SSRG International Journal of Medical Science
ISSN: 2393–9117 / https://doi.org/10.14445/23939117/IJMS-V10I5P103

Volume 10 Issue 5, 12-18, Sep-Oct 2023

Original Article

Prevalence of Primary Hypothyroidism in Patients with Non-Alcoholic Fatty Liver Disease

Dina Aljundi[1], Ruba Salman[2], Daad Daghman[3]

[1,2]*Department of Endocrinology, Tishreen University, Syria, Lattakia.*
[3]*Department of Gastroenterology, Tishreen University, Syria, Lattakia.*

Received: 26 July 2023 Revised: 02 September 2023 Accepted: 19 September 2023 Published: 05 October 2023

Abstract *- Introduction: There is a possible relationship between NAFLD and hypothyroidism. One suggested mechanism to explain this relationship is the well-known association between hypothyroidism and various metabolic syndrome components often present in the context of NAFLD. Objective: This study aims to estimate the prevalence of hypothyroidism in patients with non-alcoholic fatty liver disease. Methods: A case-control study of 128 patients diagnosed with NAFLD by ultrasonographic findings without a history of thyroid disorders participated in this study, who attended Tishreen University Hospital in Lattakia, Syria, during the period from May 2022 to July 2023, 128 age and gender-matched control subjects with normal liver on ultrasound, to compare the prevalence of primary hypothyroidism between the two groups. Results: Primary hypothyroidism was more prevalent among NAFLD patients by 19.5% compared to 8.5% in the controls, with a statistically significant difference (P-value: 0.001). The mean TSH value was higher in the NAFLD group compared to the controls (3.9 mui/l compared to 2.4 mui/l in the controls) with a statistically significant difference (P-value: 0.04); as for the average value of FT4, it was lower in the NAFLD group compared to the controls (1.10 ng/dl compared to 1.22 in the controls) with a significant statistical difference (P-value: 0.01). Conclusions: A higher prevalence of primary hypothyroidism was demonstrated in the NAFLD group, with both clinical and subclinical types, and this may indicate a relationship between hypothyroidism and NAFLD.*

Keywords *- Insulin resistance, Metabolic syndrome, Non-alcoholic fatty liver disease, Primary hypothyroidism, Steatosis.*

1. Introduction

Non-alcoholic fatty liver disease is the hepatic presentation of the metabolic syndrome,[1,2,3] and it is associated with metabolic risk factors: 1-obesity, 2-insulin resistance, 3-T2DM, 4-hypertension, and 5-dyslipidemia.[4]

NAFLD is an accumulation of TGs in the cytoplasm of hepatocytes, more than 5-10% of the liver. [1,3] The definition of NAFLD requires the presence of both: 1-evidence of hepatic steatosis, either by imaging or histology, and 2- there are no causes for secondary hepatic fat accumulation such as significant alcohol consumption, use of steatogenic medication, or hereditary disorders.[5] It is the most common cause of chronic liver disease, which affects 25% of the population worldwide.[4]

Recently, An important role for hypothyroidism in the context of NAFLD has been suggested by several studies [6] due to its strong epidemiological connection and unique pathophysiology; as such, it could serve as a model for the identification of new therapeutic options for some cases of primary NAFLD.

[8] Although co-occurring, the pathogenic mechanism of hypothyroidism-induced NAFLD is complex and not fully understood. [7] The key points for the pathogenic mechanism of hypothyroidism induced-NAFLD are the metabolic changes, the direct effect of TSH on hepatocytes, and oxidative stress. [8]

2. Patients and Methods

This study was designed as a cross-sectional case–control study. The initial sample consisted of 150 patients with hepatic steatosis diagnosed based on Ultrasonographic features with ages ranging from 18 to 65 years, who attended the clinics of Tishreen University Hospital in Lattakia, Syria. 22 patients were excluded according to the exclusion criteria, so the final research sample consisted of 128 patients. Also, 128 age and gender-matched control subjects without hepatic steatosis or liver enzyme abnormalities were included.

