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Original Article

Metabolic Syndrome among NAFLD Patients: A Single-Center Prospective Observational Study in A South Indian Teritary Care Hospital

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ABSTRACT

Background: Non-Alcoholic Fatty Liver Disease (NAFLD) is characterized by abnormal hepatic cholesterol accumulation, leading to metabolic disturbances and chronic liver conditions. The liver's role in glucose, cholesterol, and toxin regulation highlights the need for early intervention. With a projected 30% prevalence, NAFLD is a growing public health concern, particularly among diabetics and female in India (9-32%). It is strongly linked to metabolic syndrome, obesity, hyperlipidemia, and insulin resistance, increasing mortality risks. **Materials and Methods:** This study investigates the prevalence of metabolic syndrome in NAFLD patients and assesses the severity of steatosis using ultrasonography criteria. This prospective observational study was conducted over six months (September 2018-March 2019) at the master health checkup in hospital. Ultrasonography confirmed hepatic steatosis, and metabolic parameters (lipid profile, glucose levels) were recorded. **Results:** Among 136 NAFLD patients, 77.9% (*n*=106) were diagnosed with metabolic syndrome based on NCEP/ATP-III Criteria. The majority of patients were male (*n*=87), and metabolic syndrome prevalence was higher among males (81.6%) compared to females (71.4%). Common metabolic abnormalities included increased waist circumference (84.5%), low HDL levels (76.4%), and elevated fasting blood sugar (71.3%). Ultrasonography grading showed Grade I steatosis in 74.2%, Grade II in 25% and Grade III in 0.73% of patients. A significant correlation ($p<0.05$) was observed between NAFLD and metabolic syndrome components, highlighting a strong association with obesity, dyslipidemia, and insulin resistance. **Conclusion:** NAFLD is strongly linked to metabolic syndrome, especially in males. Early lifestyle intervention and multidisciplinary care are essential to prevent further complications.

Keywords: Liver Function Tests, Metabolic Syndrome, NAFLD, Obesity, Ultrasonography.

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INTRODUCTION

NAFLD can be defined as an elevated level of cholesterol in the liver with no evident cause. It is a novel component that results in chronic hepatic disorders and increased tests to evaluate liver function.[1] The liver regulates cholesterol, glucose, and poisons. Taking pre-emptive measures is critical to avoiding future issues. The 30% pandemic prevalence estimate immediate attention as well as major initiatives to encourage the identification and reporting of all possible NAFLD on a local, regional, and global scale.[2] Metabolic syndrome, type II diabetes, obesity, hyperlipidemia, insulin resistance, and steatosis are all associated with NAFLD, which increases mortality. This Hepatic condition is a main cause of chronic liver disease worldwide, and Indian patients are progressively affected. Epidemiologically, according to WHO, Non-Alcoholic Fatty Liver Disease (NAFLD) affects 9-32% of the general population in India, with a higher incidence in those with diabetes or pre-diabetes and a higher likelihood for females 60% than males 54.3%. The WHO ranks liver illness as India's ninth leading cause of mortality. Liver illness kills 3% of Indians.[3]

NAFLD is associated with metabolic syndrome, type II diabetes, obesity, hyperlipidemia, insulin resistance, and steatosis, all of which contribute to increased mortality.[4] Asymptomatic NAFLD patients are predominant. Hepatomegaly, abdominal discomfort, right upper quadrant abdominal pain, overall malaise and other symptoms may occur in study participants.[5] Thus, AST and ALT biochemical markers are essential for NAFLD diagnosis. NAFLD is diagnosed by liver biopsy, Ultrasonography,

