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# THE ASSOCIATION OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) WITH VARIOUS CARDIOVASCULAR RISK FACTORS AMONG PATIENTS OF CORONARY ARTERY DISEASE

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**Abstract**

***OBJECTIVE:*** *To determine the frequency of coronary artery disease (CAD) in patients with non-alcoholic fatty liver disease (NAFLD) and to assess the association of NAFLD with cardiovascular risk factors in patients with CAD*

***METHODOLOGY:*** *This cross-sectional study was carried out among confirmed cases of CAD for evaluation of an association of NAFLD with various cardiovascular risk factors at Department of Cardiology Liaquat University of Medical & Health Sciences, Jamshoro. A total of 92 eligible individuals were selected for the cohort (both men and women, between 20 to 80 years) who were pre-booked for a coronary angiography. The participants in the study were stratified into two distinct cohorts based on the presence or absence of comorbidity with nonalcoholic fatty liver disease (NAFLD), designated as the non-NAFLD-CAD cohort and the CAD cohort. The data were subjected to analysis utilizing SPSS version 26 statistical software, with statistical significance established at $p \leq 0.05$.*

***RESULTS:*** *The study involved a sample of 92 subjects with an average age of 52.36±14.01 years. A substantial proportion of the participants (51.1%) fell within the age bracket of >50 years, and 52.2% of the individuals were classified as female. The coronary artery disease was noted in 57.6% patients. In distribution of association of cardiovascular risk factors with NAFLD, obesity was noted in (65.6%; p=0.019), hypertension (66.7%; p=0.025), dyslipidemia (43.3%; p=0.054), smoking (84.6%; p=0.030), family history of CAD (63.6%; p=0.666), and metabolic syndrome (76.7%; p=0.001).*

***CONCLUSION:*** *Among patients with coronary artery disease (CAD), non-alcoholic fatty liver disease (NAFLD) was significantly associated with major cardiovascular risk factors including obesity, and hypertension, tobacco consumption, and metabolic syndrome. These observations imply that NAFLD may assume a contributory function in the elevation of cardiovascular risk levels. Systematic screening for NAFLD in patients with CAD is recommended to facilitate prompt intervention and comprehensive management strategies aimed at alleviating the incidence of cardiovascular complications*

## INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is increasingly being recognized as a significant risk factor independent of cardiovascular disease (CVD), including heart failure. Such association is of particular concern in the context of the increasing prevalence of NAFLD, which affects >25% of the adult population globally. The relationship between NAFLD and cardiovascular risk factors is intricate and consists of various pathways. NAFLD shares its multiple comorbidities with the metabolic syndrome, such as obesity, insulin resistance, and dyslipidemia, which adversely affect the development and progression of both diseases and resulting in the CVD. Patients with NAFLD are frequently presented with a higher prevalence of hypertension and type 2 diabetes, which are well-acknowledged as great risk factors for CVD [2]. A relation exists between NAFLD and subclinical atherosclerosis as indicated by a high coronary artery calcium score and a thickened carotid intima-media thickness. This association means that patients with NAFLD are at an increased risk of important cardiovascular disease events that actually affect clinical outcomes, such as myocardial infarction or stroke . NAFLD is marked by chronic low-graded inflammation and oxidative stress, and they closely correlate with endothelial dysfunction and atherogenesis. In addition, increased levels of inflammatory markers, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), have been shown in patients with NAFLD, may increase cardiovascular risk [4]. NAFLD has risk factors in common with metabolic syndrome, such as insulin resistance, obesity, hypertension and dyslipidaemia. NAFLD is strongly associated with its comorbidities, which themselves augment cardiovascular risk. Empirically, patients with NAFLD have shown increased prevalence of coronary atherosclerosis and an increased risk of cardiovascular events, such as myocardial infarction and heart failure, after adjusting for traditional risk factors [1,2,5]. Recent investigations have elucidated a substantial association between non-alcoholic fatty liver disease (NAFLD) and cardiovascular risk. In a cohort subjected to coronary angiography, NAFLD was identified in 58.2% of the subjects, exhibiting a markedly elevated incidence of significant coronary stenosis in comparison to their non-NAFLD counterparts (84.6% vs. 64.1%, $p < 0.001$). Consequently, there was a higher frequency of percutaneous coronary interventions conducted among NAFLD patients (68.3% vs. 43.4%, $p < 0.001$) [6]. The prevalence of coronary artery disease (CAD) was significantly greater in the NAFLD subgroup (60.5%) when juxtaposed with the non-NAFLD subgroup (45.2%). Furthermore, subjects in the high-normal UAER/low GFR group had more frequent presence of hypertension, smoking and obesity (assessed by BMI), central obesity (assessed by waist circumference and waist-to-hip ratio), increased HbA1c concentrations, increased triglycerides, low high-density lipoprotein (HDL), and a greater mean carotid intima-media thickness (CIMT) [7]. In view of the increasing incidence of NAFLD and CVD, the potential role of NAFLD as an independent CVD risk factor needs to be defined. This study aims to fill a current gap in our understanding related to the association of NAFLD with CVD. Through the analysis of the socio-demographic and clinical attributes of individuals both with and without NAFLD, this research aspires to elucidate critical determinants that heighten cardiovascular risk among those afflicted with NAFLD. Moreover, the outcomes derived from this study could facilitate future inquiries aimed at ascertaining the prognostic significance of NAFLD in forecasting CVD, ultimately enhancing patient outcomes.

