ORIGINAL ARTICLE

Hypothyroidism in Nonalcoholic Fatty Liver Disease

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Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) is a leading cause of chronic liver disease with increasing global prevalence. Thyroid dysfunction, particularly hypothyroidism, has been implicated in its pathogenesis and progression.

Objectives: To evaluate the prevalence and pattern of hypothyroidism in NAFLD patients and assess its association with hepatic steatosis and fibrosis severity using imaging and noninvasive fibrosis scoring systems.

Materials and methods: This cross-sectional observational study was conducted on 158 adult NAFLD patients at a tertiary care hospital in northern India over 1 year. Patients with significant alcohol intake or other chronic liver diseases were excluded. Hepatic steatosis and fibrosis were assessed by ultrasonography and transient elastography, respectively. Fibrosis severity was categorized using FibroScan and the FIB-4 index. Thyroid function was evaluated by serum TSH, FT3, and FT4. Statistical analysis included intergroup comparisons and correlation assessments using SPSS v26, with $p < 0.05$ considered significant.

Results: Among 158 NAFLD patients, 41.14% were hypothyroid. The prevalence of hypothyroidism increased with disease severity: 71.43% in fibrotic NASH and 44.44% in cirrhosis (FibroScan-based). A dose-response trend was observed between steatosis grade and hypothyroidism, reaching 80% in grade 3 steatosis. FT4 showed a significant positive correlation with liver stiffness ($r = 0.432$, $p < 0.001$). Additional associations included positive correlations of liver stiffness with urea and INR, and negative correlations with serum protein, fasting glucose, and LDL. Overall, hypothyroidism emerged as a significant cofactor in NAFLD pathogenesis and fibrosis progression.

Conclusion: This study demonstrates a strong association between hypothyroidism and both hepatic steatosis and fibrosis in NAFLD. Routine thyroid function screening is recommended in NAFLD patients, particularly those with metabolic syndrome or suspected fibrosis. Early detection and treatment of hypothyroidism may provide therapeutic benefits in slowing or reversing NAFLD progression.

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is a major public health concern characterized by excessive triglyceride deposition in hepatocytes among individuals consuming minimal or no alcohol. Its diagnosis is based on imaging or histology in the absence of secondary causes such as alcohol abuse, medications, or genetic liver disorders.[1] Globally, NAFLD affects 20–30% of adults and is considered the hepatic component of metabolic syndrome.[1,2] In patients with type 2 diabetes mellitus, prevalence may reach 70%, highlighting its close association with insulin resistance and cardiometabolic disturbances.[2] The disease spectrum ranges from simple steatosis to nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma.[3] Although early stages are often asymptomatic, advanced fibrosis increases the risk of severe liver-related outcomes. Recent advances in noninvasive diagnostics, including transient elastography and scoring indices such as FIB-4, have improved fibrosis assessment and reduced reliance on biopsy.[4]

Hypothyroidism, defined as reduced thyroid hormone production or action, is increasingly recognized as a contributor to NAFLD. Globally, iodine deficiency remains the most common cause, though autoimmune thyroiditis predominates in iodine-sufficient regions.[5,6] Its clinical features are often nonspecific, and diagnosis is established biochemically with elevated TSH and reduced FT4.[7] Thyroid hormones regulate lipid metabolism and mitochondrial function, and their deficiency promotes hepatic lipid accumulation, impaired β-oxidation, and oxidative stress.[8,9] Furthermore, TSH receptors expressed on hepatocytes may directly stimulate lipid synthesis.[10]

Epidemiological data and meta-analyses have shown that both overt and subclinical hypothyroidism increase the risk of NAFLD and are associated with more severe fibrosis.[11] Certain cohorts report NAFLD, particularly among patients with histologically confirmed NASH prevalence as high as 46% in hypothyroid patients.[12,13] Emerging therapeutic studies suggest levothyroxine replacement may reduce hepatic steatosis and improve metabolic parameters.[14]

In this context, the present study was designed to evaluate the association between hypothyroidism and NAFLD in an Indian population. The objectives included assessing the prevalence of thyroid dysfunction in NAFLD patients, determining its distribution across different stages of liver disease, and exploring correlations between thyroid hormone levels and fibrosis severity. Through this analysis, we aimed to better understand the endocrine-metabolic interface underlying NAFLD and to highlight the relevance of routine thyroid function screening in this population.

