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Original Research Article

Plasma Thyroid Hormone Concentration is Associated with Hepatic Triglyceride Content in Patients with Type 2 Diabetes

Prabhakar[1], Rahul Anand[2], Sumbul Kazmi[3]

[1]Senior Resident, Department of Emergency Medicine, Patna Medical College and Hospital, Patna, Bihar, India

[2]Senior Resident, Department of General Medicine, Patna Medical College and Hospital, Patna, Bihar, India

[3]Senior Resident, Department of Emergency Medicine, Patna Medical College and Hospital, Patna, Bihar, India

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Corresponding Author: Prabhakar

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Abstract:

Background: Type 2 diabetes mellitus (T2DM) is frequently associated with non-alcoholic fatty liver disease (NAFLD), in which hepatic triglyceride accumulation plays a central pathogenic role. Thyroid hormones regulate lipid oxidation and hepatic metabolism, and subtle alterations in thyroid function may contribute to hepatic steatosis in diabetic patients. This study aimed to evaluate the association between plasma thyroid hormone concentrations and hepatic triglyceride content in patients with T2DM.

Methods: This retrospective observational study included 106 adults with T2DM who attended Patna Medical College and Hospital between November 2023 and July 2024. Demographic data, thyroid hormone profile (TSH, FT3, FT4), biochemical markers, and imaging-based hepatic steatosis grades were collected from medical records. Statistical analyses included correlation tests and group comparisons using ANOVA or non-parametric equivalents, with $p < 0.05$ considered significant.

Results: Hepatic steatosis was present in 79.2% of patients. FT3 levels declined progressively with steatosis severity ($p < 0.05$), while TSH levels increased significantly across grades ($p < 0.01$). FT4 showed no significant variation. FT3 exhibited a significant negative correlation with hepatic triglyceride content ($r = –0.42$, $p = 0.002$), whereas TSH demonstrated a positive correlation ($r = 0.48$, $p < 0.001$). BMI, triglycerides, and ALT also increased significantly with worsening steatosis.

Conclusion: Lower FT3 levels and higher TSH concentrations are significantly associated with increased hepatic triglyceride accumulation in T2DM. These findings highlight the importance of evaluating subtle thyroid dysfunction in diabetic patients as part of metabolic risk assessment for NAFLD.

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, impaired insulin secretion, and progressive β-cell dysfunction, and it continues to rise globally as a major public health concern. The International Diabetes Federation estimates that more than 530 million adults are currently living with diabetes, with projections approaching 643 million by 2030, reflecting a significant burden of cardiometabolic complications and health-care utilization worldwide [1]. Among the various complications associated with T2DM, non-alcoholic fatty liver disease (NAFLD) has emerged as one of the most prevalent hepatic manifestations, occurring in nearly 60–70% of patients with diabetes [2,3]. Hepatic triglyceride accumulation, a hallmark of NAFLD, plays a central role in the development of insulin resistance and contributes to the progression from simple steatosis to non-alcoholic steatohepatitis (NASH) and cirrhosis [4].

Thyroid hormones have pivotal regulatory effects on lipid metabolism, hepatic mitochondrial function, and energy homeostasis. Experimental and clinical studies have demonstrated that thyroxine (T4) and triiodothyronine (T3) influence hepatic lipid oxidation, de novo lipogenesis, and triglyceride secretion, thereby modulating hepatic fat content [5,6]. Even subtle variations within the normal reference range of thyroid hormone levels, termed "euthyroid dysfunction," have been reported to influence metabolic risk, including dyslipidemia, adiposity, and hepatic fat accumulation [7]. Several studies suggest that low-normal free T3 (FT3) and elevated thyroid-stimulating hormone (TSH) levels may be associated with increased hepatic steatosis

and metabolic syndrome components [8,9]. However, findings remain inconsistent across populations, with some studies reporting weak or no correlation between thyroid hormone status and hepatic triglyceride content [10].

