Original Article

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Association between Non Alcoholic Fatty Liver Disease and Coronary Artery Disease.

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Abstract

Background: To study the association of Non Alcoholic Fatty Liver Disease in patients of Coronary Artery Disease. **Subjects and Methods:** 100 patients of established CAD admitted were included in the study. Patients were screened for NAFLD with USG. 2 groups were made: CAD with NAFLD & CAD without NAFLD and comorbidities were identified and evaluated for Risk Factors and Correlation was identified. **Result:** Majority of study subjects (79%) were males and 21% were females. Highest proportion of subjects (29%) were in 51-60 years of age and lowest (9%) in above 70 years of age. Chest pain was the commonest presenting symptom preceding breathlessness and sweating. In the fatty liver group, a high proportion of subjects had history of Type-II DM (31% vs 4%) and Hypertension (18% vs 11%) in comparison to normal liver group. The mean BMI of study participants in the present study was 29.5 kg/m^2. In fatty liver group, higher proportion of subjects had fasting blood glucose levels > 126 (66.7%) than the non-fatty liver subjects (3.8%). higher proportion of subjects had total cholesterol levels higher than 200 (14.6%) than the non-fatty liver subjects (1.9%). In group with non-fatty liver, greater proportion of subjects had LDL levels higher than 100 (40.4%) than the fatty liver group (33.3%). it was found that 37.5% subjects had mild grade of NAFLD whereas 43.8% had moderate grade and 18.7% had severe grade of NAFLD. **Conclusion:** There is a significant relationship between NAFLD and an elevated CVD risk in those with or without Metabolic Syndrome.

Keywords: Non Alcoholic Fatty Liver Disease, Coronary Artery Disease.

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Introduction

Non Alcoholic Fatty Liver Disease is one of the most common chronic hepatic pathology and a major community health issue that affects people all over the world.[1,2] Approximately 15-30% population is affected by NAFLD with its high prevalence up to 60-70% with T2DM with obesity. NAFLD represents hepatic manifestation of metabolic syndrome (MetS).[2]

The link between NAFLD and MetS has sparked curiosity in the possibility of a link between cardiovascular disease (CVD) and NAFLD.[2]

Increased occurrence of obesity, type-II DM, resistance of insulin & other metabolic disorders have all contributed to higher prevalence of NAFLD in present world with insulin resistance being major risk factor.[3]

NAFLD is unrelated to CVD with or without age, gender, smoking, low-density lipoproteins or MetS predilection. Furthermore, carotid artery intima-media thickness, a marker of atherosclerosis have been found to be increased in NAFLD.[4]

Occurrence of CVD is not only significantly higher in NAFLD,[5–9] butalso the commonest cause of mortality.[10]

Increased CV Risk in NAFLD appears to have a complex cause. Enhanced serum VLDL, LDL, and APO-B appear to be caused by increased insulin-induced hepatic lipogenesis, which is a feature of NAFLD.[11]

Increased factor VIII and lower protein C levels in NAFLD may raise the risk of cardiovascular disease. Insulin resistance, genetic predisposition, atherogenic dyslipidemia, chronic inflammation, oxidative stress, lower adiponectin levels, and alterations in anticoagulant factors production have all

been proposed mechanisms for accelerated atherosclerosis in NAFLD.

Patients with acute myocardial infarction have higher NAFLD prevalence than general population, also predicting severity and extent of infarction. NAFLD patients are sixty-four times more likely than non-NAFLD individuals to suffer a fatal or non-fatal cardiac incident.[12]

Multiple risk factors are implicated in CAD, both modifiable as well as non-modifiable. Obesity, type 2 diabetes, hypertension, dyslipidemia, sedentary lifestyle, and smoking are changeable risk factors, whereas age, sex, race, genetic predisposition, and personality type A are non-modifiable risk factors.[3]

As a result, in cases of NAFLD, an increased incidence of CAD has been found, making it the primary cause. The current study will look at coronary risk variables in patients with NAFLD who have acquired CAD. Detecting and treating identifiable risk factors for CAD, early in NAFLD patients can assist to avoid, stop, or delay the course of atherosclerotic coronary artery disease.

Subjects and Methods

Hospital-based Observational Cross-sectional study conducted in adult patients admitted at ICU/Medical wards of TMMC&RC, Moradabad

Inclusion Criteria

- All patients of CAD having
- Chronic Stable Angina
- Unstable Angina
- ST Elevation MI
- Non-ST Elevation MI

Exclusion Criteria

- Patients with old/documented chronic liver disease
- Patients who test positive for HBsAg and HCV.
- Patients with intake of alcohol >30gm/day in males and >20gm/day in females.
- Patients with history of drug intake - steroids, synthetic estrogens.

Procedure

Total of 100 patients were enrolled in the study

Study Method

- Detailed history including that of alcohol consumption, smoking, hypertension, past history of any cardiovascular event, family history, lifestyle, coexisting previous diseases and history of intake of medications were taken.
- Detailed clinical examination of each patient was done.
- Ultrasound was used as diagnostic tool to detect fatty liver.
- BMI of the patients was calculated.
- Blood samples for Fasting/PPBS, HbA1C, lipid profile, LFT, KFT were taken.

