# Fibroscan and Low-Density Lipoprotein Versus Non-invasive Markers (APRI test and FIB-4) As Determinants of Severe Liver Fibrosis in Egyptian Diabetic Patients With Non-Alcoholic Fatty Liver Disease

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# ORIGINAL ARTICLE

# Fibroscan and Low-density Lipoprotein Versus Noninvasive Markers (APRI Test and FIB-4) as Determinants of Severe Liver Fibrosis in Egyptian Diabetic Patients with Nonalcoholic Fatty Liver Disease

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## Abstract

*Background*: Type 2 Diabetes Mellitus (T2DM) cases commonly have nonalcoholic fatty liver disease (NAFLD) that can develop into severe liver fibrosis. Clinical implications might arise from the early detection of hepatic fibrosis.

*Aim*: The aim of this study is to evaluate the role of noninvasive scores (APRI score and FIB-4), Fibroscan and low-density lipoprotein in predicting Egyptian patients with NAFLD who have severe liver fibrosis.

*Patients and methods*: A prospective cohort study was carried out in the heptogastroentrology and infectious disease Al-Hussien University Hospital and The National Hepatology and Tropical Research Institute (NHTMRI) over a 3-years period. 90 patients attended the outpatient clinic who had NAFLD were enrolled in the study on a prospective basis, aged 18 to 70 years old.

*Results*: The cases was separated into two groups diabetic and nondiabetic Concerning the correlation between APRI test and (FIB-4, fibrosis LSM, steatosis CAP, and lab tests show significant positive correlation as regard Fib-4, fibrosis Lsm, AST, and ALT, and significant negative correlation as regard platelet and FBS, and the relationship between Fib-4 and fibrosis LSM and steatosis CAP and lab tests show significant positive correlation as regard fibrosis LSM, Age, and AST, and significant negative correlation as regard platelets and urea.

*Conclusion*: The combination of Fibroscan, APRI score,LDL-c and FIB-4 techniques gives a useful approach for evaluating liver fibrosis in NAFLD cases.

*Keywords:* Diabetic patients, Fibroscan, Liver fibrosis, Non alcoholic fatty liver disease

## 1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is one of the most frequent causes of liver disease around the world. It is expected to overcome alcoholic liver disease as the most frequent reason for end-stage hepatic disease in the next 10 years.[1]

It includes a wide range of clinical and histological signs, starting from simple steatosis to steatohepatitis, fibrosis, and cirrhosis.[2]

NAFLD is associated with an abnormal buildup of fat in the liver that is not caused by excessive alcohol usage, viral hepatitis, or drugs which be able to cause fatty liver.[3]

There are Important risk factors for NAFLD as type 2 diabetes (T2DM), hypertension, hypertriglyceridemia, hyperlipidemia and obesity.[4]

The liver is a major cause of insulin resistance which is a key part of how T2DM develops and how it gets worse. NAFLD is mostly happen if you have

DM, and about 70% of people with T2DM have NAFLD.[5]

A leading reason for chronic liver disease is NAFLD which frequently has severe effects as decompensated hepatic cirrhosis and hepatocellular cancer.[6]

Only 24% of people with high cholesterol have NAFLD. This happens more often with persons who have hypertriglyceridemia and mixed hyperlipidemia, where the rates are 50% and 60%, respectively. Hypertriglyceridemia, low HDL-C, more dense and small LDL-C are all linked to NAFLD. About 60–70% of people with NAFLD also have dyslipidemia.[7]

Abdominal ultrasonography, measurement of the lipid profile and liver functions, excluding the presence of hepatitis B and C, alcohol poisoning, and testing for insulin resistance (IR) are all required for primary assessment of early stages of fatty liver.[8]

Liver biopsy is the best way to find out if someone has NAFLD, although it occasionally causes complications, including bleeding, bile leakage, infections, and other potentially catastrophic problems.[9]

New noninvasive laboratory and radiographic diagnostic methods have developed during the previous ten years to avoid the problems of liver biopsies when finding out hepatic fibrosis in NAFLD.[10]

Numerous researches had indicated the use of imaging and serological markers as non-invasive techniques for assessing fibrosis in NAFLD.[11]

Recent research demonstrates that the ultrasound-based controlled attenuation parameter value applied in the TE method may be used to predict the extent of steatosis in NAFLD patients.[10]

Aim of the study to evaluate the role of noninvasive scores (APRI score and FIB-4), fibroscan and low-density lipoprotein in predicting Egyptian patients with NAFLD who have severe liver fibrosis.

