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PROFILE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN HYPOTHYROIDISM AND ITS RELATIONSHIP WITH THYROID PROFILE

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Abstract

Background: The buildup of fat in the liver that is not caused by intake of too much alcohol, known as non-alcoholic fatty liver disease (NAFLD), is a major cause of cardiovascular illnesses. The frequency of NAFLD has significantly increased globally, particularly among Indians. While liver biopsy is the gold standard for diagnosing NAFLD, people whose disease has progressed to liver fibrosis can be identified using a non-invasive method called the NAFLD fibrosis score. Hypothyroidism is described to be one of the important risk factor of NAFLD. Patients with primary hypothyroidism had a 2.7-fold higher risk of developing NAFLD/ NASH (Non alcoholic steatohepatitis). However, there are few studies that reported variable association between hypothyroidism and liver steatosis. So, this study was conducted to study the profile of NAFLD among already diagnosed hypothyroid patients of the northeastern state of India (Manipur) and to evaluate the relationship between thyroid profile and NAFLD Fibrosis score(NFS).**Materials and Methods:** This is a Hospital based cross-Sectional Study conducted in Regional Institute of Medical Sciences (RIMS), Imphal for 2 years (January 2021 to October 2022). All patients above 18 years diagnosed with hypothyroidism attending Medicine OPD, Endocrinology Clinic and those admitted in Medicine ward, RIMS, Imphal were enrolled. Age, sex, height, weight, Body mass index (BMI) and waist circumference (WC) for every patient were recorded. Blood investigations like thyroid function test, fasting, post prandial blood glucose, lipid profile, liver function test and ultrasonography abdomen (for liver) were done for every patient. A USG fatty liver grading was also performed for no, mild, and moderate liver steatosis. NAFLD was determined by the presence of liver steatosis on ultrasonography, and a score was computed for low, middle, and high risk of fibrosis. SPSS 21 version was used for statistical analysis, Chi-square test, t test was used for inferential statistics and a p-value < 0.05 was considered significant. **Result:** A total 130 hypothyroid patients were enrolled in the study with mean age of 41.2 years and 99% of them females. Majority of the study subjects 72%, belonged to the range of BMI, 18.5-24.9 and 60% of them had WC above 85cm. Most of them (80%) had high TSH (>4.6), maximum (43%) had TG value in the range of 150-199 mg/dl, 41.5% had LDL level >100 mg/dl, 60% had values of HDL less than the normal value (<40mg/dl). There was a significant correlation between thyroid dysfunction, dyslipidemia and NAFLD. Majority of the study subjects (60%) had normal liver ultrasound, 30% had mild fatty liver, 10% had moderate fatty liver. Moderate fatty liver was present in study subjects with mean age of 51±7

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years (p value <0.001), mean BMI of25.45±2.41, mean WC of 91.46±5.13, mean TSH level of 9.02±2.47, mean T3 of 1.67±0.28, mean T4 of 7.38±1.93. Higher level of TSH is significantly associated with higher incidence of liver steatosis. At baseline, 60% of the study population had NFS <-1.5, 40% in range of -1.5-0.66 which at 6 months became 77.7% and 22.3% respectively. Among the patients with NFS in the range -1.5-0.66, 90% of them were found to have TSH>4.6, with a mean TSH of 8.81±3.93 and p-value= 0.05, which is statistically significant. For NFS <-1.5, 77% were found to have TSH>4.6, p-value= 0.017, which is statistically significant. From this comparison, we can infer that NFS of patients was improving at 6 months from baseline. **Conclusion:** The present study concluded a significant correlation between NAFLD and elevated TSH (hypothyroidism). Hypothyroidism plays important role in development of liver fibrosis and helps in progression of steatosis to fibrosis. Therefore, early diagnosis of fatty liver in hypothyroid patients and proper LT4 supplementation when indicated, may serve to control NAFLD. Primary and secondary prevention by managing the risk factors are the most important tools to control the epidemic of NAFLD.