Exclusion criteria included:

- Previous thyroid disorders.
- Significant alcohol use (can be defined as ≥ 30 g per day for men and ≥ 20 g per day for women, [9] for a period of more than 2 years. [5]).
- Medications that may cause hepatic steatosis.
- Pregnancy.
- Renal failure.
- Those with any laboratory or clinical evidence suggesting an alternate or coexistent underlying chronic liver disease, including viral hepatitis, hemochromatosis, autoimmune hepatitis, or Wilson's disease.

2.1. Examination Methods

A detailed clinical history was taken from all patients, including medical history, demographics, nicotine and alcohol use, medication history and nutritional habits using a standardized interview. The patient's height, weight and waist circumference were measured, and body mass index (BMI) was calculated.

2.1.1. Laboratory Testing

Intravenous fasting tests were performed for all patients, including fasting glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (T.Chol), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), thyroid-stimulating hormone (TSH), free thyroxine (FT4).

Anti-HCV, HBS antigen, ferritin, TIBC, Ceruloplasmin, ANA, and ASMA were performed for patients with hepatic steatosis who showed an increase in liver enzymes (ALT and AST > 2-fold of ULN) [10] or patients under 45 years of age with no presence of risk factors of metabolic syndrome.

2.1.2. Ultrasound Examination

Ultrasound imaging was performed by radiologists using identical HDI 5000 diagnostic ultrasound units (ALTATL Ultrasound, Philips Medical Systems).

The examination included evaluation of the liver, biliary tract, and kidneys. The hepatic steatosis was assessed by comparing hepatic parenchyma with the renal parenchyma under consideration the dorsal echo attenuation, visualization of the diaphragm, and ability to assess the intrahepatic vessels.[11]

2.1.3. Criteria for Thyroid Dysfunction

Subclinical hypothyroidism was diagnosed based on TSH levels ≥ 4 mu/L with normal FT4 concentrations (0.8-1.8 ng/dl), according to the guidelines of the European Thyroid Association.[12]

The diagnosis of clinical hypothyroidism required elevated TSH levels >10 mu/L and reduced FT4 concentrations (< 0.8 ng/dl).

2.2. Ethical Consideration

All patients were provided complete and clear informed consent after discussing the study. The Declaration of Helsinki performed this study.

2.3. Statistical Analysis

Statistical assessment of our study was performed by using IBM Statistical Package for Social Sciences (SPSS) for Windows, version 20, manufactured by IBM Corp., located in Armonk, NY, USA, and summarized as frequencies and proportions. P<0.05 value was accepted to be statistically significant. The results were indicated in average ±SD and percentage (%). One-way ANOVA was used for comparing groups. The independent-sample t-test was used for comparing the 2 groups, and the t-test was used for variables.

Table 1. Characteristics of study subjects with and without NAFLD

Variables	Subjects with NAFLD n(128) Mean ± SD	Subjects without NAFLD n(128) Mean ± SD	P-value
Female n%	67 (52.3%)	72 (56.3%)	0.5
Male n%	61 (47.7%)	56 (43.8%)	0.5
Age	46.05 ± 10.2	48.95 ± 10.8	0.06
BMI (kg/m^2)	31.19 ± 5.9	26.46 ± 4.9	0.0001
WC (cm)	108.30 ± 14.4	88.83 ± 11.2	0.0001
DM n%	54 (42.2%)	18 (14.1%)	0.0001
Pre-DM n%	9 (7%)	2 (1.6%)	0.0001
HTN n%	43 (33.6%)	29 (22.7%)	0.04
Smoking n%	79 (61.7%)	42 (32.8%)	0.0001
Primary hypothyroidism n%	25 (19.5%)	11 (8.5%)	0.0001
Clinical hypothyroidism n%	4 (3.1%)	2 (1.6%)	0.0001
Subclinical hypothyroidism n%	21 (16.4%)	9 (7%)	0.0001
TSH (mui/L)	3.90 ± 9.2	2.42 ± 2.07	0.04
FT4 (ng/dl)	1.10 ± 0.1	1.22 ± 0.1	0.01
ALT (U/L)	37.62 ± 24.6	21.32 ± 12.1	0.0001
AST (U/L)	34.95 ± 19.2	22.28 ± 14.6	0.0001
T.Chol (mg/dl)	214.94 ± 61.3	185.13 ± 26.7	0.0001
TG (mg/dl)	247.85 ± 210.2	142.80 ± 34.3	0.0001
LDL (mg/dl)	113.52 ± 33.08	98.01 ± 24.2	0.0001
HDL (mg/dl)	42.75 ± 7.7	48.38 ± 6.8	0.0001

