International Journal of Research in Medical Sciences
Bitey S et al. Int J Res Med Sci. 2026 Jun;14(6):2375-2379
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20261673

Original Research Article

Study of serum ferritin levels in patients of non-alcoholic fatty liver disease with and without metabolic syndrome

Shobhana Bitey[1], Sunkari Ramya[1]*, Amol Bitey[2]

[1]Department of General Medicine, Indira Gandhi Government Medical College, Nagpur, Maharashtra, India
[2]Consultant Radiologist, Nagpur, Maharashtra, India

Received: 14 February 2026
Revised: 17 March 2026
Accepted: 20 May 2026

***Correspondence:**
Dr. Sunkari Ramya,
E-mail: ramyasunkari1628@gmail.com

ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD), defined as excessive deposition of fat >5% of liver weight is considered as liver manifestation of systemic metabolic dysregulation. Abdominal imaging is not able to determine which individuals with NAFLD have associated liver-cell death and inflammation (i.e., NASH), and specific blood tests to diagnose NASH are not yet available. Serum ferritin is a protein, expressed in an acute phase, elevated in the case of liver necrosis, inflammation. Therefore, this study aims to analyze the correlations between serum ferritin levels and NAFLD in patients with and without metabolic syndrome to explore a new biological marker for diagnosis and treatment.
Methods: A prospective study was performed among 100 cases of metabolic syndrome and 100 controls without metabolic syndrome, from November 2022-August 2024. Patients fulfilling inclusion criteria underwent ultrasonography for diagnosis and grading of NAFLD and their serum ferritin, clinical and lipid profiles were assessed in both the groups with and without metabolic syndrome.
Results: Serum ferritin levels were higher in cases across NAFLD grades compared to controls, and a strong positive correlation was observed between serum ferritin levels and NAFLD severity.
Conclusions: Patients with NAFLD exhibited a strong positive relationship between serum ferritin levels and NAFLD severity, suggesting that elevated ferritin levels may be an important marker for NAFLD progression. The findings underscore the importance of monitoring metabolic parameters and serum ferritin in assessing severity of NAFLD and adds value to the available armamentarium to tackle the syndrome.

Keywords: Metabolic syndrome, NAFLD, Serum ferritin

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD), defined a excessive deposition of fat >5% of the liver weight which is considered as a liver manifestation of systemic metabolic dysregulation. Due to the rising epidemic of obesity and the metabolic syndrome, NAFLD is now the most common liver disease with high prevalence of about 20-34% of western population.[1] NAFLD is strongly associated with insulin resistance, overweight/obesity. However, it can also occur in lean individuals and is particularly common in those with a paucity of adipose depots (i.e., lipodystrophy).[2] NAFLD is a composite term that includes the entire spectrum of fatty liver disease from simple steatosis to progressive steatosis with inflammation, fibrosis, cirrhosis, and hepatocellular carcinoma (HCC).[3] NAFLD has two subtypes: the nonprogressive form- non-alcoholic fatty liver (NAFL)- and the progressive form- non-alcoholic steatohepatitis (NASH). Epidemiological studies suggest the prevalence is around 9% to 32% of the general population in India with a higher prevalence in those with obesity and in those

with prediabetes and diabetes.[4] The gold standard for diagnosis and staging of NAFLD is liver biopsy, which is not well accepted by patients due to its invasive nature and consequently potential risks, and the accuracy is limited by sampling errors and interobserver variations.[5,6] Recent studies have pointed to hyperinsulinemia and insulin resistance as pathogenic factors in NAFLD. The strong association of NAFLD with other features of the metabolic syndrome (obesity, central fat distribution, diabetes, dyslipidemia, hypertension, and atherosclerotic cardiovascular disease) supports this hypothesis. Serum ferritin is a protein, expressed in an acute phase, so its level is elevated in the case of liver necrosis, inflammation.[7] Some recent investigations have stated that the level of SFL can be an irrespective indicator to assess the progression of hepatic fibrosis in the patients with NAFLD because of its association with hepatic iron storage and hepatic inflammation. Researchers came to a conclusion that SFL is higher in patients with NAFLD that might be linked with insulin resistance and hepatocyte damage.[8,9] NAFLD encompasses a spectrum of liver pathology with different clinical prognoses. MS affects almost the 20-30% of general population and half of the elderly, with differences between ethnic groups and economic and geographical areas.[10,11]

This study aimed to analyze the correlations between serum ferritin levels and NAFLD in patients with and without metabolic syndrome in order to further explore a new biological marker for the diagnosis and treatment of patients with NAFLD. This study further aimed compare the clinical and lipid profile changes seen in patients of NAFLD with or without metabolic syndrome.

METHODS

A prospective study was performed among 100 cases of metabolic syndrome and 100 controls without metabolic syndrome,

Study design

It was a hospital based cross sectional study.

