

Prevalance of Non-alcoholic Fatty Liver Disease in Hypothyroid Patients and its Correlation with Serum Ferritin Levels

Mridul Chaturvedi*, Kushal Pal**, Rajkumar Verma***, Paramjeet**

Abstract

NAFLD is a relatively newly recognised entity among clinicians, presented with vague symptoms and upper quadrant abdominal pain. With growing epidemic of obesity, more and more cases of NAFLD are seen in clinical practises due to better availability of ultrasonographic facilities. The disease has an unpredictable course, may remain stationary through out life or may progress to hepatic cirrhosis. Search of a biomarker like serum ferritin may be useful in routine clinical practise to predict the natural history of NAFLD. In this small study, 100 patients were included which shows raised TSH in 33% patients of NAFLD, and out of 33 patient 20 patients has raised serum ferritin. To prove that it has more of a prognostic as compared to diagnostic value, a larger sample size is needed.

Key words: Hypothyroidism, NAFLD, serum ferritin, ultrasonography.

Introduction

Nonalcoholic fatty liver disease (NAFLD) comprises a broad spectrum ranging from simple steatosis, nonalcoholic steatohepatitis with fibrosis, which can eventually progress to cirrhosis and hepatocellular carcinoma¹. Nonalcoholic fatty liver disease (NAFLD) means accumulation of fat mainly triglycerides exceeding 5% of liver weight, affecting approximately 20% of population in developed countries². In recent years, a growing body of evidence has led to speculations on the association between NAFLD and hypothyroidism. Disturbances in thyroid hormone concentrations may promote hyperlipidaemia and obesity, thus contributing to NAFLD^{3,4}. Early identification of at-risk patients is important since treatment of hypothyroidism may reduce the risk of NAFLD and potential complications⁵.

Hyperferritinaemia with mild hepatic iron accumulation is observed in 20 - 30% of patients with NAFLD, and is commonly referred to as dysmetabolic iron overload syndrome⁶. Iron overload is found in as many as one-third of the patients with NAFLD⁷. To know the actual prevalence of NAFLD in hypothyroid patients, there is a search for various biochemical markers, out of which serum ferritin has emerged to be a promising one which can be easily used in various indoor and out door clinical setting as predictors for the presence of NASH versus simple steatosis^{8,9}. The present study also shows its prognostic value in NAFLD.

Material and methods

The study was conducted in the Department of Medicine, SN Medical College and Hospital, Agra, on all newly

diagnosed and old cases of hypothyroidism attending the OPD or admitted in the wards. In the present cross-sectional prospective study, demographic, clinical, laboratory, and radiological data of 100 adult patients with hypothyroidism was analysed.

The liver was assessed with respect to size, the presence of focal lesions, the presence of hepatic steatosis, and also whether steatohepatitis has progressed to cirrhosis. Different scoring systems have been designed, hoping to diagnose and stage NASH without histological data, but the debate on their accuracy is still ongoing¹⁰. On the basis of USG examination, diagnosis of fatty liver disease was made if large fat vacuoles were present in the liver parenchyma, displacing the nuclei to the border of the cells. Steatosis was graded as 1 if less than 33% of the hepatocytes were affected, grade 2 when 33 - 66% of the hepatocytes were affected, and grade 3 if more than 66% of the hepatocytes were affected. Staging and grading were performed according to the Brunt *et al* scoring¹¹.

Serum ferritin was measured by ELISA method (Monobind, USA) within two weeks after performing the USG. Serum iron and total iron-binding capacity (TIBC) were measured by calorimetric methods at the same time.

Observations and results

The present study consisted of 100 patients of which 67 were female and 33 were male. We tried to correlate the levels of TSH with grading of NAFLD, correlation of serum ferritin with TSH, and correlation of NAFLD and hypothyroidism as shown in the Table I - IV.

*Professor, **Junior Resident, ***Assistant Professor, Post-Graduate Department of Medicine, Sarojini Naidu Medical College, Agra - 282 002, Uttar Pradesh.

Corresponding Author: Dr Mridul Chaturvedi, Professor, Post-Graduate Department of Medicine, Sarojini Naidu Medical College, Agra - 282 002, Uttar Pradesh. Tel: 9719206386, E-mail: drmridul@gmail.com.

Table I: TSH in patients having non alcoholic fatty liver disease with hypothyroidism (n = 100).

