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Original Research Article

An Observational Study to Estimate the Prevalence of NAFLD in Individuals with Hypothyroidism

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Abstract

Aim: The aim of the present study was to estimate the prevalence of NAFLD in individuals with hypothyroidism.
Material & Methods: This cross-sectional comparative study was conducted on Department of General Medicine.100 patients who qualified for the eligibility criteria. Proper history, examination, anthropometric measurements, and biochemical parameters were estimated. The collected data were entered in Excel and analyzed using the Statistical Package for Social Science 25 version developed by IBM (International Business Machine), IBM is a USA based company and the Student's t-test and the Chi-square test were applied.
Results: Out of 100 subjects, 55% were males and 45% were females. The age distribution among the study patients showed that majority of the patients are in a late age group with 58% patients belonged to >50 years of age. In this study smoking, diabetes and hypertension was present in 9%, 40% and 51% patients respectively among the subjects having thyroid dysfunction. 45% were in grade 1 followed by grade 2 and grade 3 according to grades of fatty liver. With the increasing grades of fatty liver more percentage of patients had high serum TSH and with increasing grades of fatty liver more percentage of patients had low free T4 levels and this relationship was statistically significant. In patients having grade 1 fatty liver on ultrasonography, out of 45 patients, 44 had a normal thyroid function, whereas only 1 patient was having overt hypothyroidism. In patients having grade 2 fatty liver on ultrasonography, out of 40 patients, 32 had a normal thyroid function.
Conclusion: Free T3 levels had no significant relationship with grades of fatty liver. Free T4 showed an inverse relationship with the increasing grades of fatty liver. Serum TSH showed a positive correlation with increasing grades of fatty liver.
Keywords: Non-alcoholic fatty liver disease, overt hypothyroid, subclinical hypothyroid

Introduction

Thyroid hormones are totally involved in the regulation of body weight, lipid metabolism, and insulin resistance. Therefore it is anticipated that thyroid hormones may have a role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH). [1] Non-alcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease. With a worldwide prevalence of 25%, NAFLD has become the leading cause of liver disease globally. NAFLD refers to a range of liver damage that includes simple steatosis to non-alcoholic steatohepatitis (NASH), characterized by steatosis with inflammation, hepatocyte ballooning, and varying degree of fibrosis(FIB).

NASH is a progressive type of NAFLD that can lead to liver cirrhosis and hepatocellular cancer. [2] NAFLD is diagnosed when hepatic steatosis is present in imaging or histology, while excluding secondary causes of hepatic fat accumulation. [3] NAFLD is a rapidly growing diagnosis, and it is the most common cause of abnormal liver function tests worldwide. [4] The growing pattern of NAFLD prevalence is generally attributed to a global increase in the prevalence of obesity and other metabolic risk factors. [5] Advanced age and metabolic disorders, such as diabetes type 2, impaired glucose tolerance, and central obesity, are among the risk factors for NAFLD. [6] There is a bidirectional relationship of metabolic syndrome and NAFLD. For the development of cardiovascular events and death in patients with NAFLD, metabolic syndrome is a key factor. [7]

Non-alcoholic fatty liver disease (NAFLD) represents a broad clinical spectrum ranging from simple fatty liver to non- alcoholic steatohepatitis (NASH), which may progress to liver fibrosis, cirrhosis and hepatocellular carcinoma. [8] NAFLD is a rapidly growing diagnosis, and it is the most common cause of abnormal liver function tests worldwide. [9] The growing pattern of NAFLD prevalence is generally attributed to a global increase in the prevalence of obesity and other metabolic risk factors. [10] Advanced age and metabolic disorders, such as diabetes type 2, impaired glucose tolerance, and central obesity, are among the risk factors for NAFLD. [11] Cryptogenic cirrhosis is a term used for those patients with liver cirrhosis who lack any identifiable viral, alcoholic, autoimmune or drug-related cause of the condition. Many clinicians now believe that a considerable number of these patients have cirrhosis due to NASH. [12]

Considering the increasing incidence of NAFLD/NASH, especially in developed and developing countries, it is anticipated that cirrhosis due to these conditions may surpass other causes of cirrhosis in a near future. Therefore, understanding the pathophysiology, risk factors and new treatment options of NAFLD / NASH should be among the priorities in the field of hepatology. [11] Thyroid gland is thoroughly involved in cell metabolism, energy homeostasis, regulation of body weight, thermogenesis, lipid and carbohydrate metabolism, and adipogenesis. [13]

The aim of the present study was to estimate the prevalence of NAFLD in individuals with hypothyroidism.

