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Research Article

Comparison of Aspartate Aminotransferase Platelet Ratio Index (APRI) Score and Insulin Resistance in Type 2 Diabetes Mellitus with Non-Alcoholic Fatty Liver Disease

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ABSTRACT

Introduction: Nonalcoholic Fatty Liver Disease (NAFLD) is a spectrum of liver diseases characterized by the presence of ectopic fat in the liver and steatosis, which cannot be explained by alcohol consumption. The association between NAFLD and Type 2 Diabetes Mellitus (T2DM) is well established. As liver fibrosis progresses in a patient with NAFLD, Insulin Resistance (IR) increases and may worsen diabetes control. The APRI score is a simple, inexpensive bedside marker that can detect liver fibrosis and cirrhosis. Several studies have shown an association between APRI and NAFLD. However, there is a gap in correlation with IR in patients with diabetes. In this study, we sought to correlate IR and NAFLD in diabetes using the APRI score.

Methods: This observational cross-sectional hospital based study was conducted in the Department of General Medicine, one of the tertiary care hospitals in North India, from February 2019 to July 2020. A total of 70 patients were taken for the study. Patients with type 2 diabetes mellitus, aged>30 years, who had no history of alcohol use and who had or were newly diagnosed with NAFLD were enrolled in the study.

Results: From our study, there was a significant difference in mean Homeostatic Model Assessment-2 Insulin Resistance (HOMA2 IR) between NAFLD grade 1, grade 2 and grade 3. The inter-group comparison of mean HOMA2 IR was done using the post-hoc Bonferroni test. We applied Pearson correlation to the overall values of APRI and HOMA2 IR and found a significant positive correlation between the two.

Conclusion: In conclusion, we found that APRI can also be used to assess the degree of insulin resistance and may provide important information for improving glycemic control in T2DM with NAFLD.

Keywords: APRI; Insulin Resistance; Type 2 Diabetes Mellitus; Nonalcoholic Fatty Liver Disease

INTRODUCTION

Nonalcoholic Fatty Liver Disease (NAFLD) is a spectrum of liver diseases characterized by the presence of ectopic fat in the liver and steatosis, which cannot be explained by alcohol consumption [1]. NAFLD is now recognized as one of the most important chronic liver diseases in developed countries [2]. The association between NAFLD and Type 2 Diabetes Mellitus (T2DM) is well established, which could be explained by insulin resistance and compensatory hyperinsulinemia leading to impaired lipid metabolism and accumulation of hepatic Triglycerides (TG) in NAFLD or β-cell dysfunction in T2DM The clinical associations of NAFLD with the elements of the metabolic syndrome, including obesity, hypertension, and dyslipidemia, are also well established Type 2 Diabetes Mellitus is a multifactorial disease in which the body no longer responds properly to physiological insulin concentrations, usually due to chronic overeating and obesity [3-5]. Hepatic Insulin Resistance

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(IR) appears to be an important underlying mechanism of NAFLD, along with chronic dyslipidemia Epidemiological studies have shown that 18% to 33% of individuals with NAFLD also have T2DM and as many as 66% to 83% of individuals with fatty liver disease have a dim of insulin resistance [6-8].

Fatty liver or steatosis is said to occur when more than 5% of hepatocytes in a liver biopsy show ectopic lipid droplets [9]. Recently, experts agree that NAFLD does not reflect current knowledge and propose Metabolic (dysfunction) Associated Fatty Liver Disease (MAFLD) as a more appropriate term. The new definition places greater emphasis on the important role of metabolic dysfunction. NAFLD is associated not only with hepatic morbidity and mortality but also with increased cardiovascular risk. NAFLD and cardiovascular disease share several risk factors, such as obesity, metabolic syndrome, hypertension, dyslipidemia, type 2 diabetes, and chronic kidney disease [10-12].