NAFLD grading on the basis of USG findings was done as below: 80

- **Grade 1 (Mild):** Minimal diffuse increase in hepatic echogenicity with normal visualization of diaphragm and intrahepatic vessel borders.
- **Grade 2 (Moderate):** Moderate diffuse increase in hepatic echogenicity with slightly impaired visualization of intrahepatic vessels and diaphragm.
- **Grade 3 (Severe):** Marked increase in echogenicity with poor penetration of posterior segment of right lobe of liver and poor or no visualization of hepatic vessels and diaphragm."

Results

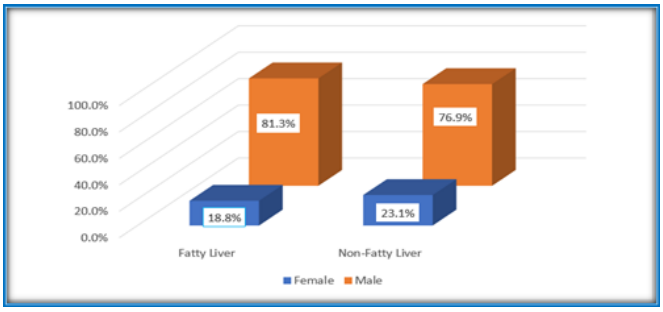

Figure 1: Graphical representation of Study participants according to Gender

Majority of study subjects (79%) were males and 21% were females. Both males and females had similar proportion of fatty liver cases. [Table 1]

[Table 2], majority of subjects (55%) were in 40 – 60 years age group. Highest proportion of subjects (29%) were in 51-60 years of age and lowest (9%) in above 70 years of age. There was similar age distribution in both the groups.

Chest pain was the most common presenting symptom followed by breathlessness and sweating. In the fatty liver group, a high proportion of subjects had Type 2 Diabetes Mellitus (31% vs 4%) and Hypertension (18% vs 11%) in comparison to the non-fatty liver group. [Table 3]

In fatty liver group, higher proportion of subjects had history of consuming either alcohol (22% vs 13%) or smoking (29% vs 25%) than the non-fatty liver group. [Table 4]

Table 1: Distribution of Study participants according to Gender

Gender	Fatty Liver		Non-Fatty Liver		Total	
	Frequency (n)	(%)	Frequency (n)	(%)	Frequency (n)	(%)
Female	9	18.8%	12	23.1%	21	21.0%
Male	39	81.3%	40	76.9%	79	79.0%

Table 2: Study participants Distribution according to Age

AGE	Fatty Liver		Non-Fatty Liver		Total	
	Frequency (n)	(%)	Frequency (n)	(%)	Frequency (n)	(%)
31-40	4	8.3%	7	13.5%	11	11.0%
41-50	12	25.0%	14	26.9%	26	26.0%
51-60	13	27.1%	16	30.8%	29	29.0%
61-70	14	29.2%	11	21.2%	25	25.0%
71 Above	5	10.4%	4	7.7%	9	9.0%

Table 3: Study participant's distribution according to Clinical Symptoms

Characteristic	Fatty Liver	Non-Fatty Liver
Chest Pain	48	51
Breathlessness	20	21
Sweating	12	16
T2DM	31	4
HTN	18	11

Table 4: Distribution of Study participants according to Personal History

Characteristic	Fatty Liver	Non-Fatty Liver
Alcohol	22	13
Smoker	29	25
Tobacco Chewing	4	5

Table 5: Distribution of Study participants according to BMI

BMI	Fatty Liver		Non-Fatty Liver		Total		p-value
	Frequency (n)	(%)	Frequency (n)	(%)	Frequency (n)	(%)	
<27.8	3	6.3	23	44.2	26	26	<0.001
>27.8	45	93.8	29	55.8	74	74	

In fatty liver group, higher proportion of subjects had BMI higher than 27.8 (93.8%) than the non-fatty liver group (55.8%). This comparison was statistically significant (p< 0.001). [Table 5]

In the non-fatty liver group, higher proportion of subjects had LDL levels higher than 100 (40.4%) than the fatty liver group (33.3%). [Table 6]

In fatty liver group, higher proportion of subjects had fasting blood glucose levels > 126 (66.7%) than the non-fatty liver group (3.8%). This comparison statistically significant (p< 0.001). [Table 7]

Both the groups had similar proportion of subjects as having positive Trop-I test. [Table 8]

In fatty-liver group, larger proportion of subjects had Triglycerides levels > 200 (43.8%) than the non-fatty liver group

Table 6: Study participants Distribution according to LDL levels

LDL	Fatty Liver		Non-Fatty Liver		Total		p-value
	Frequency (n)	(%)	Frequency (n)	(%)	Frequency (n)	(%)	
<100	32	66.7	31	59.6	63	63	0.466
>100	16	33.3	21	40.4	37	37	