Study period

The study took place from November 2022 to August 2024.

Study setting

Medicine wards and OPD of IGGMC (Indira Gandhi Government Medical College), Nagpur, Maharashtra, India.

Study subjects

Patients coming to our hospital with non-alcoholic fatty liver disease.

Selection of cases

Inclusion criteria

Patients with metabolic syndrome diagnosed according to NCEP- ATP iii criteria were taken as cases and patients without metabolic syndrome as controls; and patients willing to give informed consent.

Exclusion criteria

Patients with malignant tumors, acute infection, hemochromatosis, chronic inflammatory diseases, acute inflammation of the liver, elevated liver enzymes due to unknown causes, iron deficiency anemia, acute and chronic blood loss, excessive drinking (weekly alcohol intake >140 gm for men and >70 gm for women), drug-induced hepatitis, autoimmune hepatitis, viral hepatitis, and other diseases that may cause NAFLD were excluded. Age <18 years

Patients fulfilling inclusion criteria underwent ultrasonography for diagnosis and grading of NAFLD and their serum ferritin, clinical and lipid profiles were assessed in both the groups with and without metabolic syndrome.

Statistical analysis

Data was recorded on a Microsoft Excel spreadsheet. Statistical analysis was performed using Epi Info version 7.2.0.1 and SPSS student version 16.0 (SPSS Inc, Chicago, USA). Multivariate regression was applied to see the risk factors for metabolic syndrome and NAFLD. The p value of <0.05 was considered significant.

RESULTS

The study revealed that the mean age of participants with NAFLD (50.82 years) was slightly higher than that of the controls (47.21 years). The most common age group for both cases and controls was between 41 and 50 years. Gender distribution was similar between groups, with a predominance of females in both cases (79%) and controls (77%). Regarding NAFLD grading, cases exhibited higher proportions in grades 1 and 2 compared to controls, with statistical significance (p value =0.001). Cases had higher rates of comorbidities, including hypertension (82%), diabetes mellitus (85%), coronary artery disease (22%), and obesity (3%), compared to controls. Cases had a higher average BMI (24.47) and waist circumference (87.98 cm) compared to controls (BMI of 23.32 and waist circumference of 86.47 cm), both differences being statistically significant (p values =0.0001 and 0.02, respectively). Additionally, fasting blood sugar, triglycerides, and total cholesterol levels were higher in cases, while HDL cholesterol was lower, with all differences being statistically significant (p values ≤0.04).

Serum ferritin levels were higher in cases across NAFLD grades compared to controls, and a strong positive correlation was observed between serum ferritin levels and NAFLD severity (Pearson's r=0.77, p value =0.001).

Table 1: Characteristics of the study population with and without metabolic syndrome.

	Cases (with MetS)	Controls (without MetS)	P value
N	100	100	
Age (years)	50.82±14.36	47.21±13.23	
Gender N (%)	Males: 21 (21.00)	males: 23 (23.00)	
	Females: 79 (79.00)	females: 77 (77.00)	
Ferritin (µg/dl)	266.64	92.21	0.0001* (Mann Whitney U test)
BMI (kg/m^2)	24.47	23.32	0.0001
Waist circumference (cm)	87.98	86.47	0.02
WHR	0.85	0.84	0.66
Fasting blood sugar	162.49	156.37	0.04* (Mann Whitney U test)
Triglycerides	195.81	122.98	0.0001* (Mann Whitney U test)
Cholesterol	186.33	147.11	0.0001*
HDL	43.76	56.23	0.0001*
SGOT	25.01	25.28	0.91
SGPT	23.87	18.84	0.72 (Mann Whitney U test)
NAFLD, N (%)			
NAFLD 0	16 (16)	17 (17)	
NAFLD 1	35 (35)	15 (15)	0.001 (chi square test)
NAFLD 2	48 (48)	08 (08)	
NAFLD 3	01 (01)	00 (00)	

BMI - body mass index, WHR - waist to hip ratio, NAFLD- non-alcoholic fatty liver disease. *statistically significant

Table 2: Comparison of serum ferritin levels in cases and controls.

Serum ferritin levels	Cases n=100 (%)	Controls n=100 (%)	Chi square test P value
<200	38 (38.00)	93 (93.00)	0.0001
201-550	55 (55.00)	07 (7.00)	
551-1000	07 (7.00)	00 (00)	
Total	100 (100.00)	100 (100.00)	

Table 3: Comparison of mean serum ferritin levels in different grades of non-alcoholic fatty disease in cases and controls.

