Men's Health Journal. 2021; 5(1): e17

ORIGINAL RESEARCH

The Evaluation of the Effect of Hypothyroidism Treatment on Non-Alcoholic Fatty Liver Disease

Seyed Alireza Ebadi[1], Shayesteh khalili[2], Romina Rafiei[3], Mehdi Pishgahi[4]*, Mohammad karim Shahrzad5†

1. Department of Internal Medicine, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Department of Internal Medicine, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3. Shahid Beheshti University of Medical Sciences, Tehran, Iran.
4. Cardiology Department, Shohadaye Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
5. Internal Medicine and Endocrinology, Shohada Tajrish Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Received: February 2021; Accepted: February 2021; Published online: March 2021

Abstract: Introduction: There is still controversy over the existence of a relation between hypothyroidism and fatty liver disease. The scale by which hypothyroidism can affect fatty liver disease progression is also to be determined. Therefore, our study aims to contribute in the determination of this relation. Materials and methods: This observational analytical-before and after study with 53 patients was conducted. The subjects were categorized as having either primary or subclinical hypothyroidism. The serum levels of thyroid stimulation hormone (TSH), free T3 (FT3), free T4 (FT4), alanine transaminase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were measured and liver ultrasound was done to screen nonalcoholic fatty liver disease (NAFLD). Results: The study consisted of 41 women and 12 men with the mean age of 48.3 years. The mean TSH levels decreased after hypothyroidism treatment in patients. The mean levels of FT4 did not have a significant increase after treatment, although in patients with subclinical hypothyroidism this increase was significant. T3 levels increased significantly after treatment. Statistical studies showed that there was a significant change in the degree of fatty liver before and after hypothyroidism treatment. Conclusion: There was an explicit relation between hypothyroidism and non-alcoholic fatty liver disease as Hypothyroidism treatment can prevent non-alcoholic fatty liver disease progression.

Keywords: hypothyroidism; NAFLD, Non-Alcoholic Fatty Liver Disease

Cite this article as: Ebadi S A, Khalili Sh, Rafiei R, Pishgahi M, Shahrzad M K. The Evaluation of the Effect of Hypothyroidism Treatment on Non-Alcoholic Fatty Liver Disease. Mens Health J. 2021; 5(1): e17.

1. Introduction

In recent decades, with the rapid advancement of technology and lifestyle changes, the face of common diseases has changed from infections to emerging diseases. One of these diseases is non- alcoholic fatty liver disease (NAFLD) and cirrhosis and liver failure as a result.

Non-alcoholic steatohepatitis (NASH) is a title for a clinical topic in which patients, without a clear history of alcohol use, have indistinguishable findings from alcoholic steatohepatitis in their liver biopsy specimens(1, 2). The prevalence of NASH in the general population has not been well established(3). This limitation is due to sensitivity limitations in non-invasive NASH diagnostic evaluation methods. The prevalence of NAFLD can be better assessed in the community, because it can be detected by non-invasive methods. Fatty liver has become a common disorder in western industrialized societies, affecting 20 to 40% of the population(4). Fatty liver disease is more common around puberty(5, 6). NAFLD and NASH are more common in men(6, 7), perhaps due to the fact that men are more likely to develop metabolic syndrome. The main risk factors for NAFLD include: central obesity, type 2 diabetes, dyslipidemia, and metabolic syndrome.

Hypothyroidism is the most common endocrine disease af-

*Corresponding Author: Mehdi Pishgahi; Address: Cardiology Department, Shohadaye Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: mpishgahi.cr@gmail.com.

†Corresponding Author: Mohammad Karim Shahrzad; Address: Internal Medicine and Endocrinology, Shohada Tajrish Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: mk_shahrzad@yahoo.com.

ter diabetes. It occurs when the thyroid gland is unable to produce enough hormones. Hypothyroidism is classified into primary hypothyroidism (symptomatic hypothyroidism) and subclinical hypothyroidism (asymptomatic hypothyroidism), secondary hypothyroidism (pituitary) and tertiary hypothyroidism (Hypothalamic). (7-10) The Clinical signs of hypothyroidism are very diverse. It depends on the age of onset, the duration of the infection, and the severity of the hormone deficiency.

