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Association of Elevated Lipid Profiles and Fatty Liver Prevalence in Uncontrolled Hypothyroidism: A Case - Control Study

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Abstract: ***Nonalcoholic fatty liver disease is a chronic condition due to increased accumulation of fat in the liver in the absence of excess alcohol consumption. Identifying the risk factors and diseases linked to the pathophysiology of fatty liver is important in effectively employing preventive interventions against nonalcoholic fatty liver disease owing to its progressive complications. Hypothyroidism is the common endocrine disease implicated in the derangement of lipid metabolism promoting the development of fatty liver. Aim of the study: The study aims to identify the prevalence of fatty liver in uncontrolled hypothyroid patients and controlled hypothyroid patients and its relation with the lipid profile parameters. Materials and Methodology: A case control study was performed between 25 Uncontrolled hypothyroid patients and 25 controlled hypothyroid patients. Results: The increased levels of lipid profile in uncontrolled hypothyroid group compared to controlled hypothyroid group were statistically significant (p<0.001). The prevalence of fatty liver is 3.5 times increased in uncontrolled hypothyroid group compared to controlled hypothyroid group. Conclusion: The study clearly states that control of hypothyroidism is mandatory to minimize its effect on development of fatty liver.***

Keywords: Hypothyroidism, fatty liver, dyslipidemia

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is a chronic condition due to increased accumulation of fat in the liver in the absence of excess alcohol consumption. It can be classified into simple fatty infiltration (steatosis), fat and inflammation (non - alcoholic steatohepatitis) and cirrhosis in the absence of excessive alcohol consumption. Simple steatosis does not cause morbidity, while non - alcoholic steatohepatitis is linked to progressive fibrosis, cirrhosis and hepatocellular cancer. NAFLD is strongly associated with obesity, dyslipidemia, insulin resistance and type 2 diabetes mellitus and so may be considered to be the hepatic manifestation of the metabolic syndrome. Several studies state that its metabolic substrates share the pathogenic factors with hypothyroidism also. The prevention and treatment of NAFLD have become the focus of medical research in recent years, and identifying the risk factors for NAFLD is critical to develop effective preventive interventions against NAFLD[1]. Identifying the risk factors and diseases linked to the pathophysiology of fatty liver is important in effectively employing preventive interventions against nonalcoholic fatty liver disease. Hypothyroidism which is the common endocrine disease implicated in the derangement of lipid metabolism causing dyslipidemia. Several studies suggested its crucial role in development of nonalcoholic fatty liver disease and treatment to hormone deficiency may improve liver condition[2]. This study was conducted in the hope to raise awareness among clinicians about the possible liver impairment in endocrine pathologies as well as the need for evaluation of NAFLD in hypothyroid patients for better management and outcome.

The aim of the study was to compare the lipid profile between controlled hypothyroidism and uncontrolled hypothyroidism and to identify the prevalence of fatty liver in controlled and uncontrolled hypothyroid patients.

2. Materials and Methodology

Study type

A case control study was conducted on 50 patients with 25 uncontrolled hypothyroid patients and 25 controlled hypothyroid patients in a tertiary care hospital in Coimbatore. The variables measured were age, sex, hypothyroid status, tT3, tT4, TSH, total cholesterol, serum triglyceride, HDL - C, LDL - C, USG Abdomen.

Inclusion criteria:

Controlled hypothyroid group - previously diagnosed with hypothyroidism on regular treatment with no history of alcoholism

Uncontrolled hypothyroid group – previously diagnosed with hypothyroidism on irregular treatment or persistent symptoms even after treatment (refractory to treatment), inappropriately reduced dose of thyroxine supplement with no history of alcoholism.

Exclusion criteria:

Alcoholics, Hypertension, diabetes mellitus, renal failure and liver cirrhosis

Age of the study population was 25 - 45 years with female predominance. The present thyroid status was identified by measuring total T3, total T4, Thyroid stimulating hormone (TSH) using Chemiluminescence immunoassay technique. Total cholesterol, Serum triglyceride, HDL - C were

measured using Fully automated analyzer ERBA XL640. LDL - C was calculated using Friedewald formula.

In this study, tT3, Tt4, TSH, Total cholesterol, serum triglyceride, HDL - C, LDL - C were estimated and compared between controlled hypothyroid patients and uncontrolled hypothyroid patients. Also, Ultrasound abdomen was taken to identify and compare the prevalence of fatty liver in both the groups.

