Original Research Article

Relation between non-alcoholic fatty liver disease and ischemic heart disease studied at rural tertiary care centre in Uttar Pradesh, India

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease in the United States and other industrialized countries, many study has identified NAFLD as a risk factor not only for premature coronary artery disease and cardiovascular events, but also for early subclinical abnormalities in myocardial structure and function. Aim of this study was to the presence of NAFLD in patients with Ischemic Heart Disease (IHD) and Relation of NAFLD with other risk factors of IHD.

Methods: The study group consisted of 150 patients that comply with inclusion criteria and selected of 100 consecutive patients who underwent coronary angiographies. Coronary artery disease was defined as a stenosis at least 50% in at least one major coronary artery. Fatty liver was diagnosed by abdominal ultrasonography (4 stages: Grades 0, 1, 2 and 3). Statistical evaluations were performed using T test, Chi- square test.

Results: The present study was done in 100 patients of coronary artery disease divided into two groups i.e. Non NAFLD group n= 62 (62%) and NAFLD group n= 38 (38%). 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).

Conclusions: The presence of fatty liver and its severity should be carefully considered as independent risk factors for IHD. The study results suggest the synergistic effect in between fatty liver and deranged lipid profile for developing IHD. Abdominal ultrasonography may provide valuable information about IHD risk assessment.

Keywords: Ischemic heart disease, Metabolic syndrome, Non-alcoholic fatty liver disease, Rural area

INTRODUCTION

Non-Alcoholic Fatty Liver Disease is the most common cause of Chronic Liver Disease (CLD) in the general population and is present when fatty infiltration affects >5% of hepatocytes, in the presence of <20g of alcohol consumption per day without the evidence of other cause of liver disease.[1] IHD is the generic designation for a group of pathophysiologically related syndromes resulting from myocardial ischemia - an imbalance between the supply (perfusion) and demand of the heart for oxygenated blood. In more than 90% cases, the cause of myocardial ischemia is obstructive atherosclerotic lesions in the coronary arteries. Thus, IHD is often termed CAD or Coronary Heart Disease (CHD).[2]

The presence of fatty liver is strongly associated with increased CAD risk and CAD is a major cause of death in patients with NAFLD.[3] This could also be explained by the fact that hepatic fat is often associated to the cardiac fat and increased insulin resistance in these patients affects not only the liver but also the other tissues like the heart.[4]

The clinical manifestations of NAFLD, such as steatosis and inflammation, are additional risk factors of CVD, although the precise mechanisms by which NAFLD contributes to CVD are still the subject of ongoing research.

The age of onset of CVD events in NAFLD patients ranged from 45 to 65 years.[5] All had significantly higher estimated CVD risk at 10 years (17% vs 10%) by the Framingham risk score than NAFLD patients without new CVD events.[6]

METHODS

Study is a total number of patients attending Department of Medicine, UPUMS, Saifai, during the study period between Jan 2015 to July 2016 were taken. An informed consent was taken from all the cases before their inclusion into the study. The study was approved by ethical committee of UPUMS, Saifai, Etawah.

Inclusion criteria

All the patients of coronary artery disease above 18 years of age.

Exclusion criteria

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'-diethlyaminethoxyhexesterol, 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]

Diffuse steatosis will be classified as follows

Mild

Minimal diffuse increase in hepatic echogenicity,

Moderate

Moderate diffuse increase in hepatic echogenicity. Slightly impaired visualization of intrahepatic vessels and diaphragm.

Severe

Marked increase in echogenicity. Poor penetration of posterior liver. Poor and no visualization of hepatic vessels and diaphragm.

Patients were classified having significant HDL value, high fasting blood sugar, high systolic blood pressure, high diastolic blood pressure, high Total Cholesterol value and high serum Triglyceride values according to IDF criteria.[8] Patients were classified having low Density Lipoprotein values according to NCEP ATP III criteria.[9]

All 100 cases of coronary artery disease were studied of presence of Non-Alcoholic Fatty Liver Disease. Descriptive analysis of the collected data was done and the association of various parameters with presence or absence of NAFLD was studying using T test, Chi square test and correlation with taking 5% as the level of significance (p value ≤0.01).

RESULTS

The present study was by enrolling 100 patients of coronary artery disease divided into two groups i.e. Non NAFLD group n= 62 (62%) and NAFLD group n= 38 (38%).
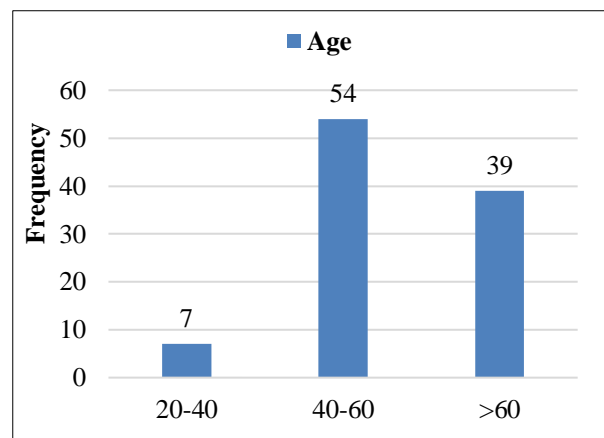

Figure 1: Distribution of age among the study subjects.