TSH (μ IU/ml)	Male		Female		Overall	
	No.	%	No.	%	No.	%
≤ 5.0	0	0.00	0	0.00	0	0.00
5.1 - 20.0	5	15.15	5	7.46	10	10.00
20.1 - 35.0	6	18.18	8	11.94	14	14.00
35.1 - 50.0	11	33.33	22	32.84	33	33.00
50.1 - 65.0	2	6.06	17	25.37	19	19.00
> 65.0	9	27.27	15	22.39	24	24.00
Total	33	100.00	67	100.00	100	100.00

The TSH value in patients of non alcoholic fatty liver disease with hypothyroidism was highest (33%) in the range of 35.1 - 50.0 μ IU/ml, followed by 24% in the range of > 65.0 μ IU/ml, 19% in the range of 50.1 - 65.0 μ IU/ml, 14% in range of 20.1 - 35.0 μ IU/ml and 10% in the range of 5.1 - 20.0 μ IU/ml. No patient was found to have TSH value ≤ 5.0 .

Table II: Grading of fatty liver in non alcoholic fatty liver disease with hypothyroid patients (n = 100).

Grade	Male (N = 33)		Female (N = 67)		Overall (N = 100)	
	No.	%	No.	%	No.	%
Fatty liver grade-I	5	15.15	10	14.93	15	15.00
Fatty liver grade-II	3	9.09	9	13.43	12	12.00
Fatty liver grade-III	5	15.15	1	1.49	6	6.00

$\chi^2 = 6.12$, p - value = 0.047.

Out of all the subjects (N = 100) included in our study, most (15%) of the patients had grade-I fatty liver followed by 12% who had grade-II fatty liver, and only 6% had grade-III fatty liver. Grade-I fatty liver and grade-II fatty liver were seen in 15.15% and 9.09% of males respectively. Most (14.93%) of the females showed grade-I fatty liver. Only one female was found to have grade-III fatty liver.

Table III: Correlation of serum ferritin level with serum TSH level.

S. TSH	Serum ferritin level					
	Male			Female		
	N	Mean	SD	N	Mean	SD
≤ 5.0	0			0		
5.1-20.0	5	139.80	95.70	5	36.00	0
20.1-35.0	6	180.33	96.29	8	180.33	63.08
35.1-50.0	11	223.73	170.16	22	208.49	143.66
50.1-65.0	2	503.00	231.93	17	162.71	64.45
> 65.0	9	371.11	161.63	15	218.23	189.21
f - value		3.900			2.913	
p - value	0.012			0.028		

The study conducted between serum TSH levels and serum ferritin levels showed that higher levels of serum ferritin were present in patients with raised serum TSH.

Table IV: Correlation between grading of fatty liver and serum ferritin level in non alcoholic fatty liver disease with hypothyroid patients.

Fatty liver Grade	Serum ferritin level					
	Male			Female		
	N	Mean	SD	N	Mean	SD
Grade I	5	163.60	148.28	10	171.68	202.00
Grade II	3	527.33	144.20	9	241.71	105.67
Grade III	5	590.40	110.59	1	364.00	0
f - value		10.076			0.876	
p - value		0.004			0.043	

The study conducted comparing the serum ferritin levels and grades of fatty liver on ultrasonography showed that patients with higher grades of fatty liver on ultrasonography had higher serum ferritin levels too.

Discussion

In the present study, 33% of patients showed fatty liver of variable grades on ultrasonography. From this study, it has been observed that there is high incidence of fatty liver in patients whose TSH level was more than 35. Around 66% patients with fatty liver had TSH more than 35. The value was calculated for the relationship which came to be less than 0.001 which is significant.

In the present study, out of 33 patients of fatty liver of various grades, grade 1 fatty liver is seen in maximum no. of patients. TSH value was found to be more in patients with higher grades of fatty liver. Out of 33 patients of NAFLD with hypothyroidism, it was found that serum ferritin was significantly high in 20 patients, it was shown that serum ferritin level was significantly high with high TSH and higher grades of NAFLD, which is statistically significant with p value < 0.1 . In the rest 13 patients, serum ferritin level was normal. Thus it has more of prognostic value as compared to diagnostic value.

Although a role of hypothyroidism in the pathogenesis of non alcoholic fatty liver disease (NAFLD) has not been established, a number of possible mechanisms could be involved. Hypothyroidism has been associated with insulin resistance, dyslipidaemia and obesity, all of which are important components of the metabolic syndrome.

Seyed Reza Modares Mousavi (2018) conducted a prospective cross-sectional study on 30 patients with biopsy proven NAFLD/NASH and found no significant correlation between the histopathological stages of the disease with

serum ferritin levels. The prevalence of NAFLD and its severity increased with age. Our patients were relatively young and with less severe disease as expected.

