Volume 3, Issue 3, 2025

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

ASSOCIATION BETWEEN NON-ALCOHOLIC FATTY LIVER DISEASE AND METABOLIC SYNDROME

Dr Gohar Ayub[1], Dr Iqbal Haider[*2], Dr Khalid Anwar[3], Dr Taimoor Sikandar Zaman Khan[4], Dr Syed Junaid Shah[5], Dr Fawad Ullah[6]

[1,4,5]*PGR FCPS Medicine, Department of Medicine, MTI-KTH, Peshawar*
[*2]*Professor of Medicine, Department of Medicine, MTI-KTH, Peshawar*
[3]*PGR FCPS General Medicine, Department of Medicine, MTI-KTH, Peshawar*
[6]*PGR FCPS General Medicine, Department of Medicine*

[1]goharayub259@gmail.com, [*2]driqbalhaiderkth@gmail.com, [3]khalidsmc229@gmail.com, [4]taimoorzaman1995@gmail.com, [5]syedjunaidshah755@gmail.com, [6]fawadullah303@gmail.com

DOI: http://doi.org/10.5281/zenodo.19414949

Keywords
Non-alcoholic fatty liver disease, Metabolic syndrome, Association, Ultrasound, Case-control study.

Article History
Received: 20 April 2025
Accepted: 25 April 2025
Published: 07 May 2025

Corresponding Author: *
Dr Iqbal Haider

Abstract

Background:
Non-alcoholic fatty liver disease (NAFLD) is a growing global health problem closely linked with metabolic abnormalities. Its relationship with metabolic syndrome (MetS) remains complex and variable across populations, necessitating further local research to clarify this association.

Objective:
To determine the association between non-alcoholic fatty liver disease and metabolic syndrome.

Methods:
This case-control study was conducted in the Department of Medicine, Khyber Teaching Hospital, Peshawar, from 15th October 2024 to 16th April 2025. A total of 164 participants (82 cases with metabolic syndrome and 82 healthy controls) aged 18–60 years were included using non-probability consecutive sampling. NAFLD was diagnosed using abdominal ultrasonography (US-FLI >1). Metabolic syndrome was defined according to NCEP-ATP III criteria. Data were analyzed using SPSS version 25. Association was assessed using chi-square test and odds ratio with 95% confidence interval.

Results:
The mean age was comparable between cases and controls (49.40±7.50 vs 49.62±7.42 years). NAFLD was present in 22 (26.8%) cases and 11 (13.4%) controls. A statistically significant association was found (p=0.032) with an odds ratio of 2.36 (95% CI: 1.06–5.27). Stratification showed a significant association with socioeconomic status (p=0.036), while age, gender, BMI, residence, and profession were not significantly associated.

Conclusion:
Metabolic syndrome is significantly associated with an increased risk of NAFLD. Early identification and management of metabolic risk factors are essential to reduce disease burden.

INTRODUCTION

Simple steatosis, steatohepatitis, severe fibrosis, and cirrhosis are all included in the category of non-alcoholic fatty liver disease (NAFLD). Weight gain and heart disease are intimately linked to nonalcoholic fatty liver disease (NAFLD), which is currently the most prevalent persistent liver condition in many affluent

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

nations. In addition, as overweight and aging grow more common, NAFLD is predicted to evolve into a further significant public health concern.[1]

The gold standard for identifying NAFLD now is liver biopsy. Although sophisticated imaging techniques have also been employed, community-based surveys and epidemiological research cannot make use of them. Although it cannot identify fewer than ten percent steatosis of hepatocytes, US is comparatively cheap and readily accessible in clinical settings when contrasted with invasive biopsy and costly MRS and CT.[2,3]

Patients with non-alcoholic fatty liver disease (NAFLD) are more likely to develop metabolic syndrome (MetS), a collection of metabolic disorders that is a risk factor for heart disease. Additionally, NAFLD has been shown to raise mortality risk and be irrespective of the usual risk variables for preclinical plaque buildup, cardiovascular illness, and MetS.[4]

several chemokines and inflammatory mediators govern the interaction in both MetS and NAFLD. Some studies have suggested that NAFLD is a hepatic feature of MetS.[5] On the other hand, some data has shown that NAFLD differs from the characteristics of MetS, indicating that further investigation is necessary on the relationship between NAFLD and MetS.[6] In a study by Yang KC and colleagues, NAFLD was observed in 17.1% patients with metabolic syndrome while 3.7% healthy controls were found having NAFLD.[1]