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). The disease distribution showed male predominance (79%) (Figure 2).
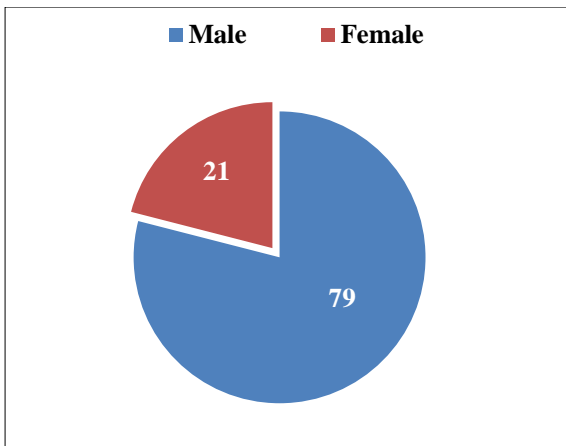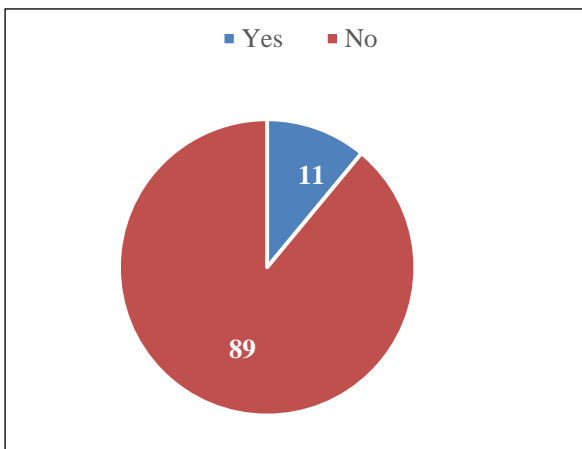
Figure 2: Gender distribution of study subjects.

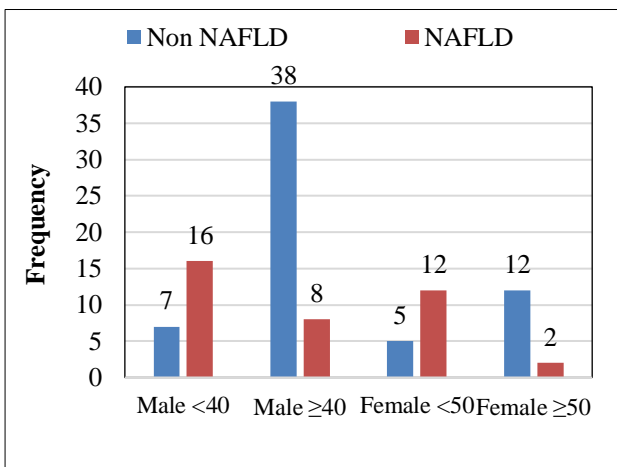**Figure 3: Proportion of metabolic syndrome among study subjects.**

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

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).
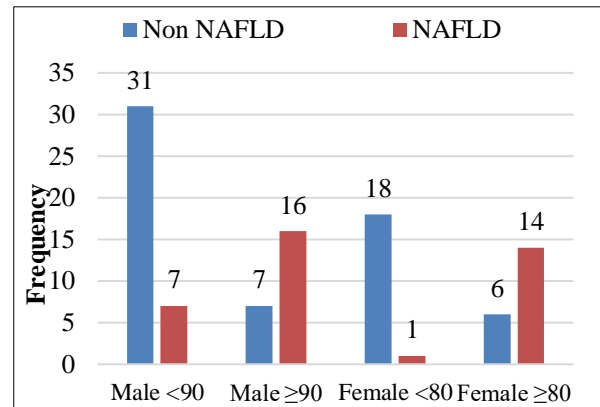

Figure 5: Gender wise proportion of NAFLD and non NAFLD with waist circumference.

Figure 5 displays the pattern of distribution of patients according to their obesity status and gender. Female patients showed that 35% of obese individuals compared to 26% among men. Females had increased proportion of obese NAFLD patients (93.3%) compared to 69.5% of male NAFLD patients.

The distribution of disease (Table 1) among the age groups shows NAFLD more among below 60years age group whereas the proportion of diseased were more among below 60 years age group (Non NAFLD- 68%) and the difference was statistically significant.