5mL of venous blood sample was collected in a plain serum tube and centrifuged at 300rpm for 15 minutes and serum was separated and used for estimation of analytes tT3, tT4, TSH, Total cholesterol, serum triglyceride, HDL - C.

Results are presented as Mean ± SD. Student t test was performed to find the significance of study parameters between the groups. Statistical analysis was done using GraphPad Prism8 and p value < 0.001 was considered to be statistically significant.

3. Results

On comparison of the general characteristics of the study groups, the mean age of the both the study groups were 35±10 years. The gender distribution was predominantly females with 85% of sample population. The Mean ± SD are as shown in Table 1. The levels of tT3, tT4 and TSH in both the groups were statistically significant (p<0.001) showing increased levels of thyroid hormones in uncontrolled hypothyroid group compared to controlled hypothyroid group as in Fig 1.

The Mean ± SD of total cholesterol and serum triglyceride and LDL - C in controlled and uncontrolled hypothyroid groups were 200 ± 34.37, 142 ± 13.95, 131 ± 34.33 and 383 ± 71.71, 448 ± 100.01, 263 ± 56.8 respectively. The Mean ± SD values of HDL - C in controlled and uncontrolled hypothyroid groups were 41 ± 2.59 and 30 ± 3.24 respectively. This lipid profile clearly shows statistical significance (p<0.001) in both the groups showing striking dyslipidemia in uncontrolled hypothyroid group compared to controlled hypothyroid group as in Fig 2.

The prevalence of fatty liver identified by USG Abdomen showed a 3.5 times higher prevalence in uncontrolled hypothyroid group compared to controlled hypothyroid group as in Fig 3.

Table 1: This table explains the Mean ± SD and statistical significance of tT3, tT4, TSH, total cholesterol, serum triglyceride, HDL - C, LDL - C in controlled hypothyroid and uncontrolled hypothyroid groups.

	Controlled Hypothyroidism	Uncontrolled Hypothyroidism	P Value
T3	1.68 ± 0.33	0.47 ± 0.13	<0.001
T4	8.5 ± 2.0	3.77 ± 0.85	<0.001
TSH	3.06 ± 0.93	84 ± 8.56	<0.001
Total Cholesterol	200 ± 34.37	383 ± 71.71	<0.001
Triglyceride	142 ± 13.95	448 ± 100.01	<0.001
HDL - C	41 ± 2.59	30 ± 3.24	<0.001
LDL - C	131 ± 34.33	263 ± 56.8	<0.001

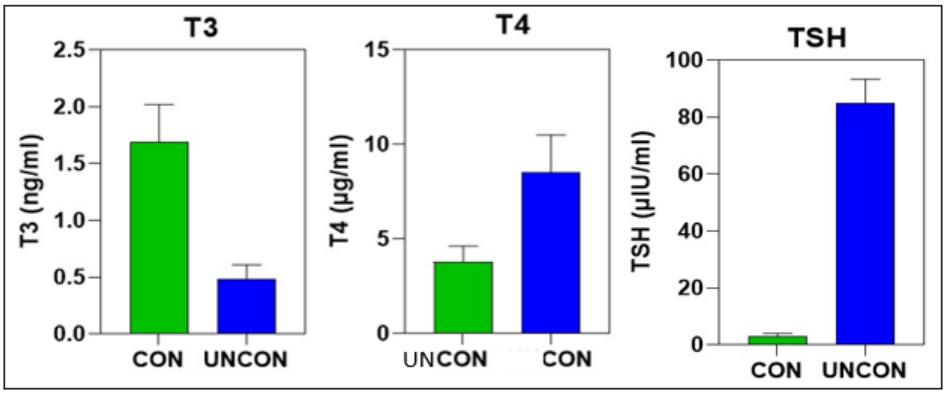

Figure 1: The bar diagram shows the significance of tT3, tT4, TSH between the controlled hypothyroid and uncontrolled hypothyroid group

