Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Using liver fatty acid binding protein as a diagnostic marker for metabolic dysfunction and associated steatotic liver disease (MASLD) in Egyptian patients.: A Case-Controlled Study.

Sherihan Yussef

sherihanm373@gmail.com

Ehab Ahmed Abdelatti
Eman Abdelsameea
Hany Abdelbari
Ezzat Abdalla
Belal Abd Elmohsen

Research Article

Keywords: MASLD, L-FABP, steatosis, fibrosis

Posted Date: May 28th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9431115/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background: MASLD is the leading cause of chronic liver disease, which can result in cirrhosis and liver cancer. Even though hepatic biopsy is the benchmark for diagnosis, non-invasive techniques are becoming more popular for MASLD diagnosis, progression tracking, and treatment monitoring. Recently, hepatic injury and fibrosis have been linked to liver fatty acid-binding protein (L-FABP). The diagnostic utility of L-FABP in Egyptian patients with MASLD is assessed in this study.

Methods: Case-control study of 80 participants, which includes 20 age-and sex-matched healthy controls, and 60 patients with MASLD. Patients from Menoufia University Hospitals were enlisted between October 2024 and June 2025. Every patient underwent clinical evaluation, laboratory testing, and serum L-FABP measurement using the ELISA technique. Additionally, FibroScan with CAP and LSM, and abdominal ultrasonography were performed on the patients. NAFLD FIB-4, fibrosis scores, and APRI were computed. ROC curve analysis was accustomed to determining the accuracy of the data**.**

Results: Patients with MASLD had significantly greater serum levels of L-FABP than controls ($p < 0.001$). ALT, AST, APRI, FIB-4,and NAFLD fibrosis scores were significantly correlated with L-FABP. L-FABP levels and steatosis grade, however, did not significantly correlate. An L-FABP cut-off of 4.05 ng/mL was shown to have acceptable diagnostic accuracy for MASLD (AUC = 0.90, 95% sensitivity). An L-FABP cut-off of 6.5 ng/mL was shown to have excellent accuracy (AUC = 0.963) for the prediction of liver fibrosis. L-FABP was an independent predictor of liver fibrosis, according to multivariable analysis.

Conclusion: Serum L-FABP is a promising noninvasive biomarker for detecting MASLD and assessing its fibrotic progression. It correlates with conventional liver injury markers, fibrosis scores, and steatosis levels, thereby enhancing the identification of patients at danger of developing advanced fibrosis.

Introduction

liver steatosis in over 5% of hepatocytes is the hallmark of Previously referred to as non-alcoholic fatty liver disease (NAFLD), metabolic dysfunction-associated steatotic liver disease (MASLD), which is frequently accompanied by insulin resistance. It is a type of steatotic liver disease (SLD) without substantial alcohol consumption that is linked to one or more cardiometabolic risk factors. MASLD encompasses several conditions, including cirrhosis, progressive fibrosis, MASH-related hepatocellular carcinoma (HCC), metabolic dysfunction-associated steatohepatitis (MASH, formerly NASH), and simple steatosis. (1–3).

Between 25 and 29% of people worldwide have MASLD. By 2040, it is expected to reach 30.7% (4, 5). With an estimated 31.8% of people affected, North Africa and the Middle East have one of the greatest incidence MASLD rate overall. Egypt is among the top ten nations for the incidence of obesity; however, precise statistics about the prevalence of MASLD and NAFLD are lacking (5, 6)

A family of small, highly conserved lipid chaperone molecules with a range of roles is known as fatty acid-binding proteins (FABPs) (7). In tissues involved in active lipid metabolism, such as hepatocytes, adipocytes, and cardiac myocytes, where fatty acids are necessary substrates for lipid synthesis, storage, or breakdown, different members of the FABP family exhibit different patterns of tissue expression. One to five percent of all soluble cytosolic proteins are the equivalent FABPs.(8).

The L-FABP protein is involved in several biological activities, like hepatic fatty acid oxidation, phospholipid and cholesterol metabolism, and intracellular fatty acid transport. Hepatocytes in the hepatic lobule express it in a gradient that decreases from the portal to the center. (9). According to certain research, MASLD patients had higher L-FABP levels(10). In clinical settings, It is known that serum L-FABP levels are a reliable biomarker for identifying drug-induced liver injury (11). L-FABP serves as a diagnostic biomarker for non-alcoholic fatty pancreatic disease (12).

Liver biopsy remains the gold standard for diagnosing MASLD (13, 14). Therefore, it is better to identify MASLD, track disease processes, and monitor therapy results in clinical practice using effective noninvasive approaches. (15). Biological markers are helpful noninvasive diagnostic techniques for MASLD, according to numerous research.(16). However, a significant drawback of liver biopsy is its invasive and painful nature, which can lead to several post-procedure consequences. Other drawbacks of liver biopsy include its high cost and the potential for sample errors during specimen collection and handling(17).

A non-invasive diagnostic method for assessing liver health is FibroScan, commonly known as Elastography. Its primary goal is to measure the stiffness or elasticity of liver tissue in order to determine the extent of hepatic fibrosis(18). Compared to traditional liver biopsy, FibroScan offers a non-invasive, reasonably quick, and secure detection method. However, hepatic inflammation may affect tissue flexibility, resulting in elevated FibroScan results.(19).

It is essential to do additional study to assess the diagnosis and prognostic value of L-FABP in MASLD and examine its correlation with non-invasive imaging modalities like FibroScan to enhance early detection, risk stratification, and disease monitoring while reducing reliance on liver biopsy. This The purpose of this study is to evaluate L-FABP's diagnostic utility in Egyptian Patients with MASLD.

Patients and Methods

Study Design and Population

Between October 2024 and June 2025, 80 patients from the hepatology clinics at Menoufia University Hospitals participated in this case-control study. Patients were split into two groups: Group B comprised 20 healthy individuals who were matched to the patient group in terms of age and sex, and Group A comprised 60 patients with MASLD.

The Menoufia University Faculty of Medicine's Institutional Review Board granted ethical approval for the study. Before being included in the study, each subject provided written informed consent.

Inclusion and Exclusion Criteria

Individuals with abdominal ultrasonography and FibroScan evidence of hepatic steatosis, with or without increased liver transaminases, were included in the study. Exclusion criteria included a history of substantial alcohol usage over 20 grams per day for females and 30 grams per day for male, age below 18 years, use of steatogenic medications such as amiodarone, valproic acid, corticosteroids, or tetracycline, pregnancy, acute or Wilson's illness, autoimmune hepatitis, hemochromatosis, chronic viral hepatitis B or C, chronic renal disease, body mass index less than 40 kg/m², liver enzyme levels that are more than three times the upper 102 limit of normal, age above 65 years, refusal to provide give informed consent, and the presence of hepatic or extrahepatic malignancy.

Clinical and Laboratory Assessment

A comprehensive medical history was obtained from each participant, including information about prior medical conditions, medication use, alcohol consumption, and smoking status. People who quit smoking for more than a year were considered ex-smokers, whereas current smokers were defined as people who had smoked within a year before the test. Participants were categorized as minimal drinkers (< 20 g/day) or abstainers based on their alcohol consumption.

A comprehensive clinical examination was performed on each participant, which included measurements of body height, weight, waist circumference, and hip circumference, with the hip circumference being measured at its widest point and the waist circumference at its narrowest point. A mercury column sphygmomanometer was used to take the participant's blood pressure after they had rested in a sitting position for at least five minutes. Two readings were taken on the right upper arm at heart level, separated by at least two minutes.