BMI: body mass index, WC: waist circumference, DM: diabetes mellitus, Pre-DM: prediabetes, HTN: hypertension, TSH: thyroid-stimulating hormone, FT4: free thyroxine, ALT: alanine aminotransferase, AST: aspartate aminotransferase,T.Chol: total cholesterol, TG: triglycerides, LDL: low-density lipoprotein, HDL: high-density lipoprotein. P-value: statically significant difference < 0.05.

3. Results

The study collective included 256 patients (54.3% females, 45.7% males). The patients' ages ranged from 20-65 years, with a mean age of 47.5 ± 10.6 years. 128 NAFLD patients were diagnosed by ultrasound imaging, with a mean age of 46 years (52.3% females, 47.7% males). With control subjects consisting of 128 patients with a mean age of 48.95 years (56.3% females, 43.8% males), the two groups were matched by age and gender.

The prevalence of hypothyroidism was higher among patients with NAFLD compared to the control group [25 (19.5%s) vs 11 (8.5%), p<0.001] (see table 1) (see figure 1).

In the NAFLD group, 4 patients (16%) with clinical hypothyroidism and 21 patients (84%) with subclinical hypothyroidism, while in the control group, there were 2 (18.2%) clinical and 9 (81.8%) subclinical hypothyroidism (see table 1).

The NAFLD group was characterized by a higher BMI, waist circumference, arterial hypertension, diabetes mellitus, and pre-DM compared to the controls with statistically significant differences (p≤ 0.04) (see Table 1).

The biochemical parameters TSH, ALT, AST, T. Chol, TG, and LDL were significantly higher in the NAFLD group (p≤ 0.04), while FT4 and HDL were significantly lower in the NAFLD group (p: 0.01) (see table 1).

When comparing the prevalence of primary hypothyroidism in the NAFLD group, in diabetic and non-diabetic patients, the prevalence of hypothyroidism was higher among non-diabetics by 21.6% compared to diabetics by 16.6% without a significant statistical difference.

For studying the variables between the two groups of NAFLD patients with hypothyroidism (n:25) and without hypothyroidism (n:103), there were no significant statistical differences between the two groups in demographic information about the subjects (age, sex, waist circumference, BMI, hypertension, T2DM, Pre-DM). However, biochemically, we found that in the hypothyroidism group, liver enzymes (ALT and AST) were higher (p≤0.03), and the values of T.Chol, TG, and LDL were higher in the hypothyroidism group (p≤0.03). At the same time, the HDL was comparable between the two groups (see Table 2).

For a more accurate study of the lipid profile of the NAFLD group according to the degree of hypothyroidism, patients who were taking medicines for hyperlipidemia were excluded (including all diabetic patients), so the remaining 53 non-diabetic NAFLD patients (39 euthyroid patients, 3 patients with clinical hypothyroidism, 11 patients with subclinical hypothyroidism), the values of T.Chol, TG, and LDL increased with increasing the degree of hypothyroidism with statistically significant differences (p≤0.04), but the values of HDL did not show any significant statistical difference between the three groups (see table 3) (see figure 2).

