A Study to Determine the Incidence of Non-Alcoholic Fatty Liver Disease in Patient with Thyroid Dysfunction

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ABSTRACT

Introdcution: Non-Alcoholic Fatty Liver Disease (NAFLD) has been recognized as the most common cause of abnormal liver function worldwide. Presence of metabolic syndrome (MetS) in an individual is the strongest risk factor for NAFLD and Non-Alcoholic Steatohepatitis (NASH), which is also linked to subclinical hypothyroidism. Here we tried to evaluate incidence of non-alcoholic fatty liver disease in patients with thyroid dysfunction.

Material and methods: A cross-sectional study was conducted on 100 patients attended the out-patient and in-patient department of general medicine of Chhatrapati Shivaji Subharti Hospital, Meerut. After the purpose and the contents of the study have been fully explained, written informed consent obtained from all patients fulfilling the inclusion criteria. A detailed history was taken.

Results: Out of 100 subjects, 53% were males and 47% were females in which majority of the patients are in a late age group with 58% patients belonged to >50 years of age. Smoking, diabetes and hypertension was present in 9%, 40% and 51% patients respectively among the subjects having thyroid dysfunction. Mean Free Thyroxine (FT4) and Thyroid-Stimulating Hormone (TSH) was 1.19 ng/dl and 6.3 µU/L among the study subjects. The incidence of non-alcoholic fatty liver disease (NAFLD) among the subjects having thyroid dysfunction was 36%.Univariate and multivariate analysis revealed that thyroid dysfunction and age > 50 years were independent risk factor of NAFLD.

Conclusion: Thyroid function is associated with NAFLD. This is an important finding because it opens a discussion if the adequacy of the TSH level to a lower reference could prevent the emergence of NAFLD.

Keywords: Non-Alcoholic Fatty Liver Disease, Metabolic Syndromes, Non-Alcoholic Steatohepatitis, Thyroid-Stimulating Hormone

INTRODUCTION

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.[1,2] The global prevalence of NAFLD is 24%, with the highest rates are reported from South America, the Middle East, and Asia.[3]

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.[4,5]

NAFLD is strongly associated with metabolic syndrome, which is also linked to subclinical hypothyroidism. Considering the important role of thyroid hormone in lipid metabolism, hypothyroidism may cause hyperlipidemia, which plays a crucial role in the pathogenesis of NAFLD.[6,7] Low thyroid hormone levels are related with hypometabolism. The prevalence of overt hypothyroidism in the general population varies between 0·3% and 3·7% in the USA and between 0·2% and 5·3% in Europe, depending on the definition used.[8]

At present, there are a number of observational studies, which have explored the relationship between hypothyroidism and NAFLD. Some studies suggested a strong correlation between hypothyroidism and NAFLD, but there were also studies pointing out that there was no correlation.[9] Therefore, the association between hypothyroidism and NAFLD risk remains in dispute up to now. Hence the present study was planned to determine the incidence of non-alcoholic fatty liver disease in patients with thyroid dysfunction.

MATERIAL AND METHODS

A cross-sectional study was conducted on 100 patients attending the out-patient and in-patient department of general medicine of Chhatrapati Shivaji Subharti Hospital, Meerut within 2 years of approval by the university. Ethical committee clearance was obtained.

Inclusion criteria

Patient age more than and equal to 18 years with thyroid dysfunction and patients who give consent were involved in this study

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Exclusion criteria

Patients diagnosed with viral hepatitis.(hepB,hep C), known cases of autoimmune hepatic diseases, alcohol intake, chronic liver disease, chronic kidney disease and patients consuming long-term drugs which affect thyroid functions (steroids, β-blockers) were excluded from the study.

Methods

After the purpose and the contents of the study have been fully explained, written informed consent was obtained from all patients fulfilling the inclusion criteria. A detailed history was taken with reference to the onset, duration, and progression of the symptoms, anorexia, malaise, fatigue, weight loss, constipation, reflux, nausea, hematemesis, vomiting, pain in abdomen, itching, melena, fullness of abdomen, alcohol intake and amount, long-term diseases like diabetes mellitus, hypertension, iron storage disorders, celiac disease, TPN, history of jejuno-ileal bypass, abetalipoproteinemia, disorders of copper metabolism, personal history and habits, family history, drug history, and such other relevant history. Liver function test (LFT) including aspartate aminotransferase (AST) and alanine transaminase (ALT) was performed for all the patients and findings were recorded.

STATISTICAL ANALYSIS

Collected data was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Univariate analysis was done using Anova (analysis of variance) and multivariate analysis was conducted with the help of linear and logistic regressions to determine the odds ratios. The level of significance was set at $p < 0.05$.

RESULTS

The present cross sectional study was conducted among 100 patients with thyroid dysfunction to evaluate the relationship and prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD). Out of 100 subjects, 53% were males and 47% 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.

