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Cardiometabolic Risk Factors and Their Association with NAFLD Severity and Progression: Evidence from a Prospective Hospital-Based Cohort

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Abstract | **Original Research Article**

Background: Non-alcoholic fatty liver disease (NAFLD) represents a major hepatic manifestation of the metabolic syndrome and is closely intertwined with a constellation of cardiometabolic risk factors including insulin resistance, dyslipidaemia, central obesity, hypertension, and type 2 diabetes mellitus (T2DM). Understanding the burden and trajectory of these risk factors across NAFLD severity grades is essential for clinical risk stratification and timely intervention. ***Objective:*** This prospective hospital-based cohort study aimed to characterise the cardiometabolic risk factor profile among patients with NAFLD of varying severity grades and to evaluate the association between these risk factors and disease progression over a 15-month observation period at a tertiary care centre in Hyderabad, Telangana, India. ***Methods:*** A total of 30 patients diagnosed with NAFLD via ultrasound and transient elastography (FibroScan) between January 2021 and April 2022 were enrolled. Clinical, anthropometric, and biochemical parameters were recorded at baseline and follow-up. Severity was graded as mild, moderate, or severe. Multivariate logistic regression was employed to identify independent predictors of advanced NAFLD. ***Results:*** The mean age of patients was 43.2±9.8 years (63.3% male). Dyslipidaemia was the most prevalent comorbidity (73.3%), followed by hypertension (60.0%), obesity (53.3%), T2DM (46.7%), and metabolic syndrome (36.7%). Insulin resistance (HOMA-IR), BMI, and triglyceride levels were significantly higher with increasing NAFLD severity ($p<0.001$ for all). On multivariate analysis, HOMA-IR (OR 1.98; 95% CI 1.38–2.84), BMI (OR 1.69; 95% CI 1.23–2.32), and hypertriglyceridaemia (OR 1.51; 95% CI 1.15–1.98) emerged as independent predictors of severe NAFLD. Disease progression was documented in 23.3% of patients at follow-up. ***Conclusion:*** Cardiometabolic risk factors are highly prevalent in NAFLD patients and demonstrate a graded relationship with disease severity. Comprehensive metabolic risk assessment and aggressive management of insulin resistance and dyslipidaemia are imperative for halting NAFLD progression and reducing cardiovascular morbidity.

Keywords: NAFLD; cardiometabolic risk; insulin resistance; HOMA-IR; dyslipidaemia; metabolic syndrome; liver fibrosis; FibroScan; prospective cohort; Hyderabad.

1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has emerged as the most prevalent chronic liver disease globally, affecting an estimated 25–30% of the adult population worldwide and up to 38% in parts of South Asia [1]. NAFLD encompasses a wide disease spectrum, ranging from simple steatosis (non-alcoholic fatty liver, NAFL) to the more aggressive non-alcoholic steatohepatitis (NASH), progressive fibrosis, cirrhosis, and ultimately hepatocellular carcinoma [2]. Its pathogenesis is rooted in the "multiple-hit hypothesis," wherein insulin resistance, oxidative stress, lipotoxicity, gut dysbiosis, and systemic inflammation act synergistically to promote hepatocyte injury and fibrogenesis [3]. The condition is widely recognised as the hepatic manifestation of the metabolic syndrome, and its rising prevalence parallels the global epidemic of obesity and type 2 diabetes mellitus (T2DM). In India, epidemiological surveys have reported NAFLD prevalence rates of 9–32% in the general population, with significantly higher rates observed in urban, sedentary populations [4].

The bidirectional relationship between NAFLD and cardiometabolic risk factors is well established. Patients with NAFLD are at substantially increased risk of cardiovascular disease (CVD), T2DM, chronic kidney disease, and certain extrahepatic malignancies [5,6]. Conversely, each cardiometabolic risk factor insulin resistance, central obesity, atherogenic dyslipidaemia, and hypertension individually and collectively accelerates hepatic fat accumulation, inflammatory activity, and fibrosis progression [7]. Insulin resistance, in particular, is considered the cornerstone pathophysiological mechanism of NAFLD. It promotes de novo lipogenesis, impairs hepatic lipid export, and sensitises hepatocytes to cytokine-mediated injury, thereby driving the transition from simple steatosis to NASH [8]. The homeostatic model assessment of insulin resistance (HOMA-IR) is a validated, accessible surrogate marker for quantifying insulin resistance in clinical and research settings, and elevated HOMA-IR has been consistently associated with advanced hepatic histological grades in NAFLD patients [9].