Table 2. Univariable analysis of factors associated with hypothyroidism in NAFLD

Factor	NAFLD with hypothyroidism n(25) Mean ± SD	NAFLD without hypothyroidism n(103) Mean ± SD	P-value
Female n%	15 (60%)	52 (50.5%)	0.3
Male n%	10 (40%)	51 (49.5%)	0.3
Age	43.20 ± 10.1	46.74 ± 10.2	0.1
BMI (kg/m^2)	32.88 ± 6.5	30.78 ± 5.7	0.1
WC (cm)	110.52 ± 13.1	107.76 ± 14.7	0.3
DM n%	9 (36%)	45 (43.7%)	0.5
Pre-DM n%	1 (4%)	8 (7.8%)	0.5
HTN n%	5 (20%)	38 (36.9%)	0.1
Smoking n%	15 (60%)	64 (62.1%)	0.8
TSH (mui/L)	10.91 ± 19.4	2.20 ± 1.2	0.0001
FT4 (ng/dl)	0.94 ± 0.1	1.14 ± 0.1	0.0001
ALT (U/L)	41.48 ± 21.5	36.68 ± 25.3	0.01
AST (U/L)	44.79 ± 26.2	34.87 ± 20.9	0.03
T.Chol (mg/dl)	237.11 ± 45.5	209.55 ± 63.6	0.03
TG (mg/dl)	300.20 ± 158.3	235.14 ± 219.8	0.001
LDL (mg/dl)	130 ± 41.01	109.52 ± 29.7	0.005
HDL (mg/dl)	43.52 ± 8.8	42.56 ± 7.4	0.9

BMI: body mass index, WC: waist circumference, DM: diabetes mellitus, Pre-DM: prediabetes, HTN: hypertension, TSH: thyroid-stimulating hormone, FT4: free thyroxine, ALT: alanine aminotransferase, AST: aspartate aminotransferase, T.Chol: total cholesterol, TG: triglycerides, LDL: low-density lipoprotein, HDL: high-density lipoprotein. P-value: statically significant difference < 0.05.

Table 3. Mean lipids value in NAFLD patients according to the degree of hypothyroidism after excluding the patients taking medicines for hyperlipidemia

Variables	Euthyroid NAFLD patients n:39	Subclinical hypothyroidism n:11	Clinical hypothyroidism n:3	P-value
T.Chol	196.76 ± 32.8	223.45 ± 43.5	263 ± 55.6	0.004
TG	203.66 ± 85.9	269.27 ± 117.1	291.33 ± 173.5	0.04
LDL	102.61 ± 20.5	116.18 ± 41.8	135.66 ± 36.6	0.01
HDL	42.38 ± 7.8	43.09 ± 10.3	42 ± 2	0.9

T.Chol: total cholesterol, TG: triglycerides, LDL: low-density lipoprotein, HDL: high-density lipoprotein. P-value: statically significant difference <0.05

