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RESEARCH ARTICLE
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"Prevalence of NAFLD in Patients with Ischemic Heart Disease-A Study in Enam Medical College and Hospital in Bangladesh"

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Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) has an in-creasing prevalence worldwide. It has also been closely associated with obesity and metabolic syndrome - two conditions known to be asso-ciated with ischemic heart disease (IHD). Several common metabolic risk factors contribute to development of both nonalcoholic fatty liver disease (NAFLD) and Ischemic Heart Disease worldwide with a preva-lence as high as 30% in the general population.

Objective: To deter-mine prevalence of NAFLD in patients with Ischemic Heart Disease.

Methods: The prospective study was conducted in the Department of Cardiology, Enam Medical College & Hospital, Savar, Bangladesh between January 2020 to December 2020. The study was conducted on 100 patients (62 patients with NAFLD and 38 Non-NAFLD) subjects were selected. Full history taking, clinical examination and laboratory tests including blood sugar, lipid profile and liver profile were done. Ultrasonography was performed to prove NAFLD while ECG and echocardiography were used for detection of myocardial ischemia.

Results: The present study was by enrolling 100 patients of coronary artery disease divided into two groups i.e. NAFLD group n= 62 (62%) and Non NAFLD group n= 38 (38%). Participants were selected and divided into two groups; NAFLD group included 62 patients with ultrasonography NAFLD (45 males & 21 females) with mean age 45.81±12.46 years and non-NAFLD group of 38 subjects with mean age 45.32± 10.56 years. The present study shows that the prevalence of NAFLD was highest (86.8%) in more than 40 years of age group. The present study shows that the prevalence of NAFLD was more in males (84.2%) as compare to females (15.8%). The present study also shows significantly high incidence of metabolic syndrome in patients with NAFLD (23.7%) as compared to Non-NAFLD (3.2%) patients with Coronary Artery (CAD). Of the NAFLD group, the frequency of mild, moderate and severe NAFLD was 42.9%, 30% and 29.1% respectively. Subjects with NAFLD had a significantly higher BMI, waist circumference and weight compared to those of non NAFLD group (p=0.014, 0.0218 and <0.001 respectively). Independent risk factors for NAFLD were obesity, DM, high LDL, low HDL, waist circumference, glycated hemoglobin and IHD with odds ratios 1.09, 2.12, 1.01, 1.15, 1.13, 1.37 and 1.17 respectively. While independent risk factors for IHD included obesity, DM, high LDL, total cholesterol, triglycerides and the presence of NAFLD with odds ratios 1.31, 1.23, 1.19, 1.132, 1.68 respectively.

Conclusion: The current study revealed that presence of NAFLD is associated with increased risk of IHD. This association was not only due to common risk factors shared between the two entities such as obesity, dyslipidemia and diabetes, but also a direct independent positive relationship was found between them. So NAFLD can be considered as an independent predictor of myocardial ischemia. The present study indicated a high prevalence of NAFLD in patients with documented Ischemic Heart Disease.

Keywords: NonAlcoholic Fatty Liver Disease, Ischemic Heart Disease, Ultrasound

1 | INTRODUCTION

NAFLD has become the predominant cause of chronic liver disease in many parts of the world. An overall global prevalence of 25.24% was reported with the highest figures were derived from the Middle East (31.79%) and South America (30.45%) (1). NAFLD is considered a multisystem disease affecting several extrahepatic organs and regulatory pathways (2). The major focus of NAFLD-related diseases has involved chronic liver disease, cardiovascular diseases and type 2 DM. There is also emerging evidence that NAFLD is linked to other diseases such as sleep apnea, colorectal cancer, osteoporosis, psoriasis and polycystic ovary syndrome (3). Liver biopsy is considered the gold standard for diagnosing steatosis, but it is an invasive method associated with many adverse effects. Since ultrasonogram is relatively precise for the diagnosis of NAFLD, low-cost, risk-free and widely available, it has been a frequently used method (4). CT scan magnetic resonance imaging either by spectroscopy or by proton density fat fraction is an excellent noninvasive quantitative modality for assessment of steatosis and is being widely used in NAFLD clinical trials (5). Patients with NAFLD have been shown to have increased mortality. The main cause of morbidity and mortality in these patients was cardiovascular disease (6). Several studies have linked fatty liver to ischemic heart disease but they present controversial results. Some demonstrated an increased cardiovascular risk in NAFLD while others argued against this relationship. So, the role of NAFLD as an independent cardiovascular risk factor is still debated (7).

