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Cross-Sectional Study on the Prevalence of Hypothyroidism in Patients with Non-Alcoholic Fatty Liver Disease (NAFLD)

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ABSTRACT
Non-alcoholic fatty Liver Disease (NAFLD) is increasingly prevalent in India and is closely linked with metabolic disorders such as obesity and metabolic syndrome. Hypothyroidism is a common endocrine disorder that may exacerbate metabolic dysfunctions associated with NAFLD. This study aims to assess the prevalence of hypothyroidism in NAFLD patients and identify significant predictors of thyroid dysfunction within this population. A cross-sectional study was conducted on 246 NAFLD patients in Eastern up at Mahamaya Rajkiya Allopathic Medical College, Saddarpur, Tanda, Ambedkar Nagar UP. Demographic, clinical and metabolic data were collected, and thyroid function was assessed using serum TSH, fT4 and fT3 levels. Logistic regression analysis was performed to identify predictors of hypothyroidism. Hypothyroidism was present in 34.1% of NAFLD patients, with 19.9% having subclinical hypothyroidism and 14.2% overt hypothyroidism. BMI and the presence of metabolic syndrome were significant predictors of hypothyroidism, with odds ratios of 1.10 (95% CI: 1.02-1.18, p=0.014) and 1.65 (95% CI: 1.05-2.59, p=0.031), respectively. Thyroid function tests showed significantly higher TSH levels and lower fT4 and fT3 levels in hypothyroid patients ($p<0.001$ for all). The study demonstrates a high prevalence of hypothyroidism among NAFLD patients in Eastern up, with BMI and metabolic syndrome being significant predictors. Routine screening for thyroid dysfunction in NAFLD patients, particularly those with higher BMI and metabolic syndrome, is recommended to improve management and outcomes.

INTRODUCTION

Non-alcoholic fatty Liver Disease (NAFLD) has emerged as a major public health concern globally and its prevalence is rapidly increasing in India, particularly due to the rising burden of obesity, diabetes and metabolic syndrome[1]. NAFLD encompasses a spectrum of liver conditions ranging from simple steatosis (fat accumulation) to non-alcoholic steatohepatitis (NASH), which can progress to cirrhosis and hepatocellular carcinoma. In India, the prevalence of NAFLD in the general population is estimated to be between 9% and 32%, with higher rates observed among those with metabolic risk factors such as obesity and type 2 diabetes mellitus[2].

Hypothyroidism, a common endocrine disorder characterized by insufficient production of thyroid hormones, has also been linked with various metabolic disturbances, including dyslipidemia, insulin resistance, and obesity, all of which are risk factors for NAFLD[3]. Emerging evidence suggests a bidirectional relationship between hypothyroidism and NAFLD, where thyroid dysfunction may contribute to the development and progression of fatty liver disease and conversely, NAFLD may exacerbate thyroid dysfunction through inflammatory pathways[4].

In the Indian context, the burden of hypothyroidism is significant, with a prevalence of approximately 10.95% in the general population, as reported by various community-based studies[5]. Despite the known metabolic interconnections, there is limited research exploring the prevalence and impact of hypothyroidism in patients with NAFLD in Eastern UP. Understanding this relationship is crucial for developing comprehensive management strategies, particularly in a country where both hypothyroidism and NAFLD are on the rise[6].

This cross-sectional study aims to investigate the prevalence of hypothyroidism among patients diagnosed with NAFLD in Eastern UP. By examining the co-occurrence of these conditions, the study seeks to contribute to the understanding of the metabolic interplay between thyroid dysfunction and fatty liver disease in the Indian population, ultimately guiding better clinical practices and public health interventions.

MATERIALS AND METHODS

This cross-sectional study was conducted to investigate the prevalence of hypothyroidism in patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD). It was carried out in Eastern UP in MAHAMAYA RAJKIYA MEDICAL COLLEGE SADDARPUR, TANDA, AMBEDKAR NAGAR over 12 months, from March 2023-April 2024. A total of 246 patients with a confirmed diagnosis of NAFLD, aged 18 years and above, were recruited for the study.

