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Hepatogastroenterology

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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ABSTRACT

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

Aim of the work: To evaluate the role of non-invasive 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. Ninty patients attended the outpatient clinic who had NAFLD were enrolled in the study on aprospective basis, aged18 to 70 years old.

Result: the cases was separated into two groups diabetic and non diabetic 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.*

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INTRODUCTION

Non-alcoholic 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 ten 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 type 2diabetes develops and how it gets worse. NAFLD is mostly happen if you have diabetes, and about 70 percent 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% to 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 non-invasive 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 non-invasive 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). Ninty patients attended the outpatient clinic who had NAFLD over a 3-years period

FIB-4 = *age (year) × AST (IU/L)/platelet count (×10^9/L) × √ALT (IU/L).* [12]

APRI Score = (AST/Upper Limit Normal AST) x 100] / Platelets (10^9/L). [13]

Inclusions Criteria: Age (18-70 years), gender (male or female), diabetes mellitus (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 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).

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, gender, 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

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).

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-square 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.

RESULTS

This study included 90 cases divided into (50 Diabetic and 40 non Diabetic) 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

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

Table 1: Description of symptoms of all studied patients

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

Clinical symptoms	DM				Chi-Square	
	Non-Diabetic		Diabetic			
	N	%	N	%	X^2	P-value
Asymptomatic	7	17.50	3	6.00	3.499	0.478
Fatigue	9	22.50	11	22.00		
Malaise	7	17.50	8	16.00		
RUQ Abdominal pain	15	37.50	25	50.00		
Nausea	2	5.00	3	6.00		

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

		DM						T-Test	
		Non-Diabetic			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**		**%**	X^2	**P-value**
Gender	**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	1.315	0.518
	Overweight	25		62.50	34		68.00		
	Obese	14		35.00	13		26.00		

Table 3: baseline demographic data of the whole studied patients

this table shows that : there was significant increase in age in diabetic patients (p value 0.002)

		DM						T-Test	
		Non-Diabetic			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 4: Comparison between diabetic and non-diabetic patients as regard lab investigations

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)

		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**	**%**	**X^2**	**P-value**
APRI grades	**Low**	16	40.00	17	34.00	0.344	0.557
	Intermediate	24	60.00	33	66.00		

Table 5: Comparison of APRI score in diabetic and nondiabetic patients

This table shows: There was non significant comparison between two groups as regard APRI titre (P-value=0.481) and APRI grades(P-value=0.557)

		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**	**%**	**X^2**	**P-value**
FIB-4 grades	**Low**	13	32.50	11	22.00	2.186	0.335
	Intermediate	25	62.50	33	66.00		
	High	2	5.00	6	12.00		

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

This table shows: there was a significant comparison between two groups as regard FIB-4 titre (P-value =0.022)and non significant comparison between two groups as regard FIB-4 grades (p =0.335)

		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**	**%**	**X^2**	**P-value**
Fibrosis grades	**F0**	15	37.50	2	4.00	29.285	<0.001*
	F1	15	37.50	10	20.00		
	F2	7	17.50	16	32.00		
	F3	3	7.50	11	22.00		
	F4	0	0.00	11	22.00		

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

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)

		APRI grades				Chi-Square	
		Low		Intermediate			
		N	%	N	%	X^2	P-value
FIB-4 grades	**Low**	20	60.61	4	7.02	32.213	<0.001*
	Intermediate	13	39.39	45	78.95		
	High	0	0.00	8	14.04		
Gender	**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	1.516	0.469
	Overweight	19	57.58	40	70.18		
	Obese	12	36.36	15	26.32		
Fibrosis grades	**F0**	12	36.36	5	8.77	16.505	0.002*
	F1	12	36.36	13	22.81		
	F2	4	12.12	19	33.33		
	F3	3	9.09	11	19.30		
	F4	2	6.06	9	15.79		
Steatosis gardes	**S0**	6	18.18	10	17.54	0.117	0.990
	S1	9	27.27	17	29.82		
	S2	9	27.27	14	24.56		
	S3	9	27.27	16	28.07		

Table 8: Relation between APRI grades and (FIB-4grades, gender, BMI Group, fibrosis grades, and steatosis grades)