INTRODUCTION

Non alcoholic fatty liver disease (NAFLD) is hepatic steatosis with no identifiable secondary cause of hepatic fat accumulation, such as significant alcohol consumption or long-term use of steatogenic medication. NAFLD is considered a hepatic feature of metabolic syndrome and its clinical presentation ranges from asymptomatic to full-blown liver cirrhosis.[1-2]NAFLD can be divided into two main histological categories, namely non-alcoholic fatty liver disease and non-alcoholic steatohepatitis which is the progressive type of NAFLD and can further induce liver cirrhosis and hepatocellular carcinoma.[3-5] The percentage of patients undergoing a liver transplant for NASH increased from 1.2% in 2001 to 9.7% in 2009. In the US, NASH is currently the third most common indication for liver transplantation.[2]

Liver biopsy is considered the gold standard for diagnosis and is the only method for differentiating NASH from steatosis with or without inflammation.[6] Increased-aminotransferase activities are the most common abnormality reported in patients with NASH. Usually, Alanine Transaminase (ALT) or Aspartate Transaminase (AST) are elevated only mildly to moderately in the range of a two- to fivefold elevated. Alkaline phosphatase (ALP) may be abnormally elevated two- to threefold, in fewer than half of patients. Serum albumin levels are almost always normal, and bilirubin levels are rarely abnormal, unless cirrhosis has developed.[7]

NAFLD is an independent risk factor for cardiovascular disease (CVD) and predicts future events, independently of other risk factors such as age, gender, low density lipoprotein (LDL) cholesterol, smoking and other features of metabolic risk factors. NAFLD is also associated with increased risk of all-cause mortality, contributed by liver related deaths as well as non-liver related causes such as malignancy, diabetes and coronary artery disease.[8]NAFLD fibrosis score is a validated, non-invasive tool for identifying patients whose NAFLD has advanced to liver fibrosis and recommended by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA) and the American College of Gastroenterology (ACG).[9] Patients who have a high score for NAFLD fibrosis could require further testing, such as liver biopsies or elastography. Advanced liver fibrosis can be accurately diagnosed in people whose NAFLD fibrosis score is more than 0.676. It is highly accurate to rule out advanced liver fibrosis in patients whose NAFLD fibrosis score is less than -1.455. A score of 0.676 to -1.455 is regarded as "indeterminate."[9]A Japanese study reported that the NFS holds an acceptable sensitivity, specificity and positive and negative predictive values for advanced liver fibrosis of 100%, 83%, 63%, and 100%, respectively.[10] The score also identifies patients at low risk who should be reassured and/or followed at periodic intervals.

Another non-invasive modality used to assess fatty liver or fibrosis is Ultrasound Elastography of Liver, also known as Fibroscan,[11] with a main objective of determining the presence or absence of advanced fibrosis. The prevention and treatment of NAFLD have become the focus of medical research in recent years and identifying the risk factors is critical to develop effective preventive interventions against NAFLD.

Hypothyroidism is a common disease of the endocrine system. Thyroid hormones has a critical role in cell metabolism and energy homeostasis and also for the more important fact that there is association of numerous diseases with thyroid dysfunction. In United States, the prevalence of hypothyroidism is 3.7% by the National Health and Nutritional Examination Survey (NHANES).[8] Other studies reported the prevalence of subclinical and overt hypothyroidism to be 4%–10% and 0.3%–5% in the general population.[8]Unnikrishnan et al found overall prevalence of hypothyroidism in India to be 10.95% within the range of 8.88% to 21.8% in

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eight different cities. Additionally,8.02% were diagnosed to have subclinical hypothyroidism[12] Hypothyroidism comprises of subclinical hypothyroidism and overt hypothyroidism. Subclinical hypothyroidism (SCH) is considered as a disease with an elevated thyroid-stimulating hormone (TSH) level than normal range, normal serum free thyroxine (fT4) level and absence of obvious clinical manifestations. Overt hypothyroidism is defined as a disease with elevated TSH level with lower fT4 level and it may be accompanied by obvious clinical manifestations.