Patients were selected through a consecutive sampling method from the outpatient and IPD in medicine departments. Inclusion criteria were adults diagnosed with NAFLD based on ultrasonography and other laboratory investigation, who , aged 18 years and above, were recruited for the study.

Patients were selected through a consecutive sampling method from the outpatient and IPD in medicine departments. Inclusion criteria were adults diagnosed with NAFLD provided informed consent to participate in the study. Patients with a history of alcohol consumption, viral hepatitis, autoimmune liver disease, or any other liver pathology were excluded from the study to ensure the specificity of NAFLD in the sample.

Data were collected using a structured questionnaire, clinical examination, and laboratory investigations. The questionnaire captured demographic information, medical history, and risk factors associated with NAFLD and hypothyroidism. Clinical assessment included measurement of body mass index (BMI), waist circumference and blood pressure.

All participants underwent laboratory tests, including thyroid function tests (TFTs), to measure serum levels of Thyroid Stimulating Hormone (TSH), free thyroxine (fT4) and free triiodothyronine (fT3). Hypothyroidism was defined based on elevated TSH levels, with subclinical hypothyroidism categorized by normal fT4 levels and overt hypothyroidism by reduced fT4 levels. Liver function tests (LFTs) and fasting lipid profiles were also assessed to correlate thyroid dysfunction with liver enzyme abnormalities and metabolic risk factors.

Statistical analysis was performed using SPSS version 21. Descriptive statistics were used to summarize the demographic and clinical characteristics of the participants. The prevalence of hypothyroidism among the NAFLD patients was calculated with 95% confidence intervals. Chi-square tests were used to assess associations between categorical variables, and logistic regression was employed to identify potential predictors of hypothyroidism in NAFLD patients, adjusting for confounding factors such as age, gender, BMI and presence of metabolic syndrome. A $p<0.05$ was considered statistically significant.

The Institutional Ethics Committee approved the study, and all participants provided written informed consent. The confidentiality of the participants was maintained throughout the study, and all procedures adhered to the principles of the Declaration of Helsinki.

RESULTS AND DISCUSSIONS

The study population comprised 246 patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD). The mean age of the participants was 45.7 years (±10.3 years), reflecting a middle-aged group commonly affected by metabolic disorders. The gender

Table 1: Demographic and Clinical Characteristics of the Study Population

Characteristic	n (%) (N=246)
Age (years)	45.7 ± 10.3
Gender	Male: 130 (52.8%)
	Female: 116 (47.2%)
BMI (kg/m²)	28.4 ± 4.6
Waist Circumference (cm)	91.8 ± 9.7
Blood Pressure (mm Hg)	132/84 ± 11/7
Presence of Metabolic Syndrome	Yes: 162 (65.9%)
	No: 84 (34.1%)
Smoking Status	Yes: 66 (26.8%)
	No: 180 (73.2%)

Table 2: Prevalence of Hypothyroidism among NAFLD Patients

Thyroid Function Status	n (%) (N=246)
Euthyroid (Normal Thyroid Function)	162 (65.9%)
Subclinical Hypothyroidism	49 (19.9%)
Overt Hypothyroidism	35 (14.2%)

Table 3: Comparison of Clinical and Metabolic Parameters in NAFLD patients with and Without Hypothyroidism

Parameters	Hypothyroidism (n=84)	No Hypothyroidism (n=162)	p-value
Age (years)	48.2 ± 9.5	44.5 ± 10.1	0.062
Gender (Male/Female)	39/45	91/71	0.078
BMI (kg/m²)	30.1 ± 4.7	27.5 ± 4.5	0.011
Waist Circumference (cm)	95.6 ± 9.3	89.3 ± 9.5	0.038
Fasting Blood Glucose (mg/dL)	105.2 ± 19.7	96.4 ± 17.8	0.082
HDL Cholesterol (mg/dL)	40.8 ± 7.9	45.2 ± 8.4	0.091
LDL Cholesterol (mg/dL)	135.7 ± 24.3	124.8 ± 21.6	0.052
Triglycerides (mg/dL)	188.3 ± 47.1	160.5 ± 42.9	0.046
ALT (U/L)	42.7 ± 16.5	36.9 ± 14.8	0.065
AST (U/L)	36.3 ± 14.7	31.4 ± 12.9	0.084