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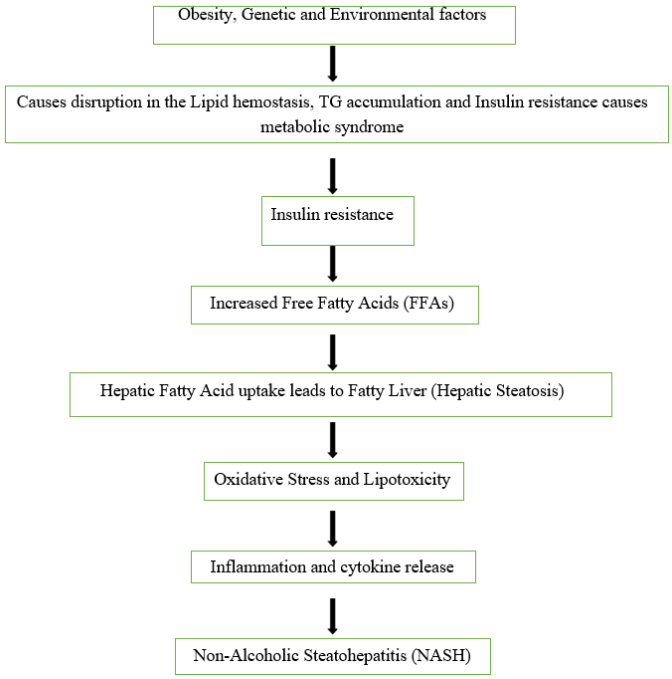
Computed Tomography, Magnetic Resonance Spectroscopy, and other indices including Fatty Liver Index.[6] Reduced FAO and increased TG production cause lipid clearance abnormalities in NAFLD.[7] Increased FAO reduces fat storage and obesity. The buildup of fat in over 5% of hepatocytes without alcohol use causes non-alcoholic fatty liver disease, which has primary or secondary clinical effects.[8] NAFLD's complex pathophysiology involves obesity, environmental factors, microbiome alterations, and predisposing genetic variations. These interactions disrupt lipid homeostasis and TG accumulation in hepatocytes.[9] Insulin resistance is a primary cause of NAFLD. Hyperinsulinemia and insulin resistance cause Metabolic Syndrome.[10] Metabolic Syndrome develops from obesity. NAFLD has emerged as a significant element of metabolic syndrome, recognizing its strong association with insulin resistance and obesity.[11] NAFLD has been associated, with scientific evidence, with an increased risk of osteoporotic fractures due to the possible mechanisms of deficiency of vitamin-D, chronic inflammation, or reduced physical activity.[12] Another avenue of exploration was into the relationship of bone mineral content to fat mass, which strengthens our hypothesis in a most enlightening way.[13]

This study explored the association between NAFLD and the prevalence of metabolic syndrome. After receiving approval from the Institutional Ethics Committee of Sri Ramachandra Institute of Higher Education and Research (Deemed to be University), and subjects fulfilling the eligibility criteria were requested to sign the informed consent form.

PATHOPHYSIOLOGY



PATIENTS AND METHODS

Methodology

This prospective observational study was conducted over 6 months, from September 2018 to March 2019, at the Department of Master Health Checkup, Sri Ramachandra Institute of Higher Education and Research (Deemed to be University) under IEC reference number CSP/18/SEP/73/245.

Study design

The study followed a prospective observational design to estimate the prevalence of Metabolic Syndrome (MetS) in individuals with NAFLD and explore different treatment approaches.

Study population

This study includes patients aged between 18 and 65 years, of both genders, who had no alcohol consumption. Eligible participants were required to have an ultrasonography impression confirming fatty liver and abnormal altered liver function tests which are not attributed to viral hepatitis, hepatobiliary or systemic diseases, or drug causes (glucocorticoids, synthetic estrogens, ATT amiodarone, aspirin, etc.,).

Sample Size Determination

The sample size was calculated using Epi software literature, with a 95% confidence interval. The calculated sample was 128 patients. To account for a 10% attrition rate, the final sample size was determined to be 136 patients.

Inclusion Criteria

- Age between 18 and 65 years in both genders.
- Ultrasonography impression showing fatty liver.
- Normal or altered liver function tests are not attributed to specific causes.

Exclusion Criteria

- Patients below 18 years of age.
- Changes in liver function tests due to drugs, chronic liver conditions, hepatobiliary or systemic diseases, or viral hepatitis.
- Active illicit drug users.
- Pregnant women.
- Seropositive for HIV.
- Patients with dyslipidemia taking lipid-lowering agents.

Data Collection

Subjects fulfilling the eligibility criteria provided informed consent, and data was collected using a specially designed proforma for the study. Complete anthropometric measurements, laboratory tests, and abdominal ultrasonography were performed to screen NAFLD and determine its grade. Mets were diagnosed in all participants based on the National Cholesterol Education Program Adult Treatment Panel III (2001) criteria (NCEP/ATP-III).

Metabolic Syndrome Detection

Metabolic Syndrome Detection was assessed using the following criteria:

- Basal glucose: ≥100 mg/dL.
- HDL Cholesterol <40 mg/dL in male and <50 mg/dl in female.
- Hypertension ≥130/85 mmHg.
- Hypertriglyceridemia ≥150 mg/dL.
- Abdominal Obesity: circumference >102 cm in male and >88cm in female.

