ORIGINAL ARTICLE

Prevalence and Predictors for Lean Fatty Liver Disease in General Population Attending a COVID-19 Vaccination Center in a Tertiary Care Hospital in India

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Abstract

Background: There is an international consensus among experts advocating for the classification of fatty liver disease as a metabolic condition. However, some authors have raised concerns that this metabolic-centric framing may result in the underdiagnosis of metabolicdysfunction-associated steatotic liver disease (MASLD) in lean individuals. The present study was carried out with the objective of describing metabolic characteristics in MASLD and the prevalence of lean MASLD in the general population.

Methods: We carried out a hospital-based cross-sectional study. A pre-tested proforma was used to collect data on socio-demographic factors, lifestyle factors, and medical history. Transient elastography and blood investigations were carried out in all patients. The identification of independent predictors for MASLD and liver fibrosis was carried out using multivariable logistic regression. A test of interaction was conducted for studying effect modification in the association of diabetes and MASLD by subgroups of body mass index (BMI).

Results: A total of 1,243 participants were interviewed and screened for MASLD. The overall prevalence of MASLD was 43.7% ($n = 543$), with the prevalence of lean MASLD being 4.3% ($n = 53$). The prevalence of MASLD in lean vs non-lean subjects differed (21.3 vs 66.7%, $p < 0.001$). Of the total MASLD cases, lean MASLD constituted 9.7% of cases. The association of diabetes and MASLD did not differ in subgroups by BMI. The test for interaction to detect effect modification was not statistically significant ($p = 0.673$).

Conclusion: The results support laying emphasis on metabolic dysfunction as a key criterion when defining fatty liver disease. The findings emphasize the shared metabolic underpinnings between lean and non-lean MASLD and advocate for inclusive approaches in diagnosis, management, and public health initiatives.

Keywords: Lean, Metabolically associated steatotic liver disease, MAFLD, Metabolic dysfunction, Obesity.

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Introduction

Metabolically dysfunction-associated steatotic liver disease (MASLD) represents a contemporary public health problem on a global scale, bi-directionally associated with the escalating rates of obesity, type 2 diabetes, and metabolic syndrome. Historically, MASLD has been primarily recognized in individuals with obesity. However, lean MASLD has emerged as a distinctive form of MASLD and has cast new light on the complex and multifaceted nature of the disease.

Lean MASLD is characterized by the presence of hepatic steatosis in individuals with a body mass index (BMI) within the normal range. While the exact prevalence remains variable across different populations and geographic regions, mounting evidence suggests that lean MASLD constitutes a substantial proportion of all MASLD cases. This phenomenon underscores the need to examine other factors beyond adiposity that contribute to the development of hepatic steatosis.

The international consensus among experts urges to define fatty liver disease inclusively as being a metabolic condition.[1] However, some authors have argued that framing it based on metabolic dysfunction will lead to the underdiagnosis of MASLD among lean individuals.[2] Studying subgroup effects in the association of metabolic dysfunction and the occurrence of MASLD is important because it will provide a perspective on the continuing debate over how much emphasis metabolic dysfunction should be rendered while defining fatty liver disease. Evidence from large, community-based studies powered to detect effect modification is required in order to provide evidence on the association of metabolic dysfunction with types of MASLD by BMI. Moreover, studying this association will provide novel pathophysiological insights, improve our predictive models and risk stratification, and help to tailor therapies for individuals.

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Prior research has primarily concentrated on ascertaining the occurrence of MASLD among lean individuals.[3,4] However, there exists a scarcity of literature concerning the prevalence and strength of association with metabolic dysfunction in individuals diagnosed with lean MASLD, as well as the juxtaposition of this dysfunction with cases of non-lean MASLD.

The present study aimed to ascertain subgroup differences in the association of MASLD with metabolic risk factors by BMI. We further attempted to calculate the prevalence of lean and non-lean MASLD in the general population and the degree of steatosis and fibrosis in lean vs non-lean MASLD.

Materials and Methods

Study Design

We carried out a hospital-based cross-sectional study.

Study Setting

The study setting was the vaccination center for COVID-19 in the Institute of Liver and Biliary Sciences, New Delhi, which catered to the general population.

Study Duration

Between June 2021 and April 2022.

