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Original Research Article

Association of Non-Alcoholic Fatty Liver Disease with Metabolic Syndrome Components and Inflammatory Biomarkers in Adults: A Cross-Sectional Study

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Abstract:

Background: Non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of metabolic syndrome and has emerged as one of the most common chronic liver disorders worldwide. NAFLD is closely associated with central obesity, insulin resistance, dyslipidemia, hypertension, and chronic low-grade inflammation. Inflammatory biomarkers such as high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and serum ferritin may reflect the inflammatory and metabolic processes underlying NAFLD progression. Understanding the relationship between NAFLD, metabolic syndrome components, and inflammatory biomarkers is important for early cardiovascular and hepatic risk stratification.

Objective: To evaluate the association of non-alcoholic fatty liver disease with metabolic syndrome components and inflammatory biomarkers among adults.

Materials and Methods: This cross-sectional observational study included 220 adults aged 30–65 years. NAFLD was diagnosed by abdominal ultrasonography after exclusion of significant alcohol consumption and other chronic liver diseases. Metabolic syndrome was assessed using the International Diabetes Federation (IDF) criteria. Anthropometric measurements, blood pressure, fasting blood glucose, HbA1c, lipid profile, liver enzymes, and inflammatory biomarkers (hs-CRP, IL-6, TNF-α, and serum ferritin) were measured. Associations between NAFLD severity, metabolic syndrome components, and inflammatory biomarkers were analyzed using Pearson correlation, logistic regression, and multivariable regression analyses.

Results: Among the 220 participants, 132 (60.0%) had ultrasonographic evidence of NAFLD. Participants with NAFLD had significantly higher body mass index, waist circumference, systolic and diastolic blood pressure, fasting glucose, triglycerides, HbA1c, hs-CRP, IL-6, TNF-α, and serum ferritin compared with those without NAFLD (all $p < 0.001$). The prevalence of metabolic syndrome was 72.7% in the NAFLD group versus 28.4% in the non-NAFLD group. NAFLD severity showed significant positive correlations with waist circumference ($r = 0.51$), triglycerides ($r = 0.44$), fasting glucose ($r = 0.39$), hs-CRP ($r = 0.48$), IL-6 ($r = 0.42$), TNF-α ($r = 0.37$), and ferritin ($r = 0.40$) (all $p < 0.001$). In multivariable analysis, waist circumference, triglycerides, and hs-CRP remained independent predictors of NAFLD.

Conclusion: Non-alcoholic fatty liver disease was strongly associated with metabolic syndrome components and elevated inflammatory biomarkers in adults. These findings support the concept that NAFLD represents a systemic metabolic-inflammatory disorder and highlight the importance of early identification of obesity, insulin resistance, dyslipidemia, and chronic inflammation in individuals with fatty liver disease.

Keywords: non-alcoholic fatty liver disease, metabolic syndrome, hs-CRP, interleukin-6, TNF-α, ferritin, obesity, insulin resistance.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) has become one of the most common chronic liver diseases worldwide and represents a major public health challenge. It encompasses a spectrum of hepatic abnormalities ranging from simple steatosis (non-alcoholic fatty liver) to non-alcoholic steatohepatitis (NASH), progressive fibrosis, cirrhosis, and hepatocellular carcinoma. [1] The global prevalence of NAFLD is estimated to be approximately 25-30%, with even higher rates reported among individuals with obesity, type 2 diabetes mellitus, and metabolic syndrome. In

many developing countries, including India, the prevalence of NAFLD has increased rapidly in parallel with urbanization, sedentary lifestyle, and increasing rates of obesity and diabetes. [2]NAFLD is widely regarded as the hepatic manifestation of metabolic syndrome. The close relationship between hepatic steatosis and central obesity, insulin resistance, dyslipidemia, hypertension, and impaired glucose metabolism suggests that NAFLD is not merely a liver disease but a multisystem metabolic disorder. [3] Accumulating evidence indicates that patients with NAFLD are at increased risk of cardiovascular disease, chronic kidney disease, type 2 diabetes mellitus, and all-cause mortality. [4] In fact, cardiovascular disease remains the leading cause of death among patients with NAFLD, emphasizing the need for early identification of metabolic and inflammatory abnormalities in affected individuals. [5]

The pathogenesis of NAFLD is complex and multifactorial. The traditional two-hit hypothesis has largely been replaced by the multiple-hit model, which proposes that hepatic fat accumulation results from interactions among insulin resistance, adipose tissue dysfunction, oxidative stress, mitochondrial dysfunction, inflammatory cytokines, altered gut microbiota, and genetic susceptibility. [6] Insulin resistance plays a central role by increasing lipolysis in adipose tissue, enhancing hepatic free fatty acid influx, stimulating de novo lipogenesis, and impairing hepatic lipid export. These mechanisms lead to triglyceride accumulation within hepatocytes and promote hepatic steatosis. [7]

Chronic low-grade inflammation is another key mechanism linking NAFLD with metabolic syndrome. [8] Adipose tissue, particularly visceral adipose tissue, functions as an active endocrine organ that secretes numerous inflammatory mediators and adipokines. [9] Increased production of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) contributes to insulin resistance, endothelial dysfunction, and hepatic inflammation. [9] Elevated high-sensitivity C-reactive protein (hs-CRP) is considered a marker of systemic inflammation and has been associated with obesity, metabolic syndrome, NAFLD severity, and cardiovascular risk. [10]

