Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

Assessment of Apolipoprotein B, A1, And the Risk of Apo B/Apoa1 Ratio in Metabolic Dysfunction-Associated Steatotic Liver Disease: A Cross-Sectional Study from South India

Dr. Mohith Hanumappa Narayanaswamy[1], Dr. Deepak Suvarna[2], Dr. Nandeesh H.P[3], Dr. Aradya H.V[4], Dr. Vinod Kumar L[5], Dr. Ashwin Paul[6], Dr. Gurrala Rajashekar[7]

Corresponding Author:

Dr.Deepak suvarna

[1] Senior Resident, Department of Medical Gastroenterology, JSS Academy of Higher Education and Research (JSSAHER), Mysuru
[2] Professor and Head, Department of Medical Gastroenterology, JSSAHER, Mysuru *(Corresponding Author)*
[3] Senior Professor, Department of Medical Gastroenterology, JSSAHER, Mysuru
[4] Associate, Department of Medical Gastroenterology, JSSAHER, Mysuru
[5] Senior Resident, Department of Medical Gastroenterology, JSSAHER, Mysuru
[6]Senior Resident, Department of Medical Gastroenterology, JSSAHER, Mysuru
[7]Senior Resident, Department of Medical Gastroenterology, JSSAHER, Mysuru

Conflicts of interest: None declared.

Funding: None.

(Received: 27 September 2025 Revised: 05 October 2025 Accepted: 01 November 2025)

KEYWORDS

Metabolic dysfunction-associated steatotic liver disease; MASLD; Apolipoprotein B; Apolipoprotein A1; Dyslipidemia;

ABSTRACT:

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is strongly associated with dyslipidemia. The apolipoprotein B/A1 ratio may provide superior metabolic risk assessment compared to conventional lipid parameters.

Aim: To assess apolipoprotein B, A1 levels and the B/A1 ratio in MASLD patients and evaluate their association with disease severity.

Methods: This cross-sectional study enrolled 150 MASLD patients at a tertiary care center in South India. Clinical evaluation, anthropometry, conventional lipid profile, apolipoprotein measurements, ultrasonography, and transient elastography (FibroScan) were performed. Correlation analysis, multiple regression, and ROC curve analysis were conducted.

Results: Mean age was 48.31±11.42 years with 61.3% males. Comorbidities included hypertension (88%), diabetes (84%), and dyslipidemia (81.3%). Lean MASLD comprised 23.3% of patients; 34.3% of lean patients had elevated Apo B/A1 ratio. Mean Apo B/A1 ratio was 1.14±0.34, with 60% having high cardiovascular risk (ratio >1.0). The ratio correlated strongly with controlled attenuation parameter ($r=0.532$, $p<0.001$) and liver stiffness ($r=0.392$, $p<0.001$). Notably, 10.7% had normal conventional lipids but elevated Apo B/A1 ratio. Dyslipidemia was the strongest predictor (OR 3.84, 95% CI 2.12-6.96), while normal lipids with increased ratio independently predicted MASLD risk (OR 2.67, 95% CI 1.23-5.79). ROC analysis showed AUC of 0.682 for moderate-severe steatosis and 0.714 for patients with normal lipids but metabolic risk.

Conclusion: Apo B/A1 ratio is a valuable biomarker for MASLD severity, identifying high-risk phenotypes including lean MASLD and metabolic dysfunction despite normal conventional lipids.

INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), recently renamed from metabolic dysfunction-associated fatty liver disease (MAFLD) and historically known as non-alcoholic fatty liver disease (NAFLD), represents the most common chronic liver disease worldwide, affecting 25-30% of the global population.[1,2] In June 2023, an international multi-society Delphi consensus introduced the MASLD

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

nomenclature, emphasizing metabolic dysfunction as the core pathophysiological feature while reducing stigmatizing terminology.[3] This study, initiated under MAFLD terminology, adopts the current MASLD nomenclature while recognizing that diagnostic criteria remain fundamentally consistent.

The global burden of MASLD continues to escalate parallel to obesity and diabetes epidemics, with projections indicating substantial increases in disease prevalence and associated complications through 2030.[4] In South Asia, including India, MASLD prevalence is particularly concerning due to unique metabolic phenotypes characterized by higher susceptibility to metabolic dysfunction at lower body mass index (BMI) thresholds compared to Western populations.[5] Meta-analyses estimate MASLD prevalence in India at approximately 38.6%, with strong associations with diabetes mellitus, hypertension, and dyslipidemia.[67]

The disease spectrum ranges from simple steatosis to metabolic dysfunction-associated steatohepatitis (MASH), advanced fibrosis, and cirrhosis. Importantly, MASLD is associated with increased cardiovascular mortality independent of traditional risk factors, with cardiovascular disease representing the leading cause of death in these patients.[8],[9] The presence and stage of liver fibrosis represents the most critical prognostic factor, making accurate non-invasive assessment of disease severity paramount for risk stratification.[10]

Dyslipidemia constitutes a cardinal feature of MASLD pathophysiology, present in 70-80% of affected individuals.[11] The characteristic pattern includes elevated triglycerides, reduced high-density lipoprotein (HDL) cholesterol, increased small dense low-density lipoprotein (LDL) particles, and elevated apolipoprotein B (Apo B) levels.[12] However, conventional lipid parameters provide incomplete information about atherogenic risk, reflecting cholesterol mass rather than lipoprotein particle number.[13]

Apolipoprotein B represents the primary structural protein in all atherogenic lipoproteins (very low-density lipoproteins, intermediate-density lipoproteins, LDL, and lipoprotein(a)). Each atherogenic particle contains exactly one Apo B molecule, making Apo B concentration a direct measure of total atherogenic particle number.[14] Apolipoprotein A1 (Apo A1) constitutes the major protein component of HDL particles, reflecting reverse cholesterol transport capacity.[15] The apolipoprotein B/A1 ratio integrates information about both atherogenic burden and protective mechanisms, potentially providing superior cardiovascular and metabolic risk assessment compared to conventional lipid parameters.[16],[17]

Emerging evidence links apolipoprotein abnormalities with MASLD presence and severity. Studies have demonstrated that elevated Apo B/A1 ratio is significantly associated with MASLD risk across different lipid profiles and BMI categories, with the highest tertile showing 3-4 fold increased odds compared to the lowest tertile.[18],[19] This association persists even in individuals with normal conventional lipid profiles, suggesting that apolipoprotein dysregulation represents a distinct pathophysiological pathway operating independently of conventional dyslipidemia.[20],[21]

Despite emerging evidence, critical gaps remain. Most studies have been conducted in East Asian populations, with limited data from South Asian cohorts despite their unique metabolic phenotypes. The relationship between apolipoprotein abnormalities and liver fibrosis progression remains incompletely characterized. The clinical utility of Apo B/A1 ratio for identifying high-risk phenotypes such as lean MASLD and individuals with occult metabolic risk requires systematic evaluation. Optimal cut-off values for clinical application have not been established.

