ORIGINAL ARTICLE

Characterizing Nonalcoholic Fatty Liver Disease (NAFLD) in Lean Individuals at a Tertiary Care Hospital: A Cross-sectional Study

Shamim Nazir[1], Zaigham Abbas[2], Darayus P Gazder[3], Sania Maqbool[4], Shaukat Ali Samejo[5], Manesh Kumar[6]

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Abstract

Background: Fat accumulation in the liver is affecting 38% of the global population. It can also occur in normal-weight individuals, termed lean non-alcoholic fatty liver disease (NAFLD). This study examines Asian and Western body mass index (BMI) criteria, as well as metabolic dysfunction-associated fatty liver disease (MAFLD) and metabolic dysfunction-associated steatotic liver disease (MASLD) diagnostic guidelines, in lean fatty liver cases within a healthcare setting.

Materials and methods: This study was cross-sectional included 111 lean patients diagnosed with NAFLD using either ultrasound or VCTE from January 2023 to March 2024. Anthropometric, laboratory and non-invasive liver fibrosis evaluation parameters were used. The study assessed clinical characteristics and metabolic risk factors of patients with BMI $\leq$ 23 kg/m^2 and BMI between 23 and $\leq$ 25 kg/m^2 using MASLD and MAFLD diagnostic criteria.

Results: The cohort included NAFLD patients with a mean age of 43.3 years ($\pm$13.2 years). Of the participants, 33% were diagnosed through ultrasonography, whereas 67% diagnosis were made via Fibro scan. Majority were male 92 (83%), while females were 19 (17%) of the entire group. The lean NAFLD criteria for Asia and the West were satisfied by 43 (39%) persons with a BMI $\leq$ 23 kg/m^2 and 68 (61%) individuals with a BMI between 23 and $\leq$ 25 kg/m^2, respectively. The average body mass index (BMI) was 23.0 $\pm$ 1.5 kg/m^2. Diabetes was observed in 16%, hypertension 11%, and ischemic heart disease in 2%. Out of the total individuals, 92 satisfied the MASLD-MAFLD criteria, whereas 18 did not qualify the MAFLD criteria for diagnosis and were classed as MASLD-Alone. Elevated triglycerides, insulin resistance (HOMA-IR $\geq$ 2), and three or more cardiometabolic risk factors (CMRF) were significant in the MASLD-MAFLD group compared to the MASLD-Alone group ($p < 0.05$). Comparing BMI criteria, no significant differences were found in terms of fibrosis between the Western and Asian lean NAFLD BMI criteria's ($p = 0.243$).

Conclusion: Lean NAFLD is a major global health concern. Applying non-Asian BMI criteria (BMI $\leq$ 25 kg/m^2) for lean Asians improves early detection and intervention for at-risk individuals. Accurate use of MAFLD and MASLD criteria is essential to prevent confusion in diagnosing lean NAFLD. Further multicenter investigations with larger sample numbers are required to corroborate these results in our community.

Keywords: Body mass index, Cardiometabolic risk factors, Insulin resistance, Lean non-alcoholic fatty liver disease, Metabolic dysfunction-associated steatotic liver disease, Metabolic dysfunction-associated fatty liver disease.

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Introduction

In terms of chronic liver illness, steatosis belongs to one of the most common causes. Non-alcoholic fatty liver disease (NAFLD) prevalence has risen significantly, increasing from 25% between 1990 and 2006 to 38% from 2016 to 2019, and the trend is not declining [1,2] This has made it most especially common and the leading reason for liver transplants in the US [3,4] Non-alcoholic fatty liver disease encompasses a broad range of conditions, from mild fatty liver to more advanced stages like steatohepatitis, cirrhosis, and hepatocellular carcinoma.[5,6] Previously only associated with obesity, NAFLD can also develop in people who appear to be at a healthy body weight, an entity known as lean NAFLD that accounts for around 20% of NAFLD patients.[7] Being obese is the primary risk factor; nevertheless, the identification of NAFLD in non-obese persons has risen since its first documentation in Asian populations and subsequently observed in European and US populations.[8]

