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Clinical Study Of Hepatic Dysfunction In Hypothyroidism

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ABSTRACT

BACKGROUND

Non alcoholic fatty liver disease (NAFLD) is one of the most common disorders of the liver worldwide. Over the past decade, numerous studies have confirmed an association between thyroid dysfunction and NAFLD. Unfortunately, most studies have been characterized by a relatively small or selected study collection. Correlation between Hypothyroidism and NAFLD may be grounded in the association of reduced FT4 levels with hypertriglyceridemia and overweight.

NAFLD is defined as hepatic accumulation of fat in the absence of excess alcohol consumption. It is now the leading cause of the liver disease worldwide. Insulin resistance (IR) and genetic predisposition play a key role in its pathogenesis. NAFLD can be divided into two main histological categories: nonalcoholic fatty liver and nonalcoholic steatohepatitis (2). An increasing number of diseases such as cardiovascular disease, type 2 diabetes, chronic kidney disease, and cancer have been reported to be linked to NAFLD. 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.

Hypothyroidism is a common disease of the endocrine system that affects lifelong health. The physiological role of the thyroid gland, is not just due to the critical role of thyroid hormones but also on the cell metabolism and energy homeostasis. Hypothyroidism comprises subclinical hypothyroidism and overt hypothyroidism. Subclinical hypothyroidism is considered as a disease with elevated thyroid-stimulating hormone (TSH) level, normal serum free thyroxine (fT4) level and absence of obvious clinical manifestation. Overt hypothyroidism is defined as a disease with elevated TSH level and a lower fT4 level, and it may be accompanied by obvious clinical symptoms. Some studies have found that both overt hypothyroidism and subclinical hypothyroidism are associated with cardiovascular diseases and mortality. Some studies report that the prevalence of hypothyroidism is from 15.2 to 36.3% among patients with NAFLD, indicating that hypothyroidism is a common concomitant disease of NAFLD and may be related to the development of NAFLD. Thus, it is necessary to study the relationship between hypothyroidism and NAFLD risk.

This study aims to deduce the correlation of Hypothyroidism with NAFLD in a case control study.

MATERIALS AND METHODS

STUDY DESIGN ***:*** *Hospital based case control study.*
LOCATION OF STUDY : Tertiary Care Hospital in Assam.
STUDY POPULATION : Hypothyroid patients both male and female of age 13 years or more coming to outpatient or ward.
SAMPLE SIZE ***:*** *Taking into account 95 % confidence interval, odds ratio 3 and power of study 80 %, the number of cases was calculates as 103. An equal number of age and sex matched healthy individuals were also included in the study as controls with informed consent.*

RESULTS AND OBSERVATIONS

The majority of cases of hypothyroidism were in the age group of 41-50 years with mean age of 40.48+13.80. The majority of patients were female. The most common symptoms of overt hypothyroidism was fatigue and lethargy. It was also found that fatty liver, lower hemoglobin levels were significantly more in cases, than controls. The LFT values had greater derangement in cases than in controls. The derangement was further more in the overt hypothyroidism group.

CONCLUSIONS

The present study shows that both overt as well as sub-clinical hypothyroidism are associated with altered liver function in comparison to euthyroid individuals. The levels of liver enzymes progressively increase with the degree of hypothyroidism. The current study also reveals a direct association between TSH levels and the

subsequent risk of NAFLD and an inverse association between T4 levels and the subsequent development of NAFLD.
KEY WORDS ALT-Alanine Aminotransferase, AST- Aspartate Aminotransferase
BMI-Body Mass Index ,FT3-Free Triiodthyronine,FT4- Free Thyroxine
NAFLD-Non Alcoholic Fatty Liver Disease,NASH-Non Alcoholic Steatohepatitis
TSH-Thyroid Stimulating Hormone,WHR – Waist –to- Hip -Ratio

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I. Introduction

Hypothyroidism is the deficiency of thyroid hormones. Hypothyroidism may be subclinical or overt. Patients with Subclinical hypothyroidism have elevated TSH levels but normal T3 and T4 levels. Overt hypothyroidism describes moderate to severe thyroid failure resulting in high serum TSH levels and with low serum concentration of free T4. Thyroid hormones are essential for normal organ growth, development and function.