The study aimed to determine the association between non-alcoholic fatty liver disease and metabolic syndrome. Dissociation of association between NAFLD and metabolic syndrome has been reported on certain occasions which warrants further research. Moreover, no study has been carried out on the association of fatty liver with metabolic syndrome locally and most of the information comes from leading international research. Hence the study was planned. Results of this study not only addressed the research gap arising from inconsistency in the results of international studies but also provided useful local information.

MATERIALS AND METHODS

This case control study was conducted at the department of Medicine, Khyber Teaching Hospital, Peshawar from 15-10-2024 to 16-04-2025 after taking approval from research review board. Male and female patients aging 18 to 60 years diagnosed with metabolic syndrome were compared with healthy controls. The study participants were evaluated for the presence non-alcoholic fatty liver disease. Patients with history of alcohol intake, chronic liver disease or viral hepatitis and pregnant females were excluded. Metabolic syndrome was defined using NCEP-ATP III criteria by the presence of any three including waist circumference ≥90 cm for men or ≥80 cm for women, hypertension, hyperglycemia, hypertriglyceridemia and low HDL-C. NAFLD was on abdominal ultrasound scanning with a 3.5–5 MHz transducer. US-FLI (ultrasound fatty liver index) score more than 1 will be considered confirmatory for the presence of non-alcoholic fatty liver disease. Patients with metabolic syndrome were called cases and without metabolic syndrome were called controls. It was hypothesized that patients with metabolic syndrome are more likely to have non-alcoholic fatty liver disease compared to healthy controls. Sample size was 164 (82 in each group) calculated Open Epi software taking anticipated proportion of NAFLD in metabolic syndrome as 17.1% and 3.7% among healthy controls,[1] 80% power of test and 5% significance level. Participants were enrolled using non-probability consecutive sampling technique.

Patients who met the selection parameters were enlisted from the hospital's outside medical department after receiving clearance from the study review board. All registered individuals were informed of the study's goals, risks, and advantages before giving their informed permission. Age (years), gender (male/female), BMI (weight in kg/height in m2), domicile (rural/urban), education, occupation, smoking history, and socioeconomic position were all reported as baseline data. Cases and controls were matched for age and gender of the patients. Anthropometric and metabolic data was collected by routine physical examinations. Body mass index (BMI) was recorded as the weight divided by height squared (kg/m^2). Waist circumference (WC) was measured at the

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

mid-level between the costal margins and the iliac crests. Fasting plasma glucose (FPG), total cholesterol (TCH), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C) and triglycerides (TG) was measured after an 8-hour overnight fast. Insulin resistance was measured using HOMA-IR based on using the calculator (http://www.dtu.ox.ac.uk/homacalculator).

Abdominal US scanning was performed after an 8-hour overnight fast by consultant radiologist blinded to clinical data with a 3.5–5 MHz transducer and a high-resolution B-mode scanner (Hitachi Aloka ProSound). The presence and severity of NAFLD was calculated using the US-FLI score, which ranges from 0 to 8. Presence of NAFLD was noted as US-FLI > 1.

IBM SPSS version 25, a statistical analysis application, was used to examine the data. For continuous data, such as age and BMI, means ± SD were recorded; for categorical variables, such as gender, residency, SE status, and NAFLD, frequencies and percentages were recorded. NAFLD and metabolic syndrome were found to be associated using the chi square or Fisher exact test at the 5% significance level. Using a 2x2 table, the odds ratio was calculated to gauge the degree of correlation. Significance was defined as 95% CI excluding 1. To control the impact modifiers, NAFLD was stratified by age, gender, place of residence, occupation, and SE status. Fisher exact or chi square tests were used after stratification at the 5% significance level.