Materials and Methods

This was a cross-sectional observational study conducted over 1 year in the Department of Medicine in collaboration with the Department of Medical Gastroenterology at a tertiary care hospital in northern India. Ethical approval was obtained from the Institutional Ethics Committee (IEC) prior to study initiation, and informed written consent was taken from all participants.

Study Population

Adult male and female patients above 18 years of age diagnosed with NAFLD were

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included. The diagnosis of NAFLD was based on abdominal ultrasonography (USG) showing hepatic steatosis, defined as:

- Increased echogenicity of the liver compared with the renal cortex.
- Blurring of intrahepatic vessel walls.
- Posterior beam attenuation.

Inclusion Criteria

- Patients with ultrasonographic evidence of fatty liver.
- Both diabetic and non-diabetic patients.
- Adults willing to provide written informed consent.

Exclusion Criteria

- History of significant alcohol consumption (>11–15 gm/day in females, >2 drinks/day in males for ≥10 years).
- Pregnant women.
- Patients with hepatitis B or C infection (confirmed by viral markers).
- Autoimmune hepatitis or metabolic liver diseases (e.g., Wilson's disease, hemochromatosis) confirmed by serology.
- Renal impairment (acute or chronic kidney disease).
- Critically ill patients or those with multi-organ dysfunction.

Sample Size

The required sample size was calculated as 158 based on an assumed hypothyroidism prevalence of 12% among NAFLD patients, with a 95% confidence interval and 5% absolute error, using the formula:

$$n = Z^2 \times P(1-P)/d^2$$

where $Z = 1.96$, $P = 0.12$, and $d = 0.05$.

Table 1: Ultrasonographic findings of study population

Parameter	*Count (n = 158)*	*Percentage (100%)*
Ultrasound findings		
Grade 1 fatty liver	41	25.95
Grade 2 fatty liver	15	9.40
Grade 3 fatty liver	7	4.44
Hepatomegaly	95	60.12

Investigations and Data Collection

All patients underwent a detailed clinical history and physical examination. Laboratory tests included complete blood count, liver function tests, fasting and postprandial blood glucose, HbA1c, serum protein, albumin, lipid profile, urea, creatinine, electrolytes, PT/INR, and thyroid function tests (TSH, FT3, FT4). Viral markers, autoimmune profiles, and relevant tests for Wilson's disease and hemochromatosis were performed to exclude secondary causes of liver disease.

Imaging

Ultrasonography was used for grading fatty liver and hepatomegaly.

Transient elastography (FibroScan, Echosens, France) measured liver stiffness (in kilopascals) and controlled attenuation parameter (CAP) for steatosis, using the median of 10 valid readings. Fibrosis stages were categorized as:

- NAFL: <7 kPa
- Early NASH (F0–F1): 7–9.9 kPa
- Fibrotic NASH (F2–F3): 10–14.9 kPa
- NASH Cirrhosis (F4): ≥15 kPa

Noninvasive Scoring

The FIB-4 index was calculated as: FIB-4 = Age × AST/platelet count × √ALT.

Scores were interpreted as:

- <1.45: Stage 0–1 fibrosis
- 1.45–3.25: Stage 2–3 fibrosis
- >3.25: Stage 4–6 fibrosis

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS v26. Continuous variables were expressed as mean ± SD or median with interquartile range. Categorical variables were expressed as percentages. Intergroup comparisons were performed using Student's *t*-test or Chi-square test, where applicable. Correlations were tested using Pearson's or Spearman's coefficients. Chi-square test was applied to assess the association of thyroid status (hypothyroid vs euthyroid) with NAFLD severity across steatosis grades (ultrasound) and fibrosis stages (FibroScan, FIB-4). A p-value < 0.05 was considered statistically significant.

Results

This study included 158 NAFLD patients, predominantly middle-aged, with a male predominance. The majority (31.65%) were in the 21–40 year group, followed by 41–60 years (31.01%) and ≥61 years (32.27%).

Ultrasonographic Findings

Grade 1 steatosis was the most frequent, followed by grade 2 and grade 3. Hepatomegaly was seen in 60.12% of participants (Table 1).