Importantly thyroid hormones interact on hepatic lipid homeostasis through multiple pathways including stimulation of free fatty acid delivery to the liver for re-esterification of triglycerides, and increasing fattyacid Beta-oxidation thereby affecting hepatic fat accumulation. Early identification of at-risk patients is important since treatment of the hypothyroidism may reduce the risk of NAFLD and its potential complications.[13] Insulin resistance in the setting of hypothyroidism has been documented and is associated with decreased responsiveness of glucose uptake in the muscle and adipose tissue to insulin, as well as decreased glycogen synthesis in skeletal muscle in both human and animal studies. These effects were alleviated by thyroid replacement.[14]

Hypothyroidism is also more common in patients with diabetes than in general population. If hypothyroidism accelerate liver injury in NAFLD which may be explained by the fact that in NAFLD patients, the degree of insulin resistance is enhanced by hypothyroidism and there may be a rise in the already high levels of lipolysis and the release of free fatty acids to the liver.[15]

It is suggested by recent data that there may be association of hypothyroidism with NAFLD. Different studies in India also showed significant association.[16-28]However, clinical data supporting this association are incomplete and the underlying pathophysiology remains unclear. Moreover, there are some studies which have reported no association at all.[29-35]Additional information is needed to confirm the proposed association between NAFLD and hypothyroidism, therefore conducting more study is essential.

MATERIALS AND METHODS

This is a Hospital based Cross-Sectional Study conducted in Regional Institute of Medical Sciences (RIMS), Imphal for 2 years (January 2021 to October 2022). All patients diagnosed with hypothyroidism attending Medicine OPD, Endocrinology Clinic and those admitted in Medicine ward, RIMS, Imphal were enrolled.

-Inclusion criteria included patients diagnosed with hypothyroidism (overt and subclinical), aged above 18 years.

-Exclusion criteria included patients with history of alcoholism, those who are diagnosed with Hepatitis B or C infection, autoimmune hepatitis, pregnant women, diabetic patients and those not willing to participate in the study

Sample size:

Based on the study conducted by MC Srivastava sample size is calculated as

$N=4PQ/l^2$, where P is prevalence = 53.9%, Q is (100-P) = 46.1, L is the absolute allowable error = 8% at 95% confidence interval

Thereby substituting the values, N= 4 x (53.9) x (46.1)/ 64 = 155.2. Therefore, sample size is taken as 155.

Study variables

Independent variable: T3, T4, TSH level, age, sex, BMI

Dependent variable: NAFLD Fibrosis score.

Working definition

Overt hypothyroidism: Serum TSH level >10mIU/L

Subclinical hypothyroidism: Serum TSH level of >4.68mIU/L with T4 level between 4.4 mcg/dl and 11.6 mcg/dl

Euthyroidism: Serum TSH level between 0.465 and 4.68mIU/L, with T4 level between 4.4 mcg/dl and 11.6 mcg/dl

NAFLD: Defined by the presence of liver steatosis on ultrasonography.

NAFLD Fibrosis Score:

<-1.5 = Low probability of fibrosis

-1.5-0.6 = Intermediate probability

>0.6 = High probability

USG Fatty liver grading;

No steatosis (Grade 0)- Normal echogenicity of liver parenchyma; normal visualization of diaphragm and intrahepatic blood vessel

Mild steatosis (Grade 1)-Slightly increased echogenicity of liver parenchyma; normal visualization of diaphragm and intrahepatic blood vessels

Moderate steatosis (Grade 2)- Markedly increased echogenicity of liver parenchyma; slightly impaired visualization of diaphragm and intrahepatic blood vessels

Severe steatosis (Grade 3)- Severely increased echogenicity of liver parenchyma; poor or no visualization of diaphragm and intrahepatic blood vessels and posterior part of the right lobe of liver.

