**Journal of Neonatal Surgery**
***ISSN(Online): 2226-0439***
***Vol. 14, Issue 12s (2025)***
*https://www.jneonatalsurg.com*

OPEN ACCESS

# An Investigation To Look Into The Relationship Between Steatotic Liver Damage And Metabolic Syndrome. Problems: A Thorough Perspective On A Complicated Issue

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Cite this paper as: Dai Decai, Satheesh Babu Natarajan, (2025) An Investigation To Look Into The Relationship Between Steatotic Liver Damage And Metabolic Syndrome. Problems: A Thorough Perspective On A Complicated Issue. *Journal of Neonatal Surgery*, 14 (12s), 640-645.

**ABSTRACT**

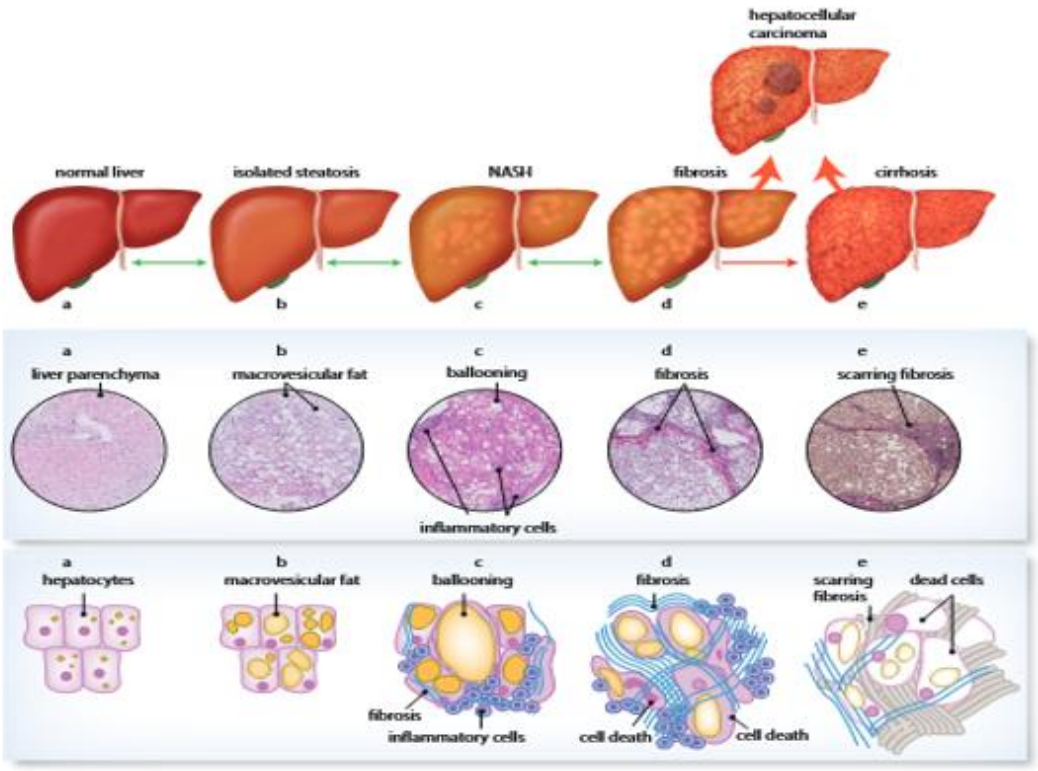
More and more people are being affected by nonalcoholic fatty liver disease (the ailment), which affects more than 25% of the world's population and more than 60% of those at a higher risk. As part of metabolic syndrome, it raises the risk of developing specific illnesses related to the cardiovascular system and liver. Because NAFLD is a complicated illness with many associated comorbidities and difficulties, its treatment requires a multidisciplinary approach. But many medical experts are unsure about how to proceed after a diagnosis of non-alcoholic fatty liver disease (NAFLD), its comorbidities, and the severity of the condition and its potential consequences. Cirrhosis, inflexible simple steatosis, hepatocellular cancer, and cardiovascular disease are among of the conditions that may coexist with actively metabolizing non-alcoholic steatosis (NASH). It may be difficult to decide on the optimal diagnostic and treatment procedures due to the contradicting advice. In this article, researchers will review the history of NAFLD, its symptoms, and available treatments before shifting gears to talk about where researchers can see multidisciplinary care pathways going in the future.