Symptoms such as fatigue, cold intolerance, weight gain, constipation, myalgia and Menstrual irregularities are common among people with hypothyroidism. Diagnosis of hypothyroidism is based on lab test results. (11-13)

There are few studies on the direct effect of hypothyroidism on the incidence of NASH, however, these studies suggest that hypothyroidism may cause NASH through hyperlipidemia and obesity. (14, 15) In this study, we intend to investigate the effect of primary hypothyroidism treatment on this common disease by examining the changes in the severity of fatty liver before and after treatment of primary hypothyroidism in patients referred to Imam Hossein Hospital.

2. Materials and Methods

This observational analytical-before and after study was performed in the endocrinology clinic of Imam Hossein Medical Center. At the clinic, patients who had not received treatment due to hypothyroidism, were given full explanations about the present study and its objectives, and were invited to participate in the research project with written consent.

Patients were given questionnaires regarding these comorbidities: smoking, history of cardiovascular disease, hyperlipidemia and hypertension. The patients' age was also included in their information form and their body mass index (BMI) was then calculated as follows: BMI=body weight (kg)/height squared (m2). Exclusion criteria from this study included history of hypothyroidism treatment, history of fatty liver treatment, diagnosis or development of fatty liver disease, history of regular alcohol consumption, use of liver dysfunction drugs, hepatitis B & C and cirrhosis.

Finally, 53 patients, including 12 men and 41 women were have been included, who they did not meet the exclusion criteria and were willing to participate in this study . For these patients, tests were performed to determine the serum levels of TSH, FT3, FT4, ALT, AST and ALP, and liver ultrasound was performed by a specialist to determine the presence of fatty liver and its severity for these patients. After 8 weeks of starting hypothyroidism treatment, TSH, FT3 and FT4 tests were performed again to adjust the dose of the drug, and if these tests were normal, after 3 months, TSH, FT3, FT4, ALT, AST and ALP tests and liver ultrasound were performed and then patients' information was entered in a form for statistical examinations.

For statistical analysis, SPSS software version 16 was used. Analysis of qualitative variables was performed by ANOVA, Chi2, Wilcoxon signed rank and Friedman tests and quantitative variables were analyzed by T-test. The acceptable alpha error was considered to be 0.05 and the beta error was considered to be 0.2.

All researchers of this study heed the Declaration of Helsinki. And the patient's names amongst their other personal information are confidential and no payment was received from the patients.

3. Results

In this study, 53 patients with newly diagnosed primary hypothyroidism who had not yet received treatment were studied. The study looked at 41 women and 12 men between the ages of 21 and 73 and the mean age of these patients was 48.3 years. 20 patients had subclinical hypothyroidism and 33 patients had primary hypothyroidism.

The review of the patients' files showed that 24 of the patients did not have comorbidities, 29 people had at least one form of hypertension, cardiovascular disease, and HLP, of which HLP was the most common.

In general, the mean TSH levels before and after hypothyroidism in patients were 13.43± 8.41 and 3.80 ±1.60 respectively, which statistically decreased TSH levels after treatment. ($P < 0.05$). The mean levels of FT4 before and after hypothyroidism in patients were 1.49±1.16 and 1.55±1.25 respectively, which did not have a statistically significant increase after treatment, although in patients with subclinical hypothyroidism this increase is significant.