## 2. Patients and methods

A prospective cohort study was carried out in the heptogastroentrology and infectious disease Al-Hussien University Hospital and The National Hepatology and Tropical Research Institute (NHTMRI). 90 patients attended the outpatient clinic who had NAFLD over a 3-years period.

(1) $\text{FIB-4} = \text{age (year)} \times \text{AST (IU/l)/platelet count} (\times 10^9/l) \times \sqrt{\text{ALT (IU/l)}}$.[12]
(2) APRI Score = (AST/Upper Limit Normal AST) $\times$ 100]/Platelets $(10^9/l)$.[13]

Inclusions Criteria: Age (18–70 years), sex (male or female), DM (fasting blood sugar levels more than 126 g/dl), nondiabetic patients, patients identified as having NAFLD based on abdominal ultrasound examination (Hyperechoic liver, in which the liver echo-texture was brighter than that of the kidney, with indistinct vascular boundaries and a significant decrease in ultrasound signal), and cases who agreed to take part in the research.

Exclusions Criteria: Patients with alcoholic liver disease, patients taking Hepatotoxic drugs like methotrexate and corticosteroids, patients with advanced hepatic disease, cardiac failure, and hepatic congestion, patients that could not do a fibroscan examination due to a very high body mass index (BMI) and other causes of liver disease as viral, metabolic, autoimmune diseases.

Ethical Considerations: before enrollment, each participant gave their signed, informed permission. Written consents were approved by the ethical committee of Al Hussein Hepatology, Gastroenterology department and the National Hepatology and Tropical Medicine Research Institute (NHTMRI).

### 2.1. Methods

Initial Assessment: The outpatient clinic was the first place where all patients were checked. A comprehensive investigation and evaluation were conducted. This included:

History: Name, age, sex, place of residence, employment, marital status, certain behaviors of medical and surgical relevance are all examples of demographic information.

Examination: General examination for vital signs are heart rate, respiratory rate, blood pressure, and temperature. Other systems examination, local examination of the liver was done to show site, size, surface, border, and presence of lymph node metastases. Physical examination included: BMI: Weight (Kg)/Height (m)$^2$ (Normal: <25) waist Circumference, which is calculated horizontally at the level of the navel without compressing the skin (Normal: Males 78:94 cm, Females 64:80 cm).

Laboratory investigations: Complete blood count (CBC) is including total leucocytic count (Total and Differential), red blood cells (RBCs), hemoglobin (Hb), and platelet count, among the laboratory tests that were performed. Bilirubin (total and direct), total proteins, serum albumin, alanine transferase (ALT), aspartate transferase (AST), and alkaline phosphatase (ALP) are all included in the list of liver function tests (LFTs), kidney function tests (KFTs), such as serum urea and creatinine. Prothrombin time (PT) and the International Normalization Ratio are two components of the coagulation profile (INR). Lipid profile is including Serum cholesterol, triglycerides and low-density lipoproteins (LDL), viral

markers like hepatitis B surface antigen (HBsAg) and hepatitis C antibodies (HCV Ab).

Abdominal ultrasonography: equipment: philips envisor C HD.

### 2.2. Fibroscan

Study Procedures: (Fibro Scan 502, Echosens, and Paris, France).

The Fibroscan 502 touch has two probes, M+ and XL+, and can be used to measure LSM and CAP at any participating medical center (TBRI). Each study was conducted by a devoted study coordinator who followed the manufacturer set of rules (Fibro Scan 502, Echosens, and Paris, France).

### 2.3. Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 22 for Microsoft Windows was used to code, process, and analyze the data (IBM SPSS Inc, Chicago, IL, USA). The normality of the data distribution was determined using the Shapiro-Wilk test. We utilized frequency counts and relative percentages to demonstrate qualitative data. Use the $\chi^2$ test to discover differences between two or more sets of qualitative variables (2). A ROC curve is utilized to determine a cutoff for a certain outcome. The quantitative data were reported as mean ± standard deviation (Standard deviation). Using the independent samples $t$-test, two sets of normally distributed variables with independent distributions were compared (parametric data). $P$ values below 0.05 were considered significant.

## 3. Results

This study included 90 cases divided into (50 Diabetic and 40 nonDiabetic) with NAFLD. As regards age, the mean age of all studied patients was 41.878 ± 8.828 years. As regards sex, there were 28 males (31.11%) and 62 females (68.89%) in all the studied patients Table 1.

This table shows that: 10% of patients with NAFLD are asymptomatic, 40% complaining of right quadrant pain, 20% complaining of fatigue, 15% complaining of malaise, and 5% have nausea Tables 2 and 3.

