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# Relationship Between The Thyroid-Stimulating Hormone (Tsh) Levels And The Presence Of Non-Alcoholic Fatty Liver Disease (Nafld) Among The Asymptomatic Egyptian Individuals

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**Abstract:**

**Introduction:** Thyroid hormones play a vital role in body distribution, lipid metabolism, and insulin resistance management. As a result, they could be involved in the aetiology of non-alcoholic fatty liver disease (NAFLD). However, the impact of thyroid function on NAFLD is unclear.

**Aim and objectives:** To evaluate the association between thyroid function and the presence of NAFLD in asymptomatic Egyptian individuals.

**Subjects and methods:** We selected 200 patients (both sexes) with (NAFLD) and 100 normal individuals as control. Both groups were subjected to complete clinical examination after thorough history taking, anthropometric measurements, laboratory investigations, thyroid and abdominal ultrasound.

**Results:** There was a statistically significant difference between the two studied groups regarding TSH, FT3 and FT4 as TSH was higher among the NAFLD group and FT3 and FT4 were lower among the NAFLD group.

**Conclusion:** Thyroid function, even when within normal limits, is linked to metabolic syndrome and may play a role in NAFLD. This is a noteworthy finding because it offers the possibility that lowering TSH levels could reduce metabolic syndrome risk factors and, as a result, NAFLD onset.

**Keywords:** Metabolic syndrome, Non-alcoholic fatty liver disease, Obesity, NAFLD, Thyroid function, and Thyroid-stimulating hormone

## Introduction:

Thyroid hormone (TH) effects on lipid metabolism have been known for over a century. Hypothyroidism is associated with weight gain and higher serum TAG and LDLC levels in the clinical setting, whereas hyperthyroidism has opposite effects.[1,2] Because of a decrease in LDL receptor activation and triglyceride-rich lipoprotein clearance, hypothyroidism has been associated with elevated levels of LDL-cholesterol and triglycerides.[3]Hypothyroidism has a positive relation to metabolic syndrome and may be considered a cause or risk factor.[4] Steatosis is a condition in which the liver accumulates abnormal levels of triglycerides. It's a part of non-alcoholic fatty liver disease (NAFLD), also known as non-alcoholic steatohepatitis.[5]

NAFLD is a hepatic characteristic of metabolic syndrome that has long been recognized. If not treated properly, this condition can progress to hepatic fibrosis, cirrhosis, and hepatocellular carcinoma.[6] Previous research has attempted to determine the link between hypothyroidism and NAFLD.[7] The majority of them found that hypothyroidism, whether overt or subclinical, is independently linked with NAFLD, implying that hypothyroidism may cause NAFLD without the involvement of other metabolic risk factors. Lower thyroxin (T4) levels were linked to an increased incidence of NAFLD in another trial.[8]

So, this study aimed to evaluate the link between thyroid function and the presence of NAFLD in asymptomatic Egyptian individuals.

**Methods:**

This study included 200 patients of (both sexes) with (NAFLD) and 100 normal individuals as control. **Inclusion criteria:** We included 200 Egyptian patients between 20 and 80 years and known to be NAFLD and 100 normal Egyptian individuals of the same age group as a control. **Exclusion criteria:** Patients with a history of liver or thyroid disease and those using a thyroid-related medication and alcoholics were excluded.

Both groups were subjected to: **1-Thorough history taking.2-complete clinical examination.3-Anthropometric measurements:** Waist circumference was measured, and anything over 94 cm for men and 80 cm for women was considered abnormal. The weight/height2 (kg/m2) formula was used to calculate the body mass index (BMI). **4-Laboratory investigations:** Lipid profile; plasma concentrations of total cholesterol, high-density lipoprotein-cholesterol (HDL-C), liver function test for exclusion of previous liver diseases, serum TSH, free T3, free T4 for exclusion of previous thyroid disease and finally complete blood count and renal function test. **5-Abdominal ultrasound:** For NAFLD evaluation. According to established criteria, NAFLD is defined as hepatic steatosis detected by ultrasonography in the absence of alcohol consumption or previous liver disease.[9] After a 6-hour fast, qualified radiologists detected steatosis by looking for an ultrasonographic pattern of a bright liver with visible contrast between the hepatic and renal parenchyma. **6-Thyroid ultrasound:** For exclusion of thyroid pathology.

**Ethics and patient consent:** All procedures followed Al-Azhar university ethical committee regulations, taking the consent from all patients.

**Statistical analysis**: Microsoft Excel software was used to code, enter, and analyze data obtained while taking the history, essential clinical examination, laboratory tests, and outcome measures. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the data type, qualitative data is represented as number and percentage, and the continuous quantitative data is represented by mean ± standard deviation (SD). The following tests were used to test differences for significance: Differences between frequencies (qualitative variables) and percentages in groups were compared by the Chi-square test. P-value was set at <0.05 for significant results and < 0.001 for highly significant results.