Thyroid hormones regulate the basal metabolic rate of all the cells, including hepatocytes, and thereby modulate hepatic function. The liver in-turn metabolizes the thyroid hormones and regulates their systemic endocrine effects. Therefore, normal thyroid function, essential for normal growth, development and regulation of energy metabolism within cells, depends on a normally functioning thyroid and liver axis. This study highlights the intricate relations between the thyroid gland and the liver in health and diseases.

AIMS AND OBJECTIVES OF THE STUDY
To study the alteration in hepatic function in patients of overt and subclinical hypothyroidism.

II. Materials and Methods

Study Design- Hospital Based Case control study
Study Population:- Hypothyroid patients of age 13 years or more attending a tertiary care centre in Assam
Inclusion Criteria

- Patients aged 13 years and above, presenting with signs, symptoms and thyroid function tests suggestive of overt or subclinical hypothyroidism.

EXCLUTION CRITERIA:

- Age less than 13 years.
- Individuals with significant alcohol consumption.
- Pregnant females.
- Patients with hepatocellular carcinoma and acute & chronic viral hepatitis.
- Chronic Kidney diseases.
- Previous history of abnormal surgery.
- Patients on drugs like OCP's, diuretics, tamoxifen, amiodarone, interferon, perchlorate, nitroprusside, sulfonylureas.

Ethical Aspect:- The protocol for the study was approved by the Institutional Ethics Committee and data were collected after receiving informed and written consent from the patient.
Diagnostic Tool
103 cases of Hypothyroidism and equal number of age and sex matched apparently healthy controls were selected for the study. The two groups were compared for ultrasonographic and biochemical evidence of hepatic dysfunction.
The diagnosis of Hypothyroidism was made on the basis of history, clinical examination and Thyroid function tests.
As per INDIAN THYROID SOCIETY AND ASSOCIATION OF PHYSICIANS, INDIA guidelines, serum reference ranges of thyroid function tests in adults are:

PARAMETER	NORMAL VALUES
T_3	0.9-2.78 mmol/L
T_4	58-140 mmol/L

TSH	0.5-4.7 mU/L
Free T_3	0.22-6.78 pmol/L
Free T_4	10.3-35 pmol/L

In our tertiary care hospital reference ranges of thyroid profile--

PARAMETER	NORMAL VALUES
T_3	0.7-2.2 ng/ml
T_4	5.5-135 ng/ml
TSH	0.5-4.5 µIU/ml

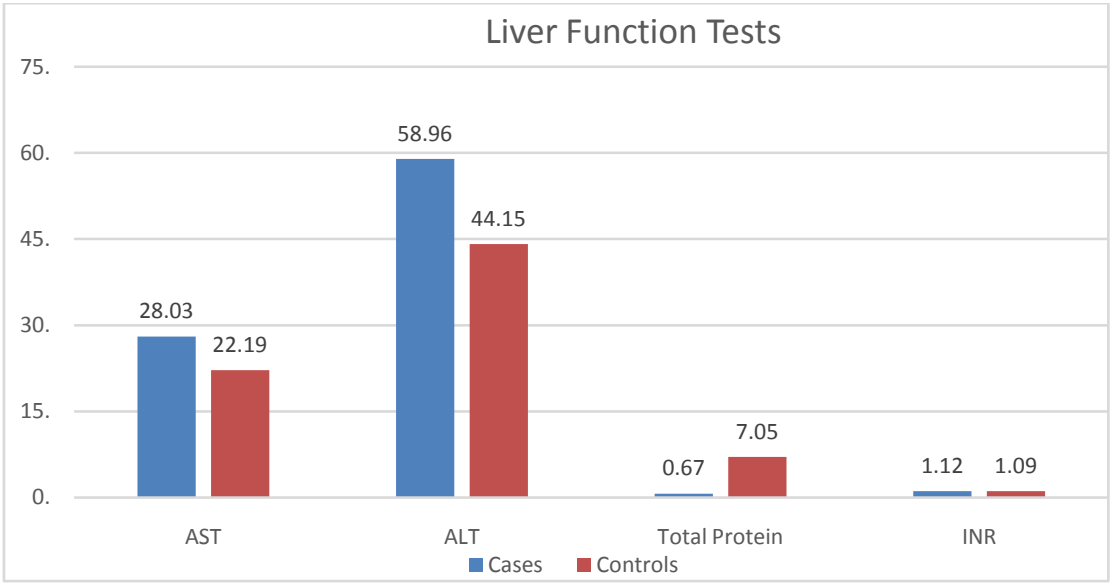
Haemoglobin, Renal Function Tests, Thyroid function tests, Liver function tests, Prothrombin time and INR, and Ultrasound of Abdomen were done in all patients.
Statistical Analysis
The obtained data were then statistically analysed