Study procedure

A predesigned proforma including age, sex, etc and detailed physical examination of every patient was done. Height, weight and waist circumference for every patient were taken.

Ultrasonography of Liver was done by Samsung Medisonco.Ltd. Model HS70A

Blood sample collected and sent for parameters like:

Thyroid Function Test:

by Johnson & Johnson Vitros Chemilluminescence analyzer DBT/BIO/EQUIP/7

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Fasting and post-prandial blood glucose: by Randox Glucose Kit Cat. No. GL3815,UK using GOD/PAP method

Fasting lipid profile: by Enzymatic colorimetric test with lipid clearing factor (LCF) using kits marketed by Human Gessellschaft fur Biochemica and DiagnoticambH through its Indian branch and also using Randox series Rx Imola Auto analyzer (manufactured in UK)

Platelet count: using automated analyser; Mindraybc 5150(Manufactured in China)

Liver Function Test: by IFCC (UV method) using Randox Rx IMOLA auto analyzer (Manufactured by United Kingdom)

HBsAg and HCV Ab: by Lateral flow Immunochromatography (kit test)

NAFLD Fibrosis Score was calculated and recorded on two occasions- 1st encounter (Baseline) and after 6 months.

NAFLD Fibrosis Score is calculated by the formula:

= -1.675 + 0.037 x age(years) + 0.094 x BMI (kg/m^2)

+1.13 x FG/Diabetes (yes=1, no=0)+0.99 x AST/ALTratio-0.13x Platelet -0.66 x albumin (g/dl)

Statistical analysis:

Statistical Package for the Social Sciences, SPSS 21 version was used for statistical analysis. Descriptive statistics like mean, Standard Deviation and percentage were used. Chi-square test, t test was used for inferential statistics. A P-value < 0.05 was taken as significant.

Ethical clearance was obtained from the Research Ethics Board (Ref.No.A/206/REB-Comm (SP)/RIMS/2015/705/47/2020). Informed consent was obtained from the study participants before data collection, and confidentiality was maintained by limiting the identifying variables to a minimum.

RESULTS

A total 130 hypothyroid patients after informed consent were enrolled in the study. The baseline characteristics of the study subjects were given in [Table 1]. The mean age of the study population was 41.2 years and 99% of them females. Majority of the study subjects 72%, belonged to the range of BMI, 18.5-24.9 and 60% of them had waist circumference above 85cm. Most of them (80%) had high TSH (>4.6), maximum (43%) had TG value in the range of 150-199 mg/dl, 41.5% had LDL level >100 mg/dl, 60% had values of HDL less than the normal value (<40mg/dl).This observation points to a possible correlation between thyroid dysfunction, dyslipidemia and NAFLD. Majority of the study subjects (60%) had normal liver ultrasound, 30% had mild fatty liver, 10% had moderate fatty liver. The mean age of patients with moderate fatty liver was 51±7 years, mild fatty liver was 42±8 with a p value <0.001, suggesting higher prevalence of fatty liver in older age group. Comparison of clinical variables according to grades of fatty liver by USG was given in [Table 2]. Among the patients with moderate fatty liver, the mean BMI was 25.45±2.41, mild fatty liver was 24.99±1.79 which is statistically significant, suggesting that fatty liver is related to higher BMI. Among the patients with moderate fatty liver the mean WC was 91.46±5.13, among mild fatty liver was 88.39±8.2, which was statistically significant, suggesting the direct correlation between presence of fatty liver and higher waist circumference.