FibroScan Staging

Nearly half (47.47%) had early NASH (F0–F1), while 8.86% and 11.39% were classified as fibrotic NASH (F2–F3) and NASH cirrhosis (F4), respectively. About one-third (32.28%) were in the NAFL stage (Table 2). FIB-4 scoring further showed that 63.29% had minimal fibrosis, whereas 27.84% and 8.80% were in stages 2–3 and 4–6, respectively (Table 3).

Cross-comparison of USG Grade with FibroScan Stage

Among the 63 patients who were graded for steatosis on USG, advanced steatosis grades were significantly associated with higher fibrosis stages (χ^2 test, $p < 0.05$). In grade 3 steatosis, 50% were in fibrotic or cirrhotic categories, compared to only 7.3% in grade 1 (Table 4).

Table 2: FibroScan staging

Parameter	*Count (n = 158)*	*Percentage (100%)*
NAFL	51	32.28
Early NASH (F0–F1)	75	47.47
Fibrotic NASH (F2–F3)	14	8.86
NASH cirrhosis (F4)	18	11.39

Table 3: FIB-4 staging

Parameter	*Count (n = 158)*	*Percentage (100%)*
Stage 0–1 (<1.45)	100	63.29
Stage 2–3 (1.45–3.25)	44	27.84
Stage 4–6 (>3.25)	14	8.80

Table 4: Fatty liver grade (USG) vs NAFLD stage (FibroScan)

USG fatty liver grade	*NAFL (n, %)*	*Early NASH (n, %)*	*Fibrotic NASH (n, %)*	*NASH Cirrhosis (n, %)*
Grade 1 ($n = 41$)	25 (60.98%)	13 (31.71%)	2 (4.88%)	1 (2.44%)
Grade 2 ($n = 12$)	6 (50.00%)	4 (33.33%)	1 (8.33%)	1 (8.33%)
Grade 3 ($n = 10$)	2 (20.00%)	3 (30.00%)	3 (30.00%)	2 (20.00%)
Total ($n = 63$)	33 (52.38%)	20 (31.75%)	6 (9.52%)	4 (6.35%)

Thyroid Function

Of the total cohort, 41.14% were hypothyroid, 55.70% euthyroid, and 3.16% hyperthyroid (Table 5). The prevalence of hypothyroidism increased with NAFLD severity on both ultrasound and FibroScan. On ultrasound, hypothyroidism was observed in 53.66% of grade 1, 75% of grade 2, and 80% of grade 3 patients. Similarly, prevalence rose from 33.33% in NAFL to 71.43% in fibrotic NASH, while 44.44% of cirrhosis patients were hypothyroid (Table 6). Chi-square analysis showed no statistically significant association between hypothyroidism and both steatosis grade and fibrosis stage ($p < 0.05$).

Table 5: Thyroid status in NAFLD

Parameter	*Count (n = 158)*	*Percentage (100%)*
Euthyroid	88	55.70
Hyperthyroid	5	3.16
Hypothyroid	65	41.14

Biochemical and Metabolic Profile

Patients showed mild anemia, slightly reduced protein/albumin, borderline dyslipidemia, and impaired glucose regulation. Correlation analysis revealed:

- Positive associations of FibroScan stiffness with FT4 (0.432, $p < 0.001$), serum urea, and INR.
- Negative associations with serum protein, fasting glucose, and LDL cholesterol (Table 7).
- Other parameters, including hemoglobin, platelets, albumin, SGOT, SGPT, TSH, and FT3, did not correlate significantly with liver stiffness.

Table 6: Distribution of hypothyroidism across the NAFLD spectrum

Parameter	*Count*	*Percentage (100%)*
Hypothyroidism by USG grade		
Grade 1 fatty liver	22	53.66
Grade 2 fatty liver	9	75.00
Grade 3 fatty liver	8	80.00
Hypothyroidism by FibroScan		
NAFL	17	33.33
Early NASH (F0–F1)	30	40.00
Fibrotic NASH (F2–F3)	10	71.43
NASH Cirrhosis (F4)	8	44.44
Chi-square = 4.26; $p = 0.234$		
Hypothyroidism by FIB-4		
Stage 0–1	34	34.00
Stage 2–3	26	59.09
Stage 4–6	5	35.71