Material & Methods

The cross-sectional study involving 100 patients was conducted in the Department of General Medicine Gouri Devi Institute of Medical Sciences and Hospital, Durgapur, West Bengal, India . The study was performed over a period of 2 years

Methodology

All the hypothyroid patients underwent anthropometric measurements such as weight, height, body mass index (BMI), and waist circumference. Biochemical parameters such as liver function test, thyroid profile, and lipid profile test were done. Ultrasonography of the abdomen was done to diagnose the NAFLD. Blood was collected by aseptic methods and transferred to a plain bulb. Blood was analyzed for biochemical parameters by VITROS 5600. An experienced radiologist performed a single abdominal ultrasonography (USG) on all patients to check for fatty deposits in the liver. A Prosound Alpha 7 high-resolution B-mode ultrasonography equipment with curved linear arrays mid-frequency probe of 3–5MHz was used for the procedure.

Statistical Analysis

Epi info is a statistical software for epidemiology developed by centers for disease control and prevention in Atlanta, Georgia. The Centers for Disease Control and Prevention holds the trademark EPI INFO (CDC). The Student's t-test was used to assess the continuous data, whereas the Chi-square test was employed to compare the categorical variables. As percentages (%), the qualitative data were presented. To determine the association between the two statistical statistics, the odds ratio (OR) and confidence interval (CI) were determined. When appropriate, data were graphically represented using whisker plots, histograms, box and pie charts, and bar charts for continuous, categorical data, respectively. Wilcoxon test was employed when it was determined that the data were not normally distributed. For group comparisons of categorical data, one-way ANOVA was utilized. P values under 0.05 and above 0.05 were regarded as insignificant, respectively, whereas P values under 0.001 were considered extremely significant.

Results

Table 1: Demographic details

Gender	**N**	**%**
Male	55	55
Female	45	45
Age groups in years		
<50 years	42	42
>50 years	58	58
Co-morbidities		
Diabetes	9	9
Hypertension	40	40
Thyroid dysfunction	51	51
Grades of fatty liver		
Grade 1	45	45

Grade 2	40	40
Grade 3	15	15

Out of 100 subjects, 55% were males and 45% were females. The age distribution among the study patients showed that majority of the patients are in a late age group with 58% patients belonged to >50 years of age. In this study smoking, diabetes and hypertension was present in 9%, 40% and 51% patients respectively among the subjects having thyroid dysfunction. 45% were in grade 1 followed by grade 2 and grade 3 according to grades of fatty liver.

Table 2: Relationship of Serum TSH Levels, Serum Free t4 Levels with Grades of Fatty Liver

Serum TSH Levels TSH Levels	**Grades of Fatty Liver**			**Total**	**Chi- Square**	**P- Value**
	Grade 1	**Grade 2**	**Grade 3**			
<5 mIU	44	32	6	82	31.672	0.001
>5 mIU	1	8	9	18		
Serum Free t4 Levels						
Normal	42	32	5	79	16.032	0.000
Low	3	8	10	21		

Out of 45 patients having grade 1 fatty liver, 44 had a normal TSH levels, whereas only 1 patient was having TSH levels of more than > 5 mIU. Out of 40 patients having grade 2 fatty liver, 32 had a normal TSH levels, whereas 8 had TSH levels > 5mIU. Out of 15 patients having grade 3 fatty liver, 6 had a normal TSH levels, whereas 9 were having TSH levels between > 5 mIU. With the increasing grades of fatty liver more percentage of patients had high serum TSH and this relationship was statistically significant (p = 0.001).Out of 45 patients having grade 1 fatty liver, 42 had normal free T4 levels, whereas only 3 patients were having decreased free T4 levels. Out of 40 patients having grade 2 fatty liver, 32 had a normal free T4 levels, whereas 8 had decreased free T4 levels. Thus with increasing grades of fatty liver more percentage of patients had low free T4 levels which was statistically significant (p = 0.000).