RESULTS

The mean age of participants in cases group was 49.40±7.50 years versus 49.62±7.42 years among control group as shown in table 1.

Table 1. Descriptive statistics of study participants (n = 164)

Parameters	Cases (n = 82)	Controls (n = 82)
Age (years)	49.40±7.50	49.62±7.42
BMI (kg/m^2)	24.44±1.38	24.08±1.28

Participants aging more than 45 years were 51(51.5%) among cases versus 48(48.5%) among controls while male participants among cases and controls were 39(49.4%) and 40(50.6%) respectively. With respect to residence, 39 patients (43.3%) belong to rural areas among vases versus 51(56.7%) among controls as reported in table 2.

Table 2. Baseline clinical and sociodemographic parameters of study participants (n = 164)

		Group		Total
		Cases	Controls	
Age(years)	45 or below	31	34	65
		47.7%	52.3%	100.0%
	More than 45	51	48	99
		51.5%	48.5%	100.0%
Gender	Male	39	40	79
		49.4%	50.6%	100.0%
	Female	43	42	85
		50.6%	49.4%	100.0%
BMI (kg/m^2)	24.0 or below	29	49	78
		37.2%	62.8%	100.0%
	More than 24.0	53	33	86
		61.6%	38.4%	100.0%
Residence	Rural	39	51	90
		43.3%	56.7%	100.0%
	Urban	43	31	74
		58.1%	41.9%	100.0%
Education	Matric or below	41	35	76

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

		53.9%	46.1%	100.0%
	Above matric	41	47	88
		46.6%	53.4%	100.0%
Profession	Salaried	34	41	75
		45.3%	54.7%	100.0%
	Business	48	41	89
		53.9%	46.1%	100.0%
SES	Fair	55	43	98
		56.1%	43.9%	100.0%
	Poor	27	39	66
		40.9%	59.1%	100.0%

Non-alcoholic fatty liver disease was observed in 22 (66.7%) cases and 11 (33.3%) controls. The chi square p value for association was 0.032 and odds ratio with 95% CI was 2.36(1.06-5.27) as shown in table 3.

Table 3. 2x2 table analysis of NAFLD among study participants (n = 164)

		Group		Total	Chi square p value	Odds ratio 95% CI
		Cases	Controls			
NAFLD	Yes	22	11	33	0.032	2.36(1.06-5.27)
		66.7%	33.3%	100.0%		
	No	60	71	131		
		45.8%	54.2%	100.0%		
Total		82	82	164		
		50.0%	50.0%	100.0%		

Male patients were slightly more frequently having NAFLD compared to female (22.8% versus 17.6%). The p value for difference in distribution was 0.412. Similarly, patients with business profession were more frequently having NAFLD compared to salaried class (21.3% versus 18.7%, p value 0.670. the p value for difference in distribution of NAFLD among with respect to SE status was 0.036 with participants with fair SE level were more frequently affected compared to poor SE level (25.5% versus 12.1%) as shown in table 4.

Table 4. stratification of NAFLD with baseline parameters (n = 164)

		NAFLD		Total	P value
		Yes (n = 33)	No (n = 131)		
Age (years)	45 or below	16	49	65	0.245
		24.6%	75.4%	100.0%	
	More than 45	17	82	99	
		17.2%	82.8%	100.0%	
Gender	Male	18	61	79	0.412
		22.8%	77.2%	100.0%	
	Female	15	70	85	
		17.6%	82.4%	100.0%	
BMI (kg/m^2)	24.0 or below	16	62	78	0.905
		20.5%	79.5%	100.0%	
	More than 24.0	17	69	86	
		19.8%	80.2%	100.0%	
Residence	Rural	16	74	90	0.409
		17.8%	82.2%	100.0%	

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

	Urban	17	57	74	
		23.0%	77.0%	100.0%	
Education	Matric or below	15	61	76	0.909
		19.7%	80.3%	100.0%	
	Above matric	18	70	88	
		20.5%	79.5%	100.0%	
Profession	Salaried	14	61	75	0.670
		18.7%	81.3%	100.0%	
	Business	19	70	89	
		21.3%	78.7%	100.0%	
SE status	Fair	25	73	98	0.036
		25.5%	74.5%	100.0%	
	Poor	8	58	66	
		12.1%	87.9%	100.0%	

