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Research Article

Thyroid-Stimulating Hormone Levels in Non-Alcoholic Fatty Liver Disease: Implications for Type 2 Diabetes Risk and Adiponectin Association in Euthyroid Subjects

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Abstract

Background: In order to control insulin resistance, lipid metabolism, and overall body weight, thyroid hormones play a key role. Some researchers think that thyroid hormones contribute to the development of NAFLD. **Aim:** the aim of this study was biochemical evaluation of serum thyroid stimulating hormone (TSH) and serum Adiponectin levels in non-alcoholic fatty liver disease (NAFLD), euthyroid subjects as a risk for T2DM. **Patient and methods:** a prospective study was held in Internal medicine department and clinical pathology department. The study lasted from March 2023 to December 2023, 82 subjects were collected from outpatient clinic, divided into three groups, first group 24 fatty liver only patients, second group24 fatty liver and type 2 diabetic patients, 34third control group. Serum TSH, also Adiponectin were assessed in the three groups. **Results**:TSH levels exhibited significant differences among the groups ($p < 0.001$). Post-hoc analysis indicated a significant increase in TSH levels in NAFLD and type 2 diabetic group compared to NAFLD only group I (p value < 0.001) and control group (p value< 0.001). Serum Adiponectin level was significantly lower in type2 diabetic and NAFLD patients in comparison with NAFLD only group with (P value <0.003). **Conclusion:** In those with fatty liver who have adequate thyroid function, the risk of developing type 2 diabetes may be increased by elevated thyroid-stimulating hormone levels and reduced adiponectin levels.

Keywords: NAFLD, type 2diabetes, (TSH) Thyroid stimulating hormone.

Introduction

An pandemic on a global scale, type 2 diabetes mellitus (T2DM) can lead to a cascade of complications affecting several bodily systems, such as the heart, kidneys, and liver. Type 2 Diabetes Mellitus is characterized by insulin resistance, which leads to the accumulation of triglycerides in the liver.(1)

A lack of inhibition of lipolysis occurs as a result of diminished sensitivity to insulin. Nonalcoholic fatty liver disease (NAFLD) is more common in those with type 2 diabetes, raising the risk of adverse clinical outcomes and death. Patients with type 2 diabetes who also have non-alcoholic fatty liver disease (NAFLD) are not specifically addressed in the current clinical guidelines for NAFLD management. two (2)

Thermogenesis, lipid metabolism, and glucose metabolism are just a few of the crucial metabolic processes that thyroid hormone controls. Hepatocyte lipid metabolism is significantly impacted by thyroid hormone. No alcoholic fatty liver disease (NAFLD) is associated with hypothyroidism and subclinical hypothyroidism, according to multiple studies (3). The third the link between euthyroid people's thyroid hormone levels and their risk of non-alcoholic fatty liver disease (NAFLD) has been clarified by multiple research. In

individuals with type 2 diabetes mellitus (T2DM), there is insufficient information regarding the correlation between NAFLD and blood thyroid hormone levels within the normal range.[4]

Among all chronic liver diseases, NAFLD is by far the most frequent. The range encompasses a multitude of liver disorders, ranging from nonalcoholic steatohepatitis with fibrosis to cirrhosis and hepatocellular carcinoma, among others. By 2030, cirrhosis caused by nonalcoholic steatohepatitis may overtake cirrhosis from alcoholic liver disease as the primary indication for liver transplantation. Further, mounting evidence connects non-alcoholic fatty liver disease (NAFLD) to extrahepatic complications including cardiovascular disease, type 2 diabetes, chronic kidney disease (CKD), cancer, and overall mortality. [5]

Patients & Methods

This prospective case control study involved 82 patients 48 of them have Non-Alcoholic Fatty Liver Disease (NAFLD) and 34 healthy control subjects matched for age and sex. These patients were selected from attendants to outpatient clinic of hepatology and gastroe-nterology Minia university hospital and outpatient clinic of Diabetes and Endocrinology unit from March 2023 to October 2023.patients were classified into three groups, Group I involved 24 NAFLD only patients, Group II involved 24 NAFLD patients with type II diabetes, Group III involved 34 healthy individuals.