Study Population

The study included an adult population without any diagnosed liver disorders. Pregnant women, individuals with severe illnesses, and participants who did not furnish informed consent were excluded from the study.

Sample Size

The previous study from India has shown that the prevalence of NAFLD ranged around 9–32%[2,3] considering the average prevalence of 20%. Using this data and keeping an absolute precision of 2%, the minimum required sample size calculated using Open Epi version 3.01 was 1100. After adjusting for a non-response rate of 10%, the sample size required for the primary objective was 1210.

Sampling Strategy

Consecutive and universal sampling was adopted for enrolling participants until the sample size was reached.

Operational Definitions

Case Definitions

Hepatic steatosis: Diagnosed by transient elastography (Fibroscan®). The following cut-offs were used to define grades of steatosis:[4–10]

S0: CAP<248 dB/m
S1: 248–267 dB/m
S2: 268–279 dB/m
S3: ≥280 dB/m

Metabolic dysfunction-associated steatotic liver disease: In the present study, adults with hepatic steatosis in the absence of any of the following conditions were considered to have MASLD:[11]

i. AUDIT-C cut-off score of ≥3 (women) and ≥4 (men) for detecting hazardous or harmful drinking[12]
ii. Positive for Hepatitis B or/and C infection

Significant liver fibrosis: Diagnosed by transient elastography (Fibroscan®). Participants were considered to have significant liver fibrosis (≥F2) if the participant's liver stiffness measurement (LSM) was ≥7.9 KPa.[13]

Type 2 diabetes (T2DM): Diabetes mellitus type 2 was defined as:

i. Fasting plasma glucose as ≥126 mg/dL (≥7 mmol/L)[14] and/or
ii. 2 hours glucose as ≥200 mg/dL (plasma) and/or
iii. HbA1c more than or equal to 6.5% and/or
iv. Self-reported and/or on treatment for diabetes.

Hypertension: Known cases of hypertension were considered to be hypertensive. Individuals having SBP ≥ 140 mm Hg or/and DBP ≥90 mm Hg on measurement of blood pressure were also considered hypertensives.

Dyslipidemia: The following criteria were used:[15]

i. Hypercholesterolemia/cholesterol level greater than 200 mg/dL and/or
ii. Hypertriglyceridemia/triglyceride level greater than 150 mg/dL and/or
iii. Individuals reporting regular use of lipid-lowering drugs such as statins.

Overweight and Obesity: Defined as:[16,17]

i. Underweight: <18.5 kg/m^2
ii. Normal/Healthy weight: 18.5–22.9 kg/m^2
iii. Overweight: 23.0–24.9 kg/m^2
iv. Obese I: 25.0– 29.9 kg/m^2
v. Obese II: ≥30 kg/m^2

Lean MASLD: Presence of MASLD in those with BMI less than 23 kg/m.^{2}

Study Procedure

After obtaining informed consent, a pre-tested proforma was administered to collect data on socio-demographic characteristics, history of liver disease, existing co-morbidities, medication usage, HBV vaccination status, and potential risk factors associated with hepatic steatosis and liver fibrosis. Additionally, lifestyle factors such as alcohol consumption (using the Alcohol Use Disorder Identification Test – AUDIT questionnaire), diet, and physical activity levels (using the International Physical Activity Questionnaire – IPAQ) were documented.

Following the questionnaire-based interview, trained personnel performed anthropometric measurements, including BMI, waist circumference, and hip circumference. A skilled nurse conducted transient elastography (Fibroscan 430 mini, Echosens) to measure the controlled attenuated parameter (CAP) and LSM of each participant. To ensure accuracy, a minimum of ten valid readings were collected from each participant for LSM and CAP, measured in kPa and dB/m, respectively.

A venous blood sample was then collected by a lab technician. The following blood investigations were carried out: liver function tests, total cholesterol, triglycerides, fasting blood sugar, and complete blood count. Rapid diagnostic tests for HBsAg and anti-HCV were performed using rapid card tests from SD Biosensor Healthcare Pvt Ltd.

Statistical Analysis

The prevalence of MASLD and liver fibrosis was reported as proportions with accompanying 95% confidence intervals (CI), with Chi-square tests and *t*-tests used to study associations.