Patients with T2DM represent a unique cohort in whom alterations in thyroid hormone metabolism—such as reduced peripheral conversion of T4 to T3, chronic inflammation, and hepatic insulin resistance—may enhance susceptibility to hepatic fat accumulation [11]. Furthermore, thyroid dysfunction is more common among individuals with T2DM than in the general population, with prevalence ranging between 10% and 15% [12]. Despite this, limited data exist from the eastern Indian population, particularly from Bihar, where the coexistence of diabetes, obesity, and NAFLD is increasingly reported in clinical settings. Understanding the association between plasma thyroid hormone concentrations and hepatic triglyceride content may help identify high-risk diabetic patients and refine metabolic management strategies.

Given these gaps, the present retrospective study conducted at Patna Medical College and Hospital from November 2023 to July 2024, involving 106 patients with T2DM, aims to evaluate the association between plasma thyroid hormone levels and hepatic triglyceride content. This may contribute to improved risk stratification and early therapeutic interventions for metabolic liver disease in diabetic populations.

Materials and Methods

Study Design and Setting: This retrospective observational study was conducted in the Department of Medicine, Patna Medical College and Hospital, Patna. Medical records of patients registered between November 2023, and July 2024 were reviewed to evaluate the association between plasma thyroid hormone concentrations and hepatic triglyceride content.

Study Population: A total of 106 adults with an established diagnosis of type 2 diabetes mellitus (T2DM) were identified from the hospital database. Patients aged 18 years or older with documented thyroid function tests and available liver imaging during the study period were eligible for inclusion.

Inclusion Criteria

1. Confirmed diagnosis of type 2 diabetes mellitus
2. Age ≥18 years
3. Availability of thyroid profile (TSH, FT3, FT4)
4. Availability of liver imaging report assessing hepatic steatosis

Exclusion Criteria

1. History of significant alcohol consumption (>20 g/day for women, >30 g/day for men)
2. Chronic liver diseases (autoimmune, drug-induced, or metabolic liver disorders)
3. Positive viral hepatitis markers (HBsAg or anti-HCV)
4. Known thyroid disease under treatment (hypothyroidism, hyperthyroidism)
5. Pregnancy
6. Incomplete clinical or laboratory data

Data Collection: Demographic details (age, sex), duration of diabetes, anthropometric measurements (BMI), blood pressure, and relevant biochemical parameters (HbA1c, lipid profile, liver function tests) were extracted from patient files. Thyroid hormone levels—TSH, FT3, and FT4—were obtained from chemiluminescent immunoassays performed in the hospital's central laboratory. Hepatic triglyceride content was assessed indirectly using imaging reports, primarily abdominal ultrasonography, and classified according to documented grades of hepatic steatosis.

Laboratory and Imaging Assessment: All laboratory investigations were conducted using standardized automated analyzers. Liver imaging reports interpreted by qualified radiologists at the time of examination were used for grading hepatic steatosis. Patients were categorized according to the degree of hepatic triglyceride accumulation based on these imaging findings.

Statistical Analysis: Data were anonymized prior to analysis. Continuous variables were summarized as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Correlations between thyroid hormone concentrations and hepatic steatosis grades were assessed using Pearson's or Spearman's correlation coefficients depending on data distribution. Group comparisons were performed using ANOVA or the Kruskal–Wallis test as appropriate. A p-value <0.05 was considered statistically significant. Statistical analysis was carried out using standard statistical software.

Results

A total of 106 patients with type 2 diabetes mellitus were included. The results are presented systematically below with corresponding tables.

Baseline Characteristics

The baseline demographic and clinical characteristics of the study population are summarized in **Table 1**. The mean age was 54.8 ± 9.6 years, with males comprising 61.3% of the study cohort. The mean duration of diabetes was 7.2 ± 3.4 years. The average BMI was 27.6 ± 3.8 kg/m², indicating that most participants were overweight.

Mean HbA1c was 8.2 ± 1.4%, suggesting suboptimal glycemic control.

Table 1: Baseline Characteristics of the Study Population (N = 106)

Variable	Mean ± SD / n (%)
Age (years)	54.8 ± 9.6
Male: Female	65 (61.3%): 41 (38.7%)
Duration of diabetes (years)	7.2 ± 3.4
BMI (kg/m²)	27.6 ± 3.8
HbA1c (%)	8.2 ± 1.4
Total cholesterol (mg/dL)	189.3 ± 32.6
Triglycerides (mg/dL)	176.8 ± 46.2
ALT (U/L)	42.7 ± 12.3

Thyroid Hormone Profile: Thyroid hormone data are presented in Table 2. The mean TSH was 3.14 ± 1.26 mIU/L, mean FT3 was 2.98 ± 0.42 pg/mL, and mean FT4 was 1.14 ± 0.23 ng/dL. Subclinical hypothyroidism was detected in 14.1% (n = 15) of the patients.