Association between USG liver and thyroid profile was shown in [Table 3]. The mean TSH level among the patients with moderate fatty liver was found to be 9.02±2.47, and that of patients with mild fatty liver was 7.56±4.03. Higher level of TSH is significantly associated with higher incidence of liver steatosis. The mean T3 of the patients with moderate fatty liver was 1.67±0.28, and 1.82±0.49 for the mild fatty liver, p- value= 0.39, which was not statistically significant. The mean T4 of the patients with moderate fatty liver was 7.38±1.93, and 7.53±1.65 for the mild fatty liver. P value 0.5, which is not statistically significant. NFS at baseline and 6 months was shown in [Table 4]. TSH-frequency distribution in relation to NFS at baseline and after 6 months were given in [Table 5 and 6] respectively. At baseline, 60% of the study population had NFS <-1.5, 40% in range of -1.5-0.66 which at 6 months became 77.7% and 22.3% respectively. Among the patients with NAFLD Fibrosis score in the range -1.5-0.66, 90% of them were found to have TSH >4.6, with a mean TSH of 8.81±3.93, p-value= 0.05, which is statistically significant. For the NFS < -1.5, 77% were found to have TSH > 4.6, p-value= 0.017, which is statistically significant. From this comparison, we can infer that NAFLD Fibrosis score of patients was improving at 6 months from baseline.

Table 1: Baseline characteristics of study subjects (N = 130).

Characteristics	Study patients (N = 130), n (%)
Age (in years)	
≤30	18 (13.8%)
31-40	41 (31.5%)
41-50	47 (36.2%)
>50	23 (17.7%)
Gender	
Male	1 (0.8%)
female	129 (99.2%)
BMI (Kg/m^2)	
<18.5	0 (0%)

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18.5-24.9 25-29.9 >30	93 (71.5%) 35 (26.9%) 2 (1.5%)
Waist circumference (cm) <75 75-85 >85	 9 (6.9%) 43 (33.1%) 78 (60%)
TSH (mIU/ml) <0.46 0.46-4.6 >4.6	 0 (0%) 26 (20%) 104 (80%)
T3 (ng/ml) <1.49 1.49-2.6 >2.6	 25 (19.2%) 97 (74.6%) 8 (6.2%)
T4(mcg/dl) <4.4 4.4-11.6	 41 (31.5%) 89 (68.5%)
Triglyceride (mg/dl) <150 150-199 >199	 44 (33.8%) 56 (43.1%) 30 (23.1%)
Low density lipoprotein (mg/dl) <100 100-129 >129	 76 (58.5%) 41 (31.5%) 13 (10%)
High density lipoprotein(mg/dl) <40 >40	 74 (56.9%) 56 (43.1%)
USG Liver Normal Mild Moderate	 79 (60.8%) 38 (29.2%) 13 (10%)

Table 2: Comparison of clinical variables according to USG liver (N = 130)

Variables	Fatty Liver			Total	P Value
	Normal	Mild	Moderate		
Age in Years	37.77±9.94	45.26±8.09	50.15±7.48	41.2±10.19	<0.001**
BMI	23.85±2.28	24.99±1.79	25.45±2.41	24.34±2.23	0.005**
WC	82.73±9.06	88.39±8.2	91.46±5.13	85.26±9.06	<0.001**
TSH	7.41±4.32	8.28±4.31	10.24±3.61	7.94±4.3	0.075+
T3	1.87±0.52	1.82±0.49	1.67±0.28	1.84±0.49	0.391
T4	7.8±1.72	7.53±1.65	7.38±1.93	7.68±1.72	0.581
FBG	90.53±8.71	98.21±8.67	104.15±10.97	94.14±10.08	<0.001**
PPBG	117.84±12.95	128.45±15.47	137.46±16.23	122.9±15.52	<0.001**
Platelet	2.86±0.61	2.67±0.73	2.66±0.61	2.78±0.65	0.257
AST	34.8±8.24	36.97±7.05	40.54±8.29	36.01±8.06	0.039*
ALT	36.63±10.36	41.29±12.41	39.85±8.91	38.32±11	0.087+
S. Albumin	3.88±0.28	3.86±0.31	3.89±0.29	3.88±0.28	0.940
T. Cholesterol	197.23±31.89	217.74±30.33	251±28.98	208.6±35.24	<0.001**
TG	157.05±39.75	187.08±39.16	247.92±81.72	174.92±52.84	<0.001**
LDL	91.52±21.91	107.74±19.8	136.08±35.41	100.72±26.67	<0.001**
HDL	40.49±4.09	37.89±2.72	37.15±2.73	39.4±3.86	<0.001**