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 non significant comparison between two groups as regard (gender ,BMI group and steatosis grades)

		FIB-4 grades						Chi-Square	
		Low		Intermediate		High			
		N	%	N	%	N	%	X^2	P-value
Gender	**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	0.00	38.923	<0.001*
	F1	12	50.00	13	22.41	0	0.00		
	F2	2	8.33	20	34.48	1	12.50		
	F3	0	0.00	10	17.24	4	50.00		
	F4	0	0.00	8	13.79	3	37.50		
Steatosis grades	**S0**	5	20.83	11	18.97	0	0.00	2.987	0.810
	S1	6	25.00	18	31.03	2	25.00		
	S2	7	29.17	13	22.41	3	37.50		
	S3	6	25.00	16	27.59	3	37.50		

Table 9: Relation between FIB-4 grades and (gender, fibrosis grades, and steatosis grades)

This table shows: there was statistically significant comparison between two groups as regard fibrosis grades ((P-value<0.001), and There was non significant comparison between FIB-4 grades as regard (Gender and Steatosis grades)

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

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)

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)

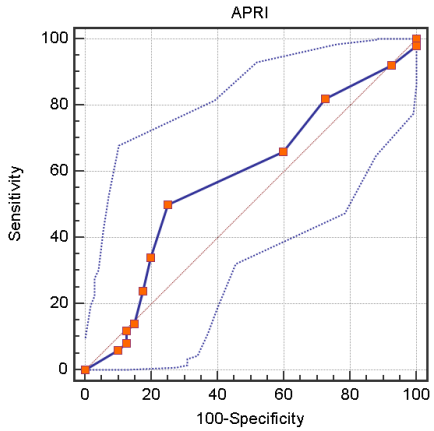

Fig. 1: receiving operating characteristic curve for apri score in diabetic and non diabetic patients (Cutoff >0.5) Sens.= 50 Spec.= 75 Accuracy=58.2%

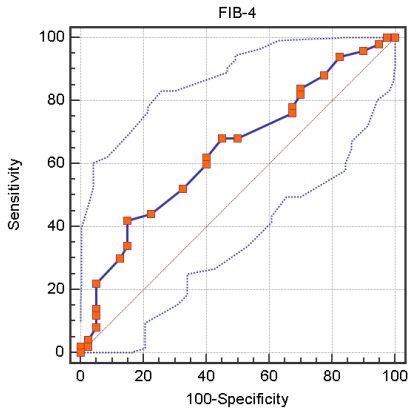

Fig.2: receiving operating characteristic curve for FIB-4 in diabetic and non diabetic patients (Cutoff >2) Sens.= 42 Spec.= 85 Accuracy=64.4%

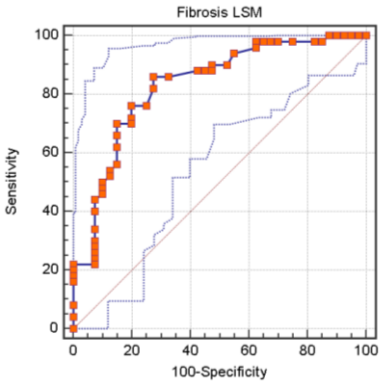

Fig.3: receiving operating characteristic curve for Fibrosis LSM in diabetic and non diabetic patients (Cutoff >0.5) Sens.= 86 Spec.= 72.5 Accuracy=83.1%

DISCUSSION

The aim of this study is to assess the impact of diabetes on NAFLD development and identify markers of 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 et al., [14] found that the average age of the diabetic and nondiabetics 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 et al., [15] patients with NAFLD were noticeably older than those in the controls.

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

Jaafar et al., [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 et al., [16]

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

Fib-4 was statistically substantially higher in diabetes than in the nondiabetic group, according to Hemida et al., [17]

There were significant variations among the three groups in terms of FIB-4, according to Cassinotto et al., [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 et al., [18] (p=0.023).

According to Hemida et al., [17] diabetes group fibrosis grades were statistically substantially higher than nondiabetic group fibrosis grades.

