Section: General Medicine

Original Research Article

A PROSPECTIVE STUDY TO ANALYZE THE RELATIONSHIP AND THE TREND OF THYROID FUNCTION WITH SEVERITY OF NON-ALCOHOLIC FATTY LIVER DISEASE AT NEWLY ESTABLISHED TERTIARY CARE CENTER

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ABSTRACT

Background: Nonalcoholic fatty liver disease (NAFLD) is an emerging worldwide problem and its association with other metabolic pathologies. Metabolic derangements are suggested to be the main cause of NAFLD. As thyroid hormone is the main regulator of energy metabolism, there may be a link between NAFLD and thyroid function. This is a prospective study to analyze the relationship and the trend of thyroid function with severity of non-alcoholic fatty liver disease at newly established tertiary care center.

Materials and Methods: The present hospital based cross sectional study was proposed to be undertaken with a total number of 50 patients above 20 years of age of NAFLD diagnosed by ultrasonography whole abdomen, attending the department of medicine, Government Medical college, Barmer, Rajasthan, India during one-year period. Detailed history and clinical examinations were conducted on all patients, and they underwent routine investigations and thyroid function tests (free T3, free T4, and TSH). The statistical tests applied for analysis were Pearson's chi-square test, test and one-way analysis of variance.

Results: The present study consisted of 50 patients having Non-alcoholic fatty liver disease diagnosed on ultrasonography, 48% were having grade 1, 42% were having grade 2 and 10% were having grade 3 fatty liver. In the present study, 58% were having normal FT3 levels and 42 % patients had low FT3 levels which showed no significant relationship with increasing grades of fatty liver ($P>0.05$). Free T4 levels showed inverse relationship with increasing grades of fatty liver ($P<0.05$*). 18% of patients with NAFLD had hypothyroidism (4% subclinical and 14% overt hypothyroid) and a more percentage of patients with grade 2 and 3 fatty liver had hypothyroidism.

Conclusion: We concluded that free T4 and serum TSH levels had significant correlation with increasing grades of fatty liver. Hence, a statistically significant association was found between hypothyroidism and NAFLD.

Keywords: Hypothyroidism, Nonalcoholic Fatty Liver Disease (NAFLD), TSH, Free T4, Free T3.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a rapidly growing diagnosis, and it is the most common cause of abnormal liver function tests worldwide.[1] The growing pattern of NAFLD prevalence is generally attributed to a global increase in the prevalence of obesity and other

metabolic risk factors.[2] Non-alcoholic fatty liver disease (NAFLD) represents a broad clinical spectrum ranging from simple fatty liver to nonalcoholic steatohepatitis (NASH), which may progress to liver fibrosis, cirrhosis and hepatocellular carcinoma.[3]

Advanced age and metabolic disorders, such as diabetes type 2, impaired glucose tolerance, and central obesity, are among the risk factors for NAFLD.[4-6] 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.[7] 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.

Endocrine hormones are generally involved in cell metabolism, regulation of energy expenditure and fat distribution in the human body and thereby play an important role in the development of metabolic abnormalities. Thyroid gland is thoroughly involved in cell metabolism, energy homeostasis, regulation of body weight, thermogenesis, lipid and carbohydrate metabolism, and adipogenesis.[8] Subclinical hypothyroidism has been reported to be associated with metabolic syndrome, cardiovascular mortality, and disturbance of lipid metabolism.[9]

The prevalence of non-alcoholic fatty liver disease (NAFLD) in adults has been reported to be as high as 33 % making it the most common cause of chronic liver disease. Metabolic derangements are suggested to be the main cause of NAFLD. As thyroid hormone is the main regulator of energy metabolism, there may be a link between NAFLD and thyroid function. Considering this evidence, some studies were conducted to investigate the association between thyroid dysfunction and NAFLD / NASH. This is a prospective study to analyze the relationship and the trend of thyroid function with severity of non-alcoholic fatty liver disease at newly established tertiary care center.

MATERIALS AND METHODS

The present hospital based cross sectional study was proposed to be undertaken with a total number of 50 patients above 20 years of age of NAFLD diagnosed by ultrasonography whole abdomen, attending the department of medicine, Government Medical college, Barmer, Rajasthan, India during one-year period.

Exclusion Criteria

1. Presence of hepatitis B or C infection.
2. Presence of haemochromatosis.
3. Intake of iodine, antithyroid agents or thyroid hormones.
4. Chronic alcoholic liver disease.
5. Diabetes Mellitus.
6. Intake of drugs like Dopamine, Corticosteroids, Amiodarone and Phenytoin.