According to two comprehensive studies, the global rates of non-obese and lean fatty liver illness are estimated at 12.1% and 5.1%, respectively. The highest incidence of lean NAFLD was observed in Asia, with a rate of 4.8%, followed by Oceania at 3.5%, and North America at 3.1%. Europe reported the lowest prevalence (2.2%). By country, the United States has the lowest prevalence of lean NAFLD at 3.1%, while China has the highest at 5.5%.[5,9] Initially,

[1,4–6]Department of Gastroenterology and Hepatology, Dr. Ziauddin Hospital Clifton Campus, Karachi, Pakistan

[2]Department of Gastroenterology, Dr. Ziauddin Hospital Clifton Campus, Karachi, Pakistan

[3]Department of Gastroenterology and Hepatology, Dr. Ziauddin University Hospital, Karachi, Pakistan

Corresponding Author: Zaigham Abbas, Department of Gastroenterology, Dr. Ziauddin Hospital Clifton Campus, Karachi, Pakistan, Phone: +92135862937, e-mail: drzabbas@gmail.com

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lean NAFLD was believed to be comparatively benign with favorable outcomes compared to overweight or obese NAFLD patients. However, as seen in other studies, higher rates of mortality have been reported for lean NAFLD.[7,10,11]

A healthy weight is defined by a body mass index (BMI) of 18.5 – 24.9 kg/m^2, while a BMI over 30 kg/m^2 is considered obese.[12] For non-Asian populations, similar BMI standards apply, but the criteria for Asian individuals are adjusted, with normal weight classified as a BMI of 18.5–22.9 kg/m^2 and obesity defined as a BMI above 25 kg/m^2. Furthermore, waist circumference measurements deemed abnormal are set at 102 cm or more for men and 88 cm or more for women among non-Asians, whereas for Asians, these thresholds are reduced to 85 cm for men and between 74 and 80 cm for women.[13]

This study investigates lean fatty liver disease and evaluates BMI standards from both Asian and Western perspectives. It also reviews the diagnostic criteria for metabolic dysfunction-associated fatty liver disease (MAFLD) and metabolic dysfunction-associated steatotic liver disease (MASLD) for lean individuals and aims to enhance the identification and classification of lean steatotic in our population. Additionally, fatty liver disease now serves as a broad term for various types of steatosis, and non-alcoholic steatohepatitis (NASH), that has evolved into metabolic dysfunction-associated steatohepatitis (MASH).[14,15]

Materials and Methods

This prospective cross-sectional investigation, executed between January 2023 and March 2024, enrolled 111 individuals aged 18–85 years who were diagnosed with fatty liver disease. The diagnosis was confirmed using ultrasonography, which revealed increased echogenicity of the liver parenchyma, impaired intrahepatic artery visibility, and diaphragm-related changes. To quantify liver fibrosis and fat accumulation, vibration-controlled transient elastography (VCTE) was done using FibroTouch® equipment from HiSKY Medical Technologies.[16] Control attenuation parameters (CAP) and liver stiffness measures (LSM) were applied to determine the degree of fat and scarring. The sample was estimated based on an anticipated lean fatty liver disease prevalence of 5%, with a 95% confidence level and a 5% margin of error.[17] To account for probable dropouts and non-compliance, a total of 111 participants were recruited. Participants with a BMI up to 25 kg/m^2 were included, except for those with secondary causes of hepatic steatosis or fibrosis, such as autoimmune liver diseases, Wilson's disease, drug-induced hepatic steatosis, viral hepatitis (hepatitis B or C), pregnancy, or excessive alcohol intake (>30 g/day for men and >20 gm/day for women).[18–21] Elevated ALT levels were over 33 IU/L for males and 19–25 IU/L for women.[22]