According to Jaafar et al. 2019.[12] only 46 (26.3%) nondiabetics had significant liver fibrosis, compared to 35 (47.9%) diabetic patients.

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

According to Dai et al., [19] T2D 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.

LDL levels were shown to be considerably lower in diabetes patients by Jaafar et al., [14]. LDL levels were 101 ±13.1 mg/dl in diabetic patients compared to 120 ±15.5 mg/dl in non-diabetic 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 et al., [20].

According to the degree of fibrosis, Itakura et al., [21] 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.

Alhankawi et al., [22] 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 et al., [23] 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 et al.[24] showed that although there was no inflammation in the samples used for the study, FIB-4 was substantially linked with the existence of fibrosis.

This was also backed up by research by Kumar et al., [25] 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 et al., [26] discovered a significant connection among the levels of FIB-4, platelet count, and AST.

According to Cassinotto et al., [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.
. A previous study by Fallatah et al., [27] 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
Mansour et al., [28] 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 et al.[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.

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 diseae 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)

Conflict of interest : none

REFERENCES

1. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nature reviews Gastroenterology & hepatology. 2018; 15(1):11-20.
2. McPherson S, Hardy T, Henderson E, Burt AD, Day CP, Anstee QM. Evidence of NAFLD progression from steatosis to fibrosing-steatohepatitis using paired biopsies: implications for prognosis and clinical management. Journal of hepatology. 2015; 62(5):1148-55.
3. Marjot T, Moolla A, Cobbold JF, Hodson L, Tomlinson JW. Nonalcoholic fatty liver disease in adults: current concepts in etiology, outcomes, and management. Endocrine Reviews. 2020; 41(1):66-117.
4. Dharmalingam M, Yamasandhi PG. Non-alcoholic fatty liver disease and type 2 diabetes mellitus. Indian Journalof Endocrinology and Metabolism 2018; 22(3):421
5. Goh GB, Pagadala MR, Dasarathy J, Unalp-Arida A, Sargent R, Hawkins C, et al. Clinical spectrum of non-alcoholic fatty liver disease in diabetic and non-diabetic patients. BBA clinical. 2015; 3:141-5.
6. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The diagnosis and management of non-alcoholic fatty liver disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 2012; 55(6):2005-2023.
7. Hemida K, Haroun H, Mohamed IE, Mahmoud M. Non-invasive Methods in Diagnosis of Nonalcoholic Fatty Liver Disease. The Egyptian Journal of Hospital Medicine. 2021; 83(1):1038-42.
8. Wong VW, Adams LA, de Lédinghen V, Wong GL, Sookoian S. Noninvasive biomarkers in NAFLD and NASH—current progress and future promise. Nature reviews Gastroenterology & hepatology. 2018;15(8):461-78.
9. Esterson YB, Grimaldi GM. Radiologic imaging in nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Clinics in liver disease. 2018; 22(1):93-108.
10. Kwok R, Tse YK, Wong GH, Ha Y, Lee AU, Ngu MC, et al. Systematic review with meta-analysis: non-invasive assessment of non-alcoholic fatty liver disease–the role of transient elastography and plasma cytokeratin-18 fragments. Alimentary pharmacology & therapeutics. 2014; 39(3):254-69.
11. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328-57.
12. Shah, Amy G., et al. "Comparison of noninvasive markers of fibrosis in patients with nonalcoholic fatty liver disease." *Clinical gastroenterology and hepatology* 7.10(2009):1104-1112.
13. Loaeza-del-Castillo, Aurora, et al. "AST to platelet ratio index (APRI) for the noninvasive evaluation of liver fibrosis." *Annals of hepatology* 7.4 (2008): 350-357.
14. Jaafar RF, Ali AM, Zaghal AM, Kanso M, Habib SG, Halaoui AF, et al. Fibroscan and low-density lipoprotein as determinants of severe liver fibrosis in diabetic patients with nonalcoholic fatty liver disease. European journal of gastroenterology & hepatology. 2019; 31(12):1540-4.
15. Mohamed AA, Shousha WG, Shaker O, Mahdy ME, Ibrahim EM, Aal HA, et al. Insulin resistance in Egyptian nonalcoholic fatty liver disease patients. British Journal of Medicine and Medical Research. 2015; 6(5):463.
16. Cassinotto C, Boursier J, de Lédinghen V, Lebigot J, Lapuyade B, Cales P, et al. Liver stiffness in nonalcoholic fatty liver disease: a comparison of supersonic shear imaging, FibroScan, and ARFI with liver biopsy. Hepatology. 2016; 63(6):1817-27.