All factors demonstrating significance with a *p*-value less than 0.20 were subsequently included in the multivariable logistic regression model. The identification of independent predictors for MASLD and liver fibrosis was carried out using multivariable logistic regression. A test of interaction was conducted to study effect modification. Statistical significance was considered at a threshold of $p < 0.05$ for all analyses. All analyses were carried out using SPSS version 21.

Ethical Consideration

Ethics clearance was obtained from the Institute ethics committee vide order No. F.37/(1)/9/ILBS/DOA/2020/20217/351).

Results

Study Population

A total of 1,243 participants were interviewed and screened for MASLD using transient elastography. Out of them, 41% were male. The mean age of the study subjects was 48.7 years. The majority of the sample was married, of Hindu religion, and most participants belonged to lower-middle socio-economic status (Table 1).

The prevalence of hypertension and diabetes among the population was 12 and 15%, respectively. Around 2.2% of the population has dyslipidemia, and 1.2% have a history of coronary artery disease. The mean BMI of the sample was 26.3 kg/m^2. The results of the physical and blood examinations are summarized in Table 1.

Prevalence of MASLD in Lean vs Non-lean Individuals

Overall, MASLD was present in 543 (43.7%) subjects.

The prevalence of hepatic steatosis in lean subjects was 21.3% and in non-lean subjects was 66.7% ($p < 0.01$). Most subjects had grade III steatosis in either group. Of the total MASLD cases, lean MASLD constituted 9.7% of cases, with the remaining being non-lean MASLD.

The prevalence of significant liver fibrosis (LSM ≥ 7.9 kPa) was 5.4% ($n = 67$) overall, with prevalence in lean and non-lean being 2.8 and 7%, respectively.

The characteristics of lean and non-lean individuals differed in terms of age, gender, socio-economic status, and prevalence of diabetes, hypertension, and other risk factors.

Characteristics and Risk Factors in Lean vs Non-lean MASLD

The socio-demographic characteristics of lean and non-lean MASLD are depicted in Table 2. A greater number of males constituted lean

Table 1: Socio-demographic, Clinical, biochemical characteristics of study participants ($n = 1,243$)

Demographic characteristics	*n (%) Overall*
Socio-demographic characteristics	
Mean Age (SD) years	48.77 ± 16.2
Gender	
Male	508 (41)
Educational qualification	
Not educated/No formal education	300 (24.2)
Up to primary/Middle school	246 (19.8)
Up to class 10th/High school	222 (17.9)
Class 12th/Intermediate	179 (14.4)
Graduation and above	296 (23.8)
Religion	
Hindu	1,053 (84)
Muslim	149 (12)
Others	47 (4)
Socio-economic status (Using BG Prasad classification – 2021)	
Class I (7770 and above)	196 (16)
Class II (3808–7769)	280 (22.9)
Class III (2253–3808)	417 (33.4)
Class IV (1166–2253)	277 (22.3)
Class V (<1166)	73 (6)
Diabetes	186 (15)
History of hypertension	149 (12)
History of hypothyroidism	94 (7.6)
History of myocardial infarction	10 (1.2)
Dyslipidemia	27 (2.2)
Mean body mass index (kg/m^2) ± SD	26.33 ± 7.67
BMI category	
Underweight (<18.5)	87 (7)
Normal (18.5–22.9)	300 (24.2)
Overweight (23.0–24.9)	348 (28)
Obese I (25.0–29.9)	389 (31.2)
Obese II (>30)	119 (9.6)
Blood pressure	
Mean systolic blood pressure (SD)	128.74 ± 22.79
Mean diastolic blood pressure (SD)	79.41 ± 15.3
Median ALT (IQR)	23.4 ± 19.5
Median AST (IQR)	29 ± 18.4
Median GGT (IQR)	23 ± 18.7
Mean cholesterol (SD)	176.33 ± 42.71
Median triglycerides (IQR)	112.95 ± 84
Mean fasting blood sugar (SD)	119.13 ± .84
Mean hemoglobin (SD)	16.94 ± 1.97
Mean platelets (SD)	206.83 ± 86.23
Physical activity	
Less or no exercise	850 (68.4)
Moderate or vigorous exercise	393 (31.6)
Smoking status: Ever smoked	42 (3.4)
Presence of MASLD (CAP ≥248 dB/m)	543 (43.7)
Grading of steatosis	
No steatosis (<248)	700 (56.3)
S1 (248–268)	199 (16)
S2 (268–280)	73 (5.9)
S3 (≥ 280)	271 (21.8)
Significant liver fibrosis (LSM ≥7.9 kPa)	67 (5.4)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuated parameter; GGT, γ-Glutamyl transferase; IQR, interquartile range; LSM, liver stiffness measurement; SD, standard deviation