Table 2: Thyroid Hormone Profile of Patients

Parameter	Mean ± SD
TSH (mIU/L)	3.14 ± 1.26
FT3 (pg/mL)	2.98 ± 0.42
FT4 (ng/dL)	1.14 ± 0.23
Subclinical hypothyroidism	15 (14.1%)

Distribution of Hepatic Steatosis: Imaging-based grading of hepatic steatosis is shown in Table 3. A majority of patients (79.2%) exhibited some degree of hepatic triglyceride accumulation. Grade I steatosis was most common (38.7%), followed by Grade II (26.4%) and Grade III (14.1%).

Table 3: Distribution of Hepatic Steatosis

Steatosis Grade	n (%)
Grade 0	22 (20.8%)
Grade I	41 (38.7%)
Grade II	28 (26.4%)
Grade III	15 (14.1%)
Total with steatosis	**84 (79.2%)**

Thyroid Hormones Across Steatosis Grades: The comparison of thyroid hormone levels across hepatic steatosis grades is presented in Table 4. FT3 levels showed a significant declining trend with increasing steatosis severity ($p < 0.05$), whereas TSH levels increased significantly across grades ($p < 0.01$). FT4 levels did not show meaningful variation.

Patients with Grade II and Grade III steatosis had significantly lower FT3 and higher TSH levels compared with those without steatosis.

Table 4: Thyroid Hormone Levels Across Steatosis Grades

Steatosis Grade	FT3 (pg/mL)	TSH (mIU/L)	FT4 (ng/dL)
Grade 0	3.18 ± 0.39	2.41 ± 0.88	1.17 ± 0.21
Grade I	3.01 ± 0.34	3.02 ± 1.04	1.15 ± 0.22
Grade II	2.87 ± 0.28	3.39 ± 1.15	1.12 ± 0.25
Grade III	2.74 ± 0.25	4.12 ± 1.29	1.11 ± 0.24
p-value	**<0.05**	**<0.01**	>0.05

Correlation Between Thyroid Hormones and Hepatic Triglyceride Content: Correlation coefficients are summarized in Table 5. There was a statistically significant negative correlation between FT3 and hepatic steatosis ($r = –0.42$, $p = 0.002$), indicating that lower FT3 was associated with higher hepatic fat content. TSH demonstrated a positive correlation with steatosis severity ($r = 0.48$, $p < 0.001$). FT4 showed no significant association.

Table 5: Correlation Between Thyroid Hormones and Hepatic Triglyceride Content

Parameter	r	p-value	Interpretation
FT3 vs Steatosis	–0.42	0.002	Significant negative correlation
TSH vs Steatosis	+0.48	<0.001	Significant positive correlation
FT4 vs Steatosis	–0.09	>0.05	Not significant

Other Metabolic Parameters Across Steatosis Grades: The comparison of metabolic variables is detailed in Table 6. BMI, triglycerides, and ALT levels increased significantly with worsening hepatic steatosis ($p < 0.05$ for each). Although HbA1c increased progressively from Grade 0 to Grade III, the trend was not statistically significant.

Table 6: Comparison of Metabolic Parameters Across Steatosis Grades

Parameter	Grade 0	Grade I	Grade II	Grade III	p-value
BMI (kg/m²)	25.4 ± 3.1	27.2 ± 3.4	28.5 ± 3.9	29.1 ± 4.2	<0.05
Triglycerides (mg/dL)	148.6 ± 36.4	173.8 ± 42.1	185.2 ± 48.9	198.3 ± 54.6	<0.05
ALT (U/L)	36.2 ± 10.9	41.7 ± 11.5	45.3 ± 12.1	49.4 ± 13.2	<0.05
HbA1c (%)	7.9 ± 1.2	8.1 ± 1.3	8.4 ± 1.5	8.6 ± 1.6	>0.05

Discussion

In this retrospective study of 106 patients with type 2 diabetes, we found a significant association between plasma thyroid hormone concentrations and hepatic triglyceride content. Specifically, lower FT3 levels and higher TSH concentrations were associated with higher grades of hepatic steatosis, whereas FT4 levels did not show a significant relationship. These findings support the concept of a thyroid–liver metabolic axis influencing hepatic fat accumulation in diabetes and are consistent with recent studies that link subtle thyroid dysfunction with NAFLD progression [13].