We designed this study to systematically evaluate apolipoprotein B, A1, and the B/A1 ratio in MASLD patients at a tertiary care center in South India, examining their associations with disease severity markers and evaluating their performance for identifying high-risk phenotypes.

AIMS

Primary Objective: To assess serum apolipoprotein B and apolipoprotein A1 levels in patients with metabolic dysfunction-associated steatotic liver disease.

Secondary Objectives: To evaluate the apolipoprotein B/A1 ratio and its association with MASLD severity indicators; to identify patients with occult metabolic risk despite normal conventional lipids; and to determine the discriminative ability of Apo B/A1 ratio for predicting disease severity.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional observational study was conducted at the Department of Medical Gastroenterology, JSS Medical College and Hospital, Mysuru, Karnataka, India, from January 2023 to June 2024. The study was approved by the Institutional Ethics Committee (approval number: JSSMC/IEC/02/2023) and conducted according to Declaration of Helsinki principles. Written informed consent was obtained from all participants.

Study Population and Sample Size

Consecutive patients diagnosed with MASLD attending the outpatient and inpatient departments were enrolled. Sample size was calculated based on 26% MASLD prevalence in Indian studies,[6] using the formula: $n = Z^2 \times P \times Q / D^2$, where Z=1.96, P=0.26, Q=0.74, and D=0.07, yielding n=150.

Eligibility Criteria

Inclusion criteria: Patients aged ≥18 years with MASLD diagnosed by hepatic steatosis on ultrasonography plus evidence of metabolic dysfunction (overweight/obesity [BMI ≥23 kg/m²], type 2 diabetes, or ≥2 metabolic risk factors including waist circumference >90 cm [men] or >80 cm [women], blood pressure ≥130/85 mmHg, triglycerides ≥150 mg/dL, HDL <40 mg/dL [men] or <50 mg/dL [women], or prediabetes).

Exclusion criteria: Age <18 years; excessive alcohol consumption (>30 g/day men, >20 g/day women); other chronic liver diseases (viral hepatitis, autoimmune hepatitis, Wilson disease, hemochromatosis); current lipid-lowering medication use; decompensated liver disease; malignancy; severe systemic illness; pregnancy/lactation; unwillingness to participate.

Data Collection and Measurements

Demographic data, medical history, and physical examination were recorded using standardized forms. Anthropometric measurements included height, weight, and waist circumference were done using calibrated instruments. BMI was calculated and classified according to Asian criteria: normal (<23 kg/m²), overweight (23-24.9 kg/m²), obese (≥25 kg/m²).

Laboratory Investigations

After 8-10 hours overnight fasting, venous blood samples were collected. Complete blood count, liver function tests (AST, ALT, total bilirubin, albumin), renal function tests, glycemic parameters (fasting glucose, postprandial glucose, HbA1c), and viral serology (HBsAg, anti-HCV) were performed using automated analyzers.

Fasting lipid profile included total cholesterol, triglycerides, HDL cholesterol, and calculated LDL cholesterol (Friedewald formula). Dyslipidemia was defined per NCEP ATP III guidelines.

Apolipoprotein measurements: Serum Apo B and Apo A1 levels were measured using immunoturbidimetric assay. Apo B/A1 ratio was calculated and categorized: low risk (<0.8), moderate risk (0.8-1.0), high risk (>1.0).

Radiological Investigations

Ultrasonography: Hepatic steatosis was assessed using high-resolution ultrasound and graded: Grade I (mild), Grade II (moderate), Grade III (severe) based on liver echogenicity, vascular blurring, and beam attenuation.

Transient elastography (FibroScan): Controlled attenuation parameter (CAP, dB/m) quantified steatosis: S0 (<238), S1 (238-259), S2 (260-290), S3 (>290). Liver stiffness measurement (LSM, kPa) assessed fibrosis: F0 (<6.0), F1 (6.0-7.9), F2 (8.0-9.9), F3 (10.0-13.9).

Statistical Analysis

Data were analyzed using SPSS version 28.0. Continuous variables were expressed as mean±SD and median (IQR). Categorical variables were expressed as frequencies and percentages. Independent samples t-test compared two groups; one-way ANOVA compared multiple groups. Chi-square test compared categorical variables. Pearson correlation assessed relationships between continuous variables. Multiple linear regression identified predictors of Apo B/A1 ratio. Binary logistic regression calculated odds ratios for high Apo B/A1 ratio. ROC curve analysis evaluated discriminative ability, calculating AUC, sensitivity, specificity, PPV, and NPV. P<0.05 was considered significant.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

RESULTS

Demographic and Clinical Characteristics

A total of 150 MASLD patients were included. The mean age was 48.31±11.42 years (median 49, range 31–69). 62% patients were aged 41–60 years. Males comprised 61.3% (n=92), females 38.7% (n=58), giving a ratio of 1.6:1.

Metabolic comorbidities were highly prevalent: hypertension in 88%, diabetes in 84%, and dyslipidemia in 81.3%. Among 28 patients (18.7%) with normal lipid profiles, 16 (10.7%) had elevated Apo B/A1 ratio, while only 12 (8%) had both normal lipids and normal ratio.

Anthropometric and Body Composition

Mean BMI was 26.03±4.62 kg/m² and waist circumference 91.19±6.75 cm. Of 150 patients, 35 (23.3%) were lean (BMI <23 kg/m²), 46 (30.7%) overweight, and 69 (46%) obese—indicating 76.7% were overweight or had obesity.

Lean MASLD Phenotype

Among 35 lean MASLD patients, 12 (34.3%) exhibited elevated Apo B/A1 ratio despite normal BMI, while 23 (65.7%) had normal ratio, showing that one-third of lean patients demonstrated metabolic dysfunction.

Hepatic Steatosis and Fibrosis

Ultrasound grades revealed Grade II fatty liver in 45.3%, Grade I in 36%, and Grade III in 18.7%. Overall, 64% had moderate to severe steatosis (Grades II–III).

Mean CAP was 289.47±34.82 dB/m, with S0 in 4.7%, S1 in 17.3%, S2 in 39.3%, and S3 in 38.7%, indicating 78% with moderate to severe steatosis (S2–S3).

Mean liver stiffness (LSM) was 8.41±2.50 kPa. Fibrosis stages were F0 (7.3%), F1 (19.3%), F2 (43.3%), and F3 (30.0%), with 73.3% showing F2–F3 (significant to advanced fibrosis).