Following an overnight fast, venous blood samples were taken in the morning for laboratory testing. Kidney function (serum creatinine, blood urea), lipid profile (triglycerides, total cholesterol, LDL-C, HDL-C), glycemic evaluation (fasting glucose, glycated hemoglobin), complete blood count, and liver function (ALT, AST, serum albumin, bilirubin, prothrombin time, partial thromboplastin time, international normalized ratio) were all tested.

Serum FABP1 was measured using the enzyme-linked immunosorbent assay (ELISA) technique. Sample processing and washing steps were performed using an automated ELISA plate washer (BioTek® ELx50, BioTek Instruments Inc., USA).

Radiological Assessment

The radiological evaluation employed abdominal ultrasonography to assess the size of the liver and spleen, detect focal lesions, and measure the diameter of the portal vein. Conventional B-mode ultrasonography screening was used to diagnose MASLD and NASH. Indicators of liver steatosis in MASLD patients included generalized elevated near-field ultrasound echo (bright liver), gradual attenuation of far-field ultrasound echo, vascular blurring, and greater echogenicity in the liver compared to the kidneys (20). This was verified by using the Controlled Attenuation Parameter (CAP) to evaluate the radiofrequency wave attenuation (dB/m) concurrently with the liver stiffness measurement. For the diagnosis of mild steatosis (≥ S1), moderate steatosis (≥ S2), and severe steatosis (= S3), the ideal cutoff was 248 dB/m, 268 dB/m, and 280 dB/m, respectively (21) The stiffness of the liver was measured using Fibro Scan, a noninvasive method for assessing hepatic fibrosis.

Fibrosis Scoring Systems

Using Controlled Attenuation Parameter (CAP) to measure fat (steatosis) and Liver Stiffness Measurement (LSM) to evaluate scarring (fibrosis/cirrhosis) concurrently in a painless ultrasound, FibroScan aids in the fatty liver diagnosis (MAFLD/NAFLD) and offers a non-invasive method to stage the disease (S0-S3 for fat, F0-F4 for fibrosis) and monitor its progression without the need for a biopsy. (22).

The Fibrosis-4 (FIB-4) index is computed as follows: Age (years) × AST (U/L) / [Platelet count (10∘/L) × √ALT (U/L)]. If the score is less than 0.5, there is no major fibrosis; if it is greater than 0.5, there is liver fibrosis; if it is greater than 1.5, there is likely cirrhosis. The platelet count (×10−/L) divided by the AST (IU/L) yields the AST to Platelet Ratio Index (APRI), which is then multiplied by 100. The NAFLD Fibrosis Score (NFS) is used to classify patients based on their fibrosis risk; values < − 1.5 indicate low probability, scores between − 1.5 and 1.67 indicate intermediate probability, and scores > 0.67 indicate high probability of advanced fibrosis.

Statistical analysis

SPSS version 26 was used to analyze the data using both analytical and descriptive statistics. Both quantitative and qualitative metrics, such as mean, standard deviation, median, and interquartile range, were included in descriptive statistics. Several tests were used in analytical statistics: For normally distributed data, use the student’s t-test; for non-normally distributed data, use the Mann-Whitney test; for qualitative variable associations, use the Chi-square test; and for correlations, use the Pearson correlation coefficient. From no correlation to perfect correlation, the coefficient of correlation varies. Sensitivity and specificity metrics were used to determine the ideal cut-off value, and the AUC value indicated diagnostic accuracy.

Results

Case-control research was conducted with 80 participants in total. Two groups of patients were set up. Group B comprised 20 seemingly healthy individuals who were age and sex matched to the patient group, while Group A had 60 patients with MASLD diagnoses.

The MASLD and control groups do not differ statistically substantially in terms of age, sex distribution, weight, height, body mass index, or waist circumference ($p > 0.05$ for all). The MASLD group had significantly higher rates of hypertension and diabetes mellitus than the control group ($p = 0.022$ and 0.030, respectively). **(**Table 1**).**

Liver enzyme values, including AST and ALT, were considerably higher in the MASLD patients than in the control group. Serum albumin was considerably lower in the MASLD group, despite modest but significantly greater total protein levels. Total and direct bilirubin levels did not significantly differ between the two groups. **(Table 2).**

Significant hematological and metabolic abnormalities, including reduced hemoglobin levels and dyslipidemia—a condition characterized by elevated triglyceride and cholesterol levels and decreased HDL—were observed in MASLD patients. The MASLD group also had inadequate postprandial glucose control. Despite comparable regular hematological values, these findings demonstrate the connection between MASLD, dyslipidemia, and postprandial hyperglycemia **(Table 3).**

There is a clear association between raised L-FABP and MASLD, as seen by the much greater serum L-FABP levels in the MASLD group when compared to controls ($p < 0.001$). This result lends credence to L-FABP's possible function as a liver biomarker involvement and hepatic metabolic dysfunction in MASLD patients (**Table 4).**

The average FIB-4 score in the MASLD group was low (0.33 ± 0.1), indicating minimal fibrosis. The APRI score showed a low mean value (0.99 ± 0.38; range 0.21–1.6**).(Table 5)**

Most patients had early fibrosis (F0–F1: 66.7%), and fewer had advanced fibrosis (F2–F4: 33.4%), according to the Fibrosis stages by FibroScan. According to these noninvasive fibrosis indices, the majority of MASLD patients in this group appeared to have mild to moderate liver fibrosis Also, most patients had moderate to severe steatosis. S2 and S3 made up 75% of the cases, which means there was a high amount of fat in the studied MASLD group. Only 25% had mild or no steatosis (S0-S1) **(Table 6).**

Patients with severe fibrosis (NFS > 2) had considerably higher L-FABP levels (8.1 ± 1.5 ng/ml) than those without fibrosis (5.6 ± 0.9 ng/ml), with a highly important difference ($p < 0.001$). (**Table 7).**

Higher levels of L-FABP are linked to increased hepatocellular damage, with significant positive correlations to liver enzymes ALT ($r = 0.559$, $p < 0.001$) and AST ($r = 0.574$, $p < 0.001$). A slight negative correlation with total protein ($r = -0.282$, $p = 0.029$) suggests potential hepatic synthetic dysfunction. L-FABP is a more reliable marker of liver injury than demographic or general biochemical factors, as no

significant correlations with age, BMI, waist circumference, albumin, total bilirubin, or direct bilirubin were found. **(Table 8**, Fig. 1**).**

The fibrosis indices FIB-4 ($r = 0.446$, $p < 0.001$), APRI score ($r = 0.561$, $p < 0.001$), and NAFLD fibrosis score ($r = 0.885$, $p < 0.001$) all had strong positive correlations with L-FABP, as shown in **Table 9 and** Fig. 2.

