http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i12.88

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

A study on the prevalence of non-alcoholic fatty liver disease in hypothyroid patients in a tertiary care hospital in north India

Authors
Dr MC Srivastava[1], Dr Rajendra Kumar[2*]
[1]Assistant Professor, Department of Medicine, Prasad Institute of Medical Sciences, Sarai Shahzadi, Banthara, Lucknow-226401
[2]Assistant Professor, Department of Pharmacology, Prasad Institute of Medical Sciences, Sarai Shahzadi, Banthara, Lucknow-226401
*Corresponding Author
Dr Rajendra Kumar
Assistant Professor, Department of Pharmacology, Prasad Institute of Medical Sciences, Sarai Shahzadi, Banthara, Lucknow-226401, India

Abstract
Objective: *to assess the prevalence of non-alcoholic fatty liver disease in hypothyroid patients in a tertiary care hospital in north India.*
Methods: *This was a cross-sectional study. A total of 102 hypothyroid patients were included in the study. All diagnosed hypothyroid patient with a serum TSH> 5.5mIU/L with or without treatment were included in the study. On the basis of abdominal ultrasonography, NAFLD was diagnosed.*
Results: *The prevalence of NAFLD was 53.9%. The prevalence of NAFLD was 4.05 times significantly higher among the patients of age 30-40 years than <30 years (OR=4.05, 95%CI=1.58-10.39, p=0.004). The prevalence of NAFLD was 30% insignificantly lower among male patients than females (OR=0.22, 95% CI=0.21-2.24, p>0.05). The prevalence of NAFLD was 7.80 times significantly higher among patients with BMI ≥25 than BMI<18.5 (OR=7.80, 95%CI=1.46-41.41, p=0.01). Both AST and ALT were significantly (p<0.05) increased among the patients with NAFLD than without NAFLD. Both triglyceride and cholesterol were significantly (p=0.0001) increased among the patients with NAFLD than without NAFLD.*
Conclusion: *This study found a higher prevalence of NAFLD among hypothyroid patients. Age, BMI, ALT, AST, triglyceride and cholesterol were significantly associated with the prevalence of NAFLD among hypothyroid patients.*
Keywords: *Hypothyroid patients, Prevalence, Liver function tests, Lipid profile.*

Introduction

Non-alcoholic fatty liver disease (NAFLD) includes diseases of liver ranging from simple fatty liver to non-alcoholic steatohepatitis (NASH), which if untreated may lead to cirrhosis of liver and hepatocellular carcinoma[(1)]. It is the commonest liver disease worldwide. The increased prevalence of NAFLD is directly related to increased incidence of obesity, metabolic disorders such as insulin resistance, diabetes mellitus, and hypertension and dyslipidaemia[(2)]. Since thyroid hormones are

thoroughly involved in cell metabolism, energy homoeostasis, regulation of body weight, lipid and carbohydrate metabolism, and adipogenesis, there is chance of association between thyroid dysfunction and NAFLD/NASH. There is growing dataabout higher prevalence of thyroid dysfunction in the form of overt or subclinical hypothyroidism among patients with NAFLD/ NASH[3]. The prevalence of hypothyroidism was reported to range from 15.2 % to 36.3 % among patients with NAFLD/NASH[4].

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[5]. 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. The thyroid gland is significantly involved in energy homeostasis, lipid and carbohydrate metabolism, regulation of body weight and adipogenesis[6,7].

The present study conducted to assess the prevalence of non-alcoholic fatty liver disease in hypothyroid patients in a tertiary care hospital in north India.

Material and Methods

This was a cross-sectional study conducted in a tertiary care hospital in north India. The study was approved by the Ethical Committee of the Institute and consent was taken from each participant before including in the study. A total of 102 hypothyroid patients were included in the study.

All diagnosed hypothyroid patient with a serum TSH> 5.5mIU/L with or without treatment were included in the study. Diabetic patients (as per ADA criteria), patients with hypertension BP>130/80mmHg, alcohol consumption of > 20gm/day for men and >10gm/day for women, past history of jaundice and ongoing pregnancy were excluded from the study.

The patients were subjected to a questionnaire which included a short history about the illness. Patients were asked to come early morning for fasting for blood investigation as well as abdominal ultasonography. All blood investigations were performed at the institution's biochemical lab. On the basis of abdominal ultrasonography, NAFLD was diagnosed.

Statistical Analysis

The results are presented in frequencies, percentages and mean±SD. Unpaired t-test was used to compare continuous variables between the groups. The Pearson correlation coefficient was calculated. The univariate binary logistic regression was used to find the strength of associations of various factors with the prevalence of NAFLD. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

Results

The prevalence of NAFLD was 53.9% (Fig.1).