***Keywords:*** *Metabolic dysfunction, steatotic liver disease, and diagnostic tests.*

## 1. INTRODUCTION

According to (Premkumar & Anand, 2023), there has been a significant increase in the number of individuals adhering to the "Western lifestyle," which comprises an excessive calorie intake and an inadequate exercise regimen. A "Western lifestyle" is linked to obesity and metabolic syndrome, a group of symptoms that includes abnormal lipid profiles, excessively high blood pressure, abnormally high blood sugar, and an accumulation of belly fat. There is a metabolic condition that affects the liver known as "nonalcoholic fatty liver disease (NAFLD)." When other hepatic steatosis reasons, such heavy alcohol use, specific metabolic problems, or medication usage, are absent, "Non-alcoholic fatty liver disease" is defined as imaging or histology evidence showing intracellular fat accumulation in more than 5% of hepatocytes. The prevalence of non-alcoholic fatty liver disease has surged in recent decades, impacting more than 25% of the global population. This alarming trend parallels the enormous increases in obesity and metabolic disorders. Type 2 diabetes mellitus (T2DM) and other high-risk groups have a prevalence estimate that is more than 60%5. Treatment costs, healthcare expenditure, quality of life, and death rates related to "Non-alcoholic fatty liver disease" and its comorbidities, such as cardiovascular disease and type 2 diabetes, are on the rise. According to Quek et al. (2023), NAFLD may show up in several ways when a person is sick. Liver diseases may progress through many stages, such as fibrosis, cirrhosis, "Nonalcoholic fatty liver," and "Hepatocellular carcinoma (HCC)". Despite the prevalence of "Nonalcoholic fatty liver disease" only a small percentage of people with hepatic steatosis will develop severe liver disease. Liver failure, hepatic encephalopathy, esophageal varices, ascites, and HCC are more probable outcomes of severe NAFLD. Metabolically active NASH should be diagnosed in people who are at risk of HCC, cirrhosis, or heart attacks before non-progressive simple steatosis should be diagnosed in those who are at low risk of these problems. Finding these susceptible people may be difficult, and there are different opinions on how to diagnose and help them. This leaves many doctors and nurses confused on what to do in the case of a new NAFLD diagnosis or suspicion. According to (Allen et al., 2023), one of the major issues is the lack of a comprehensive strategy for treating NAFLD that considers all the many features of the illness and its possible implications.

**Figure 1: The range of symptoms associated with NAFLD is wide.**

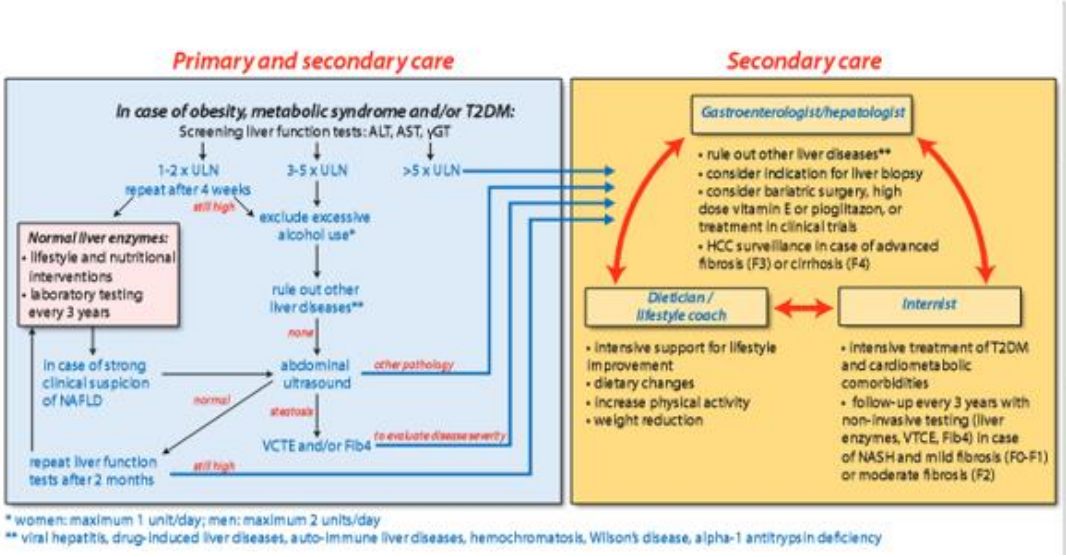



In this article, the authors discuss the causes, symptoms, non-alcoholic fatty liver disease and its potential treatments. They aim to provide a comprehensive overview of the diagnostic options, clinical care procedures, and therapy recommendations.