17. Hemida K, Haroun H, Mohamed IE, Mahmoud M. Non-invasive Methods in Diagnosis of Nonalcoholic Fatty Liver Disease. The Egyptian Journal of Hospital Medicine. 2021; 83(1):1038-42.

18. Hanan HS, Nasrat M, Mohammed I, Esheba NE. Fibroscan for Assessment of Non Alcoholic Fatty Liver Disease in Type 2 Diabetic Patients in Tanta University Hospital. The Medical Journal of Cairo University. 2018; 86:4209-17.

19. Dai CY, Fang TJ, Hung WW, Tsai HJ, Tsai YC. The Determinants of Liver Fibrosis in Patients with Nonalcoholic Fatty Liver Disease and Type 2 Diabetes Mellitus. Biomedicines. 2022;10(7):1487.

20. Kolhe KM, Amarapurkar A, Parikh P, Chaubal A, Chauhan S, Khairnar H, et al. Aspartate transaminase to platelet ratio index (APRI) but not FIB-5 or FIB-4 is accurate in ruling out significant fibrosis in patients with non-alcoholic fatty liver disease (NAFLD) in an urban slum-dwelling population. BMJ open gastroenterology. 2019; 6(1):288.

21. Itakura J, Kurosaki M, Setoyama H, Simakami T, Oza N, Korenaga M, et al. Applicability of APRI and FIB-4 as a transition indicator of liver fibrosis in patients with chronic viral hepatitis. Journal of gastroenterology. 2021; 56(5):470-8.

22. Alhankawi D, HunJung K, Sharma S, Park J. Transient Elastography (Fibroscan) Compared to FIB-4, APRI, and AST/ALT Ratio for Assessment of Significant Liver Fibrosis in Patients with Chronic Hepatitis C: 989. Official journal of the American College of Gastroenterology| ACG. 2018; 113:556-7.

23. Ucar F, Sezer S, Ginis Z, Ozturk G, Albayrak A, Basar O, et al. APRI, the FIB-4 score, and Forn's index have noninvasive diagnostic value for liver fibrosis in patients with chronic hepatitis B. European journal of gastroenterology & hepatology. 2013; 25(9):1076-81.

24. Eletreby R, Abdellatif Z, Gaber Y, Ramadan A, Ahmad N, Khattab H, et al. Validity of routine biochemical and ultrasound scores for prediction of hepatic fibrosis and steatosis in NAFLD. Egyptian Liver Journal. 2021; 11(1):1-0.

25. Kumar R, Rastogi A, Sharma MK, Bhatia V, Tyagi P, Sharma P, et al. Liver stiffness measurements in patients with different stages of nonalcoholic fatty liver disease: diagnostic performance and clinicopathological correlation. Digestive Diseases and Sciences. 2013; 58(1):265-74.

26. El Nakeeb NA, Helmy A, Saleh SA, Abdellah HM, Aleem MH, Elshennawy D. Comparison between FIB-4 index and fibroscan as marker of fibrosis in chronic HCV infection in Egyptian patients. Open Journal of Gastroenterology. 2014; 4(12):383.

27. Fallatah HI, Akbar HO, Fallatah AM. Fibroscan compared to FIB-4, APRI, and AST/ALT ratio for assessment of liver fibrosis in Saudi patients with nonalcoholic fatty liver disease. Hepatitis Monthly. 2016; 16(7).

28. Mansour RH, Zaky S, El Kassas M, Mamdouh H, Esmat G. Evaluating the effect of direct-acting agents on liver fibrosis, by real-time elastography, Fibroscan and FIB4 score in chronic HCV patients. The Scientific Journal of Al-Azhar Medical Faculty, Girls. 2019; 3(1):237.