To establish a diagnosis of MAFLD, we followed the 2020 expert consensus, which requires proof of hepatic steatosis (detected via ultrasonography or VCTE) and one of the following: overweight/obesity (BMI $\geq$ 25 kg/m^2) or lean/normal weight (BMI $\leq$ 25 kg/m^2) along with metabolic dysregulation.[23] Metabolic dysregulation was defined by the presence of at least two factors such as type 2 diabetes, high blood pressure (≥130/85 mm Hg), elevated triglycerides (>150 mg/dL), low high-density lip protein (HDL) cholesterol (<40 mg/dL for men and <50 mg/dL for women), or prediabetes (fasting glucose 100–125 mg/dL or HbA1c 5.7–6.4%). In contrast, the 2023 MASLD criteria required hepatic steatosis and at least one metabolic abnormality, with different BMI cutoffs for Asians (BMI $\geq$ 23 kg/m^2).[15] The study collected data on demographics, such as age, gender, height, weight, BMI, and waist circumference. Laboratory profiles included various parameters like hemoglobin, ALT, AST, alkaline phosphatase, albumin, cholesterol levels, triglycerides, and uric acid HOMA-IR (cutoff of 2 for insulin resistance),[24] APRI, NAFLD fibrosis score, FIB-4 Index, CAP, and LSM (kPa) were compared between MASLD-MAFLD and MASLD alone, as well as between normal BMI by Asian criteria (BMI $\leq$ 23 kg/m^2) and normal BMI by Western criteria but overweight by Asian BMI ($\geq$ 23 kg/m^2 $\leq$ 25 kg/m^2). Fibrosis was assessed via liver stiffness, and steatosis was evaluated using CAP. CAP values were categorized as follows: <247 dB/m (S0, normal liver, <5% fat), 247–280 dB/m (S1, mild fatty liver, 5–33% fat), 280–299 dB/m (S2, moderate fatty liver, 34–66% fat), and >299 dB/m (S3, severe fatty liver, >67% fat).[16] Liver stiffness cutoffs were 6.3 kPa for stage F2, 8.3 kPa for F3, and 10.5 kPa for F4.[25]

Continuous data presented as frequencies and percentages. To explore associations between categorical variables, we applied the Chi-square test. For comparisons of continuous variables between groups, the Student's *t*-test (with appropriate adjustments) was used. Correlations between metabolic parameters) were analyzed using Spearman's rank correlation for non-parametric data and Pearson's correlation coefficient (PCC) for parametric data. A *p*-value of less than 0.05 was considered statistically significant across all analyses. All statistical analyses were conducted using SPSS software (version 26, IBM, Armonk, NY, USA).

Results

The baseline features of 111 people diagnosed with NAFLD are presented in Table 1. Among the participants, the males were 92 (83%). Diagnosis modalities included ultrasonography for 37 (33%) and FibroScan for 74 (67%) individuals. The average age of the participants was 43.3 ± 13.2 years, and the mean waist circumference was 88.2 ± 8.4 cm). Among the males, 45 (40%) had a waist circumference greater than 90 cm, while among females, 13 (12%) exceeded 80 cm. Common comorbidities included diabetes mellitus 18 (16%), hypertension 12 (11%), and ischemic heart disease 2 (2%).

The laboratory profiles revealed an average hemoglobin of 13.2 ± 1.7, white blood cell count of 6.2 ± 2.1, and platelet count of 250.4 ± 82.6. Bilirubin levels averaged 0.71 ± 0.56, ALT levels averaged 55.0 ± 37.4, with 53% of patients exhibiting elevated ALT. Aspartate aminotransferase averaged 36.0 ± 20.0, gamma-glutamyl transferase (GGT) 56.6 ± 50.4), and ALP 103.2 ± 60.9. Albumin levels were on average 3.8 ± 0.43, cholesterol 182.4 ± 39.7 with 68% showing elevated levels, and triglycerides 180.0 ± 110.7 with half of the patients showing elevated levels. High-density lipoprotein averaged 36.6 ± 12.9 with 52% having low HDL levels, and low-density lipoprotein (LDL) averaged 101.6 ± 36.4. Very low-density lipoprotein (VLDL) levels averaged 39.6 ± 31.3. Fasting insulin were 17.5 ± 9.3 and fasting blood sugar (FBS) levels 105.3 mg/dL ± 37.4, with half of the patients having FBS above 100 mg/dL. The homeostatic model assessment for insulin resistance (HOMA-IR) averaged 3.5 ± 2.9, with 65% of patients showing a HOMA-IR of 2 or higher. The mean creatinine was 0.87 ± 0.19 and uric acid 5.4 ± 1.3. The NAFLD fibrosis score averaged 1.6 ± 0.87 and the FIB-4 Index 1.0 ± 0.71. The CAP was 274.8 ± 57.0, and liver stiffness averaged 11.5 ± 26.9, with 26% showing stiffness greater than 7.9 kPa. The aspartate aminotransferase to platelet ratio index (APRI) averaged 0.65 ± 0.55.