Table 2: Determinants of Lean MASLD on multivariable logistic regression

Characteristics	*Adjusted OR (95% CI)*	*p-value*
Age	1.4 (1.08–5.65)	0.02
Male gender	1.83 (1.28–5.98)	0.03
Diabetes mellitus	1.48 (1.18–3.98)	<0.01

Variables included were age, gender, educational qualification, SES, presence of diabetes mellitus, hypertension, dyslipidemia, and physical activity

MASLD. Hypertension (15.3 vs 21.1%, $p = 0.01$) and hypothyroidism (6.2 vs 3.5%, p-value <0.01) were less common in lean MASLD vs non-lean MASLD. Though the prevalence of diabetes was slightly higher in non-lean MASLD (28.2 vs 25.1%), this difference was not statistically significant ($p = 0.298$).

There was a statistically significant difference in mean values of CAP (276.7 vs 237.5, $p < 0.001$) and median LSM (4.5 vs 5.2, p-value <0.001) among the two groups, with both parameters being less raised in lean MASLD.

There was a statistically significant difference in the mean values of ALT, AST, GGT, and fasting blood sugar among the two groups. The differences in mean/median values of laboratory parameters are presented in Table 1.

Prevalence and Determinants of Lean MASLD

The prevalence of lean MASLD was 4.3% ($n = 53$). The following factors were independent determinants of lean MASLD among the total population with statistically significant association on multivariable logistic regression: increasing age (OR 1.4; 95% CI: 1.08–5.65; p-value = 0.02), male gender (OR 1.83; 95% CI: 1.28–5.98, p-value = 0.03) and diabetes mellitus (OR 1.48; 95% CI: 1.18–3.98; p-value < 0.01) (Table 2).

Subgroup Differences in Association of Diabetes with MASLD in Lean vs Non-lean Patients

The association of diabetes and MASLD, adjusted for possible confounders, did not differ by subgroups based on BMI, i.e., lean vs non-lean, though the sample size was not powered for detection of subgroup differences. The test for interaction to detect effect modification was not statistically significant ($p = 0.673$).

Discussion

Main Findings

The present study represents an important contribution to the growing body of research addressing the complex interplay between metabolic dysfunction and non-alcoholic fatty liver disease, with a specific focus on the intriguing subtype of lean MASLD. Leveraging a comprehensive community-based approach and employing advanced techniques such as transient elastography, this study elucidated the associated metabolic dysfunction in lean MASLD and compared it to MASLD in overweight and obese populations.

The study found that MASLD in lean patients constituted about 10% of all MASLD cases. The prevalence of MASLD in lean individuals was around 20%, whereas that in non-lean was 67%. Though grades of steatosis and fibrosis differed in the two subgroups, there was no statistically significant difference in the prevalence of diabetes. Furthermore, we did not observe a statistically significant subgroup difference in the magnitude of the association of MASLD with diabetes in lean vs non-lean.

The observed prevalence of lean MASLD among the studied cohort adds to the mounting evidence that this distinct phenotype constitutes a noteworthy proportion of MASLD cases. The unexpected presence of hepatic steatosis in lean individuals challenges established paradigms surrounding the relationship between obesity and MASLD. The current findings accentuate the importance of recognizing lean individuals as a significant subgroup vulnerable to MASLD, emphasizing the need for tailored diagnostic and therapeutic strategies catering to this population.

Metabolic dysfunction, a hallmark of MASLD pathogenesis, is conventionally linked with obesity and its associated co-morbidities. However, the present study underscores the fact that metabolic disturbances extend beyond the confines of obesity and are indeed instrumental in the pathogenesis of lean MASLD. The observed derangements in key biochemical parameters, including ALT, AST, GGT, and lipid profile, illuminate the underlying metabolic irregularities that may be driving hepatic lipid accumulation in lean individuals. These findings hint at a commonality of metabolic factors bridging the gap between lean and non-lean MASLD.