Table 1. Description of symptoms of all studied patients.

| Studied patients ($N = 90$) | $N$ (%) |
|---|---|
| Asymptomatic | 10 (11.11) |
| Fatigue | 20 (22.22) |
| Malaise | 15 (16.67) |
| RUQ Abdominal pain | 40 (44.44) |
| Nausea | 5 (5.56) |

This table shows that: there was significant increase in age in diabetic patients ($P$ value 0.002) Table 4.

This table shows: There was significantly decrease LDL in diabetic patients ($P$ value < 0.001)and significantly high AST in diabetic patients ($P$ value < 0.001) Table 5.

This table shows: There was nonsignificant comparison between two groups as regard APRI titre ($P$ value = 0.481) and APRI grades ($P$ value = 0.557) Table 6.

This table shows: there was a significant comparison between two groups as regard FIB-4 titre ($P$ value = 0.022) and nonsignificant comparison between two groups as regard FIB-4 grades ($P = 0.335$) Table 7.

This table shows: there was a significant comparison between two groups as regard Fibrosis LSM ($P$ value < 0.001) and fibrosis grades ($P$ value < 0.001) Table 8.

This table shows: there was a significant comparison between two groups as regard fib-4 grades ($P$ value < 0.001) and fibrosis grades ($P$ value = 0.002) and nonsignificant comparison between two groups as regard (sex, BMI group and steatosis grades) Table 9.

This table shows: there was statistically significant comparison between two groups as regard fibrosis grades ($P$ value < 0.001), and There was nonsignificant comparison between FIB-4 grades as regard (Sex and Steatosis grades) Table 10.

This table shows: there was a significant positive correlation between APRI as regard (FIB-4, fibrosis LSM, ASTand ALT) and significant negative correlation as regard (platelet and FBS) and a significant positive correlation between FIB-4 as regard (fibrosis LSM, age and AST) and significant negative correlation as regard (platelet and urea) Figs. 1−3.

## 4. Discussion

The aim of this study is to assess the impact of DM on NAFLD development and identify markers of

Table 2. This table shows that: there was non significant comparison between two groups as regrard clinical symptoms (P-value = 0.478).

| Clinical symptoms | DM | | Chi-Square | |
|---|---|---|---|---|
| | NonDiabetic N (%) | Diabetics (%) | $\chi^2$ | $P$-value |
| Asymptomatic | 7 (17.50) | 3 (6.00) | | |
| Fatigue | 9 (22.50) | 11 (22.00) | | |
| Malaise | 7 (17.50) | 8 (16.00) | 3.499 | 0.478 |
| RUQ Abdominal pain | 15 (37.50) | 25 (50.00) | | |
| Nausea | 2 (5.00) | 3 (6.00) | | |

Table 3. Baseline demographic data of the whole studied patients.

| | DM | | T-Test | |
| | NonDiabetic | Diabetic | t | P-value |
| --- | --- | --- | --- | --- |
| Age | | | | |
|   Range | 20–55 | 32–65 | −3.210 | 0.002* |
|   Mean ± SD | 38.700 ± 8.933 | 44.420 ± 7.949 | | |
| Weight | | | | |
|   Range | 67–120 | 53–126 | −0.006 | 0.995 |
|   Mean ± SD | 92.000 ± 15.319 | 92.020 ± 16.245 | | |
| Height | | | | |
|   Range | 145–179 | 146–188 | −1.461 | 0.148 |
|   Mean ± SD | 159.425 ± 7.292 | 161.900 ± 8.498 | | |
| BMI | | | | |
|   Range | 23.1–51.31 | 18.78–48.01 | 0.744 | 0.459 |
|   Mean ± SD | 36.469 ± 7.173 | 35.354 ± 6.970 | | |
| WC | | | | |
|   Range | 88–144 | 86–144 | 0.500 | 0.618 |
|   Mean ± SD | 110.150 ± 11.857 | 108.920 ± 11.393 | | |
| Chi-Square | N (%) | N (%) | $\chi^2$ | P-value |
| Sex | | | | |
|   Male | 12 (30.00) | 16 (32.00) | 0.041 | 0.839 |
|   Female | 28 (70.00) | 34 (68.00) | | |
| Smoking | | | | |
|   No | 23 (57.50) | 30 (60.00) | 0.057 | 0.811 |
|   Yes | 17 (42.50) | 20 (40.00) | | |
| BMI group | | | | |
|   Normal | 1 (2.50) | 3 (6.00) | | |
|   Overweight | 25 (62.50) | 34 (68.00) | 1.315 | 0.518 |
|   Obese | 14 (35.00) | 13 (26.00) | | |

severe liver fibrosis and to assess the usefulness of Fibroscan and noninvasive parameters in determining liver status.

