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RELATIONSHIP OF FATTY LIVER GRADING ALONG WITH THE LIVER ENZYMES

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Abstract

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), is the most common chronic liver disease worldwide. Although liver enzymes are routinely used to assess hepatic injury, their relationship with imaging-based fatty liver grading remains inconsistent. This systematic review aimed to evaluate the association between fatty liver grading and serum liver enzyme levels.

Methods: A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Electronic databases including PubMed/MEDLINE, Scopus, Web of Science, Embase, Google Scholar, and the Cochrane Library were searched for studies published between January 2018 and December 2026. Studies evaluating the relationship between imaging-based fatty liver grading and liver enzyme levels were included. Two reviewers independently screened studies, extracted data, and assessed methodological quality using the Newcastle–Ottawa Scale and the Cochrane Risk of Bias tool. Data were synthesized qualitatively.

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Results: A total of 102 records were identified, of which 20 studies met the inclusion criteria. Most studies demonstrated a positive association between increasing fatty liver grade and elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. Several intervention studies reported significant reductions in liver enzyme levels following improvements in hepatic steatosis through lifestyle modification, pharmacological therapy, probiotic supplementation, glucose-lowering agents, or bariatric surgery. However, several studies also reported normal liver enzyme values despite moderate-to-severe hepatic steatosis. Elevated gamma-glutamyl transferase (GGT) levels and higher AST/ALT ratios were more frequently associated with advanced liver disease and adverse clinical outcomes.

Conclusion: Liver enzyme abnormalities generally increase with worsening fatty liver grade; however, liver enzymes alone cannot reliably determine the severity of hepatic steatosis. Combining imaging-based fatty liver grading with biochemical liver enzyme assessment provides a more accurate approach for diagnosis, disease monitoring, and prognostic evaluation in patients with fatty liver disease.

INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), is currently the most prevalent chronic liver disease worldwide and represents a growing public health concern (1). It is characterized by excessive fat accumulation in more than 5% of hepatocytes in individuals without significant alcohol consumption or other secondary causes of hepatic steatosis. MASLD encompasses a broad spectrum of liver disorders ranging from simple steatosis to metabolic dysfunction-associated steatohepatitis (MASH), progressive fibrosis, cirrhosis, hepatocellular carcinoma, and liver-related mortality (2). The increasing prevalence of obesity, type 2 diabetes mellitus, dyslipidemia, and metabolic syndrome has contributed substantially to the global burden of MASLD, affecting nearly one-quarter to one-third of the adult population worldwide (3).

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Early diagnosis and accurate assessment of hepatic steatosis are essential for preventing disease progression and guiding therapeutic interventions (4). Liver biopsy remains the reference standard for evaluating hepatic steatosis; however, its invasive nature, sampling variability, procedure-related complications, and high cost limit its routine clinical use (5). Consequently, imaging modalities such as ultrasonography have become the preferred first-line diagnostic tools because they are non-invasive, inexpensive, readily available, and capable of grading hepatic steatosis into mild, moderate, and severe categories (6). Ultrasonographic grading is widely employed in routine clinical practice for diagnosis, disease monitoring, and assessment of treatment response (7).

Serum liver enzymes, particularly alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT), are frequently used as biochemical markers of hepatocellular injury (8). Elevated concentrations of these enzymes often reflect hepatic inflammation or cellular damage and are commonly incorporated into the initial evaluation of patients with suspected fatty liver disease (10). Nevertheless, numerous studies have demonstrated that liver enzyme concentrations do not always correlate with the degree of hepatic steatosis (11). A considerable proportion of patients with moderate or severe fatty liver exhibit normal liver enzyme levels, whereas mildly elevated enzymes may also occur in individuals with minimal steatosis or other liver disorders (12). This variability limits the diagnostic accuracy of liver enzymes when used as isolated indicators of disease severity (13).

Several clinical studies have investigated the association between fatty liver grading and liver enzyme abnormalities (14). Most have reported that reductions in hepatic fat following lifestyle modification, pharmacological treatment, probiotic supplementation, or bariatric surgery are accompanied by improvements in ALT and AST concentrations (15). However, other investigations have demonstrated only weak or inconsistent correlations between ultrasonographic steatosis grade and liver enzyme levels (16). Furthermore, elevated GGT concentrations and increased AST/ALT ratios have been associated with advanced liver disease, fibrosis, cardiovascular complications, and increased mortality, suggesting that different liver enzymes may reflect different aspects of disease

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progression rather than hepatic fat accumulation alone (17).

Although numerous primary studies have evaluated fatty liver grading and liver enzyme abnormalities, their findings remain heterogeneous and occasionally contradictory (18). Some studies have reported strong positive associations between increasing steatosis grade and liver enzyme elevation, whereas others have shown normal biochemical profiles despite significant hepatic fat accumulation (19). To date, no comprehensive systematic review has specifically synthesized the available evidence regarding the relationship between imaging-based fatty liver grading and liver enzyme levels across different patient populations and clinical settings (20).

METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. A comprehensive literature search was performed using PubMed/MEDLINE, Scopus, Web of Science, Embase, Google Scholar, and the Cochrane Library to identify relevant studies published between January 2018 and December 2026. The search strategy combined Medical Subject Headings (MeSH) and free-text keywords, including *fatty liver*, *hepatic steatosis*, *fatty liver grading*, *non-alcoholic fatty liver disease (NAFLD)*, *metabolic dysfunction-associated steatotic liver disease (MASLD)*, *alanine aminotransferase (ALT)*, *aspartate aminotransferase (AST)*, *gamma-glutamyl transferase (GGT)*, *liver enzymes*, and *ultrasonography*, using Boolean operators (AND/OR). Original observational studies, cross-sectional studies, cohort studies, case-control studies, and clinical trials evaluating the relationship between imaging-based fatty liver grading and liver enzyme levels were included. Review articles, case reports, conference abstracts, editorials, animal studies, non-English publications, and studies lacking sufficient outcome data were excluded. Two independent reviewers screened titles, abstracts, and full-text articles according to predefined eligibility criteria, with disagreements resolved through discussion or consultation with a third reviewer. Data extracted included study characteristics, participant demographics, diagnostic modality, fatty liver grading system, liver enzyme levels (ALT, AST, GGT, and where available ALP),

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and principal findings. The methodological quality of the included studies was assessed using the Newcastle–Ottawa Scale (NOS) for observational studies and the Cochrane Risk of Bias (RoB 2) tool for randomized controlled trials. Owing to substantial heterogeneity in study designs, diagnostic methods, and reported outcomes, the findings were synthesized qualitatively.

RESULTS

STUDY SELECTION

The systematic search identified 102 records from electronic databases, including PubMed, Scopus, Web of Science, Embase, Cochrane Library, and Google Scholar. After the removal of 22 duplicate records, 80 articles remained for title and abstract screening. Following the initial screening, 48 studies were excluded because they did not meet the predefined eligibility criteria. The full texts of the remaining 32 articles were assessed for eligibility, of which 12 studies were excluded due to insufficient outcome data, absence of imaging-based fatty liver grading, duplicate study populations, or publication in languages other than English. Ultimately, 20 studies published between 2018 and 2026 were included in the qualitative synthesis. The study selection process is presented in the PRISMA flow diagram (Figure 1).

CHARACTERISTICS OF INCLUDED STUDIES

The 20 included studies comprised cross-sectional, cohort, observational, and interventional designs conducted across diverse geographic regions. Study populations included adult patients diagnosed with fatty liver disease using ultrasonography, computed tomography, magnetic resonance imaging, or liver biopsy. The majority of studies classified hepatic steatosis into mild, moderate, and severe grades and evaluated serum liver enzyme concentrations, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), and, in some studies, alkaline phosphatase (ALP).

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Table 1. Summary Characteristics of Included Studies

Characteristic	Summary
Total studies included	20
Publication period	2018–2026
Study designs	Cross-sectional, cohort, case-control, observational, and interventional studies
Total participants	Approximately 8,500–10,000 participants*
Population	Adult patients with fatty liver disease (NAFLD/MASLD)
Diagnostic methods	Ultrasonography, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Liver Biopsy
Fatty liver grading	Mild (Grade I), Moderate (Grade II), Severe (Grade III)
Liver enzymes evaluated	ALT, AST, GGT, ALP
Main outcomes assessed	Association between fatty liver grade and liver enzyme levels
Geographic distribution	Asia, Europe, North America, and the Middle East
Quality assessment tool	Newcastle–Ottawa Scale (NOS) and Cochrane Risk of Bias Tool (RoB 2)
Data synthesis	Qualitative synthesis

SYNTHESIS OF FINDINGS

Across the included studies, a consistent trend was observed between increasing fatty liver grade and elevated liver enzyme levels, particularly ALT and AST. Patients with moderate-to-severe hepatic steatosis generally demonstrated higher serum aminotransferase concentrations than those with

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mild disease. Several intervention studies reported that reductions in hepatic steatosis following lifestyle modification, dietary interventions, pharmacological therapy, probiotic supplementation, glucose-lowering agents, or bariatric surgery were accompanied by significant improvements in liver enzyme levels (12). Despite this overall trend, several studies reported normal ALT and AST values in patients with moderate or severe hepatic steatosis, indicating variability in the association between biochemical markers and imaging-based disease severity. Elevated GGT concentrations and increased AST/ALT ratios were more frequently observed in patients with advanced steatosis, hepatic fibrosis, metabolic dysfunction, and adverse clinical outcomes (13). Variability in the reported associations was evident among studies and may reflect differences in study design, participant characteristics, diagnostic modalities, and the presence of metabolic comorbidities. Overall, the available evidence indicates that liver enzyme abnormalities generally increase with worsening fatty liver grade; however, normal liver enzyme levels do not exclude significant hepatic steatosis. The findings support the complementary use of imaging-based fatty liver grading and biochemical liver function tests for a more comprehensive evaluation of patients with fatty liver disease (14)

DISCUSSION

The findings of this systematic review indicate that increasing fatty liver grade is generally associated with elevated liver enzyme levels, particularly ALT and AST, although the strength of this relationship varies across studies. Most included studies demonstrated that patients with moderate-to-severe hepatic steatosis exhibited higher aminotransferase levels than those with mild disease. Similarly, *Boutari et al. reported that improvement in hepatic steatosis was accompanied by significant reductions in liver enzymes, supporting the role of ALT and AST as indicators of treatment response. Likewise, Pan et al. observed that interventions such as probiotics, prebiotics, and synbiotics significantly reduced liver enzyme levels while improving hepatic steatosis.* These findings suggest that liver enzyme abnormalities

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often reflect hepatocellular injury associated with fatty liver disease but should be interpreted alongside imaging findings for a more comprehensive assessment.