Dyslipidaemia characterised by elevated triglycerides, elevated low-density lipoprotein cholesterol (LDL-C), and reduced high-density lipoprotein cholesterol (HDL-C) is the most prevalent cardiometabolic comorbidity in NAFLD cohorts [10]. The atherogenic lipid milieu not only promotes hepatic lipid accumulation but also independently predicts cardiovascular events, making it a critical therapeutic target in NAFLD management. Hypertension, present in approximately 40–70% of NAFLD patients, contributes to hepatic fibrosis through renin-angiotensin-aldosterone system (RAAS) activation and endothelial dysfunction, further compounding the cardiovascular risk [11]. Obesity, particularly visceral adiposity, drives lipotoxic stress and proinflammatory adipokine dysregulation, both of which are critically implicated in NASH development and progression [12]. The co-occurrence of multiple cardiometabolic risk factors as components of the metabolic syndrome exponentially amplifies the risk of advanced liver disease, making comprehensive metabolic assessment indispensable in the clinical evaluation of NAFLD patients.

Despite the enormous global burden of NAFLD, published data from South Indian hospital-based cohorts specifically examining the graded relationship between cardiometabolic risk factor profiles and NAFLD severity remain limited. Most existing Indian studies are either cross-sectional, community-based, or focus narrowly on biochemical markers without prospective follow-up data on disease progression [13]. There is a critical need for prospective studies that systematically evaluate the entire cardiometabolic risk burden spanning glycaemic parameters, lipid indices, anthropometric measures, and blood pressure across well-defined NAFLD severity strata. Such data would provide valuable real-world evidence to guide clinicians in risk stratification and in prioritising interventions in resource-constrained settings. The present study was therefore designed as a prospective hospital-based cohort to address this knowledge gap, focusing on patients attending a tertiary medical institution in Hyderabad, Telangana, over a 15-month observation window from January 2021 to April 2022.

2. OBJECTIVE

The primary objective of this study was to evaluate the prevalence and distribution of cardiometabolic risk factors including insulin resistance (HOMA-IR), central obesity, atherogenic dyslipidaemia, hypertension, and type 2 diabetes mellitus across different severity grades of non-alcoholic fatty liver disease in a hospital-based prospective cohort. A secondary objective was to identify independent cardiometabolic predictors of advanced NAFLD (moderate to severe grade) using multivariate logistic regression modelling, thereby contributing to a clinically actionable risk stratification framework for South Indian populations.

Additionally, the study aimed to document short-term disease progression in terms of worsening metabolic parameters and NAFLD grade over the 15-month follow-up period from January 2021 to April 2022. The findings were intended to generate evidence that could inform the design of integrated cardiometabolic-hepatological care pathways in tertiary care settings, with particular relevance to the rapidly increasing burden of NAFLD and metabolic syndrome in the urban population of Telangana, India [14].

3. METHODOLOGY AND MATERIALS

Study Design and Setting

This was a prospective observational hospital-based cohort study conducted in the Department of General Medicine, Mallareddy Medical College for Women, Hyderabad, Telangana, India, over a period of 16 months from January 2021 to April 2022. The study was approved by the Institutional Ethics Committee (IEC Ref. No. MMCW/IEC/2020/114) and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all enrolled participants prior to study initiation. Patients were recruited from the outpatient department (OPD) and medical wards of the institution. NAFLD was diagnosed by abdominal ultrasound (performed by an experienced radiologist) supplemented by transient elastography (FibroScan, Echosens, France) for liver stiffness measurement

(LSM) and hepatic fat quantification using the controlled attenuation parameter (CAP). Disease severity was graded as mild (CAP 248–267 dB/m, LSM <7.0 kPa), moderate (CAP 268–279 dB/m, LSM 7.0–9.9 kPa), and severe (CAP ≥280 dB/m, LSM ≥10.0 kPa) in accordance with established FibroScan criteria [2,9].