The gold standard for diagnosis is liver biopsy, especially for diagnosis NASH and staging of fibrosis. Liver biopsy cannot be used routinely because it is an invasive and expensive procedure, prone to sampling errors, captures only an insignificant volume of the liver, and represents a disease in which lesions are unevenly distributed throughout the liver, leading to false exclusion of NASH and misclassification of the degree of fibrosis in a quarter of cases [13]. On the other hand, it is highly dependent on the pathologist, especially in the diagnosis of NASH. In recent years, an index composed of routinely available laboratory tests, namely the aspartate Aminotransferase To Platelet Ratio Index (APRI) has been developed for the evaluation of liver fibrosis in patients with chronic hepatitis B and C. This index is used to assess the degree of fibrosis [14,15].

It is well documented that both NAFLD and Diabetes Mellitus (DM) are interrelated and have a bidirectional relationship. Insulin resistance is an important risk factor that applies to both NAFLD and DM. As liver fibrosis progresses in a patient with NAFLD, IR increases and may worsen diabetes control. The APRI score is a simple, inexpensive bedside marker that can detect liver fibrosis and cirrhosis. Several studies have shown an association between APRI and NAFLD [16,17]. However, there is a gap in correlation with IR in patients with DM. In addition, it needs to be clarified whether APRI correlates with different grades of NAFLD and whether it can be used to support the association between NAFLD and IR in type 2 diabetes mellitus. In this study, we sought to correlate IR and NAFLD in diabetes using the APRI score.

MATERIALS AND METHODS

This observational cross-sectional hospital based study was conducted in the department of general medicine, one of the tertiary care hospitals in North India, from February 2019 to July 2020. A total of 70 patients who attended an OPD and/or were admitted for study purposes, gave written consent, and met the inclusion criteria were recruited for this study. The research procedure used was in accordance with the approved ethical standards of the institution under notification number SU/SMS and R/76-A/2019/61. Patients with type 2 diabetes mellitus, aged>30 years, who had no history of alcohol use and who had or were newly diagnosed with NAFLD were enrolled in the study. A total of 85 patients were screened, 8 declined to participate in the study, and 7 did not meet the inclusion criteria. Finally, 70 patients with NAFLD and T2DM were found eligible according to the inclusion criteria.

Inclusion criteria

- All patients of diabetes mellitus type 2 aged>30 yrs.
- No history of alcohol intake.
- History of or newly diagnosed NAFLD.

Exclusion criteria

- Patients in any stage of pregnancy.
- Patients with hepatitis B or hepatitis C.
- Patients with a history of any liver disease, apart from NAFLD or any hematological disorder.
- Patients with a history of repeated blood transfusions.
- Patients of thrombocytosis or thrombocytopenia.
- Patients admitted or with a history of any acute illness in the last 4 weeks.
- Patients with autoimmune disorders.
- Patients with a history of use of hepatotoxic drugs.

After written informed consent was obtained, a detailed history of the presenting symptoms and their occurrence was taken. A detailed history was obtained from all patients such as demographic information; patient's age, clinical details, blood pressure, heart rate, and Body Mass Index (BMI) were noted on the patient's proforma. Ultrasonography, fasting blood glucose and HBA1c determination, ELISA for fasting insulin level and HOMA2 software, Liver Function Test (LFT) and Complete Blood Count (CBC) for APRI score calculation were also performed.

Patients were diagnosed as diabetic according to the latest American Diabetes Association guidelines [18]. Patients were also diagnosed as having NAFLD on the basis of undergoing a sonographic scan and the degree of NAFLD was recorded. When the echogenicity is just increased, it is a grade I; when the echogenic liver obscures the echogenic walls of portal vein branches, it is grade II, and, when the echogenic liver obscures the diaphragmatic outline, it is grade III fatty infiltration [19,20].

APRI score were calculated using the following formula:

APRI=(AST in IU/L)/(AST Upper Limit of Normal in IU/L)/(Platelets in 10^9/L)

Based on a 2011 meta-analysis in Hepatology by Lin, et al.

- APRI threshold of 0.7 was 77% sensitive and 72% specific.
- APRI threshold of 1.0 was 61% sensitive and 64% specific.
- APRI threshold of 1.0 was 76% sensitive and 72% specific.

