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Prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) Among Coronary Artery Disease Patients and its Association with CAD Severity

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ABSTRACT

Background: The relationship between NAFLD and CVD remains debated, and non-invasive diagnostic methods for NAFLD are recommended. This study aimed to estimate the prevalence of NAFLD among patients with CAD and explore the association between CAD severity and the probability of developing NAFLD.

Methodology: A cross-sectional study was conducted among CAD patients. Patients with a history of infectious liver disease, pregnant or lactating individuals, and with excessive alcohol consumption were excluded. Coronary angiography was performed to assess CAD severity using the Gensini score. Ultrasonography and non-invasive assessments, such as the Fibrosis-4 (FIB-4) index, were used to diagnose and stage NAFLD.

Result: The study included 156 CAD patients, with 79 (50.6%) being male. Out of total, 31 (19.8%) had severe, 79(50.6%) had moderate, and 46 (29.48%) had mild NAFLD. Male patients showed a significantly higher prevalence of severe NAFLD compared to females. There was no significant difference in the mean age of CAD patients across NAFLD severities. Severe NAFLD was associated with higher mean Gensini scores and FIB-4 values compared to mild to moderate NAFLD patients. A positive correlation was found between Gensini score and FIB4, suggesting that Gensini score could be an alternative to FIB4 in diagnosing NAFLD severity among CAD patients.

Conclusion: The study revealed a high prevalence of NAFLD among CAD patients, with severe NAFLD being associated with higher CAD severity.

BACKGROUND

Although it is predicted that NAFLD will be the primary cause of liver transplants by 2025[1] and is a risk factor for end-stage liver disease and hepatocellular carcinoma, people with NAFLD mostly die from cardiovascular disease (CVD). [2]

According to a prior meta-analysis, those who were having NAFLD are at risk for 64% greater chance of experiencing a fatal or non-fatal CVD event.[3] It should be noted that the majority of the studies that made up this meta-analysis used computed tomography or ultrasound to diagnose NAFLD[3], which can only detect early stages of the disease such as simple steatosis. A relatively small sample size and a select group who received a liver biopsy,

however, hampered one of the few studies that included histologically verified NAFLD and demonstrated that advanced hepatic fibrosis particularly accounted for the higher CVD risk.[4] As recently reviewed[5], there is continuous debate about whether NAFLD actually plays a role in the emergence of CVD or is merely a passive observer. It is noteworthy that in people with impaired fasting glucose and/or impaired glucose tolerance, NAFLD was found to be the strongest determinant of increased intima-media thickness, independent of the potential confounding effects of age, sex, visceral fat mass, state of hyperglycemia, insulin resistance, and insulin secretion. However, it should be highlighted that some of these variables could not be confounders but rather operate as mediators in the association between NAFLD and CVD. NAFLD and CVD must be connected by mediating variables because they are biologically distinct features. As a good alternative to diagnosing and staging NAFLD, non-invasive diagnostics such clinical ratings should be utilized in all patients with NAFLD, according to European recommendations.[6] In this research we tried to estimate the prevalence of NAFLD among Coronary Artery Disease patients. Study also determines the association between CAD severity and probability to develop NAFLD.

METHODOLOGY

Present Cross-sectional study was conducted From May 2023 to July 2023 among coronary artery disease patients selected with nonprobable convenience sampling technique. CAD patients having past history of any infectious liver disease, pregnant and lactating mothers or person with positive history of alcohol were excluded from the study. Additionally, patients with ALT >400 IU/L were excluded from the study to avoid high FIB-4 levels due to an artifact caused by acute liver disease.[7] All of the participants underwent coronary angiography. The coronary artery lesion site and degree of stenosis were examined and graded as follows: 1 point for less than 25% narrowing, 2 points for 26-50% narrowing, 4 points for 51-75% narrowing, 8 points for between 76 and 90% narrowing, 16 points for 91-99% narrowing, and 32 points for complete occlusion. The importance of the lesion's location in the coronary circulation is then determined by multiplying each lesion score by a certain number (5 for the left main coronary artery, 2.5 for the proximal segment of the left anterior descending coronary artery, 2.5 for the proximal segment of the circumflex artery, 1.5 for the mid-segment of the left anterior descending coronary artery, 1.0 for the right coronary artery, the distal segment of the left anterior descending. [8,9]

Finally, the individual coronary segment scores were added up to determine the Gensini score. First tertile (Gensini score <11 points), second tertile (Gensini score 11–38 points), and third tertile (Gensini score >38 points) were used to divide the patients into three groups.