Inclusion and Exclusion Criteria

Inclusion Criteria: Patients aged 18–65 years attending the General Medicine Department between January 2021 and April 2022; diagnosis of NAFLD confirmed by ultrasound and FibroScan; willingness to participate and provide written informed consent; availability for follow-up over the study duration.

Exclusion Criteria: Patients with significant alcohol consumption (>20 g/day for women or >30 g/day for men); secondary causes of hepatic steatosis including hepatitis B and C virus infection, autoimmune hepatitis, drug-induced liver injury, Wilson's disease, or haemochromatosis; pre-existing cirrhosis or hepatocellular carcinoma; pregnancy or lactation; severe renal impairment (eGFR <30 mL/min/1.73 m²); thyroid dysfunction; patients on medications known to cause steatosis (corticosteroids, amiodarone, tamoxifen, valproate); inability to provide informed consent or complete follow-up visits.

Data Collection Procedure

At enrolment (baseline: January–June 2021), all participants underwent a standardised clinical assessment including detailed medical history, physical examination, and anthropometric measurements (body weight, height, body mass index [BMI], waist circumference [WC], hip circumference, waist-to-hip ratio [WHR]). Blood pressure was measured using a calibrated mercury sphygmomanometer after five minutes of rest in the seated position, with the mean of two readings recorded. Fasting venous blood samples (12 hours overnight fast) were collected for the following biochemical analyses: fasting plasma glucose (FPG), glycated haemoglobin (HbA1c), fasting serum insulin, complete lipid profile (total cholesterol, LDL-C, HDL-C, VLDL-C, and triglycerides), liver function tests (ALT, AST, GGT, ALP, albumin, total and direct bilirubin), complete blood count, serum creatinine, uric acid, and high-sensitivity C-reactive protein (hsCRP). Insulin resistance was calculated using the HOMA-IR formula: HOMA-IR = [Fasting insulin (μU/mL) × Fasting glucose (mmol/L)] / 22.5. Metabolic syndrome was defined per the International Diabetes Federation (IDF) 2009 consensus criteria [15]. All laboratory analyses were performed in the accredited central laboratory of Mallareddy Medical College Hospital using standardised, quality-controlled analytical platforms. Follow-up assessments (April 2022) replicated all baseline procedures, including repeat FibroScan and biochemical profiling.

Statistical Data Analysis

All data were entered into Microsoft Excel and analysed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as frequencies and percentages. The Kolmogorov-Smirnov test was used to assess normality of continuous variables. Between-group comparisons for continuous variables were performed using one-way ANOVA with Tukey's post-hoc test. Chi-square test or Fisher's exact test was used for categorical variables. Pearson's correlation coefficient (r) was used to assess bivariate associations between cardiometabolic parameters and NAFLD severity grade (coded as an ordinal variable: 1 = mild, 2 = moderate, 3 = severe). Multivariate binary logistic regression (dependent variable: moderate-to-severe NAFLD vs. mild NAFLD) was performed including variables that were significant ($p<0.05$) on univariate analysis. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). Paired t-test was used for comparing baseline and follow-up continuous variables. A p-value of <0.05 (two-tailed) was considered statistically significant for all analyses [3,10].

4. RESULTS

A total of 30 patients with confirmed NAFLD were enrolled during the study period. The sample comprised 19 males (63.3%) and 11 females (36.7%), with a mean age of 43.2±9.8 years (range: 24–64 years). The sample was stratified by disease severity: 12 patients (40.0%) with mild NAFLD, 11 patients (36.7%) with moderate NAFLD, and 7 patients (23.3%) with severe NAFLD. There were no statistically significant differences in gender distribution across severity groups ($p=0.94$). However, patients with severe NAFLD were significantly older (50.3±10.1 years) compared to those with mild disease (38.4±8.2 years; $p=0.008$). Mean BMI was 26.3±2.1 kg/m² in the mild group, rising to 29.8±2.8 kg/m² in the moderate group and 33.6±3.4 kg/m² in the severe group ($p<0.001$), reflecting a clear gradient of worsening adiposity with disease progression. Dyslipidaemia was the most prevalent comorbidity in the overall cohort (73.3%), present in 100% of severe NAFLD patients, compared to 72.7% in moderate and 58.3% in mild cases. Hypertension was documented in 60.0% of patients overall, with a strikingly higher prevalence of 85.7% in the severe NAFLD group versus 41.7% in the mild group. T2DM was present in 46.7% of the total cohort, with significantly higher prevalence in severe (71.4%) and moderate (54.5%) NAFLD compared to mild