Interleukin-6 plays an important role in hepatic lipid metabolism and inflammatory signaling, while TNF-α promotes hepatocyte apoptosis, insulin resistance, and activation of hepatic stellate cells involved in fibrosis. Serum ferritin, an acute-phase reactant as well as a marker of body iron stores, is frequently elevated in NAFLD and has been associated with hepatic inflammation, fibrosis progression, and metabolic syndrome. [11] These inflammatory biomarkers may therefore provide valuable insight into the metabolic-inflammatory pathways underlying NAFLD. [12]

The diagnostic evaluation of NAFLD commonly relies on abdominal ultrasonography, which is a widely available, non-invasive, and cost-effective imaging modality for detecting hepatic steatosis. Ultrasonographic grading of fatty liver allows assessment of disease severity and can be correlated with metabolic and biochemical parameters. Although liver biopsy remains the gold standard for diagnosing NASH and fibrosis, ultrasonography is particularly useful for epidemiological studies and clinical screening. [13]

Several studies have demonstrated associations between NAFLD and individual components of metabolic syndrome, including abdominal obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), hypertension, and hyperglycemia. [14] However, the simultaneous evaluation of metabolic syndrome components together with inflammatory biomarkers provides a more comprehensive understanding of the systemic nature of NAFLD. Identifying inflammatory markers associated with NAFLD may also help predict disease progression and cardiovascular risk. [15]

Despite the increasing burden of NAFLD, data regarding the relationship between NAFLD severity, metabolic syndrome components, and inflammatory biomarkers in adult populations remain limited in many regions. Understanding these associations may facilitate early risk stratification, targeted lifestyle interventions, and prevention of both hepatic and cardiovascular complications.

Aim of the Study: To evaluate the association between non-alcoholic fatty liver disease, metabolic syndrome components, and inflammatory biomarkers among adults.

Objectives

1. To determine the prevalence of NAFLD among adults using abdominal ultrasonography.
2. To assess the prevalence of metabolic syndrome among adults with and without NAFLD.
3. To compare anthropometric, blood pressure, glycemic, lipid, and inflammatory parameters between NAFLD and non-NAFLD groups.
4. To evaluate the correlation between NAFLD severity and inflammatory biomarkers (hs-CRP, IL-6, TNF-α, and serum ferritin).
5. To identify independent predictors of NAFLD using multivariable regression analysis.

Research Hypothesis: Non-alcoholic fatty liver disease is significantly associated with metabolic

syndrome components and elevated inflammatory biomarkers in adults.

Materials and Methods

Study Design and Setting: This study was designed as a cross-sectional observational study conducted in the tertiary care teaching hospital. The study period was assumed to extend over 12 months.

Study Population: Adult participants attending the outpatient and health screening clinics of the participating institution were screened for eligibility. Individuals with suspected or incidentally detected fatty liver on abdominal ultrasonography were evaluated after exclusion of significant alcohol intake and other chronic liver diseases.

Sample Size: The sample size was estimated using the formula for prevalence and association studies, assuming an expected NAFLD prevalence of 30%, a 95% confidence level, and 80% statistical power. The calculated minimum sample size was 200 participants. To compensate for incomplete data and possible exclusions, a final sample size of 220 participants was considered adequate.

Study Sample: A total of 220 adults were included in the study:

- 118 males
- 102 females

Inclusion Criteria

1. Age between 30 and 65 years
2. Apparently healthy adults or patients attending outpatient clinics for routine evaluation
3. Willingness to provide written informed consent
4. Availability of complete anthropometric, biochemical, and ultrasonographic assessment

Exclusion Criteria

1. Significant alcohol consumption (>20 g/day in women and >30 g/day in men)
2. Viral hepatitis (HBV or HCV)
3. Autoimmune liver disease
4. Drug-induced liver disease
5. Wilson disease, hemochromatosis, or other chronic liver disorders
6. Pregnancy
7. Known malignancy
8. Acute systemic infection or inflammatory disease
9. Chronic kidney disease stage 4 or 5
10. Current corticosteroid or immunosuppressive therapy

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of the participating institution. Written informed consent was obtained from all participants before enrollment. Confidentiality of participant information was maintained throughout the study in accordance with the Declaration of Helsinki (2013 revision).

Study Procedure: Participants reported to the laboratory after an overnight fast of 10–12 hours. The following assessments were performed in sequence:

1. Recording of demographic and clinical information
2. Anthropometric measurements
3. Blood pressure measurement
4. Venous blood sampling
5. Abdominal ultrasonography
6. Laboratory analysis of metabolic and inflammatory biomarkers

Demographic and Clinical Variables

The following variables were recorded:

- Age (years)
- Sex
- Occupation
- Physical activity level
- Smoking status
- Alcohol consumption
- History of diabetes mellitus
- Hypertension
- Dyslipidemia
- Current medications

Anthropometric Measurements

- Height was measured using a wall-mounted stadiometer to the nearest 0.1 cm.
- Weight was measured using a calibrated digital weighing scale to the nearest 0.1 kg.
- Body mass index was calculated as:

BMI (kg/m²) = Weight (kg) / Height (m²)

- Waist circumference was measured midway between the lower costal margin and the iliac crest at the end of normal expiration.
- Hip circumference was measured at the level of the greater trochanters.
- Waist-to-hip ratio (WHR) was calculated as:

WHR = Waist circumference / Hip circumference

Blood Pressure Measurement

- Blood pressure was measured using a calibrated automated sphygmomanometer according to American Heart Association recommendations.
- Participants rested in the sitting position for 10 minutes before measurement.
- Three readings were obtained at 2-minute intervals, and the average of the final two readings was used for analysis.