Among all patients, T3 levels before and after hypothyroidism treatment were 72.61±14.18 and 90.35±15.62 respectively, and statistically, T3 levels increased significantly after treatment. ($P < 0.05$)

Figure 1 shows the frequency of different degrees of fatty liver before hypothyroidism treatment. Grade 1 fatty liver is more common than other degrees, and Figure 2 shows the frequency of different degrees of fatty liver after hypothyroidism treatment. At this stage, grade 1 fatty liver is still more common and the number of people with grade 1 fatty liver has increased. Statistical studies showed that there was a significant change in the degree of fatty liver before and after hypothyroidism treatment. In general, in 12 patients the degree of fatty liver decreased, in 41 patients there was no change and in none of the patients there was an increase in the degree of fatty liver.

ALT levels before and after hypothyroidism treatment were 42.15±21.84 and 39.26±18.14 respectively, which did not show a statistically significant decrease after treatment.

ALP levels before and after hypothyroidism in patients were

60.03±1.57 and 40.11±1.59 respectively, indicating no significant change in its level after hypothyroidism.
In the study population, AST levels before and after hypothyroidism treatment were 37.67±16.62 and 34.07±13.74 respectively, indicating a decrease in the level of patients after hypothyroidism treatment.
Patients' BMI decreased generally after hypothyroidism, so that the mean was 30.67±5.31 before treatment and 29.95±5.28 after treatment. Studies also showed that 21 people were non-smokers, 10 were smokers, 17 were inactive smokers and 5 were already smokers.

4. Discussion

Non-alcoholic fatty liver disease is among the prevalent causes of chronic hepatitis and cirrhosis; on the other hand, hypothyroidism is a condition affecting lifelong health in patients. As these two conditions are common health issues affecting the quality of lives of many patients, studying the association between them could result in significant findings. Currently, there are not enough studies on the direct effect of hypothyroidism on NAFLD. In this study, the rate of change in the severity of fatty liver disease before and after treatment of hypothyroidism in patients referred to Imam Hossein Hospital has been investigated. Our study suggests significant impact of hypothyroidism treatment on the suppression of fatty liver disease.
Liver enzymes (AST, ALT, and ALP) are found in liver cells and released into the patient's serum after a damage to the liver tissue. Therefore, the increase in AST, ALT, and ALP serum levels shows the destruction of liver cells (16). In this study an insignificant decrease in ALT and ALP levels and a significant decrease in AST levels was seen which shows a decrease in the liver tissue damage. Although some of these enzymes did not appear to have significant decrease in their serum levels, data depicts the process of liver damage to be restricted.
The average BMI of patients significantly decreased after the treatment of hypothyroidism. One study shows a meaningful relation between BMI and NAFLD (17). A study demonstrates that hypothyroidism can cause hyperlipidemia and obesity and thereby cause NASH. Hence, the decline in BMI can be effective in the suppression of liver damage (14).
As obesity, hypertension, type II diabetes, and other metabolic disorders have an important role in the increased risk of NAFLD, regular physical activity and exercise, and a low-fat diet is recommended to reduce the risk of NAFLD and liver damage (18). Many studies show a change in lifestyle, especially weight loss and increased physical activity, has an explicit effect on the improvement of NAFLD stage (19).
Another study also found a significant difference between the liver enzyme levels of patients with hypothyroidism and the patients with normal thyroid function. This study also shows a dose-dependent relation between the hypothyroidism spectrum and NAFLD. Several other studies also confirm these findings. (20-23)
There is also an opposing study which states that there is no association between hypothyroidism and fatty liver disease. This study has reviewed different articles and therefore its results could be compromised by statistical heterogenicity. The study also mentions that its result could be due to the limitation of races that have been assessed up to now, consisting of only Caucasians and Asians. (24)
Our study not only shows a relation between hypothyroidism and NAFLD, but also measures the impact. Therefore, this study provides quantitative information on the association. Furthermore, TSH, T3, FT4, AST, ALT, and ALP levels were all assessed in this study which is an advantage amongst some of the other similar articles.
In this study, certain comorbidities-which were mentioned earlier- were considered as potential interfering factors, and thus have been included in the gathering of data. Passive smoking has also been considered in our study as a comorbidity.
Our study was carried out on patients newly diagnosed with hypothyroidism, which is an advantage amongst other similar studies. Moreover, to our knowledge this study was the first to measure the association between hypothyroidism and fatty liver disease in its own population; which can help provide information about Middle Eastern people as well, and therefore confirm the previous studies on a new population.
Limitations of our study include; the use of imaging techniques for screening of NAFLD, instead of liver biopsy –which is the gold standard- could fault the results to some extent, all the laboratory tests were carried out in one (but reliable) clinical laboratory so further study is still needed on the matter, especially in different populations and races.