All participants met the MASLD diagnostic criteria, yet 18 lean NAFLD patients did not meet the MAFLD criteria and were classified as MASLD-Alone. Comparisons between the MASLD-MAFLD and MASLD-Alone groups showed significant differences in elevated

Table 1: Demographic, clinical, and laboratory characteristics of Lean NAFLD patients

Variable	*Lean NAFLD N = 111*
Age (years)	43.3 ± 13.2
Male (%)	92 (83%)
BMI (kg/m^2)	23.1 ± 1.5
Up to 23	43 (39%)
Up to 25	68 (61%)
Waist circumference (cm)	88.2 ± 8.4
According to male cut-of points *n* = 92	
≥90 (cm) *n*	45 (40%)
<90 (cm) *n*	47 (42%)
According to female cut-of points *n* = 19	
≥80 (cm) *n*	13 (12%)
<80 (cm) *n*	6 (5%)
Diabetic (%)	18 (16%)
Hypertension (%)	12 (11%)
Ischemic heart disease (%)	2 (2%)
Hemoglobin (gm/dL)	13.2 ± 1.7
White blood cell count (1,000 cells/µL)	6.2 ± 2.1
Platelet count (1,000 cells/µL)	250.4 ± 82.6
Bilirubin (mg/dL)	0.71 ± 0.56
ALT (U/L)	55.0 ± 37.4
Elevated ALT (%)	59 (53%)
AST (U/L)	36.0 ± 20.0
GGT (IU/L)	56.6 ± 50.4
Alkaline phosphatase (U/L)	103.2 ± 60.9
Albumin (gm/dL)	3.8 ± 0.43
Cholesterol (mg/dL)	182.4 ± 39.7
Elevated cholesterol (%)	75 (68%)
Triglycerides (mg/dL)	180.0 ± 110.7
Elevated triglycerides (%)	56 (50%)
HDL (mg/dL)	36.6 ± 12.9
Low HDL	58 (52%)
LDL (mg/dL)	101.6 ± 36.4
VLDL (mg/dL)	39.6 ± 31.3
Insulin (µIU/mL)	17.5 ± 9.3
FBS (mg/dL)	105.3 ± 37.4
> 100 (mg/dL)	56 (50%)
< 100 (mg/dL)	55 (50%)
HOMA-IR	3.5 ± 2.9
HOMA-IR ≥ 2 (%)	72 (65%)
Creatinine (mg/dL)	0.87 ± 0.19
Uric acid (mg/dL)	5.4 ± 1.3
NAFLD fibrosis score	1.6 ± 0.87
FIB-4 Index	1.0 ± 0.71
CAP	274.8 ± 57.0
Liver stiffness (kPa)	11.5 ± 26.9
kPa > 7.9 (%)	29 (26%)
APRI score	0.65 ± 0.55
≥ 3 CMRF *n*	75

ALT, alanine aminotransferase; APRI, AST to platelet ratio index; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; CMRF, cardiometabolic risk factor; FBS, fasting blood sugar; GGT, gamma-glutamyl transferase; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, low-density lipoprotein; MAFLD, metabolic associated fatty liver disease; MASLD, metabolic dysfunction associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease; VLDL, very low density lipoprotein

triglycerides and HOMA-IR, both with *p*-values less than 0.05 (Table 2).

Further comparisons between those with a normal BMI under Asia Pacific criteria (BMI ≤ 23) and those with a normal non-Asian BMI but considered overweight by Asia Pacific standards (BMI between 23 and ≤25) indicated significant differences in waist circumference and insulin resistance, also with p-values below 0.05, while fibrosis measurements via noninvasive tests such as CAP, FIB-4 Index, and NAFLD Fibrosis scores showed no significant differences (Table 3). Pearson correlation analysis conducted to explore the relationships among clinical and biochemical parameters in lean NAFLD patients highlighted significant positive correlations among cardiometabolic risk factors, HOMA-IR, CAP, FIB-4 Index, and NAFLD Fibrosis score, all with *p*-values less than 0.001.