6 ml of fasting (8-12 hours) venous blood samples were taken from all subjects participating in the study and divided into 3 parts: The 1st part was put in a plain tube and left to clot and the blood was centrifuged at 3000 xg (xg-times gravity) for 15

minutes. The plasma was then stored at -20°C for determination of serum insulin levels.

Fasting serum insulin levels were measured using an EDI™ Human Insulin ELISA kit in 70 selected sera. The assay utilizes the "sandwich" technique with selected antibodies that bind to various epitopes of insulin. Intra-and inter-assay Co-efficient of Variations (CVs) were 7.8% and 9.4% for insulin, respectively.

The 2nd part was put in a tube containing EDTA and transferred to the central laboratory of the hospital for determination of fasting blood glucose, HBA1c and platelet count. Fasting blood glucose was measured by the GOD-POD method. HBA1c was measured using an auto analyzer. Platelet count was obtained by hydrodynamic focusing on automated Sysmex XT1800i.

The 3rd part was put in a plain tube and left to clot. The serum was then separated using a centrifuge at 3000 xg for 15 minutes. The serum was then used to measure the AST levels by kinetic with pyridoxal 5 phos-on VITROS FS 5.1, respectively.

Once the data was collected for all the patients, the Homeostatic Model Assessment-2 (HOMA 2) calculator provided by the university of Oxford, diabetes trial unit, was used to calculate%B (measure of β-cell activity), %S (insulin sensitivity) and insulin resistance by inputting the fasting blood glucose and fasting serum insulin values [21].

Statistical analysis: Microsoft Excel was used in creating the database and producing graphs, while the data were analysed using the Statistical Package for the Social Sciences (SPSS) version 23.0 for Windows. Mean and standard deviation (± SD) were used to describe quantitative data meeting normal distribution. Continuous two independent groups were compared by parametric independent student's t-test. ANOVA (one way) was used to perform intergroup analysis involving more than two groups. Pearson coefficient was calculated to evaluate the correlation between two sets of data. P values less than 0.05 ($p<0.05$) was considered statistically significant.

RESULTS

Of the 70 patients recruited for this study, 38 were male (54.3%) and 32 were female (45.7%). The subjects were divided on the basis of grades of NAFLD as ascertained on ultrasonography.

There were 30 patients with grade 1 (42.9%), 30 patients with grade 2 (42.9) and 10 patients with grade 3 (14.3%) NAFLD. The mean age of each group of NAFLD along with standard deviation is shown in Table 1.

Table 1: Mean age distribution according to grades of NAFLD.

Grades of NAFLD	Age			
	Mean	Std. Deviation	F-value	p-value
Grade 1	46.6	13.56	1.375	0.26
Grade 2	42.37	10.92		
Grade 3	47.8	2.49		

BMI and grades of NAFLD: The mean BMI was compared between NAFLD grade 1, grade 2 and grade 3 using the one-way ANOVA test as shown in Table 2. There was no significant difference in mean BMI between NAFLD grade 1, grade 2 and grade 3.

Table 2: BMI and NAFLD grades.

Grades of NAFLD	BMI			
	Mean	Std. Deviation	F-value	p-value
Grade 1	28.78	3.24	0.546	0.582
Grade 2	28.23	2.68		
Grade 3	29.18	1.14		
One-way ANOVA test				

The inter-group comparison of mean BMI was done using the post-hoc Bonferroni test as shown in Table 3. No significant difference was found for the inter-group comparisons of mean BMI between NAFLD grade 1, grade 2 and grade 3.

Table 3: Inter-group comparison of mean BMI and Grades of NAFLD.

Grades of NAFLD		Mean difference	p-value
Grade 1	Grade 2	0.55	1
Grade 1	Grade 3	-0.4	1
Grade 2	Grade 3	-0.95	1

Post-hoc Bonferroni test

The mean HBA1c was compared between NAFLD grade 1, grade 2 and grade 3 using the one-way ANOVA test. There was a significant difference in mean HBA1c between NAFLD grade 1, grade 2 and grade 3 as shown in Table 4. The inter-group comparison of mean HBA1c was done using the post-hoc Bonferroni test. The mean HBA1c was significantly more among NAFLD grade 3 compared to grades 1 and 2 as shown in Tables 4 and 5.