With an AUC of 0.9 ($p < 0.001$), an L-FABP cut-off point of 4.05 ng/ml demonstrated good diagnostic performance for MASLD and high overall accuracy. The specificity was 50%, indicating a moderate ability to exclude non-MASLD cases, while the sensitivity was 95%, indicating that the majority of MASLD cases were correctly identified. This predictive value's robustness is confirmed by the 95% confidence interval (0.831–0.972), **(Table 10, Fig. 3).**

For predicting fibrosis among MASLD patients, an L-FABP cut-off of 6.5 ng/ml showed excellent diagnostic accuracy with an AUC of 0.963 ($p < 0.001$). The sensitivity was 95%, indicating most patients with fibrosis were correctly identified, and specificity was 80%, reflecting a high ability to correctly exclude patients without fibrosis. The 95% CI (0.921–1) confirms the reliability of this cut-off as a noninvasive liver fibrosis **(table 11**, Fig. 4**).**

Univariate analysis identified L-FABP as a strong predictor of liver fibrosis (OR = 0.047, 95% CI: 0.008–0.266, $p < 0.001$), with higher levels correlating to increased fibrosis risk. Other predictors included ALT, AST, APRI score, and hypertension. In multivariable analysis, L-FABP remained an independent predictor of liver fibrosis (OR = 0.025, 95% CI: 0.001–0.882, $p = 0.043$) after adjusting for confounders, confirming its role as a noninvasive indicator in MASLD individuals **(Table 12).**

As the fibrosis stages of MASLD patients progress, **Table 13** shows a statistically significant increase in serum L-FABP levels. The degree of fibrosis shown a strong correlation with mean L-FABP concentrations, which increased from 4.9 ± 0.66 ng/mL at F0 to 10.4 ± 2.5 ng/mL at F4. Significant variations in L-FABP levels across fibrosis grades were confirmed by one-way ANOVA ($F = 59.789$, $p < 0.001$), indicating its potential as a non-invasive biomarker for evaluating and differentiating liver fibrosis stages.

Patients who had hepatic steatosis (grades S1–S3) had higher mean serum L-FABP levels compared to those without steatosis (S0); however, this increase did not exhibit a consistent pattern with steatosis severity. Statistical analysis indicated no significant correlation between serum L-FABP levels and steatosis degree, with no notable differences in L-FABP across the groups ($F = 1.51$, $p = 0.207$). **(Table 14)**

Discussion

According to Ando and Jou (23)In the industrialized world, MASLD is the most common cause of chronic liver disease, and includes a range of conditions, with some individuals developing cirrhosis and hepatocellular cancer (24). The liver biopsy is still the most accurate for diagnosis (13). Effective noninvasive techniques are preferred in clinical practice for MASLD identification, illness process tracking, and therapy impact monitoring (15).

Our findings regarding demographic and anthropometric parameters are consistent with those reported by **Abdulaziz et al. and Bahnasawy et al.**, who found that there was no obvious age difference., gender, and height in MASLD group and control group (25, 26). Furthermore, according to **Akbal et al.**, there was no age or gender difference between individuals with NAFLD and controls, but The MASLD group's BMI was greater than the controls'.(27).

The BMI of the patients and controls did not differ. This finding contrasts with the traditional view that the association between metabolic liver disease and excess body weight is challenged by growing evidence that MASLD can also occur in people with a normal BMI, a phenotype known as lean MASLD (28, 29).

Elevated blood glucose is recognized to be closely linked to fatty liver disease. Thirty-eight patients in the MASLD group (47.5%) had diabetes mellitus, which is consistent with the findings of other publications, including **Assim et al.** (30) who reported that patients with type 2 diabetes mellitus have a high prevalence of MASLD, and **Chen et al.'s study** (31), which found a positive correlation between type 2 DM status and the prevalence of hepatic steatosis and fibrosis. Furthermore, the study by **Marieke et al.** found that 20% of Type 1 DM patients and 76% of Type 2 DM patients had fatty liver (32).

Regarding hypertension, consistent with our study, **Mohamed et al**. found that 36.25% of our MASLD patients had the condition (9). Similarly, other investigations found that MASLD independently contributed to the onset of hypertension and vice versa. There is a substantial correlation between MASLD and hypertension, according to **Yang et al.** (33)and Gerui et al(9). Insulin resistance, systemic inflammation, oxidative stress, sympathetic nervous system and renin-angiotensin-aldosterone system activation, dysbiosis of the gut microbiota, hormonal influences, and genetic factors are some of the hypothesized mechanisms underlying this relationship (34).

The L-FABP level in our study was greater in MASLD patients than in healthy controls, resulting in a statistically significant difference across all analyzed groups. This finding was consistent with that of **Abdulaziz et al.** (25). They found that, at 188.6 ± 34.94 and 137.7 ± 13.05, respectively, the L-FABP serum levels in the MASLD group (group I) were statistically substantially greater than those in the control group (group II). Furthermore, according to **Akbal et al.**, L-FABP was higher in MASLD patients than in healthy individuals. ($p < 0.001$). (27).

Similarly, **Mohamed et al.** discovered that the L-FABP levels in the blood was statistically considerably greater in the MASLD group (195.8 ng/mL ± 47.7) than in the control group (141.9 ng/mL ± 13) (9). Additionally, prior studies have indicated that serum L-FABP is a specific and sensitive biomarker for

diagnosing liver damage in MASLD.(26, 35, 36). Liver cells contain L-FABP, which has a very modest molecular weight. Due to its characteristics, LFABP increases even in cases of mild cell damage. Small proteins circulate in the blood more quickly than large proteins because hepatocytes lack an interstitial barrier and are in direct contact with the blood. (37).

In this study, non-invasive fibrosis assessments indicated a low risk of advanced fibrosis, with most patients showing minimal to mild hepatic involvement based on FIB-4 and APRI scores. The majority were classified in early fibrosis stages (F0–F1), reinforcing the utility of non-invasive scores for early risk assessment. Additionally, 75% of patients exhibited moderate to severe steatosis (S2 and S3), while only 25% had mild or no steatosis (S0-S1).

These findings are consistent with earlier research showing that early-stage fibrosis predominates in populations with MASLD and NAFLD. Using FibroScan, **Amernia et al**. found that while fewer patients had advanced fibrosis (F3: 14.1%; F4: 7.3%), most patients were classified as F1 (45.9%) or F2 (32.7%) (38). *Also*, **Alam et al.** studied 255 patients with type 2 diabetes mellitus and NAFLD (mean age 45 years), reporting that early fibrosis remained predominant (F1: 71%), with smaller proportions in F2 (8.6%), F3 (11.8%), and F4 (8.6%), underscoring the influence of metabolic comorbidities on disease progression (39).

In contrast, Larger population-based studies, on the other hand, have reported higher rates of advanced fibrosis; **Younossi et al.** found that 35% of 17,792 MASLD patients had advanced fibrosis (≥ F3), demonstrating the influence of risk profile and population size on the prevalence of fibrosis (40).

In the current investigation, MASLD patients with severe fibrosis (NFS > 2) had much greater L-FABP levels than those without fibrosis, indicating a clear correlation between elevated L-FABP and hepatic fibrotic load. Serum L-FABP may be used as a noninvasive indicator for evaluating inflammation and fibrosis in NAS patients, according to another study that discovered a relationship between elevated blood L-FABP levels and the degree of inflammation and fibrosis in individuals with non-alcoholic steatohepatitis (41). Additionally, **Akbal et al.** showed that blood levels of LFABP were greater in people with fatty liver disease that is not caused by alcohol. L-FABP levels were associated with persistent liver injury. (27).

Additionally, compared to those with grade II and I, the L-FABP level was significantly higher in group I and II cases with steatosis grade III(26). Thus, the degree of steatosis and the level of L-FABP were positively correlated. The study by **Adulaziz et al.** revealed similar results(25).

In our study, an L-FABP cut-off value of 4.05 ng/mL demonstrated excellent diagnostic accuracy for MASLD (AUC = 0.90, $p < 0.001$), with high sensitivity (95%) and moderate specificity (50%). The narrow 95% confidence interval (0.831–0.972) supports the robustness of L-FABP as a diagnostic marker.

According to **Mohamed et al.'s** study, ROC curve analysis of L-FABP as a MASLD diagnostic test revealed that, at the threshold value > 145 ng/mL, it distinguished MASLD patients from healthy individuals, with

sensitivity, specificity, positive and negative predictive values of 88.7%, 85%, 95.9%, and 65.4%, respectively. (9).