Ultrasonography and Non-invasive assessment was done to diagnose NAFLD among CAD patients. Grade for fatty liver was classified as Mild (grade-1) if echogenicity of liver is more than kidney and spleen, Moderate (grade-2) if intravascular structures are blurred and Severe (grade-3) if deep attenuation found and diaphragm could not be discerned from posterior wall of liver. As non-invasive assessment Fibrosis-4 (FIB-4) index was used. Blood investigation i.e., ALT, AST, and platelet count for FIB4 were done. The result of very first blood investigation report was consider to calculate FIB-4. other subsequent reports were excluded from the analysis.

FIB-4 index = (age × AST) / platelet count $\times\sqrt{AST}$

Risk of developing NAFLD among patients with different CAD severity was calculated. Chi square test was applied to find association between Qualitative variable. ANOVA test was applied to find significant difference among quantitative variable. Person correlation test was applied to check linearity among Gensini score and FIB4. ROC curve was derived to predict cut off for severe Non-alcoholic fatty liver disease among CAD patients. 95% confidence level was considered for statistically significant difference with p value less than 0.05.

RESULT

Current study included total 156 patients among them 79(50.6%) were male. Out of total 156 patients with coronary artery disease, 31(19.8%) had severe, 79(50.6%) had moderate and 46(29.48%) had mild NAFLD diagnosed by ultrasonography (Table 1). Not a single patient was found without sign of fatty liver disease on ultrasound.

Majority of male patients had severe NAFLD compared to female patients with CAD. Out of 31 CAD patients, 61.3% male were diagnosed with severe NAFLD, compared to 38.7% female. The association of male gender for development of severe NAFLD among CAD patients is statistically significant.

Table 1: Comparison of various study variables with severity of NAFLD of CAD patients.

Variables	NAFLD			P value
	Mild (n=46)	Moderate (n=79)	Severe (n=31)	
Gender				
Female n (%)	17 (37.00)	48(60.80)	12(38.70)	<0.001*
Male n (%)	29(63.00)	31(39.20)	19(61.30)	
Age in years (mean ± sd)	51.89±8.5	51.28±10.3	51.52±9.87	0.94#
Gensini score (mean ± sd)	17.76±7.8	27.82±7.22	35.1±6.52	<0.001#
FIB4 (mean ± sd)	1.45±0.36	1.99±0.38	2.34±0.31	<0.001#

*Chi square test; #ANOVA test19.96; p value:

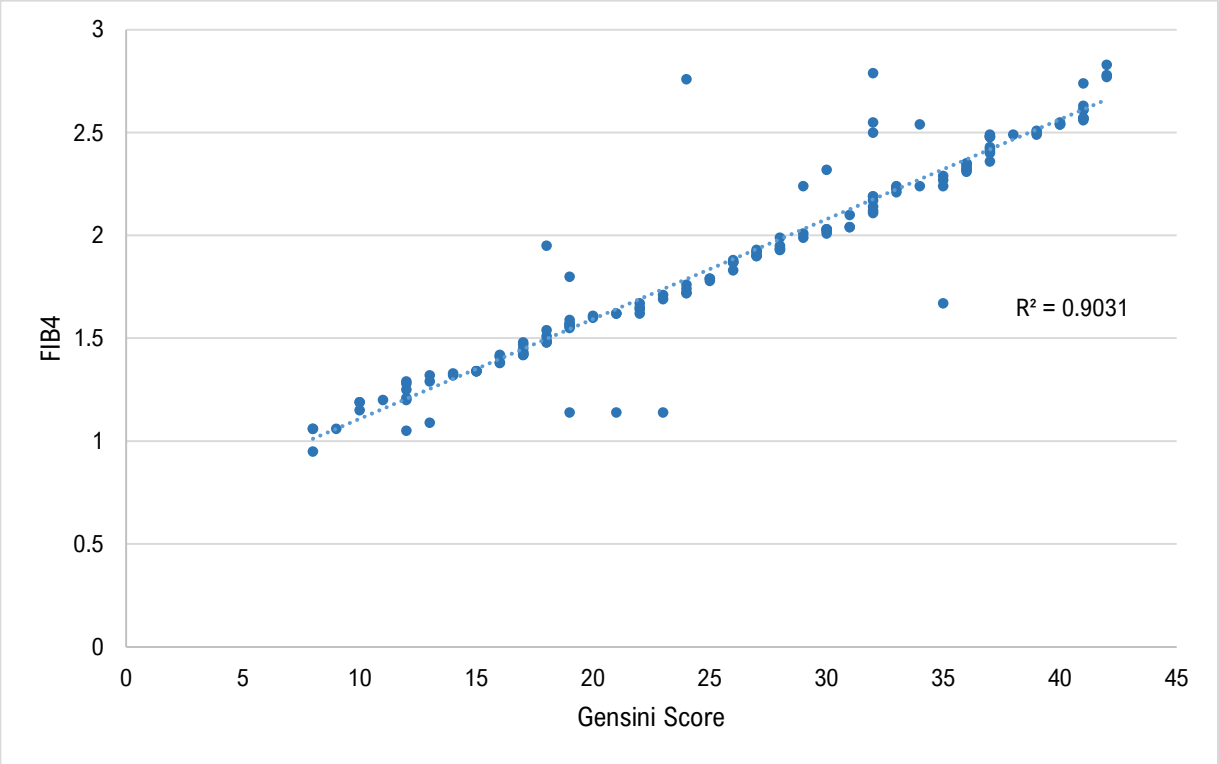

Figure 1: Correlation of Gensini score and FIB4

Current study included patient age range between 34 to 68 years with mean age 51.5±9.66 years. There is no significant difference in mean age of CAD patients with their severity for NAFLD. Among Severe NAFLD patients mean Gensini score (35.1±6.52) was higher compared to other. The difference in mean Gensini score among CAD patients with different severity of NAFLD patients was statistically significant. Severe NAFLD patients had 2.34±0.31 FIB4 which is significantly higher than other CAD patients with mild to moderate NAFLD.

There is a positive correlation was found between Gensini score and FIB4 among CAD patients and this model fit to 90.31% population (r=0.95 with p value <0.001). Above correlation suggest that to diagnose severity of NAFLD among CAD, Gensini score can be used in alternative to FIB4 score (Fig 1).

Cut of value for Gensini score to diagnose severe NAFLD with 83.3 probability is 33.5 with 74.2% sensitivity and 84.8% specificity. The Cut of value of FIB4 to diagnose severe non-alcoholic fatty liver disease among CAD patients with 83.9% probability is 2.25 with 77.4% sensitivity and 84.8% Specificity (Figure 2).

Gensini score less than 17.5 is consider protective with 67.4% sensitivity and 95.5% specificity and less likely chance to develop moderate or severe NAFLD among CAD patients. The FIB4 Cut of value for less likely to develop moderate to severe non-alcoholic fatty liver disease among CAD patients with 83.9% probability is less than 1.41 with 61% sensitivity and 98.2% Specificity.