In our study we discovered that the average age of diabetic individuals with NAFLD increased significantly (P value 0.002).

In a study to assess Fibroscan and low-density lipoprotein as determinants of severe hepatic fibrosis in diabetic cases with NAFLD, Jaafar and colleagues,[14] found that the average age of the diabetic and non-diabetics cases was 53.7 ± 14.6 (range: 27.0–80.0; median = 55.2) and 46.1 ± 14.6 (range: 18.0–82.0; median = 48.3) years, respectively (P < 0.001).

According to Mohamed and colleagues,[15] patients with NAFLD were noticeably older than those in the controls.

In this study, we found that individuals with DM and those without DM had statistically insignificantly different in APRI grades.

Jaafar and colleagues,[14] found that there was no difference observed in APRI between diabetic and nondiabetic cases.

There was an insignificant difference among the three groups in relation to APRI, according to Cassinotto and colleagues[16]

In this study, we showed that diabetic individuals with NAFLD had significantly higher FIB 4 titre.

Fib-4 was statistically substantially higher in DM than in the nondiabetic group, according to Hemida and colleagues.[7]

There were significant variations among the three groups in terms of FIB-4, according to Cassinotto and colleagues.[16]

In this study, we demonstrated that diabetic individuals had considerably greater levels of fibrosis by LSM, higher levels of fibrosis grades overall.

Cases with T2DM and obesity showed greater levels of fibrosis than controls, according to HANAN and colleagues,[17] (P = 0.023).

According to Hemida and colleagues,[7] DM group fibrosis grades were statistically substantially higher than nondiabetic group fibrosis grades.

According to Jaafar[12] only 46 (26.3%) nondiabetics had significant liver fibrosis, compared with 35 (47.9%) diabetic patients.

In this work, we demonstrated that diabetic individuals had dramatically low LDL and significantly high AST.

According to Dai and colleagues,[18] T2DM cases that had NAFLD with liver stiffness had higher levels of High BMI, serum uric acid, triglycerides, glycated hemoglobin, and HDL-C, as well as lower AST and ALT activity than those without liver stiffness.

Table 4. Comparison between diabetic and nondiabetic patients as regard lab investigations.

| | DM | | T-Test | |
| --- | --- | --- | --- | --- |
| | NonDiabetic | Diabetic | t | P-value |
| Hb | | | | |
| Range | 9.9–15.7 | 10.4–15.8 | 0.384 | 0.702 |
| Mean ± SD | 13.493 ± 1.257 | 13.386 ± 1.345 | | |
| PLTs | | | | |
| Range | 80–353 | 80–450 | 0.110 | 0.912 |
| Mean ± SD | 206.075 ± 66.683 | 204.320 ± 80.822 | | |
| WBCs | | | | |
| Range | 2.6–9.3 | 3–10 | 0.144 | 0.885 |
| Mean ± SD | 6.168 ± 1.507 | 6.114 ± 1.914 | | |
| RBCs | | | | |
| Range | 3.6–5.4 | 3.7–5.7 | 0.199 | 0.843 |
| Mean ± SD | 4.628 ± 0.474 | 4.608 ± 0.451 | | |
| T. Bil | | | | |
| Range | 0.26–1.32 | 0.39–1.29 | 0.987 | 0.326 |
| Mean ± SD | 0.756 ± 0.226 | 0.710 ± 0.213 | | |
| D. Bil | | | | |
| Range | 0.04–0.46 | 0.03–0.56 | −1.644 | 0.104 |
| Mean ± SD | 0.242 ± 0.111 | 0.282 ± 0.117 | | |
| TP | | | | |
| Range | 6.1–8.2 | 6.1–8.1 | −0.502 | 0.617 |
| Mean ± SD | 7.015 ± 0.493 | 7.064 ± 0.431 | | |
| ALB | | | | |
| Range | 3.4–5.8 | 3.1–5.8 | 0.216 | 0.830 |
| Mean ± SD | 4.370 ± 0.537 | 4.344 ± 0.592 | | |
| FBS | | | | |
| Range | 32–275 | 48–332 | −0.008 | 0.993 |
| Mean ± SD | 132.050 ± 59.652 | 132.160 ± 64.347 | | |
| AST | | | | |
| Range | 20–70 | 17–80 | −3.857 | <0.001* |
| Mean ± SD | 37.150 ± 10.458 | 45.560 ± 10.136 | | |
| ALT | | | | |
| Range | 21–75 | 17–76 | −1.324 | 0.189 |
| Mean ± SD | 33.850 ± 14.508 | 38.400 ± 17.423 | | |
| ALP | | | | |
| Range | 35–104 | 33–107 | 0.482 | 0.631 |
| Mean ± SD | 67.100 ± 17.016 | 65.340 ± 17.377 | | |
| GGT | | | | |
| Range | 8–48 | 10–54 | −1.572 | 0.119 |
| Mean ± SD | 23.625 ± 8.095 | 26.680 ± 9.925 | | |
| Urea | | | | |
| Range | 14–37 | 9–60 | 1.224 | 0.224 |
| Mean ± SD | 25.750 ± 6.640 | 23.660 ± 9.014 | | |
| Creat | | | | |
| Range | 0.08–2.9 | 0.08–2.9 | 1.609 | 0.111 |
| Mean ± SD | 0.938 ± 0.679 | 0.736 ± 0.514 | | |
| PT | | | | |
| Range | 10–11 | 10–11 | −0.782 | 0.436 |
| Mean ± SD | 10.950 ± 0.221 | 10.980 ± 0.141 | | |
| INR | | | | |
| Range | 0.9–1.1 | 0.9–1.2 | −0.691 | 0.491 |
| Mean ± SD | 1.020 ± 0.069 | 1.030 ± 0.068 | | |
| TG | | | | |
| Range | 23–359 | 67–318 | 1.157 | 0.250 |
| Mean ± SD | 169.750 ± 79.123 | 153.520 ± 53.576 | | |
| LDL | | | | |
| Range | 87–170 | 75–134 | 5.504 | <0.001* |
| Mean ± SD | 121.000 ± 21.145 | 100.600 ± 13.868 | | |
| CHOL | | | | |
| Range | 69–289 | 124–302 | −1.317 | 0.191 |
| Mean ± SD | 198.175 ± 45.071 | 210.940 ± 46.195 | | |