Discussion

This study underscores the prevalence and clinical characteristics of lean NAFLD, aligning with global observations. Predominantly affecting males, this condition manifests at an earlier age in our study population than typically seen in Western counterparts.[26] Non-alcoholic fatty liver disease is emerging as a significant contributor to liver disease mortality in Pakistan, although detailed national data remain unavailable. The incidence varies from 9 to 27% in rural regions to 21–42% in metropolitan areas.[27] Studies from Asia report the prevalence of NAFLD among those with a BMI below 25 kg/m² ranging from 7.0 to 20.0%.[28–31] When comparing MASLD-MAFLD and MASLD-Alone groups, individuals meeting MASLD-MAFLD criteria exhibited a broader spectrum of clinical and metabolic dysregulations, including a large proportion with low HDL, insulin resistance, and more than three cardiometabolic abnormalities. The MAFLD criteria identify individuals with higher metabolic risk profiles and more advanced disease since it requires at least two metabolic abnormalities, whereas MASLD requires only one risk abnormality.[32] However, MASLD may lead to overdiagnosis in individuals with lower metabolic risks, and MAFLD may underdiagnose or misclassify cases, as noted by Ramírez-Mejía MM et al., who called for further research to validate both criteria globally.[33]

Another study from India found that many lean individuals are missed under the MAFLD criteria, suggesting that MASLD criteria are more applicable to lean patients.[34] Our research did not uncover significant differences in hepatic fibrosis measures between the two criteria, showing none is better in diagnosing liver fibrosis in lean people. A substantial number of lean NAFLD patients had elevated ALT with most meeting the criteria for MASH. We included

Table 2: Comparison between MAFLD-MASLD and MAFLD alone

Variable	*MASLD-MAFLD N = 93*	*MASLD-Alone N = 18*	*p-value*
Age (years)	43.7 ± 13.2	46.1 ± 13.6	0.328
Gender			
Male (%)	75 (80%)	17 (94%)	0.155
Female (%)	18 (19%)	1 (5%)	0.155
BMI (kg/m^2)	23.1 ± 1.5	22.8 ± 1.5	0.469
Up to 23	43 (39%)	10 (55%)	0.587
Up to 25	68 (61%)	8 (45%)	0.587
Waist circumference (cm)	88.2 ± 8.4	86.1 ± 4.8	0.142
Diabetic (%)	18 (16%)	1 (6%)	0.180
Hypertension (%)	12 (11%)	1 (6%)	0.433
Ischemic heart disease (%)	2 (2%)	0 (0%)	0.530
Hemoglobin (gm/dL)	13.2 ± 1.7	14.4 ± 0.9	0.007
White blood cell count (1,000 cells/µL)	6.2 ± 2.1	6.6 ± 1.2	0.501
Platelet count (1,000 cells/µL)	250.4 ± 82.6	250.5 ± 78.8	0.999
Bilirubin (mg/dL)	0.71 ± 0.56	0.58 ± 0.30	0.290
ALT (U/L)	55.0 ± 37.4	51.4 ± 42.7	0.714
Elevated ALT (%)	51 (55%)	8 (44%)	0.419
AST (U/L)	36.0 ± 20.0	34.4 ± 17.1	0.750
GGT (IU/L)	56.6 ± 50.4	45.2 ± 15.5	0.267
Alkaline phosphatase (U/L)	103.2 ± 60.9	69.9 ± 23.4	0.008
Albumin (gm/dL)	3.8 ± 0.43	3.8 ± 0.41	0.790
Cholesterol (mg/dL)	182.4 ± 39.7	176.0 ± 35.4	0.463
Elevated Cholesterol (%)	75 (68%)	10 (55%)	0.209
Triglycerides (mg/dL)	180.0 ± 110.7	108.0 ± 44.5	0.008
Elevated triglycerides (%)	56 (50%)	2 (11%)	<0.001
HDL (mg/dL)	36.6 ± 12.9	50.8 ± 7.8	<0.001
Low HDL (mg/dL) (%)	58 (52%)	6 (33%)	<0.001
LDL (mg/dL)	101.6 ± 36.4	107.4 ± 33.4	0.543
VLDL (mg/dL)	39.6 ± 31.3	24.1 ± 13.5	0.042
Insulin (µIU/mL)	17.5 ± 9.3	8.5 ± 1.9	<0.001
FBS (mg/dL)	105.3 ± 37.4	91.5 ± 9.5	0.068
HOMA-IR	3.5 ± 2.9	1.6 ± 0.6	<0.001
HOMA-IR ≥ 2 (%)	72 (65%)	3 (16%)	<0.001
Creatinine (mg/dL)	0.87 ± 0.19	0.85 ± 0.17	0.661
Uric acid (mg/dL)	5.4 ± 1.3	5.3 ± 1.1	0.837
NAFLD fibrosis score	1.6 ± 0.87	1.3 ± 0.68	0.499
F0-F2	58 (62%)	14 (78%)	0.285
Intermediate	8 (9%)	2 (11%)	
F3-4	27 (29%)	2 (11%)	
FIB-4 Index	1.0 ± 0.71	0.9 ± 0.36	0.187
< 1.45	35 (37%)	9 (50%)	
1.45-3.25	42(45%)	7 (39%)	
> 3.25	16 (17%)	2 (11%)	
CAP (dB/m)	274.8 ± 57.0	273.4 ± 57.5	0.657
S-1	17 (23%)	4 (27%)	0.946
S-2	17 (23%)	4 (27%)	
S-3	36 (48%)	7 (47%)	