Implications of Findings

In the year 2020, a group of international experts released a consensus statement recommending a shift in nomenclature from MASLD to MAFLD.[1] This alteration in terminology removes the disease from being solely defined by exclusion criteria and instead presents it as a metabolic condition with a more inclusive perspective. This proposition has later gained support from various other expert panels and associations endorsing the same concept.[18] The present study provides supporting evidence for renaming MASLD to MAFLD. This may be a progressive step that aligns with the evolving understanding of this condition. It emphasizes the metabolic aspect, promotes inclusivity, and holds promise for advancing research and improving patient care. Metabolic Associated Fatty Liver Disease places the emphasis where it belongs – on the metabolic aspect, offering a more accurate representation of the condition. Shifting to MAFLD can stimulate research initiatives that explore the metabolic underpinnings of the disease, potentially leading to new treatment avenues and therapeutic targets. Furthermore, funding bodies may prioritize research in MAFLD, recognizing its relevance in addressing the growing global health concern of fatty liver disease.

The current study's revelations hold significant implications for clinical management and public health strategies. With lean individuals also at risk of metabolic dysfunction and liver-related complications, the identification and monitoring of such individuals become imperative. Incorporating advanced techniques like transient elastography facilitates the early detection of liver fibrosis, enabling timely intervention and risk stratification. The insights provided by this study warrant the reevaluation of screening protocols and health promotion campaigns to encompass lean individuals, thereby optimizing the prevention and management of lean MASLD.

Comparison with Other Studies

A study by Li et al.[19] on data emanating from the National Health and Nutrition Examination Survey (NHANES) found findings consistent with the present study. Li et al. reported a similar proportion of diabetes in lean and non-lean hepatic steatosis and also reported

similar association measures with diabetes in the two groups. A recent study from the UK Biobank[20] did not observe a significant difference in levels of blood glucose but a marginal difference in levels of HBA1c among MASLD in those with a BMI of <25 vs >25. A study conducted in India[3] observed a similar prevalence of diabetes in comparing lean and overweight MASLD, but differences in comparing lean and obese MASLD. In a community-based cohort, Park et al.[21] identified diabetes as a risk factor for fibrosis with the strongest association.

However, two studies done using electronic health records had a contrasting conclusion, with metabolic syndrome being more strongly associated with lean MASLD.[22,23] A systematic review found less prevalence of diabetes in lean MASLD subjects; however, the meta-analysis suffered from substantial heterogeneity ($I^2 = 99\%$).[2] Two more systematic reviews[24,25] and a study by Khayat found an increasing prevalence of diabetes with BMI.[26] The variation across studies may be explained by the complex interplay of genetic, environmental, and lifestyle factors in the multifactorial causation of this disease, with high regional variability in attributable pathogenesis.[27]

Study Strengths and Limitations

This study's strengths lie in its robust community-based design, encompassing a substantial sample size, and utilizing state-of-the-art techniques for data collection. The inclusion of transient elastography adds accuracy in assessing hepatic steatosis and fibrosis. This is, to the best of our knowledge, the largest community-based study estimating the prevalence of MASLD and associated liver fibrosis in asymptomatic adults using the transient elastography technique and the first one powered enough to study subgroup effects according to BMI. Other strengths include standardization of diagnosis techniques and regular quality control. Nevertheless, the study is not without limitations. Its cross-sectional nature limits the establishment of temporality and, thus, causal relationships. Additionally, the reliance on self-reported lifestyle factors and the lack of detailed dietary information may introduce inherent biases. Liver stiffness measurement and CAP using transient elastography, though widely validated as an accurate measure of liver fibrosis and hepatic steatosis, respectively, cannot be considered a gold standard technique. However, issues with the feasibility and invasiveness of liver biopsy must be considered in conjunction with this limitation. The high prevalence of diabetes may represent a high-risk population since it included participants reporting to Mohalla clinics for follow-up. Moreover, the social-desirability bias would have led to an underestimation of the estimated prevalence of alcohol use disorder in the existing study.