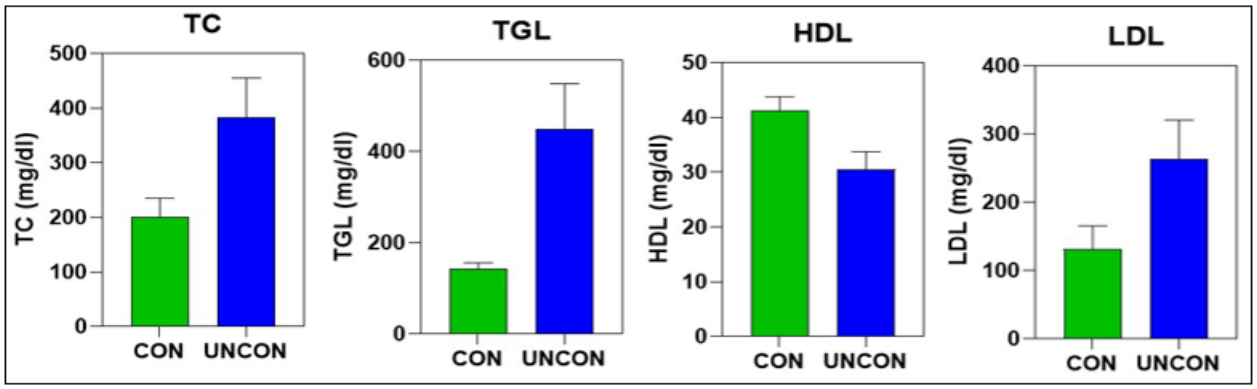

Figure 2: This is a bar diagram showing the significance of Total cholesterol, serum triglyceride, HDL - C, LDL - C in controlled and uncontrolled hypothyroid groups.

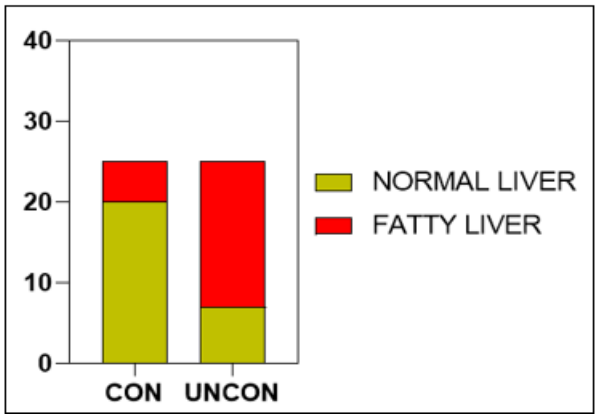

Figure 3: This bar chart shows the prevalence of fatty liver in controlled hypothyroid group and uncontrolled hypothyroid group

4. Discussion

NAFLD has become a significant public health problem due to its cardiovascular and metabolic risk factors. Hypothyroidism plays an important role in the pathogenesis of NAFLD. Weiwei He et al., Systemic review and Meta - analysis suggests epidemiological evidence for the obvious relationship between hypothyroidism and NAFLD, and the impact of hypothyroidism is independent from other known risk factors for NAFLD.4 Dyslipidaemia, obesity and insulin resistance proposed to the possible mechanisms which play a role in development of NAFLD. Insulin resistance can accelerate liver injury in NAFLD[5]. Thyroid hormones regulate lipid metabolism in the liver via thyroid hormone receptor beta, and they can decrease cholesterol and triglyceride levels. Low thyroid hormones explain the increased levels of cholesterol, triglyceride and LDL - C levels and reduced HDL - C levels. Hypercholesterolemia caused by hypothyroidism plays an important role in pathogenesis of NAFLD. Also, many studies have proposed oxidative stress can be observed in hypothyroidism patients which can increase cellular injury and insulin resistance by reducing beta oxidation of fatty acids and increasing peroxidation of lipids. Oxidative stress is one of the mechanisms of NAFLD.[5, 6]

Pagadala et al states that another hypothesis involved can be altered adipokine levels in hypothyroidism[6]. The altered adiponectin levels can promote oxygen radical release and cause liver inflammation and fibrosis.[7] High levels of leptin is seen in hypothyroid patients which can promote hepatic collagen synthesis and thereby hepatic fibrosis.[8, 9]

Patient education on screening of NAFLD in all hypothyroid patients becomes mandatory as they are more prone for developing NAFLD. Strict regular treatment and screening for NAFLD is of societal concern as the patient may present late with uncontrolled hypothyroidism and full - blown cirrhosis liver if NAFLD is left undiagnosed. Appropriate treatment with levothyroxine supplements and hypolipidemic drugs can prevent or delay the complications and progression of NAFLD.[10]

5. Conclusion

The study clearly states that control of hypothyroidism is mandatory to minimize its effect on development of fatty liver. Advice of lifestyle changes and proper control of hypothyroidism with thyroid replacement therapy could improve disease progression and lead to better outcomes. Larger clinical trials are needed to support the study finding and thus would be beneficial in management of these combined diseases.

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