(Contd...)

Table 2: *(Contd...)*

Variable	*MASLD-MAFLD N = 93*	*MASLD-Alone N = 18*	*p-value*
Liver stiffness (kPa)	11.5 ± 26.9	8.1 ± 7.3	0.252
F-2	47 (63%)	13 (87%)	
F-3	10 (13%)	2 (13%)	
F-4	13	0 (0%)	
APRI score	0.65 ± 0.55	0.63 ± 0.48	0.020
< 0.5	58 (62%)	12 (67%)	
0.5 –1.5	24 (26%)	4 (22%)	
> 1.5	11 (12%)	2 (11%)	
≥ 3 CMRF *n*	75	0	<0.001

ALT, alanine aminotransferase; APRI, AST to platelet ratio index; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; CMRF, cardiometabolic risk factor; FBS, fasting blood sugar; GGT, gamma-glutamyl transferase; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, low-density lipoprotein; MAFLD, metabolic associated fatty liver disease; MASLD, metabolic dysfunction associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease; VLDL, very low density lipoprotein

Table 3:. Comparison of individuals with normal BMI by Asian (BMI ≤ 23) vs Western criteria BMI (≥ 23 <25)

Variable	*BMI ≤ 23 N = 43*	*(BMI ≥ 23 ≤ 25) N = 68*	*p-value*
Male *n*	36	56	0.852
Age years	44.19 ± 12.1	42.74 ± 14.0	0.577
BMI (kg/m^2)	21.5 ± 1.3	24.0 ± 0.60	<0.001
DM/HTN/IHD *n*	4/4/1	14/8/1	0.116/0.684/0.741
Increased waist circumference *n* = 58	18 (16%)	40 (36%)	<0.001
According to male cut-of points *n* = 45			
≥ 90 (cm) *n*	11 (25%)	33 (48%)	<0.001
According to female cut-of points *n* = 13			
≥ 80 (cm) *n*	4 (9%)	12 (18%)	<0.001
≥ 3 CMRF *n* (%)	31 (67%)	43 (67%)	0.952
1 CMRF *n* (%)	10 (23%)	7 (10%)	
3 CMRF *n* (%)	14 (32%)	20 (29%)	
HOMA-IR ≥ 2 *n* (%)	28 (65%)	40 (59%)	<0.001
Elevated ALT (U/L) *n*	17 (40%)	35 (51%)	0.220
Elevated cholesterol (mg/dL) *n*	28 (65%)	47 (69%)	0.580
Elevated triglyceride (mg/dL) *n*	21 (49%)	35 (51%)	0.728
HDL cholesterol (mg/dL)	40.3 ± 12.2	38.4 ± 14.6	0.699
Low HDL *n* = 58	22	36	0.689
FBS (mg/dL)	109.4 ± 48.5	104.6 ± 29.3	0.517
>100 (mg/dL)	23 (51%)	33 (48%)	
<100 (mg/dL)	20 (46%)	35 (51%)	
MASLD alone *n* = 18 (%)	8 (18%)	10 (23%)	0.587
Liver stiffness (kPa) *n* = 85	14.80 ± 41.50	9.42 ± 10.33	0.377
F-2	24 (28%)	36 (42%)	
F-3	3 (3%)	9 (10%)	
F-4	6 (7%)	7 (8%)	
CAP (dB/m) *n* = 85	268.3 ± 68.4	279.0 ± 48.4	0.404
S-1	12 (14%)	9 (10%)	
S-2	7 (8%)	14 (16%)	
S-3	14 (16%)	29 (34%)	