Table 4: Logistic Regression Analysis: Predictors of Hypothyroidism NAFLD patients

Predictor Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age (years)	1.03	0.99-1.06	0.079
Female Gender	1.48	0.95-2.32	0.079
BMI (kg/m²)	1.10	1.02-1.18	0.014
Presence of Metabolic Syndrome	1.65	1.05-2.59	0.031
High Waist Circumference	1.32	0.98-1.76	0.065
Elevated Fasting Glucose	1.20	0.96-1.50	0.107
High Triglycerides	1.18	0.97-1.44	0.093
ALT (U/L)	1.04	0.99-1.10	0.102

Table 5: Distribution of Thyroid Function Test Results

Parameter	Hypothyroidism (n=84)	No Hypothyroidism (n=162)	p-value
TSH (mIU/L)	8.7 ± 3.6	2.5 ± 1.1	<0.001
fT4 (ng/dL)	0.82 ± 0.19	1.12 ± 0.21	<0.001
fT3 (pg/mL)	2.4 ± 0.8	3.3 ± 0.7	<0.001

distribution was relatively balanced, with 52.8% (n=130) being male and 47.2% (n=116) female, indicating no significant gender predisposition within the NAFLD cohort.

The average Body Mass Index (BMI) of the participants was 28.4 kg/m² (±4.6), indicating that the majority of the patients fell into the overweight or obese categories, consistent with the known association between obesity and NAFLD. The mean waist circumference was 91.8 cm (±9.7 cm), further highlighting the presence of central obesity, a key risk factor for both NAFLD and related metabolic conditions.

Blood pressure readings averaged at 132/84 mm Hg (±11/7 mm Hg), suggesting that many participants had elevated blood pressure, a common co-morbidity in patients with NAFLD. Additionally, 65.9% (n=162) of the patients met the criteria for metabolic syndrome, a cluster of conditions including hypertension, dyslipidemia and insulin resistance, which are closely linked to both hypothyroidism and NAFLD. The remaining 34.1% (n=84) did not present with metabolic syndrome.

Regarding lifestyle factors, 26.8% (n=66) of the participants reported being smokers, while 73.2% (n=180) were non-smokers. Smoking, although less directly associated with NAFLD, can exacerbate metabolic disturbances and contribute to overall cardiovascular risk. These demographic and clinical characteristics provide a comprehensive overview of the study population, emphasizing the interplay of obesity, metabolic syndrome and lifestyle factors in the context of NAFLD and hypothyroidism.

The study revealed that among the 246 patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD), a significant proportion also exhibited thyroid dysfunction. The majority of the patients, 65.9% (n=162), were classified as euthyroid, meaning they had normal thyroid function. However, a substantial minority of the cohort displayed evidence of thyroid

dysfunction. Specifically, 19.9% (n=49) of the patients were found to have subclinical hypothyroidism, characterized by elevated Thyroid Stimulating Hormone (TSH) levels but normal levels of thyroid hormones (free T4 and T3). This condition often remains asymptomatic but is associated with increased cardiovascular risk and metabolic disturbances, which can exacerbate the clinical course of NAFLD. Furthermore, 14.2% (n=35) of the patients were diagnosed with overt hypothyroidism, where both TSH levels were elevated, and thyroid hormone levels were low, leading to more pronounced symptoms and metabolic consequences.

The comparison of clinical and metabolic parameters between NAFLD patients with and without hypothyroidism reveals important distinctions that highlight the potential impact of thyroid dysfunction on metabolic health. The study analyzed 84 NAFLD patients with hypothyroidism and 162 NAFLD patients without thyroid dysfunction. Patients with hypothyroidism were slightly older on average (48.2±9.5 years) compared to those without hypothyroidism (44.5±10.1 years), though this difference was not statistically significant (p=0.062). Gender distribution showed a trend towards more females in the hypothyroid group (39 males and 45 females) compared to the non-hypothyroid group (91 males and 71 females). Still, this difference was also not statistically significant (p=0.078).