Table 3: Relationship of Thyroid Status with Grades of Fatty Liver

Thyroid status TSH Levels	**Grades of Fatty Liver**			**Total**	**Chi- Square**	**P- Value**
	Grade 1	**Grade 2**	**Grade 3**			
Normal Thyroid Function	44	32	5	81	3.244	0.000
Subclinical Hypothyroidism	0	3	1	4		
Overt Hypothyroidism	1	5	9	15		

In patients having grade 1 fatty liver on ultrasonography, out of 45 patients, 44 had a normal thyroid function, whereas only 1 patient was having overt hypothyroidism. In patients having grade 2 fatty liver on ultrasonography, out of 40 patients, 32 had a normal thyroid function.

Discussion

The frequency of non-alcoholic fatty liver disease (NAFLD) has increased significantly throughout the past periods, and it has become the prominent reason of liver disease worldwide with a global prevalence of 25%, which can be moderately recognized to the rising prevalence of obesity. [14,15] The global prevalence of NAFLD is 24%, with the highest rates are reported from South America, the Middle East, and Asia. [16] Presence of metabolic syndrome (MetS) in an individual is the strongest risk factor for NAFLD and Non-Alcoholic Steatohepatitis (NASH). Among the features of MetS, diabetes mellitus has the clearest biologic link to the progression of NAFLD, and up to 75% of individuals with type 2 diabetes have NAFLD. [7,17]

The growing pattern of NAFLD prevalence is generally attributed to a global increase in the prevalence of obesity and other metabolic risk factors. Advanced age and metabolic disorders, such as diabetes type 2, impaired glucose tolerance, and central obesity, are among the risk factors for NAFLD. [10] Cryptogenic cirrhosis is a term used for those patients with liver cirrhosis who lack any identifiable viral, alcoholic, autoimmune or drug-related cause of the condition. [18] Out of 100

subjects, 55% were males and 45% were females. The age distribution among the study patients showed that majority of the patients are in a late age group with 58% patients belonged to >50 years of age. Tahara K et al [19] in their study revealed mean age of 69.1±8.1, which is approximately similar to our study. In this study smoking, diabetes and hypertension was present in 9%, 40% and 51% patients respectively among the subjects having thyroid dysfunction. In a study by Tahara K et al [19], the prevalence of diabetes or hypertension was not significantly different between patients with subclinical hypothyroidism and those with euthyroidism.

Chung et al [20] reported that the prevalence of NAFLD and abnormal liver enzyme levels (ALT) progressively increases as the grade of hypothyroidism increases. According to Eshraghian and Jahromi, an increased serum ALT level is a surrogate biomarker for NAFLD in the absence of other causes of liver disease and an indicator for the development of diabetes, cardiovascular disease and long term adverse complications from metabolic syndrome. [21] 45% were in grade 1 followed by grade 2 and grade 3 according to grades of fatty liver. With the increasing grades of fatty liver more percentage of patients had high serum TSH and with increasing grades of fatty liver more percentage of patients had low free T4 levels and this relationship was statistically significant. In patients having grade 1 fatty liver on ultrasonography, out of 45 patients, 44 had a normal thyroid function, whereas only 1 patient was having overt hypothyroidism. In patients having grade 2 fatty liver on ultrasonography, out of 40 patients, 32 had a normal thyroid function. The thyroid gland is significantly involved in energy homeostasis, lipid and carbohydrate metabolism, regulation of body weight and adipogenesis. In a clinical setting, subclinical hypothyroidism has been associated with metabolic syndrome, cardiovascular mortality and disturbance of lipid metabolism. In recent years, growing body of evidence has led to speculation on the association between NAFLD and thyroid dysfunction. [22,23] In a study by Ittermann et al [24], a significant inverse association between the free T4 concentration of NAFLD could be demonstrated. Studies by Xu et al [25], Chung et al. [20]

Conclusion

Free T3 levels had no significant relationship with grades of fatty liver. Free T4 showed an inverse relationship with the increasing grades of fatty liver. Serum TSH showed a positive correlation with increasing grades of fatty liver.