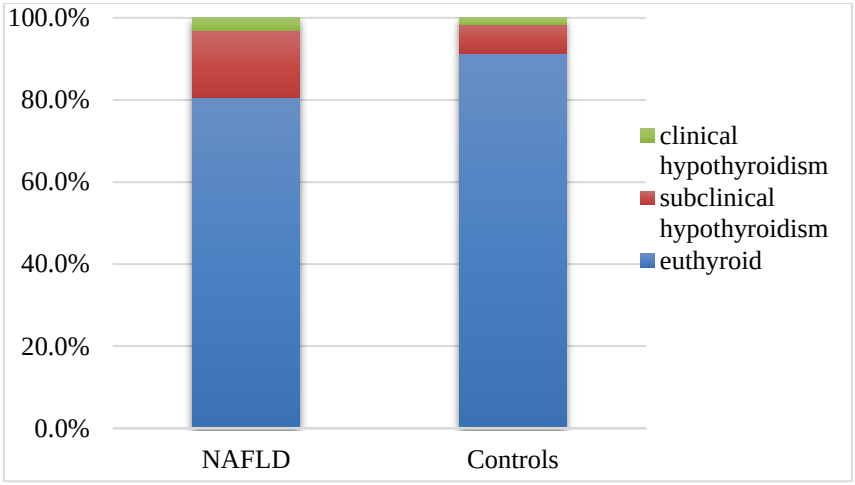

Fig. 1 Prevalence of hypothyroidism in the NAFLD group compared to control

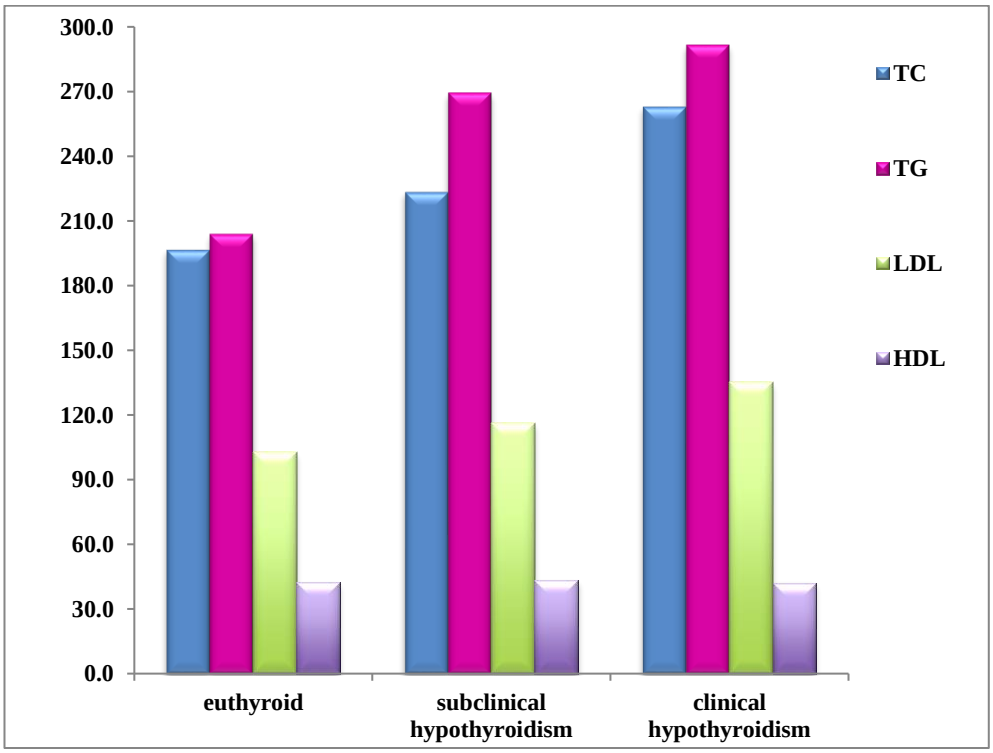

Fig. 2 Mean lipids values in the NAFLD group according to the degree of hypothyroidism

4. Discussion

NAFLD is the most common cause of chronic liver disease, affecting 25% of the world's population.[4] The prevalence of NAFLD is increasing worldwide in parallel with the increasing prevalence of obesity and metabolic comorbidities.[13] An important role for hypothyroidisim in the context of NAFLD has recently been suggested by several studies,[6] but the pathogenic mechanism of HIN is complex and not fully understood.[7] It is found an increased prevalence of hypothyroidism among patients with NAFLD compared to age and gender-matched controls (19.5% vs. 8.5%, p≤0.01); patients with NAFLD

have a two-fold increased risk of hypothyroidism (60% females, 40% males). Three previous studies also had similar results; Dhaliwal et al., this study was based on ultrasound. It showed a higher prevalence of hypothyroidism in the NAFLD group (18%) [14] Pagadala et al., Parikh et al. Two biopsy-based studies showed a higher prevalence of hypothyroidism in the NAFLD group by (21.1% and 16.8%).[15,16] These current findings confirm an association between the presence of hypothyroidism and NAFLD.