*Table 5. Comparison of APRI score in diabetic and nondiabetic patients.*

| | DM | | T-Test | |
|---|---|---|---|---|
| | Nondiabetic | Diabetic | t | P-value |
| **APRI** | | | | |
| Range | 0.2–1.3 | 0.1–1.3 | −0.707 | 0.481 |
| Mean ± SD | 0.548 ± 0.311 | 0.592 ± 0.284 | | |
| **Chi-Square** | N (%) | N (%) | $\chi^2$ | P-value |
| **APRI grades** | | | | |
| Low | 16 (40.00) | 17 (34.00) | 0.344 | 0.557 |
| Intermediate | 24 (60.00) | 33 (66.00) | | |

*Table 6. Comparison of Fib-4 in diabetic and nondiabetic patients.*

| | DM | | T-Test | |
|---|---|---|---|---|
| | Nondiabetic | Diabetic | t | P-value |
| **FIB-4** | | | | |
| Range | 0.2–3.2 | 0.4–3.7 | −2.338 | 0.022* |
| Mean ± SD | 1.463 ± 0.695 | 1.816 ± 0.726 | | |
| **Chi-Square** | N (%) | N (%) | $\chi^2$ | P-value |
| **FIB-4 grades** | | | | |
| Low | 13 (32.50) | 11 (22.00) | | |
| Intermediate | 25 (62.50) | 33 (66.00) | 2.186 | 0.335 |
| High | 2 (5.00) | 6 (12.00) | | |

LDL levels were shown to be considerably lower in DM patients by Jaafar and colleagues,[14] LDL levels were 101 ± 13.1 mg/dl in diabetic patients compared with 120 ± 15.5 mg/dl in nondiabetic individuals (P = 0.017).

This research provides evidence that APRI is significantly relevant with FIB-4 and fibrosis grades.

Significant fibrosis group had greater APRI scores (1.18 ± 0.92 vs. 0.25 ± 0.16, respectively; (P ≪ 0.0001) and FIB-4 scores (2.40 ± 2.13 vs. 0.85 ± 0.52, respectively; P = 0.0001), according to Kolhe and colleagues.[19]

According to the degree of fibrosis, Itakura and colleagues,[20] found that APRI increased considerably (P < 0.01) and FIB-4 also significantly increased (P < 0.01).

In this study, we discovered that the correlation between APRI grades and platelet, AST, fibrosis LSM, and FIB-4 is statistically significant.