Plan for Analysis

The SPSS V17.0 was used in the statistical analysis concerning the study data. For the continuous variables, descriptive statistics will offer a detailed summarization of the data through the mean, as well as standard deviation, or the median, in addition to interquartile range. The chi-square test was used to assess the correlation between NAFLD along with metabolic syndrome. Categorical variables were described via frequencies and percentages, and continuous variables were described as means with standard deviation or median with interquartile range.

RESULTS

The average age of our participants was 48.2 years, which closely aligns with a previous study conducted in Karachi by Imam S. K. *et al.*, where the mean age was 49.9 years.[14] Analyzing the age distribution, we found that a higher percentage of individuals aged above 50 years exhibited metabolic syndrome, consistent with the findings of a study by Ford E. S. *et al.*,[15-17] This suggests that age is a significant risk factor for metabolic syndrome. Furthermore, when comparing genders, the sample size indicated a higher proportion of males with metabolic syndrome than females.

Among 136 patients, the distribution of fasting blood sugar levels was as follows: 39 patients (28.67%) had normal fasting blood sugar, while 97 patients (71.3%) had abnormal fasting blood sugar. When considering blood pressure, normal blood pressure was found in 34 male (25%) and 21 female (15.4%) patients, whereas abnormal blood pressure was present in 53 male (38.9%) and 28 female (20.5%) patients. For HDL levels, normal HDL was observed in 24 males (17.6%) and 8 females (5.8%), while abnormal HDL was present in 63 males (46.3%) and 41 females (30.1%). Regarding TG levels, normal TG was found in 42 males (30.8%) and 31 females (22.7%), whereas abnormal TG was present in 45 males (33%) and 18 females (13.2%). Now focusing on waist circumference, 1 female patient (0.7%) and 20 male patients (14.7%) had normal waist circumference, while abnormal waist circumference was observed in 48 females (35.2%) and 67 males (49.2%) as follow as (Table 1 and Figure 1).

In the total NAFLD patients increased waist circumference is the commonest component in metabolic syndrome. Bhattarai S, *et al.*,[18-22] have explained that elevated waist circumference and hip/waist ratio is prevalent in females than in males.

The patients were classified into different grades based on their fatty liver condition. Grade I, which indicates increased liver echogenicity, was present in 101 patients (74.2%). Grade II, characterized by the liver obscuring the echogenic walls of the portal venous branches, was present in 34 patients (25%). Grade III, where the diaphragmatic outlines are obscured, was observed in 1 patient (0.73%) as follow as (Table 2 and Figure 2).

The mean and frequency distribution of various parameters of metabolic syndrome is as follows: waist circumference >90 cm was seen in 84.5% of the patients with a mean value of 94.28±47.28; blood pressure >130/85 mmHg was seen in 57.3% patients with a mean of 126.27; triglycerides >150 mg/dL was seen in 46.3% patients with a mean value of 158.6±81.5; HDL <40 mg/dL was seen in 76.4%% of patients with the mean of 38.7±20.37 and fasting blood sugar >100 mg/dL was seen in 71.m% patients with mean value of 132.3±52.8 as follow as (Table 3 and Figure 3).

In this study, it was found that 106 patients had metabolic syndrome among 136 patients, of which 71(81.6%) were male patients and 35(71.4%) of them were female patients. Moreover, NAFLD is a strong determinant for the future development of the metabolic syndrome[23-26] as follow as (Table 4).

Table 1: Metabolic syndrome parameters.

Parameters to Measure Metabolic Syndrome		No. of Patients	
		Male (*n*=87)	Female (*n*=49)
Waist Circumference	Normal	20	1
	Abnormal	67	48
Blood pressure	Normal (≤130/≤85 mmHg)	34	21
	Abnormal (≥130/≥85 mmHg)	53	28
Fasting blood sugar	Normal (<100 mg/dL)	22	17
	Abnormal (≥100 mg/dL)	65	32
Triglycerides	Normal (≤150 mg/dL)	42	31
	Abnormal (≥150 mg/dL)	45	18
High-density lipoprotein	Normal (<40 mg/dL)	24	8
	Abnormal (<50 mg/dL)	63	41