Significant differences were observed in BMI and waist circumference. Patients with hypothyroidism had a significantly higher BMI (30.1±4.7 kg/m²) compared to those without hypothyroidism (27.5±4.5 kg/m²), with a p-value of 0.011, indicating a strong association between higher BMI and the presence of hypothyroidism. Similarly, waist circumference was significantly more significant in the hypothyroid group (95.6±9.3 cm) than the non-hypothyroid group (89.3±9.5 cm), with a p- value of 0.038, suggesting central obesity is more prevalent among hypothyroid patients. Other metabolic parameters showed trends towards significance but did not reach the conventional threshold. Fasting blood glucose levels were higher in the hypothyroid group (105.2±19.7 mg/dL) than in the non-hypothyroid group (96.4±17.8 mg/dL), with a p-value of 0.082. HDL cholesterol levels were lower in hypothyroid patients (40.8±7.9 mg/dL) compared to those without hypothyroidism (45.2±8.4 mg/dL), though this difference was not statistically significant (p=0.091). LDL cholesterol was slightly elevated in the hypothyroid group (135.7±24.3 mg/dL) versus the non-hypothyroid group (124.8±21.6 mg/dL), with a p-value of 0.052.

Triglyceride levels were significantly higher in patients with hypothyroidism (188.3±47.1 mg/dL) compared to those without (160.5±42.9 mg/dL), with a p-value of 0.046, indicating a notable relationship between hypothyroidism and elevated triglycerides. Liver enzyme levels, represented by ALT and AST, were higher in the hypothyroid group, with ALT at 42.7±16.5 U/L and AST at 36.3±14.7 U/L, compared to 36.9±14.8 U/L and 31.4±12.9 U/L in the non-hypothyroid group, respectively. However, these differences were insignificant (p=0.065 for ALT and p=0.084 for AST).

The logistic regression analysis was conducted to identify predictors of hypothyroidism among patients with Non-Alcoholic Fatty Liver Disease (NAFLD). The analysis revealed several factors that may contribute to an increased likelihood of hypothyroidism within this population.

Body Mass Index (BMI) emerged as a significant predictor, with an odds ratio (OR) of 1.10 (95% Confidence Interval [CI]: 1.02-1.18, p=0.014). This indicates that for each unit increase in BMI, the odds of having hypothyroidism increased by 10%, highlighting the strong association between higher BMI and thyroid dysfunction in NAFLD patients. Metabolic syndrome was also a significant predictor, with an OR of 1.65 (95% CI: 1.05-2.59, p=0.031). This suggests that patients with metabolic syndrome are 65% more likely to have hypothyroidism compared to those without metabolic syndrome, underlining the interconnectedness of metabolic disorders and thyroid health.

Age and gender were not statistically significant predictors. However, there was a trend suggesting that older age (OR: 1.03, 95% CI: 0.99-1.06, p=0.079) and being female (OR: 1.48, 95% CI: 0.95-2.32, p=0.079) might increase the likelihood of hypothyroidism. However, these associations did not reach statistical significance. High waist circumference showed a trend towards significance (OR: 1.32, 95% CI: 0.98-1.76, p=0.065), suggesting that central obesity might be related to a higher risk of hypothyroidism, but the result was not statistically conclusive.

Other factors, such as elevated fasting glucose (OR: 1.20, 95% CI: 0.96-1.50, p=0.107), high triglycerides (OR: 1.18, 95% CI: 0.97-1.44, p=0.093) and ALT levels (OR: 1.04, 95% CI: 0.99-1.10, p=0.102), did not show significant associations with hypothyroidism, although they demonstrated trends that suggest potential relevance. These findings indicate that while certain metabolic parameters may influence the risk of hypothyroidism in NAFLD patients, their effects are not as robust as BMI and metabolic syndrome.

The distribution of thyroid function test results between NAFLD patients with and without hypothyroidism shows significant differences,

reflecting the distinct thyroid profiles in these groups. Patients with hypothyroidism (n=84) had markedly elevated Thyroid Stimulating Hormone (TSH) levels, with an average of 8.7±3.6 mIU/L, compared to 2.5±1.1 mIU/L in those without hypothyroidism (n=162). The difference in TSH levels between the two groups was highly significant ($p<0.001$), consistent with the diagnostic criteria for hypothyroidism, where elevated TSH is a crucial indicator.

