ORIGINAL ARTICLE

Frequency of NAFLD among Patients of Coronary Artery Disease

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ABSTRACT

Objective: The purpose of this study was to assess the prevalence of NAFLD in coronary artery disease patients. **Study Design:** Prospective study

Place and Duration: Department of General Medicine, Khyber Teaching Hospital, MTI Peshawar in the duration from June, 2022 to November, 2022.

Methods: Total 125 patients of both genders with age 25-75 years were presented. Patients were included if they had a verified diagnosis of CAD and stenosis in either of the main coronary arteries or one of the branches. Hepatic steatosis was diagnosed with ultrasound of the liver in all individuals. Likewise, steatosis severity was ranked from 0 (no steatosis present) to 3 (moderate steatosis present) (severe steatosis). At last, the patients' NAFLD prevalence was calculated. The data was analyzed using SPSS 23.0.

Results: In all, 73 (58.4%) patients were males and 52 (41.6%) cases were females. Mean age of the patients was 44.6±18.37 years and had mean BMI 26.9±11.65 kg/m². Most common comorbidity was hypertension, followed by diabetes mellitus, obesity and hyperlipidemia. There were 60 (48%) smokers among all cases. Frequency of NAFLD was found in 62 (49.6%) cases. Among 62 cases of NAFLD, 40 cases were had normal NAFLD (grade 1) and 22 cases were had mild NAFLD (grade 2). Majority of the NAFLD patients were had hyperlipidemia, obesity and hypertension.

Conclusion: We found that obese, HTN, and hyperlipidemic NAFLD individuals were more common. The prevalence and severity of NAFLD were also independently linked with CAD. Normal vascular and NOB patients had mild NAFLD, while extensive CAD patients with multi-vessel disease had severe NAFLD.

Keywords: CAD, NAFLD, Obesity, Hyperlipidemia, HTN

INTRODUCTION

Abnormal buildup of triglycerides (steatosis) in the liver is the hallmark of non-alcoholic fatty liver disease (NAFLD) [1]. Initial stages often show no signs of hepatocellular damage or fibrosis and are thus considered benign. Histology (liver biopsy) is commonly used to arrive at a conclusive diagnosis [3]. Nevertheless, imaging techniques including ultrasound, computed tomography, and magnetic resonance imaging (MRI) are frequently utilized since they are painless and accurate ways to identify NAFLD. The presence of metabolic risk factors increases the likelihood that NAFLD will advance to liver inflammation, hepatocellular damage, fibrosis, and end-stage liver failure [4, 5], highlighting the need of early identification of NAFLD. In addition, NAFLD has been proposed as a potential risk factor for CVD [5]. It has been demonstrated in many studies [6, 7] that individuals with NAFLD had a greater 10-year chance of cardiovascular disease events. The prevalence of cardiovascular, cerebrovascular, and peripheral vascular disease was shown to be considerably greater in individuals with NAFLD compared to people without NAFLD. A meta-analysis confirmed these findings, concluding that individuals with NAFLD had an increased risk of both fatal and nonfatal CVD events [7].

The potential link between NAFLD and CAD [8] is of relevance because of the relationship between NAFLD and metabolic syndrome. In contrast, research shows that NAFLD is linked with cardiovascular events regardless of age, sex, LDL cholesterol, smoking, and other markers of the metabolic syndrome [8]. Moreover, some authors have shown that individuals with NAFLD had a much higher than average carotid artery intimamedia thickness, an indication of subclinical atherosclerosis [9].

The importance of detecting and treating CAD in patients with NAFLD [10] is underscored by the fact that cardiovascular disease is the major cause of mortality in individuals with NAFLD and accounts for more than 30 percent of fatalities in the United States overall. NAFLD is more common in those who have had an acute myocardial infarction and can be used as a predictor of the disease's severity and progression [11].

It was anticipated that non-alcoholic fatty liver disease (NAFLD) connects with coronary artery disease (CAD), one of the leading causes of death globally, because NAFLD is strongly connected with metabolic syndrome and insulin resistance.