5. Conclusion

Our study demonstrates a significant association between hypothyroidism and fatty liver disease. Hypothyroidism causes the progression of NAFLD by increasing the risk of hyperlipidemia and obesity. Therefore, hypothyroidism treatment can improve fatty liver disease and prevent its further progression.

6. Appendix

6.1. Acknowledgment

None.

6.2. Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

6.3. Funding and support

None

6.4. Author's contributions

All the authors had the same contribution.

References

1. Ludwig J, Viggiano TR, Mcgill DB, Oh B, editors. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. Mayo Clinic Proceedings; 1980.
2. Sheth SG, Gordon FD, Chopra S. Nonalcoholic steatohepatitis. Annals of internal medicine. 1997;126(2):137-45. 3. Brunt EM. Pathology of fatty liver disease. Modern Pathology. 2007;20(1):S40-S8.
4. Lee RG. Nonalcoholic steatohepatitis: a study of 49 patients. Human pathology. 1989;20(6):594-8.
5. Papandreou D, Rousso I, Mavromichalis I. Update on non-alcoholic fatty liver disease in children. Clinical nutrition. 2007;26(4):409-15.
6. Patton HM, Sirlin C, Behling C, Middleton M, Schwimmer JB, Lavine JE. Pediatric nonalcoholic fatty liver disease: a critical appraisal of current data and implications for future research. Journal of pediatric gastroenterology and nutrition. 2006;43(4):413-27.
7. Nonomura A, Mizukam Y, Unoura M, Kobayashi K, Takeda Y, Takeda R. Clinicopathologic study of alcohol-like liver disease in non-alcoholics; non-alcoholic steatohepatitis and fibrosis. Gastroenterologia Japonica. 1992;27(4):521-8.
8. Arun J, Clements RH, Lazenby AJ, Leeth RR, Abrams GA. The prevalence of nonalcoholic steatohepatitis is greater in morbidly obese men compared to women. Obesity surgery. 2006;16(10):1351-8.
9. Tunbridge W, Evered D, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Whickham survey. Clinical endocrinology. 1977;7(6):481-93.
10. Vanderpump M, Tunbrldge W, French J, Appleton D, Bates D, Clark F, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. Clinical endocrinology. 1995;43(1):55-68.
11. Vanderpump MP, Tunbridge WMG. The epidemiology of thyroid diseases. Werner and Ingbar's the thyroid: a fundamental and clinical text. 2005:398-406.
12. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Archives of internal medicine. 2000;160(4):526-34.
13. Kajantie E, Phillips DI, Osmond C, Barker DJ, Forsen T, Eriksson JG. Spontaneous hypothyroidism in adult women is predicted by small body size at birth and during childhood. The Journal of Clinical Endocrinology & Metabolism. 2006;91(12):4953-6.
14. Surks MI, Hollowell JG. Age-specific distribution of serum thyrotropin and antithyroid antibodies in the US population: implications for the prevalence of subclinical hypothyroidism. The Journal of Clinical Endocrinology & Metabolism. 2007;92(12):4575-82.
15. Fauci A, Kasper D, Longo D. Harrison's Principles of Internal Medicine Vol 11. 2008.
16. Brunt EM, Janney CG, Di Bisceglie AM, Neuschwander-Tetri BA, Bacon BR. Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. The American journal of gastroenterology. 1999;94(9):2467-74.
17. L'age M, Meinhold H, Wenzel K, Schleusener H. Relations between serum levels of TSH, TBG, T 4, T 3, rT 3 and various histologically classified chronic liver diseases. Journal of endocrinological investigation. 1980;3(4):379-83.
18. Jamali R, Khonsari M, Merat S, Khoshnia M, Jafari E, Kalhori AB, et al. Persistent alanine aminotransferase elevation among the general Iranian population: prevalence and causes. World journal of Gastroenterology: WJG. 2008;14(18):2867.
19. Targher G, Byrne CD. Metabolically healthy obesity and NAFLD. Nature reviews gastroenterology & hepatology. 2016;13(8):442-4.
20. Ueno T, Sugawara H, Sujaku K, Hashimoto O, Tsuji R, Tamaki S, et al. Therapeutic effects of restricted diet and exercise in obese patients with fatty liver. Journal of hepatology. 1997;27(1):103-7.
21. Chung GE, Kim D, Kim W, Yim JY, Park MJ, Kim YJ, et al. Non-alcoholic fatty liver disease across the spectrum of hypothyroidism. Journal of hepatology. 2012;57(1):150-6.
22. Pagadala MR, Zein CO, Dasarathy S, Yerian LM, Lopez R, McCullough AJ. Prevalence of hypothyroidism in nonalcoholic fatty liver disease. Digestive diseases and sciences. 2012;57(2):528-34.
23. He W, An X, Li L, Shao X, Li Q, Yao Q, et al. Relationship between hypothyroidism and non-alcoholic fatty liver disease: a systematic review and meta-analysis. Frontiers in endocrinology. 2017;8:335.
24. Mantovani A, Nascimbeni F, Lonardo A, Zoppini G, Bonora E, Mantzoros CS, et al. Association between primary hypothyroidism and nonalcoholic fatty liver disease: a systematic review and meta-analysis. Thyroid. 2018;28(10):1270-84.