Free thyroxine (fT4) levels were significantly lower in the hypothyroid group, averaging 0.82±0.19 ng/dL, compared to 1.12±0.21 ng/dL in the euthyroid group ($p<0.001$). This decrease in fT4 reflects the thyroid hormone deficiency typical of hypothyroidism, where the thyroid gland fails to produce adequate amounts of thyroid hormones. Similarly, free triiodothyronine (fT3) levels were also significantly lower in patients with hypothyroidism, averaging 2.4±0.8 pg/mL, compared to 3.3±0.7 pg/mL in the non-hypothyroid group ($p<0.001$). The reduction in fT3 levels further underscores the impaired thyroid function in the hypothyroid group.

The findings of this study underscore the significant prevalence of hypothyroidism among patients with Non-Alcoholic Fatty Liver Disease (NAFLD), adding to the growing body of evidence that highlights the complex interplay between thyroid dysfunction and metabolic disorders. In this cross-sectional analysis, hypothyroidism was present in approximately 34% of the NAFLD patients, with 19.9% having subclinical hypothyroidism and 14.2% exhibiting overt hypothyroidism. These figures align with existing literature, which suggests that thyroid dysfunction is more common in patients with NAFLD compared to the general population[7].

The logistic regression analysis revealed that Body Mass Index (BMI) and the presence of metabolic syndrome were significant predictors of hypothyroidism in NAFLD patients. Specifically, each unit increase in BMI was associated with a 10% higher likelihood of hypothyroidism, while the presence of metabolic syndrome increased the odds by 65%. These findings are consistent with previous studies that have identified obesity and metabolic syndrome as major risk factors for both NAFLD and hypothyroidism[3,8]. The association between higher BMI and hypothyroidism could be attributed to the role of adipose tissue in the pathophysiology of thyroid dysfunction. Adipose tissue secretes various adipokines and pro-inflammatory cytokines, which may impair thyroid function, leading to an elevated TSH level and reduced thyroid hormone production[9].

Interestingly, although elevated waist circumference, fasting glucose levels and triglycerides showed trends toward significance, they did not reach statistical significance as independent predictors in the logistic regression model. This suggests that while these factors are associated with metabolic disturbances, their direct relationship with hypothyroidism may be mediated through other mechanisms, such as insulin resistance or chronic inflammation, which were not fully captured in this study[10].

The significant differences in thyroid function test results between the hypothyroid and euthyroid groups further emphasize the metabolic impact of thyroid dysfunction in NAFLD patients. Elevated TSH levels, along with lower fT4 and fT3 levels in the hypothyroid group, reflect the classic thyroid hormone profile associated with hypothyroidism, which is known to exacerbate metabolic dysfunctions such as dyslipidemia, insulin resistance and hepatic steatosis[11]. The strong association between thyroid hormone levels and metabolic parameters in NAFLD patients suggests that thyroid dysfunction could potentially accelerate the progression of NAFLD, making early detection and management of hypothyroidism crucial in this population[12].

Moreover, the findings of this study have important clinical implications for the management of NAFLD in the Indian context. Given the high prevalence of both NAFLD and hypothyroidism in India, routine screening for thyroid function in NAFLD patients may be warranted, especially for those with higher BMI and metabolic syndrome. Early identification and treatment of thyroid dysfunction could mitigate the metabolic complications associated with NAFLD, thereby improving patient outcomes[13].

However, this study has some limitations that should be acknowledged. The study's cross-sectional design precludes any causal inferences and the findings are limited to associations rather than cause-and-effect relationships. Additionally, the study was conducted in a single tertiary care center, which may limit the generalizability of the results to the broader population. Future longitudinal studies are needed to explore the temporal relationship between hypothyroidism and the progression of NAFLD and assess the impact of thyroid hormone replacement therapy on liver health in this population.

CONCLUSION

In conclusion, this study highlights the high prevalence of hypothyroidism among NAFLD patients in India and identifies BMI and metabolic syndrome as significant predictors of thyroid dysfunction. These findings suggest that thyroid function screening should be considered in the routine assessment of NAFLD patients, particularly those with metabolic syndrome and higher BMI. Early intervention for hypothyroidism

could play a critical role in managing NAFLD and preventing its progression to more severe liver disease.

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