About half of patients were between 30-40 years (49%) followed by <30 (31.4%) and >40 (19.6%). More than half of patients were females (87.3%). About half of patients had BMI 18.5-24.99 (49%) followed by ≥25 (42.2%) and <18.5 (8.8%). The prevalence of NAFLD was higher among the patients of age 30-40 years (68%) than >40 (50%) and <30 (34.4%). The prevalence of NAFLD was 4.05 times significantly higher among the patients of age 30-40 years than <30 years (OR=4.05, 95%CI=1.58-10.39, p=0.004). The prevalence of NAFLD was higher among female patients (87.3%) than males (55.6%). The prevalence of NAFLD was 30% insignificantly lower among male patients than females (OR=0.22, 95% CI=0.21-2.24, p>0.05). The prevalence of NAFLD was higher among the patients of BMI ≥25 (90.7%) than <18.5 (55.6%) and 18.5-24.99 (22%). The prevalence of NAFLD was 7.80 times

significantly higher among patients with BMI ≥25 than BMI<18.5 (OR=7.80, 95%CI=1.46-41.41, p=0.01) (Table-1).

Both AST and ALT were significantly (p<0.05) increased among the patients with NAFLD than without NAFLD (Table-2).

Both triglyceride and cholesterol were significantly (p=0.0001) increased among the patients with NAFLD than without NAFLD (Table-3).

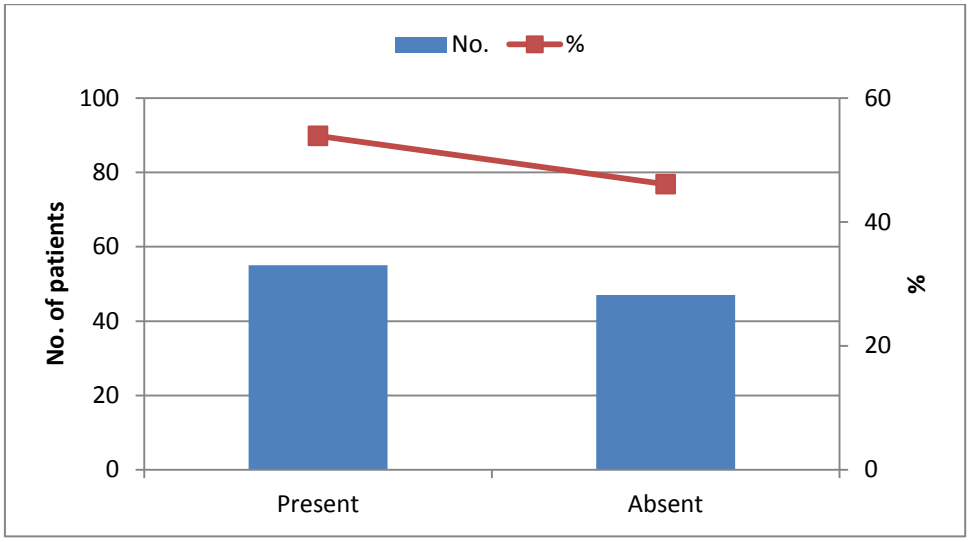

Fig. 1: Distribution of prevalence of NAFLD among the patients

Table-1: Association of prevalence of NAFLD with age, gender and BMI

Variables	No. of patients		With NAFLD		Without NAFLD		OR (95%CI)	p-value
	No.	%	No.	%	No.	%		
Age in years								
<30	32	31.4	11	34.4	21	65.6	1.00 (Ref.)	
30-40	50	49.0	34	68.0	16	32.0	4.05 (1.58-10.39)	0.004*
>40	20	19.6	10	50.0	10	50.0	1.90 (0.61-5.97)	0.26
Gender								
Male	13	12.7	6	46.2	7	53.8	0.70 (0.21-2.24)	0.54
Female	89	87.3	49	55.1	40	44.9	1.00 (Ref.)	
BMI								
<18.5	9	8.8	5	55.6	4	44.4	1.00 (Ref.)	
18.5-24.99	50	49.0	11	22.0	39	78.0	0.22 (0.05-0.98)	0.04*
≥25	43	42.2	39	90.7	4	9.3	7.80 (1.46-41.41)	0.01*

OR-Odds ratio, CI-Confidence interval, Ref.: Reference, *Significant

Table-2: Comparison of LFT between with and without NAFLD

LFT	With NAFLD	Without NAFLD	p-value[1]
AST	39.07±23.83	28.71±17.37	0.01*
ALT	38.93±28.19	26.31±14.33	0.02*
ALB	4.26±0.34	4.24±0.39	0.99

[1]Unpaired t-test, *Significant

Table-3: Comparison of Lipid profile between with and without NAFLD

Lipid profile	With NAFLD	Without NAFLD	p-value[1]
Triglyceride	159.73±66.48	108.20±41.87	0.0001*
Cholesterol	199.44±34.00	154.91±41.48	0.0001*
HDL	41.42±6.96	41.71±8.72	0.46
LDL	144.77±33.22	117.11±29.09	0.0001*
Cholesterol/HDL	4.96±1.26	3.93±1.82	0.004*

[1]Unpaired t-test, *Significant

Discussion

In this study, a total of 102 hypothyroid patients were included and USG was done on every patient to detect presence of NAFLD and USG grading of NAFLD was done.