2 | MATERIALS AND METHODS

The prospective study was conducted in the Department of Cardiology, Enam Medical College & Hospital, Savar, Bangladesh between January 2020 to December 2020. The study was conducted on 100 patients (66 patients with NAFLD and 34 non-NAFLD) subjects were selected. Full history taking, clinical examination and laboratory tests including blood sugar, lipid profile and liver profile were done. Ultrasonography and CT scan were performed to prove NAFLD while ECG, echocardiography, coronary angiogram were used for detection of myocardial ischemia.

Inclusion criteria:

- Patients of both sexes were included.
- Age: 18-65.
- Ultrasonography/CT scan proven NAFLD.

Exclusion criteria:

- Advanced liver disease.
- Hepatocellular carcinoma.
- Comorbid liver disease and life threatening illness.
- Alcohol intake >20g/day, Presence of chronic liver disease, hepatitis B surface antigen or anti HCV antibody. Subjects those who were exposed to drugs and toxins such as: L-Asparaginase, Azaserine, Bleomycin, Methotrexate, Azacitidine, Puromycin, Tetracyclin, Amiodarone, 4,4'- diethlyaminethoxy-hexesterol, Dichloroethylene, Ethionine, Ethyl bromide, Estrogen, Highly active retroviral therapy, Hydrazine, orotate, Perhexilene maleate, Safrole, Tamoxifen. Subjects who were exposed to metals such as Antimony, Barium salts, Chromates, Phosphorus, Thallium compounds and Uranium compounds, and undergone surgical procedures such as biliopancreatic diversion, extensive small bowel resection, gastric bypass, jejunoileal bypass. Sonography of fatty infiltration varies depending on the amount of fat whether deposits are diffuse or focal (7).

All Patients were subjected to thorough history taking, clinical examination including body mass index, weight and waist circumference and laboratory assessment including aspartate aminotransferase (AST), alanine aminotransferase (ALT), total & direct bilirubin, total serum cholesterol, serum triglycerides (TG), serum high-density lipoprotein (HDL) cholesterol, fasting glucose, HbA1C, hepatitis B surface antigen, and an antibody to hepatitis C virus.

Supplementary information The online version of this article (https://doi.org/10.15520/jmrhs.v4i7.366) contains supplementary material, which is available to authorized users.

Diagnosis of NAFLD: Abdominal ultrasonography performed by an experienced radiologist and CT scan of abdomen were used for diagnosis of fatty liver. The criteria used were: increased echogenicity relative to the kidney, distal attenuation and loss of intra-hepatic architectural details. Fatty liver was classified according to the following items: echogenicity relative to kidneys (0-3), blurring of gall bladder wall (0-3), blurring of hepatic veins (0-3), blurring of portal vein (0-3), far gain attenuation (0-3). Grading was defined as mild (total scores of 2-6), moderate (7-10), and severe (11-15) fatty liver (8). Diagnosis of NALFD was done following exclusion of significant alcohol intake, other causes of chronic liver disease and use of drugs that could cause fatty liver.

Statistical M ethods: The collected data were analyzed using SPSS software (statistical package for social science) version 22.0 on IBM compatible computer. Continuous variables were expressed as mean ± standard deviation (M ± SD), and analyzed using Student's t-test. Categorical variables were expressed as number and percentage and analyzed using Chi-square test or Fisher's exact test. Multivariate logistic regression analysis was used. Variables found to be significant on the univariate analysis to identify independent factors associated with NAFLD and IHD. The level of significance was set at a P-value of <0.05.