NAFLD is on the rise, and with it come a number of risk factors, the most notable of which are obesity and type 2 diabetes mellitus (T2DM). Around ninety-five percent of individuals with extreme obesity and/or obesity who undergo bariatric surgery have NAFLD [13]. Patients with type 2 diabetes mellitus had a prevalence as high as 60%. Elevated levels of alanine aminotransferase (ALT) and gamma-glutamyltransferase (GGT) are two liver enzymes that are also linked to NAFLD [14]. The metabolic syndrome is consistent with these clinical findings (MetS). There is some evidence in the literature [15] to imply that NAFLD is the hepatic manifestation of MetS. Nevertheless, because much of the available research on NAFLD has been undertaken in hospitals and other tertiary facilities, we know very little about the risk factors for this condition in primary care in Malaysia.

Due to the symptomatic nature of CAD, the discovery of a strong correlation between the two conditions may suggest that individuals with a CAD diagnosis might benefit from screening for NAFLD. Hence, the current investigation was conceived of and executed to ascertain the incidence of NAFLD in CAD patients.

MATERIAL AND METHODS

This prospective study was conducted at Department of General Medicine, Khyber Teaching Hospital, MTI Peshawar in the duration from June, 2022 to November, 2022 and comprised of 125 cases of CAD. Individuals who had undergone coronary artery angiography at the center for acute coronary syndrome, chest discomfort, or a positive exercise test were chosen from that group. In the trial, patients were enrolled at random with out any degree of stenosis in the coronary arteries or their branches after coronary angiography. The study excluded patients with heart failure, a history of coronary artery bypass graft (CABG), heavy alcohol use, any hepatic problem, cor pulmonale, chronic renal

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disease, cancer, acute or chronic infections, or positive serology for hepatitis B or C, HIV, or syphilis.

Based on the results of the ultrasonography, NAFLD was identified. After 12 hours of fasting, one radiologist performed each ultrasound examination using the same equipment and standards. Using the following grading system: grade 0, no fatty liver; grade 1, mild disease; grade 2, moderate illness; and grade 3, severe disease, the echogenicity of the liver was compared to the echogenicity of the left kidney. The Saverymuttu et al. approach was used to evaluate the degree of hepatic steatosis. The approach relies on the liver-kidney difference in echo amplitude, echo penetration into the deep region of the liver, and clarity of the liver's vascular pattern. It also relies on abnormally intense, high level echoes from the hepatic parenchyma.

Categorical and continuous variables were analyzed using Fisher's exact test and Student's independent t-test, respectively. P-values of 0.05 or below were regarded as statistically significant. SPSS 23.0 was used to analyze the data.

RESULTS

In all, 73 (58.4%) patients were males and 52 (41.6%) cases were females. Mean age of the patients was 44.6 ± 18.37 years and had mean BMI 26.9 ± 11.65 kg/m². Most common comorbidity was hypertension, followed by diabetes mellitus, obesity and hyperlipidemia. There were 60 (48%) smokers among all cases. (table 1)

Table-1. Daseline details of enfolied cases	Table-1:	Baseline	details of	f enrolled	cases
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Variables	Frequency	Percentage
Mean age (years)	44.6±18.37	
Mean BMI (kg/m ²)	26.9±11.65	
Gender		
Male	73	58.4
Female	52	41.6
Comorbidities		
Hypertension	40	32
DM	35	28
Obesity	32	25.6
Hyperlipidemia	23	18.4
Smokers		
Yes	60	48
No	65	52

Frequency of NAFLD was found in 62 (49.6%) cases.(figure 1)





Among 62 cases of NAFLD, 40 cases were had normal NAFLD (grade 1) and 22 cases were had mild NAFLD (grade 2).(table 2)

Table-1: Severity of NAFLD among CAD cases

Variables	Frequency (62)	Percentage
NAFLD		
Normal	40	64.5
Mild	22	35.5
Total	62	100

Majority of the NAFLD patients were had hyperlipidemia, obesity and hypertension.(table 2)

Variables	Frequency (n=62)	Percentage
Comorbidities		
Hyperlipidemia	19	30.6
Obesity	18	29.03
Hypertension	15	24.1
DM	10	16.1

DISCUSSION

Many studies have looked at the possible links between CAD and NAFLD. The research by Kim et al. included 4023 people who had no history of ischemic heart disease or liver illness. [16] Independent of other known risk factors for CAD, such as abdominal fat, they discovered that NAFLD was linked to coronary artery calcification. In their opinion, NAFLD should be seen as a separate risk factor of CAD.

