Original Article

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Hypothyroidism in Patients with Non Alcoholic Fatty Liver Disease (NAFLD)

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[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [2,4]Active participation in active methodology, analysis, or interpretation of data for the work, [5,6]Drafting the work or revising it critically for important intellectual content

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ABSTRACT

Objective: To determine the frequency of hypothyroidism in patients diagnosed with Non-alcoholic fatty liver disease (NAFLD) presenting at Liaquat University Hospital, Hyderabad.

Methodology: A descriptive cross-sectional study was conducted over six months, from January to July 2023, in the Department of Medicine, Liaquat University Hospital, Hyderabad. Patients aged 20 to 60 years of either gender with a clinical diagnosis of NAFLD for at least three months were included. Each patient was evaluated for hypothyroidism through laboratory analysis of a 2cc venous blood sample, and relevant data were recorded using a predesigned proforma. Post-stratification associations were analyzed using chi-square test taking a p-value ≤ 0.05 as statistically significant.

Results: An overall mean age of the patients was 39.56 ± 10.45 years, comprising 54.7% males and 45.3% females. Overall hypothyroidism was detected in 93 individuals (38.0%). Additionally post-stratification analysis showed that hypothyroidism was significantly more common among females (57.9%), rural residents (54.4%), patients with longer disease duration, hypertension, obesity and smokers (p-0.001), while no significant difference was found across different age groups (p = 0.93).

Conclusion: A high frequency of hypothyroidism was observed among patients with NAFLD, suggesting a potential link between thyroid dysfunction and fatty liver disease.

Keywords: Hypothyroidism, Thyroid disorders, Non-alcoholic fatty liver disease, Non-alcoholic steatohepatitis.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) has emerged as most frequently reported chronic hepatic disorder around the word. This medical condition results from the deposition of lipid in hepatocytes. It covers a variety of hepatic pathologies from simple Fatty Liver Disease (or hepatic steatosis) to metabolic dysfunction-associated steatohepatitis (MASH) (previously termed as non-alcoholic steatohepatitis (NASH)). MASH can potentially develop into fibrosis and then into cirrhosis, which is an ultimate irreversible end stage of liver failure.[1] A recent shift of name from NAFLD to metabolic dysfunction-associated fatty liver disease (MASLD) has made it easy to understand the underlying cause.[2]

NAFLD has been shown to have strong relationship with lifestyle, metabolic dysfunction, genetic factors, and endocrine abnormalities.[3] Obesity, Dyslipidemia, hypertension, Diabetes (Type 2), and sedentary lifestyle are among the primary risk factors for NAFLD, where NAFLD has been found among more than 90% of individuals with severe obesity and 69% of people with Diabetes (Type 2).[4,5] Polymorphisms in TM6SF2 and

PNPLA3 genes have also been linked to NAFLD. [6] NAFLD has been found more commonly among male gender and exacerbates with increasing age.[3] A recent study found strong correlation between age and NAFLD.[7] A longitudinal study also found significant association of NAFLD with increasing age ($P < 0.001$).[8] A cross-sectional study found significant correlation between NAFLD with higher risk of Type 2 diabetes in male gender of middle and older age than the female gender.[9]

Recent studies have reported significantly higher levels of thyroid stimulating hormone (TSH) among NAFLD patients, suggesting a possible link between Hypothyroidism and NAFLD. However, the extent and clinical relevance of this association are constantly under investigation. [10]

Hypothyroidism refers to endocrine disorder wherein thyroid gland fails to produce sufficient thyroid hormone, affecting nearly 10-32% of the global population, with a rising trends in morbid condition and mortality rate.[11-13] Thyroid hormone hormones are vital for lipid metabolism, metabolic functions, and mitochondrial function and even a slight thyroid dysfunction may result in lipid accumulation in hepatocytes and fibrosis. [11,14,15] Recent research suggests hypothyroidism as an under-recognized risk factor of NAFLD, where Thyroid-stimulating hormone (TSH) significantly contributes to hepatic steatosis through modulating the lipid regulatory genes and direct effect on liver regardless of circulating thyroid hormone levels.[13]