3 | RESULTS

The present study was by enrolling 100 patients of coronary artery disease divided into two groups i.e. NAFLD group n= 62 (62%) and Non NAFLD group n= 38 (38%). Participants were selected and divided into two groups; NAFLD group included 62 patients with ultrasonography NAFLD (45 males & 21 females) with mean age 45.81±12.46 years and non-NAFLD group of 38 subjects with mean age 45.32± 10.56 years. The age distribution of the study participants revealed that the proportion of diseased were more (N=54) among the age group of 40-60 years, followed 39 patients belong to >60 years and 7 belong to 20-40 years group (Figure 1). Among the coronary artery disease subjects 89% had metabolic syndrome (Figure 3). Gender wise proportion of NAFLD and Non NAFLD showed HDL level was low in Non-NAFLD in both older male and females and HDL was relatively increased in young participants compared to Non NAFLD group (Figure 4). Of the NAFLD group, the frequency of mild, moderate and severe NAFLD was 42.9%, 30% and 29.1% respectively. Subjects with NAFLD had a significantly higher BMI, waist circumference and weight compared to those of non NAFLD group (p=0.014, 0.0218 and <0.001 respectively). On the other hand, no significant difference was found between the two groups regarding the age, sex or height. Regarding the evidence of myocardial ischemia, a statistically significant difference was found between NAFLD and non NAFLD groups with respect to the presence wall motion abnormalities and ischemic changes in ECG as shown in (Table 2).