## 2. BACKGROUND OF THE STUDY

The prevalence of cardiovascular and metabolic disorders in patients with non-alcoholic fatty liver disease (NAFLD) is a relatively new issue in public health. Primary care physicians, vascular specialists, hepatologists, internists-endocrinologists, and assistant nurses must work together to identify patients at high risk for developing nonalcoholic steatohepatitis (NASH) (Sanyal et al., 2021). With the hope of fostering such cooperation, several hospitals throughout the world have sought to establish a NASH workgroup. Metabolically active non-alcoholic steatohepatitis (NASH), cirrhosis, non-progressive simple steatosis, or hepatocellular carcinoma (HCC) are sometimes not immediately apparent in patients diagnosed with non-alcoholic fatty liver disease (NAFLD). Cardiovascular disease and other serious complications are associated with the fourth group. Screening, liver disease stage differentiation, and risk assessment of cirrhotic consequences like HCC may all benefit from more precise and non-invasive diagnostic methods, which the research community is now lacking. While we wait for a non-invasive diagnostic technology that is both accurate and widely accessible, Fig. 2 lays out some guidelines for screening, diagnosing, and monitoring people who might have NAFLD. Ultrasonography or serum liver enzyme testing for NAFLD should be performed every three years on people at high risk for the disease. It is recommended to check HCC every six months if significant fibrosis or cirrhosis is found. According to (Brunt et al., 2021), patients who report with portal hypertension should undergo further assessment for esophageal varices.

**Figure 2: Approaching non-alcoholic fats liver disease (NAFLD) from several perspectives.**




## 3. PURPOSE OF THE RESEARCH

In this study, we aimed to determine if faecal microbiota transplantation (FMT) improved outcomes for patients with metabolic syndrome-related non-alcoholic fatty liver disease (NAFLD). The objective of the research was to evaluate treatment-naïve NAFLD patients' reactions to autologous (donor-derived) and allogeneic (self-derived) FMT. Investigate how FMT influences many biological systems connected to NAFLD, such as the make-up of the gut microbiota, metabolomics in plasma, and patterns of DNA methylation in the liver. Using these biological indicators, train and test a machine learning model that can differentiate between patients receiving autologous and heterologous FMT after 24 weeks. Help scientists learn more about NAFLD and the gut-liver axis, which might lead to new treatments. Explore the potential of integrating multi-omics data to predict and tailor the responses of NAFLD patients to FMT therapy. As a first step, researchers should determine if FMT is effective in treating NAFLD and, if so, how it works. This work aimed to fill this knowledge gap regarding the function of the gut microbiota in NAFLD (non-alcoholic fatty liver disease) and its treatment. Additionally, it paved the way for better, more personalized therapies for a condition that is becoming more common (Lim et al., 2023).

## 4. LITERATURE REVIEW

Even in those who do not partake in excessive drinking, cirrhosis of the liver may occur, which shares symptoms with alcoholic hepatitis. According to (Dwinata et al., 2020), most of the patients were moderately obese and had diabetes mellitus. The liver is affected by this condition, which is known as non-alcoholic steatohepatitis. Ultrasonography data may be used to identify non-alcoholic fatty liver disease (NAFLD) once other chronic liver disease causes, such as excessive alcohol use or medications that induce hepatic stenosis, have been ruled out, according to the Asian-Pacific Sitting Party for NAFLD. In a subsequent policy statement, the European Association for the Study of Liver (EASL) recognized that NAFLD was previously diagnosed by ruling out other chronic liver disease causes. The robust correlation with metabolic syndrome and other long-term liver diseases, however, offered compelling reasons to change the name. Despite the term NAFLD being used in significant international recommendations 4-6, a shift was on the way. Remember to think about the 2016 EASL guidelines; while discussing "primary NAFLD," they said that NAFLD is "associated with metabolic risk factors." Van Dijk (2023) states that in its 2017 recommendations, the Asian-Pacific Research Party provided a "positive" definition of NAFLD. For adults who have a history of type 2 diabetes (T2DM), obesity, imaging-detected steatosis of the liver, bloodstream biomarkers, or a liver biopsy, or a combination of these metabolic risk factors, a new term called metabolic processes dysfunction-associated fatty liver condition (MAFLD) has been suggested. This has received the blessing of several international organizations and associations, such as the Asian Pacific Association for the Statistical Investigation of the Liver and the Malaysian Society of Gastro and Hepatology. The revised definition of fatty liver disease was released in June 2022 via a Delphi compromise statement that included many societies. The condition known as mitochondrial dysfunction-associated steatosis hepatitis disease has mostly superseded the NAFLD moniker. Since they both go into deeper depth on the same subject, MAFLD and MASLD are both superior choices. As previously stated by Brunner et al. (2019).