In this study, about half of patients were between 30-40 years (49%) and more than half of patients were females (87.3%). In a study[8], in treated group, maximum number of patients 27 (54%) belonged to age group of 40-59 years and in untreated group also maximum number of patients 28 (56%) belonged to age group of 40-59 years. Among all hypothyroid cases, 68 (68%) were male and 32 (32%) were female. In treated group, 28 (56%) were male and 22 (44%) were female, whereas in the untreated group 40 (80%) were male and 10 (20%) were female. In the study by Liangpunsakul and Chalasani[9], the association between thyroid dysfunction and NAFLD have been characterised by relatively small sample and gender imbalance showing female preponderance.

The prevalence of NAFLD was 53.9% in this study. Mohanty et al(8) reported that among 100 hypothyroid cases (treated and untreated), 77 had TSH ≥4.1 mIU/L, of which 27 (35%) had NAFLD and 23 had TSH. In a study in Saudi Arabia, the prevalence of NAFLD diagnosed with ultrasonography was 16.6%[10].

This found that the prevalence of NAFLD was higher among the patients of age 30-40 years (68%) than >40 (50%) and <30 (34.4%). The prevalence of NAFLD was 4.05 times significantly higher among the patients of age 30-40 years than <30 years (OR=4.05, 95%CI=1.58-10.39, p=0.004). The prevalence of NAFLD was higher among female patients (87.3%) than males (55.6%). The prevalence of NAFLD was 30% insignificantly lower among male patients than females (OR=0.22, 95%CI=0.21-2.24, p>0.05). Study by Loria et al[11] demonstrated that prevalence of NAFLD increases with age, 13 but in our study majority of NAFLD cases i.e. 56.6% were found in the age group 40-59 yrs., P=1.563 which is statistically insignificant. In the study Mohanty et al[8], out of 30 NAFLD cases, 19 (63.3%) were male and 11 (36.7%) were female. From 19 male NAFLD cases, majority cases i.e. 8 cases (42.1%) were having NAFLD USG grade-II and out of 11 female NAFLD cases, 5 (45.4%) were having NAFLD USG grade-II. P= 0.063, which was statistically insignificant showing no significant relationship between gender & USG grading of NAFLD. So far as age is concerned, majority NAFLD cases i.e. 17 (56.7%) were of age group 40-59 yrs. and no NAFLD case was detected above 60 yrs. of age

In the present study, the prevalence of NAFLD was higher among the patients of BMI ≥25 (90.7%) than <18.5 (55.6%) and 18.5-24.99 (22%). The prevalence of NAFLD was 7.80 times significantly higher among patients with BMI ≥25 than BMI<18.5 (OR=7.80, 95%CI=1.46-41.41, p=0.01). In Taiwan, Japan, China and India proportion of non-obese subjects in a reported series of nonalcoholic fatty liver diseases from Asia with BMI <25kg/m^2 were 17%, 44%, 21% and 75% respectively[12].

In this study, both AST and ALT were significantly (p<0.05) increased among the patients with NAFLD than without NAFLD. Both triglyceride and cholesterol were significantly (p=0.0001) increased among the patients with NAFLD than without NAFLD. Eshraghian et al[13] reported that metabolic syndrome, higher BMI, waist circumference, hip circumference, advanced age, hypertension, diabetes, hyperlipidemia, elevated ALT, and AST levels were all associated with presence of NAFLD in univariate analysis.

Several studies have been recently conducted to investigate the association between thyroid dysfunction especially hypothyroidism and NAFLD/NASH. A cross-sectional study showed that increased serum TSH level is an independent risk factor for biopsyproven NASH[14]. Another cross-sectional study on elderly Chinese population revealed that higher freeT4 level was an independent risk factor for NAFLD[15].

Patients with hypothyroidism have abnormal lipid profiles mostly in the form of elevated serum levels of LDL[16]. Elevated TSH level has been

associated with diminished hepatic lipoprotein lipase activity and consequent elevation in serum triglyceride level[17,18]. Elevated serum makers of oxidative stress have been reported in patients with hypothyroidism and oxidative stress is one of the mechanisms involved in NAFLD. Hypothyroid patients were found to have elevated serum leptin levels, a hormone which is increased in obesity and insulin resistance[19,20].