**Results:**

Table 1 shows that group 1 was 48.5 ±17.2 years old, Group 2 was 47.9 ±19.2 years old. In terms of age, there was no statistically significant difference between the two groups. The first group included 59 % males and 41 % females, whereas the second had 48 % males and 52 % females. In terms of gender, there was no statistically significant difference between the two groups. There were 51.5 % smokers and 48.5 % nonsmokers in Group 1, and 51 % smokers and 49 % nonsmokers in Group2. There was no statistically significant difference between the two groups evaluated when it came to smoking.

Group 1 had a mean height of 168.4 ±6.3, while group 2 had a mean height of 169.7 ±6.1, as seen in Table 1. There was no statistically significant difference in height between the two groups investigated. The average weight in Group 1 was 105.7 ±14.2, while the average weight in Group 2 was 85.2 ±10.8. Group 1 had a statistically significant higher weight. The average BMI in Group 1 was 25.8 ±3.0, while the average BMI in Group 2 was 21.8 ±1.8. Group 1 had a statistically significantly higher BMI. In groups 1 and 2, the mean waist circumference was 86.4 ±9.9 in group 1 and 84.6 ±3.3 in group 2. There was no statistically significant difference in waist circumference between the two groups. Groups 1 and 2 had mean hip circumferences of 104.9 ±5.9 and 105.1 ±5.9, respectively, with no significant difference.

The mean systolic blood pressure in groups 1 and 2 was 125.5 ±8.8 and 118.2 ±4.9, respectively, as shown in Table 2. Group 1 systolic blood pressure was statistically significantly higher. In groups 1 and 2, the mean diastolic blood pressure was 81.4 ±4.9 and 73.2 ±3.0, respectively. In group 2, the diastolic blood pressure was statistically significantly higher. Groups 1 and 2 had mean pulses of 88.4 ±12.7 and 88.8 ±12.7, respectively. There was no statistically significant difference between the two groups investigated when it came to pulse.

Table 3 demonstrates that the mean ALT of group 1 was statistically significantly higher. Group 1 mean GGT was statistically significantly higher. There was no statistically significant difference between the two groups studied in terms of AST. There was no statistically significant difference in serum creatinine between the two groups studied. Group 1 had a statistically significant rise in HDL-C.In group 1, the mean LDL-C was statistically significantly higher. There was no statistically significant difference between the two groups in terms of total cholesterol and triglycerides.

As shown in table 4, there was a statistically significant difference between the two studied groups regarding TSH, FT3 and FT4 as TSH was higher among group 1, FT3 was lower among group 1, and FT4 was lower among group 1.

In terms of abdominal and neck ultrasound, there was a statistically significant difference between the two studied groups, as indicated in table 5, with group 1 having more fatty liver by abdominal ultrasound and more abnormal neck ultrasound.

As table 6 shows, there was a statistically significant difference between the two studied groups regarding haemoglobin. Group 1 had a higher level of haemoglobin than group 2. There was no statistically significant difference between the two studied groups regarding platelets, RBCs, WBCs and lymphocytes.

There was no statistically significant correlation between TSH and ALT, AST, GGT, LDL-C, HDL-C, total cholesterol and serum creatinine, as shown in table 7.

**Discussion:**

This study has been conducted at Al-Sayed Galal university hospital, one of Al-Azhar university hospitals, to evaluate the association between thyroid function and the presence of NAFLD in asymptomatic Egyptian individuals. This study's major and primary finding is that high TSH levels were associated with NAFLD among the Egyptian population. We also found that the NAFLD group had low FT3 and FT4 levels compared with the non-NAFLD group, which means that hypothyroidism is associated with developing NAFLD. This finding agrees with the previous studies as this systematic review demonstrated that high TSH levels might be a vital risk factor for developing NAFLD irrespective of thyroid hormone levels.[10] Another systematic review reported that the results of present studies are still conflicted and reported that increased TSH levels associated with developing NAFLD and play a vital role in the progression of the disease, as the TSH levels increased with the progression of the NAFLD. So, thyroid hormone profile may consider as an initial assessment in patients with NAFLD. [11]