- The following parameters were recorded:
- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)

Diagnosis of Non-Alcoholic Fatty Liver Disease: NAFLD was diagnosed by abdominal ultrasonography using a 3.5–5 MHz convex transducer performed by an experienced radiologist blinded to laboratory findings.

Ultrasonographic Criteria: Fatty liver was diagnosed based on the presence of at least two of the following:

- Increased hepatic echogenicity compared with the renal cortex
- Increased posterior attenuation of the ultrasound beam
- Loss of visualization of intrahepatic vascular margins
- Poor visualization of the diaphragm

Grading of Fatty Liver

Grade 0 (Normal):

- Normal liver echotexture

Grade I (Mild):

- Slight diffuse increase in hepatic echogenicity
- Normal visualization of diaphragm and intrahepatic vessels

Grade II (Moderate):

- Moderate increase in hepatic echogenicity
- Slight impairment of visualization of diaphragm and portal vein walls

Grade III (Severe):

- Marked increase in hepatic echogenicity
- Poor or absent visualization of diaphragm and intrahepatic vessels

Participants with Grades I–III steatosis were classified as having NAFLD after exclusion of secondary causes.

Assessment of Metabolic Syndrome: Metabolic syndrome was diagnosed according to the International Diabetes Federation (IDF) criteria. Central obesity was defined as:

- **Men:** Waist circumference ≥90 cm (South Asian cut-off)
- **Women:** Waist circumference ≥80 cm

Plus any two of the following:

1. Triglycerides ≥150 mg/dL
2. HDL cholesterol <40 mg/dL in men or <50 mg/dL in women
3. Blood pressure ≥130/85 mmHg or treatment for hypertension
4. Fasting plasma glucose ≥100 mg/dL or previously diagnosed diabetes mellitus

Laboratory Investigations: Approximately 10 mL of venous blood was collected under aseptic precautions. The following investigations were performed:

Glycemic Parameters

- Fasting blood glucose (FBG)
- HbA1c

Lipid Profile

- Total cholesterol
- Triglycerides
- HDL cholesterol
- LDL cholesterol
- VLDL cholesterol

Liver Function Tests

- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)
- Gamma-glutamyl transferase (GGT)
- Alkaline phosphatase (ALP)

Renal Function

- Serum creatinine

HbA1c was measured using high-performance liquid chromatography (HPLC). Liver enzymes and lipid parameters were analyzed using an automated clinical chemistry analyzer.

Estimation of Inflammatory Biomarkers

High-Sensitivity C - reactive protein (hs-CRP): Serum hs-CRP was measured by high-sensitivity immunoturbidimetric assay. Results were expressed in mg/L.

Interleukin-6 (IL-6): Serum IL-6 was measured using a sandwich enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions. Results were expressed in pg/mL.

Tumor Necrosis Factor-Alpha (TNF-α): Serum TNF-α was measured using a commercial ELISA kit. Results were expressed in pg/mL.

Serum Ferritin: Serum ferritin was estimated using chemiluminescent immunoassay (CLIA). Results were expressed in ng/mL. Internal quality control sera and calibration standards were used for all assays.

Outcome Measures

Primary Outcome: Association between NAFLD and metabolic syndrome.

Secondary Outcomes

1. Association between NAFLD and individual metabolic syndrome components.
2. Correlation between NAFLD severity and inflammatory biomarkers.

3. Identification of independent predictors of NAFLD using multivariable regression analysis.

Statistical Analysis

- Data were analyzed using IBM SPSS Statistics version 26.0.
- Continuous variables were expressed as mean ± standard deviation (SD).
- Categorical variables were expressed as frequency and percentage.
- Normality was assessed using the Shapiro-Wilk test.

Comparisons between NAFLD and non-NAFLD groups were performed using:

- Independent Student's t-test for normally distributed variables
- Mann-Whitney U test for non-normally distributed variables

Categorical variables were compared using the Chi-square test.

Correlations were analyzed using:
- Pearson correlation coefficient
- Spearman correlation where appropriate

Independent predictors of NAFLD were evaluated using binary logistic regression analysis.

Factors associated with NAFLD severity were assessed using multiple linear regression analysis with adjustment for:

- age,
- sex,
- body mass index,
- waist circumference,
- fasting glucose,
- triglycerides,
- HDL cholesterol,
- systolic blood pressure,
- hs-CRP,
- IL-6,
- TNF-α,
- Serum ferritin.

A p-value < 0.05 was considered statistically significant.

Data Management: All data were entered into a structured Microsoft Excel spreadsheet and cross-verified for accuracy prior to statistical analysis. Missing values and outliers were assessed before analysis, and only complete datasets were included in the final evaluation.

Observations and Results

A total of 220 adults aged 30–65 years were included in the study. The study population comprised 118 males (53.6%) and 102 females (46.4%). All participants underwent anthropometric assessment, blood pressure measurement, biochemical investigations, inflammatory biomarker analysis, and abdominal ultrasonography.