Laboratory Parameters

Mean AST was 49.35±24.82 U/L and ALT 62.81±38.53 U/L. Lipid analysis showed mean total cholesterol 211.23±52.76 mg/dL, triglycerides 183.95±56.12 mg/dL, HDL 42.47±10.42 mg/dL, and LDL 128.31±36.42 mg/dL.

Apolipoprotein Profile

Mean Apo B was 107.29±21.53 mg/dL, Apo A1 was 94.53±16.78 mg/dL, and Apo B/A1 ratio 1.14±0.34. Based on ratio categories, 16.7% were low-risk (<0.8), 23.3% moderate-risk (0.8–1.0), and 60% high-risk (>1.0), making 83.3% moderate-to-high **risk for cardiovascular disease** overall.

Association with Demographic Variables

No significant difference was observed in Apo B/A1 ratio across age groups (p=0.447). Males had slightly higher mean ratio (1.16±0.35) than females (1.10±0.32, p=0.057).

Association with Clinical Parameters

BMI showed a non-significant trend (p=0.122). Significant associations were observed for hypertension (higher ratio 1.16±0.34 vs 1.05±0.32; p=0.016), diabetes (1.17±0.34 vs 1.04±0.31; p=0.004), and dyslipidemia (1.18±0.33 vs 0.96±0.28; p<0.001). Among normal lipid patients with elevated ratio, mean was 1.14±0.15.

Association with MASLD Severity

Apo B/A1 ratio increased significantly with ultrasound grade (p<0.001): Grade I (1.05±0.32), Grade II (1.14±0.33), and Grade III (1.26±0.35).

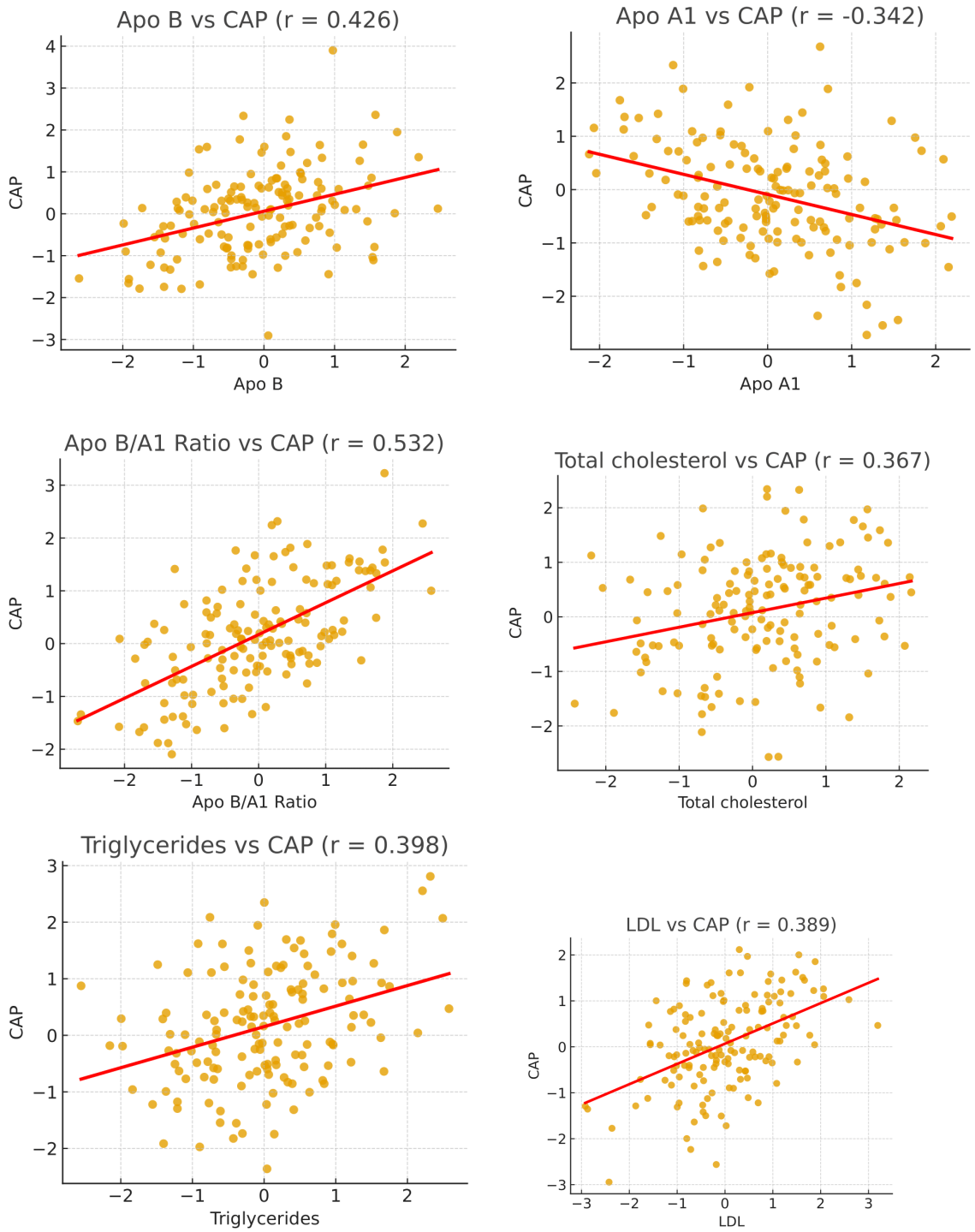
This pattern persisted after lipid stratification. In dyslipidemic patients (p=0.001), ratios rose from 1.08 (Grade I) to 1.17 (Grade II) to 1.29 (Grade III). In normal lipid patients (p=0.048), ratios increased from 0.92 to 0.97 to 1.06, reflecting consistent severity correlation.

Correlation Analysis

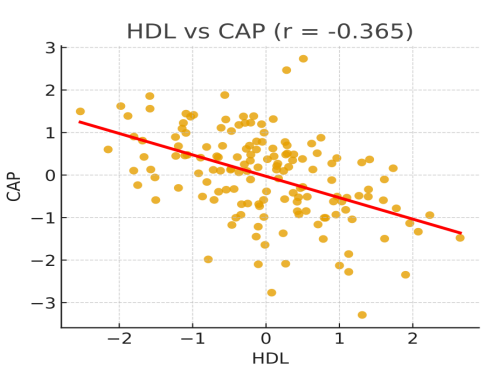
Apo B correlated with CAP (r=0.426) and LSM (r=0.318); LDL with CAP (r=0.389) and LSM (r=0.294). Apo A1 and HDL correlated negatively with CAP (r=-0.342 and -0.365) and LSM (r=-0.287 and -0.276). Apo B/A1 ratio showed the strongest associations—CAP (r=0.532, p<0.001) and LSM (r=0.392, p<0.001)—outperforming all other lipid indices.