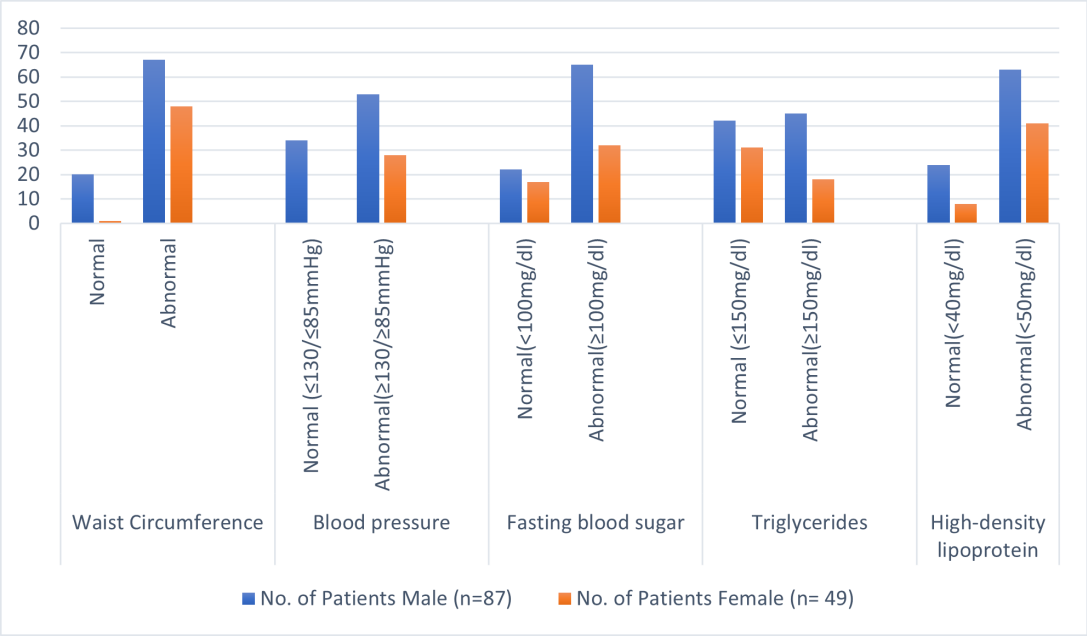


Figure 1: Parameters to Measure Metabolic Syndrome.

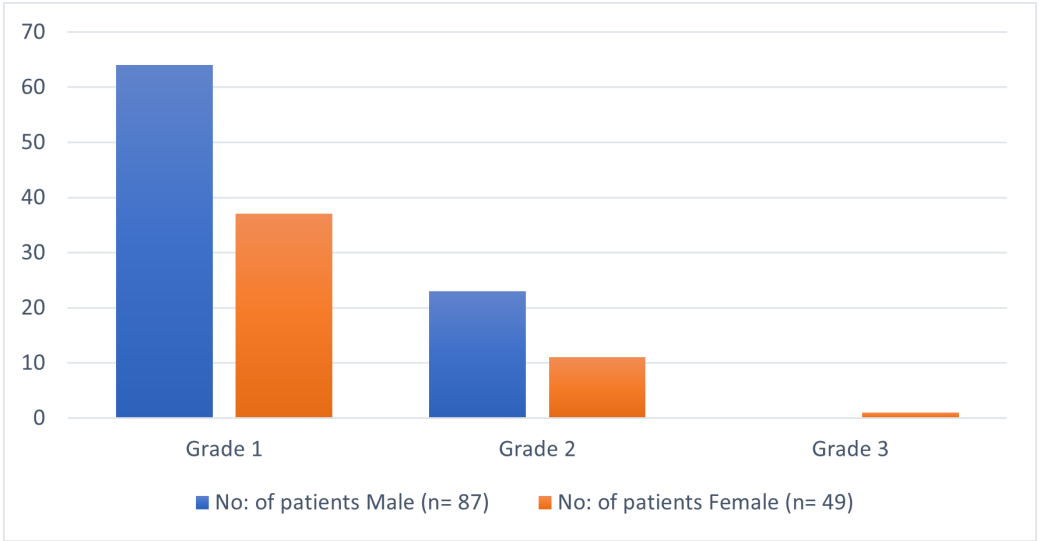


Figure 2: Fatty liver grading.