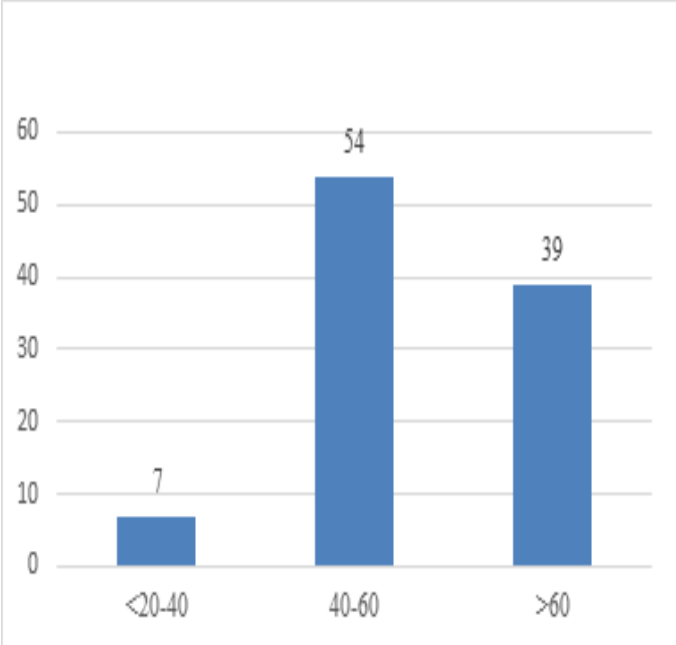

FIGURE 1: Distribution of age among the study subjects

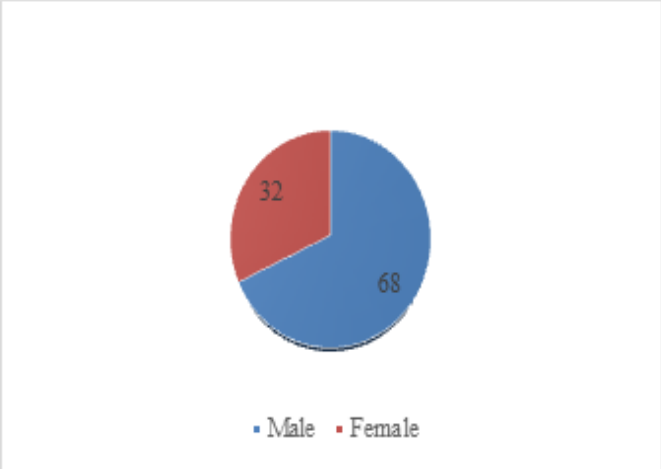

FIGURE 2: Gender distribution of study subjects

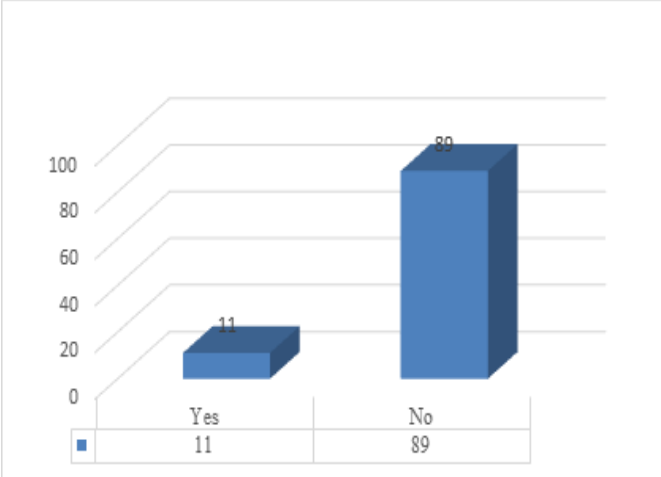

FIGURE 3: Proportion of metabolic syndrome among study subjects.

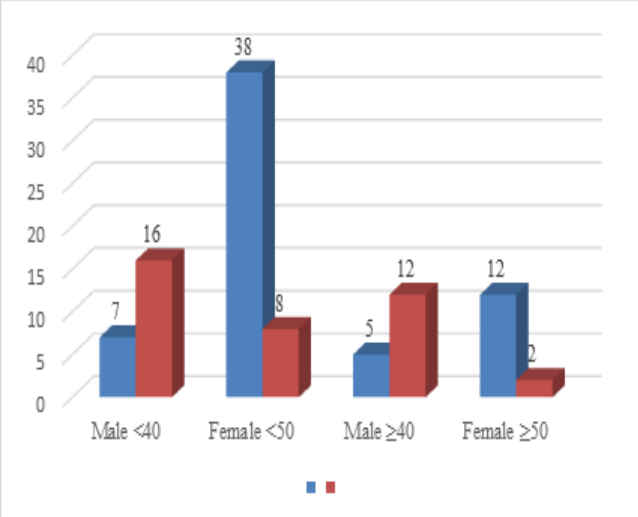

FIGURE 4: Gender wise proportion of NAFLD and Non NAFLD with HDL.

TABLE 1: 1: Clinical and laboratory characteristics of NAFLD and non-NAFLD groups.

	NAFLD	Non NAFLD	Chi-square/ *t*-test	
	No (%)	No (%)	t/X^2	p-value
Sex				
Male	45 (68.1%)	23 (67.6%)	0.10	0.922
Female	21 (32.8%)	11 (32.3%)		
Smoking	41 (41.0%)	10 (10.0%)	1.287	0.257
Family History Of CAD	55 (55.0%)	45 (45.0%)		
BMI				
Normal	12 (17.91%)	6 (18.18%)	6.802	0.033*
Over weight	20 (29.85%)	16 (48.48%)		
Obese	35 (52.23%)	11 (33.33%)		
DM	45 (67.16%)	7 (21.21%)	58.372	<0.001**
FBS				
<126	23 (50.0%)	47 (87.0%)		
≥126	23 (50.0%)	7 (13.0%)		
	Mean ± SD	Mean ± SD	t/X^2	P-value
Age (year)	48.81 ± 12.46	49.32 ±10.56		
Height (cm)	159.0 ± 7.4	161.4 ± 8.4	25.146	0.321
Weight (kg)	75.5 ± 10.0	65.9 ± 8.2	9.422	<0.001**
Waist circumference (cm)	96.5 ± 11.4	90.3 ± 12.9	11.393	0.0218*
BMI (kg/m2)	31.81±5.23	25.4±3.45	4.713	0.014*
HDL (mg/dL)	38.4 ± 12.1	48.2 ± 12.2	3.487	0.004*
LDL (mg/dL)	125.5 ± 32.3	104.3 ± 24.1	5.461	0.013*
Total cholesterol (mg/dL)	215.6 ± 39.1	177.1 ± 30.8	3.730	0.009*
Serum triglycerides (mg/dL)	179.7 ± 64.7	129.9 ± 52.8	3.256	0.012*

TABLE 2: 2: ECG and echocardiographic findings in different grades of NAFLD.