Our study demonstrated that regardless of age, obesity is associated with high TSH levels alone and with the development of NAFLD in Egyptian individuals, and this finding agrees with the previous studies. A previous study conducted in Tanta university hospital in Egypt evaluating the thyroid function in obese patients with NAFLD demonstrated that obesity is associated with the presence of NAFLD and low levels of thyroid hormones, agreeing with our results.[12] Regarding Vital signs among the two studied groups, our results revealed that the mean systolic blood pressure was statistically significantly higher among group 1. The diastolic blood pressure was statistically significantly higher among group 1. But there was no statistically significant difference between the two studied groups regarding pulse. Our results regarding vital signs supported by other studies as NAFLD as a part of metabolic syndrome was associated with increased blood pressure, systolic and diastolic, which was the second finding in our research. Moreover, high blood pressure may consider as a risk factor for developing NAFLD.[13,14]

The relation between thyroid dysfunction and subsequently TSH levels and lipid profile in our study was that the NAFLD group was associated with high levels of HDL-C and LDL-C. There was no statistically significant difference between the two studied groups regarding total cholesterol and triglyceride. Some studies a gree with our results[13,14], and others disagree with our results[17,18] which still makes this point controversial.

Regarding thyroid function tests, this point is still controversial and need further studies to make it clear. Our results reveal that TSH level was higher among group 1, FT3 and FT4 were lower among group 1. In agreement with our results, the study conducted in Tanta university hospital[12] revealed a statistically significant difference between the two groups regarding TSH and FT4. In contrast with our results, there was no statistically significant difference between the two groups regarding FT3. Another study revealed that there was no statistically significant difference between the two groups regarding TSH and FT4. In comparison, there was a statistically significant difference between the two groups regarding FT3.12. In contrast, the study conducted by Wang et al.[19] reported a statistically significant difference between the two groups regarding FT3 and FT4, while there was no statistically significant difference between the two groups regarding TSH.

Our results showed that there was no statistically significant difference between the two studied groups regarding serum creatinine. However, our results were not supported by previous studies as according to Liu et al.[17]there was a statistically significant difference in serum creatinine levels between the two groups studied, as NAFLD had higher levels of creatinine.

We also found a statistically significant difference between the two studied groups regarding abdominal and neck ultrasound as fatty liver by abdominal us was higher among group 1 and abnormal neck ultrasound was higher among group 1. Regarding Blood indices among the two studied groups, we found a statistically significant difference regarding Hg between the two studied groups. There was no statistically significant difference between the two studied groups regarding platelets, RBCs, WBCs and lymphocytes.

**Conclusion:**

These findings could add to our understanding of the thyroid hormone's involvement in regulating liver fat content and NAFLD. Overall, our findings imply that thyroid function, even when within normal limits, is linked to metabolic syndrome and that it may play a role in NAFLD through this pathway. This is a significant finding because it raises the question of whether the TSH level should be compared to a lower reference level in order to reduce metabolic syndrome risk factors and, as a result, the onset of NAFLD. So, We recommend that further clinical and histopathological research is essential to determine the relationship between hypothyroidism and TSH levels irrespective of thyroid hormone levels and developing and progression of NAFLD and to understand the underlying pathogenesis. In addition, the efficacy of using thyroid-related drugs to prevent steatosis and the development of non-alcohol steatohepatitis must be explored in animal and cell culture models.

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**El-Shanawany MNT:** Whole work of the study.

**Al-Alfy MN:** Continous supervision on whole work and guidance of selection of cases and broad instructions.

**Hashish MA:** Direct supervision on laboratory work of the researc.

**Abo Hassan AM:** Direct supervision and close monitoring of cases.

**Amin MAA:** Direct supervision on radiological assessments, thyroid US and abdominal "liver" US.

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**Tables:**

| Variables | Group 1 | Group 2 | Test value | P-value |
|---|---|---|---|---|
| **Age**<br>**Mean± SD** | 48.5± 17.2 | 47.9± 19.2 | 0.251 | 0.802[1] |
| **Gender**<br>**Male n (%)**<br>**Female n (%)** | <br>118 (59)<br>82 (41) | <br>48 (48)<br>52 (52) | 3.264 | 0.085[2] |
| **Smoking**<br>**No n (%)**<br>**Yes n (%)** | <br>97 (48.5)<br>103 (51.5) | <br>49 (49)<br>51 (51) | 0.007 | 0.999[2] |
| **Height**<br>**Mean± SD** | 168.4± 6.3 | 169.7± 6.1 | 1.661 | 0.098 |
| **Weight**<br>**Mean± SD** | 105.7± 14.2 | 85.2± 10.8 | 12.721 | **<0.001*** |
| **BMI**<br>**Mean± SD** | 25.8± 3.0 | 21.8± 1.8 | 12.476 | **<0.001*** |
| **Waist circumference**<br>**Mean± SD** | 86.4± 9.9 | 84.6± 3.3 | 1.754 | 0.080 |
| **Hip circumference**<br>**Mean± SD** | 104.9± 5.9 | 105.1± 5.9 | 0.340 | 0.734 |