LFABP can be used to distinguish MASLD from healthy controls with a cut-off value of 222.54 ng/mL (80% sensitivity and 80% specificity) and positive and negative predictive values of 82% and 81%, respectively. At a cut-off value of 284 ng/mL, L-FABP demonstrated 73% sensitivity and 100% specificity, with positive and negative predictive values of 79% and 100%, respectively. (27).

Furthermore, the receiver operating curve (ROC) for L-FABP showed an area under the curve (AUC) of 0.839 at a cut-off point of 151.1 ng/mL, with sensitivity, specificity, positive and negative predictive values of 83.3%, 71.8%, 31.3%, and 96.6%, respectively; at a cut-off point of 189.5 ng/mL, the AUC was 90%, 85%, 95.4%, and 70.8%, respectively, which was statistically significant ($p < 0.001$) (25).

Our study identified significant positive correlations between serum L-FABP levels and noninvasive fibrosis indices, especially with the NAFLD fibrosis score. Higher L-FABP levels were associated with worsening hepatic fibrosis. Furthermore, with a cut-off value of 6.5 ng/ml producing high sensitivity and specificity in differentiating fibrotic from non-fibrotic cases, L-FABP showed excellent diagnostic performance for predicting liver fibrosis in MASLD patients.

A similar study by **Mohamed et al.** discovered a favorable correlation between LFABP and the level of fatty liver steatosis identified by fibroscan and ultrasound, as well as the degree of fibrosis ($p < 0.001$) (9). Additionally, **Badawy et al.** found associations between LFABP and ultrasound grades in the identification of MASLD (25).

Also, A positive association was observed ($p < 0.001$) between LFABP and the Fatty Liver Index (FLI) score. This indicates that the identification of fibrosis grades is significantly correlated with LFABP and FibroScan (9).

The regression analysis further supports the role of L-FABP as a strong predictor of liver fibrosis in MASLD. In univariate analysis, Along with well-known indicators of liver injury and fibrosis like ALT, AST, APRI score, and hypertension, L-FABP demonstrated a strong correlation with the risk of fibrosis, highlighting its intimate connection to hepatic damage and the advancement of fibrosis.

This result also corroborated those of **Akbal et al.** (27), who found a connection between high LFABP levels and BMI, diabetes, AST, ALT, and GGT levels. These results suggest that liver cell injury, fatty infiltration, and dyslipidemia may raise the serum level of L-FABP.

In this study, serum L-FABP levels were compared among patients with varying degrees of hepatic steatosis (S1–S3) and those without (S0). Although L-FABP levels were higher in steatosis patients, these differences were not statistically significant, nor was there a direct correlation between the severity of steatosis and L-FABP levels. The findings suggest that L-FABP may not reliably indicate hepatic fat storage degree, indicating its closer association with fibrosis or hepatocellular damage than with steatosis itself.

Conclusion

A possible noninvasive biomarker for identifying MASLD and evaluating its fibrotic development is serum L-FABP. It improves the identification of patients at risk for advanced fibrosis by correlating fibrosis scores, steatosis levels, and traditional liver damage markers.

Abbreviations

Abbreviation	Full Term
MASLD	Metabolic Dysfunction-Associated Steatotic Liver Disease
NAFLD	Non-Alcoholic Fatty Liver Disease
MASH	Metabolic Dysfunction-Associated Steatohepatitis
NASH	Non-Alcoholic Steatohepatitis
HCC	Hepatocellular Carcinoma
L-FABP (FABP1)	Liver Fatty Acid-Binding Protein
FABPs	Fatty Acid-Binding Proteins
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
FIB-4	Fibrosis-4 Index
APRI	AST to Platelet Ratio Index
NFS	NAFLD Fibrosis Score
CAP	Controlled Attenuation Parameter
LSM	Liver Stiffness Measurement
ELISA	Enzyme-Linked Immunosorbent Assay
BMI	Body Mass Index
CBC	Complete Blood Count
LDL-C	Low-Density Lipoprotein Cholesterol
HDL-C	High-Density Lipoprotein Cholesterol
ROC	Receiver Operating Characteristic
AUC	Area Under the Curve
CI	Confidence Interval
OR	Odds Ratio
DM	Diabetes Mellitus

Declarations

Ethics approval and consent to participate:

The Institutional Review Board of Menoufia University's Faculty of Medicine granted ethical approval for the study. Before being included in the study, each subject provided written informed consent.

Consent for publication:

The publication was authorized in writing by each participant or their legal guardian.

Availability of data and material:

The datasets generated and/or examined in this study are not accessible to the public due to patient confidentiality and governmental data protection regulations; however, they can be obtained from the corresponding author upon reasonable request.

Competing interests

According to the writers, they have no conflicting interests.

Funding

The authors declare no funding**.**

Authors' contributions

- Sherihan Mohamed Mohamed Yussef: study design, data collection, statistical analysis, manuscript drafting.
- Prof. Ehab Ahmed Abdelatti: supervision, critical revision of manuscript.
- Prof. Eman Abdelsamie Mahmoud: supervision and study guidance.
- Dr. Hany Abdelbari Elbasuony: data interpretation and clinical supervision.
- Dr. Ezzat Mohamed Abdalla: laboratory analysis and interpretation.
- Dr. Belal Abd Elmohsen Montaser: statistical analysis and revision of the manuscript.
- All authors read and approved the final manuscript.

Acknowledgements

None

References

1. Jeong S, Lim Y, Lee SK, Han HW (2023) Letter regarding "Non-alcoholic fatty liver disease: definition and subtypes". Clin Mol Hepatol 29:810.
2. Hashimoto Y, Hamaguchi M, Okamura T, Nakanishi N, Obora A, Kojima T et al (2022) Metabolic associated fatty liver disease is a risk factor for chronic kidney disease. J Diabetes Investig 13:308–316.

3. European Association for the Study of the Liver, European Association for the Study of Diabetes, European Association for the Study of Obesity (2024) EASL-EASD-EASO clinical practice guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). Obes Facts 17:374–444.
4. Li J, Ha A, Rui F, Zou B, Yang H, Xue Q et al (2022) Meta-analysis: global prevalence, trend and forecasting of non-alcoholic fatty liver disease in children and adolescents, 2000–2021. Aliment Pharmacol Ther 56:396–406.
5. Riazi K, Azhari H, Charette JH, Underwood FE, King JA, Afshar EE et al (2022) The prevalence and incidence of NAFLD worldwide: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 7:851–861.
6. Tomah S, Hamdy O, Abuelmagd MM, Hassan AH, Alkhouri N, Al-Badri MR et al (2021) Prevalence of and risk factors for non-alcoholic fatty liver disease (NAFLD) and fibrosis among young adults in Egypt. BMJ Open Gastroenterol 8:e000780.
7. Younossi ZM, Karrar A, Pierobon M, Birerdinc A, Stepanova M, Abdelatif D et al (2018) An exploratory study examining how nano-liquid chromatography–mass spectrometry and phosphoproteomics differentiate patients with advanced fibrosis in non-alcoholic fatty liver disease. BMC Med 16:170.
8. Higuchi N, Kato M, Tanaka M, Miyazaki M, Takao S, Kohjima M et al (2011) Effects of insulin resistance and hepatic lipid accumulation on hepatic mRNA expression levels of apoB, MTP and L-FABP in non-alcoholic fatty liver disease. Exp Ther Med 2:1077–1081.
9. Mohamed MM, Mohamed MS, Salama MM, Ahmed GA, Hassan HM, George TMA (2024) Liver fatty acid-binding protein as a diagnostic marker for non-alcoholic fatty liver disease. QJM 117(Suppl 2):hcae175.
10. Başar Ö, Akbal E, Köklü S, Tuna Y, Koçak E, Başar N et al (2013) Increased H-FABP concentrations in nonalcoholic fatty liver disease. Herz 38:417–422.
11. Church RJ, Kullak-Ublick GA, Aubrecht J, Bonkovsky HL, Chalasani N, Fontana RJ et al (2019) Candidate biomarkers for the diagnosis and prognosis of drug-induced liver injury. Hepatology 69:760–773.
12. El-Sayed Awadallah A, Mohamed Amer Afify M, Hendawy El-Shahat A, Mohamed Abu-Mohamed N (2022) Role of FABP1 as a diagnostic biomarker for non-alcoholic fatty pancreatic disease. Al-Azhar Med J 51:1619–1636.
13. Wong VWS, Chan WK, Chitturi S, Chawla Y, Dan YY, Duseja A et al (2018) Asia–Pacific Working Party on NAFLD guidelines 2017—part 1: definition, risk factors and assessment. J Gastroenterol Hepatol 33:70–85.
14. Brunt EM, Wong VW-S, Nobili V, Day CP, Sookoian S, Maher JJ et al (2015) Nonalcoholic fatty liver disease. Nat Rev Dis Primers 1:15080.
15. Cai J, Zhang XJ, Li H (2019) Progress and challenges in the prevention and control of nonalcoholic fatty liver disease. Med Res Rev 39:328–348.

16. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M et al (2018) The diagnosis and management of nonalcoholic fatty liver disease. Hepatology 67:328–357.
17. Chin JL, Pavlides M, Moolla A, Ryan JD (2016) Non-invasive markers of liver fibrosis: adjuncts or alternatives to liver biopsy? Front Pharmacol 7:159.
18. Newsome PN, Sasso M, Deeks JJ, Paredes A, Boursier J, Chan WK et al (2020) FibroScan-AST (FAST) score for identifying patients with NASH and fibrosis. Lancet Gastroenterol Hepatol 5:362–373.
19. Sanyal AJ, Foucquier J, Younossi ZM, Harrison SA, Newsome PN, Chan WK et al (2023) Enhanced diagnosis of advanced fibrosis using FibroScan-based scores. J Hepatol 78:247–259.
20. Farrell GC, Chitturi S, Lau GK, Sollano JD (2007) Guidelines for NAFLD management in Asia–Pacific region. J Gastroenterol Hepatol 22:775–777.
21. Zhang X, Wong GL-H, Wong VW-S (2019) Application of transient elastography in NAFLD. Clin Mol Hepatol 26:128.
22. Oeda S, Tanaka K, Oshima A, Matsumoto Y, Sueoka E, Takahashi H (2020) Diagnostic accuracy of FibroScan. Diagnostics 10:940.
23. Ando Y, Jou JH (2021) Nonalcoholic fatty liver disease and recent guideline updates. Clin Liver Dis 17:23–28.
24. McPherson S, Hardy T, Henderson E, Burt AD, Day CP, Anstee QM (2015) Evidence of NAFLD progression using paired biopsies. J Hepatol 62:1148–1155.
25. Bahnasawy SAM, El Gammal NES, El Attar NI, El-Gebaly AM (2023) Liver fatty acid-binding protein as a diagnostic marker for NAFLD. Egypt J Hosp Med 91:5345–5352.
26. Abdulaziz BA, Abdu SA, Amin AM, El Menyawi AKAH, Ahmed A, Khalil MA et al (2019) Assessment of L-FABP as a diagnostic marker in NAFLD. Open J Gastroenterol 9:113–124.
27. Akbal E, Koçak E, Akyürek Ö, Köklü S, Batgi H, Şenes M (2016) L-FABP as a diagnostic marker for NAFLD. Wien Klin Wochenschr 128:48–52.
28. Wattacheril J, Sanyal AJ (2016) Lean NAFLD: an underrecognized outlier. Curr Hepatol Rep 15:134–139.
29. Denkmayr L, Feldman A, Stechemesser L, Eder SK, Zandanell S, Schranz M et al (2018) Lean NAFLD histological phenotype. J Clin Med 7:562.
30. Alfadda AA, Sherbeeni SM, Alqutub AN, Aldosary AS, Aldaghri NM, Taylor-Robinson SD et al (2022) Transient elastography in NAFLD. Saudi J Gastroenterol 28:426–433.
31. Chen J, Hu P, Wang Y, Zhu Z (2022) Association between diabetes and liver fibrosis. BMC Endocr Disord 22:128.
32. de Vries M, El-Morabit F, van Erpecum KJ, Westerink J, Bac ST, Kaasjager HK et al (2022) NAFLD in type 1 and type 2 diabetes. Eur J Intern Med 100:77–82.
33. Yang D, Lan J, Cen J, Han Y, Hu H (2023) Hypertension and NAFLD association. Diabetes Metab Syndr Obes 16:345–363.

34. Golubeva JA, Sheptulina AF, Elkina AY, Liusina EO, Kiselev AR, Drapkina OM (2023) NAFLD and hypertension relationship. Biomedicines 11:2465.
35. Al Mazrouei N, ElGharbawy MM, Gamal M, Emad S, Mohamed AA, Ibrahim OM et al (2025) L-FABP as biomarker in MASLD pediatric patients. PLoS One 20:e0333581.
36. Şen İ, Dumlu Ş (2024) L-FABP as a biomarker in liver injury. Turk J Gastroenterol 35:568.
37. Pelsers MM, Morovat A, Alexander GJ, Hermens WT, Trull AK, Glatz JF (2002) L-FABP as a sensitive marker of hepatocellular damage. Clin Chem 48:2055–2057.
38. Amernia B, Moosavy SH, Banookh F, Zoghi G (2021) FIB-4 and APRI vs FibroScan in NAFLD. BMC Gastroenterol 21:453.
39. Alam MS, Kalam ST, Khan MI, Ahmed J, Saha R, Kamrul-Hasan A (2025) Comparison of FIB-4, APRI and AST/ALT ratio with FibroScan. Egypt Liver J 15:38.
40. Younossi ZM, De Avila L, Petta S, Hagström H, Kim SU, Nakajima A et al (2025) Predictors of fibrosis, clinical events and mortality in MASLD. Hepatology. doi:10.1097/HEP.0000000000000000.
41. Özenirler S, Degertekin CK, Erkan G, Elbeğ Ş, Tuncer C, Kandilc U et al (2013) Serum L-FABP correlation with liver histology in NASH. Hepatogastroenterology 60:1095–1100.

Tables

Table 1: Comparison between the studied group regarding sociodemographic data and medical history.

sociodemographic data	MASLD group (n=60)	Control group (n=20)	Test	p-value
Age			t=0.96	0.341
Mean ±SD	43.4±7.5	41.6±7.3		
Range	32 – 57	32 – 54		
Sex (n %)			χ2 =0.29	0.588
Male	20 (33.3)	8 (40)		
Female	40 (66.7)	12 (60)		
Weight(Kg)			t=0.19	0.846
Mean ±SD	95.3±8.4	95.7±6.5		
Range	80 – 125	88 – 110		
Height(m)			t=0.31	0.762
Mean ±SD	1.7±0.1	1.7±0.1		
Range	1.46 – 1.90	1.53 – 1.82		
BMI			t=0.50	0.618
Mean ±SD	33.9±3.3	34.3±3.2		
Range	29.03 - 41.79	30.37 – 40.40		
Waist circumference (cm)			t=0.08	0.935
Mean ±SD				
Range	113.9±12.8	113.7±12.4		
	96 – 140	100 – 135		
Medical History (n% %)				
DM				**0.030***
Yes	25 (41.7)	3 (15)	χ2 =4.69	
No	35 (58.3)	17 (85)		
HTN			χ2 =5.21	**0.022***
Yes	26 (43.3)	3 (15)		
No	34 (56.7)	17 (85)		

kg: kilogram; m: meter; **BMI:** body mass index; **cm:** centimeter; **DM**: diabetes mellitus; **HTN:** hypertension; **t:** student t-test **χ2**: Chi-square test. SD: Standard deviation. **BMI**: body mass index ***:** Statistically significant.