Conclusion

This study found a higher prevalence of NAFLD among hypothyroid patients. Age, BMI, ALT, AST, triglyceride and cholesterol were significantly associated with the prevalence of NAFLD among hypothyroid patients.

References

1. Law K, Brunt EM. Non-alcoholic fatty liver diseases. Clin Liver Dis 2010;14 (4): 591-604.
2. Day CP. Non-alcoholic fatty liver disease: a massive problem. Clin Med (Lond) 2011;11(2):176-8.
3. Pucci E, Chiovato L, Pinchera A. Thyroid and lipid metabolism. Int J Obes Relat Metab Disord 2000;24(Suppl 2):S109-12.
4. Chung GE, Kim D, Kim W, et al. Non-alcoholic fatty liver disease across the spectrum of hypothyroidism. J Hepatol 2012;57(1):150-6.
5. 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: 346-352.
6. Michalaki MA, Vagenakis AG, Leonardou AS, Argentou MN, Habeos IG, Makri MG, Psyrogiannis AI, Kalfarentzos FE, Kyriazopoulou VE. Thyroid function in humans with morbid obesity. Thyroid 2006; 16: 73-78.
7. Raftopoulos Y, Gagné DJ, Papasavas P, Hayetian F, Maurer J, Bononi P, Caushaj PF. Improvement of hypothyroidism after laparoscopic Roux-en-Y gastric bypass for morbid obesity. ObesSurg 2004; 14: 509-513.
8. Mohanty R, Das SN, Jena AK, et al. Prevalence of non-alcoholic fatty liver disease in hypothyroidism in a tertiary care hospital in eastern India. J. Evolution Med. Dent. Sci. 2017;6(79):5589-5593,
9. Liangpunsakul S, Chalasani N. Is hypothyroidism a risk factor for non-alcoholic steatohepatitis? J Clin Gastroenterol 2003;37(4):340–3.
10. Al-Hamoudi W, El-Sabbah M, Ali S, Altuwaijri M, Bedewi M, Adam M, et al. Epidemiological, clinical, and biochemical characteristics of Saudi patients with nonalcoholic fatty liver disease: a hospital-based study. Ann Saudi Med. 2012; 32: 288 – 292.
11. Loria P, Carulli L, Bertolotti M, et al. Endocrine and liver interaction: the role of endocrine pathways in NASH. Nat Rev Gastroenterol Hepatol 2009;6(4):236- 47.
12. Das K, Das K, Mukherjee PS et al. Nonobese population in a developing country has a high prevalence of non-alcoholic fatty liver and significant liver disease. Hepatology. 2010,51: 1593-602.
13. Eshraghian A, Dabbaghmanesh MH, Eshraghian H, Fattahi MR, Omrani G. R. Nonalcoholic Fatty Liver Disease in a Cluster of Iranian Population: Thyroid Status and Metabolic Risk Factors. Arch Iran Med. 2013; 16(10): 584 – 589.
14. Carulli L, Ballestri S, Lonardo A, Lami F, Violi E, Losi L, et al. Is nonalcoholic steatohepatitis associated with a high-though-normal thyroid stimulating hormone level and lower cholesterol levels? Intern Emerg Med. 2013; 8: 297 – 305.
15. Xu C, Xu L, Yu C, Miao M, Li Y. Association between thyroid function and nonalcoholic fatty liver disease in

euthyroid elderly Chinese. Clin Endocrinol (Oxf). 2011; 75: 240 – 246.

16. Musso G, Gambino R, Cassader M. Recent insights into hepatic lipid metabolism in nonalcoholic fatty liver disease (NAFLD). Prog Lipid Res. 2009; 48: 1 – 26.
17. Brenta G, Berg G, Arias P, Zago V, Schnitman M, Muzzio ML, et al. Lipoprotein alterations, hepatic lipase activity, and insulin sensitivity in subclinical hypothyroidism: response to L-T(4) treatment. Thyroid. 2007; 17: 453 – 460
18. Duntas LH. Thyroid disease and lipids. Thyroid.2002; 12: 287 – 293.
19. Torun AN, Kulaksizoglu S, Kulaksizoglu M, Pamuk BO, Isbilen E, Tutuncu NB. Serum total antioxidant status and lipid peroxidation marker malondialdehyde levels in overt and subclinical hypothyroidism. Clin Endocrinol (Oxf). 2009; 70: 469 – 474.
20. Rolo AP, Teodoro JS, Palmeira CM. Role of oxidative stress in the pathogenesis of nonalcoholic steatohepatitis. Free Radic Biol Med. 2012; 52: 59 – 69.