**Table 1 Basic characteristics and anthropometric measures of the two studied groups**
1: student t-test 2: chi-square test, BMI: body mass index

| Variables | Group 1 | Group 2 | Test value | P-value |
|---|---|---|---|---|
| **SBP**<br>**Mean± SD** | 125.5± 8.8 | 118.2± 4.9 | 7.817 | <0.001* |
| **DBP**<br>**Mean± SD** | 81.4± 4.9 | 73.2± 3.0 | 9.632 | <0.001* |
| **Pulse**<br>**Mean± SD** | 88.4± 12.7 | 88.8± 12.7 | 0.251 | 0.802 |

**Table 2 Vital signs among the two studied groups**
*Student t-test
SBP: systolic blood pressure, DBP: diastolic blood pressure

| Variables | Group 1 | Group 2 | Test value | P-value |
|---|---|---|---|---|
| **ALT**<br>**Mean± SD** | 24.2± 3.3 | 22.8± 2.7 | 3.446 | **0.001*** |
| **AST**<br>**Mean± SD** | 27.6± 5.2 | 26.7± 5.2 | 1.362 | 0.174 |
| **GGT**<br>**Mean± SD** | 40.6± 11.3 | 31.3± 7.3 | 7.490 | **<0.001*** |
| **Serum creatinine**<br>**Mean± SD** | 73.7± 6.7 | 73.9± 7.4 | 0.252 | 0.801* |
| **Total cholesterol**<br>**Mean± SD** | 4.9± 1.2 | 4.7± 1.1 | 1.858 | 0.064 |
| **Triglyceride**<br>**Mean± SD** | 1.8± 0.7 | 1.8± 0.8 | 0.075 | 0.940 |
| **HDL-C**<br>**Mean± SD** | 1.5± 0.6 | 0.7± 0.5 | 11.595 | **<0.001*** |
| **LDL-C**<br>**Mean± SD** | 2.3±0.8 | 1.7± 0.8 | 5.777 | **<0.001*** |

**Table 3 Liver function tests, serum creatinine and lipid profile among the two studied groups**
*Student t-test
ALT: Alanine aminotransferase, AST: aspartate aminotransferase, GGT: gamma-glutamyl transferase, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol

| Variables | Group1 | Group 2 | Test value | P-value |
|---|---|---|---|---|
| **TSH**<br>**Mean± SD** | 3.1± 1.0 | 2.0± 0.9 | 0.366 | **0.015*** |
| **FT3**<br>**Mean± SD** | 1.1± 0.9 | 2.2± 0.9 | 1.044 | **0.007*** |

| | | | | |
|---|---|---|---|---|
| **FT4 Mean± SD** | 8.5± 1.1 | 16.8± 1.1 | 1.716 | **0.021*** |

**Table 4 Thyroid function tests among the two studied groups**
*Student t-test
TSH: thyroid-stimulating hormone, FT3: Free triiodothyronine, FT4: Free thyroxine

| Variable | Group 1 n (%) | Group 2 n (%) | P-value |
|---|---|---|---|
| **Abdominal US** | | | |
| **Normal** | 8 (4) | 100 (100) | |
| **Fatty liver** | 192 (96) | 0 (0) | **<0.001*** |
| **Neck US** | | | |
| **Normal** | 87 (43.5) | 19 (19) | |
| **Abnormal** | 113 (56.5) | 81 (81) | **0.015*** |

**T**
**able 5 Abdominal and neck ultrasound among the two studied groups**
*Student t-test

| Variable | Group 1 n (%) | Group 2 n (%) | P value |
|---|---|---|---|
| **Hg** | 13.8± 2.6 | 12.4± 1.6 | **0.017*** |
| **Platelets** | 259.3± 101.5 | 255.7± 122.5 | 0.317 |
| **RBCs** | 4.8± 0.1 | 4.7± 0.01 | 0.129 |
| **WBCs** | 6.5± 1.1 | 6.3± 1.7 | 0.720 |
| **Lymphocytes** | 41.1± 8.3 | 40.9± 9.1 | 0.513 |

**Table 6 Blood indices among the two studied groups**
*Student t-test

**Table 7 Correlation between TSH and liver function tests**

| Variable | TSH | P value |
|---|---|---|
| **ALT** | 0.030 | 0.607 |
| **AST** | 0.034 | 0.561 |
| **GGT** | 0.015 | 0.793 |

| | | |
|---|---|---|
| **LDL-C** | 0.066 | 0.254 |
| **HDL-C** | -0.013 | 0.816 |
| **Total cholesterol** | -0.014 | 0.804 |
| **Serum creatinine** | -.054 | 0.353 |