Demographic and Clinical Characteristics: The mean age of the study population was 47.9 ± 8.7 years. Participants with NAFLD had significantly higher body mass index, waist circumference, systolic blood pressure, fasting glucose, HbA1c, triglycerides, and inflammatory biomarker levels compared with those without NAFLD.

Table 1: Demographic and clinical characteristics of study participants (n = 220)

Variable	NAFLD (n = 132)	Non-NAFLD (n = 88)	Total (n = 220)	p-value
Age (years)	48.6 ± 8.5	46.9 ± 8.9	47.9 ± 8.7	0.156
Male sex, n (%)	74 (56.1)	44 (50.0)	118 (53.6)	0.372
BMI (kg/m²)	29.1 ± 3.8	24.8 ± 3.1	27.4 ± 4.1	<0.001
Waist circumference (cm)	97.8 ± 8.6	85.4 ± 7.3	92.8 ± 9.8	<0.001
Waist-hip ratio	0.94 ± 0.06	0.88 ± 0.05	0.92 ± 0.07	<0.001
Systolic BP (mmHg)	134.6 ± 12.4	122.8 ± 10.6	129.9 ± 12.9	<0.001
Diastolic BP (mmHg)	84.8 ± 8.3	76.9 ± 7.2	81.6 ± 8.7	<0.001
Fasting glucose (mg/dL)	118.6 ± 21.4	97.8 ± 16.8	110.3 ± 22.5	<0.001
HbA1c (%)	6.8 ± 1.1	5.9 ± 0.8	6.4 ± 1.1	<0.001

Prevalence and Ultrasonographic Grading of NAFLD: Among the 220 participants, 132 (60.0%) had ultrasonographic evidence of NAFLD.

Table 2: Ultrasonographic grading of fatty liver

NAFLD grade	Number (n)	Percentage (%)
Grade I (Mild)	62	28.2
Grade II (Moderate)	48	21.8
Grade III (Severe)	22	10.0
No NAFLD	88	40.0
Total	**220**	**100.0**

Mild steatosis was the most common ultrasonographic grade observed among participants with NAFLD.

Metabolic Syndrome Components: The prevalence of metabolic syndrome was significantly higher among participants with NAFLD.

Table 3: Prevalence of metabolic syndrome and its components

Parameter	NAFLD (n = 132)	Non-NAFLD (n = 88)	p-value
Central obesity	112 (84.8%)	38 (43.2%)	<0.001
Elevated triglycerides	92 (69.7%)	26 (29.5%)	<0.001
Low HDL cholesterol	76 (57.6%)	24 (27.3%)	<0.001
Elevated blood pressure	88 (66.7%)	28 (31.8%)	<0.001
Elevated fasting glucose	81 (61.4%)	21 (23.9%)	<0.001
Metabolic syndrome	**96 (72.7%)**	**25 (28.4%)**	**<0.001**

Participants with NAFLD had significantly greater prevalence of all five metabolic syndrome components.

Lipid Profile and Liver Enzymes

Table 4: Biochemical profile of study participants

Parameter	NAFLD (n = 132)	Non-NAFLD (n = 88)	p-value
Total cholesterol (mg/dL)	212.6 ± 34.2	186.8 ± 29.6	<0.001
Triglycerides (mg/dL)	186.4 ± 48.8	132.6 ± 34.7	<0.001
HDL cholesterol (mg/dL)	39.8 ± 7.2	47.1 ± 8.1	<0.001
LDL cholesterol (mg/dL)	132.4 ± 29.6	114.8 ± 24.9	<0.001
ALT (U/L)	48.6 ± 18.2	27.4 ± 10.6	<0.001
AST (U/L)	39.8 ± 14.1	25.6 ± 9.8	<0.001
GGT (U/L)	52.1 ± 19.6	31.8 ± 12.4	<0.001

Inflammatory Biomarkers: Participants with NAFLD had significantly elevated inflammatory biomarker levels.

Table 5: Inflammatory biomarkers in NAFLD and non-NAFLD groups

Biomarker	NAFLD (n = 132)	Non-NAFLD (n = 88)	p-value
hs-CRP (mg/L)	4.8 ± 1.9	2.3 ± 1.1	<0.001
IL-6 (pg/mL)	5.9 ± 2.1	3.4 ± 1.4	<0.001
TNF-α (pg/mL)	8.6 ± 2.8	5.7 ± 1.9	<0.001
Ferritin (ng/mL)	218 ± 84	142 ± 56	<0.001

All inflammatory biomarkers were significantly elevated in participants with NAFLD.