In current study 125 cases of CAD were presented. In all, 73 (58.4%) patients were males and 52 (41.6%) cases were females. Mean age of the patients was 44.6±18.37 years and had mean BMI 26.9±11.65 kg/m². Our findings demonstrate a correlation between NAFLD prevalence and severity and CAD risk. It is interesting to note that moderate NAFLD is seen in normal and NOB individuals, but severe NAFLD is more common in patients with severe CAD and multi-vessel disease.

Participants undergoing elective coronary angiography were evaluated, and it was discovered that 49.6% of them had NAFLD. Our findings are in line with those of Perera et al., who discovered that NAFLD was present in 46.67 percent of patients with nonfatal ACS in Sri Lanka. Our findings are compatible with those of Perera et al. [17] Individuals diagnosed with ACS who had diagnostic coronary angiography in Finland (53.78 percent), Turkey (53.16%), and Brazil (55.2 percent) all had NAFLD. Participants with a body mass index (BMI) of above 27.5 had 2.89 times the risk of developing NAFLD compared to those with a BMI of less than or equal to 27.5 (Adj. OR 2.89, 95%CI 1.21, 6.91). Overweight people (BMI > 25 kg/m2) were also more likely to develop NAFLD, according to a research conducted in Asia (OR 1.05 (95%CI 1.004,1.09) p = 0.031. [18] In our analysis, people with high fasting plasma glucose levels (FPG 5.6 mmol/L) were 2.79 times more likely to have NAFLD than those with normal FPG (Adj OR 2.79, 95%CI 1.44, 5.43) compared to those with normal FPG. Similar results were seen in Sri Lanka, with an odds ratio (OR) for NAFLD of 1.7 (95%CI 1.39, 2.08) for an increased FPG of 5.6 mmol/L or higher [19,20].

Atherogenic dyslipidemia (increased LDL-c, triglycerides, and apolipoprotein B and decreased HDL) and increased carotid intima-media thickness may be exacerbated by the systemic inflammatory state seen in NAFLD patients, leading to an increased risk of CVE [21]. There is a substantial correlation between the histological severity of NAFLD and inflammation and an elevated risk of CVD and this atherogenic lipid profile. Although the presence of conventional CAD risk factors and components of the metabolic syndrome exacerbates the pathogenesis of NAFLD, it appears that people with NAFLD are immune to the development of coronary artery atherosclerosis. NAFLD has also been linked to endothelial dysfunction, increased inflammatory biomarkers, and subclinical atherosclerosis in the carotid artery. [22] Consistent with earlier reports, we discovered that patients with greater BMI were more likely to develop NAFLD.

Those without NAFLD were more likely to have normal angiography, but 2VD was seen in those with the most severe

NAFLD. NAFLD patients also tended to have an early form of atherosclerosis called non-obstructive bronchitis (NOB). Wong et alfindings .'s indicating CAD is more common in NAFLD patients (84.6% vs. 64.1% of the general population) are consistent with ours. They discovered a correlation between NAFLD and CAD (OR = 2.31, 95% CI = 1.46-3.64). [23]

CONCLUSION

We found that obese, HTN, and hyperlipidemic NAFLD individuals were more common. The prevalence and severity of NAFLD were also independently linked with CAD. Normal vascular and NOB patients had mild NAFLD, while extensive CAD patients with multivessel disease had severe NAFLD.

REFERENCES

- Labrecque DR, Abbas Z, Anania F, Ferenci P, Khan AG, Goh KL, et al. World gastroenterology organisation global guidelines: nonalcoholic fatty liver disease and nonalcoholic steatohepatitisbrecq. J Clin Gastroenterol. 2014;48(6):467–73.
- 2 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.
- 3 Cleveland E, Bandy A, VanWagner LB. Diagnostic challenges of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. Clin Liver Dis. 2018;11(4):98–104.
- 4 Ahmed MH, Abu EO, Byrne CD. Non-alcoholic fatty liver disease (NAFLD): new challenge for general practitioners and important burden for health authorities? Primary care diabetes; 2010.
- 5 Treeprasertsuk S, Leverage S, Adams LA, Lindor KD, St Sauver J, Angulo P. The Framingham risk score and heart disease in nonalcoholic fatty liver disease. Liver Int. 2012;32(6):945–050.
- 6 Alkagiet S, Papagiannis A, Tziomalos K. World journal of Hepatolgy. World J Hepatol. 2018;10(7):474–8.
- 7 Targher G, Byrne CD, Lonardo A, Zoppini G, Barbui C, BCh M. Nonalcoholic fatty liver disease and risk of incident cardiovascular disease: a meta-analysis of observational studies. J Hepatol. 2016;65(3):1–29.
- 8 E. Lerchbaum, S. Pilz, T. B. Grammer et al., "The fatty liver index is associated with increased mortality in subjects referred to coronary angiography," Nutrition, Metabolism & Cardiovascular Diseases, vol. 23, pp. 1231–1238, 2013.
- 9 G. Targher and G. Arcaro, "Non-alcoholic fatty liver disease and increased risk of cardiovascular disease," Atherosclerosis, vol. 191, no. 2, pp. 235–240, 2007.