*Table 7. Comparison of Fibrosis by LSM and fibrosis grades in diabetic and nondiabetic patients.*

| | DM | | T-Test | |
|---|---|---|---|---|
| | Nondiabetic | Diabetic | t | P-value |
| **Fibrosis LSM** | | | | |
| Range | 2.4–10.3 | 3.9–15.5 | −5.797 | <0.001* |
| Mean ± SD | 6.100 ± 1.985 | 9.394 ± 3.122 | | |
| **Chi-Square** | N (%) | N (%) | $\chi^2$ | P-value |
| **Fibrosis grades** | | | | |
| F0 | 15 (37.50) | 2 (4.00) | | |
| F1 | 15 (37.50) | 10 (20.00) | | |
| F2 | 7 (17.50) | 16 (32.00) | 29.285 | <0.001* |
| F3 | 3 (7.50) | 11 (22.00) | | |
| F4 | 0 | 11 (22.00) | | |

*Table 8. Relation between APRI grades and (FIB-4 grades, sex, BMI Group, fibrosis grades, and steatosis grades).*

| | APRI grades | | Chi-Square | |
|---|---|---|---|---|
| | Low N (%) | Intermediate N (%) | $\chi^2$ | P-value |
| **FIB-4 grades** | | | | |
| Low | 20 (60.61) | 4 (7.02) | | |
| Intermediate | 13 (39.39) | 45 (78.95) | 32.213 | <0.001* |
| High | 0 | 8 (14.04) | | |
| **Sex** | | | | |
| Male | 10 (30.30) | 18 (31.58) | 0.016 | 0.900 |
| Female | 23 (69.70) | 39 (68.42) | | |
| **BMI group** | | | | |
| Normal | 2 (6.06) | 2 (3.51) | | |
| Overweight | 19 (57.58) | 40 (70.18) | 1.516 | 0.469 |
| Obese | 12 (36.36) | 15 (26.32) | | |
| **Fibrosis grades** | | | | |
| F0 | 12 (36.36) | 5 (8.77) | | |
| F1 | 12 (36.36) | 13 (22.81) | | |
| F2 | 4 (12.12) | 19 (33.33) | 16.505 | 0.002* |
| F3 | 3 (9.09) | 11 (19.30) | | |
| F4 | 2 (6.06) | 9 (15.79) | | |
| **Steatosis gardes** | | | | |
| S0 | 6 (18.18) | 10 (17.54) | | |
| S1 | 9 (27.27) | 17 (29.82) | 0.117 | 0.990 |
| S2 | 9 (27.27) | 14 (24.56) | | |
| S3 | 9 (27.27) | 16 (28.07) | | |

Alhankawi and colleagues,[21] found that FIB-4, APRI score, and AST/ALT ratio substantially connected with Fibroscan score (r = 0.472, P < 0.0001; r = 0.418, P < 0.0001; r = 0.219, P = 0.003).

Ucar and colleagues,[22] discovered that cases with extensive fibrosis had significantly increased APRI score and FIB-4 (P < 0.05).

In this work, we showed that the correlation between FIB-4 grades and fibrosis grades was quite strong.

Eletreby and colleagues[23] showed that although there was no inflammation in the samples used for

*Table 9. Relation between FIB-4 grades and (sex, fibrosis grades, and steatosis grades).*

| | FIB-4 grades | | | Chi-Square | |
|---|---|---|---|---|---|
| | Low N (%) | Intermediate N (%) | High N (%) | $\chi^{22}$ | P-value |
| **Sex** | | | | | |
| Male | 4 (16.67) | 23 (39.66) | 1 (12.50) | 5.605 | 0.061 |
| Female | 20 (83.33) | 35 (60.34) | 7 (87.50) | | |
| **Fibrosis grades** | | | | | |
| F0 | 10 (41.67) | 7 (12.07) | 0 | | |
| F1 | 12 (50.00) | 13 (22.41) | 0 | | |
| F2 | 2 (8.33) | 20 (34.48) | 1 (12.50) | 38.923 | <0.001* |
| F3 | 0 | 10 (17.24) | 4 (50.00) | | |
| F4 | 0 | 8 (13.79) | 3 (37.50) | | |
| **Steatosis grades** | | | | | |
| S0 | 5 (20.83) | 11 (18.97) | 0 | | |
| S1 | 6 (25.00) | 18 (31.03) | 2 (25.00) | 2.987 | 0.810 |
| S2 | 7 (29.17) | 13 (22.41) | 3 (37.50) | | |
| S3 | 6 (25.00) | 16 (27.59) | 3 (37.50) | | |

Table 10. Correlation between APRI score and (FIB-4, fibrosis LSM and steatosis and lab tests) and Correlation between Fib-4 and (fibrosis LSM, steatosis CAP and lab tests).