## METHODOLOGY

This was a cross-sectional study carried out at Department of Cardiology, Liaquat University of Medical and Health Sciences, Jamshoro/Hyderabad. Ninety-two patients aged 20–80 years who were scheduled for coronarography were enrolled after informed consent was given and non-random consecutive sampling was applied. Inclusion criteria consisted of adult patients undergoing coronary angiography, whereas patients with a history of chronic liver disease, alcohol consumption, or pregnancy were excluded. The diagnosis of coronary artery disease (CAD) was based on coronary angiography findings showing ≥50% stenosis in one or more coronary arteries, or a clinical history of myocardial infarction, coronary revascularization procedures, or documented angina.The diagnosis of

non-alcoholic fatty liver disease (NAFLD) was made on the basis of abdominal USG by a consultant radiologist blinded to the study. The NAFLD diagnosis criteria were liver echogenicity higher than the renal cortex and spleen, attenuation of the ultrasound beam, indistinct diaphragm profile, and changes in visibility of periportal structure. Patients were categorized into CAD with NAFLD and without NAFLD. Information was obtained with structured questionnaires and from medical records. Body measurements were taken using standard protocol. Arterial blood pressure was recorded using a standard digital monitor, after the patient rested for 15 minutes. Cardiovascular risk factors were evaluated: obesity (BMI ≥30 kg/m2), hypertension (BP ≥130/85 mmHg or use of anti-hypertensive drugs), dyslipidemia (abnormal lipid profile), type 1 diabetes or type 2 diabetes (diagnosed by the standard glucose or HbA1c criteria), the metabolic syndrome (central obesity plus ≥ 2 additional criteria), and current smoking (> 1 cigarette/day in the last year). Data was entered and analyzed using SPSS version 26. Categorical variables were expressed as frequencies and percentages, and continuous variables as mean ± standard deviation. Chi-square test and independent sample t-tests were applied to compare groups. A p-value ≤ 0.05 was considered statistically significant.

## RESULTS

A total of 92 participants with a mean age of 52.36 ± 14.01 years were enrolled in the study. The age distribution was almost balanced, 48.9% of the subjects were aged 20–50 years, and 51.1% above 50 years. In the sample, females were slightly more than males, with about 52.2% versus 47.8%. (Table I)

The relationship between non-alcoholic fatty liver disease (NAFLD) and several cardiovascular risk factors was prospectively evaluated in 92 subjects. The prevalence of NAFLD was much more common in females (68.8%) as compared to males (45.5%) (p= 0.024). There was a significant relationship between obesity and NAFLD; 65.6% of patients who had NAFLD were obese while 34.4% were not (p = 0.019). Similarly, hypertension was significantly more common in the NAFLD group (66.7%) than in the non-NAFLD (33.3%) group with a p-value of 0.025. Moreover, smoking was also significantly associated, presented more in the NAFLD (84.6%) than non-NAFLD subjects (15.4%) (p = 0.030).