Recommendations for Future Research

This study urges a deeper evaluation of the traditional paradigms surrounding the development and progression of MASLD. In an era where metabolic disorders continue to exert a considerable health burden, the recognition and exploration of lean MASLD is imperative for gaining new insights into the spectrum of metabolic diseases. A thorough understanding of the prevalence of metabolic dysfunction in lean MASLD and its other determinants may ultimately pave the way for more tailored diagnostic and therapeutic strategies, fostering improved patient outcomes and public health measures.

There remain several avenues for future research. Longitudinal studies are needed in order to precisely project the trajectory of metabolic dysfunction in lean individuals over time along with the progression of hepatic complications. Molecular and genetic investigations may unveil novel pathways underlying metabolic perturbations in lean MASLD. Moreover, interventional studies targeting metabolic dysregulation in both lean and non-lean MASLD could elucidate effective therapeutic approaches.

The findings of the present study have important implications for policy and future research. The high burden of MASLD as reported in the present study makes a strong case for advancing the public health agenda for this liver disease. Prevention and management of non-alcoholic fatty liver disease must be viewed as a fundamental aim of primary care, including action toward other components of metabolic syndrome, with consistent advocacy measures for stronger policies.

Conclusion

In conclusion, the present community-based study underscores the substantial prevalence of metabolic dysfunction within the realm of lean MASLD. The findings emphasize the shared metabolic underpinnings between lean and non-lean MASLD and advocate for inclusive approaches in diagnosis, management, and public health initiatives.

References

1. Eslam M, Newsome PN, Sarin SK, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol 2020;73(1):202–209. DOI: 10.1016/j.jhep.2020.03.039.
2. Tang A, Ng CH, Phang PH, et al. Comparative burden of metabolic dysfunction in lean MASLD vs non-lean MASLD – A systematic review and meta-analysis. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc 2023;21(7):1750–1760.e12. DOI: 10.1016/j.cgh.2022.06.029.
3. Kumar R, Rastogi A, Sharma MK, et al. Clinicopathological characteristics and metabolic profiles of non-alcoholic fatty liver disease in Indian patients with normal body mass index: Do they differ from obese or overweight non-alcoholic fatty liver disease? Indian J Endocrinol Metab 2013;17(4):665–671. DOI: 10.4103/2230-8210.113758.
4. Xu R, Pan J, Zhou W, et al. Recent advances in lean MASLD. Biomed Pharmacother Biomedecine Pharmacother 2022;153:113331. DOI: 10.1016/j.biopha.2022.113331.
5. Younossi ZM, Golabi P, Paik JM, et al. The global epidemiology of nonalcoholic fatty liver disease (MASLD) and nonalcoholic steatohepatitis (NASH): A systematic review. Hepatol Baltim MD 2023;77(4):1335–1347. DOI: 10.1097/HEP.0000000000000004.
6. Ranasinghe P, Jayawardena R, Gamage N, et al. Prevalence and trends of the diabetes epidemic in urban and rural India: A pooled systematic review and meta-analysis of 1.7 million adults. Ann Epidemiol 2021;58:128–148. DOI: 10.1016/j.annepidem.2021.02.016.
7. Venkatrao M, Nagarathna R, Majumdar V, et al. Prevalence of obesity in India and its neurological implications: A multifactor analysis of a nationwide cross-sectional study. Ann Neurosci 2020;27(3–4):153–161. DOI: 10.1177/0972753120987465.
8. Morrison AE, Zaccardi F, Khunti K, et al. Causality between non-alcoholic fatty liver disease and risk of cardiovascular disease and type 2 diabetes: A meta-analysis with bias analysis. Liver Int Off J Int Assoc Study Liver 2019;39(3):557–567. DOI: 10.1111/liv.13994.
9. Ali A, Alfajjam S, Gasana J. Diabetes mellitus and its risk factors among migrant workers in Kuwait. Int J Environ Res Public Health 2022;19(7):3943. DOI: 10.3390/ijerph19073943.
10. Karlas T, Petroff D, Sasso M, et al. Individual patient data meta-analysis of controlled attenuation parameter (CAP) technology for assessing steatosis. J Hepatol 2017;66(5):1022–1030. DOI: 10.1016/j.jhep.2016.12.022.