disease (25.0%). Detailed baseline sociodemographic and clinical characteristics are presented in Table 1.

Table 1: Baseline Sociodemographic and Clinical Characteristics by NAFLD Severity Grade

Characteristic	Mild NAFLD (n=12)	Moderate NAFLD (n=11)	Severe NAFLD (n=7)
Age (years), mean±SD	38.4±8.2	44.1±9.6	50.3±10.1
Male, n (%)	7 (58.3)	6 (54.5)	4 (57.1)
Female, n (%)	5 (41.7)	5 (45.5)	3 (42.9)
BMI (kg/m²), mean±SD	26.3±2.1	29.8±2.8	33.6±3.4
Hypertension, n (%)	5 (41.7)	7 (63.6)	6 (85.7)
Type 2 Diabetes, n (%)	3 (25.0)	6 (54.5)	5 (71.4)
Dyslipidaemia, n (%)	7 (58.3)	8 (72.7)	7 (100.0)
MetS, n (%)	2 (16.7)	4 (36.4)	5 (71.4)

SD: standard deviation; BMI: body mass index; MetS: metabolic syndrome. p-values derived from one-way ANOVA (continuous variables) or chi-square test (categorical variables). Significance threshold: $p<0.05$.

Analysis of cardiometabolic and biochemical parameters revealed a highly significant and consistent gradient across NAFLD severity groups. Fasting plasma glucose escalated from 102.4±10.2 mg/dL in mild NAFLD to 138.2±18.4 mg/dL in severe NAFLD ($p<0.001$). Similarly, HbA1c values increased from 5.8±0.4% in mild to 7.4±0.8% in severe disease ($p<0.001$), reflecting progressive glycaemic deterioration. The atherogenic lipid phenotype was accentuated with increasing severity: LDL-C rose from 118.2±14.6 to 148.9±20.4 mg/dL ($p=0.003$), while triglycerides escalated markedly from 148.6±22.4 to 224.8±34.2 mg/dL ($p<0.001$). Conversely, HDL-C demonstrated a significant inverse relationship with disease severity, declining from 48.6±6.2 mg/dL in mild to 36.8±5.1 mg/dL in severe NAFLD ($p=0.001$). The most striking metabolic finding was the dramatic rise in insulin resistance: HOMA-IR increased from 2.8±0.8 in mild NAFLD to 7.6±1.8 in severe disease ($p<0.001$), confirming insulin resistance as the dominant metabolic driver of NAFLD severity in this cohort. Corresponding liver function test (LFT) data showed significantly elevated transaminases, with ALT reaching 108.4±22.8 U/L and AST 96.2±20.4 U/L in the severe group, alongside substantially elevated GGT and reduced albumin levels, indicating progressive hepatocellular dysfunction. These data are summarised in Tables 2 and 3, and the metabolic parameter gradient is visually depicted in Figure 1.

