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A STUDY OF COMPARISON OF VARIOUS FIBROSIS SCORES - APRI, NAFLD FIBROSIS SCORE & FIB 4 SCORE WITH THE RESULTS OF FIBROSCAN IN TYPE 2 DIABETES MELLITUS PATIENTS

Gastroenterology

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ABSTRACT

NAFLD and T2DM often coexist. Prevalence of NAFLD in patients with type 2 diabetes mellitus is more than 2-fold higher than in the general population. Mean Fibroscan value is 8.94 + 2.71. 38% of subjects are in the F3 group i.e. advanced fibrosis. 47% of subjects fall in the category of advanced fibrosis/cirrhosis group. 53% subjects comprise the F0 — F2 group. Indeterminate or intermediate values constituted 21%, 51%, 38% of the total values in APRI, NFS, FIB 4 respectively. Of these intermediate values 19%, 29%, 22% constituted the advanced fibrosis (F3/F4) group respectively. 47 % of subjects had advanced fibrosis (F3/F4). APRI, NFS and FIB 4 correlated significantly with Fibroscan ($r=0.374$, $p < 0.001$; $r= 0.594$, $p < 0.001$; $r = 0.411$, $p<0.001$ respectively). FIB4 had higher accuracy for prediction of advanced fibrosis ($p<0.001$). NFS and APRI had intermittent accuracy ($p=0.003$; $p=0.002$).

KEYWORDS

NAFLD – Non Alcoholic Fatty Liver Disease, APRI - AST to Platelet Ratio Index, FIB-4 – Fibrosis 4 Score, Fibroscan, Type 2 Diabetes mellitus

INTRODUCTION

The prevalence of the metabolic disease, Type 2 Diabetes Mellitus (T2DM) has experienced an extremely rapid increase, affecting currently over 463 million people worldwide. Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease, affecting 15%–40% of the population worldwide[1].

NAFLD and T2DM often coexist. Prevalence of NAFLD in patients with type 2 diabetes mellitus is more than 2-fold higher than in the general population. The overall prevalence of NAFLD among patients with T2DM is 55.5% with South Asia showing 57.87%[2].

AIMS AND OBJECTIVES :

- To assess the liver stiffness in Type 2 diabetic individuals without overt liver disease.
- Comparison of various fibrosis scores - APRI, NAFLD Fibrosis score & FIB 4 score with the results of Fibroscan.

MATERIALS AND METHODS:

100 cases attended to outpatient departments of General Medicine and Endocrinology of King George Hospital, Andhra Medical College, Visakhapatnam were selected. Patients aged above 40 yrs with Type2 DM showing steatosis on Ultrasound were included. Patients aged < 40 yrs, with overt liver disease, congestive heart failure, ascites, positive for HIV/HBsAg/HCV, alcohol intake (men who consumed >20 g and women who consumed >10 g of alcohol per day), usage of drugs known to cause steatosis such as amiodarone, corticosteroids, tamoxifen, methotrexate and high dose estrogen, history of jejunoileal bypass or extensive small bowel resection, findings in favour of metabolic liver diseases including wilson's disease, hemochromatosis and positive alpha-1 antitrypsin and BMI > 35 kg/m2 were excluded.

DATA COLLECTION :

Patients satisfying the inclusion criteria were enrolled in this study, after providing written informed consent. A thorough medical history and physical examination was performed for each individual, which included measurements of weight and height. BMI was calculated as a measure of obesity. Blood investigations such as Complete blood count, Liver function tests (Total Bilirubin, AST, ALT, Albumin), HbA1c, Lipid profile (Triglycerides, Total Cholesterol, LDL, HDL) will be done for all the patients. Fibroscan was performed on all the patients. APRI, NAFLD Fibrosis score and FIB 4 - Index was calculated for all the patients.

STATISTICAL ANALYSIS :

Data was entered in MS-Excel and analyzed in SPSS V21. Descriptive statistics were represented with percentages and Mean was represented with Standard Deviation(SD). Shapiro wilk test was applied to find normality. Chi-square test and ANOVA were applied to find significance. Spearman correlation was applied. $P<0.05$ was considered as statistically significant. Multivariate analysis was applied for the factors which were significant on univariate analysis.

RESULTS:

Table 1: Age And Sex Distribution

Age	Frequency	Percent
40-50	31	31.0
51-60	35	35.0
61-70	19	19.0
71-80	12	12.0
>80	3	3.0
Sex	Frequency	Percent
Female	41	41.0
Male	59	59.0

Table 2: Fibroscan

Fibroscan	Value (kpa)	Frequency	Percent
F0 – F1	< 6.5	23	23.0
F2	6.6 – 9.0	30	30.0
F3	9.1 – 11.4	38	38.0
F4	≥ 11.5	9	9.0

Table 3: Distribution Of Fibrosis Scores

APRI	Frequency	Percent
Low (≤0.5)	79	79.0
Intermediate(0.6-1.4)	21	21.0
NFS	Frequency	Percent
Low (≤ -1.455)	25	25.0
Intermediate (-1.455 to 0.675)	58	58.0
High (>0.675)	17	17.0
FIB4	Frequency	Percent
Low (<1.30)	47	47.0
Intermediate (1.30-2.67)	38	38.0
High (>2.67)	15	15.0

Table 4: Fibroscan And Apri

APRI	Fibroscan			
	F0-F1	F2	F3	F4
F0-F2 Low (≤ 0.5)	23	28	25	3
	100.0%	93.3%	65.8%	33.3%
Intermediate (0.6-1.4)	0	2	13	6
	0.0%	6.7%	34.2%	66.7%
P<0.001				