Table 4: Comparison of HBA1c and grades of NAFLD.

Grades of NAFLD	HBA1c%			
	Mean	Std. Deviation	F-value	p-value
Grade 1	7.086	0.657	36.608	<0.001*
Grade 2	7.583	0.988		
Grade 3	10.69	2.261		

One-way ANOVA test *Significant difference

Table 5: Inter-group comparison of mean HBA1c with grades of NAFLD.

Grades of NAFLD		Mean difference	p-value
Grade 1	Grade 2	0.496	0.025*
Grade 2	Grade 3	3.106	<0.001*
Grade 3	Grade 1	-3.603	<0.001*

Post-hoc Bonferroni test *Significant difference

The mean serum AST (IU/L) was compared between NAFLD grade 1, grade 2 and grade 3 using the one-way ANOVA test. There was a significant difference in mean serum AST between NAFLD grade 1, grade 2 and grade 3 as shown in Table 6.

Table 6: Comparison of mean AST and grades of NAFLD.

Grades of NAFLD	AST			
	Mean	Std. Deviation	F-value	p-value
Grade 1	43.22	16.93	16.31	<0.001*
Grade 2	60.94	23.37		
Grade 3	86.36	26.21		

One-way ANOVA test *Significant difference

From Table 7, the inter-group comparison of mean AST was done using the post-hoc Bonferroni test. The mean AST was significantly more among NAFLD grade 3 compared to grades 1 and 2.

Table 7: Inter group comparison of mean AST and grades of NAFLD.

Grades of NAFLD		Mean difference	p-value
Grade 1	Grade 2	17.72	0.001
Grade 2	Grade 3	25.42	0.006*
Grade 3	Grade 1	-43.14	< 0.001*

Post-hoc Bonferroni test *Significant difference

Platelet Count and NAFLD: The mean platelet count was compared between NAFLD grade 1, grade 2 and grade 3 using the one-way ANOVA test as shown in Table 8. There was no significant difference in mean platelet count between NAFLD grade 1, grade 2 and grade 3.

Table 8: Comparison of mean platelet count and grades of NAFLD.

Grades of NAFLD	Platelet count			
	Mean	Std. Deviation	F-value	p-value
Grade 1	258.033	58.24	2.193	0.119#
Grade 2	273.566	65.921		
Grade 3	226.9	56.779		

One-way ANOVA test #Nonsignificant difference

In Table 9, the inter-group comparison of mean platelet count was done using the post-hoc Bonferroni test. There was no significant difference among NAFLD grades 1, 2 and 3.

Table 9: Inter-group comparison of mean platelet count and grades of NAFLD.

Grades of NAFLD		Mean difference	p-value
Grade 1	Grade 2	15.533	0.337
Grade 2	Grade 3	-46.666	0.052
Grade 3	Grade 1	31.133	0.149

Post-hoc Bonferroni test

The mean serum insulin levels (IU/ml) was compared between NAFLD grade 1, grade 2 and grade 3 using the one-way ANOVA test. There was a significant difference in mean serum insulin levels (IU/ml) between NAFLD grade 1, grade 2 and grade 3 as shown in Table 10. The inter-group comparison of mean serum insulin levels (IU/ml) was done using the post-hoc Bonferroni test. The mean serum insulin levels (IU/ml) was significantly more among NAFLD grades 2 and 3 compared to grade 1 as shown in Table 11.

Table 10: Comparison of mean fasting serum insulin levels and grades of NAFLD.

Grades of NAFLD	Serum Insulin levels (IU/ml)			
	Mean	Std. Deviation	F-value	p-value
Grade 1	8.85	3.19	27.5	<0.001*
Grade 2	11.69	3.95		
Grade 3	19.9	6.36		

One-way ANOVA test *Significant difference

Table 11: Inter-group comparison of mean fasting serum insulin levels and grades of NAFL.