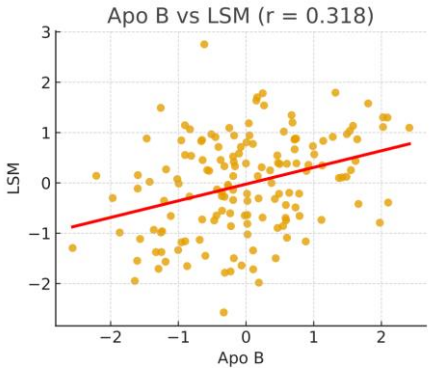
Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

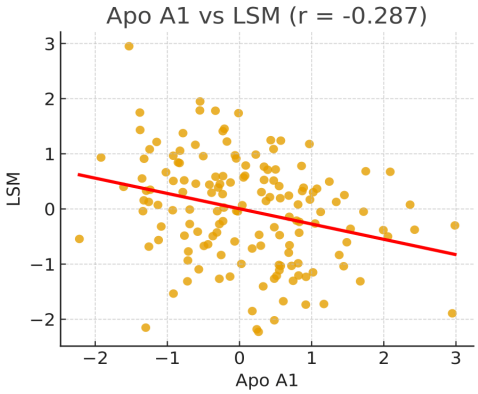
Figure 1: Correlation of all lipid markers with Fibroscan parameters (CAP and LSM)

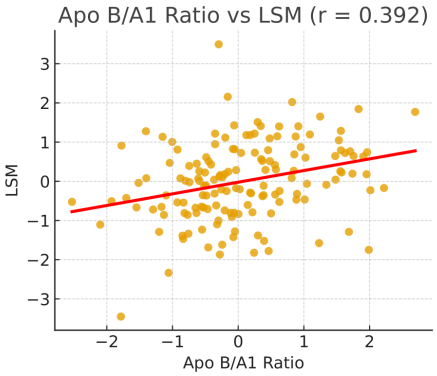


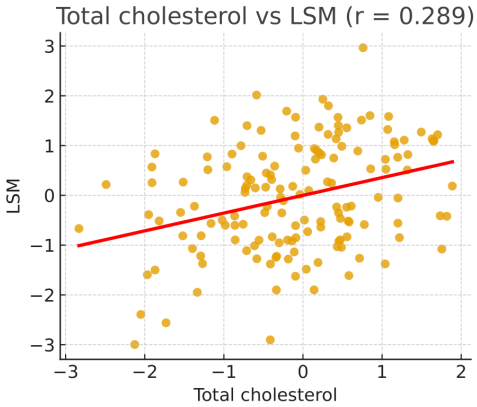
Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

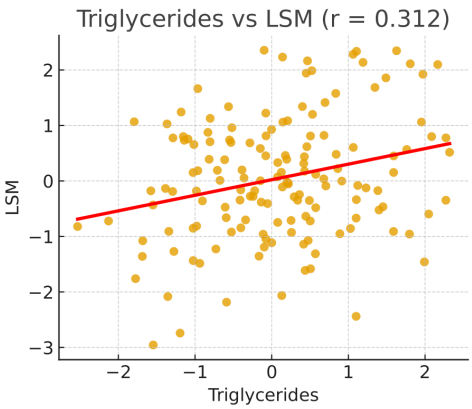


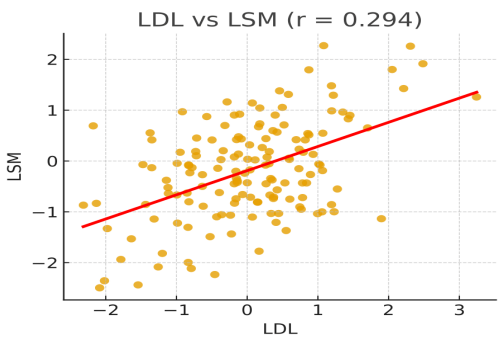


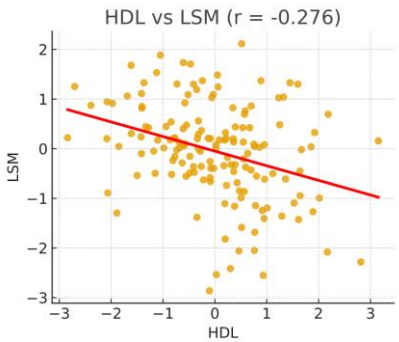












Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

Multiple Linear Regression

Regression with Apo B/A1 ratio as dependent variable confirmed model significance (R^2=0.428; p<0.001). Dyslipidemia (β=0.189, p<0.001) and CAP (β=0.004, p<0.001) were independent predictors. Age, sex, BMI, diabetes, and hypertension were not significant after adjustment.

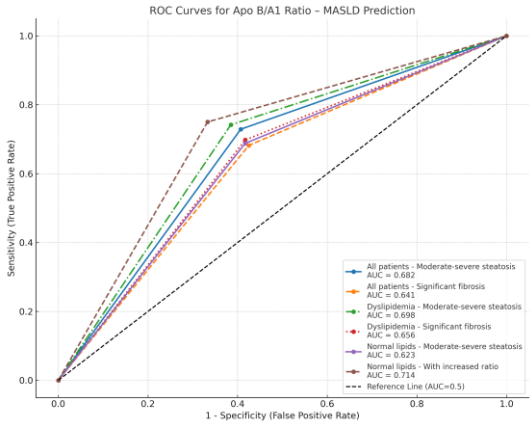
ROC Analysis

In the total cohort, Apo B/A1 ratio predicted moderate-severe steatosis (AUC 0.682; cut-off >1.10) with 72.9% sensitivity and 59.3% specificity; for significant fibrosis (AUC 0.641; cut-off >1.12) with 68.2% sensitivity and 57.5% specificity.

Stratification enhanced performance:

- **Dyslipidemic patients:** AUC 0.698 (cut-off >1.15) for steatosis; 0.656 (cut-off >1.16) for fibrosis.
- **Normal lipid patients:** AUC 0.623 (cut-off >0.95) for steatosis, and in those with raised ratio, AUC 0.714 (cut-off >1.05), showing good discrimination in this high-risk subgroup.

Figure 2 : ROC Curves of ApoB/ApoA1 ratio with MASLD prediction



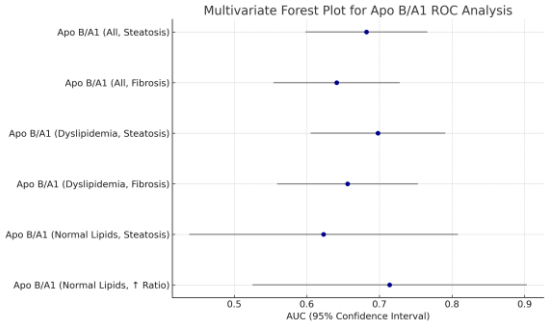
Lipid Parameter Progression

All lipid variables worsened with ultrasound grade. LDL rose from 118.4 to 130.2 to 139.6 mg/dL (p=0.022); Apo B from 99.8 to 108.2 to 116.6 mg/dL (p=0.002). HDL decreased from 45.6 to 38.1 mg/dL (p=0.006), Apo A1 from 99.9 to 88.0 mg/dL (p=0.004), and Apo B/A1 ratio rose from 1.05 to 1.26 (p<0.001).