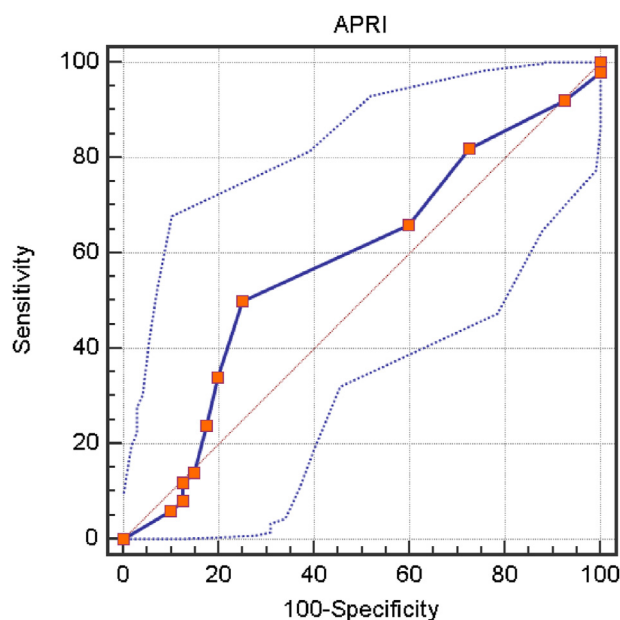| Correlations | | | | |
| --- | --- | --- | --- | --- |
| | APRI | | FIB-4 | |
| | r | P-value | r | P-value |
| FIB-4 | 0.704 | <0.001* | | |
| Fibrosis LSM | 0.370 | <0.001* | 0.596 | <0.001* |
| Steatosis CAP | −0.067 | 0.532 | 0.112 | 0.295 |
| Age | −0.025 | 0.815 | 0.450 | <0.001* |
| Weight | −0.101 | 0.345 | −0.101 | 0.343 |
| Height | −0.094 | 0.380 | −0.024 | 0.821 |
| BMI | −0.055 | 0.607 | −0.094 | 0.377 |
| WC | 0.061 | 0.567 | −0.003 | 0.975 |
| Hb | 0.048 | 0.655 | 0.016 | 0.878 |
| PLTs | −0.616 | <0.001* | −0.476 | <0.001* |
| WBCs | 0.029 | 0.783 | −0.056 | 0.598 |
| RBCs | −0.179 | 0.092 | −0.181 | 0.088 |
| T. Bil | −0.031 | 0.769 | 0.009 | 0.935 |
| D. Bil | 0.067 | 0.532 | 0.049 | 0.644 |
| TP | 0.059 | 0.584 | 0.003 | 0.978 |
| ALB | −0.064 | 0.549 | −0.054 | 0.611 |
| FBS | −0.244 | 0.021* | −0.179 | 0.091 |
| AST | 0.359 | 0.001* | 0.535 | <0.001* |
| ALT | 0.481 | <0.001* | 0.014 | 0.896 |
| ALP | 0.017 | 0.873 | 0.029 | 0.787 |
| GGT | 0.016 | 0.877 | 0.197 | 0.063 |
| Urea | −0.144 | 0.175 | −0.320 | 0.002* |
| Creat | −0.131 | 0.218 | −0.117 | 0.273 |
| PT | 0.109 | 0.307 | 0.092 | 0.390 |
| INR | −0.098 | 0.356 | −0.148 | 0.163 |
| TG | −0.113 | 0.288 | −0.042 | 0.692 |
| LDL | −0.144 | 0.175 | −0.133 | 0.211 |
| CHOL | 0.005 | 0.964 | 0.022 | 0.839 |



Fig. 1. Receiving operating characteristic curve for apri score in diabetic and nondiabetic patients (Cutoff >0.5) Sens. = 50 Spec. = 75 Accuracy = 58.2%.