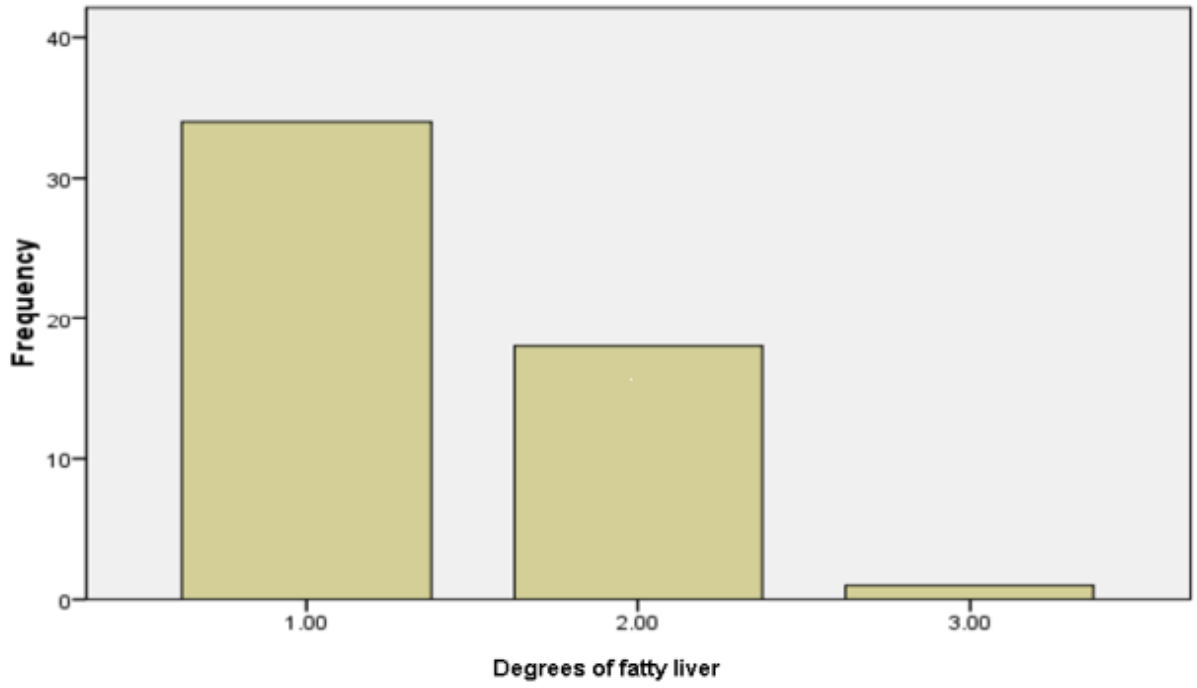

Figure 1: Shows the frequency of different degrees of fatty liver before hypothyroidism treatment.