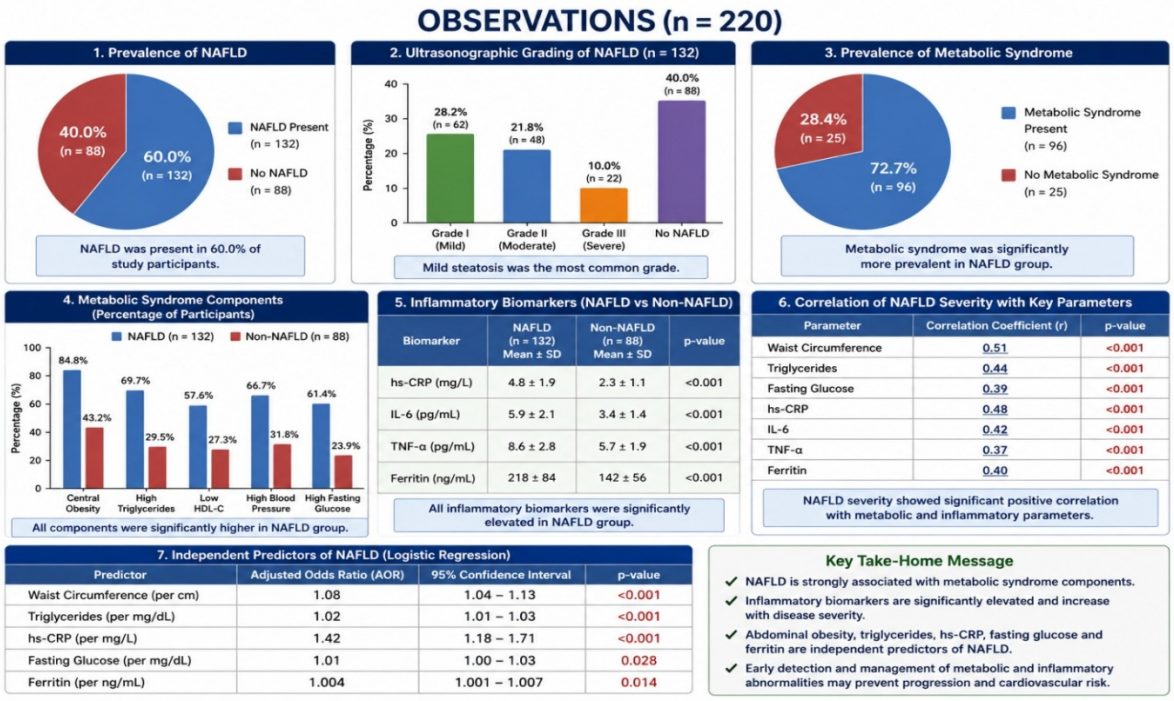

Figure 1: Observations (n=20)

Inflammatory Biomarkers across NAFLD Severity

Table 6. Inflammatory biomarkers according to ultrasonographic NAFLD grade

Biomarker	Grade I	Grade II	Grade III	p-value
hs-CRP (mg/L)	3.8 ± 1.4	5.1 ± 1.6	6.6 ± 2.0	<0.001
IL-6 (pg/mL)	4.8 ± 1.6	6.1 ± 1.9	7.5 ± 2.2	<0.001
TNF-α (pg/mL)	7.4 ± 2.2	8.9 ± 2.4	10.4 ± 3.1	<0.001
Ferritin (ng/mL)	184 ± 62	224 ± 71	292 ± 96	<0.001

Inflammatory biomarker concentrations increased progressively with increasing severity of hepatic steatosis.

Correlation between NAFLD Severity and Metabolic Parameters: Pearson correlation analysis showed significant positive correlations between NAFLD severity and metabolic syndrome components.

Table 7: Correlation between NAFLD severity and metabolic parameters

Variable	Correlation coefficient (r)	p-value
BMI	0.46	<0.001
Waist circumference	0.51	<0.001
Systolic BP	0.34	<0.001
Diastolic BP	0.29	<0.001
Fasting glucose	0.39	<0.001
HbA1c	0.36	<0.001
Triglycerides	0.44	<0.001
HDL cholesterol	−0.32	<0.001

Correlation between NAFLD Severity and Inflammatory Biomarkers: NAFLD severity showed significant positive correlations with all inflammatory biomarkers.

Table 8: Correlation between NAFLD severity and inflammatory biomarkers

Biomarker	Correlation coefficient (r)	p-value
hs-CRP	0.48	<0.001
IL-6	0.42	<0.001
TNF-α	0.37	<0.001
Ferritin	0.40	<0.001

The strongest correlation was observed between NAFLD severity and hs-CRP.

Correlation Matrix of Major Study Variables

Table 9: Pearson correlation matrix

Variable	NAFLD grade	Waist circumference	Triglycerides	hs-CRP	IL-6
NAFLD grade	1.00	0.51	0.44	0.48	0.42
Waist circumference	0.51	1.00	0.39	0.36	0.32
Triglycerides	0.44	0.39	1.00	0.34	0.30
hs-CRP	0.48	0.36	0.34	1.00	0.58
IL-6	0.42	0.32	0.30	0.58	1.00

All displayed correlations were statistically significant at $p < 0.01$.

Logistic Regression Analysis for Predictors of NAFLD: Binary logistic regression was performed with presence of NAFLD as the dependent variable.

Table 10: Independent predictors of NAFLD

Predictor	Adjusted Odds Ratio (AOR)	95% Confidence Interval	p-value
Waist circumference	**1.08**	1.04–1.13	**<0.001**
BMI	1.05	0.98–1.13	0.148
Triglycerides	**1.02**	1.01–1.03	**<0.001**
HDL cholesterol	**0.96**	0.93–0.99	**0.012**
Fasting glucose	**1.01**	1.00–1.03	**0.028**
hs-CRP	**1.42**	1.18–1.71	**<0.001**
IL-6	1.09	0.98–1.21	0.106
TNF-α	1.05	0.96–1.16	0.242
Ferritin	**1.004**	1.001–1.007	**0.014**

Waist circumference, triglycerides, hs-CRP, fasting glucose, and ferritin remained independent predictors of NAFLD.