Table 2: Cardiometabolic and Glycaemic Parameters Across NAFLD Severity Groups

Parameter	Mild NAFLD (n=12)	Moderate NAFLD (n=11)	Severe NAFLD (n=7)	p-value
FPG (mg/dL)	102.4±10.2	118.6±14.8	138.2±18.4	<0.001
HbA1c (%)	5.8±0.4	6.6±0.6	7.4±0.8	<0.001
Total Cholesterol (mg/dL)	188.4±18.2	208.6±22.4	234.8±26.1	<0.001
LDL-C (mg/dL)	118.2±14.6	132.5±18.2	148.9±20.4	0.003
HDL-C (mg/dL)	48.6±6.2	42.4±5.8	36.8±5.1	0.001
Triglycerides (mg/dL)	148.6±22.4	186.4±28.6	224.8±34.2	<0.001
Fasting Insulin (μU/mL)	10.8±3.2	16.4±4.6	22.8±6.4	<0.001
HOMA-IR	2.8±0.8	4.8±1.2	7.6±1.8	<0.001

FPG: fasting plasma glucose; HbA1c: glycated haemoglobin; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; HOMA-IR: homeostatic model assessment of insulin resistance. Values expressed as mean ± SD. p-values from one-way ANOVA.

Table 3: Liver Function and Elastography Parameters Across NAFLD Severity Groups

Liver Parameter	Mild NAFLD (n=12)	Moderate NAFLD (n=11)	Severe NAFLD (n=7)	p-value
ALT (U/L)	42.6±8.4	72.8±14.6	108.4±22.8	<0.001
AST (U/L)	34.2±6.8	58.4±12.2	96.2±20.4	<0.001
GGT (U/L)	38.4±8.8	62.6±14.4	98.8±22.6	<0.001
ALP (U/L)	82.4±12.4	102.8±18.6	138.6±26.8	0.002
Albumin (g/dL)	4.2±0.3	3.9±0.4	3.4±0.5	0.003
Total Bilirubin (mg/dL)	0.8±0.2	1.2±0.4	1.8±0.6	0.008
Fibroscan (kPa)	5.8±1.2	9.4±1.8	14.6±3.2	<0.001

ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyl transferase; ALP: alkaline phosphatase. Values expressed as mean ± SD. p-values from one-way ANOVA.

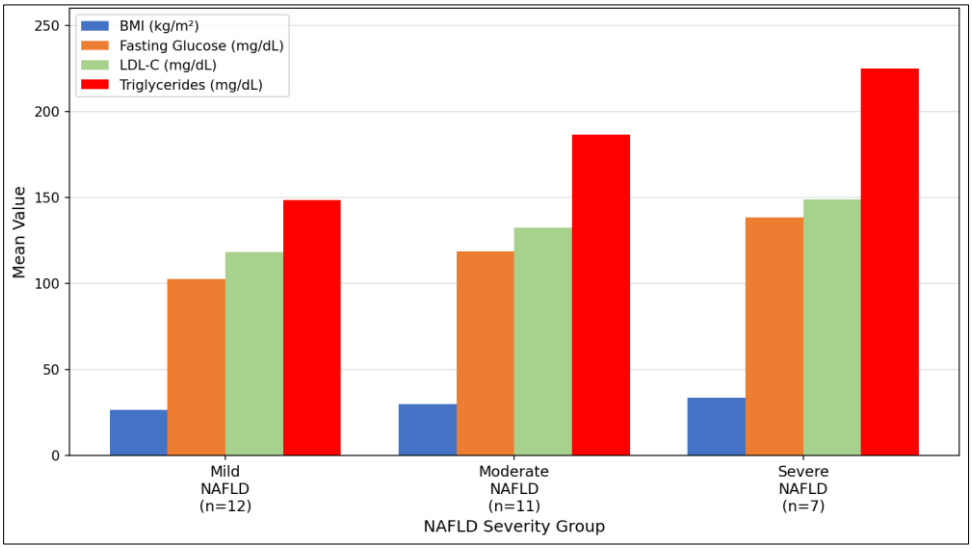

Figure 1: Mean cardiometabolic risk parameters (BMI, fasting glucose, LDL-C, triglycerides) stratified by NAFLD severity grade

Multivariate binary logistic regression identified HOMA-IR (OR 1.98; 95% CI 1.38–2.84; p<0.001), BMI (OR 1.69; 95% CI 1.23–2.32; p=0.001), and serum triglycerides (OR 1.51; 95% CI 1.15–1.98; p=0.003) as the most potent independent predictors of moderate-to-severe NAFLD. HbA1c (OR 1.47) and the presence of hypertension (OR 1.35) also reached statistical significance as independent risk determinants (Table 4). HDL-C demonstrated a protective inverse association (OR 0.71; 95% CI 0.55–0.91; p=0.007). On prospective follow-up (April 2022), seven patients (23.3%) demonstrated disease progression (upgrade in FibroScan severity grade). This subgroup showed significantly greater deterioration in HOMA-IR, BMI, triglycerides, and HbA1c over the follow-up interval compared to non-progressors (Table 5). The distribution of cardiometabolic comorbidities in the overall cohort is illustrated in Figure 2.