References

1. Eshraghian A, Jahromi AH. Non-alcoholic fatty liver disease and thyroid dysfunction: a systematic review. World journal of gastroenterology: WJG. 2014 Jul 7;20(25):8102.
2. Younossi Z, Tacke F, Arrese M, Chander Sharma B, Mostafa I, Bugianesi E, et al. Global Perspectives on Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. Hepatology 2019;69:2672-82.
3. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, Harrison SA, Brunt EM, Sanyal AJ. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018 Jan;67(1):328-57.
4. Angulo P. GI epidemiology: nonalcoholic fatty liver disease. Aliment Pharmacol Ther 2007; 25: 883-889.
5. Day CP. Non-alcoholic fatty liver disease: a massive problem. Clin Med 2011; 11: 176-178.
6. Eshraghian A, Jahromi AH. Non-alcoholic fatty liver disease and thyroid dysfunction: a systematic review. World J Gastroenterol 201 4;20(25):8102-8109.
7. Käräjämäki AJ, Bloigu R, Kauma H, Kesäniemi YA, Koivurova OP, Perkiömäki J, Huikuri H, Ukkola O. Non-alcoholic fatty liver disease with and without metabolic syndrome: different long-term outcomes. Metabolism. 20 17 Jan 1;66:55-63.
8. Law K, Brunt EM. Nonalcoholic fatty liver disease. Clin Liver Dis 2010;14(4):591-604.
9. Angulo P. GI epidemiology: nonalcoholic fatty liver disease. Aliment Pharmacol Ther 2007; 25(8):883-889.
10. Day CP. Non-alcoholic fatty liver disease: a massive problem. Clinical medicine. 2011;11 (2):176-178.
11. Eshraghian A, Jahromi AH. Non-alcoholic fatty liver disease and thyroid dysfunction: a systematic review. World J Gastroenterol 20 14;20(25):8102-8109.
12. Caldwell SH, Lee VD, Kleiner DE, et al. NASH and cryptogenic cirrhosis: a histological analysis. Ann Hepatol 2009;8(4):346-352.
13. Michalaki MA, Vagenakis AG, Leonardou AS, et al. Thyroid function in humans with morbid obesity. Thyroid 2006;16(1):73-78.
14. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016 Jul;64(1):73-84.
15. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. Jama. 2015 Jun 9;313(22): 2263-73.
16. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, George J, Bugianesi E. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nature

reviews Gastroenterology & hepatology. 2018 Jan;15(1):11-20.
17. Allen AM, Therneau TM, Larson JJ, Coward A, Somers VK, Kamath PS. Nonalcoholic fatty liver disease incidence and impact on metabolic burden and death: a 20 year-community study. Hepatology. 2018 May;67(5):1726-36.
18. Ortiz-Lopez C, Lomonaco R, Orsak B, Finch J, Chang Z, Kochunov VG, Hardies J, Cusi K. Prevalence of prediabetes and diabetes and metabolic profile of patients with nonalcoholic fatty liver disease (NAFLD). Diabetes care. 2012 Apr 1;35(4):873-8.
19. Tahara K, Akahane T, Namisaki T, Moriya K, Kawaratani H, Kaji K, Takaya H, Sawada Y, Shimozato N, Sato S, Saikawa S. Thyroid-stimulating hormone is an independent risk factor of non-alcoholic fatty liver disease. JGH Open. 2020 Jun;4(3):400-4.
20. Chung GE, Kim D, Kim W, Yim JY, Park MJ, Kim YJ, Yoon JH, Lee HS. Non-alcoholic fatty liver disease across the spectrum of hypothyroidism. Journal of hepatology. 2012 Jul 1; 57(1):150-6.
21. Eshraghian A, Dabbaghmanesh MH, Eshraghian H, Fattahi MR, Omrani GR. Nonalcoholic fatty liver disease in a cluster of Iranian population: thyroid status and metabolic risk factors. Archives of Iranian medicine. 2013 Oct 1;16(10):0-.
22. Yamada T, Fukatsu M, Suzuki S, Wada T, Yoshida T, Joh T. Fatty liver predicts impaired fasting glucose and type 2 diabetes mellitus in Japanese undergoing a health checkup. Journal of gastroenterology and hepatology. 2010 Feb; 25(2):352-6.
23. Rodondi N, den Elzen WP, Bauer DC, Cappola AR, Razvi S, Walsh JP, Åsvold BO, Iervasi G, Imaizumi M, Collet TH, Bremner A. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. Jama. 2010 Sep 22;304(12):1365-74.
24. Ittermann T, Haring R, Wallaschofski H, et al. Inverse association between serum free thyroxine levels and hepatic steatosis: results from the Study of Health in Pomerania. Thyroid 2012;22(6):568-574.
25. Xu C, Xu L, Yu C, et al. Association between thyroid function and nonalcoholic fatty liver disease in euthyroid elderly Chinese. Clin Endocrinol 2011;75(2):240-246.