Although dyslipidemia was more common in non-NAFLD participants, the difference approached but did not reach statistical significance (p = 0.054). No significant association was found between NAFLD and a family history of coronary artery disease (p = 0.666). However, metabolic syndrome showed a strong and significant association with NAFLD, present in 76.7% of affected individuals compared to 23.3% without NAFLD (p = 0.001). (Table II)

## DISCUSSION

This study was conducted to determine the association of non-alcoholic fatty liver disease (NAFLD)with cluster of cardiovascular risk factor in patients of coronary artery disease (CAD). According to our study, significantly higher prevalence of NAFLD was found to be associated with obesity (65.6%; P=0.019), hypertension (66.7%; P=0.025), tobacco use (84.6%; P=0.030), and metabolic syndrome (76.7%; P=0.001). There was a trend toward significance of dyslipidemia (43.3%; p=0.054) which, however, did not reach the set statistical threshold at last. There was no significant correlation in the family history of CAD (63.6%; p=0.666).

These results are consistent with the several published reports showing high association between NAFLD and cardiovascular risk factors. Montemezzo et al. stressed that NAFLD is common in the presence of CAD, particularly in patients with acute coronary syndrome, and that both diseases share pathogenic mechanisms including systemic inflammation and insulin resistance [8]. Saraya et al. similarly observed that NAFLD was associated with key risk factors such as hypertension (32.7%; p=0.01), diabetes mellitus (27.3%; p=0.001), smoking (14.5%; p=0.014) and dyslipidemia (28.6%; p=0.001) [9], these findings further support the observations in our population.

Mundi et al. elaborated on the progressive comprehension of non-alcoholic fatty liver disease (NAFLD) as a complex, multisystemic condition, emphasizing its capability to intensify cardiovascular risk beyond complications directly associated with liver pathology [10]. Arslan and Yenerçağ similarly articulated a reciprocal relationship between NAFLD and coronary heart disease, thereby corroborating the

notion that NAFLD serves as both an indicator and a potential catalyst for atherosclerotic processes [11].

Furthermore, the results of the study by Gholoobi et al. have shown that the existence and severity of NAFLD is highly correlated with the CAD degree among patients who are undergoing angiographic testing. In their discussion, they concluded that "an independent correlation between NAFLD and CAD is confirmed by our findings from diagnostic angiography". Moreover, the study by Dai et al. demonstrates the relationship between NAFLD and the risk of the development of the type 2 diabetes and CAD among non-obese individuals. Our observations, in the same way, demonstrated the strong connection between NAFLD and metabolic syndrome at (76.7%).

Similarly, this study also found high percentage of association between smoking and NAFLD (84.6) which adds to the evidence that modifiable lifestyle factors play an important role in the manifestation of liver disease just as it does cardiovascular disease [54]. Liu et al. apart NAFLD has been recently identified as an independent predictor of adverse cardiovascular events in those with stable CAD [14], consistent with the results of our investigation and supports the opinions that NAFLD should be screened on a daily basis.

Moreover, Toh et al. executed a comprehensive global meta-analysis that substantiated the elevated prevalence and robust correlation of coronary heart disease among individuals with non-alcoholic fatty liver disease (NAFLD), thereby advocating for the implementation of proactive screening and risk management strategies within this demographic [15]. Chiriac et al. further emphasized that NAFLD ought to be acknowledged as an integral element of cardiovascular risk assessments, thereby playing a contributory role in both clinical manifestations and subclinical presentations of cardiovascular pathology [16].

The current study emphasizes a strong relationship of NAFLD to established ongoing CVD risk factors in CAD patients. These results contribute to increasing evidence that NAFLD must be systematically integrated in the "risk prediction" of cardiovascular complications and managed through an integrated clinical approach.