Patients included in our study were 30-70 years old, diagnosed by ultrasound as having fatty liver, and Type II diabetes which is diagnosed according to American diabetes Association (ADA) 2022, WHO 2022, Centers for Disease Control and Prevention (CDC) 2022 and guidelines of Egyptian ministry of Health 2022.[6]

we excluded patients known to have viral hepatitis e.g.: HCV and HBV, Wilson`s disease, Autoimmune hepatitis disorders, Haemochromatosis, Hepatic decompensation, Hepatocellular carcinoma, Renal failure, Hypothyroidism, Drug induced liver injury (corticosteroids, tamoxifen, antipsychotics, antidepressants, amiodarone, and metho-trexate), Any advanced systemic disease, Pregnancy, IBD, Females using oral contraceptive pills, and patients on any hormonal therapy.

All patients included underwent the following: Thorough history collection, meticulous clinical assessment, and laboratory tests: Thyroid-stimulating hormone The TSH ELISA Kit is an enzyme immunoassay designed to detect and measure the human TSH protein, specifically Cat. No. DCM076-9Hu kit.

Adiponectin Human by Adiponectin ELISA kit: This sandwich kit is for the accurate quantitative detection of human adiponectin (also known as ADIPOQ) in serum, plasma, ascitic fluid and other biological fluids, Assay principle:

This kit is an Enzyme linked Immunosorbent Assay (ELISA).[1] specifically Cat. No. E1550Hu kit.

Ethical approval was obtained from the ethical committee of faculty of medicine, Minia University. Code no. 682/march.2023

Statistical analysis:

Data were gathered and analyzed using the SPSS program, version 24. Mean and standard deviation were utilized for quantitative data, whilst percentage and number were used for categorical data.

An independent t-test was utilized to analyze the parametric quantitative data differences between the groups.

The Chi-square test was utilized to analyze the quantitative data, with the option to employ Fisher's Exact test if more than 20% of cells have an anticipated count less than 5.

Results

Demographic and anthropometric data of the studied groups Shown in Table (1) as regard age was ranged in all groups from 30 to70 yrs., the age was ranged in NAFLD only group from (35-61) with mean ± SD (41.2 ± 12.4), NAFLD with type 2 diabetes ranged from (37-70) with mean ± SD (51.8 ± 10.5), control group ranged from (31-55) with mean ± SD (34.6 ± 8.7).

Females were more precipitated in this study 18 (75.0%) for NAFLD only group, 16 (66.7%) for NAFLD and diabetic group, 26 (76.5%) in control group.

There was significant relatively higher level of TSH in NAFLD and type 2 diabetic group than NAFLD only with p value <0.001, serum Adiponectin level was significantly low in NAFLD and type 2 diabetic group than NAFLD only and control groups with p value <0.001, (Table 2).

Table 1: Demographic and clinical data of studied participants

Personal History		**Group I n= 24**	**Group II n= 24**	**Group III n= 34**	**p value**		
					I vs II	**I vs III**	**II vs III**
Age	**Mean ± SD**	35-61 41.2 ± 12.4	37-70 51.8 ± 10.5	31-55 34.6 ± 8.7	**<0.001***		
					<0.001*	**0.019***	**<0.001***
Gender: **Male** **Female**	**n (%)**	6 (25.0%) 18 (75.0%)	8 (33.3%) 16 (66.7%)	8 (23.5%) 26 (76.5%)	0.688		

- **ANOVA test for parametric quantitative data between the three groups followed by LSD test.**
- **Chi-square test for qualitative data.**
- ***: significant level at p value <0.05**

Table 2: Comparison between serum TSH and serum Adiponectin levels in the studied groups