DISCUSSION

The study's findings support a strong link between metabolic syndrome and nonalcoholic fatty liver disease (NAFLD), with those with MetS having a 2.36-fold increased risk of developing NAFLD in comparison to healthy controls. This result aligns with the current notion of NAFLD serving as the hepatic analog of MetS, which has been repeatedly confirmed in recent research. Mantovani et al.'s 2022 systematic review and meta-analysis confirmed that MetS constituents work in concert to raise the risk of NAFLD development, with pooled odds ratios uniformly over 2.0 throughout populations.[7]

Crucially, age and gender were evenly distributed in our research groups, removing them as significant confounders. Both cases and controls had mean BMIs that were overweight. This finding is crucial since new research shows that NAFLD is becoming more common in non-obese people, especially in Asian populations where cardiovascular and metabolic risk goes up at lower BMI boundaries.[8] The AGA 2021 recommendations, which emphasize the waist circumference and metabolic dysfunction as more trustworthy warning signs than BMI alone in NAFLD development, are consistent with our findings.[9]

Comprehensive findings were obtained by stratified assessment. In contrast to many major epidemiological investigations, our sample did not show a statistically significant correlation between NAFLD and either gender or age. For instance, a 2023 research of the worldwide load of NAFLD revealed an increase in cases with age and a usually greater frequency in men.[10] Our demographic or sampling size may be the cause of the non-significant trend. According to recent study by Kim et al. (2022), shifting lifestyle variables and the waning preventive impact of estrogen, postmenopausal may be the reasons why the gender difference in the rate of NAFLD may be closing in some cohorts.[11]

The substantial correlation between socioeconomic (SE) level and the occurrence of NA was one especially notable observation. NAFLD was more common in those with better SE status than in those with "poor" condition. It is important to analyze this complicated relationship carefully. The negative relationship seen here is conceivable in some evolutionary situations, even though several research from high-income nations show that lower socioeconomic groups have a larger incidence of metabolic illnesses.[12] Increasing affluence can ultimately lead to higher amounts of processed foods, beverages with added sugar, and inactive lifestyles—key causes of NAFLD prior to health consciousness catches up, according to a 2021 comprehensive review on changes in nutrition in South Asia.[13] For middle-class populations, which the appropriate SE category would reflect, this trend establishes a distinct risk gap. Additionally, different groups may have different access to diagnostic imaging, which might result in identification discrimination.

Additionally illuminating are the insignificant correlations with occupation and place of living (rural vs. urban). Studies including one by

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Zhang and colleagues (2024) show a sharp increase in NAFLD incidence in rural China due to industrialization and changes in diet, obscuring previous risk boundaries, indicating a change in the worldwide rural-urban split in NAFLD risk.[14] According to a 2022 research on professional activity levels and NAFLD, the sedentary character of many "salaried" positions today may equate metabolic hazards with more conventional "business" occupations.[15]

There are caveats on this study. Although sufficient for the principal connection, the sample size restricts the power of subgroup testing. Since ultrasound has a modest sensitivity for early steatosis detection, it is crucial that the diagnostic criteria for NAFLD be defined.[16] For improved risk categorization, a recent consensus suggests integrating imaging with biomarkers such as the FIB-4 index.[17,18]

CONCLUSION

In summary, this study provides strong evidence for the documented connection between MetS and NAFLD. The phenomenon is ever-changing and context-specific, as evidenced by the surprising socioeconomic phasing of NAFLD risk. It emphasizes the need to transcend universal risk frameworks and adapt public health interventions to local epidemiological shifts. In order to further identify causative pathways, prospective longitudinal studies involving this cohort should include comprehensive food surveys, sophisticated non-invasive fibrosis testing, and genomic risk evaluations.

REFERENCES

Yang KC, Hung HF, Lu CW, Chang HH, Lee LT, Huang KC. Association of Non-alcoholic Fatty Liver Disease with Metabolic Syndrome Independently of Central Obesity and Insulin Resistance. Sci Rep. 2016;6:27034-9.