The global prevalence of NAFLD in adults is estimated to be approximately 38%, with age-standardized point prevalence of 15,018 cases per 100,000 populations and annual emergence of 608 fresh cases per 100,000 population. It is more common in men (15,731 cases per 100,000) than women (14,311 cases per 100,000), with highest prevalence in age groups of 45–49 years in men and 50–54 years in women. The prevalence rose from 13.2 to 16.9% during 2010-2021 in neighboring counties of Pakistan, specially India and China respectively.[16] Pakistan, on the other hand, is facing an increasing prevalence of 14-47% for NAFLD in general population.[17]

Developing epidemiological overlap between non-alcoholic fatty liver disease (NAFLD) and endocrine disorders, such as hypothyroidism, highlights the need for integrated clinical approaches that bridge hepatology and endocrinology. Despite international evidence suggesting a potential association between hypothyroidism and NAFLD, there is a lack of local data exploring this interaction in Pakistan, particularly within the Sindh province. However, this study aims to determine the frequency of hypothyroidism among clinically diagnosed NAFLD patients in this population, providing evidence to inform future clinical screening and management strategies.

Methodology

This descriptive cross-sectional study was conducted in the Department of Medicine, Liaquat University Hospital, Hyderabad, over a six-month period from January 7, 2023, to July 6, 2023. Ref No CPSP/REU/MED-2019-164-14949 Sample of 150 cases was calculated based on the lowest reported prevalence of hypothyroidism in NAFLD at 16.8%, and with a margin of error of 6% at a 95% confidence level, the calculated sample size was 150 patients with NAFLD. A non-probability consecutive sampling technique was used. All the patients aged 20 to 60 years of either gender, who had been diagnosed with NAFLD for at least three months, and presented with symptoms such as abdominal discomfort, bloating, dyspepsia, fatigue, somnolence, or weight gain for a duration of at least four weeks, were included. All the known cases with hyperthyroidism, alcohol consumption, patients on corticosteroids, immunocompromised patients, patients on pyrazinamide, thiazides, lipid-lowering or antioxidant therapy, as well as those receiving thyroxin, vitamins, or mineral supplements were excluded. Additionally patients with chronic liver disease, chronic viral hepatitis, chronic renal failure, and pregnant or lactating women were also excluded. Study was done after approval from the CPSP and informed consent from participants; eligible patients were enrolled from the outpatient department. Complete medical history, clinical examination, blood sampling, and data collection were performed by the principal investigator.

For assessment of hypothyroidism, a 2cc venous blood sample was drawn using a 5cc disposable syringe and sent to the laboratory for analysis. NAFLD was diagnosed based on characteristic ultrasound findings (bright liver, vessel blurring, and narrowed hepatic veins) in the absence of alcohol use or steatogenic medications. Hypothyroidism was defined by clinical symptoms (fatigue, somnolence, weight gain) along with elevated TSH (>4.50 μIU/mL) and normal FT4 (0.8–1.8 ng/dL) and FT3 (1.4–4.4 pg/mL) levels. All financial costs related to the study were borne by the researcher. After data collection by study proforma analysis was carried out by SPSS version 21.0. Frequencies and percentages

were calculated for categorical variables. Mean and standard deviation or median with interquartile range (IQR) was computed for quantitative variables. Stratification was performed for potential effect modifiers. Post-stratification associations were analyzed using chi-square test taking a p-value ≤ 0.05 as statistically significant.

Results

This study included 150 participants with an overall mean age of 39.56 ± 10.45 years, comprising 54.7% males and 45.3% females. A majority (58%) resided in urban areas, while 42% were from rural regions. Educational status varied, with 24.7% being illiterate and 16% having higher education. Regarding smoking habits, 47.3% were current smokers, 20.7% were ex-smokers, and 32% had never smoked. Clinically, 59.3% had hypertension and uncontrolled diabetes mellitus, while 62% presented with hyperlipidemia. Both obesity and a low AST to ALT ratio were observed in 58% of participants and 50% had low platelet counts. The average duration of disease was 8.64 ± 2.72 weeks, and the mean HbA1c level was 7.48 ± 2.08%. (Table I)

Table 1: The demographic and clinical variables information of NAFLD patients (n=150)