Table (2): Comparison between the studied group regarding liver enzymes and labs.

sociodemographic data	The MASLD group	The control group	Test	p-value
AST(u/L)			U=1.984	**0.047***
Mean±SD	42.5±31.5	21±4		
Range	11 – 131	11 – 26		
ALT(u/L)			U=2.361	**0.018***
Mean±SD	46.1±34.7	22.4±5.2		
Range	13 – 145	11– 32		
t..protein(g/dl)			t=2.03	**0.046***
Mean±SD	8.1±0.5	7.9±0.3		
Range	6 – 8.9	7.1 – 8.5		
Albumin(g/dl)			t=2.89	**0.005***
Mean±SD	4.1±0.4	4.4±0.2		
Range	2.8 – 5.0	4.1 – 4.8		
t.bil(mg/dl)			U=0.504	**0.614**
Mean±SD	0.4±0.2	0.3±0.1		
Range	0.18 – 10.6	0.23 – 0.69		
d.bil(mg/dl)			U=0.20	**0.839**
Mean±SD	0.3±1.1	0.2±0.1		
Range	0.06 – 8.80	0.10 – 0.33		

AST: aspartate aminotransferase; **ALT**: alanine aminotransferase; **t. protein**: total protein; **t. bil:** total bilirubin; **d. bil:** direct bilirubin **t**: student t-test **SD**: Standard deviation **U:** Mann-Whitney test *: Statistically significant, **: Statistically Highly significant

Table (3): Comparison between the studied group regarding the complete blood count, lipid prolife and blood glucose measurements.

sociodemographic data	The MASLD group	The control group	Test	p-value
Hb(g/dl)			t=4.47	**<0.001****
Mean ±SD	12.6±1.3	13.9±0.4		
Range	11.0 – 16.5	13.2 – 14.6		
platelets(*10^3/cmm)			t=0.15	**0.881**
Mean± SD	256.7±45.6	258.3±11.8		
Range	160 – 330	240 – 280		
WBCS(*10^3/cmm)			t=0.56	**0.578**
Mean ±SD	6.3±1.5	6.5±0.5		
Range	4.3 – 9.8	5.7 – 7.3		
Triglycerides(mg/dl)			t=7.20	**<0.001****
Mean± SD	180.6±50.7	94.4±28.8		
Range	79 – 324	45 – 150		
Cholesterol(mg/dl)			t=7.49	**<0.001****
Mean ±SD	214.9±31.5	157±24.6		
Range	141 – 330	100 – 200		
LDL(mg/dl)			t=0.37	**0.710**
Mean± SD	137.1±32.4	140.2±29.5		
Range	49 – 254	89 – 180		
HDL(mg/dl)			t=11.72	**<0.001****
Mean ±SD	43.6±7.3	67±8.9		
Range	30 – 71	45 – 80		
Fasting BS			U=0.85	**0.395**
Mean ±SD	107.9±40.5	89.7±3.0		
Range	75 – 300	84 – 95		
2 hr pp			U=2.06	**0.039***
Mean ±SD	152.9±65.9	116.8±4.0		
Range	85 – 350	108 – 123		

Hb: hemoglobin; **WBCs:** white blood cells; **platelets**: platelet count; **LDL**: low-density lipoprotein; **HDL:** high-density lipoprotein; **BS:** blood sugar; **2 hr pp**: 2-hour postprandial blood glucose. **t** = student t-test

.**SD**= Standard deviation **U**= Mann-Whitney test *****: Statistically significant, ****:** Statistically Highly significant.

Table (4): Comparison between the studied group regarding L-FABP

Variable	The MASLD group	The control group	Test	p-value
L-FABP(ng/ml)			t=5.898	<0.001**
Mean ±SD	6.4±1.6	4.1±0.99		
Range	3.9-13	2.8-6		

L-FABP: liver fatty acid–binding protein; **SD:** standard deviation; **t:** Student's t-test; *: Statistically significant.

Table (5): FIB-4 and APRI score results of the cases studied:

Variable	The MASLD group
FIB-4	
Mean ±SD	0.33±0.1
Range	0.15-0.57
APRI score	
Mean ±SD	0.99±0.38
Range	1.6 - 0.21

FIB-4: fibrosis-4 index; **APRI:** AST to platelet ratio index

Table (6): FibroScan results showing the degree of fibrosis and steatosis of the studied cases:

Fibrosis stages by FibroScan		
F0		22(36.7)
F1		18(30.0)
F2		7(11.7)
F3		10(16.7)
F4		3(5.0)
Degree of Steatosis by FibroScan	**CAP Score (dB/m)**	
S0	**150–248**	5 (8.3%)
S1	**248–260**	10 (16.7%)
S2	**260–280**	21 (35.0%)
S3	**> 280**	24 (40.0%)

F0–F4: fibrosis stages 0 to 4; SD: standard deviation; AST: aspartate aminotransferase **S0**: no steatosis; **S1**: mild steatosis; **S2** : moderate steatosis; **S3:** severe steatosis.

Table (7): Comparison between the cases with fibrosis (NFS>2) and non-fibrosis (NFS<2) regarding L-FABP

Variable	fibrosis (NFS>2)	non-fibrosis (NFS<2)	Test	p-value
L-FABP (ng/ml)			t=7.906	<0.001**
Mean ±SD	8.1±1.5	5.6±0.9		
Range	6.2 -13	3.9 – 7.1		

NFS: NAFLD Fibrosis Score

Table (8): Correlation between L-FABP and sociodemographic data and liver labs.

Variables	L-FABP	
	r	p-value
Age	0.092	0.483
BMI	0.172	0.188
Waist circumference	-0.072	0.585
ALT	0.559	<0.001**
AST	0.574	<0.001**
Total protein(g/dl)	-0.282	0.029*
Albumin(g/dl)	-0.222	0.089
Total billirubin (mg/dl)	0.155	0.238
Direct billirubin mg/dl)	0.138	0.294

L-FABP: liver fatty acid–binding protein; **BMI:** body mass index; **ALT**: alanine aminotransferase; **AST:** aspartate aminotransferase; g/dl: grams per deciliter; **r**: correlation coefficient. *: Statistically significant; **: Statistically Highly significant.

Table (9): Correlation between L-FABP and Fibro scan results

Variables	L-FABP	
	R	p-value
FIB-4	0.446	<0.001**
APRI score	0.561	<0.001**
NAFLD fibrosis score	0.885	<0.001**

L-FABP: liver fatty acid–binding protein; **FIB-4:** fibrosis-4 index; **APRI:** AST to platelet ratio index; **NAFLD**: nonalcoholic fatty liver disease; **r:** correlation coefficient; p-value: probability value indicating statistical significance; **AST**: aspartate aminotransferase; **: Statistically highly significant.

Table (10): ROC curve for L-FABP as a predictor for MASLD.