Mean BMI (kg/m2) among the study group was 20.17 kg/m2. Mean HbA1c (%) was 6.3. ALT (IU/L), AST (IU/L) and Gamma-glutamyltransferase (IU/L) were 45.8 IU/L, 45.5 IU/L, and 105.39 IU/L among the subjects having thyroid dysfunction. Mean FT4 and TSH was 1.19 ng/dl and 6.3 µU/L among the study subjects. Mean total cholesterol, triglyceride and HDL- cholesterol among the study population were 1.19 mg/dl, 134.92 mg/dl and 57.18 mg/dl. In our study, elevated ALT and AST was reported among 40% and 37% of study subjects respectively. The prevalence of non-alcoholic fatty liver disease (NAFLD) among the subjects having thyroid dysfunction was 36%.Univariate and multivariate analysis revealed that thyroid dysfunction and age > 50 years were independent risk factor of NAFLD (Table 1).

DISCUSSION

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.[11]

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.[12,13]

The present cross sectional study was conducted among 100 patients with thyroid dysfunction to evaluate the relationship and prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD). Out of 100 subjects, 53% were males and 47% were females. Kazuki Tahara et al reported similar gender distribution in their study.[14]

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 (mean age: 67.89 years) in our study. Kazuki Tahara et al in their study revealed mean age of 69.1±8.1, which is approximately similar to our study.[14]

In this study smoking, diabetes and hypertension was present

Variables	Univariate Model			Multivariate Model		
	Odds Ratio	95%CI	p value	Odds Ratio	95%CI	p value
Thyroid Dysfunction	3.38	1.43-8.12	0.004*	4.83	2.79-11.81	<0.01*
Age>50 Years	2.86	1.11-5.74	0.03*	2.71	1.02-5.16	0.04*
Gender (Male)	1.04	0.87-1.29	0.45			
BMI	1.17	1.08-1.39	0.16			
Triglyceride	0.99	0.95-1.02	0.19			
HDL-Cholesterol	0.97	0.96-1.01	0.16			
Hypertension	1.42	0.69-2.97	0.11			
Diabetes	1.32	0.81-2.18	0.24			

Table-1: Risk factors of non-alcoholic fatty liver disease assessed by univariate and multivariate analyses

in 9%, 40% and 51% of the patients respectively having thyroid dysfunction. In a study by Kazuki Tahara et al, the prevalence of diabetes or hypertension was not significantly different between patients with subclinical hypothyroidism and those with euthyroidism.[14]

Mean BMI (kg/m2) among the study group was 20.17 kg/m2. Mean HbA1c (%) was 6.3. ALT (IU/L), AST (IU/L) and Gamma-glutamyltransferase (IU/L) were 45.8 IU/L, 45.5 IU/L, 105.39 IU/L among the subjects having thyroid dysfunction in the present study. Mean total cholesterol, triglyceride and HDL- cholesterol among the study population were 1.19 mg/dl, 134.92 mg/dl and 57.18 mg/dl in our study. Kazuki Tahara et al too revealed that the total cholesterol, triglyceride, HDL cholesterol, or HbA1c level was not significantly different between patients with subclinical hypothyroidism and those with euthyroidism.[14]

In this study, mean FT4 and TSH was 1.19 ng/dl and 6.3 µU/L among the study subjects. In our study, elevated ALT and AST was reported among 40% and 37% of study subjects respectively. These findings were in accordance with study done by Tahara et al.[14] Chung et al reported that the prevalence of NAFLD and abnormal liver enzyme levels (ALT) progressively increases as the grade of hypothyroidism increases.[15] 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.[16]

In the present study, the prevalence of non-alcoholic fatty liver disease (NAFLD) among the subjects having thyroid dysfunction was 36%. Thyroid hormones act as potent regulators of metabolic and energy homeostasis and have been implicated in various metabolic diseases. Hypothyroidism reduces resting energy expenditure, lipolysis, and gluconeogenesis; increases weight; and increases cholesterol levels. Therefore, hypothyroidism leads to hyperlipidemia, obesity, and insulin resistance, which are risk factors of the metabolic syndrome associated with NAFLD.[14]

In our study, risk factors of non-alcoholic fatty liver disease were assessed by univariate and multivariate analysis in study subjects. Thyroid dysfunction and age > 50 yrs were statistically significant on both univariate analysis (p value 0.004 and 0.03 respectively) and multivariate analysis (p value <0.01 and 0.04 respectively). Gender, BMI, triglyceride, HDL-cholesterol, hypertension and diabetes were not statistically significant. Therefore, thyroid dysfunction and age > 50 years were found to be independent risk factors of NAFLD in this study. Although the mechanism was not explained by this study, it was indicated that TSH might directly contribute to the development of NAFLD.