Table 5: Fibroscan And NFS

NFS	Fibroscan			
	F0-F1	F2	F3	F4
Low (< -1.455)	10	12	3	0
	43.5%	40.0%	7.9%	0.0%
Intermediate	12	17	27	2

(-1.455 to 0.675)	52.2%	56.7%	71.1%	22.2%
High (>0.675)	1	1	8	7
	4.3%	3.3%	21.1%	77.8%
P<0.001				

Table 6: Fibroscan And Fib 4

FIB4	Fibroscan			
	F0-F1	F2	F3	F4
Low (<1.30)	15	20	12	0
	65.2%	66.7%	31.6%	0.0%
Intermediate (1.30-2.67)	8	8	20	2
	34.8%	26.7%	52.6%	22.2%
High (>2.67)	0	2	6	7
	0.0%	6.7%	15.8%	77.8%
P<0.001				

Indeterminate or intermediate values constituted 21%, 51%, 38% of the total values in APRI, NFS, FIB 4 respectively. Of these intermediate values, 19%, 29%, 22% constituted the advanced fibrosis(F3/F4) group respectively. 28% of subjects are labeled as having no advanced fibrosis on APRI (<= 0.5) but have shown advanced fibrosis(F3/F4) on Fibroscan. On evaluation of NFS, 29% and 3% subjects having intermediate and low values are classified as advanced fibrosis(F3/F4) by Fibroscan. In FIB 4, 22% and 12% subjects having intermediate and low values are classified as advanced fibrosis by Fibroscan. 9% of subjects who are classified as F4 by Fibroscan are either in the high(7%) or intermediate(2%) group on NFS and FIB4. The same above subjects are grouped as low (3%) and intermediate(6%) group on APRI.

Table 7: Correlation Between Fibroscan And Arfi / Apri / Nfs / Fib 4

Variable	Fibro scan	Mean	SD	Median	IQR	P-value
ARFI	F0-F1	1.00	0.13	1.00	0.20	**<0.001**
	F2	1.30	0.14	1.30	0.28	
	F3	1.61	0.14	1.60	0.20	
	F4	2.31	0.20	2.30	0.30	
FIB-4	F0-F1	1.27	0.52	1.10	0.86	**<0.001**
	F2	1.21	0.71	1.05	0.93	
	F3	1.63	0.75	1.52	1.08	
	F4	3.14	1.17	3.16	1.51	
NFS	F0-F1	-1.30	1.54	-1.06	2.10	**<0.001**
	F2	-1.22	1.08	-1.30	1.29	
	F3	-0.05	0.88	0.06	1.09	
	F4	1.20	0.92	1.21	1.03	
APRI	F0-F1	0.31	0.13	0.28	0.18	**0.001**
	F2	0.32	0.17	0.28	0.23	
	F3	0.46	0.25	0.41	0.45	
	F4	0.72	0.32	0.77	0.57	

In our study, we found that significant correlation was present between fibrosis scores of Fibroscan and the respective values of APRI, NFS and FIB 4.The p value is ≤ 0.001.

We calculated the AUROC for detecting advanced fibrosis for APRI, NFS, and FIB 4 by comparing with LSM values.

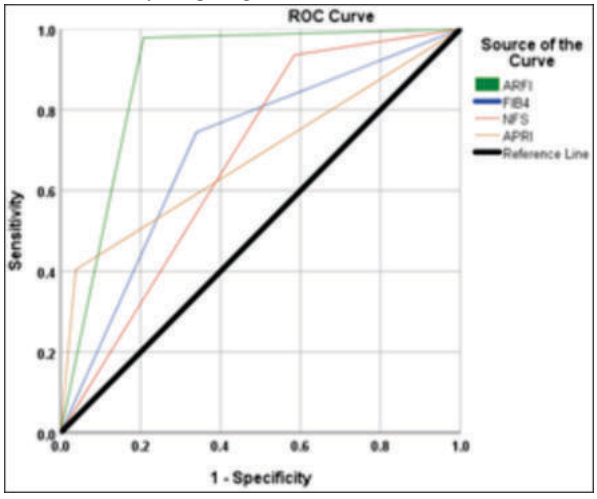

Figure 1: Area Under Roc Curve

Table 8: Area Under Roc Curve

Test Result Variable(s)	Area	P-value	95% Confidence Interval	
			Lower Bound	Upper Bound
ARFI	0.886	**< 0.001**	0.815	0.957
FIB4	0.703	**< 0.001**	0.599	0.806
NFS	0.676	**0.003**	0.570	0.781
APRI	0.683	**0.002**	0.576	0.791

Strengths Of The Study:

- Use of one of the best and widely available non invasive test to assess fibrosis.
- Comparison with the easily available non invasive scores.

Limitations Of The Study:

- Small sample size
- Gold standard for assessing fibrosis, liver biopsy is not done. However it is difficult to justify performing liver biopsy to determine the severity of liver disease in asymptomatic community based subjects.

CONCLUSIONS:

47 % of subjects had advanced fibrosis (F3/F4). APRI, NFS and FIB 4 correlated significantly with Fibroscan (r =0.374, p<0.001; r=0.594, p<0.001; r=0.411, p<0.001 respectively). The AUROC values for advanced fibrosis of APRI, NFS, FIB 4 and ARFI are 0.683, 0.676, 0.703 and 0.886 respectively. FIB4 had higher accuracy for prediction of advanced fibrosis (p<0.001). NFS and APRI had intermittent accuracy (p = 0.003; p = 0.002).

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