Methods

Detailed history and clinical examinations were conducted on all patients, and they underwent routine investigations and thyroid function tests (free T3, free T4, and TSH).

A 3D abdominal phantom Model was introduced to standardize the measured values of US H/R ratio and hepatic echo- intensity attenuation rate, finally we can compute the liver fat content as the following formula: Liver fat content (%) = 62.592 × US hepatic/renal ratio + 168.076 × US hepatic attenuation rate − 27.863.

Statistical Analysis

Descriptive statistics included computation of percentages, means and standard deviations. The statistical tests applied for analysis were Pearson's chi-square test, test and one-way analysis of variance. For all tests, confidence interval and p-value were set at 95% and ≤ 0.05 respectively.

RESULTS

The mean age was 52.58 years with maximum number of patients (30%) being in the age group of 50-60 years. Out of 50 patients 20 were females and 30 were males. The male to female ratio was 1.5:1 (table 1). On ultrasonography, 48% patients were diagnosed to be having grade 1, 42 % grade 2 and 10 % grade 3 fatty liver. Out of 24 patients having grade 1 fatty liver, 13 (54.16%) had a normal FT3 levels, whereas 11 (45.84%) were having low FT3 levels. Out of 21 patients having grade 2 fatty liver, 14 (66.66%) had a normal FT3 levels, whereas 7 (33.33%) were having decreased FT3 levels. Out of 5 patients having grade 3 fatty liver, 2 (40%) had a normal free T3 levels and 3 (60%) had decreased free T3 levels. Thus, abnormality in free T3 levels increased from 33.33 % in grade 2 to 60 % in grade 3 fatty liver, but the relationship was not statistically significant (p >0.05 NS). [Table 2]

Out of 24 patients having grade 1 fatty liver, 22 (91.66%) had a normal FT3 levels, whereas 2 (8.33%) were having low FT3 levels. Out of 21 patients having grade 2 fatty liver, 16 (76.20%) had a normal FT3 levels, whereas 5 (23.80%) had decreased FT3 levels. Out of 5 patients having grade 3 fatty liver, 2 (40%) had a normal free T3 levels and 3 (60%) had decreased free T3 levels. Thus, with increasing grades of fatty liver, a more percentage of patients had low free T4 levels which was statistically significant (p = 0.000). [Table 2]

Out of 24 patients having grade 1 fatty liver, 23 (95.83 %) had a normal TSH levels, whereas only 1 (4.16%) patient was having TSH levels of more than > 5 mIU. Out of 21 patients having grade 2 fatty liver, 16 (76.20 %) had a normal TSH levels, whereas 5 (23.80%) had TSH levels > 5mIU. Out of 5 patients having grade 3 fatty liver, 1 (20%) had a

normal TSH levels, whereas 4 (80%) were having TSH levels between > 5 mIU. As such 4.16% of patients with fatty liver grade 1, 23.80% with fatty liver grade 2 and 80% with fatty liver grade 3 had TSH level of >5 mIU. Thus, with increasing grades of fatty liver more percentage of patients had high serum TSH and this relationship was statistically significant (p <0.05*). [Table 2]

In patients having grade 1 fatty liver on ultrasonography, out of 24 patients, 23 (95.83%) had a normal thyroid function, whereas only 1 (4.16%) patient had overt hypothyroidism. In patients having grade 2 fatty liver on ultrasonography, out of 21 patients, 16 (76.19%) had a normal thyroid function, whereas 1 (4.76%) patient were having subclinical hypothyroidism with serum TSH levels >5mIU and normal free T4 levels and 4 (19.04%) patients were having overt hypothyroidism. In patients having grade 3 fatty liver on ultrasonography, out of 5 patients, 2 (40%) had a normal thyroid function, one (20%) had subclinical hypothyroidism and 2 (40%) were having overt hypothyroidism. As such in fatty liver grade 1, only one patient (4.16%) had hypothyroidism, in fatty liver grade 2, 5 patients (23.80%) had hypothyroidism out of which 1 (4.76%) had subclinical hypothyroidism and 4 (19.04%) had overt hypothyroidism and in fatty liver grade 3, 3 (60%) had hypothyroidism out of which 1 (20%) had subclinical hypothyroidism and 2 (40%) had overt hypothyroidism. Thus, with increasing grades of fatty liver there were more percentage of patients having hypothyroidism and this relationship was statistically highly significant (p<0.05*). Thus, in the present study prevalence of hypothyroidism was 18 % (4% subclinical hypothyroid, 14 % overt hypothyroid). [Table 3]