A previous study by Fallatah and colleagues,[26] reported that there was a substantial variation in liver stiffness score values, APRI, and the FIB-4 among cases had advanced fibrosis of more than F2 and those with mild to moderate fibrosis of F2 or under.
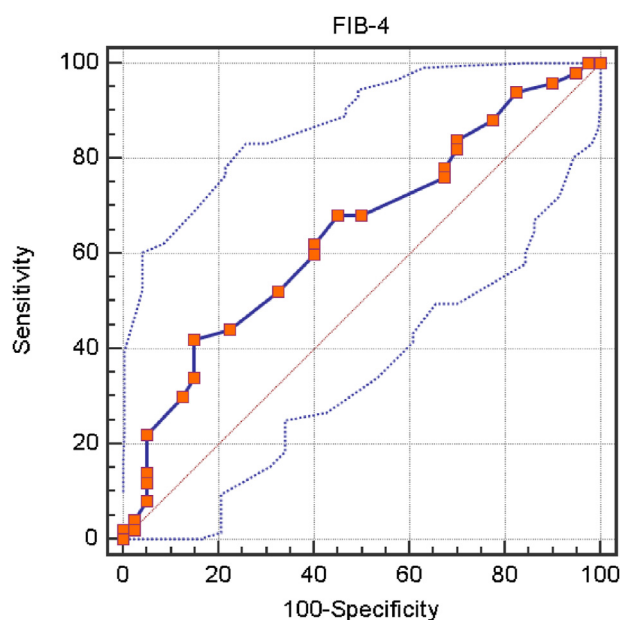
the study, FIB-4 was substantially linked with the existence of fibrosis.

This was also backed up by research by Kumar and colleagues,[24] who found a connection between liver stiffness as determined by TE and other study parameters as well as other fibrosis indicators, including NFS and FIB-4.

In the research we conducted, we discovered a substantial correlation between FIB-4 grades and age, height, platelets, AST, urea, APRI test, and LSM fibrosis.

In a study published in 2014, El Nakeeb and colleagues,[25] discovered a significant connection among the levels of FIB-4, platelet count, and AST.

According to Cassinotto and colleagues,[16] there was a significantly positive relation between the FIB4 score and the fibrosis stage as determined by fibroscan.

In this study, we discovered that the APRI score correlated positively with FIB-4, fibrosis LSM, AST, ALT, and platelet levels, whereas FIB-4 correlated positively with fibrosis LSM, age, and AST and negatively with platelet levels and urea.



Fig. 2. Receiving operating characteristic curve for FIB-4 in diabetic and nondiabetic patients (Cutoff >2) Sens. = 42 Spec. = 85 Accuracy = 64.4%.
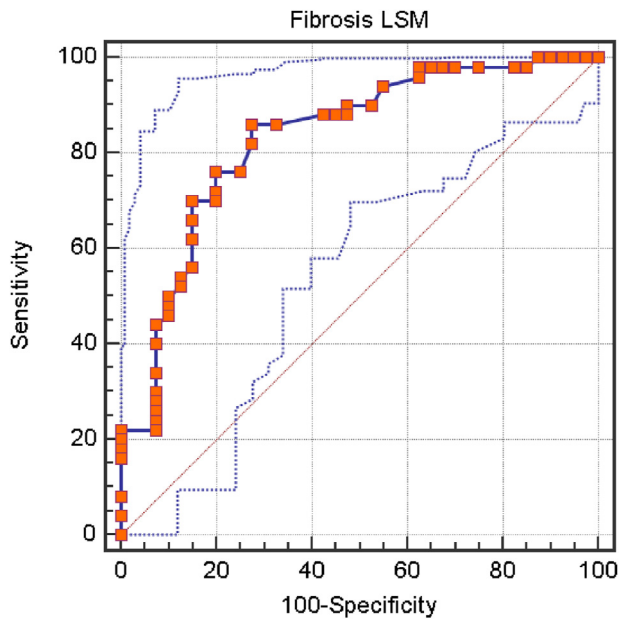
*Fig. 3. Receiving operating characteristic curve for Fibrosis LSM in diabetic and non diabetic patients (Cutoff >0.5) Sens. = 86 Spec. = 72.5 Accuracy = 83.1%.*

Mansour and colleagues,[27] found that there was a negative association between platelets and all fibrosis markers (APRI score and FIB4), and there was a positive association among AST, APRI, and FIB4.

Our results indicated a significant correlation between LDL and fibrosis severity.

According to Jaafar and colleagues[14] more severe fibrosis was evident in 47.9% of diabetic individuals, and this was linked to substantial variations in LDL levels between the two groups.

### 4.1. Conclusion

The combination of Fibroscan, APRI score,LDL-c and FIB-4 techniques gives a useful approach for evaluating liver fibrosis in NAFLD cases. This can reduce the demand for liver biopsy in cases without clear indications.

Limitations of our study include that diagnosis of non alcoholic fatty liver disease was based on the combination of clinical, laboratory and Fibroscan. This could lead to excluding patients with obesity, A narrow intercostal space, Ascites, The quality of the liver parenchyma and Large vascular structure present in the acquisition window (may lead to false results).

### Disclosure

The authors have no financial interest to declare in relation to the content of this article.

### Authorship

All authors have a substantial contribution to the article.

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### Conflicts of interest

Conflict of interest statement: The authors declared that there were NO conflicts of Interest.

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