Multiple Linear Regression Analysis for NAFLD Severity

Table 11: Independent predictors of NAFLD severity

Predictor	Standardized β	Standard Error	t-value	p-value
Waist circumference	**0.29**	0.01	4.32	**<0.001**
Triglycerides	**0.24**	0.001	3.71	**<0.001**
hs-CRP	**0.27**	0.05	4.08	**<0.001**
IL-6	0.12	0.04	1.86	0.065
Ferritin	**0.16**	0.001	2.42	**0.016**
HbA1c	0.14	0.06	2.01	0.046

Model statistics:

- $R^2 = 0.43$
- Adjusted $R^2 = 0.41$
- $F = 20.76$
- $p < 0.001$

Summary of Principal Findings

The present analysis showed that:

1. NAFLD was present in 60.0% of the study population.
2. Metabolic syndrome was significantly more prevalent among participants with NAFLD (72.7% vs 28.4%).
3. Participants with NAFLD exhibited significantly higher obesity indices, blood pressure, fasting glucose, triglycerides, and liver enzymes.
4. Inflammatory biomarkers (hs-CRP, IL-6, TNF-α, and ferritin) were significantly elevated in NAFLD and increased progressively with disease severity.
5. Waist circumference, triglycerides, hs-CRP, fasting glucose, and ferritin remained independent predictors of NAFLD after multivariable adjustment.

These findings support a strong association between non-alcoholic fatty liver disease, metabolic syndrome, and chronic systemic inflammation in adults.

Discussion

The present cross-sectional study evaluated the association between non-alcoholic fatty liver disease (NAFLD), metabolic syndrome components, and inflammatory biomarkers in adults. The principal findings were that NAFLD was highly prevalent and was significantly associated with central obesity, hyper-tension, dyslipidemia, impaired glucose metabolism, and elevated inflammatory biomarkers including hs-CRP, IL-6, TNF-α, and serum ferritin. In addition, waist circumference, triglycerides, hs-CRP, fasting glucose, and ferritin emerged as independent predictors of NAFLD after adjustment for demographic and metabolic confounders.

These findings support the concept that NAFLD is not merely a hepatic disorder but a systemic metabolic-inflammatory disease closely linked to metabolic syndrome and chronic low-grade inflammation, both of which contribute substantially to cardiovascular and hepatic morbidity. [16,17]

Prevalence of NAFLD: In the present study, 60.0% of participants had ultrasonographic evidence of NAFLD, with mild steatosis being the most common grade. [18] Although this prevalence is higher than estimates reported for the general population, it is comparable to studies involving individuals with obesity, type 2 diabetes mellitus, or metabolic syndrome, where the prevalence of NAFLD frequently exceeds 50%.[19] The increasing burden of NAFLD has paralleled the global rise in obesity, insulin resistance, sedentary life-style, and dietary transition, particularly in South Asian populations. [20] Urbanization, reduced physical activity, and increased consumption of calorie-dense foods have contributed to the rapid increase in fatty liver disease among adults.