Risk Factor Analysis

Binary logistic regression identified dyslipidemia as the strongest predictor of elevated Apo B/A1 ratio (OR 3.84, p<0.001). Combined factors increased risk: dyslipidemia with diabetes (OR 4.26), hypertension (OR 3.95), and obesity (OR 4.12) (all p<0.001). Importantly, normal lipids with elevated ratio independently predicted MASLD risk (OR 2.67, p=0.013). Age and sex were not significant predictors.

Figure 3: Multivariate analysis of ApoB/ApoA1 ratio



TABLES

Table 1: Baseline Demographic and Clinical Characteristics of Study Population (N=150)

Parameter	**Value**
Age (years)	
Mean ± SD	48.31 ± 11.42
Median (IQR)	49.0 (40.0-56.0)
Range	31-69
Age distribution, n (%)	
31-40 years	42 (28.0)
41-50 years	48 (32.0)
51-60 years	45 (30.0)
>60 years	15 (10.0)
Gender, n (%)	
Male	92 (61.3)

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

Parameter	Value
Female	58 (38.7)
BMI (kg/m²)	
Mean ± SD	26.03 ± 4.62
BMI categories, n (%)	
Normal (<23)	35 (23.3)
Overweight (23-24.9)	46 (30.7)
Obese (≥25)	69 (46.0)
Waist circumference (cm), Mean ± SD	91.19 ± 6.75
Comorbidities, n (%)	

Parameter	Value
Hypertension	132 (88.0)
Diabetes mellitus	126 (84.0)
Dyslipidemia	122 (81.3)
Lipid status, n (%)	
Dyslipidemia	122 (81.3)
Normal lipids	28 (18.7)
Normal lipids with increased Apo B/A1	16 (10.7)
Normal lipids with normal Apo B/A1	12 (8.0)

Table 2: Apolipoprotein Profile and Disease Severity Markers (N=150)

Parameter	Mean ± SD	Median (IQR)	Range
Apolipoprotein parameters			
Apo B (mg/dL)	107.29 ± 21.53	108.0 (89.0-124.0)	69-145
Apo A1 (mg/dL)	94.53 ± 16.78	92.0 (85.0-102.0)	74-130
Apo B/A1 ratio	1.14 ± 0.34	1.17 (0.94-1.35)	0.40-1.70
Apo B/A1 risk categories, n (%)			
Low risk (<0.8)	25 (16.7)		
Moderate risk (0.8-1.0)	35 (23.3)		
High risk (>1.0)	90 (60.0)		
Conventional lipid parameters			
Total cholesterol (mg/dL)	211.23 ± 52.76	194.0 (168.0-239.0)	121-333
Triglycerides (mg/dL)	183.95 ± 56.12	171.0 (141.0-225.0)	108-294
HDL cholesterol (mg/dL)	42.47 ± 10.42	39.0 (35.0-50.0)	27-66
LDL cholesterol (mg/dL)	128.31 ± 36.42	118.0 (99.0-147.0)	70-236

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

Parameter	Mean ± SD	Median (IQR)	Range
Liver enzymes			
AST (U/L)	49.35 ± 24.82	43.0 (33.0-57.0)	23-123
ALT (U/L)	62.81 ± 38.53	50.0 (38.0-74.0)	30-192
FibroScan parameters			
CAP (dB/m)	289.47 ± 34.82	286.4 (263.4-304.4)	-
LSM (kPa)	8.41 ± 2.50	8.2 (6.78-9.87)	-
USG grading, n (%)			
Grade I	54 (36.0)		
Grade II	68 (45.3)		
Grade III	28 (18.7)		
Fibrosis stage, n (%)			
F0	11 (7.3)		
F1	29 (19.3)		
F2	65 (43.3)		
F3	45 (30.0)		

Abbreviations: Apo, Apolipoprotein; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; CAP, Controlled attenuation parameter; LSM, Liver stiffness measurement; USG, Ultrasonography

Table 3: Association of Apo B/A1 Ratio with Clinical Parameters

Variable	Category	Mean Apo B/A1 ± SD	Test statistic	p-value
Age groups			F = 0.89	0.447
	31-40 years	1.11 ± 0.36		
	41-50 years	1.15 ± 0.32		
	51-60 years	1.14 ± 0.35		
	>60 years	1.12 ± 0.33		
Gender			t = 1.92	0.057

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

Variable	Category	Mean Apo B/A1 ± SD	Test statistic	p-value
	Male	1.16 ± 0.35		
	Female	1.10 ± 0.32		
BMI categories			F = 2.13	0.122
	Normal	1.09 ± 0.31		
	Overweight	1.13 ± 0.35		
	Obese	1.17 ± 0.35		
Hypertension			t = 2.44	0.016*
	Yes	1.16 ± 0.34		
	No	1.05 ± 0.32		
Diabetes mellitus			t = 2.89	0.004*
	Yes	1.17 ± 0.34		
	No	1.04 ± 0.31		
Lipid status			t = 4.62	<0.001*
	Dyslipidemia	1.18 ± 0.33		
	Normal lipids	0.96 ± 0.28		
	Normal with ↑ratio	1.14 ± 0.15		

*Statistically significant ($p<0.05$)

Table 4: Association of Apo B/A1 Ratio with MASLD Severity Indicators

Severity indicator	Category	Mean Apo B/A1 ± SD	Test statistic	p-value
USG grade (overall)			F = 8.24	<0.001*
	Grade I	1.05 ± 0.32		
	Grade II	1.14 ± 0.33		
	Grade III	1.26 ± 0.35		
USG grade (dyslipidemia)			F = 6.89	0.001*
	Grade I	1.08 ± 0.31		
	Grade II	1.17 ± 0.32		

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

Severity indicator	Category	Mean Apo B/A1 ± SD	Test statistic	p-value
	Grade III	1.29 ± 0.34		
USG grade (normal lipids)			F = 3.21	0.048*
	Grade I	0.92 ± 0.26		
	Grade II	0.97 ± 0.28		
	Grade III	1.06 ± 0.30		

*Statistically significant (p<0.05)