III. Results And Observations

Results and Observations
A total of 103 cases and 103 age and sex matched individuals were included in the study.
The maximum number of cases were found between the age of 41-50 years with the mean age of 40.18±13.31. The mean age of controls were 42.54±13.77. Hypothyroidism was seen more in females (n=78; 75.7%) with a male to Female ratio of 1:3.4.
The most common symptom of hypothyroidism seen was fatigue, that was seen in 35% (n=36) cases; followed by muscle cramps seen in 28.1% (n=29) patients.
The mean TSH value of cases was 20.99 ±17.45 and that of controls was 2.63±0.92.
` Presence of fatty liver in Ultrasound was significantly higher in cases (n=30; 27.5%) than the controls(n=16; 15.5%) (p=0.0296).

AST, ALT and INR values were significantly higher in cases than controls.
LIVER FUNCTION TEST LFTs BETWEEN CASES AND CONTROLS

Variables	Cases		Controls		p-value
	Mean	SD	Mean	SD	
AST	28.03	7.91	22.19	3.95	<0.0001
ALT	58.96	23.6	44.15	13.85	<0.0001
INR	1.12	0.13	1.09	0.09	0.0555



Amongst the patients with Fatty liver, the mean TSH was 34.51±22.42 and amongst those without fatty liver, the mean TSH was 15.20±10.94.

Categories	With fatty liver		Without fatty liver		p value
	N	Mean TSH	N	Mean TSH	
Cases	30	35.51 ± 22.42	73	15.20± 10.94	<0.0001
Controls	16	3.34 ± 0.70	87	2.5 ± 0.9	0.0006

IV. Discussion

The mean age of the study participants was 40.18 ±13.31 years. In the present study, it was found that hypothyroidism was more common in females 78 (75.7%) than the male cases 25 (24.3%). The male:female ratio was 1 : 3.4.

Unnikrishnan AG et al., (2013, India) in their study reported that hypothyroidism was maximum in the age group of 46-54 years. The mean age in their study was 46 ±14.68 years. There was also a female preponderance in their study. A significantly higher ($p<0.05$) proportion of females vs. males (15.86% vs 5.02%) were diagnosed. Arora et al. (2009, New-Delhi, India)" in their study reported the mean age of hypothyroid patients to be 46.55 1.8 years and majority of the patients were females (72.5%). Pandey et al., (2013, Nepal)" in their study reported 65.45% of hypothyroid patients to be females. Streeten DH et al. (1988, USA)75 reported the mean age of hypothyroid patients to be 49.8 ±2.5 years. Indra R et al (2004. Kashmir, India) reported the mean age of study population to be 44 ±13 years. Females comprised of 78.46% of the study population. The Colorado Thyroid Prevalence Study 26 also showed that hypothyroidism was more common in the female population.

The results in the present study were more or less comparable with the previous studies. Moreover, similar demographic profile was also reported in Harrison's Principles of Internal Medicine and William's Textbook of Endocrinology." 19,22

In the present study, it was observed that 27.50% of cases (30 cases) had fatty liver in Ultrasound of whole abdomen and 72.50% (73 cases) had normal ultrasound. In the control group, 15.53% (16 had fatty liver and 84.47% (87 individuals) had normal ultrasound. Presence of fatty liver in Ultrasound was significantly higher in cases than the controls ($p=0.0296$).