Table 4: Multivariate Logistic Regression - Independent Predictors of Moderate-to-Severe NAFLD

Variable	β Coefficient	SE	Wald χ^2	OR (95% CI)	p-value
HOMA-IR	0.682	0.184	13.74	1.98 (1.38–2.84)	<0.001
BMI (kg/m²)	0.524	0.162	10.46	1.69 (1.23–2.32)	0.001
Triglycerides	0.412	0.138	8.92	1.51 (1.15–1.98)	0.003
HbA1c (%)	0.388	0.144	7.26	1.47 (1.11–1.95)	0.007
HDL-C (mg/dL)	-0.342	0.126	7.38	0.71 (0.55–0.91)	0.007
Hypertension	0.298	0.118	6.38	1.35 (1.07–1.70)	0.012
LDL-C (mg/dL)	0.264	0.112	5.56	1.30 (1.05–1.62)	0.018

SE: standard error; OR: odds ratio; CI: confidence interval; Reference category: mild NAFLD. Hosmer-Lemeshow goodness-of-fit p=0.72. Model Nagelkerke R^2 = 0.61.

Table 5: Longitudinal Changes in Cardiometabolic Parameters: Baseline vs. Follow-up (n=30)

Risk Factor	Baseline (Jan–Jun 2021) n=30	Follow-up (Jan–Apr 2022) n=30	p-value
Mean BMI (kg/m²)	29.2±4.6	30.8±4.9	0.028
Mean FPG (mg/dL)	116.4±20.8	122.6±22.4	0.042
Mean HbA1c (%)	6.4±0.9	6.8±1.0	0.038
Mean Triglycerides (mg/dL)	181.4±42.6	194.8±48.2	0.044
Mean HOMA-IR	4.8±2.2	5.6±2.6	0.031
Proportion with MetS (%)	36.7	46.7	0.038
Proportion with HTN (%)	60.0	66.7	0.041
Disease Progression (%)		23.3	

FPG: fasting plasma glucose; MetS: metabolic syndrome; HTN: hypertension. Continuous variables compared by paired t-test; categorical variables by McNemar test. denotes not applicable.

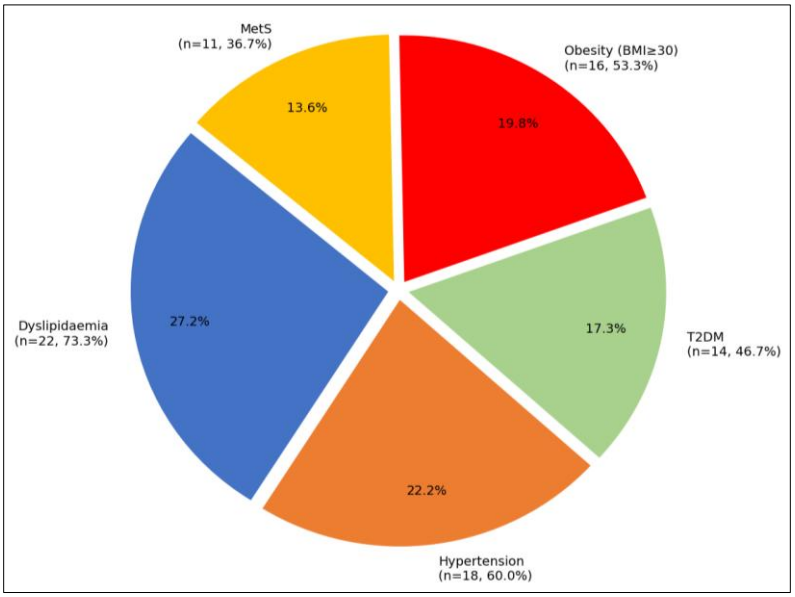

Figure 2: Proportional distribution of cardiometabolic comorbidities among NAFLD patients in the study cohort (n=30)