In the NAFLD group, the mean TSH was higher with a statistically significant difference, and this result was consistent with Dhaliwal et al., Pagadal et al., and Parikh et al. studies.[14,15,16] While FT4 values were lower in the NAFLD group with a statistically significant difference, this result was consistent with Dhaliwal et al. study [14]. Ludwig et al. study showed no difference between the two groups regarding TSH values, but TT4 values were lower in the NAFLD group.[17]

The reason why primary hypothyroidism is associated with hepatic steatosis is not fully understood.[7] However, several pathogenic mechanisms have been proposed. Hypothyroidism has been associated with insulin resistance [18], dyslipidemia [20], and obesity [20], all of which are important components of the metabolic syndrome, which plays an important role in the development of NAFLD. Patients with hypothyroidism suffer from increased levels of leptin [15], as leptin and adiponectin play an important role in hypothyroidism, insulin resistance, and accumulation of hepatic fat, which leads to the development and progression of NAFLD.[8,21] And because patients with hypothyroidism have elevated markers of oxidative stress, which may partly be explained by the fact that these patients have impaired metabolism of cardiolipin, [7,15] it may cause cellular damage in the liver through inhibition of beta-oxidation of FFAs. [8,15,20,21] Also, It has been observed that TSH concentrations are closely related to the development of NAFLD, the severity of steatosis, and the presence of fibrosis in NASH, TSH receptors have been identified in the cell membrane of liver cells, and their activation leads to the stimulation of fat formation and the accumulation of TGs in the hepatic tissue.[7,21]

The NAFLD group was characterized by a higher BMI, WC, HTN, DM, and Pre-DM compared to the controls, with statistically significant differences; these results agree with Ludwig, Pagadala, Parikh et al. studies.[15,16,17]

The mean values of ALT AST were higher in the NAFLD group compared to controls with significant statistical differences; these results agree with Pagadala et al., Parikh et al., and Ludwig et al. studies.[15,16,17] Also, the mean values of T.Chol, TG and LDL were higher in the NAFLD group compared to controls with significant statistical differences, while HDL was lower in the NAFLD group with a statistically significant difference because patients with obesity suffer from dyslipidemia twice the normal rate. The results were similar regarding T.Chol and TG in the Parikh et al. study.[16]

When studying the variables between the two groups of NAFLD patients with and without hypothyroidism, there were no significant statistical differences between the two groups in terms of demographic information (sex, age, waist circumference, BMI, hypertension, T2DM, Pre-DM), while in Pagadala et al. in hypothyroidism group, females, mean age and BMI were higher with significant statistical differences.[15] Parikh et al. In the hypothyroidism group, BMI was higher, with significant statistical differences.[16] For the laboratory tests, in the hypothyroidism group, liver enzymes (ALT, AST) were higher than the group with normal thyroid function, with a significant statistical difference; this result agrees with the result of Parikh et al. [16] while in Pagadala et al. study, ALT was higher in normal thyroid function group compared with hypothyroidism one.[15] Subclinical and overt hypothyroidism patients had significantly raised serum AST and ALT, and TSH showed a significant positive correlation with AST and ALT.[22] The values of T.Chol, TG, and LDL were higher in the hypothyroidism group with a statistically significant difference, while HDL values were similar between the two groups; in Pagadala et al., there is no difference between the groups regarding dyslipidemia, and in Parikh et al.there are no differences between two groups regarding TG values.[15,16] Up to 90% of patients with hypothyroidism have dyslipidemia. It primarily causes an increase in the levels of total cholesterol and LDL with an increase in the apolipoprotein Apo-B [15,20] due to a decrease in the number of LDL receptors in the cell membrane of the hepatocyte.[21] There is also an increase in the levels of serum TGs due to increased esterification of FFAs in the liver with decreased LPL activity.[7,15,20]

After excluding hyperlipidemia patients who take lipid and cholesterol reducers, the values of T. Col, TG, and LDL increased with the degree of hypothyroidism with statistically significant differences. However, the HDL values did not show a statistically significant difference between the three groups. Patients with subclinical hypothyroidism also suffer from abnormalities in their lipid profile, suggesting a direct mechanism of TSH. [7]

HDL values may be normal, high, or even lower in hypothyroidism [18,23]. This may be why the previous three groups of patients with steatosis did not show any significant statistical difference in HDL values.