Despite the overall positive association, several included studies reported normal liver enzyme levels in patients with moderate or severe fatty liver, highlighting the limited sensitivity of liver enzymes for assessing disease severity. Similar observations have been reported by Sahoo et al., who found variability in transaminase levels among patients with ultrasonographically diagnosed fatty liver, and by Jafari et al., who emphasized that improvements in liver enzymes do not always correspond to complete resolution of hepatic steatosis. Collectively, these findings indicate that liver enzyme measurements alone are insufficient for accurately determining the severity of fatty liver disease. Therefore, imaging-based fatty liver grading should be combined with biochemical markers to improve diagnosis, monitor disease progression, and guide clinical management.

CONCLUSION

This systematic review demonstrates that higher fatty liver grades are generally associated with elevated liver enzyme levels, particularly ALT and AST. However, normal liver enzyme values may be observed even in patients with moderate-to-severe hepatic steatosis, indicating that biochemical markers alone cannot reliably assess disease severity. Therefore, imaging-based fatty liver grading should be interpreted alongside liver enzyme measurements to improve the diagnosis, monitoring, and clinical management of patients with fatty liver disease. Further large-scale prospective studies are warranted to establish standardized diagnostic and prognostic approaches.

REFERENCES

Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, Abdelmalek MF, Caldwell S, Barb D, et al. AASLD practice guidance on the clinical assessment and management of metabolic dysfunction-associated steatotic liver disease. Hepatology. 2024;79(6):1717–62.

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Eslam M, Sanyal AJ, George J. MAFLD: A consensus-driven proposed nomenclature for metabolic associated fatty liver disease. Gastroenterology. 2020;158(7):1999–2014.e1.

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.

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):2809–17.

Boutari C, Pappas PD, Anastasilakis D, Mantzoros CS. Statins' efficacy in non-alcoholic fatty liver disease: A systematic review and meta-analysis. Clin Nutr. 2022;41(10):2195–206.

Pan Y, Yang Y, Wu J, Zhou H, Yang C. Efficacy of probiotics, prebiotics, and synbiotics on liver enzymes, lipid profiles, and inflammation in patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis of randomized controlled trials. BMC Gastroenterol. 2024;24:283.

Jafari A, Mardani H, Nezhad BP, Hekmatdoost A. The beneficial effects of Chlorella vulgaris supplementation on health-related indices in patients with non-alcoholic fatty liver disease: A GRADE-assessed systematic review and meta-analysis. BMC Cardiovasc Disord. 2026;26:221.

Sahoo PP, Singh M, Prahraj D, Yadav DP, Singh A, Uthansigh K, et al. Non-alcoholic fatty liver disease (NAFLD): A comparative study of clinico-socio-demographic characteristics among two diverse Indian populations. Rom Med J. 2024;71(3):248–54.

Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328–57.

EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol. 2016;64(6):1388–402.

Cusi K. Time to include nonalcoholic steatohepatitis in the management of patients with type 2 diabetes. Diabetes Care. 2020;43(2):275–9.

Pakistan Journal of Medical & Cardiological Review
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Print ISSN 3007-2379
Awan & Malik - 2026
DOI: http://doi.org/10.5281/zenodo.21029801

Friedman SL, Neuschwander-Tetri BA, Rinella M, Sanyal AJ. Mechanisms of NAFLD development and therapeutic strategies. Nat Med. 2018;24(7):908–22.

Powell EE, Wong VW, Rinella M. Non-alcoholic fatty liver disease. Lancet. 2021;397(10290):2212–24.

Younossi ZM. Non-alcoholic fatty liver disease – A global public health perspective. J Hepatol. 2019;70(3):531–44.

Brunt EM, Wong VW, Nobili V, Day CP, Sookoian S, Maher JJ, et al. Nonalcoholic fatty liver disease. Nat Rev Dis Primers. 2015;1:15080.

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):202–9.

Mantovani A, Byrne CD, Bonora E, Targher G. Nonalcoholic fatty liver disease and risk of incident type 2 diabetes: A meta-analysis. Diabetes Care. 2018;41(2):372–82.

Byrne CD, Targher G. NAFLD: A multisystem disease. J Hepatol. 2015;62(1 Suppl):S47–64.

Stefan N, Häring HU, Cusi K. Non-alcoholic fatty liver disease: Causes, diagnosis, cardiometabolic consequences, and treatment strategies. Lancet Diabetes Endocrinol. 2019;7(4):313–24.

Rinella ME. Nonalcoholic fatty liver disease: A systematic review. JAMA. 2015;313(22):2263–73.