PARAMETER	(n=150)	(%)
GENDER		
Male	82	54.7
Female	68	45.3
RESIDENCE		
Urban	87	58.0
Rural	63	42.0
EDUCATIONAL STATUS		
Illiterate	37	24.7
Primary	28	18.7
Middle	26	17.3
Secondary	35	23.3
Higher	24	16.0
Smoking		
Yes	71	47.3
No	48	32.0
Ex-smoker	31	20.7
Hypertension		
Yes	89	59.3
No	61	40.7
Hyperlipidemia		
Yes	93	62.0
No	57	38.0
Uncontrolled Diabetes Mellitus		
Yes	89	59.3
No	61	40.7
OBESITY		
Yes	87	58.0
No	63	42.0
LOW AST TO ALT RATIO		
Yes	87	58.0
No	63	42.0
LOW PLATELET COUNT		
Yes	75	50.0
No	75	50.0
Quantitative variables		
Age (yrs)	39.56 ± 10.45	
Duration of disease (wks)	8.64 ± 2.72	
HbA1c (%)	7.48 ± 2.08	

Overall hypothyroidism frequency was 28%. (**Figure 1)**

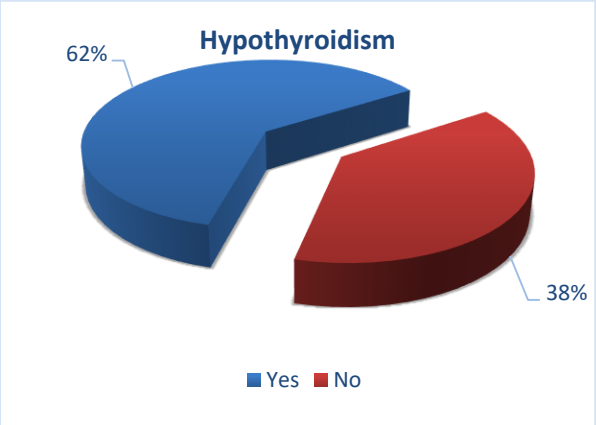

Figure I: Distribution of Hypothyroidism.

According to the post-stratification analysis among 150 patients showed that hypothyroidism was significantly more common in females (57.9%) than males (42.1%) and in rural residents (54.4%) compared to urban (45.6%) (p- 0.01). Additionally, there was also significant association of hypothyroidism with and longer disease duration, Hypertension (p = 0.04), obesity and smoking status (p-0.001), while no significant difference was found across different age groups (p = 0.93). (Table II)

Table II: Post stratification for hypothyroidism. (n=150)

Demographic Variables	HYPOTHYROIDISM No 93 (62%)	HYPOTHYROIDISM Yes 93(38%)	Total	P-Value
Age (years)				
20-29	13(14.0%)	10(17.5%)	23(15.3%)	
30-39	20(21.5%)	12(21.1%)	32(21.3%)	
40-49	29(31.2%)	16(28.1%)	45(30.0%	**0.93**
50-60	31(33.3%)	19(33.3%)	50(33.3%)	
Total	93(100.0%	57(100.0%)	150(100.0%)	
Gender				
Male	58(62.4%)	24(42.1%)	82(54.7%)	
Female	35(37.6%)	33(57.9%)	68(45.3%)	**0.01**
Total	93(100.0%)	57(100.0%)	150(100.0%)	
Residence				
Urban	61(65.6%)	26(45.6%)	87(58.0%)	
Rural	32(34.4%)	31(54.4%)	63(42.0%)	**0.01**
Total	93(100.0%)	57(100.0%)	150(100.0%)	