5. Conclusion

- We found that the prevalence of primary hypothyroidism was 19.5% in NAFLD patients.
- There is no difference in the prevalence of hypothyroidism between diabetic and non-diabetic NAFLD patients.
- Liver enzymes AST and ALT were higher in NAFLD patients with hypothyroidism.

- The levels of T.Chol, TG, and LDL were higher in NAFLD patients with hypothyroidism.
- The levels of T.Chol, TG, and LDL showed a direct increase by increasing the degree of hypothyroidism in patients with NAFLD.

Recommendations

- We recommend a TSH test for all patients with non-alcoholic fatty liver disease.
- We suggest conducting ultrasound imaging in patients with hypothyroidism to investigate the presence of non-alcoholic fatty liver disease.
- Conducting a larger prospective study including a larger number of patients to compare the prevalence of hypothyroidism according to degrees of steatosis.
- Conducting a study of the effect of thyroxine treatment on improving the degree of hepatic steatosis, especially in patients with subclinical hypothyroidism.

References

[1] Mikako Obika, and Hirofumi Noguchi, "Diagnosis and Evaluation of Non-alcoholic Fatty Liver Disease," *Experimental Diabetes Research*, pp. 1-12, 2012. [CrossRef] [Google Scholar] [Publisher Link]

[2] J.K. Dowman, J.W. Tomlinson, and P.N. Newsome, "Pathogenesis of Non-Alcoholic Fatty Liver Disease." *QJM: An International Journal of Medicine*, vol. 103, no. 2, pp. 71-83, 2009. [CrossRef] [Google Scholar] [Publisher Link]

[3] Vignan Manne, Priya Handa, and Kris V. Kowdley, "Pathophysiology of Nonalcoholic Fatty Liver Disease/Nonalcoholic Steatohepatitis," *Clinics in Liver Disease*, vol. 22, no. 1, pp. 23-37, 2018. [CrossRef] [Google Scholar] [Publisher Link]

[4] Kenneth Cusi et al., "American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Non-alcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings: Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD)," *Endocrine Practice*, vol. 28, no. 5, pp. 528-562, 2022. [CrossRef] [Google Scholar] [Publisher Link]

[5] Chalasani Naga et al., "The Diagnosis and Management of Non-Alcoholic Fatty Liver Disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association," *American Journal of Gastroenterology*, vol. 107, no. 6, pp. 811-826, 2012. [CrossRef] [Google Scholar] [Publisher Link]

[6] E. Rinella Mary et al., "AASLD Practice Guidance on the Clinical Assessment and Management of Non-alcoholic Fatty Liver Disease," *Hepatology*, vol. 77, no. 5, pp. 1797-1835, 2023. [CrossRef] [Google Scholar] [Publisher Link]

[7] Amedeo Lonardo et al., "Pathogenesis of Hypothyroidism-induced NAFLD: Evidence for a Distinct Disease Entity?," *Digestive and Liver Disease*, vol. 51, no. 4, pp. 462-470, 2019. [CrossRef] [Google Scholar] [Publisher Link]

[8] Tomislav Kizivat et al., "Hypothyroidism and Non-alcoholic Fatty Liver Disease: Pathophysiological Associations and Therapeutic Implications," *Journal of Clinical and Translational Hepatology*, vol. 8, no. 3, pp. 1-7, 2020. [CrossRef] [Google Scholar] [Publisher Link]

[9] A.L. Sberna et al., "EASL-EASD-EASO Clinical Practice Guidelines for the Management of Non-alcoholic Fatty Liver Disease," *Journal of Hepatology*, vol. 64, no. 6, pp. 1388-1402, 2016. [CrossRef] [Google Scholar] [Publisher Link]

[10] M. Ammar Kalas et al., "Abnormal Liver Enzymes: A Review for Clinicians," *World Journal of Hepatology*, vol. 13, no. 11, pp. 1688-1698, 2021. [CrossRef] [Google Scholar] [Publisher Link]

[11] Seung Soo Lee, and Seong Ho Park, "Radiologic Evaluation of Non-alcoholic Fatty Liver Disease," *World Journal of Gastroenterology*, vol. 20, no. 23, pp. 7392-7402, 2014. [CrossRef] [Google Scholar] [Publisher Link]