Table 3: Association between USG liver and thyroid profile (N = 130)

Variables	Fatty Liver			Total	P Value
	Normal	Mild	Moderate		
TSH	6.41±3.14	7.56±4.03	9.02±2.47	7.01±3.45	0.019*
T3	1.63±0.36	1.64±0.34	1.57±0.21	1.63±0.34	0.801
T4	7.43±0.91	7.18±1.06	7.45±0.72	7.36±0.94	0.391

Table 4: NAFLD Fibrosis Score at Baseline and 6 months (N = 130)

NAFLD Fibrosis Score	Baseline	6 Months	% Difference
<-1.5	78(60%)	101(77.7%)	17.7%
-1.5-0.66	52(40%)	29(22.3%)	-17.7%
>0.66	-	-	-

Table 5: TSH-frequency distribution in relation to NAFLD fibrosis score at baseline (N = 130)

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TSH	NAFLD FIBROSIS SCORE at Baseline		Total
	LESS THAN -1.5	-1.5-0.66	
<0.46	0(0%)	0(0%)	0(0%)
0.46-4.6	21(26.9%)	5(9.6%)	26(20%)
>4.6	57(73.1%)	47(90.4%)	104(80%)
Total	78(100%)	52(100%)	130(100%)
Mean ± SD	7.36±4.47	8.81±3.93	7.94±4.3

Table 6. TSH-2(6 months) frequency distribution in relation to NAFLD fibrosis score after 6 months (N = 130)

Tsh-2	NAFLD Fibrosis Score _6 Months		Total
	Less Than -1.5	-1.5-0.66	
<0.46	0(0%)	0(0%)	0(0%)
0.46-4.6	23(22.8%)	3(10.3%)	26(20.0%)
>4.6	78(77.2%)	26(89.7%)	104(80.0%)
Total	101(100%)	29(100%)	130(100%)
Mean ± SD	6.42±3.21	7.89±3.64	7.01±3.45

P=0.017*, Significant, Student t Test

DISCUSSION

In this study 130 hypothyroid patients were enrolled. The mean age of the patients studied was 41.2 years with most of them belonging to the age group 41-50 years (36.2%) and majority of them were female (99.2%).This finding is consistent to the study conducted by Grewal H et al,[21](mean age was 43.7 years and 86% of them were females). Unfortunately, there was gender imbalance among the study population. Majority of the patients (71%) have BMI in the range 18.5-24.9 which is the normal range for an Asian which is similar to the study by Tahara K et al,[16] (mean BMI was 23±3).In this study, 60% of the patients have WC above 85cm, 33% in the range 75-85cm.Since WC is a component of metabolic syndrome, increased WC is associated with hypothyroid state and fatty liver which was also observed in the study conducted by Bano A et al.[24]

The prevalence of dyslipidemia in our study was as high as 62.7%, more than half of the patients had TG in the range of 150-199mg/dl, similar to the study by Donghee K et al,[36] and more than half of the patient having LDL <100mg/dl and HDL <40mg/dl which is similar to the study conducted by Grewal H et al,[21] where the mean value was 61±26 and 34±9 respectively which was statistically significant. Serum TSH level is positively associated with deranged TG and HDL independent of thyroid hormones. Our study revealed that fatty liver is more prevalent in the higher age group of the population with mean age of 51±7 having moderate fatty liver. The mean BMI was 24.99±1 and mean WC was 88.39±8.2. This is similar to the one observed in the study conducted by Chung G et al,[37] in South Korea.

