Original Research Article

Incidence of non-alcoholic liver diseases in hypothyroidism

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Abstract

Prevalence of hypothyroidisms is an alarming condition in India. It has been also observed that hypothyroidism is also associated with various other co morbidities of metabolic syndrome due to the crucial role of thyroid hormone in metabolism. Hypothyroidism has been identified as an important risk factor for both hepatic and cardiometabolic mortality. Endocrine hormones play an important role in various key metabolic processes and their dysfunction leads to metabolic abnormalities. Thyroid hormone plays an important role in energy homeostasis, lipid and carbohydrate metabolism, regulation of body weight and adipogenesis. Its dysfunction may alter various metabolic processes. Abnormal lipid metabolism may lead storage of fat in liver which is known as non alcoholic fatty liver disease (NAFLD) and non alcoholic steatohepatitis (NASH). Hypothyroidism is prevalent among patients with NAFLD/NASH. The present study observed significant increase in circulatory levels of ALT and AST in hypothyroidism patients than control.

Key Word: Thyroid dysfunction, Hypothyroidism, Non alcoholic steatohepatitis, Non alcoholic fatty liver disease

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INTRODUCTION

Endocrine hormones play an important role in various key metabolic processes and their dysfunction leads to metabolic abnormalities. Thyroid hormone is needed for energy homeostasis, lipid and carbohydrate metabolism, regulation of body weight and adipogenesis[1,2]. Hypothyroidism is one of the common conditions in India. Many young patients have been reported to suffering with this condition. It has been observed that stress, and autoimmune mechanisms are major factors associated with hypothyroidism. A large population of hypothyroidism is suffering with underlined fatty liver disease which remains undiagnosed most of the time. Non alcoholic fatty liver disease (NAFLD) has a broader spectrum from simple fatty liver to non alcoholic steatohepatitis (NASH), which may progress to liver fibrosis, cirrhosis and hepatocellular carcinoma[3]. NAFLD is the most common cause of abnormal liver function tests worldwide in the people with sedentary life style, stress and food habits[4]. High incidence of NAFLD is suggests the abnormal lipid storage in liver in obesity and co morbidities.[5] Visceral obesity is one of the major risk factor for NAFLD[6-8]. In forth coming years NAFLD and NASH becoming the major cause of liver diseases than any other causes. Therefore, understanding the pathophysiology, risk factors can provide a new insight for newer treatment modalities of NAFLD/NASH. It has been observed that hypothyroidism has been associated weight gain and most of the fat storage take place in visceral cavity which leads to visceral obesity and with other co morbidities it develops metabolic syndrome[9,10]. The present study aimed to evaluate the association between NAFLD/NASH and hypothyroidism, and the proposed underlying mechanisms of this relationship. Many scientists studied the incidence of NAFLD and NASH in hypothyroidism. Chung *et al*[11], observed the prevalence of NAFLD with elevated alanine

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aminotransferase (ALT) and it was higher in patients with hypothyroidism. It has been also observed that the increased serum ALT level is a surrogate biomarker for NAFLD in the absence of other causes of liver disease. It is an indicator for the development of diabetes, cardiovascular disease and long term adverse complications from metabolic syndrome. They confirm the association between the severity of NAFLD and hypothyroidism. In another study Pagadala *et al*[12] reported that hypothyroidism was more common in patients with NASH compared to patients with NAFLD. This finding remained statistically significant after adjusting for other variables including age, diabetes, dyslipidemia and hypertension but not gender. The association between the severity of liver fatty infiltration and hypothyroidism is confirmed by liver biopsy and the NAFLD activity score to distinguish NASH from NAFLD. Mazo and co-workers did not find any statistically significant association between hypothyroidism, simple steatosis and NASH[13]. Some other studies also supported Mazo findings and reported no statistical significance[14,15]. TSH plays an important role in diagnosis of hypothyroidism. Hence increase in degree of TSH concentration can give a better idea about the undiagnosed hypothyroidism and relate the occurrence of fatty liver. In a study Carulli *et al*[16] observed that an increased serum TSH level is an independent risk factor for NASH compared to patients with NAFLD.

METHODOLOGY

The present study was conducted in Dr. D.Y. Patil Medical College and Hospital, Nerul, Navi Mumbai. Outpatient department (OPD) and Indoor patient department (IPD) were recruited in this study. A written informed consent was collected from all the study subjects. The study has been approved by the Institutional Ethics Committee.

Inclusion criteria: Hypothyroism patients were included as per the clinical diagnosis. Age and sex matched healthy individuals without clinical evidence of thyroid disorder and liver diseases were included as controls.

Exclusion criteria: Pregnant women, patients < 20 years of age, with Congenital Heart disease, acute or chronic infection, chronic liver and kidney disease.