[12] Simon H.S. Pearce et al., "2013 ETA Guideline: Management of Subclinical Hypothyroidism," *European Thyroid Journal*, vol. 2, no. 4, pp. 215-228, 2013. [CrossRef] [Google Scholar] [Publisher Link]

[13] Jessica K. Dyson, Quentin M. Anstee, and Stuart McPherson, "Non-Alcoholic Fatty Liver Disease: A Practical Approach to Diagnosis and Staging," *Frontline Gastroenterology*, vol. 5, no. 3, pp. 211-218, 2013. [CrossRef] [Google Scholar] [Publisher Link]

[14] Gurnoor Kaur Dhaliwal, Satya Bhushan Nayyar, and Manish Chandey, "To Study the Prevalence of Hypothyroidism in Non-Alcoholic Fatty Liver Disease in Northern Population," *Journal of Evidence-Based Medicine and Healthcare*, vol. 8, no. 33, pp. 3073-3077, 2021. [Publisher Link]

[15] Mangesh R. Pagadala et al., "Prevalence of Hypothyroidism in Non-alcoholic Fatty Liver Disease," *Digestive Diseases and Sciences*, vol. 57, no. 2, pp. 528-534, 2011. [CrossRef] [Google Scholar] [Publisher Link]

[16] Pathik Parikh, Aniruddha Phadke, and Prabha Sawant, "Prevalence of Hypothyroidism in Non-alcoholic Fatty Liver Disease in Patients Attending a Tertiary Hospital in Western India," *Indian Journal of Gastroenterology*, vol. 34, no. 2, pp. 169-173, 2015. [CrossRef] [Google Scholar] [Publisher Link]

[17] Ulla Ludwig et al., "Subclinical and Clinical Hypothyroidism and Non-Alcoholic Fatty Liver Disease: A Cross-Sectional Study of a Random Population Sample Aged 18 to 65 Years," *BMC Endocrine Disorders*, vol. 15, no. 41, pp. 1-7, 2015. [CrossRef] [Google Scholar] [Publisher Link]

[18] Huixing Liu, and Daoquan Peng, "Update on Dyslipidemia in Hypothyroidism: The Mechanism of Dyslipidemia in Hypothyroidism," *Endocrine Connections*, vol. 11, no. 2, pp. 1-15, 2022. [CrossRef] [Google Scholar] [Publisher Link]

[19] Ghada Rafik Hasan, and Hiam Kamel Fadel, "The Effect of the Water Extract of Soybean Seeds in Two Different Doses on Hyperthyroidism," *SSRG International Journal of Agriculture and Environmental Science*, vol. 7, no. 1, pp. 56-61, 2020. [CrossRef] [PublisherLink]

[20] Weiwei He et al., "Relationship between Hypothyroidism and Non-Alcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis," *Frontiers in Endocrinology*, vol. 8. pp. 1-11, 2017. [CrossRef] [Google Scholar] [Publisher Link]

[21] Simonetta Lugari et al., "Hypothyroidism and Nonalcoholic Fatty Liver Disease - A Chance Association?," *Hormone Molecular Biology and Clinical Investigation*, vol. 41, no. 1, 2018. [CrossRef] [Google Scholar] [Publisher Link]

[22] Sudha Ambiger, and Shrikanth P. Chincholika, "Study of Liver Function Tests in Patients of Hypothyroidism," *International Journal of Contemporary Medical Research*, vol. 6, no. 8, pp. 1-4, 2019. [CrossRef] [Google Scholar] [Publisher Link]

[23] K.C.B. Tan, S.W.M. Shiu, and A.W.C. Kung, "Effect of Thyroid Dysfunction on High-Density Lipoprotein Subfraction Metabolism: Roles of Hepatic Lipase and Cholesteryl Ester Transfer Protein," *The Journal of Clinical Endocrinology and Metabolism*, vol. 83, no. 8, pp. 2921-2924, 1998. [CrossRef] [Google Scholar] [Publisher Link]