Recently, multiple studies reported extra-thyroid tissues expressing the TSH receptor. It was reported that functional TSH receptors were expressed in hepatocytes and that the cAMP/PKA/CREB pathway of the liver was involved in the induction of cholesterol synthesis by TSH62. Similarly Kazuki Tahara et al in their study found that TSH levels were independently associated with NAFLD, adjusted by metabolic-related factors such as BMI, triglyceride, HDL-cholesterol, hypertension, and diabetes, as assessed by multivariate analysis.[14]

Guo et al have reported that the association between NAFLD and FT3 and FT4 levels was heterogeneous among the population, and the TSH level may be an important risk factor for the development and progression of NAFLD, independent of thyroid hormones.[17] He et al have reported that the correlation between overt hypothyroidism and NAFLD was more significant than that between subclinical hypothyroidism and NAFLD.[18] Mantovani et al reported that subclinical hypothyroidism was not independently associated with the risk of incident NAFLD.[19] In addition, Kim et al reported that an increase in the TSH level, even within the normal clinical range of T4, was associated with biopsy-proven non-alcoholic steatohepatitis (NASH) and advanced fibrosis.[20]

The present study had some limitations. First, this was a cross-sectional study. Second, as NAFLD was diagnosed by ultrasonography, there was limited accuracy for the detection of mild steatosis.

CONCLUSION

It was found that thyroid function has a strong association with NAFLD. It is an important finding because it opens a discussion if the adequacy of the TSH level to a lower reference could prevent the emergence of NAFLD. The study findings highlight the need for future investigations on preventive measures (eg, screening of thyroid function in NAFLD patients) and possible therapeutic interventions (eg, decision of treatment in subclinical thyroid dysfunction).

REFERENCE

1. 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; 64:73-84.
2. Rinella ME. Nonalcoholic fatty liver disease: a systematic review. JAMA. 2015; 313:2263–73.
3. Younossi Z, Anstee QM, Marietti M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol. 2018; 15:11–20.
4. Käräjämäki AJ. Non-alcoholic fatty liver disease with and without metabolic syndrome: different long-term outcomes. Metabolism 2017; 66:55–63.
5. Allen AM. Nonalcoholic fatty liver disease incidence and impact on metabolic burden and death: a 20 year-community study. Hepatology 2018;67:1726–1736
6. Chen SH, He F, Zhou HL, Wu HR, Xia C, Li YM. Relationship between nonalcoholic fatty liver disease and metabolic syndrome. J Dig Dis. 2011; 12:125–30.
7. Mazo DF de C, Lima VMR de, Stefano JT, Rabelo F, Faintuch J, Oliveira CP de. Gluco-lipidic indices in treated hypothyroidism associated with nonalcoholic fatty liver disease. Arq Gastroenterol. 2011; 48:186–9.
8. McLeod DS, Caturegli P, Cooper DS, Matos PG, Hutfless S. Variation in rates of autoimmune thyroid

disease by race/ethnicity in US military personnel. JAMA 2014; 311: 1563–65.
9. 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. Arch Iran Med 2013; 16:584–9.
10. Day CP. Non-alcoholic fatty liver disease: a massive problem. Clin Med 2011; 11: 176-178.
11. Ortiz-Lopez C, Lomonaco R, Orsak B, Fet al. Prevalence of prediabetes and diabetes and metabolic profile of patients with nonalcoholic fatty liver disease (NAFLD). Diabetes Care 2012; 35:873-878.
12. 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. J Gastroenterol Hepatol 2010; 25: 352-356.
13. Rodondi N, den Elzen WP, Bauer DC, et al. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA 2010; 304: 1365-1374.
14. Tahara K, Akahane T, Namisaki T, et al. Thyroid-stimulating hormone is an independent risk factor of non-alcoholic fatty liver disease. Journal of gastroenterology and hepatology 2019:1–5.
15. Chung GE, Kim D, Kim W, et al. Non-alcoholic fatty liver disease across the spectrum of hypothyroidism. J Hepatol 2012; 57: 150-56.
16. 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. Arch Iran Med 2013;16:584–9.
17. Guo Z, Li M, Han B, Qi X. Association of non-alcoholic fatty liver disease with thyroid function: a systematic review and meta-analysis. Dig. Liver Dis. 2018; 50: 1153–62.
18. He W, An X, Li L et al. Relationship between hypothyroidism and non-alcoholic fatty liver disease: a systematic review and meta-analysis. Front. Endocrinol. 2017; 8: 335.
19. Mantovani A, Nascimbeni F, Lonardo A, et al Association between primary hypothyroidism and nonalcoholic fatty liver disease: a systematic review and meta-analysis. Thyroid. 2018; 28:1270-84.
20. Kim D, Kim W, Joo SK, Bae JM, Kim JH, Ahmed A. Subclinical hypothyroidism and low-normal thyroid function are associated with nonalcoholic steatohepatitis and fibrosis. Clin. Gastroenterol. Hepatol. 2018; 16: 123–31.

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