without them the study could not have been done. We are thankful to the supporting staff of our hospital who were involved in patient care of the study group.

List of abbreviations:

TSH: Thyroid Stimulating Hormone

T4: Thyroxine

T2DM: Type 2 Diabetes Mellitus

BMI: Body Mass Index

HbA1c: Glycated Hemoglobin

ELISA: Enzyme-Linked Immunosorbent Assay

CLIA: Chemiluminescence Immunoassay

FT3: Free Triiodothyronine

OR: Odds Ratio

CI: Confidence Interval

mg/dL: Milligrams per deciliter

eGFR: Estimated Glomerular Filtration Rate

HPLC: High-Performance Liquid Chromatography

LDL: Low-Density Lipoprotein

HDL: High-Density Lipoprotein

ACR: Albumin-to-Creatinine Ratio

Source of funding: No funding received.

References

1. Shimizu, Y., Nabeshima-Kimura, Y., Kawashiri, S., Noguchi, Y., Minami, S., Nagata, Y., Maeda, T., & Hayashida, N. Association between thyroid-stimulating hormone (TSH) and proteinuria in relation to thyroid cyst in a euthyroid general population. Journal of Physiological Anthropology, 2021;40.
2. Yasuda, T., Kaneto, H., Kuroda, A., Yamamoto, T., Takahara, M., Naka, T., Miyashita, K., Fujisawa, K., Sakamoto, F., Katakami, N., Matsuoka, T., & Shimomura, I. Subclinical hypothyroidism is independently associated with albuminuria in people with type 2 diabetes. Diabetes research and clinical practice,2011; 943:e75-7.
3. Wang, Y., Lu, J., Ni, J., Wang, M., Shen, Y., Lu, W., Zhu, W., Bao, Y., & Zhou, J. Association of thyroid stimulating hormone and time in range with risk of diabetic retinopathy in euthyroid type 2 diabetes. Diabetes/Metabolism Research and Reviews, 2023;39.
4. Yang, J., Ding, W., Wang, H., & Shi, Y. Association Between Sensitivity to Thyroid Hormone Indices and Diabetic Retinopathy in Euthyroid Patients with Type 2 Diabetes Mellitus. Diabetes, Metabolic Syndrome and Obesity, 2023;16: 535 - 545.
5. Wang, J., Li, H., Tan, M., Gao, G., Zhang, Y., Ding, B., Su, X., Kong, X., & Ma, J. Association between thyroid function and diabetic nephropathy in euthyroid subjects with type 2 diabetes mellitus: a cross-sectional study in China. Oncotarget, 2019;10: 88 - 97.
6. Hu, Y., Hu, Z., Tang, W., Liu, W., Wu, X., & Pan, C. Association of Thyroid Hormone Levels with Microvascular Complications in Euthyroid Type 2 Diabetes Mellitus Patients. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 2022; 15: 2467 - 2477.
7. El-Eshmawy, M., El-Hafez, H., Shabrawy, W., & Aal, I. Subclinical Hypothyroidism Is Independently Associated with Microalbuminuria in a Cohort of Prediabetic Egyptian Adults. Diabetes & Metabolism Journal, 2013; 37: 450-457.
8. Aljabri, K., Alnasser, I., Facharatz, F., Bokhari, S., Alshareef, M., Khan, P., Mallosho, A., Abuelsaoud, H., Jalal, M., Safwat, R., Boraie, R., Aljabri, N., Aljabri, B., Alsuraihi, A., & Hawsawi, A. Association of Serum Thyroid Stimulating Hormone and Free Thyroxine with Urinary Albumin Excretion in Euthyroid Subjects with Type 2 Diabetes Mellitus. International Journal of Diabetes and Clinical Research. 2019.