In his study, it was found that 3 males and 9 females had both hypothyroidism and grade II non alcoholic fatty liver. These subjects showed a mean serum ferritin level of 527.33 and 241.71 respectively with a standard deviation of ± 144.20 and ± 105.67 respectively. They found 5 males and only 1 female with both hypothyroidism and grade III non alcoholic fatty liver, these subjects showed a mean serum ferritin level of 490.40 and 364.00 respectively with a standard deviation of ± 110.59 and ± 0 respectively. p value of correlation of serum ferritin level in patients of hypothyroidism with non alcoholic fatty liver was found to be 0.004 and 0.434 for males and females respectively.

Out of all the subjects (N = 100) included in our study, most (15%) of the patients had grade-I fatty liver followed by 12% having grade-II fatty liver and only 6% had grade-III fatty liver. Grade-I fatty liver was seen in 15.15% of males whereas only 9.09% of males showed grade-II fatty liver. Most (14.93%) of the females showed grade-I fatty liver. Only one female was found to have grade-III fatty liver.

Conclusion

With increase in obesity and sedentary lifestyle in developing countries like India, more and more cases of NAFLD are reported. More reporting of NAFLD cases is possible due to easy accessibility and sophisticated technique of ultrasonography, but the prognosis and natural history of NAFLD is still unpredictable. A biochemical marker like serum ferritin could help in predicting the natural history of NAFLD in hypothyroidism patients. Thus a better and suitable preventive strategy can be formulated to limit the development and progression of hepatic cirrhosis. In the present study, it was found that there was increased prevalence of fatty liver in patients of hypothyroidism and the levels of serum TSH correlated with grades of fatty liver. Also, serum ferritin levels were found to be increased in patients of fatty liver with hypothyroidism which also correlated with the grade of fatty liver.

References

1. Law K, Brunt EM. Nonalcoholic fatty liver disease. *Clin Liver Dis* 2010; 14: 591-604.
2. Kassem A, Khalil F, Ramadan MR *et al.* Association and impact of non-alcoholic fatty liver disease on thyroid function. *Int J Curr Res Med Sci* 2017; 3 (7): 94-107.
3. Chung GE, Kim D, Kim W *et al.* Non-alcoholic fatty liver disease across the spectrum of hypothyroidism. *J Hepatol* 2012; 57: 150-6.
4. 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: 236-47.

5. Ineck BA, Ng TM. Effects of subclinical hypothyroidism and its treatment on serum lipids. *Ann Pharmacother* 2003; 37: 725-30.
6. Angulo P. Non-alcoholic fatty liver disease. *N Engl J Med* 2002; 346: 1221-31.
7. Datz C, Muller E, Aigner E. Iron overload and non-alcoholic fatty liver disease. *Minerva Endocrinol* 2017; 42: 173-83. doi: 10.23736/S0391-1977.16.02565-7.
8. Feldstein AE, Wieckowska A, Lopez AR *et al.* Cytokeratin-18 fragment levels as noninvasive biomarkers for nonalcoholic steatohepatitis: a multicenter validation study. *Hepatology* 2009; 50: 1072-8. doi: 10.1002/hep.23050.
9. Sumida Y, Yoneda M, Hyogo H *et al.* A simple clinical scoring system using ferritin, fasting insulin, and type IV collagen 7S for predicting steatohepatitis in nonalcoholic fatty liver disease. *J Gastroenterol* 2011; 46: 257-68. doi: 10.1007/s00535-010-0305-6.
10. Buzzetti E, Lombardi R, De Luca L *et al.* Noninvasive Assessment of Fibrosis in Patients with Nonalcoholic Fatty Liver Disease. *Int J Endocrinol* 2015; 2015: 343-828. doi: 10.1155/2015/343828.
11. Brunt EM, Janney CG, Di Bisceglie AM *et al.* Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. *Am J Gastroenterol* 1999; 94: 2467-74. doi: 10.1111/j.1572-0241.1999.01377.

ADVERTISEMENT TARIFF

Journal, Indian Academy of Clinical Medicine
Advertisement Tariff effective January, 2020

Position	Single Issue	Consecutive Four Issues
(a) Back cover	₹ 20,000/-	₹ 60,000/-
(b) Inside back and inside front cover	₹ 15,000/-	₹ 45,000/-
(c) Full page	₹ 10,000/-	₹ 30,000/-
(d) Half page	₹ 6,000/-	₹ 18,000/-

Note: Artworks/positives (processing)/art pulls of advertisements for Back cover, Inside front cover, Inside back cover and Full page should not exceed 28 cm (H) x 21 cm (W) – (for bleed); and 25 cm (H) x 18 cm (W) – (for non-bleed). For half page advertisements the artwork should not exceed 12 cm (H) x 18 cm (W).

Size of the Journal is 28 cm x 21 cm.

For advertisement assistance & queries, contact:

Dr. Amit Aggarwal, Secretary, JIACM
 Mobile: +91-9716112232