Table 5: Correlation Between Lipid Parameters and Fibroscan parameters

Lipid parameter	CAP (dB/m)		LSM (kPa)	
	Pearson's r	p-value	Pearson's r	p-value
Apo B	0.426	<0.001*	0.318	<0.001*
Apo A1	-0.342	<0.001*	-0.287	<0.001*
Apo B/A1 ratio	**0.532**	**<0.001***	**0.392**	**<0.001***
Total cholesterol	0.367	<0.001*	0.289	<0.001*
Triglycerides	0.398	<0.001*	0.312	<0.001*
LDL cholesterol	0.389	<0.001*	0.294	<0.001*
HDL cholesterol	-0.365	<0.001*	-0.276	<0.001*

*Statistically significant (p<0.05) CAP, Controlled attenuation parameter; LSM, Liver stiffness measurement

Table 6: ROC Analysis for Apo B/A1 Ratio in Predicting MASLD Severity

Population	Outcome	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
All patients							
	Moderate-severe steatosis	0.682 (0.598-0.766)	>1.10	72.9	59.3	75.8	55.2
	Significant fibrosis	0.641 (0.554-0.728)	>1.12	68.2	57.5	78.4	44.2
Dyslipidemia							
	Moderate-severe steatosis	0.698 (0.605-0.791)	>1.15	74.2	61.5	78.1	56.3

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

Population	Outcome	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	Significant fibrosis	0.656 (0.559-0.753)	>1.16	69.8	58.3	80.2	44.7
Normal lipids							
	Moderate-severe steatosis	0.623 (0.438-0.808)	>0.95	68.8	58.3	73.3	53.8
	With increased ratio	0.714 (0.525-0.903)	>1.05	75.0	66.7	75.0	66.7

AUC, Area under curve; CI, Confidence interval; PPV, Positive predictive value; NPV, Negative predictive value

DISCUSSION

This cross-sectional study of 150 MASLD patients in South India demonstrates that the apolipoprotein B/A1 ratio represents a valuable biomarker for assessing disease severity and cardiovascular risk. The data highlight metabolic heterogeneity across phenotypes, particularly within the lean MASLD subgroup, providing new insights into lipid dysregulation in MASLD.

Demographics and Metabolic Comorbidity Burden

Our cohort (mean age 48.3 years, 61.3% male) reflected the global male predominance in MASLD (ratio 1.6:1) and the highest prevalence among adults aged 41–60 years, underscoring socioeconomic implications. The exceptionally high metabolic comorbidity burden—hypertension (88%), diabetes (84%), and dyslipidemia (81.3%)—exceeds Western data[22] but is consistent with South Asian trends[23],[24] where metabolic syndrome manifests at lower BMI thresholds. Factors contributing include referral bias to tertiary centers, ethnic susceptibility, and delayed diagnosis due to limited resources.

The Lean MASLD Phenotype

Lean MASLD constituted 23.3% (35 patients) of our cohort, with 34.3% (12 patients; 8% overall) showing elevated Apo B/A1 ratios despite normal BMI. This agrees with Asian data reporting 20–35% lean MASLD prevalence.[25],[26] The finding challenges BMI-based risk models and aligns with reports that Apo B/A1 ratio independently associates with MASLD in non-obese individuals.[27] Lean patients often evade metabolic screening and present later with advanced fibrosis, emphasizing the need for apolipoprotein assessment beyond anthropometric indices—especially in South Asian populations predisposed to metabolic dysfunction at lower BMI values.

Apolipoprotein B/A1 Ratio: Primary Outcome Analysis

The mean Apo B/A1 ratio (1.14±0.34) revealed high atherogenic burden, with 60% of patients at high cardiovascular risk (ratio >1.0). Comparable studies report mean ratios around 1.08±0.31 in MASLD versus 0.82±0.24 in controls,[18],[28] confirming the marker's discriminative value. Elevated Apo B (107.3 mg/dL) with relatively reduced Apo A1 (94.5 mg/dL) reflects characteristic MASLD dyslipidemia—excess atherogenic particles and reduced reverse cholesterol transport capacity—explaining why the ratio outperforms traditional lipid parameters.

Association with Disease Severity

Apo B/A1 ratio correlated strongly with MASLD severity, increasing progressively across ultrasound grades—Grade I (1.05±0.32), Grade II (1.14±0.33), and Grade III (1.26±0.35) ($F=8.24$, $p<0.001$)—a pattern consistent across lipid strata. Correlation analyses revealed the strongest association with hepatic steatosis (CAP: $r=0.532$, $p<0.001$), surpassing Apo B ($r=0.426$) or LDL ($r=0.389$). Inverse correlations with Apo A1 ($r=-0.342$) and HDL ($r=-0.365$) further support apolipoprotein dysregulation as central to hepatic lipid accumulation.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

The ratio also correlated with liver stiffness (r=0.392, p<0.001), implicating it in fibrosis progression, possibly mediated by increased hepatic lipid influx, impaired HDL-mediated efflux, oxidized lipoprotein–driven oxidative stress, and pro-inflammatory cascades.[29,30] Together, these findings link apolipoprotein imbalance to both steatosis and fibroinflammatory progression.

Lipid Status Stratification: A Critical Refinement

A key finding was that 16 patients (10.7%) exhibited elevated Apo B/A1 ratios despite normal lipid profiles, forming an occult high-risk group with mean ratio 1.14±0.15, similar to the total cohort. This subset (57% of normal-lipid individuals) exemplifies metabolic risk hidden by standard lipid panels.

Multivariate analysis identified dyslipidemia (β=0.189, p<0.001) and CAP (β=0.004, p<0.001) as independent predictors of high ratios, explaining 42.8% of variance, while conventional factors (age, sex, BMI, diabetes, hypertension) were non-predictive after adjustment. Dyslipidemia showed the strongest association (OR 3.84, 95% CI 2.12–6.96, p<0.001), and importantly, normal lipid status with increased ApoB/ApoA1 ratio independently predicted MASLD risk (OR 2.67, 95% CI 1.23–5.79, p=0.013), confirming a distinct metabolic phenotype warranting clinical recognition and targeted prevention.

ROC Analysis and Clinical Utility

ROC analysis confirmed the Apo B/A1 ratio's discriminative ability for predicting steatosis and fibrosis severity. In the overall cohort, AUC values were 0.682 for steatosis and 0.641 for fibrosis. Lipid status stratification improved performance in dyslipidemic patients, AUCs rose to 0.698 and 0.656, respectively; in normal-lipid patients with elevated ratio, AUC reached 0.714, indicating good predictive capacity in this "metabolically unhealthy normal-lipid" group.

The identified cut-offs (>1.15 for dyslipidemic, >1.05 for normal-lipid with metabolic risk, >0.95 overall) provide actionable clinical guidance for evaluating atherogenic and hepatic risk profiles. Although these thresholds require external validation, they represent a foundation for precision screening algorithms incorporating baseline lipid status.