11. Ando Y, Jou JH. Nonalcoholic fatty liver disease and recent guideline updates. Clin Liver Dis [Internet] 2021 [cited 2022 Feb 1];17(1):23–28. DOI: 10.1002/cld.1045.
12. Reinert DF, Allen JP. The alcohol use disorders identification test: An update of research findings. Alcohol Clin Exp Res 2007;31(2):185–199. DOI: 10.1111/j.1530-0277.2006.00295.x.
13. Abeysekera KWM, Fernandes GS, Hammerton G, et al. Prevalence of steatosis and fibrosis in young adults in the UK: A population-based study. Lancet Gastroenterol Hepatol 2020;5(3):295–305. DOI: 10.1016/S2468-1253(19)30419-4.
14. Standards of medical care in diabetes-2016: Summary of revisions. Diabetes Care 2016;39 Suppl 1:S4–S5. DOI: 10.2337/dc16-S003.
15. Goff David C, Bertoni Alain G, Kramer Holly, et al. Dyslipidemia prevalence, treatment, and control in the multi-ethnic study of atherosclerosis (MESA). Circulation [Internet] 2006 [cited 2020 Nov 24];113(5):647–656. Available from: https://www.ahajournals.org/doi/10.1161/circulationaha.105.552737.
16. WHO expert consultation*. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet [Internet] 2004 [cited 2022 Jan 29];363(9403):157–163. DOI: 10.1016/S0140-6736(03)15268-3.
17. Misra A, Chowbey P, Makkar BM, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India 2009;57:163–170. PMID: 19582986.
18. Rinella ME, Lazarus JV, Ratziu V, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. Ann Hepatol 2024;29(1):101133. DOI: 10.1016/j.aohep.2023.101133.
19. Li M, Zhang W, Li X, et al. Metabolic and risk profiles of lean and non-lean hepatic steatosis among US adults. Nutrients 2023;15(13):2856. DOI: 10.3390/nu15132856.
20. Chahal D, Sharma D, Keshavarzi S, et al. Distinctive clinical and genetic features of lean vs overweight fatty liver disease using the UK Biobank. Hepatol Int 2022;16(2):325–336. DOI: 10.1007/s12072-022-10304-z.
21. Park H, Yoon EL, Cho S, et al. Diabetes is the strongest risk factor of hepatic fibrosis in lean patients with non-alcoholic fatty liver disease. Gut 2022;71(5):1035–1036. DOI: 10.1136/gutjnl-2021-325102.
22. Almomani A, Kumar P, Onwuzo S, et al. Epidemiology and prevalence of lean nonalcoholic fatty liver disease and associated cirrhosis, hepatocellular carcinoma, and cardiovascular outcomes in the United States: A population-based study and review of literature. J Gastroenterol Hepatol 2023;38(2):269–273. DOI: 10.1111/jgh.16049.
23. Semmler G, Wernly S, Bachmayer S, et al. Nonalcoholic fatty liver disease in lean subjects: Associations with metabolic dysregulation and cardiovascular risk-a single-center cross-sectional study. Clin Transl Gastroenterol 2021;12(4):e00326. DOI: 10.14309/ctg.0000000000000326.
24. Lu FB, Zheng KI, Rios RS, et al. Global epidemiology of lean non-alcoholic fatty liver disease: A systematic review and meta-analysis. J Gastroenterol Hepatol 2020;35(12):2041–2050. DOI: 10.1111/jgh.15156.
25. Shi Y, Wang Q, Sun Y, et al. The prevalence of lean/nonobese nonalcoholic fatty liver disease: A systematic review and meta-analysis. J Clin Gastroenterol 2020;54(4):378–387. DOI: 10.1097/MCG.0000000000001270.
26. Khayyat YM. Lean non-alcoholic fatty liver disease and associated metabolic disturbance: A Saudi Arabian cross-sectional study. Physiol Rep 2021;9(14):e14949. DOI: 10.14814/phy2.14949.
27. Long MT, Zhang X, Xu H, et al. Hepatic fibrosis associates with multiple cardiometabolic disease risk factors: The Framingham heart study. Hepatology 2021;73(2):548–559. DOI: 10.1002/hep.31608.