Table 1: Distribution of patients According to Age Groups

Age group (yrs)	No. of patients (N=50)	Percentage
20-30 yrs	6	12%
31-40 yrs	10	20%
41-50 yrs	12	24%
51-60 yrs	15	30%
>60 yrs	7	14%

Table 2: Relationship of Serum Free T4 levels and TSH Levels with Grades of Fatty Liver

BIOCHEMICAL ANALYSIS	Grades of Fatty Liver			P-value
	Grade 1 (N=24)	Grade 2 (N=21)	Grade 3 (N=5)	
SERUM FREE T4 LEVELS				
Normal (N=40)	22 (91.66%)	16 (76.20%)	2 (40%)	<0.05*
Low (N=10)	2 (8.33%)	5 (23.80%)	3 (60%)	
SERUM FREE T3 LEVELS				
Normal (N=29)	13 (54.16%)	14 (66.66%)	2 (40%)	>0.05
Low (N=21)	11 (45.83%)	7 (33.33%)	3 (60%)	
SERUM TSH LEVELS				
<5mIU	23 (95.83%)	16 (76.20%)	1 (20%)	<0.05*
>5mIU	1 (4.16%)	5 (23.80%)	4 (80%)	

Table 3: Relationship of thyroid status with Grades of Fatty Liver

Thyroid status	Grades of Fatty Liver			P-value
	Grade 1 (N=24)	Grade 2 (N=21)	Grade 3 (N=5)	
Normal thyroid status (N=41)	23 (95.83%)	16 (76.19%)	2 (40%)	<0.05*
Subclinical hypothyroidism (N=2)	0 (0%)	1 (4.76%)	1 (20%)	
Overt hypothyroidism (N=7)	1 (4.16%)	4 (19.04%)	2 (40%)	

DISCUSSION

Nonalcoholic fatty liver disease (NAFLD) is an emerging worldwide problem and its association with other metabolic pathologies has been one of the main research topics in the last decade. 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).

In the present study, 30% patients were in the age group of 51 - 60 years of age. The mean age of the patients was 52.58 ±11.42 years. In a study by Eshraghian A et al10 the mean age of patients with NAFLD was 48.20 ± 12.82 years. In another study by Ludwig U et al,[11] the mean age of the patients with NAFLD was 47.7 ± 11.5 years. The patients in both these studies were in the younger age group as compared to the present study.

In the present study, 60% patients were males and 40% were females thus having male predominance. In a study by Ulla Ludwig 70 % of the population with NAFLD were males and the remaining 30 % were females thus having male predominance.[11] In contrast in a study by Paul Samaresh et al,[12] there was female preponderance (63.3 %) among NAFLD patients.

More percentage of patients with low free T3 levels were in higher grades of fatty liver (p>0.05). In the study by Chung et al., which presented clear evidence of the association between hypothyroidism

and NAFLD, did not also describe any diagnostic value to the FT3 concentration.[13]

8.83% of patients with fatty liver grade 1, 23.80% with grade 2 and 60% with fatty liver grade 3 had low free T4 levels. Thus, with increasing grades of fatty liver more percentage of patients had low free T4 levels which was statistically significant ($p<0.05$*). There was an inverse relationship between low free T4 levels with increasing grades of fatty liver. In a study by Ittermann et al, a significant inverse association between the free T4 concentration of NAFLD could be demonstrated.[14] Studies by Xu et al,[15] Chung et al,[13] and Ittermann et al,[14] also concluded that lower free T4 is an independent risk factor for NAFLD. Findings of these studies are consistent with the present study.

4.16% of patients with fatty liver grade 1, 23.80% with fatty liver grade 2 and 80% with fatty liver grade 3 had TSH level of > 5 mIU. Thus, with increasing grades of fatty liver more percentage of patients had high TSH and this relationship was statistically significant ($p<0.05$*). Beside the inverse association with free T4, Chung et al,[13] and Xu et al,[15] identified a positive association between NAFLD and TSH. Studies by Carulli et al,[16] and Pagadala et al,[17] in addition, suggest that the serum TSH concentration is associated with the severity of hepatic steatosis. Ittermann et al,[14] detected no consistent association of serum TSH concentrations with hepatic steatosis. Our study showed a highly significant relationship between serum TSH levels and increasing grades of fatty liver. Bano et al,[18] in 2016 prospectively investigated the association between variations in thyroid function and NAFLD. They reported that higher free T4 levels were associated with a decreased risk of NAFLD. Also, higher serum TSH levels were associated with an increased risk of having clinically relevant fibrosis in NAFLD. The study concluded that lower thyroid function is associated with increased grades of NAFLD. This is in consistency with findings of the present study as it showed significant association of free T4 and serum TSH with increasing grades of fatty liver.