Thyroid hormones regulate hepatic lipid oxidation, mitochondrial function, and de novo lipogenesis. A decline in FT3 may reduce β-oxidation and impair clearance of circulating fatty acids, facilitating hepatic lipid deposition. Previous research has shown a similar pattern where FT3 decreases progressively as the severity of steatosis increases, suggesting the possibility of an "intrahepatic hypothyroid state" even when systemic thyroid hormone levels appear normal [14].

The positive correlation between TSH and hepatic steatosis severity observed in our cohort aligns with mechanistic evidence indicating that TSH can directly stimulate hepatic lipogenesis via activation of SREBP-1c pathways [15]. This suggests that even modest elevations in TSH may have biological consequences in the liver independent of FT3 or FT4. Additionally, subclinical hypothyroidism—found in 14.1% of our patients—has been associated with dyslipidemia, increased liver enzymes, and greater hepatic fat accumulation in earlier reports [16].

Metabolic derangements observed across increasing steatosis grades in our study (higher BMI, ALT, triglycerides) further highlight the interconnected nature of thyroid function, insulin resistance, and hepatic fat metabolism. Several studies have demonstrated that thyroid dysfunction can worsen insulin resistance, alter lipid trafficking, and promote oxidative stress, contributing to NAFLD severity in diabetes [17,18]. FT4 levels, however, did not show a significant association with hepatic triglyceride content in our findings, similar to observations by Sinha and Jain [19], who reported that FT4 remains relatively stable due to compensatory peripheral conversion to FT3.

The significant negative correlation between FT3 and hepatic triglyceride content is clinically meaningful. FT3 is the biologically active form involved in stimulating hepatic fatty-acid oxidation; therefore, reduced FT3 levels could represent an early biochemical marker of worsening hepatic steatosis. Experimental studies have shown that intrahepatic T3 deficiency may precede hepatic lipid accumulation, supporting this hypothesis [20]. Conversely, the positive correlation between TSH and hepatic triglyceride content reinforces the view that TSH itself may contribute directly to hepatic lipid storage beyond its classical endocrine role [21].

These findings underscore the importance of routine thyroid function assessment in patients with type 2 diabetes, particularly those with metabolic risk factors or evidence of hepatic steatosis. Early identification of subtle thyroid abnormalities may help in the stratification of individuals at risk for progressive NAFLD. Weight reduction and lifestyle interventions have been shown to improve both thyroid and hepatic metabolic profiles [22]. Furthermore, thyroid hormone analogues and selective THR-β agonists are emerging as potential therapeutic tools for reducing hepatic triglyceride content [23].

This study has certain limitations. As a single-center retrospective study, causality cannot be confirmed, and residual confounding factors such as diet, physical activity, or medication effects may influence the results. Despite these limitations, the robustness of the associations and consistency with

previously published findings strengthen the credibility of the observed thyroid–liver link.

Overall, our results indicate that thyroid hormone imbalance—particularly low FT3 and elevated TSH—is significantly associated with increased hepatic triglyceride accumulation in type 2 diabetes. These findings support integrated metabolic and thyroid evaluation in the clinical assessment of diabetic patients at risk for hepatic steatosis.

Conclusion

In this retrospective study of 106 patients with type 2 diabetes, lower FT3 levels and elevated TSH were found to be significantly associated with higher hepatic triglyceride content, while FT4 showed no meaningful correlation. These results demonstrate a strong thyroid–liver metabolic interaction in diabetic individuals and support the concept that even mild deviations in thyroid hormone status may influence hepatic fat accumulation. Routine assessment of thyroid function in T2DM may help identify individuals at increased risk for NAFLD, enabling earlier lifestyle modification and metabolic intervention. Further multicentric prospective studies are warranted to clarify causal relationships and explore therapeutic strategies targeting the thyroid–liver axis.

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