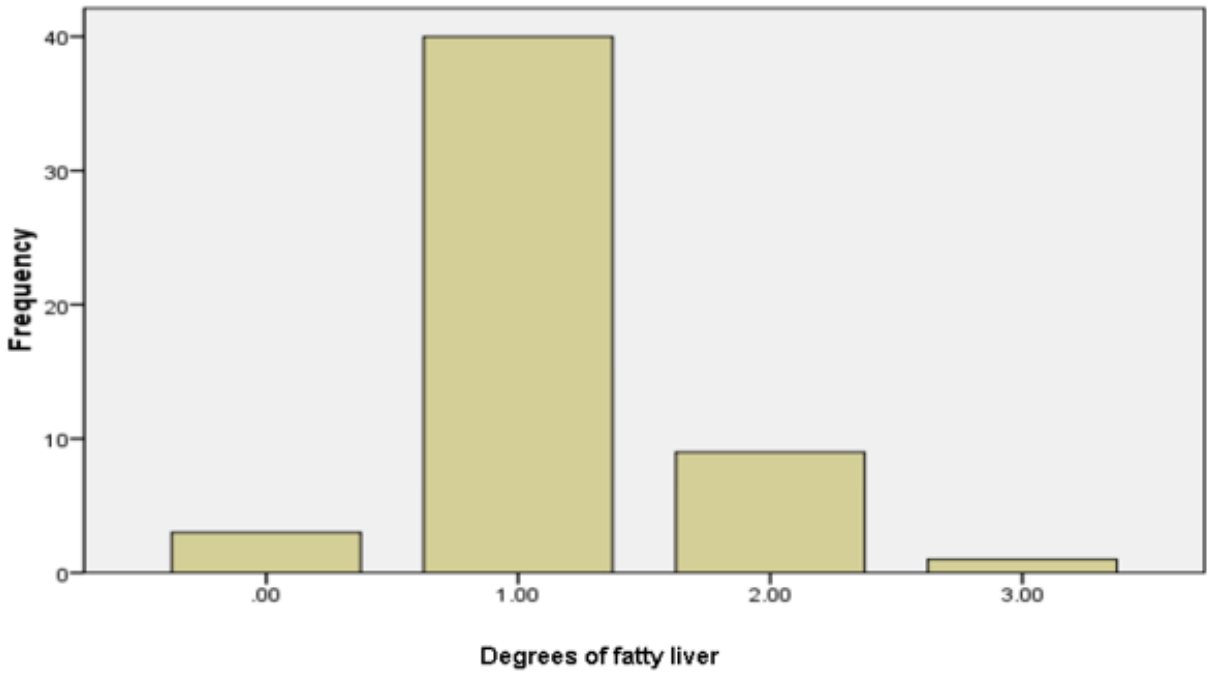

Figure 2: Shows the frequency of different degrees of fatty liver after hypothyroidism treatment.