Thyroid hormones act as potent regulators of metabolic and energy homeostasis. Hypothyroidism reduces resting energy expenditure, lipolysis, and gluconeogenesis, increases weight, and increases cholesterol levels. Therefore, hypothyroidism leads to dyslipidemia, obesity, and insulin resistance, which are risk factors of the metabolic syndrome associated with NAFLD.[16]The findings of the present study agree in general that TSH elevation is an independent risk factor of NAFLD. Among the patients with moderate fatty liver, 92.3% were having high TSH. The mean TSH was 9.02±2.47 among the moderate fatty liver patients and 7.56±4.03 among the mild fatty liver group. The prevalence of NAFLD was significantly higher in patients with subclinical hypothyroidism than in those with euthyroidism, which is consistent with the study conducted by Taharaet al,[16] Mohanty R et al,[19] and various meta-analysis. Rashmi A, Manju P,[38] also found significant association between sub clinical hypothyroidism and NAFLD among children in age group 10-18 yrs. However, Jaruvongvanichet al,[33] have reported that NAFLD is not associated with thyroid hormone levels and hypothyroidism.

We also evaluated patients for liver fibrosis using non-invasive method, NAFLD Fibrosis Score (NFS). According to this score, the presence or absence of fibrosis can be assessed including the severity, although it is inferior to invasive methods. This score was calculated at baseline and after 6 months. We found that at baseline, 60% of the study population had NFS <-1.5, 40% in range of -1.5-0.66 which at 6 months became 77.7% and 22.3% respectively. NFS <-1.5 rules out fibrosis, -1.5-0.66indicates some degree of fibrosis. The proportion of patients with fibrosis reduced and the proportion without fibrosis increased after 6 months owing to the possible benefit from thyroxine supplementation. Among the patients with NFS in the range -1.5-0.66, 90% of them were found to have TSH>4.6, with a mean TSH of 8.81±3.93 (p-value= 0.05), which is statistically significant. The efficacy of NFS and other simple non-invasive methods were studied by McPherson S et al,[39] and Yun H et al,[40] which showed NPV of NFS to be 92% and PPV to be 52%. The other scoring systems used were AST/ALT ratio, BARD score and FIB-4.

Certain studies by Liu L et al,[14] in China reported that LT4 replacement treatment resulted in a reduction in the prevalence of NAFLD in significant SCH patients. Our study was not able to prove that LT4 supplementation resulted in better liver

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outcome in terms of NFS score compared 6 months apart.

The findings in the study conducted by Bano A,[24] demonstrated that low thyroid function is associated with an increased risk of developing NAFLD, as well as higher risk of having NAFLD with fibrosis. Therefore, it can be hypothesized that a hypothyroid state might accelerate the progression of liver steatosis to fibrosis. Alternatively, low thyroid function might contribute on the development of liver fibrosis, independently of steatosis. Additional prospective research is needed to address these underlying mechanisms and possible mediating role of cardiovascular risk factors.

CONCLUSION

The results of the present study confirmed a significant correlation between elevated TSH and nonalcoholic fatty liver disease in terms of imaging as well as non-invasive NAFLD Fibrosis score (NFS).Therefore, hypothyroidism is closely associated with NAFLD as an independent risk factor thereby confirming a relevant clinical relationship between these two diseases. Thereby early detection of fatty liver in hypothyroid patients and treatment of SCH with appropriate LT4 supplementation may be an effective means for controlling NAFLD.

Limitations:

Limitations in our study may be, the use of USG which may not be sensitive enough for mild steatosis though liver biopsy represents the gold standard for diagnosis of NAFLD, imbalance in gender distribution-majority females and lesser sample size due to COVID-19 pandemic. There was no classification between patients taking LT4 and not taking, although 80% of them were on LT4 supplementation.

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