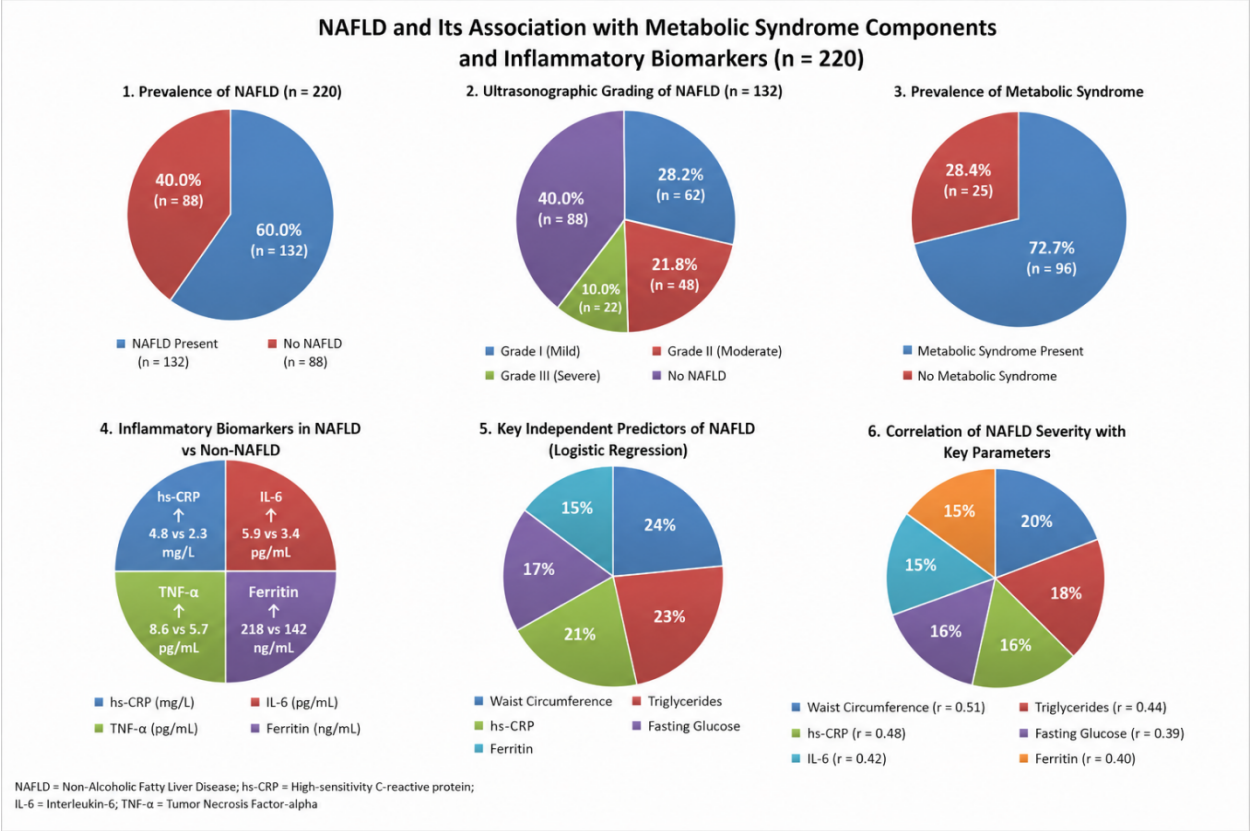

Figure 2: NAFLD and its association with metabolic syndrome components and inflammatory biomarkers (n=220)

Association with Obesity and Central Adiposity: The present study showed significantly higher BMI, waist circumference, and waist-hip ratio among participants with NAFLD. Waist circumference showed the strongest correlation with NAFLD severity (r = 0.51) and remained an independent predictor in multivariable analyses. [21]

These findings emphasize the critical role of visceral adiposity in the pathogenesis of NAFLD. Visceral adipose tissue is metabolically active and releases excessive free fatty acids (FFAs) into the portal circulation, increasing hepatic fatty acid influx and triglyceride accumulation. Visceral obesity is also associated with adipokine imbalance, including increased leptin and decreased adiponectin, which promotes insulin resistance, oxidative stress, and hepatic inflammation. [22]

The stronger association of waist circumference compared with BMI suggests that abdominal obesity is a better predictor of NAFLD than generalized obesity, a finding consistently reported in epidemiological studies.

NAFLD and Metabolic Syndrome Components: A major observation of the present study was the markedly higher prevalence of metabolic syndrome in the NAFLD group (72.7%) compared with the non-NAFLD group (28.4%).23 Participants with NAFLD had significantly higher frequencies of central obesity, hypertriglyceridemia, low HDL cholesterol, elevated blood pressure, and impaired fasting glucose. [24]

These findings reinforce the concept that NAFLD represents the hepatic manifestation of metabolic syndrome. Insulin resistance plays a central role by increasing adipose tissue lipolysis, enhancing hepatic de novo lipogenesis, reducing fatty acid oxidation, and impairing very-low-density lipoprotein (VLDL) export. [25] The resulting hepatic fat accumulation contributes to steatosis and further aggravates systemic insulin resistance.

The significant correlations observed between NAFLD severity and fasting glucose, HbA1c, triglycerides, and HDL cholesterol indicate that worsening hepatic steatosis is accompanied by progressive metabolic deterioration.

Blood Pressure and NAFLD: Participants with NAFLD exhibited significantly higher systolic and diastolic blood pressure, and blood pressure showed positive correlations with NAFLD severity. Hypertension is increasingly recognized as an important component of the NAFLD-metabolic syndrome spectrum. [26]

Potential mechanisms include endothelial dysfunction, activation of the renin-angiotensin-

aldosterone system, sympathetic overactivity, oxidative stress, and chronic inflammation. Hepatic steatosis is associated with reduced nitric oxide bioavailability and increased vascular stiffness, which contribute to elevated blood pressure and increased cardiovascular risk. [27]

Inflammatory Biomarkers and NAFLD: One of the most important findings of the present study was the significant elevation of hs-CRP, IL-6, TNF-α, and serum ferritin among participants with NAFLD, with progressive increases across Grades I–III fatty liv-er. [28]

High-Sensitivity C - reactive protein: The strongest correlation was observed between NAFLD severity and hs-CRP (r = 0.48). hs-CRP is a sensitive marker of systemic inflammation and is synthesized by the liver in response to IL-6-mediated hepatic stimulation. [29] Elevated hs-CRP reflects chronic low-grade inflammation associated with obesity, insulin resistance, endothelial dysfunction, and atheroscleross. [30]

Previous studies have consistently reported higher hs-CRP concentrations in patients with NAFLD and have demonstrated significant associations between CRP levels and hepatic steatosis, steatohepatitis, and fibrosis.

Interleukin-6: IL-6 concentrations were significantly elevated in participants with NAFLD and increased progressively with disease severity. IL-6 is produced by visceral adipose tissue, macrophages, hepatocytes, and immune cells, and plays an important role in hepatic lipid metabolism and inflammatory signaling. [31]

Experimental and clinical studies suggest that IL-6 contributes to the progression from simple steatosis to non-alcoholic steatohepatitis (NASH) through activation of inflammatory pathways and promotion of insulin resistance.

Tumor Necrosis Factor-Alpha: TNF-α was significantly elevated in participants with NAFLD and showed a positive correlation with disease severity. TNF-α is a key pro-inflammatory cytokine that promotes insulin resistance, hepatocyte apoptosis, oxidative stress, and activation of hepatic stellate cells, thereby contributing to progression toward fibro-sis. [32]

Elevated TNF-α has also been associated with obesity-related inflammation and endothelial dysfunction, further linking NAFLD with cardiovascular disease.