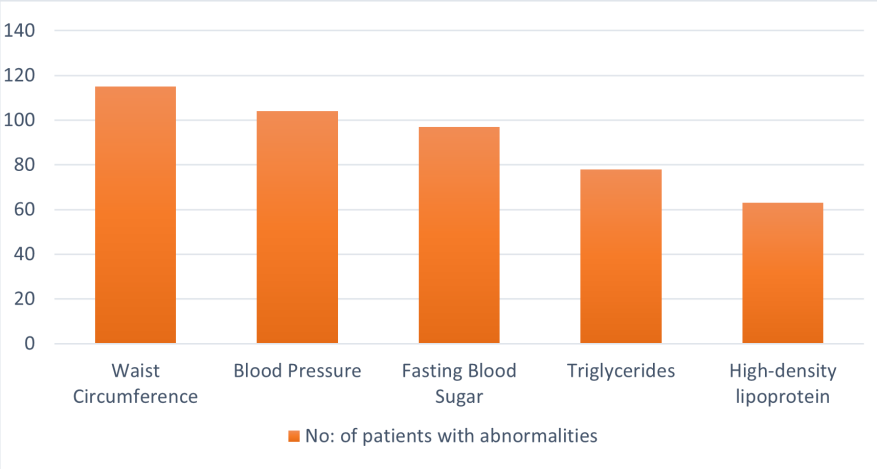


Figure 3: Metabolic syndrome variables and abnormalities.

Table 2: **Fatty liver grading.**

Fatty liver grading	No of patients	
	Male (*n*= 87)	Female (*n*=49)
Grade 1	64	37
Grade 2	23	11
Grade 3	0	1

Table 3: **Metabolic syndrome variables and abnormalities.**

Metabolic syndrome variables	No of patients with abnormalities
Waist Circumference	115
Blood Pressure	104
Fasting Blood Sugar	97
Triglycerides	78
High-density lipoprotein	63

Table 4: **Frequency of metabolic syndrome.**

Mets	Total patients enrolled in MHC (136)		Percentage (%)
	Male	Female	
With Metabolic syndrome	71(81.6%)	35(71.4%)	106(77.9%)
Without Metabolic syndrome	16(18.3%)	14(28.5%)	30(22.1%)
Total	87(100%)	49(100%)	136(100%)

CONCLUSION

The prevalence of metabolic syndrome among study patients with NAFLD was found to be significant ($p<0.05$), with 106 patients meeting the NCEP/ATP-III criteria. Our study revealed a higher occurrence of metabolic syndrome in individuals with NAFLD. Interestingly, despite a higher representation of males in us study population, the prevalence of metabolic syndrome was significantly greater among male patients compared to females. We observed a strong association between NAFLD and notable metabolic disturbances, particularly obesity in female and elevated triglyceride levels. These metabolic abnormalities are important factors contributing to the development of type 2 diabetes mellitus and cardiovascular disease.

Both in India and globally, NAFLD has emerged as a significant health concern, imposing a substantial burden on public health. The increasing prevalence of NAFLD is closely linked to the rise in obesity rates, sedentary lifestyles, unhealthy dietary habits, and metabolic syndrome. To effectively address NAFLD in patients, a comprehensive approach involving collaboration between hepatologists, endocrinologists, and cardiologists is recommended. Personalized strategies for lifestyle modifications should be developed, taking into account individual metabolic and nutritional profiles. Motivating patients to adopt healthier habits is vital for reducing components of metabolic syndrome. Regular interactions with the healthcare system can help improve patient outcomes in this regard. Moreover, the use of point-of-care technology has empowered pharmacists to assess patient risk factors independently during clinic visits, enhancing their role in managing NAFLD and metabolic syndrome.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

NAFLD: Non-Alcoholic Fatty Liver Disease; **WHO:** World Health Organization; **AST:** Aspartate Aminotransferase; **ALT:** Alanine Transaminase; **FAO:** Fatty Acid Oxidation; **TG:** Triglyceride; **FFA:** Free Fatty Acids; **NASH:** Non-alcoholic steatohepatitis; **HCC:** Hepatocellular Carcinoma; **MetS:** Metabolic Syndrome**.**

ETHICAL APPROVAL

CSP/18/SEP/73/245.

AUTHOR CONTRIBUTIONS

1. **D. Kiran Khanna:** conceptualizations, study design, data collection, methodology development and statistical analysis**.**
2. **Kesava Moorthy. G:** Manuscript review and editing. All authors have read and approved the final manuscript.

SUMMARY

This prospective observational study investigates the prevalence of metabolic syndrome among patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD) at a tertiary care hospital in south India. Given the shared pathophysiology between NAFLD and metabolic syndrome-including factors such as obesity, insulin resistance, hypertension and dyslipidemia. This study aims to identify the proportion of NAFLD patients exhibiting features of metabolic syndrome. It also evaluates associated clinical and biochemical parameters to better understand the interrelationship and guide early interventions for preventing disease progression.

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