- 10 L. A. Videla, "Oxidative stress signaling underlying liver disease and hepatoprotective mechanisms," World Journal of Hepatology, vol. 1, no. 1, pp. 72–78, 2009.
- 11 M. T. Agaç, L. Korkmaz, G. Cavusoglu et al., "Association between nonalcoholic fatty liver disease and coronary artery disease complexity in patients with acute coronary syndrome: a pilot study," Angiology, vol. 64, no. 64, pp. 604–608, 2013.
- 12 Arbab-Zadeh A, Nakano M, Virmani R, Fuster V. Acute coronary events. Circulation. 2012;125(9):1147–56.
- 13 Sweet PH, Khoo T, Nguyen S. Nonalcoholic fatty liver disease. Prim Care. 2017;44:599–607.
- 14 Caballería L, Pera G, Auladell MA, Torán P, Muñoz L, Miranda D, et al. Prevalence and factors associated with the presence of nonalcoholic fatty liver disease in an adult population in Spain. Eur J Gastroenterol Hepatol [Internet]. 2010;22(1):24–32
- 15 Singh SP, Singh A, Misra D, Misra B, Pati GK, Panigrahi MK, et al. Risk factors associated with non-alcoholic fatty liver disease in Indians: a case-control study. J Clin Exp Hepatol. 2015;5(4):295–302.
- 16 Kim D, Choi SY, Park EH, Lee W, Kang JH, Kim W, et al. Nonalcoholic fatty liver disease is associated with coronary artery calcification. Hepatology. 2012;56(2):605–13.
- 17 Perera N, Indrakumar J, Abeysinghe WV, Fernando V, Samaraweera WMCK, Lawrence JS. Non alcoholic fatty liver disease increases the mortality from acute coronary syndrome: an observational study from Sri Lanka. BMC Cardiovasc. Disord. 2016; 16: 37.
- 18 Montemezzo M, AlTurki A, Stahlschmidt F, Olandoski M, Rodrigo Tafarel J, Precoma DB. Nonalcoholic fatty liver disease and coronary artery disease: big brothers in patients with acute coronary syndrome. ScientificWorldJournal. 2020; 2020: 8489238.
- 19 Keskin M, Hayıroğlu M, Uzun AO, Güvenç TS, Şahin S, Kozan Ö. Effect of nonalcoholic fatty liver disease on in-hospital and longterm outcomes in patients with ST-segment elevation myocardial infarction. Am. J. Cardiol. 2017; 120: 1720–6.
- 20 Olubamwo OO, Virtanen JK, Voutilainen A, Kauhanen J, Pihlajamäki J, Tuomainen TP. Association of fatty liver index with the risk of incident cardiovascular disease and acute myocardial infarction. Eur. J. Gastroenterol. Hepatol. 2018; 30: 1047–54.
- 21 T. M. Haddad, S. Hamdeh, A. Kanmanthareddy, and V. M. Alla, "Nonalcoholic fatty liver disease and the risk of clinical cardiovascular events: a systematic review and meta-analysis," Diabetes & Metabolic Syndrome: Clinical Research & Reviews, vol. 11, pp. S209–S216, 2016.
- Villanova N, Moscatiello S, Ramilli S, Bugianesi E, Magalotti D, Vanni E, et al. Endothelial dysfunction and cardiovascular risk profile in nonalcoholic fatty liver disease. Hepatology. 2005;42(2):473–80.
- 23 Miptah, H.N., Ramli, A.S., Mohamad, M. et al. Non-alcoholic fatty liver disease (NAFLD) and the cardiovascular disease (CVD) risk categories in primary care: is there an association? BMC Fam Pract 21, 238 (2020).