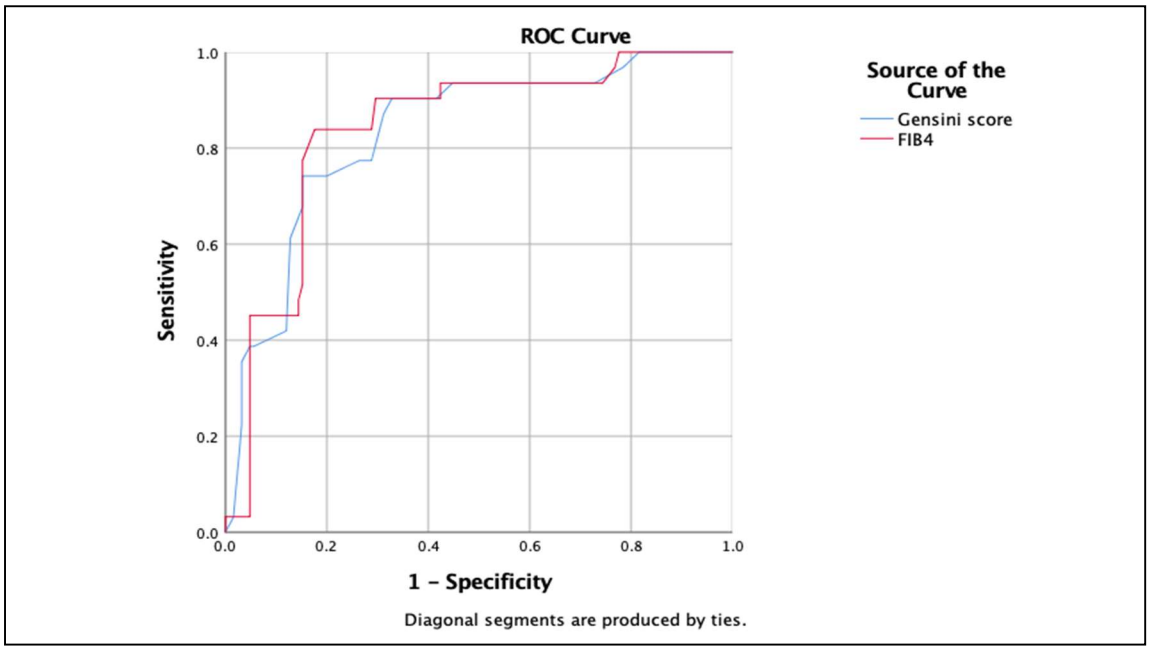

Figure 2: Receiver operating characteristic curve to predict cut of value of Gensini and FIB4 Index for severe NAFLD among CAD patients. For Gensini score AUC (95% CI) 0.833 (0.75-0.91) and for FIB4 Index AUC (95% CI) 0.839 (0.76-0.91)

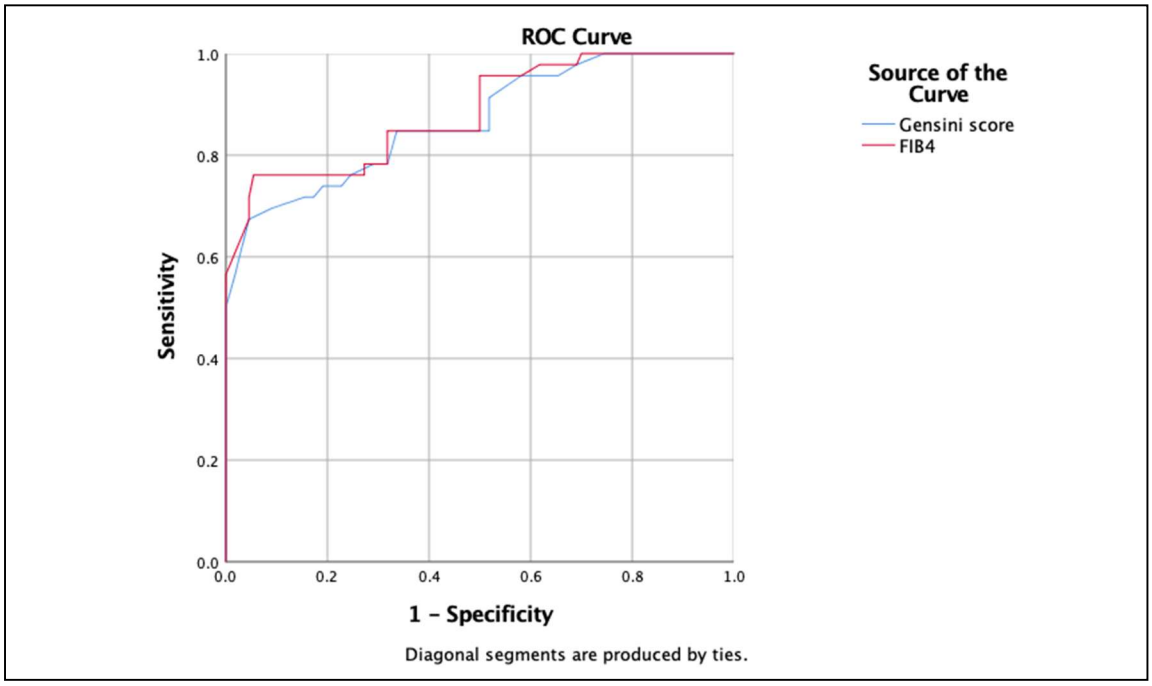

Figure 2: ROC curve to predict less likely risk to develop moderate to severe NAFLD among CAD patients. For Gensini score AUC (95% CI) 0.868 (0.80-0.93) and for FIB4 Index AUC (95% CI) 0.884 (0.82-0.95)