Comparison with Existing Literature

Our results align with global findings linking apolipoprotein abnormalities to MASLD pathogenesis and extend understanding in South Asians. Zhao et al.[18] reported elevated Apo B/A1 ratio as a significant MASLD risk factor, potentiated by dyslipidemia. Yang et al.[19] demonstrated consistent associations in both normal-weight and overweight individuals, where elevated ratios predicted MASLD even at BMI <23 kg/m² (adjusted OR 2.1). Choe et al.[20] similarly found Apo B/A1 ratio independently associated with MASLD in non-diabetic subjects (OR 1.89), independent of standard metabolic parameters.

Our study adds novel evidence by establishing apolipoprotein-based stratification in a South Asian cohort, quantifying lean MASLD with dysregulated lipid profiles, identifying practical cut-offs stratified by lipid status, and correlating these with validated non-invasive markers (CAP, LSM). The detection of occult metabolic risk in 10.7% of patients with normal lipids underscores the inadequacy of conventional panels alone and supports incorporating apolipoprotein evaluation into MASLD assessment frameworks to improve risk detection and therapeutic precision.

Clinical Implications

Our findings support integrating apolipoprotein measurement into routine MASLD assessment, particularly for individuals with normal lipid profiles who may harbor occult metabolic risk. The 10.7% of patients with normal lipids but elevated Apo B/A1 ratio represent a clinically relevant group requiring early identification and intervention.

The identified lipid status–specific cut-offs may guide risk stratification algorithms—patients with dyslipidemia and Apo B/A1 ratio >1.15 merit intensive metabolic therapy, while those with normal lipids but ratio >1.05 require enhanced surveillance despite normal conventional lipid results. This stratified approach acknowledges metabolic heterogeneity within MASLD and promotes individualized management.

Strong correlations between Apo B/A1 ratio and both CAP and LSM suggest its promise as a simple serum biomarker that could complement, or in resource-limited settings partially substitute, imaging-based evaluations. Its use may optimize patient triaging for

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

advanced imaging, improving cost-effectiveness in high-prevalence populations.

Furthermore, the association between dyslipidemia, elevated Apo B/A1 ratio (OR 3.84), and disease severity underscores lipid lowering as a key therapeutic target in MASLD, potentially improving both hepatic and cardiovascular outcomes.

Strengths and Limitations

This study's strengths include its comprehensive clinical, biochemical, and imaging evaluation, allowing multidimensional characterization of MASLD. This is the first study to correlate ApoB,ApoA1 and ApoB/ApoA1 ratio with fibroscan parameters (CAP and LSM). The inclusion of diverse BMI and lipid phenotypes enhances generalizability, while direct comparison between conventional and apolipoprotein markers addresses a critical gap, particularly in South Indian populations.

However, several limitations warrant acknowledgment: the cross-sectional design limits causal inference; longitudinal studies are required to assess temporal relationships and therapeutic effects. The single-center tertiary setting may introduce selection bias, and the moderate sample size restricts subgroup power, notably for lean MASLD analysis. Use of ultrasound and FibroScan instead of biopsy could lead to limited misclassification, though both reflect standard non-invasive practice.

Additional limitations include absence of genetic, dietary, or detailed lipoprotein profiling (e.g., lipoprotein(a), small dense LDL), and lack of cardiovascular outcome data. The proposed cut-offs require external validation to define their clinical applicability and appropriate monitoring intervals.

Future Research Directions

Future longitudinal and interventional studies should determine whether baseline or therapy-induced changes in Apo B/A1 ratio predict hepatic and cardiovascular outcomes. Mechanistic studies are needed to clarify molecular pathways linking apolipoproteins to hepatocellular injury and fibrosis. Genetic and multi-ethnic studies should assess population differences and establish ethnicity-specific thresholds. Finally, cost-effectiveness analyses should evaluate whether routine apolipoprotein screening enhances risk prediction and reduces disease burden in MASLD.

CONCLUSION

The Apo B/A1 ratio is significantly elevated in MASLD and correlates strongly with disease severity markers, providing clinically useful risk stratification particularly when interpreted in the context of conventional lipid status. A notable lean MASLD prevalence (23.3%) with metabolic dysfunction (34.3% elevated Apo B/A1 ratio) challenges BMI-based risk models, while 10.7% of patients had occult metabolic risk despite normal lipids, highlighting the utility of apolipoprotein profiling. The Apo B/A1 ratio outperformed conventional lipids with strong associations with steatosis ($r=0.532$, $p<0.001$) and fibrosis ($r=0.392$, $p<0.001$), and ROC analysis showed acceptable discriminative ability (AUC 0.682–0.714) with stratified lipid-specific thresholds. Dyslipidemia was the strongest predictor of elevated ratio (OR 3.84), while normal lipids with high ApoB/ApoA1 ratio independently predicted MASLD risk (OR 2.67), defining a hidden high-risk phenotype. These findings support including apolipoprotein assays in comprehensive MASLD evaluation, with lipid status-specific algorithms refining risk stratification and therapeutic targeting to address hepatic outcomes in MASLD.

Declarations

ACKNOWLEDGMENTS

We acknowledge the Department of Biochemistry, Department of Radiology, and FibroScan facility at JSS Medical College and Hospital for their support in conducting this study. We thank all patients who participated in this study.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING

This study received no external funding. Laboratory investigations were supported by institutional resources.

Ethical Clearance –Obtained from the Institutinal ethical committee,JSSAHER,Mysuru

Patient Consent: Obtained from all participants.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 348-364 | ISSN:2251-6727

Author Contributions:

1. **Dr. Mohith Hanumappa Narayanaswamy:** played a central role, designing the study and guiding its overall direction, while also leading the writing of the first draft

2. **Dr. Deepak Suvarna:** assisted by reviewing the literature and helping prepare the manuscript's figures and tables, making sure everything was clear and precise.

3. **Dr. Nandeesh HP:** contributed their clinical expertise, managing patient care and providing thoughtful insights that enhanced the manuscript's depth.

4. **Dr. Aradya HV:** supported the research by coordinating laboratory work and organizing important clinical information.

5. **Dr. Vinod Kumar L:** took charge of gathering the data and carefully analyzing it, helping to bring the story behind the numbers to life

6. **Dr. Ashwin Paul:** offered valuable guidance throughout the project, overseeing the work and helping refine the final manuscript with a critical eye..

7. **Dr. Gurrala Rajashekar:** handled data validation, managed communication with the journal, and ensured that all ethical and disclosure requirements were met smoothly

All authors reviewed and approved the final manuscript and takes collective responsibility for the content, accuracy, and integrity of the work.

REFERENCES

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73-84.