Cut-off point	AUC	P-value	CI (lower-upper limit)	Sensitivity	Specificity
4.05	0.9	**<0.001****	0.831 – 0.972	95.0%	50.0%

AUC: area under the curve; **CI**: confidence interval; **Sensitivity:** true positive rate; Specificity: true negative rate; **: Statistically highly significant.

Table (11): ROC curve for L-FABP as a predictor for fibrosis among the MASLD group.

Cut-off point	AUC	P-value	CI (lower-upper limit)	Sensitivity	Specificity
6.5	0.963	**<0.001****	0.921 – 1	95.0%	80%

AUC: area under the curve; **CI**: confidence interval; **Sensitivity:** true positive rate; Specificity: true negative rate; **: Statistically highly significant.

Table (12): Univariate and Multivariable analysis to assess L-FABP as a predictor of liver fibrosis, adjusting for confounders.

Variable	Formaldehyde exposure			
	Univariate analysis		Multivariable analysis	
	OR (95% CI)	P	OR (95% CI)	p
Age	0.978(0.910 – 1.051)	0.546		
Gender (Male)	2.667(0.753 – 9.450)	0.129		
BMI	0.919(0.780 – 1.082)	0.308		
Waist circumference	0.991(0.950 -1.034)	0.672		
DM	1.667(0.563 -4.934)	0.356		
HTN	3.857(1.243-11.968)	**0.019***	0.237(0.010-5.636)	0.237
ALT	0.942 (0.915-0.970)	**<0.001****	1.019(0.813-1.276)	0.872
AST	0.947(0.922 -0.973)	**<0.001****	1.072(0.835 – 1.375)	0.585
APRI score	0.869(0.806 - 0.937)	**<0.001****	0.701(0.401 – 1.375)	0.214
L-FABP	0.047 (0.008- 0.266)	**<0.001****	0.025(0.001 – 0.882)	0.043*

OR: odds ratio; **CI:** confidence interval; **BMI:** body mass index; **DM:** diabetes mellitus; **HTN:** hypertension; **ALT:** alanine aminotransferase; **AST:** aspartate aminotransferase; **APRI**: AST to platelet ratio index; **L-FABP:** liver fatty acid–binding protein; p-value: probability value indicating statistical significance.

Table (13): Comparison between the cases with fibrosis regarding L-FABP

Variable	F0	F1	F2	F3	F4	Test	p-value
L-FABP (ng/ml)						F=59.789	<0.001**
Mean ±SD							
Range	4.9±0.66	6.4±0.5	6.88±0.5	8.2±0.5	10.4±2.5		
	3.9-6	5.8 -7.1	6.2-7.6	7.3 – 9	8.1-13		

L-FABP: Liver Fatty Acid–Binding Protein; **F0–F4:** fibrosis stages (F0: no fibrosis, F1: mild, F2: moderate, F3: severe, F4: cirrhosis); **SD**: standard deviation; **F**: ANOVA F value; **p**: p value; ******: statistically significant.

Table (14): Comparison between the cases with steatosis regarding L-FABP

Variable	S0	S1	S2	S3	Test	p-value
L-FABP (ng/ml)					F=1.51	0.207
Mean ±SD						
Range	5.5±1.1	6.9±1.1	6.3±1.3	6.8±2		
	4 -8	5.3-8	3.9-9	4 - 13		

L-FABP: Liver Fatty Acid–Binding Protein; **S0–S3:** steatosis grades (S0: no steatosis, S1: mild, S2: moderate, S3: severe); **SD**: standard deviation**; F:** ANOVA F value; **p**: p value.

Figures

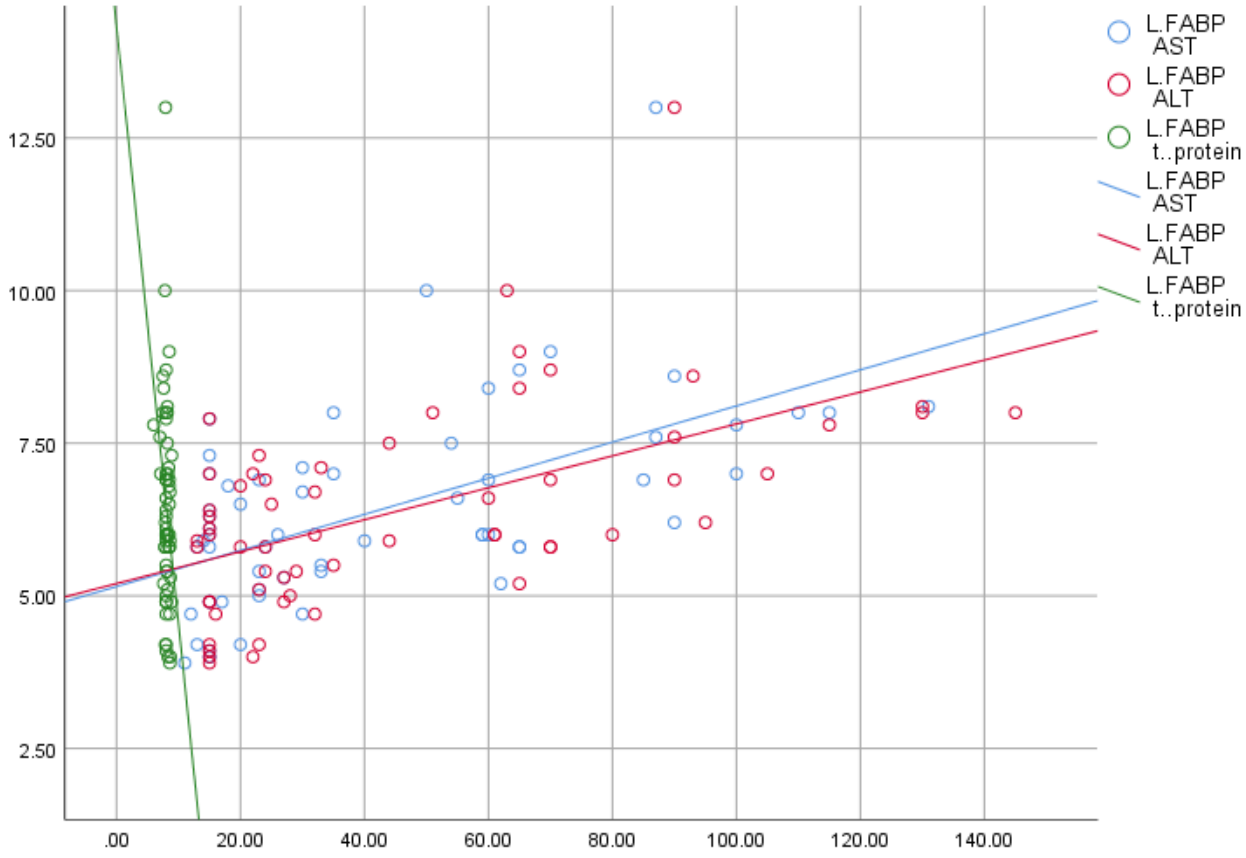


Figure 1

Correlation between L-FABP, AST, ALT, and total protein.