Table 7: Biochemical and metabolic profile of study population and correlation with liver fibrosis (FibroScan)

Parameter	*Mean ± SD*	*r (correlation coefficient)*	*p-value*
Hemoglobin (gm/dL)	9.99 ± 2.19	0.011	0.892
TLC (cells/mm^3)	9066.33 ± 11075.71	0.002	0.982
Platelets (lakh/mm^3)	2.18 ± 1.59	0.084	0.294
Serum Protein (gm/dL)	6.25 ± 0.74	−0.245	0.002
Albumin (gm/dL)	3.53 ± 2.71	−0.033	0.679
Sodium (mEq/L)	133.12 ± 14.91	−0.064	0.58
Potassium (mEq/L)	3.92 ± 2.18	0.215	0.049
Urea (mg/dL)	37.29 ± 22.77	0.263	0.001
Creatinine (mg/dL)	1.08 ± 0.96	0.082	0.308
SGOT (U/L)	57.50 ± 46.29	0.006	0.942
SGPT (U/L)	49.45 ± 62.48	−0.016	0.844
PT (sec)	13.38 ± 3.34	0.131	0.100
INR	1.17 ± 0.35	0.237	0.003
Fasting blood sugar (mg/dL)	108.59 ± 25.42	−0.223	0.005
Postprandial sugar (mg/dL)	145.39 ± 32.14	−0.061	0.445
HbA1c (%)	6.11 ± 1.64	−0.115	0.149
Cholesterol (mg/dL)	160.19 ± 53.78	−0.026	0.749
Triglycerides (mg/dL)	159.98 ± 90.94	0.105	0.191
HDL (mg/dL)	49.62 ± 25.12	0.096	0.233
LDL (mg/dL)	83.37 ± 39.89	−0.170	0.032

Discussion

The prevalence of hypothyroidism in our cohort was 41.14%, which increased with advancing disease stage, reaching 80% in grade 3 steatosis and 71.43% in fibrotic NASH. These findings support the concept that thyroid dysfunction may play a direct role in disease progression rather than being a coincidental comorbidity, consistent with earlier reports by Guo et al.[8]

The demographic profile of middle-aged predominance and male excess was in line with other metabolic syndrome studies, as noted by Lee et al.[2] Our data also confirmed that ultrasonography, despite its limitations, remains a useful first-line tool for fatty liver detection, while FibroScan provides more accurate staging, as emphasized by Loomba et al.[4] The concordance of higher ultrasound grades with advanced fibrosis on elastography in our study reinforces the practical utility of combining imaging modalities for NAFLD risk stratification.

The prevalence of hypothyroidism in our NAFLD patients was higher than that reported in some international cohorts. A recent population-based study by Almomani et al. demonstrated a significantly higher prevalence of hypothyroidism (22.4%) in NAFLD and suggested that thyroid hormone replacement may positively influence disease course.[15] Biopsy-based evidence from D'Ambrosio et al. demonstrated a prevalence to be around 21% and that abnormal thyroid function is closely related to histological severity of NAFLD.[16] Importantly, a study by Parikh et al. reported a prevalence of 16.8% of hypothyroidism in NAFLD patients in western India.[17] These observations are supported by the systematic review by Eshraghian and Jahromi, which comprehensively summarized earlier studies and concluded that thyroid dysfunction consistently increases the risk and severity of NAFLD and found the prevalence of hypothyroidism to be around 15.2–36.3%.[18] This variation may reflect differences in iodine sufficiency, autoimmunity burden,

and population-level metabolic risks. Taken together, these findings strengthen the argument that hypothyroidism contributes to NAFLD progression rather than representing a coincidental comorbidity.

Biochemical findings in our patients further reinforced the metabolic-liver-thyroid axis. The positive correlation of liver stiffness with FT4 may indicate altered hormone metabolism in chronic liver disease, while the absence of significant correlation with TSH suggests possible nonthyroidal illness effects. These findings are consistent with earlier studies showing that conventional thyroid markers may not always capture the dynamic interplay of thyroid and liver function.[11] Additionally, negative associations of fibrosis with serum protein, fasting glucose, and LDL cholesterol underline the complex interactions of hepatic synthetic function, insulin resistance, and lipid handling, as also observed in recent Indian cohorts, such as Parikh et al.[17]

From a mechanistic standpoint, thyroid hormone deficiency is known to impair β-oxidation, enhance intrahepatic lipid accumulation, and promote oxidative stress, inflammation, and fibrogenesis.[9,10] Clinical evidence, including levothyroxine intervention studies, suggests that thyroid hormone replacement may ameliorate hepatic steatosis and improve metabolic parameters.[14] These data support the possibility of thyroid-targeted interventions as adjuncts in NAFLD management.