Pagadala MR et al showed 21 % of their study population was having hypothyroidism in patients with NAFLD ($p =0.000$).17 In a study by Parikh et al the number of hypothyroid patients in NAFLD was found to be 16.8 %.19 Hypothyroidism showed a significant correlation with NAFLD with a p - value of < 0.001. In the present study 18 % patients with NAFLD had hypothyroidism (4 % subclinical and 14 % overt hypothyroid) and a higher percentage of patients with grade 2 and 3 fatty liver had hypothyroidism.

CONCLUSION

The prevalence of hypothyroidism in the present study was 18 % which is almost 2 times the prevalence in the general population. A more percentage of patients in grade 2 and 3 fatty liver had hypothyroidism. Free T4 and serum TSH levels had significant correlation with increasing grades of fatty liver. Hence, a statistically significant association was found between hypothyroidism and NAFLD. These results may provide new evidence in the role of thyroid hormone on the regulation of liver fat content and NAFLD.

REFERENCES

1. Angulo P. GI epidemiology: nonalcoholic fatty liver disease. Aliment Pharmacol Ther 2007; 25: 883-89.
2. Day CP. Non-alcoholic fatty liver disease: a massive problem. Clin Med 2011; 11: 176-78.
3. Law K, Brunt EM. Nonalcoholic fatty liver disease. Clin Liver Dis 2010;14(4):591-604.
4. Amarapurkar D, Kamani P, Patel N, Gupte P, Kumar P, Agal S, Baijal R, Lala S, Chaudhary D, Deshpande A. Prevalence of non-alcoholic fatty liver disease: population based study. Ann Hepatol 2007; 6: 161-63.
5. 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; 35: 873-78.
6. 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: 352-56.
7. Caldwell SH, Lee VD, Kleiner DE, Al-Osaimi AM, Argo CK, Northup PG, Berg CL. NASH and cryptogenic cirrhosis: a histological analysis. Ann Hepatol 2009; 8: 346-3.
8. Michalaki MA, Vagenakis AG, Leonardou AS, et al. Thyroid function in humans with morbid obesity. Thyroid 2006;16(1):73-78.
9. Rodondi N, Den Elzen WP, Bauer DC, et al. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA 2010;304(12):1365-74.
10. Eshraghian A, Dabbaghmanesh MH, Eshraghian H, et al. Nonalcoholic fatty liver disease in a cluster of Iranian population: thyroid status and metabolic risk factors. Arch Iranian Med 2013;16(10):584-89.
11. Ludwig U, Holzner D, Denzer C, 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 Dis 2015;15(1):1-7.
12. Samaresh P, Bhaumik P, Swatilekha B. Thyroid profile of patients with non-alcoholic fatty liver disease. International Journal of Scientific Study 2020;8(1):72-75.
13. Chung GE, Kim D, Kim W, et al. Non-alcoholic fatty liver disease across the spectrum of hypothyroidism. J Hepatol 2012;57(1):150-56.
14. 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):568-74.
15. 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):240-46.
16. Carulli L, Ballestri S, Lonardo A, et al. Is nonalcoholic steatohepatitis associated with a high-though-normal thyroid stimulating hormone level and lower cholesterol levels? Int Emerg Med 2013;8(4):297-05.
17. Pagadala MR, Zein CO, Dasarathy S, et al. Prevalence of hypothyroidism in nonalcoholic fatty liver disease. Digest Dis Sci 2012;57(2):528-34.
18. Bano A, Chaker L, Plompen EPC, et al. Thyroid function and the risk of nonalcoholic fatty liver disease: the Rotterdam study. J Clin Endocrinol Metab 2016;101(8):3204-11.
19. Parikh P, Phadke A, Sawant P. Prevalence of hypothyroidism in non-alcoholic fatty liver disease in patients attending a tertiary hospital in western India. Indian J Gastroenterol 2015;34(2):169-73.