2. Riazi K, Azhari H, Charette JH, Underwood FE, King JA, Afshar EE, et al. The prevalence and incidence of NAFLD worldwide: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2022;7(9):851-861.

3. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. J Hepatol. 2023;79(6):1542-1556.

4. Estes C, Anstee QM, Arias-Loste MT, Bantel H, Bellentani S, Caballeria J, et al. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030. J Hepatol. 2018;69(4):896-904.

5. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol. 2020;73(1):202-209.

6. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, et al. Prevalence of Non-alcoholic Fatty Liver Disease in India: A Systematic Review and Meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-829.

7. Niriella MA, Ediriweera DS, Withanage MY, Darshika S, De Silva ST, Janaka de Silva H. Prevalence and associated factors for non-alcoholic fatty liver disease among adults in the South Asian Region: a meta-analysis. Lancet Reg Health Southeast Asia. 2023;15:100220.

8. Targher G, Byrne CD, Tilg H. NAFLD and increased risk of cardiovascular disease: clinical associations, pathophysiological mechanisms and pharmacological implications. Gut. 2020;69(9):1691-1705.

9. Targher G, Tilg H, Byrne CD. Non-alcoholic fatty liver disease: a multisystem disease requiring a multidisciplinary and holistic approach. Lancet Gastroenterol Hepatol. 2021;6(7):578-588.

10. Dulai PS, Singh S, Patel J, Soni M, Prokop LJ, Younossi Z, et al. Increased risk of mortality by fibrosis stage in nonalcoholic fatty liver disease: Systematic review and meta-analysis. Hepatology. 2017;65(5):1557-1565.

11. Kamagaté M, Sawadogo S, Yeo K, Ouattara M, Dembélé A. Apolipoprotein

B/Apolipoprotein A1 ratio and cardiovascular risk. Mali Med. 2019;34(3):21-25.

12. Sierra-Johnson J, Romero-Corral A, Somers VK, Lopez-Jimenez F, Walldius G, Hamsten A, et al. ApoB/apoA-I ratio: an independent predictor of insulin resistance in US non-diabetic subjects. Eur Heart J. 2007;28(21):2637-2643.
13. Sniderman AD, Williams K, Contois JH, Monroe HM, McQueen MJ, de Graaf J, et al. A meta-analysis of low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and apolipoprotein B as markers of cardiovascular risk. Circ Cardiovasc Qual Outcomes. 2011;4(3):337-345.
14. Walldius G, Jungner I. The apoB/apoA-I ratio: a strong, new risk factor for cardiovascular disease and a target for lipid-lowering therapy--a review of the evidence. J Intern Med. 2006;259(5):493-519.
15. Walldius G, Jungner I, Holme I, Aastveit AH, Kolar W, Steiner E. High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study. Lancet. 2001;358(9298):2026-2033.
16. Sniderman AD. The apoB/apoA-I ratio and insulin resistance: sorting out the metabolic syndrome. Eur Heart J. 2007;28(21):2563-2564.
17. Li Y, Zheng R, Li S, Cai R, Ni X, Zheng H, et al. Association between four anthropometric indexes and metabolic syndrome in US adults. Front Endocrinol (Lausanne). 2022;13:889785.
18. Zhao Y, Zhang J, Zhang J, Wu J. Association between apolipoprotein B/A1 and the risk of metabolic dysfunction associated fatty liver disease according to different lipid profiles in a Chinese population: A cross-sectional study. Clin Chim Acta. 2022;534:138-145.
19. Yang MH, Sung J, Gwak GY. The associations between apolipoprotein B, A1, and the B/A1 ratio and nonalcoholic fatty liver disease in both normal-weight and overweight Korean population. J Clin Lipidol. 2016;10(2):289-298.
20. Choe YG, Jin W, Cho YK, Chung WG, Kim HJ, Jeon WK, et al. Apolipoprotein B/AI ratio is independently associated with non-alcoholic fatty liver disease in nondiabetic subjects. J Gastroenterol Hepatol. 2013;28(4):678-683.
21. Wu T, Zheng X, Yang M, Zhao A, Li M, Chen T, et al. Serum lipid alterations identified in chronic hepatitis B, hepatitis B virus-associated cirrhosis and carcinoma patients. Sci Rep. 2017;7(1):42710.
22. Balakrishnan M, Patel P, Dunn-Valadez S, Dao C, Khan V, Ali H, et al. Women have a lower risk of nonalcoholic fatty liver disease but a higher risk of progression vs men: A systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2021;19(1):61-71.
23. Thanopoulou AC, Karamanos BG, Angelico FV, Assaad-Khalil SH, Barbato AF, Del Ben MP, et al. Dietary fat intake as risk factor for the development of diabetes: multinational, multicenter study of the Mediterranean Group for the Study of Diabetes (MGSD). Diabetes Care. 2003;26(2):302-307.
24. Kim JY, Park JY, Kim OY, Ham BM, Kim HJ, Kwon DY, et al. Metabolic profiling of plasma in overweight/obese and lean men using ultra performance liquid chromatography and Q-TOF mass spectrometry (UPLC-Q-TOF MS). J Proteome Res. 2010;9(9):4368-4375.
25. Ye Q, Zou B, Yeo YH, Li J, Huang DQ, Wu Y, et al. Global prevalence, incidence, and outcomes of non-obese or lean non-alcoholic fatty liver disease: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2020;5(8):739-752.
26. Ghani MA, Faulkner C, Rangan P, Ahmed T, Lopez R, Ghabril MS, et al. Increased Mortality Among Lean Versus Non-Lean Adults With MASLD: A Multicenter Study. J Gastroenterol Hepatol. 2025;40(3):467-475.
27. De A, Bhagat N, Mehta M, et al. Metabolic dysfunction-associated steatotic liver disease

(MASLD) definition is better than MAFLD criteria for lean patients with NAFLD. J Hepatol. 2024;80:e61-e62.

28. Shi L, Zhou Q, Li S, Fan X, Li B, Zeng Q, et al. The correlation of apolipoprotein B and apolipoprotein A1 with metabolic dysfunction-associated steatotic liver disease in children and adolescents with obesity. Pediatr Obes. 2025;20(3):e13185.
29. Wu T, Ye J, Mo S, Ye M, Li X, Li Q, et al. Varied Relationship of Lipid and Lipoprotein Profiles to Liver Fat Content in Phenotypes of Metabolic Associated Fatty Liver Disease. Front Endocrinol (Lausanne). 2021;12:691556.
30. Nurtazina A, Kozhakhmetova D, Dautov D, Shakhanova A, Chattu VK. Apolipoprotein B/A1 ratio as a diagnostic alternative to triglycerides and HDL-cholesterol for the prediction of metabolic syndrome in Type 2 diabetes mellitus. J Diabetes Metab Disord. 2020;19:1377-1384.