(Contd...)

Table 3: *(Contd...)*

Variable	*BMI ≤ 23 N = 43*	*(BMI ≥ 23 ≤ 25) N = 68*	*p-value*
NAFLD fibrosis score F3–4	1.44 ± 0.795	1.72 ± 0.911	0.993
F0–F2	32 (28%)	40 (36%)	
Intermediate	3 (3%)	7 (6%)	
F3–F4	8 (7%)	21 (19%)	
APRI score	0.59 ± 0.59	0.65 ± 0.53	0.849
<0.5	28 (25%)	41 (36%)	
0.5–1.5	10 (9%)	21 (19%)	
>1.5	5 (4%)	6 (5%)	

ALT, alanine aminotransferase; APRI, AST to platelet ratio index; CAP, controlled attenuation parameter; CMRF, cardiometabolic risk factors; DM, diabetes mellitus; FBS, fasting blood sugar; FIB-4, fibrosis-4 index; HDL, high density lipoprotein; HOMA-IR, homeostatic model assessment for insulin resistance; HTN, hypertension; IHD, ischemic heart disease; MASLD, metabolic dysfunction associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease

individuals who were overweight by Asian BMI criteria but normal by Western standards, with 61% of lean NAFLD patients having a BMI between 23 and ≤25 kg/m^2.[35] These patients exhibited significant metabolic dysregulation, notably elevated triglycerides and insulin resistance. Insulin insensitivity is a key factor in the development of lean fatty liver illness.[36] Our findings suggest that the MASLD criteria were more inclusive and effective in identifying lean NAFLD patients, while the MAFLD criteria captured a broader spectrum of metabolic dysfunctions. In the MASLD-MAFLD group, there were significantly higher levels of elevated triglycerides, HOMA-IR, and the presence of three or more cardiometabolic risk factors when compared to the MASLD-alone group ($p < 0.05$). The definitions of normal weight and obesity differ slightly between Asian and non-Asian populations.[5,10] Our findings suggest that adopting Western BMI criteria for Asian populations may better reflect metabolic health, as no significant statistical differences were observed in key parameters between classifications. Western BMI criteria appear to encompass metabolic dysregulation more comprehensively, which is crucial for the early identification and management of lean or mildly overweight NAFLD patients. Given the genetic similarities between South Asia and Europe due to migration over the past 8,000 years, we recommend using Western BMI classification for South Asian populations in Pakistan and Northern India to increase lean NAFLD identification.[37]

Regular screening for NAFLD in lean individuals, particularly those with metabolic risk factors, is essential for early diagnosis and intervention. Enhancing healthcare provider awareness about lean NAFLD prevalence and its metabolic implications can improve patient outcomes through timely and appropriate management strategies. Our study has some limitations, such as its single-centered, a relatively small number of participants, and the lack of liver biopsies.

Conclusion

Lean NAFLD is a substantial health problem in Asian people. Our analysis underlines the necessity of a holistic strategy to detecting and addressing lean NAFLD. It proposes for adopting Western BMI criteria for the diagnosis of lean NAFLD in Asian populations may promote early identification of persons at risk for metabolic problems. While the MAFLD criteria better catch patients with a wider range of metabolic risk abnormalities. Additional multicenter investigations with larger sample size are necessary to confirm these findings for adopting adequate diagnostic criteria for lean NAFLD in our community.

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