5. DISCUSSION

The findings of this prospective hospital-based cohort study underscore the profound and graded entanglement between cardiometabolic risk factors and NAFLD severity in the South Indian population. All major cardiometabolic risk parameters glycaemic indices, lipid fractions, body mass index, blood pressure, and indices of insulin resistance demonstrated a significant stepwise worsening across NAFLD severity grades, from mild to severe, corroborating the well-established concept that NAFLD is the hepatic expression of a systemic metabolic disorder [1,5]. The near-universal prevalence of dyslipidaemia in severe NAFLD patients (100%) and the high overall prevalence of hypertension (60%) and T2DM (46.7%) align closely with published Indian cohort data [4,13], and highlight the compounded cardiovascular risk that these patients carry. The escalating cardiometabolic burden with worsening NAFLD severity observed in the present study is consistent with the bidirectional pathobiological relationship between hepatic and systemic metabolic dysregulation documented in large multinational cohorts [6,7]. Importantly, the prospective design of this study, with baseline and follow-up assessments over 15 months, adds a temporal dimension that strengthens causal inference beyond cross-sectional surveys.

The identification of HOMA-IR as the strongest independent predictor of moderate-to-severe NAFLD (OR 1.98; $p<0.001$) in our multivariate model is a critically important finding with direct clinical implications. Insulin resistance is mechanistically central to NAFLD pathogenesis: it promotes hepatic de novo lipogenesis via upregulation of SREBP-1c, increases free fatty acid flux to the liver, impairs mitochondrial beta-oxidation, and potentiates proinflammatory cytokine-mediated hepatocyte injury [8,9]. The strong predictive value of HOMA-IR observed here supports its routine clinical use as a non-invasive risk stratification tool in NAFLD patients, particularly in settings where liver biopsy is impractical. BMI emerged as the second most powerful independent predictor (OR 1.69; $p=0.001$), consistent with the pivotal role of visceral adiposity in driving lipotoxic stress, adipokine dysregulation, and systemic inflammation in NAFLD [12]. The significant inverse association of HDL-C (OR 0.71; $p=0.007$) with severe NAFLD further reinforces the atherogenic dyslipidaemia paradigm: low HDL-C not only serves as a cardiovascular risk marker but also reflects impaired reverse cholesterol transport and enhanced hepatic lipid accumulation [10]. The 23.3% disease progression rate documented on follow-up occurring within as little as 15 months is alarming and argues strongly for aggressive, early metabolic intervention rather than watchful waiting. Patients demonstrating progression showed significantly greater worsening in HOMA-IR, BMI, triglycerides, and HbA1c, suggesting that deteriorating metabolic control is the principal driver of hepatic fibrosis progression, in line with the longitudinal evidence from global NAFLD registries [11,14].

These findings have important implications for clinical practice in the Indian context. First, they validate the utility of readily available metabolic biomarkers HOMA-IR, BMI, and fasting lipids as surrogates for NAFLD severity, potentially reducing reliance on invasive liver biopsy in routine clinical assessment. Second, they reinforce the imperative for a multidisciplinary cardiometabolic-hepatological approach in NAFLD management: addressing insulin resistance through lifestyle modification and pharmacotherapy (e.g., pioglitazone, GLP-1 receptor agonists), optimising lipid control (statins, fenofibrates), and achieving stringent blood pressure targets should form the pillars of NAFLD management alongside hepatology-specific therapies [2,5,15]. Third, the high comorbidity burden observed in this cohort with metabolic syndrome present in 71.4% of severe NAFLD patients underscores the need for systematic cardiovascular risk assessment in all patients presenting with liver disease, as cardiovascular mortality remains the leading cause of death in NAFLD patients [6]. Future research should focus on larger multicentre Indian cohorts with extended follow-up, histological endpoints (NASH activity score, fibrosis stage), and head-to-head comparison of pharmacological interventions targeting specific cardiometabolic pathways in NAFLD patients. The integration of novel biomarkers such as fibroblast growth factor 21 (FGF-21), fetuin-A, and cytokeratin-18 fragments may further enhance non-invasive severity prediction in resource-limited settings.