Grades of NAFLD		Mean difference	p-value
Grade 1	Grade 2	2.84	0.003*
Grade 2	Grade 3	8.21	<0.001*
Grade 3	Grade 1	-11.05	<0.001*

The mean APRI was compared between NAFLD grade 1, grade 2 and grade 3 using the one-way ANOVA test. There was a significant difference in mean APRI between NAFLD grade 1, grade 2 and grade 3 as shown in Table 12. The inter-group comparison of mean APRI was done using the post-hoc Bonferroni test. The mean APRI was significantly more among NAFLD grade 3 compared to grades 1 and 2 as shown in Table 13.

Table 12: Comparison of mean APRI and grades of NAFLD.

Grades of NAFLD	APRI			
	Mean	Std. Deviation	F-value	p-value
Grade 1	0.426	0.201	24.501	<0.001*
Grade 2	0.566	0.198		
Grade 3	0.99	0.321		

One-way ANOVA test *Significant difference

Table 13: Inter-group comparison of mean APRI and grades of NAFLD.

Grades of NAFLD		Mean difference	p-value
Grade 1	Grade 2	0.14	0.008*
Grade 2	Grade 3	0.42	< 0.001*
Grade 3	Grade 1	-0.56	<0.001*

*Significant difference

In Table 14 the mean HOMA2 IR was compared between NAFLD grade 1, grade 2 and grade 3 using the one-way ANOVA test. There was a significant difference in mean HOMA2 IR between NAFLD grade 1, grade 2 and grade 3. The inter-group comparison of mean HOMA2 IR was done using the post-hoc Bonferroni test. There was a significant difference in the inter-group comparisons of mean HOMA2 IR between NAFLD grade 1, grade 2 and grade 3 as shown in Table 15.

Table 14: Comparison of mean HOMA2 IR and grades of NAFLD.

NAFLD Grades	HOMA2 IR			
	Mean	Std. Deviation	F-value	p-value
Grade 1	1.233	0.475	28.819	<0.001*
Grade 2	1.663	0.621		
Grade 3	3.074	1.095		

One-way ANOVA test *Non-significant difference

Table 15: Inter-group comparison of mean HOMA2 IR and grades of NAFLD.

Grades of NAFLD		Mean difference	p-value
Grade 1	Grade 2	0.43	0.003*
Grade 2	Grade 3	1.41	<0.001*
Grade 3	Grade 1	-1.841	<0.001*

*Non-significant difference

As shown in Table 16, we applied Pearson correlation to the overall values of APRI and HOMA2 IR and found a significant positive correlation between the two. Pearson correlation was also applied to the APRI score for the three grades of NAFLD and HOMA2 IR. There was a significant positive correlation between the HOMA-2 IR and APRI for all three grades of NAFLD as shown in Table 17.

Table 16: Pearson's correlation between APRI and HOMA2 IR.

HOMA2 IR	APRI	
	Pearson correlation coefficient	0.9727
	p value	<0.001*

*Non-significant difference

Table 17: Pearson's correlation between APRI score for the three grades of NAFLD and HOMA2 IR.

HOMA2 IR	Grades of NAFLD	APRI	
	Grade 1 NAFLD	Pearson correlation coefficient	0.9628
		p value	<0.001*
	Grade 2 NAFLD	Pearson correlation coefficient	0.9443
		p value	<0.001*
	Grade 3 NAFLD	Pearson correlation coefficient	0.9869
		p value	<0.001*

*Non-significant difference

DISCUSSION

To our knowledge, our study is perhaps the first of its kind to examine the association between APRI score and insulin resistance, as no studies have been conducted to date that have found this association in patients with T2DM along with NAFLD. There were 30 patients with grade 1 NAFLD (42.9%), 30 patients with grade 2 (42.9) and 10 patients with grade 3 (14.3%). The mean age of subjects in the grade 1 NAFLD group was 46.6 years+13.56 years, in the grade 2 NAFLD group was

42.37+10.92 years and in grade 3 NAFLD group was 47.8+2.49 years. There was no statistically significant difference between these groups in age (F value 1.375, P-value=0.26) (Table 1). The mean BMI (Kg/m^2) was compared between NAFLD grade 1, grade 2 and grade 3. It was 28.78+3.24, 28.23+2.68 and 29.18+1.14, respectively. There was no significant difference in mean BMI between NAFLD grade 1, grade 2 and grade 3 (P-value=0.582); however, all three groups were overweight.