Blood Sampling and Methodology: Fasting venous blood samples were collected from all the study participants. Routine biochemical tests were carried out on an autoanalyser using commercially available kits. Thyroid function tests, Liver function tests, lipid profile etc. were evaluated in clinical laboratory of D.Y Patil hospital and research center, Nerul, Navi Mumbai. Anthropometric measurements were also noted for all study participants. SPSS software (version 17) was used for Statistical analysis of the data. Demographic and biochemical data were expressed as mean ± S.D. Student't' test used to test the significance between cases and controls. The '*P*' value < 0.05 considered to be significant while < 0.01 is highly significant.

RESULTS

The study results were displayed in tabular and graphical forms. Table 1- shows the demographical characteristics of study subjects.

Table 1: Demographical Characteristics of study subjects

Variables	Controls (n=220)	Patients (n=256)	*P* value
Age	43.30(± 11.33)	47.47(± 15.53)	NS
BMI	24.80 (±3.68)	28.90 (±4.34)	0.005
WC	95.5 (±10.7)	100.44 (± 11.5)	0.001
WHR	0.96 (±0.68)	1.03(±0.35)	0.001
TG (mg%)	121.34 (±46.7)	148.46 (±76.34)	0.005
TC (mg%)	175.45 (±29.16)	200..28 (±52.56)	0.005
LDL (mg%)	100.26 (±34.24)	119.10 (±46.13)	0.005

The present study observed a significant increase anthropometric parameters and lipid parameters in patients than controls. TG and LDL have shown an increased pattern in circulatory levels in serum. TG [121.34 (±46.7)/121.34 (±46.7)] and LDL [119.10 (±46.13)/100.26 (±34.24)]

Table 2: Serum ALT and AST in Hypothyroidism

Variables	Hypothyroidism	Controls	*P* value
ALT(IU/L)	46.3± 3.8	19.24± 3.1	0.001
AST (IU/L)	36.8 ± 2.9	25.3 ± 2.6	0.005

A significant difference was found in circulatory levels of ALT in hypothyroidism patients than controls [46.3(± 3.8) /19.24(± 3.1)].

DISCUSSION

The present study observed high circulatory levels of ALT in hypothyroidism patients than normal. 45% patients with hypothyroidism reported to have higher levels of ALT. The abnormal lipid profile also indicates the importance of thyroid hormone in lipid metabolism. Hypothyroidism has been reported to be associated with obesity and metabolic syndrome [17,19]. The present study also reported high levels of TG, LDL-cholesterol in hypothyroidism patients. Metabolic abnormalities in hypothyroidism lead to NAFLD which can be converted into NASH in remain undiagnosed and untreated. While the underlying patho physiology for this association is still not clear, several mechanisms have been proposed by various study groups. A study by Brenta *et al* suggested that hypothyroidism and elevated TSH result in diminished hepatic lipoprotein lipase activity[20]. Thyroid hormones manipulate Hepatic Lipase (HL) and Lipoprotein Lipase (LPL) activities by different mechanisms. In hypothyroidism altered HL activity play an important role in the disturbance of cholesterol metabolism while higher levels of triglyceride is as a result alteration in LPL activity, which is responsible for TG lowering effect. Thyroid hormone controls the generation of cholesterol by regulating the activity of the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) enzyme and its degradation rate by regulating the expression of the SREBP-2 gene, the transcription factor that positively regulates the activity of LDL receptor [21,22]. Another mechanism is suggested that Hepatic damage through mitochondrial dysfunction is one of the theories based on oxidative stress and reactive oxygen species (ROS) production.[23]. Some studies described increased markers of oxidative stress such as serum malondialdehyde in hypothyroidism[24]. Elevated serum markers of oxidative stress have been observed in Hashimoto's thyroiditis patients with hypothyroidism [23,25]. Jarrar *et al* and Musso suggested that adipocytokines plays an important role in in NAFLD [26, 27], and some studies suggested a relationship between adipocytokines and hypothyroidism to clarify the mechanism of thyroid dysfunction and NAFLD. These studies failed to find an association between serum levels of adiponectin and hypothyroidism[28,29]. Various underlying mechanisms are associated with development of fatty liver in hypothyroidism. Hence despite the growing evidence of an association between hypothyroidism and NAFLD it's a difficult identify exact underlying mechanism for this association. In future more studies in this aspect can put some more light on this. So far some studies have failed to show an association between hypothyroidism and NAFLD. None of the present studies are interventional trials and placebo controlled clinical trials should be conducted to further elucidate the issue.

CONCLUSION

The study results concluded that high levels of ALT and AST have been observed in hypothyroidism, which is one of the risk factor for fatty liver. Hence the study suggests that patients with hypothyroidism should be screened for ALT and AST to prevent NAFLD and NASH.

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