6. Limitations of the Study

Several limitations of this study must be acknowledged. The most significant is the small sample size of 30 patients, which limits statistical power, reduces the precision of effect size estimates, and may introduce type II errors for variables with modest associations. Although this sample is appropriate for a pilot prospective cohort from a single institution, findings should be interpreted cautiously and validated in larger multicentre cohorts. Second, the absence of liver biopsy data means that histological NASH activity (NAS score) and fibrosis staging could not be directly ascertained; FibroScan-derived CAP and LSM values, while validated and widely used, are subject to operator variability and technical limitations in patients with high BMI. Third, the 15-month follow-up window may be insufficient to capture the full trajectory of NAFLD progression, which often occurs over years to decades. Fourth, this was a single-centre study from an urban tertiary care hospital, which may introduce referral bias and limit generalisability to rural or primary care populations. Fifth, dietary assessment and physical activity quantification were not performed systematically, precluding adjustment for these important confounders in regression models. Sixth, some potentially relevant biomarkers, including hsCRP, FGF-21, and liver biopsy-based adipokine profiles, were not consistently available for all participants. Despite these limitations, the prospective design, standardised data collection, and comprehensive cardiometabolic profiling represent meaningful strengths of this investigation.

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8. CONCLUSION

This prospective hospital-based cohort study provides compelling evidence that cardiometabolic risk factors insulin resistance (HOMA-IR), central obesity (BMI), atherogenic dyslipidaemia (hypertriglyceridaemia, low HDL-C), hypertension, and T2DM are not merely concurrent comorbidities in NAFLD patients but demonstrate a highly significant graded relationship with hepatic disease severity. The stepwise escalation of each major cardiometabolic parameter from mild through moderate to severe NAFLD, consistently significant across all biochemical and anthropometric indices ($p<0.001$ for most), underscores the metabolic underpinnings of NAFLD progression and validates the paradigm of NAFLD as a hepatic manifestation of systemic metabolic dysregulation. The identification of HOMA-IR as the dominant independent predictor of advanced NAFLD severity (OR 1.98) in this South Indian cohort provides strong empirical support for the routine clinical measurement of insulin resistance in all NAFLD patients as part of a standardised risk stratification protocol. The significant and independent predictive roles of BMI, triglycerides, HbA1c, and hypertension further affirm that comprehensive cardiometabolic assessment encompassing glycaemic control, lipid profiling, anthropometric evaluation, and blood pressure monitoring should be regarded as

indispensable in the hepatological workup of NAFLD, irrespective of the presenting hepatic severity grade.

The longitudinal follow-up data, demonstrating disease progression in 23.3% of patients over 15 months alongside concurrent deterioration in key metabolic parameters, carry urgent clinical implications. They suggest that NAFLD is a dynamically progressive condition in a substantial proportion of patients, driven primarily by worsening metabolic control, and that the therapeutic window for intervention may be narrow. The public health implications are equally significant: with T2DM, obesity, and the metabolic syndrome reaching epidemic proportions in urban India, NAFLD is poised to become a major driver of hepatic cirrhosis, liver failure, and hepatocellular carcinoma in coming decades, in addition to its already substantial contribution to cardiovascular morbidity and mortality. Effective management of NAFLD must therefore transcend the traditional hepatocentric paradigm and embrace an integrated cardiometabolic-hepatological framework. This entails aggressive lifestyle modification targeting weight reduction and insulin sensitisation, pharmacological optimisation of dyslipidaemia and blood pressure, glycaemic control to HbA1c targets, and regular non-invasive hepatic monitoring using validated tools such as FibroScan. Ultimately, close interdisciplinary collaboration between hepatologists, diabetologists, cardiologists, and nutritionists is essential to reduce the dual hepatic and cardiovascular burden in this high-risk population and to translate the growing mechanistic understanding of NAFLD pathobiology into improved patient outcomes.

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