Grades of NAFLD						
	Non	Mild	Moderate	Severe	Chi-square	
	N (%)	N (%)	N (%)	N (%)	X2	N (%)
Echo wall motion abnormalities						
Negative	31 (88.57%)	12 (57.2%)	14 (70.0%)	17 (70.83%)	50.066	<0.001**
Positive	4 (11.43%)	9 (42.8%)	6 (30.0%)	7 (29.17%)		
ECG changes						
Negative Wall motion abnormalities	31 (88.57%)	18 (85.71%)	13 (68.42%)	17 (68.0%)	57.875	<0.001**
Positive	4 (11.43%)	3 (14.28)	6 (31.57%)	8 (32.0%)		

TABLE 3: 3: Multivariate logistic regression analysis of the risk factors for NAFLD.

	95% Confidence Interval		Odds ratio	P-value
	Lower	Upper		
Obesity	0.527	1.237	1.09	0.004*
DM	0.875	3.547	2.12	<0.001**
IHD	0.943	2.1 65	1.17	0.005*
Age	0.087	0.271	0.16	0.252
Waist circumference	1.00	1.15	1.13	0.019 *
LDL	1.00	1.18	1.01	0.022*
HDL	0.109	1.844	1.15	0.024*
Total Cholesterol	0.498	0.977	0.52	0.156
S. Triglycerides	0.261	0.843	0.40	0.092
HBA1C	1.18	1.03	1.37	0.028*

TABLE 4: 4: Multivariate logistic regression analysis of the risk factors for IHD.

	95% Confidence Interval		Odds ratio	P value
	Lower	Upper		
Obesity	0.870	1.275	1.195	0.035*
DM	0.932	2.085	1.234	0.032*
NAFLD:	1.051	2.754	1.685	0.023*
Mild.	1.071	2.524	1.56	0.021*
Moderate.	1.356	3.341	2.11	0.016*
Severe.	1.421	3.396	2.61	0.011*
Age	0.068	0.573	0.105	0.373
Waist circumference	0.132	0.506	0.211	0.089
HDL	0.256	0.834	0.058	0.458
LDL	0.99	1.537	1.132	0.004*
Total Cholesterol	1.012	1.732	1.31	0.010*
S. Triglycerides	1.003	1.089	1.01	0.053

There was also a highly statistical significant differ-ence among different grades of NAFLD ($p<0.001$). On multivariate logistic regression analysis, inde-pendent risk factors for NAFLD were obesity, DM, high LDL, low HDL, waist circumference, glycated hemoglobin and IHD with odds ratios 1.09, 2.12, 1.01, 1.15, 1.13, 1.37 and 1.17 respectively (Table 3). While independent risk factors for IHD included obesity, DM, high LDL, total cholesterol, triglyc-erides and the presence of NAFLD with odds ratios 1.31, 1.23, 1.19, 1.13, 1.68 respectively (Table 4). Both IHD and NAFLD shared common risk fac-tors such as obesity, presence of diabetes and dys-lipidemia (increased LDL, low HDL). The risk of IHD was also significantly more in higher grades of NAFLD. The odds ratios for the different grades of NAFLD were; 1.56, 2.11 and 2.61, for mild, moderate and severe NAFLD respectively.

4 | DISCUSSION

Metabolic syndrome features are not only highly prevalent in NAFLD patients, but components of metabolic syndrome also increase the risk of de-veloping NAFLD (9). There is a growing body of evidence that NAFLD and its risk factors carry an increased risk of cardiovascular disease indepen-dent of traditional cardiovascular risk factors and metabolic syndrome (10). The most common cause of mortality in patients with NAFLD was presumed to be myocardial ischemia irrespective of other co-morbidities (11). The possible contributing mech-anisms are complex and heterogeneous including genetic predisposition, insulin resistance and dys-lipidemia, chronic inflammation, oxidative stress, adiponectin deficiency and altered production of pro- and anticoagulant factors (12). The current study aimed to investigate the association ultrasonogra-phy/CT diagnosed NAFLD and risk of IHD diag-nosed by ECG, wall motion abnormality by echocar-diography and by coronary angiogram. In this study NAFLD group had a significantly higher BMI and waist circumference than the non NAFLD group. This was also observed by Loomis et al. who reported a 5- to 10-fold increased risk of NAFLD in the