This study was limited by its single-center design and modest sample size, which may restrict generalizability. Its cross-sectional nature prevented establishing causality between hypothyroidism and NAFLD progression. Although FibroScan and FIB-4 scoring are validated tools, the absence of histopathology could have influenced staging accuracy. Confounding effects of altered thyroid hormone metabolism in advanced liver disease and unmeasured factors such as diet, physical activity, and iodine status could not be fully accounted for.

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References

1. Milic S, Stimac D. Nonalcoholic fatty liver disease/steatohepatitis: Epidemiology, pathogenesis, clinical presentation and treatment. Dig Dis 2012;30(2):158–162.
2. Lee YH, Cho Y, Lee BW, et al. Nonalcoholic fatty liver disease in diabetes. Part I: Epidemiology and diagnosis. Diabetes Metab J 2019;43(1):31–45.
3. Brown GT, Kleiner DE. Histopathology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Metabolism 2016;65(8):1080–1086.
4. Loomba R, Adams LA. Advances in non-invasive assessment of hepatic fibrosis. Gut 2020;69(7):1343–1352.
5. Taylor PN, Albrecht D, Scholz A, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol 2018;14(5):301–316.
6. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: Cosponsored by the AACE and ATA. Endocr Pract 2012;18(6):988–1028.
7. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: Prepared by the American Thyroid Association. Thyroid 2014;24(12):1670–1751.
8. Guo Z, Li M, Han B, et al. Association of non-alcoholic fatty liver disease with thyroid function: a systematic review and meta-analysis. Dig Liver Dis 2018;50(11):1153–1162.
9. Mandato C, D'Acunzo I, Vajro P. Thyroid dysfunction and its role as a risk factor for non-alcoholic fatty liver disease: What's new. Dig Liver Dis 2018;50(11):1163–1165.
10. Zhang W, Tian LM, Han Y, et al. Presence of thyrotropin receptor in hepatocytes: not a case of illegitimate transcription. J Cell Mol Med 2009;13(11–12):4636–4642.
11. He W, An X, Li L, et al. Relationship between hypothyroidism and non-alcoholic fatty liver disease: a systematic review and meta-analysis. Front Endocrinol 2017;8:335.
12. Alam MS, Ashraf H, Zafar KS, et al. The NAFLD threat in hypothyroid patients: a cross-sectional study. J ASEAN Fed Endocr Soc 2024;39(S1):4
13. Naguib R, Fayed A, Elkemary EZ, et al. Evaluation of thyroid function and thyroid autoimmune disease in patients with non-alcoholic fatty liver disease. Clin Exp Hepatol 2021;7(4):422–428.
14. Bruinstroop E, Dalan R, Cao Y, et al. Low-dose levothyroxine reduces intrahepatic lipid content in patients with type 2 diabetes mellitus and NAFLD. J Clin Endocrinol Metab 2018;103(7):2698–2706.
15. Almomani A, Hitawala AA, Kumar P, et al. Prevalence of hypothyroidism and effect of thyroid hormone replacement therapy in patients with non-alcoholic fatty liver disease: a population-based study. World J Hepatol 2022;14(3):551–558.
16. D'Ambrosio R, Campi I, Maggioni M, et al. The relationship between liver histology and thyroid function tests in patients with non-alcoholic fatty liver disease (NAFLD). PLoS One 2021;16(4):e0249614.
17. Parikh P, Phadke A, Sawant P. Prevalence of hypothyroidism in nonalcoholic fatty liver disease in patients attending a tertiary hospital in western India. Indian J Gastroenterol 2015;34(2):169–173.
18. Eshraghian A, Hamidian Jahromi A. Non-alcoholic fatty liver disease and thyroid dysfunction: a systematic review. World J Gastroenterol 2014;20(25):8102–8109.