The mean AST (IU/L) was compared between NAFLD grade 1, grade 2 and grade 3 (Table 6). The mean AST levels were 43.22+16.93, 60.94+23.37 and 86.36+ 26.21, respectively. Our study showed that there was a significant difference in mean AST between NAFLD grade 1, grade 2 and grade 3 (p-value<0.001). Our inter-group analysis showed that the mean AST was significantly more among NAFLD grade 3 compared to grades 1 and 2 (P-value<0.001). Ghamar-Chehreh ME22 revealed a significant direct relationship between ultra sono graphic grading of the NAFLD and AST (P=0.015).

We compared the platelet count (per microliter of blood) in each group of NAFLD patients (Table 8). In grade 1 NAFLD, mean platelet count was 258,033 +58,240, in grade 2 NAFLD it was 273,566+65,921 and in grade 3 NAFLD it was 226,900+56,779. We found that there was no significant difference in mean platelet count between NAFLD grade 1, grade 2 and grade 3 (p-value<0.119). However, we see that there is a rise in the platelet count in patients with grade 2 NAFLD when compared to grade 1 NAFLD and a fall in platelet count in grade 3 NAFLD when compared to grades 1 and 2. These findings correspond well with the data available since there have been a number of studies showing both a positive and a negative correlation between platelet count and the severity of NAFLD. Yoneda M, et al. in a study of 1,048 patients with liver-biopsy-confirmed NAFLD found that there was a linear decrease of the platelet count with increasing histological severity of hepatic fibrosis.

However, studies by Garjani A, et al. found that patients with mild fatty liver on ultrasonography had lower platelet counts than those with moderate and severe fatty liver. Another study by Saremi Z, et al. found a similar association between platelet count and grades of NAFLD. However, both the studies concluded that no cut-off value of platelet count could reliably distinguish different grades of fatty liver.

The reason for this discrepancy has been postulated. The negative correlation between platelet count and severity of NAFLD for liver fibrosis in some studies may be due to splenic sequestration of platelets, which might occur in patients with severe liver fibrosis and cirrhosis. It is also probable that liver injury causes reduced platelet production in the bone marrow due to defective TPO release. On the other hand, the positive correlation between platelet count and NAFLD may be due to the fact that platelet counts increase in response to inflammation, and hepatic inflammation is the channel through which hepatic steatosis leads to liver injury and fibrosis.

Our study has shown a rise in the platelet count between grades 1 and 2 NAFLD which correlates well with recent studies that have shown a rise between different stages of NAFLD. However, there is a fall in platelet count in patients of grade 3 NAFLD. This may be due increased severity of fibrosis which could only be examined on a liver biopsy.

In our study, the inter-group comparison of mean platelet count was not significantly affected among NAFLD grades 1, 2 and 3 (Table 9).

In our study the HBA1c values (in%) in grade 1, 2, and 3 NAFLD were 7.086+0.675, 7.583+0.988 and 10.69+2.261, respectively. There was a significant difference in mean HBA1c between NAFLD grade 1, grade 2 and grade 3 (p <0.001). This result was in line with studies performed by Ghamar-Chehreh, et al. and Bae JC, et al. In our intergroup analysis, the mean HBA1c was significantly more among NAFLD grade 3 compared to grades 1 and 2 which was well associated with the findings of Ghamar-Chehreh, et al.