DISCUSSION

In the current study, which included 156 patients with coronary artery disease (CAD), the prevalence of NAFLD was found to be 100%, with 19.8% having severe NAFLD, 50.6% having moderate NAFLD, and 29.48% having mild NAFLD. These findings are consistent with previous studies conducted by Ahmedi et al. where, out of 170, 63 and 17 had grade 1 and 2 hepatic steatosis in ultrasound examination, respectively, providing prevalence of 47% in studied population.[10]

The current study also revealed a significant association between gender and the development of severe NAFLD among CAD patients. Specifically, a

higher proportion of male patients (61.3%) were diagnosed with severe NAFLD compared to female patients (38.7%).

The prevalence of NAFLD in male (55%) patients was slightly higher than in female (53.5%) patients in our study; nevertheless, men had a higher prevalence of mild NAFLD, whereas women had a larger prevalence of severe NAFLD. In contrast to our findings, Agarwal et al. observed that type 2 diabetes patients with NAFLD had a prevalence of 58.1% in males and 56% in women.[11]

Perera et al. discovered that male patients with ACS (53.6%) had a greater frequency of NAFLD than female patients (46.4%). [12]

The prevalence of male patients with NAFLD was reported to rise with increasing NAFLD stages in a Korean community with a history of CVD. [13]

Furthermore, the current study found a significant difference in mean Gensini scores among CAD patients with varying severities of NAFLD. Patients with severe NAFLD had higher mean Gensini scores compared to those with mild to moderate NAFLD. With concordance to our study finding Wang et al. documented that the mean Gensini score was significantly higher in patients with fatty liver compared to those without. They also concluded that Irrespective of the presence of obesity, NAFLD is a risk factor for CHD, and the clinical effect of nonobese fatty liver (especially in women) should be carefully considered. [14]

The positive correlation found between Gensini scores and FIB4 scores in the current study. These results are consistent with the findings of Chen et al., who also observed the odds ratio (OR) for different fibrosis markers associated with one step increase was statistically significant between severity categories, including that from the ordinal regression analysis (OR = 3.33, 95% CI: 2.42-4.60, $p < 0.001$, and OR = 4.65, 95% CI: 2.92-7.43, $p < 0.001$, respectively). [15] This suggests that Gensini scores can be used as an alternative to FIB4 scores in diagnosing the severity of NAFLD among CAD patients.

Cut of value for Gensini score to diagnose severe NAFLD with 83.3 probability is 33.5 with 74.2% sensitivity and 84.8% specificity. The Cut of value of FIB4 to diagnose severe non-alcoholic fatty liver disease among CAD patients with 83.9% probability is 2.25 with 77.4% sensitivity and 84.8% Specificity.

According to Yun R. et al study if we combined the new FIB-4 cut-off with abnormal ultrasound findings (sonographic chronic liver disease or liver cirrhosis with FIB-4 > 2.68, is indicate advanced fibrosis), the accuracy of diagnosing advanced fibrosis was higher than when using FIB-4 or sonographic results alone.[16] Assuming that an unnecessary additional work-up could be avoided in patients who had a true negative or true positive test result, 81% of unnecessary work-ups would be avoided by incorporating FIB-4 and ultrasound results to evaluate subjects with advanced fibrosis.

CONCLUSION

The present study provides valuable insights into the prevalence, severity, and diagnostic thresholds of NAFLD among CAD patients. The findings highlight the importance of considering NAFLD in the management and treatment of CAD patients, particularly in relation to disease severity. The use of the Gensini score as an alternative to the FIB4 score demonstrates the potential for simplifying diagnostic approaches. Further research and validation studies are warranted to confirm these findings and to explore the clinical implications in more detail.

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