	Group I n= 24	**Group II n= 24**	**Group III n= 34**	**p value**		
				I vs II	**I vs III**	**II vs III**
TSH Mean (SD)	3.2 (0.85)	4.1 (1.02)	1.8 (0.72)	**<0.001***		
				<0.001*	**0.001***	**<0.001***
Adiponectin Median (IQR)	3.6 (2.9 – 4.4)	2.8 (2.3 – 3.7)	6.5 (3.7 – 17.3)	**<0.001***		
				0.003*	**<0.001***	**0.01***

- **Kruskal-Wallis test for non-parametric quantitative data between the three groups followed by Mann-Whitney test between each two groups.**
- **significant level at p value <0.05**

Discussion

The purpose of this prospective study is to evaluate serum TSH levels in order to determine whether there is an association between fatty liver disease and type 2 diabetes. Glucose and lipid metabolism are two of the many processes impacted by thyroid hormones including thyroid-stimulating hormone (TSH). Current research has focused on the association between TSH levels and NAFLD in T2DM patients. The 82 participants in the present study ranged in age from 30 to 70 years old, with 22 (or 25%) men and 60 (or 75%) females making up the sample. In comparison to individuals with NAFLD alone, those with both NAFLD and DM2 had significantly higher TSH levels (p value<.0001).

Huang B et. al. stated that their research demonstrated a noticeably elevated TSH level in NAFLD patients in comparison to controls (p-

value <0.001). This finding is intriguing.[7] Obesity and hyperlipidemia, brought on by lower TSH levels, could exacerbate NAFLD[8]. We agree with Carolina Castro et al. that there is a correlation between normal TSH levels and the existence of NAFLD. After controlling for metabolic syndrome variables (waist circumference-C, triglycerides, diabetes, and systemic arterial hypertension), no longer was there a significant connection between the two [9].

Kim et.al. investigated the effects of obesity and non-alcoholic fatty liver disease (NAFLD) on thyroid function and found that those who are overweight and have NAFLD are more likely to have thyroid dysfunction than those who do not have these disorders. Because thyroid hormones are so important for controlling basal metabolism and affecting fat and glucose metabolism, their levels are strongly correlated with body composition. Therefore, it is believed that thyroid dysfunction has a role in the onset of obesity and NAFLD. [10]

Martinez et al. found that TSH levels, non-alcoholic fatty liver disease (NAFLD), and liver fibrosis are all correlated. In particular, patients with TSH levels of 2.5 μIU/mL or more are significantly more likely to have NAFLD and fibrosis, irrespective of the other metabolic factors that were investigated.[11]

On the other hand, some researchers who looked at patient data found no connection between hepatic steatosis and serum TSH and FT3 values.[12]

In addition, our study showed that patients with both NAFLD and DM2 had significantly decreased Adiponectin levels compared to patients with NAFLD alone (p value <.003).

The researchers L. Zhang et al. discovered strong inverse correlations between adiponectin and body mass index (BMI), HOMA-IR, and blood sugar levels. This highlights the strong association between insulin resistance and adiponectin in a limited group of people with non-alcoholic fatty liver disease.[13]

A composite formula that incorporates these cytokines shows good accuracy in predicting non-alcoholic steatohepatitis, according to Machado et al., who found that the severity of non-alcoholic fatty liver disease (NAFLD) is associated with imbalances in the interplay of adiponectin, leptin, and ghrelin.[14] Patients with non-alcoholic steatohepatitis (NASH) who have increased liver enzyme levels also have considerably lower blood adiponectin levels, according to research by Aygun et al., especially in instances of this inflammatory form of NASH.[15]

Conclusion:

A significant rise in thyroid-stimulating hormone levels may pose an added risk for the onset of type 2 diabetes in individuals with normal thyroid function. Decreased plasma adiponectin levels are directly linked to the development and seriousness of nonalcoholic fatty liver disease (NAFLD) in individuals with type 2 diabetic mellitus (T2DM).

Conflicts of interest: No potential conflict of interest was reported by any of the authors.

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