Serum Ferritin: Serum ferritin levels were significantly higher in the NAFLD group and increased progressively with ultrasonographic severity. Ferritin is both an acute-phase reactant and a marker of body iron stores, and elevated ferritin in NAFLD may reflect hepatic inflammation, oxidative stress, macrophage activation, and altered iron metabolism. [33]

Hyperserotonaemia has been associated with advanced steatosis, fibrosis, insulin resistance, and metabolic syndrome, suggesting that ferritin may serve as a marker of metabolic-inflammatory burden in NAFLD.

Progressive Increase in Inflammation with NAFLD Severity: The progressive increase in hs-CRP, IL-6, TNF-α, and ferritin across Grades I–III NAFLD suggests that systemic inflammation intensifies with increasing hepatic fat accumulation.

This observation supports the multiple-hit hypothesis of NAFLD, in which hepatic steatosis results from interactions among insulin resistance, adipose tissue dysfunction, oxidative stress, inflammatory cytokines, mitochondrial dysfunction, and gut-derived inflammatory signals. As steatosis progresses, inflammatory media-tors amplify hepatic injury and promote fibrosis through activation of Kupffer cells and hepatic stellate cells. [34]

Independent Predictors of NAFLD: Binary logistic regression identified waist circumference, triglycerides, hs-CRP, fasting glucose, and ferri-tin as independent predictors of NAFLD. Multiple linear regression further demonstrated that waist circumference, triglycerides, hs-CRP, ferritin, and HbA1c independently predicted NAFLD severity.

These findings indicate that abdominal obesity and systemic inflammation are central determinants of NAFLD, even after accounting for other metabolic variables. The independent association of hs-CRP suggests that inflammation is not merely a consequence of hepatic steatosis but may actively contribute to disease development and progression.

Comparison with Previous Studies: The findings of the present study are consistent with numerous international studies reporting strong associations between NAFLD, metabolic syndrome, and inflammatory biomarkers.

Meta-analyses have demonstrated significant associations of CRP, IL-6, and TNF-α with increased risk of NAFLD, and inflammatory cytokine concentrations generally increase with disease severity.

Similarly, studies evaluating systemic inflammation in NAFLD have shown elevated circulating cytokines and acute-phase reactants in patients with hepatic steatosis and steatohepatitis, supporting the concept of NAFLD as a chronic low-grade inflammatory state. [35]

Cardiovascular Implications: The coexistence of central obesity, hypertension, dyslipidemia, hyperglycemia, and elevated inflammatory

biomarkers observed in participants with NAFLD has important cardiovascular implications. NAFLD is increasingly recognized as an independent risk factor for atherosclerosis, coronary artery disease, stroke, heart failure, and cardiovascular mortality.

Chronic inflammation, endothelial dysfunction, oxidative stress, and insulin resistance provide common mechanistic pathways linking NAFLD with cardiovascular disease. Elevated hs-CRP and inflammatory cytokines may therefore identify NAFLD patients at particularly high cardiovascular risk.

Strengths of the Study

The present study has several strengths:

1. Comprehensive evaluation of NAFLD, metabolic syndrome components, and multiple inflammatory biomarkers.
2. Use of standardized ultrasonographic grading of fatty liver.
3. Assessment of both metabolic and inflammatory pathways.
4. Inclusion of multivariable logistic and linear regression analyses.
5. Evaluation of NAFLD severity rather than merely presence or absence of fatty liver.

Limitations

Certain limitations should be acknowledged.

1. The cross-sectional design precludes causal inference.
2. Ultrasonography, although widely accepted for epidemiological studies, is less sensitive than MRI or liver biopsy for detecting mild steatosis.
3. Histological confirmation of NASH and fibrosis was not available.
4. Dietary intake, physical activity, and genetic polymorphisms influencing NAFLD were not assessed.
5. Additional inflammatory markers such as adiponectin, leptin, MCP-1, and oxidative stress bi-omarkers were not measured.

Future prospective cohort studies incorporating transient elastography, MRI-based hepatic fat quantification, liver fibrosis assessment, and longitudinal cardiovascular follow-up may further clarify the relationships among metabolic syndrome, inflammation, and NAFLD progression.

Conclusion

The present cross-sectional study showed that non-alcoholic fatty liver disease was highly prevalent among adults and was strongly associated with metabolic syndrome components and elevated inflammatory biomarkers. Participants with NAFLD exhibited significantly higher body mass index, waist circumference, blood pressure, fasting glucose, HbA1c, triglycerides, liver enzymes, hs-CRP, IL-6, TNF-α, and serum ferritin compared with those without NAFLD. The prevalence of metabolic syndrome was markedly higher in individuals with NAFLD, and inflammatory biomarker concentrations increased progressively with increasing ultra-sonographic severity of hepatic steatosis.

Importantly, waist circumference, triglycerides, hs-CRP, fasting glucose, and ferritin remained independent predictors of NAFLD, indicating that abdominal obesity, dyslipidemia, metabolic dysfunction, and chronic low-grade inflammation play central roles in the development and progression of fatty liver disease.

These findings support the concept that NAFLD represents a systemic metabolic-inflammatory disorder rather than an isolated hepatic condition. Early identification of visceral obesity, insulin resistance, dyslipidemia, and inflammatory activation may help prevent progression to non-alcoholic steatohepatitis, fibrosis, cirrhosis, and cardiovascular disease. Routine assessment of metabolic syndrome components and inflammatory biomarkers may therefore improve risk stratification and clinical management of adults with NAFLD.

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