When we compared the mean serum insulin levels (IU/ml) between NAFLD grade 1, grade 2 and grade 3 (Table 10). We found that there was a significant difference in mean serum insulin levels (IU/ml) between NAFLD grades 1, grade 2 and grade 3. In our study, the serum insulin levels were 8.85+3.19 IU/ml, 11.69+3.95 IU/ml and 19.9+6.36 IU/ml in grades 1,2 and 3 NAFLD respectively, (p-value<0.001). In our inter-group comparison of mean serum insulin levels (IU/ml), we found that the mean serum insulin levels (IU/ml) were significantly more among NAFLD grades 3 when compared to grades 1 and 2. Our results were similar to a study conducted by Jung CH, et al. and Das S, et al.

We also compared the mean APRI scores with NAFLD grade 1, grade 2 and grade 3 (Table 12). In grade 1 NAFLD, the mean APRI score was 0.426+0.201, in grade 2 it was 0.566+0.198 and in grade 3 it was 0.99+0.321. We found that there was a significant correlation between the NAFLD grades and APRI scores with a p-value of <0.001. In our intergroup comparison, we found that there was a significant difference in the APRI values for the three grades of NAFLD (P-value <0.001). Studies done by Yilmaz Y, et al. and Sapmaz F, et al. showed similar results.

The mean HOMA2 IR was compared between NAFLD grade 1, grade 2 and grade 3. The values for grades 1, 2 and 3 of NAFLD were 1.233+0.475, 1.663+0.621 and 3.074+1.095, respectively. There was a significant difference in mean HOMA2 IR between NAFLD grade 1, grade 2 and grade 3 (p-value<0.001). In our intergroup comparison of mean HOMA2 IR, we found that there was a significant difference in the inter-group comparisons of mean HOMA2 IR between NAFLD grade 1, grade 2 and grade 3 (p-value<0.001). Ghamar-Chehreh ME, et al. and Aller R, et al. showed similar results [21-30].

Finally, we applied Pearson's correlation to the overall values of APRI and HOMA2 IR and found a significant positive correlation between the two (t=0.9727, p-value<0.001). When the correlation was applied to APRI of individual grades of NAFLD and HOMA2 IR, we found a similarly strong correlation between them. For grade 1 NAFLD, the correlation between APRI and HOMA2 IR was 0.9628 and a p-value of <0.001. For grade 2, it was 0.9443 with a p-value of <0.001 and in grade 3 it was 0.9869 with a p-value of <0.001 (Table 17).

We could not find any study that has correlated APRI and HOMA2 IR in patients with NAFLD and diabetes. Several studies have correlated APRI and HOMA2 IR to grades of NAFLD individually but none of them has correlated the values of these two. As established above, APRI is a good non-invasive test to evaluate liver fibrosis in NAFLD. It's also well established that HOMA2 IR is a strong indicator of hepatic fibrosis. So, we postulated that APRI can be correlated with HOMA2 IR in patients of NAFLD with diabetes. Our results have shown that there is a total positive correlation between APRI and HOMA2 IR and also with different grades of NAFLD [31,32].

CONCLUSION

In conclusion, this present study suggests that the APRI score can be confidently used to assess the degree of steatosis in patients with NAFLD and diabetes. We also suggest that APRI can also be used to assess the degree of insulin resistance and may provide important information for improving glycaemic control in such patients. Further studies are required to confirm our findings and for a better understanding of the underlying mechanisms.

LIMITATIONS

This was a cross-sectional study which does not allow for conclusions regarding causality. The small sample size is a limiting factor for generalizing results. Future multicenter trials with a large population may be needed. Also, a power analysis of the sample size was not done.

We used ultrasonography to diagnose and grade NAFLD. Liver biopsy is the gold standard investigation to diagnose and understand the extent of NAFLD. Also, newer methods involving transient elastography are more sensitive and specific and can be used in future studies to improve upon the results obtained in our study.

All our patients were known cases of diabetes. The lack of a control group makes the results of this study less reliable and weak for the establishment of causal relationships between independent and dependent variables. We did not consider diabetic therapy in our study.

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CONFLICT OF INTEREST

None

CONSENT

Written

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