**Table 1**

| Characteristic | MAFLD |
|---|---|
| Positive diagnostic criteria | Yes |
| Attributes the condition to its etiology | Yes |
| Criteria | Hepatic steatosis detected either by imaging techniqu |
| Presence of other concomitant liver diseases | Other concomitant liver diseases retain their own terr |

*MetALD, i.e., weekly intake 140–350 g for female, 210–420 g for male (average daily 20–50 g for female, 30–60 g for male).

Abbreviations:
MAFLD: metabolic dysfunction-associated fatty liver disease
MASLD: metabolic dysfunction-associated steatotic liver disease
HDL: high-density lipoprotein
HbA1c: glycosylated hemoglobin
HOMA-IR: homeostatic model for assessment of insulin resistance
hs-CRP: high sensitivity C-reactive protein
BMI: body mass index
MetALD: MASLD and increased alcohol intake

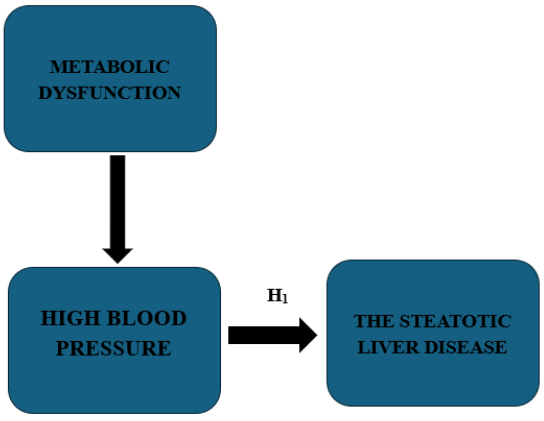
## 5. RESEARCH QUESTIONS

- What is the impact of high blood pressure on steatotic liver disease?

## 6. RESEARCH METHODOLOGY

To identify NASH and NAFLD-related fibrosis, this study is a component of the LITMUS project, an international consortium of research centers aiming to discover and verify a panel of diagnostic biomarkers. Everyone may watch while a systematic review is conducted. We used the PRISMA-DTA statement to compile this report. The researchers scoured the literature for studies that tested the diagnostic accuracy of Pro-C3 in patients with NAFLD using a sophisticated search algorithm. The whole record, including the abstract and title, was included in the search by using words from the Medical Theme Headings. In 2022, the group scoured MEDLINE (via OVID), EMBASE (via OVID and OVID as well), PubMed, Academic Citations Index, and CENTRAL (the Cochrane Library), among other databases. Scientists may be able to get all the answers they need from the supplement. To find any further studies that the search method could have missed, they contacted their LITMUS colleagues and went through the bibliographies of relevant research articles by hand. In 2022, the search was modified. It has already verified all the records that matched the criteria of the researchers.

## 7. CONCEPTUAL FRAMEWORK




## 8. RESULTS

Allogeneic (n = 10) and autologous (n = 11) FMT were used to treat hepatic steatosis and metabolic syndrome in 21 individuals who had never received therapy before. No one could participate in the trial if they had a cholecystectomy, type 2 insulin resistance, cardiovascular disease, renal illness, or compromised immune system. Medications were not administered to any of the participants. To be included or omitted, students must meet all the criteria, which are detailed elsewhere. Table 2 shows where the study participants began. Notably, neither the food consumption nor the ages of the