Gill MG, Majumdar A. Metabolic associated fatty liver disease: Addressing a new era in liver transplantation. World J Hepatol. 2020;12(12):1168-81.

Younossi ZM, Paik JM, Al Shabeeb R, Golabi P, Younossi I, Henry L. Are there outcome differences between NAFLD and metabolic-associated fatty liver disease? Hepatology. 2022;76(5):1423-37.

Muzurović E, Mikhailidis DP, Mantzoros C. Non-alcoholic fatty liver disease, insulin resistance, metabolic syndrome and their association with vascular risk. Metabolism. 2021;119:154770-5.

Wainwright P, Byrne CD. Bidirectional Relationships and Disconnects between NAFLD and Features of the Metabolic Syndrome. Int J Mol Sci. 2016;17(3):367-78.

Payne JY, Alkhouri N, Le P, Rothberg MB, Polanco P, Sakkal C, et al. Prevalence of at-risk NASH and its association with metabolic syndrome in US adults with NAFLD, 2017-2018. Hepatol Commun. 2023;7(1):e0019-25.

Mantovani A, Byrne CD, Scorletti E, Mantzoros CS, Targher G. Efficacy and safety of anti-hyperglycaemic drugs in patients with non-alcoholic fatty liver disease with or without diabetes: An updated systematic review of randomized controlled trials. Diabetes Metab. 2022;48(6):101365.

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.

Kanwal F, Shubrook JH, Adams LA, Pfotenhauer K, Wai-Sun Wong V, Wright E, et al. Clinical Care Pathway for the Risk Stratification and Management of Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology. 2021;161(5):1657-1669.

Le MH, Yeo YH, Li X, Li J, Zou B, Wu Y, et al. 2019 Global NAFLD Prevalence: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2022;20(12):2809-2817.e28.

Frontier in Medical & Health Research

ISSN: (e) 3007-1607 (p) 3007-1593

Kim D, Konyn P, Sandhu KK, Dennis BB, Cheung AC, Ahmed A. Metabolic dysfunction-associated fatty liver disease is associated with increased all-cause mortality in the United States. J Hepatol. 2021;75(6):1284-1291.

Petersen JM, Kemps E, Lewis LK, Maher C, Smith A, Tomayko EJ, et al. The relationship between lifestyle and socio-economic, demographic and health characteristics of young Australian women. Prev Med Rep. 2021;24:101560.

Popkin BM, Corvalan C, Grummer-Strawn LM. Dynamics of the double burden of malnutrition and the changing nutrition reality. Lancet. 2020;395(10217):65-74.

Zhang X, Wu M, Liu Z, Yuan H, Wu X, Shi T, et al. Increasing prevalence of NAFLD/NASH among children, adolescents and young adults from 1990 to 2017: a population-based observational study. BMJ Open. 2021;11(5):e042843.

Hallsworth K, Thoma C, Moore S, Ploetz T, Anstee QM, Taylor R, et al. Non-alcoholic fatty liver disease is associated with higher levels of objectively measured sedentary behaviour and lower levels of physical activity than matched healthy controls. Frontline Gastroenterol. 2021;12(2):132-137.

Stine JG, Wentworth BJ, Zimmet A, Rinella ME, Loomba R, Caldwell SH, et al. Systematic review with meta-analysis: risk of hepatocellular carcinoma in non-alcoholic steatohepatitis without cirrhosis. Aliment Pharmacol Ther. 2021;54(3):238-248.

Newsome PN, Cramb R, Davison SM, Dillon JF, Foulerton M, Godfrey EM, et al. Guidelines on the management of abnormal liver blood tests. Gut. 2018;67(1):6-19. (Updated in practice by 2021 EASL Clinical Practice Guidelines).

Lazarus JV, Mark HE, Anstee QM, Arab JP, Batterham RL, Castera L, et al. Advancing the global public health agenda for NAFLD: a consensus statement. Nat Rev Gastroenterol Hepatol. 2022;19(1):60-78.