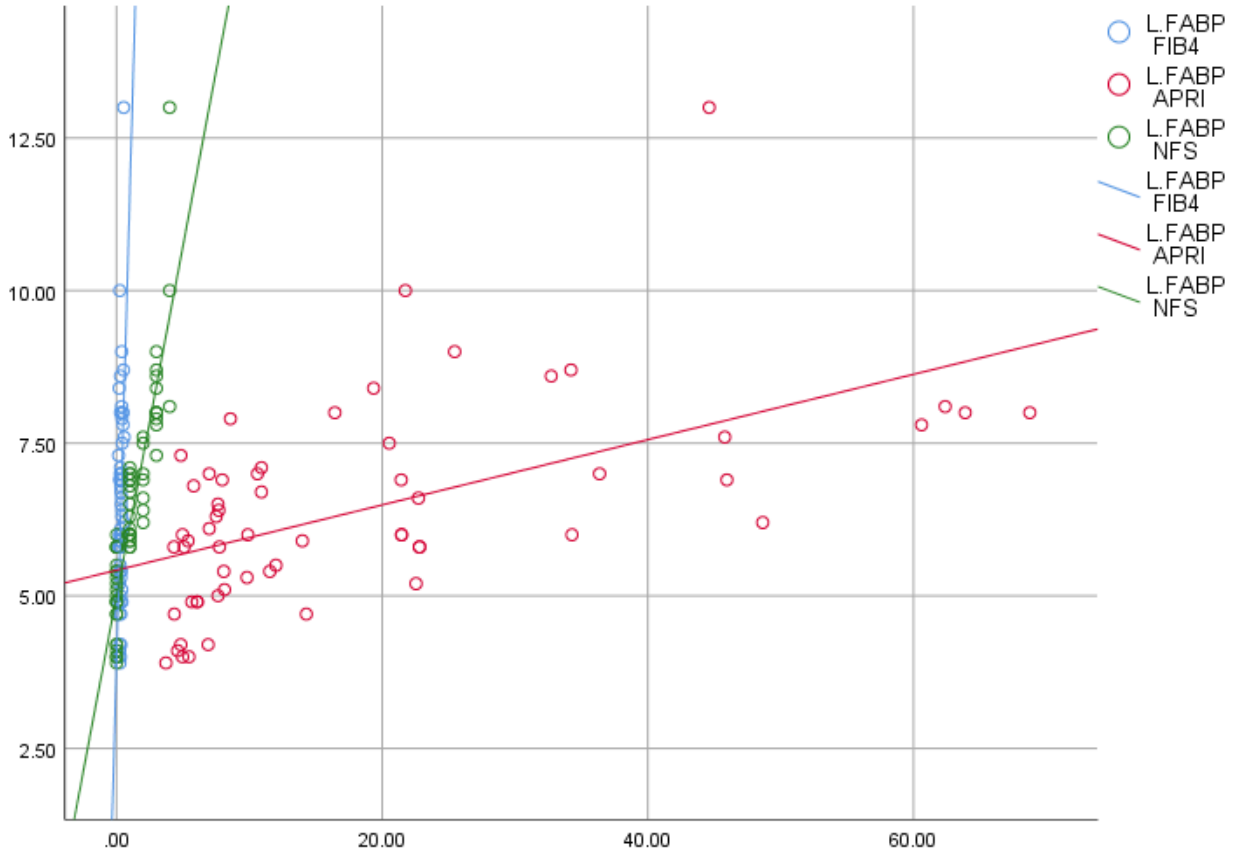


Figure 2

Correlation between L-FABP and Fibro scan results.

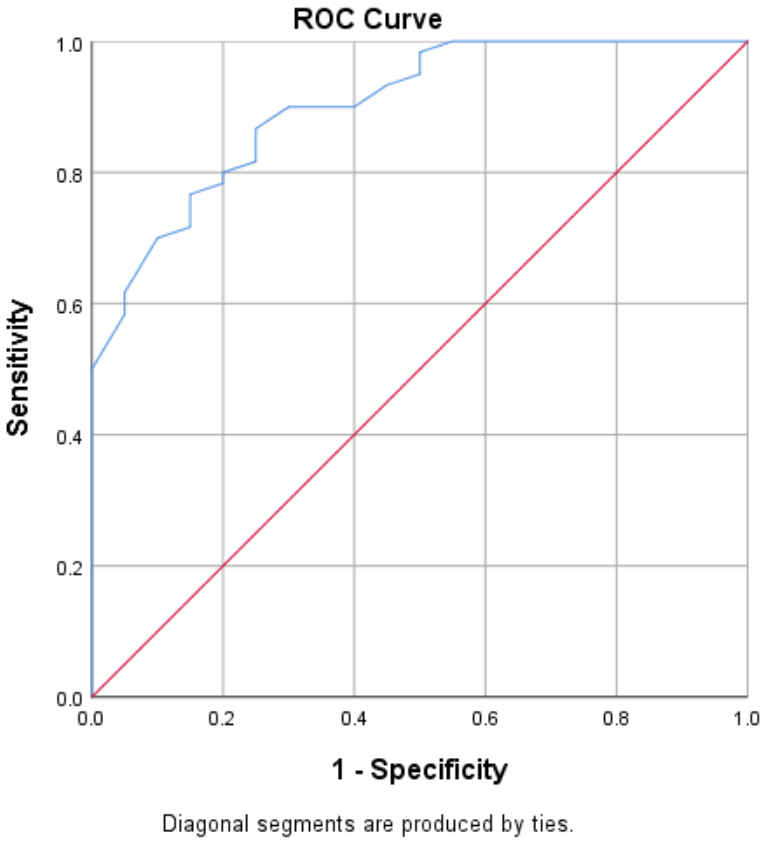


Figure 3

ROC curve showing the L-FABP as a predictor for MASLD.

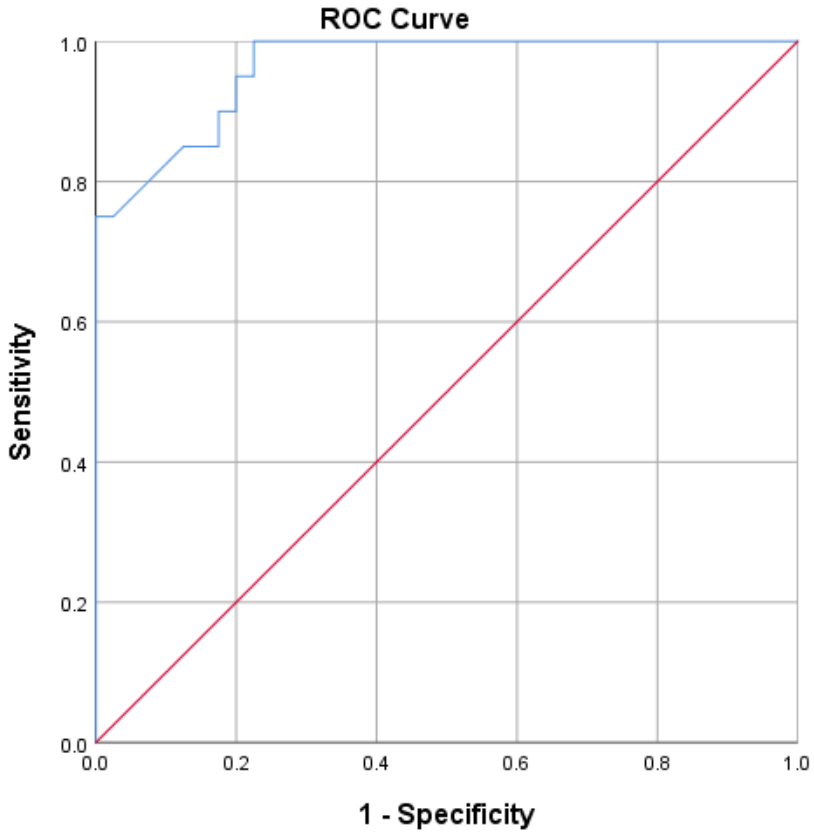


Figure 4

ROC curve showing the L-FABP as a predictor for hepatic fibrosis.