The distribution of disease was not much significant among different gender. NAFLD was shown to be significantly higher (21%) among patients with increased cholesterol level compared to that of Non NAFLD patients (3%). NAFLD was significantly increased among patients who had increased levels of triglycerides, LDL cholesterol (p<0.0001). Increased waist circumference (p<0.0001) and presence of metabolic syndrome (<0.01). HDL was reduced prevalence of NAFLD both among males and females and the difference was statistically significant.

DISCUSSION

The present study shows that the prevalence of NAFLD was highest (86.8%) in more than 40 years of age group. These findings are in line with the study conducted by Kalra et al, where they found the prevalence of NAFLD to be highest at 61.8% in 60-70 years of age group.[10] Study shows that the prevalence of NAFLD was more in males (84.2%) as compare to females (15.8%). A similar study from Turkey also found the frequency of non-alcoholic hepatic steatosis to be lower in females (32.7%).[11]

Table 1: Distribution of the patients on the basis of various variables.

Variables		Non NAFLD		NAFLD		Total	
		Freq	%	Freq	%	Freq	p value
N		62	62%	38	38%	100	
Age	20-60	30	48.30%	31	81.5%	61	0.009
	>60	32	51.7%	7	18.5%	39	
Sex	Female	15	24.2%	6	15.8%	21	0.31
	Male	47	75.8%	32	84.2%	79	
Total cholesterol	<200	60	97%	30	79%	90	<0.01
	≥200	2	3%	8	21%	10	
S. Triglyceride	<150	57	92%	19	50%	76	<0.0001
	≥150	5	8%	19	50%	24	
HDL	<40 Male	7	11.3%	16	42.1%	23	<0.0001
	≥40 Male	38	61.3%	8	21%	46	
	<50 Female	5	8%	12	31.6%	17	
	≥50 Female	12	19.4%	2	5.3%	14	
LDL	<100	54	87%	20	52.6%	70	<0.0001
	>= 100	8	13%	18	47.4%	30	
Waist circumference	<90 Male	31	50%	7	18.4%	38	<0.0001
	≥90 Male	7	11.3%	16	42.1%	23	
	<80 Female	18	29%	1	2.6%	19	
	≥80 Female	6	9.7%	14	36.9%	20	
Metabolic syndrome	Negative	60	96.8%	29	76.3%	89	<0.01
	Positive	2	3.2%	9	23.7%	11	

This study showed that 21% patients in NAFLD group had high cholesterol levels as compared to 3% patients in Non-NAFLD group and difference was found to be statistically significant (p<0.01). This finding is in correlation with the findings of Bajaj et al, who found significantly higher values of Total cholesterol in NAFLD group.[12]

This study showed that 50% patients in NAFLD group had high serum triglycerides as compared to 8% patients in Non-NAFLD group (p<0.01). This findings are in relation to findings of Kwon et al, who also found significantly higher percentage of patients in NAFLD group (28.7%) having high triglyceride levels.[13] And the study done by Kwon et al, found that significantly higher percentage of patients with low HDL in NAFLD group, (73.7% and 32.1%) respectively.[13] In another study Viswanathan et al, also found that low HDL levels were more common in NAFLD group in compared to Non-NAFLD group (53.8% vs 41.5%).[14] Interestingly waist circumference was significantly higher in this study in NAFLD group (79%). This finding are in correlation with finding of Fan et al, who found the strongest association of waist circumference with metabolic syndrome in Asia Pacific region.[15]

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 CAD. Another study done by Gupte P et al, Rocha et al, and Pagano et al in their study showed association between the metabolic syndrome and NAFLD.[16-18]

The present study shows that the prevalence of NAFLD in CAD patients was 38% as compared to 10-30% in general population as shown by study done by Browning JD et al.[19] Therefore NAFLD can be a risk factor and the cause of CAD. Gastaldelli et al, Viswanathan et al, Targher et al, Lin YC et al, and Alkhouri N et al, reported that fatty liver is significantly associated with the increased CAD risk.[14,20-23]

Several mechanistic explanations have been proposed for the relationship between CAD and NAFLD. It has been demonstrated by Schindler TH et al that there is a significant relationship between CAD and inflammation.[24] Kernar A et al, has also shown in their study that there is an increased systemic inflammatory response in metabolic syndrome patients.[25]

CONCLUSION

In this study showed a higher prevalence of NAFLD in patients of CAD and showed important clinical (waist circumference) and metabolic (fasting blood glucose, dyslipidemia, metabolic syndrome) predictor of NAFLD in Rural North Indians. It is important to note that variability in the anthropometric and biochemical parameters is predictive of NAFLD. Result from this study should sensitize practitioners to the need for frequent evaluation of NAFLD in high risk patients for CAD. Authors sincerely wish this study will be an important step in understanding prevalence of NAFLD in Indian population and designing preventive strategies as well as future studies on this condition.

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