Duration of Disease				
4-6	44(47.3%)	16(28.1%)	60(40.0%)	
7-9	24(25.8%)	24(42.1%)	48(32.0%)	**0.04**
>10	25(26.9%)	17(29.8%)	42(28.0%)	
Total	93(100.0%)	57(100.0%)	150(100.0%)	
Hypertension				
Yes	61(65.6%)	28(49.1%)	89(59.3%)	
No	32(34.4%)	29(50.9%)	61(40.7%)	**0.04**
Total	93(100.0%)	57(100.0%)	150(100.0%)	
Smoking				
Yes	52(55.9%)	19(33.3%)	71(47.3%)	
No	31(33.3%)	17(29.8%)	48(32.0%)	**<0.01**
Ex-smoker	10(10.8%)	21(36.8%)	31(20.7%)	
Total	93(100.0%)	57(100.0%)	150(100.0%)	
Obesity				
Yes	61(65.6%)	26(45.6%)	87(58.0%)	
No	32(34.4%)	31(54.4%)	63(42.0%)	**0.01**
Total	93(100.0%)	57(100.0%)	150(100.0%)	

Discussion

The NAFLD is a multifactorial and globally prevalent liver disorder that has been increasingly linked to various metabolic and endocrine abnormalities, including hypothyroidism. In the present study, the prevalence of hypothyroidism was assessed among 150 clinically diagnosed NAFLD patients aged between 20 and 60 years. The study population showed a predominance of male participants (54.7%), urban residents (58%), and individuals with no formal education (24.7%). These demographic findings were comparable to the study by Parikh et al.[18] According to this study, the most commonly observed associated conditions among NAFLD patients were smoking (47%), hypertension (59.3%), hyperlipidemia (62%), diabetes (57.3%), obesity (58%), low AST to ALT ratio (58%). These findings align with those of Mansour-Ghanaei et al[19] who reported a higher prevalence of NAFLD among patients with hypothyroidism, diabetes, hyperlipidemia, and hypertension, along with significantly elevated levels of fasting blood sugar, triglycerides, ALT, and total cholesterol ($p < 0.05$). Similarly, Abu-Freha et al[20] found that comorbid conditions such as diabetes mellitus (23.2%), obesity (58.8%), and hypertension (57.2%) were significantly more common among individuals with NAFLD ($p < 0.05$).

According to the present study, hypothyroidism was detected in 38% of patients with NAFLD. This prevalence is notably higher than that reported in previous studies like Pagadala et al[21] found a 21% prevalence of hypothyroidism in NAFLD patients and reported a 2.1-fold increased risk of NAFLD among those with hypothyroidism. Consistently, Parikh et al[22] and Almomani et al[23] reported hypothyroidism in 16.8% and 22.4% of NAFLD cases, respectively, while Hamidi et al[18] observed a prevalence of 19.5%. These consistently lower figures highlight a significant discrepancy compared to our findings and this may reflect regional, demographic, or methodological differences, but collectively, the studies underscore the important association between hypothyroidism and NAFLD. Regardless of the variation in prevalence, the overall evidence supports the need for thyroid function screening in patients with NAFLD.

Furthermore this study revealed significant associations between hypothyroidism and factors such as gender ($p < 0.01$), residence ($p = 0.01$), smoking ($p < 0.01$) and obesity ($p = 0.01$), while no significant association was found with age ($p = 0.93$). Our findings were aligned with the study by Ogbonna et al[24] where reported a significant link between thyroid dysfunction and female gender, elevated HbA1c levels, and central obesity ($p < 0.05$). Unnikrishnan et al[25] also reported consistent results, finding a strong association between vitamin D deficiency and gender ($p < 0.0001$), while age was not significantly related ($p = 0.153$), echoing our findings. However, in contrast to our results, Sajitha et al[26] found significant associations of hypothyroidism with female gender, diabetes, and older age ($p < 0.05$), and reported that age above 60 years and female were independent predictors of hypothyroidism. Additionally, unlike our study, hypertension did not show a significant association with hypothyroidism in that study. Some variations across the studies may because of the influence of population differences, comorbidity profiles, and diagnostic criteria, emphasizing the need for context-specific research and tailored clinical screening strategies.

Conclusion

The study revealed that hypothyroidism is highly prevalent among patients with NAFLD, indicating a strong association between the two conditions. It was more commonly observed in individuals with metabolic disorders such as obesity, hypertension, and diabetes. These findings underscore the importance of routine thyroid function screening in NAFLD patients, as early detection and management of hypothyroidism may help prevent progression to more severe liver complications. Future large-scale studies are essential to further explore

these associations and support integrated clinical management strategies.

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