The current study has several limitations that should be recognized. Firstly, the cross-sectional design does not enable causal inferences concerning the relationship between non-alcoholic fatty liver disease and the cardiovascular risk factors in patients with coronary artery disease. Instead, the data only provide single-time associations and do not consider the dynamics or the order of the occurrence of the mentioned phenomena. Secondly, the sample size of 92 individuals does not support the generalization of results. A larger and more heterogenic sample would ensure better statististical representation.

Moreover, there are limitations regarding the diagnostic modality for NAFLD. The diagnosis was established using ultrasonography. Despite its common use in clinical practice because it is non-invasive and relatively inexpensive, ultrasonography has low sensitivity for the diagnosis of mild or early hepatic steatosis and is unable to determine the fibrosis stage. Therefore, the assessment using more advanced imaging modalities, such as Fibro Scan or magnetic resonance imaging, could have yielded more accurate information on liver fat content and fibrosis. Additionally, several information sources, including smoking and some lifestyle-related data, were self-reported; this fact could result in recall or reporting bias. Finally, the present study was carried out solely at one tertiary care center. Thus, the risk of selection bias exists, and results cannot necessarily be generalized to community or outpatient care practice. Nevertheless, the study also has several strengths. Firstly, the researchers followed standardized descriptions and criteria for CAD, NAFLD, and CVD risk factors. Therefore, this indicates a higher level of material and criterion quality. Secondly, the application of an ultrasound assessment performed by a blinded radiologist seemed to restrict the tendency toward diagnostic bias. Lastly, the structured data collection approaches and evaluation with the aid of objective anthropometric and clinical measures seemed to guarantee the accuracy of results.

Hence, future investigations must apply the longitudinal study designs to determine the casual relationships. Meanwhile, larger, multicenter studies employing the most simultaneous imaging methods of NAFLD examination should be conducted. Based on the existing findings, general practitioners should focus on the regular screening for NAFLD among

CAD patients with identified metabolic risk to implement the early intervention and comprehensive risk management.

## CONCLUSION

Among patients with coronary artery disease (CAD), non-alcoholic fatty liver disease (NAFLD) was significantly associated with major cardiovascular risk factors including obesity, and hypertension, tobacco consumption, and metabolic syndrome. These observations imply that NAFLD may assume a contributory function in the elevation of cardiovascular risk levels. Systematic screening for NAFLD in patients with CAD is recommended to facilitate prompt intervention and comprehensive management strategies aimed at alleviating the incidence of cardiovascular complications.

| **Table I: Characteristics of Study Participants** (n=92) | |
|---|---|
| **Variable** | **n** (%) |
| **Age (Mean ± SD)** = 52.36 ± 14.01 | |
| 20 - 50 years | 45 (48.9) |
| >50 years | 47 (51.1) |
| **Gender** | |
| Male | 44 (47.8) |
| Female | 48 (52.2) |

**Table II: Association of Non-Alcoholic Fatty Liver Disease (NAFLD) with Various Cardiovascular Risk Factors** (n=92)

| **Risk Factors** | | **NAFLD** (n=53) | **Non-NAFLD** (n=39) | **95% C. I** | **P-Value** |
|---|---|---|---|---|---|
| Gender | Male | 20 (45.5) | 24 (54.5) | (0.16–0.88) | 0.024 |
| | Female | 33 (68.8) | 15 (31.3) | | |
| Obesity | | 42 (65.6) | 22 (34.4) | (1.17–7.38) | 0.019 |
| Hypertension | | 38 (66.7) | 19 (33.3) | (1.12–6.34) | 0.025 |
| Dyslipidemia | | 13 (43.3) | 17 (56.7) | (0.17–1.02) | 0.054 |
| Smoking | | 11 (84.6) | 2 (15.4) | (1.00–23.29) | 0.030 |
| Family History of CAD | | 7 (63.6) | 4 (36.4) | (0.36–4.90) | 0.666 |
| Metabolic Syndrome | | 33 (76.7) | 10 (23.3) | (1.92–11.86) | 0.001 |

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