treatment groups differed significantly from the outset (Suppl. Table 2). Groups did not differ significantly with respect to the NAFLD action score (NAS), fibrosis stage, or baseline steatosis %. Table 2: Basic information about 21 people whose NAFLD was confirmed by biopsy. Two common ways to display data are as an average plus or minus the standard deviation, or as a frequency (%) or midpoint (interquartile range). The p-values represent the outcomes of several statistical tests, such as the Mann-Whitney U test for independent data, the t-test for data with a typical distribution, and Fisher's exact test for binary analysis. The abbreviations "ALP," "an ALT," and "AST" are used for glutamate transaminase, aspartate a protein termed trans, and "BMI," respectively. Haemoglobin A and low-density lipoprotein chole are the acronyms for high-density lipoprotein lipid and low-density lipoprotein chole, respectively. Alpha-lactamase, C-reactive protein, and transplantation of feces microbiota. The score for NAFLD activity is known as the NAS score. Short for type 2 diabetes mellitus.

**Table 2**

| Characteristic | Autologous FMT (n=11) | Allogenic FMT (n=10) | p-value |
|---|---|---|---|
| Age, years | 48.5 ± 10.2 | 51.2 ± 6.6 | 0.48 |
| Sex, male/female | 10/1 | 7/3 | 0.31 |
| BMI, kg/m² | 31.5 ± 4.8 | 31.7 ± 3.5 | 0.91 |
| HbA1c, mmol/mol | 37.6 ± 3.8 | 38.2 ± 3.7 | 0.70 |
| Glucose, mmol/L | 5.7 ± 0.5 | 5.8 ± 0.7 | 0.79 |
| AST, IU/L | 29.0 [26.5-33.0] | 39.5 [37.0-49.5] | 0.001 |
| ALT, IU/L | 48.1 ± 16.5 | 70.8 ± 23.4 | 0.02 |
| ALP, IU/L | 83.0 [54.0-120.5] | 71.0 [58.8-76.8] | 0.67 |
| GGT, IU/L | 41.1 ± 21.4 | 45.1 ± 19.3 | 0.66 |
| Cholesterol, mmol/L | 5.8 ± 1.6 | 6.0 ± 0.8 | 0.75 |
| HDL-C, mmol/L | 1.2 [1.0-1.4] | 1.2 [1.0-1.4] | 0.80 |
| LDL-C, mmol/L | 4.0 ± 1.3 | 4.2 ± 0.7 | 0.71 |
| Triglycerides, mmol/L | 1.2 ± 0.6 | 1.4 ± 0.5 | 0.41 |
| CRP, mg/mL | 2.2 [0.8-4.3] | 1.5 [0.9-3.2] | 0.50 |
| Steatosis, % | 35.0 ± 20.7 | 34.1 ± 20.4 | 0.92 |
| NAS score | | | 0.38 |
| 1 | 1 (9%) | 0 (0.0%) | |
| 2 | 5 (46%) | 4 (40%) | |
| 3 | 4 (36%) | 2 (20%) | |
| 4 | 1 (9%) | 4 (40%) | |
| Necro-inflammation score | | | 0.06 |
| 0 | 1 (9%) | 0 (0%) | |
| 1 | 10 (91%) | 6 (60%) | |
| 2 | 0 (0%) | 4 (40%) | |
| Fibrosis stage | | | 1.00 |
| F0 | 3 (30%) | 2 (20%) | |
| F1 | 6 (60%) | 5 (50%) | |
| F2 | 2 (20%) | 2 (20%) | |
| F3 | 0 (0%) | 1 (10%) | |

By examining changes in the gut microbiota (AUC0.78), plasma metabolites (AUC0.74), and liver DNA methylation patterns (AUC0.75), the predictive ML system was able to differentiate between allogenic and allogeneic FMT from 0 to 24 weeks. The likelihood that the observed accuracy was attributable to chance was modest (0.88; $p< 0.001$), according to the findings of the permutation investigation. Listed below are the primary characteristics that set each group in each research apart.

## 9. CONCLUSION

This study's results inspired the creation of a new method for treatment response prediction that makes use of machine learning and data from many omics (Schaapman et al., 2021). Concerning the medical management of non-alcoholic fatty liver disease, this study's findings provide promising data on the use of FMT. The findings of this study provide fresh hope for individualizing treatment plans for the increasing prevalence of NAFLD among individuals, and they contribute to the growing body of research on the gut-liver connection in this condition (Stine et al., 2021).

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