obese and 10- to 14-fold risk in the morbidly obese subjects. They concluded that both prevention of weight gain and weight reduction are important for prevention and management of NAFLD (13). This finding also agrees with what reported by Sasaki et al. who observed that all grades of obesity are associated with NAFLD (14). In the current study, there was a statistically significant positive association between diabetes mellitus and NAFLD as the diabetic patients had an odds ratio of 2.12 regarding the risk of developing NAFLD as revealed on multivariate analysis. This result agrees with several studies reported a high prevalence of NAFLD in patients with diabetes mellitus and a mutual association between NAFLD and DM (15, 16). Our study showed also a highly statistical significant difference between NAFLD and non-NAFLD groups as regarding the frequency of dyslipidemia. Patients with NAFLD had significantly higher levels of LDL cholesterol and triglycerides and lower levels HDL cholesterol than those of non-NAFLD group. Similar to our study Alper et al., Sun et al. and Kim et al. illustrated that high levels of triglycerides, LDL-cholesterol were significantly associated with increased risk of IHD (17–19). Regarding the relationship between NAFLD and IHD, our study revealed a significantly positive association between degree of NAFLD diagnosed by ultrasonography and presence of ischemic heart disease. Finding was documented on both the univariate and the multivariate logistic regression analysis. The odds ratios for the various grades of NAFLD versus non- NAFLD group were 1.56, 2.11 and 2.61 for mild, moderate and severe NAFLD respectively. These data coincide with Pais et al. and Francque et al. who reported that there was a significant positive association between NAFLD and atherosclerotic process.They concluded that NAFLD represents an independent risk factor for coronary vascular disease (20, 21). Our results also come in accordance with Zib et al., 2016 in their prospective study on 4119 subjects after exclusion of coronary vascular disease or any known liver disease at baseline with a mean period of 7.6 years follow up (12). They concluded that NAFLD was independently associated with the risk of adverse cardiovascular events. Furthermore, in a cross-sectional study on diabetic patients, Targher et al. found ultrasonography-diagnosed NAFLD to be associated with prevalent cardiovascular disease independent of classical risk factors, glycemic control, medications and metabolic syndrome features (22). On the other hand, Chan et al. in their cross-sectional study on Asian diabetic patients reported that independent factors associated with IHD were older age, greater waist circumference, lower levels of physical activity and higher levels of HbA1c. They concluded that ultrasonography-diagnosed NAFLD was not associated with IHD. They explained this discrepancy in results by the differences in the study populations (23). Pickhardt et al. also stated that steatosis was not found to be an independent risk factor for cardiovascular events on multivariate logistic regression analysis after controlling for other confounding risk factors (24). Our study also showed that both NAFLD and IHD share common risk factors such as increased BMI, presence of diabetes and dyslipidemia. This result agree with what revealed by Lin et al. and Corey et al. who declared that the higher rates of IHD risk are associated with factors including hypertension, dyslipidemia, hyperglycemia and overweight. They also reported that IHD risk increased with the severity of fatty liver. They explained that patients with NAFLD have pro atherogenic lipid profile due to hepatic lipid concentration and insulin resistance (25, 26). Some limitations of our study warrant to be mentioned. First, NAFLD patients in our study were not histologically diagnosed by biopsy. We diagnosed NAFLD using transabdominal ultrasonography and CT scan of abdomen that does not identify fatty infiltration <30% and subjected to intra-and inter observer differences when making a diagnosis. However, it is a safe, available, of low cost, reasonably reliable and noninvasive method. To overcome this point, ultrasonography was performed by a single experienced operator. The usage of these non-invasive methods for diagnosing and grading NAFLD and also for detection of IHD risk have acceptable reliability and are practical tools of screening purpose (8). In addition, this was not a population-based study covering a wide geographic area or a large number of patients. So our results needs to be furtherly evaluated for validation on larger cohorts.

4.1 | Conclusion

The current study revealed that presence of NAFLD is associated with increased risk of IHD. This association was not only due to common risk factors shared between the two entities such as obesity, dyslipidemia and diabetes, but also a direct independent positive relationship was found between them. So NAFLD can be considered as an independent predictor of myocardial ischemia.

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