Bano et al., (2016, the Netherlands)" in their large, prospective, population-based cohort study, known as "The Rotterdam Study" found that 155 out of 536 hypothyroid individuals had NAFLD, which accounted for 28.91% in comparison to 22.19% (1035 out of 4664) in case of euthyroid individuals. They summarized that individuals with hypothyroidism are at increased risk of NAFLD compared with euthyroid subjects.

In the present study, it was seen that in the hypothyroid group, mean TSH of cases with fatty liver was 34.51±22.42 and of cases without fatty liver was 15.20 ±10.94. Thus, the TSH values of cases with fatty liver

were significantly higher than the TSH values of cases without fatty liver in overt hypothyroid group (p = <0.0001).

Rakshanaa et al., (2017, Tamil Nadu, India)" in their study found the mean TSH of NAFLD patients with hypothyroidism to be 15.31 ±4.79 compared to the non- NAFLD patients with hypothyroidism, where the mean TSH value was 12.13±7.07. They concluded that the prevalence of hepatic steatosis rises significantly with an increase in TSH concentrations.

V. Conclusion

In the present study, an approach was made to establish whether alteration of hepatic function is associated with hypothyroidism.

The present study shows that hypothyroidism is associated with altered liver function in comparison to euthyroid individuals. The study also shows that overt and sub-clinical hypothyroidism patients are at increased risk of development of NAFLD.

The results of this emphasize the need for monitoring liver enzymes in hypothyroid patients as declining liver function may be missed by single assessment, which will help in prevention and early detection of the possible liver dysfunction. Further, as there is always a risk of progression of NAFLD to NASH, Cirrhosis and/or Hepatocellular carcinoma, early treatment should be initiated for liver dysfunction in hypothyroidism even for sub-clinical cases. The findings of the study also highlight the need for possible therapeutic interventions regarding treatment of subclinical thyroid dysfunction. However, there is need for further prospective studies to assess the correlation of all the risk factors of NAFLD with Hypothyroidism.

Limitation of the Study

This study is limited by lack of resources and further higher end investigations like Fibroscan/AFRI for quantification of fibrosis. This study is also unable to assess the contribution of comorbidities like Diabetes Mellitus and obesity in the disease process of fibrosis.

Bibliography

[1]. Guber AH, Farag AF. Evaluation of Endocrine Function. In: McPherson RA, Pincus MR (eds.) Henry's Clinical Diagnosis and Management by Laboratory Methods. 22nd Edition. Saunders, Elsevier. 2012: 365-416,

[2]. Mc Dermott MT. Overview of Clinical manifestations of Hypothyroidism. In: Braverman LE, Cooper DS.Werner and Ingbar's The Thyroid: A Fundamental and Clinical text. 10" Edition.Lippincott Williams and Wilkins.2013, p 569.

[3]. Michael Braun. The Breast In: Russel RCG Williams NS. Bulstrode CJK, editors. Bailey and Love's Short Practice of Surgery. 24th ed London: HooldevAmold Oxford Uni Press 2004:835-9.

[4]. Peter AM, Kathleen MB. Lipid Transport & Storage. In: Murray RK, Granner DK, Mayes PA. Rodwell VW, editors. Harper's Illustrated Biochemistry. 28th ed. New Delhi: Lange Medical Books; 2009:110-1.

[5]. Larsen PR, Berry MJ. Nutritional and hormonal regulation of thyroid hormone deiodinases.Annu Rev Nutr. 1995;15:323-52.

[6]. Bano et al Thyroid and NAFLD J ClinEndocrinolMetab, August 2016. 101(8):3204-3211

[7]. Rakshanaa T. V. Rajalakshmi, Kumar Dr. Mahendra. Association of Fatty Liver and Hypothyroidism. International Journal of Science and Research (1JSR) ISSN (Online): 2319-7064, Volume 6 Issue 4, April 2017

[8]. Harrison, T. R., & Braunwald, E. (2022). *Harrison's principles of internal medicine* (22nd ed.). McGraw-Hill.

[9]. Melmed, Shlomo, Kenneth S. Polonsky, P. Reed Larsen, and Henry M. Kronenberg. 2019. *Williams Textbook of Endocrinology*. Philadelphia, PA: Elsevier - Health Sciences Division.

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