USG NAFLD grade	Group	Serum ferritin	T test P value
0	Cases	71.81±34.58	0.0001
	Controls	64.96±23.65	
1	Cases	216.8±83.35	0.0001
	Controls	158.9±47.61	
2	Cases	365.5±164.5	0.00001
	Controls	229.5±95.00	
3	Cases	380.0±00	--
	Controls	--	

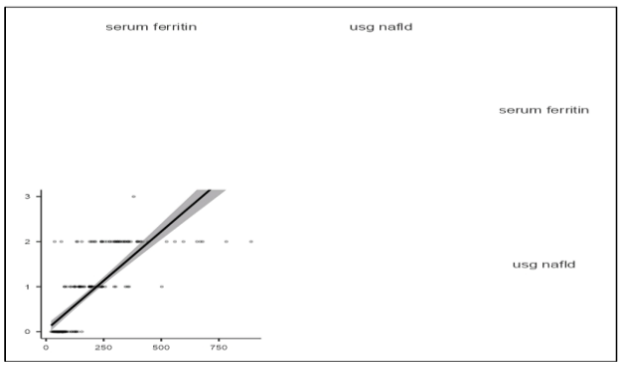

Figure 1: Correlation between serum ferritin levels and NAFLD.

Figure 1 presents the correlation between serum ferritin levels and NAFLD. The Pearson's correlation coefficient (r) is 0.77, indicating a strong positive correlation. The p value is 0.001, suggesting that the correlation is statistically significant. The degrees of freedom (df) is 198.

DISCUSSION

Age distribution

The study found that the highest proportion of cases was in the 41-50 age group (31%), followed by 51-60 (23%).

A study by Bellentani et al reported that NAFLD prevalence increases significantly with age, particularly in those over 40 years old.[12]

Gender distribution

The gender distribution in our study revealed a higher proportion of females among the cases (79%) compared to controls (77%). The higher prevalence of NAFLD in females observed in this study is consistent with Wong et al, who reported a greater female predominance in NAFLD cases.[13] This is supported by a study from Li et al, which found that hormonal and genetic factors might contribute to the higher prevalence in women.[14]

Anthropometric and biochemical parameters

The biochemical analyses showed significantly higher fasting blood sugar (FBS), triglycerides (TG), and cholesterol levels, and lower HDL levels in cases compared to controls. The higher mean values of BMI, waist circumference, fasting blood sugar, triglycerides, and cholesterol, along with lower HDL levels in cases, are consistent with research by Angulo and Marchesini et al.[3,15]

NAFLD grading

Our findings demonstrated a significant difference in NAFLD grading between cases and controls, with the majority of cases falling into NAFLD grades 1 and 2. Patients with metabolic syndrome(cases) had high grades of NAFLD as compared to controls. This is in line with research by Chalasani et al, which showed that most NAFLD patients present with mild to moderate steatosis.[16] Also by studies such as Younossi et al, which linked higher NAFLD grades with advanced stages of liver disease.[17]

Higher serum ferritin levels have higher grades of NAFLD and this is consistent with our study findings. We also found higher levels of ferritin levels in cases as compared to controls. Elevated serum ferritin levels are also consistent with studies by Cengiz et al and Neuschwander-Tetri, which linked high ferritin levels with liver inflammation and fibrosis.[18,19]

Limitations of the study are- sample size: the study had a relatively small sample size (n=100), which may limit the generalizability of the findings to broader populations. A larger sample size could provide more robust conclusions. Single-center study: this study was conducted in a single center or hospital, the results may not be representative of different regions or healthcare settings, which might have different exposure patterns, treatment protocols, or patient demographics.

CONCLUSION

The present study demonstrates a significant association between nonalcoholic fatty liver disease (NAFLD) and various metabolic risk factors. Age, blood pressure, BMI, WHR, prevalence of diabetes, hypertension and other comorbidities were higher in the MetS group compared with non-MetS group. Fasting blood sugar, triglycerides and total cholesterol were significantly higher in cases than controls whereas HDL levels were lower in cases when compared to controls. Patients with NAFLD exhibited higher mean BMI, waist circumference, and levels of fasting blood sugar, liver enzymes, triglycerides, and total cholesterol. Notably, lower high-density lipoprotein (HDL) levels and higher serum ferritin levels were observed in NAFLD cases, reflecting more severe metabolic dysregulation. The distribution of NAFLD grades showed a higher prevalence of moderate to severe steatosis in cases compared to controls. The correlation analysis revealed a strong positive relationship between serum ferritin levels and NAFLD severity, suggesting that elevated ferritin levels may be an important marker for NAFLD progression. Overall, the findings underscore the importance of monitoring metabolic parameters and serum ferritin in managing and assessing the severity of NAFLD and adds value to the available armamentarium to tackle the syndrome. The study highlights the need for targeted interventions to address metabolic dysfunctions in patients with NAFLD to potentially mitigate disease progression.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Bitey S, Ramya S, Bitey A. Study of serum ferritin levels in patients of non-alcoholic fatty liver disease with and without metabolic syndrome. Int J Res Med Sci 2026;14:2375-9.