Table 7: Distribution of Study participants according to Fasting Blood Glucose levels

FBS	Fatty Liver		Non-Fatty Liver		Total		p-value
	Frequency (n)	(%)	Frequency (n)	(%)	Frequency (n)	(%)	
<126	16	33.3	50	96.2	66	66	<0.001
>126	32	66.7	2	3.8	34	34	

Table 8: Distribution of Study participants according to Trop-I Test

Trop-I	Fatty Liver		Non-Fatty Liver		Total		p-value
	Frequency (n)	(%)	Frequency (n)	(%)	Frequency (n)	(%)	
Negative	11	22.9	10	19.2	21	21	0.65
Positive	37	77.1	42	80.8	79	79	

Table 9: Distribution of Study participants according to Triglycerides levels

Triglyceride	Fatty Liver		Non-Fatty Liver		Total		p-value
	Frequency (n)	(%)	Frequency (n)	(%)	Frequency (n)	(%)	
<150	27	56.3	39	75.0	66	66	0.048
>150	21	43.8	13	25.0	34	34	

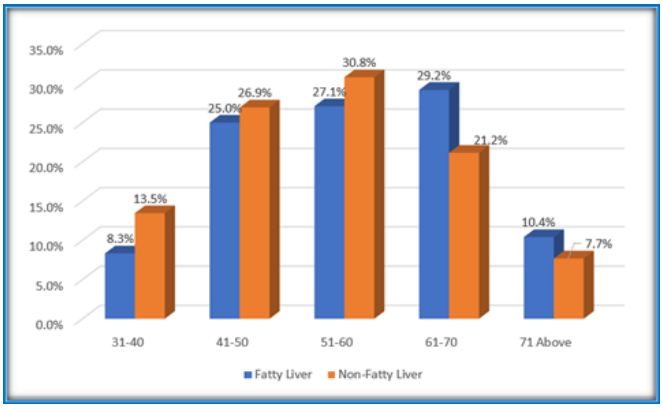

Figure 2: Graphical representation of Study participants according to Age

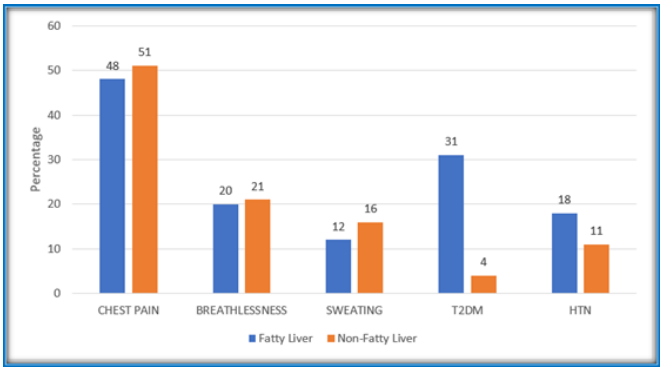

Figure 3: Graphical representation of Study participants according to Clinical Symptoms

(25%). This comparison was statistically significant ($p < 0.05$). [Table 9]

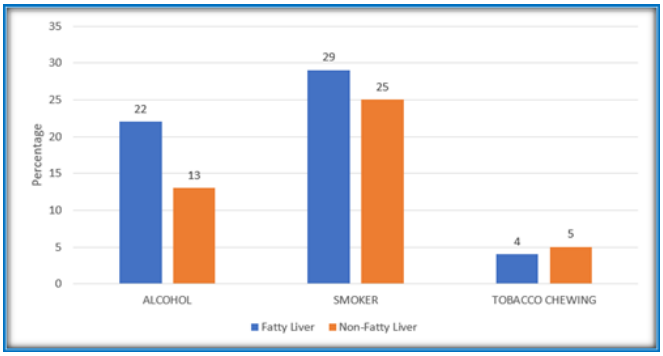

Figure 4: Graphical representation of Study participants according to Personal History

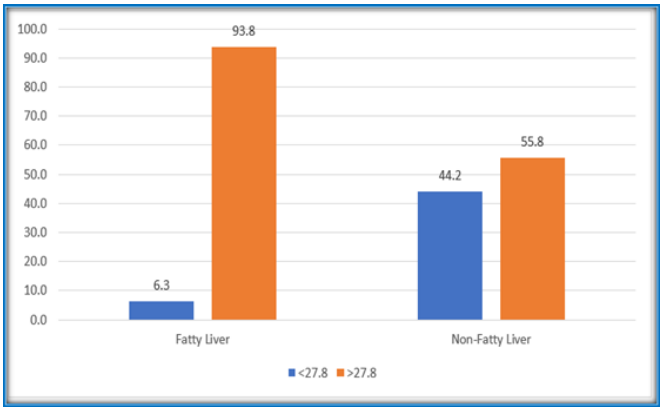

Figure 5: Graphical representation of Study participants according to BMI

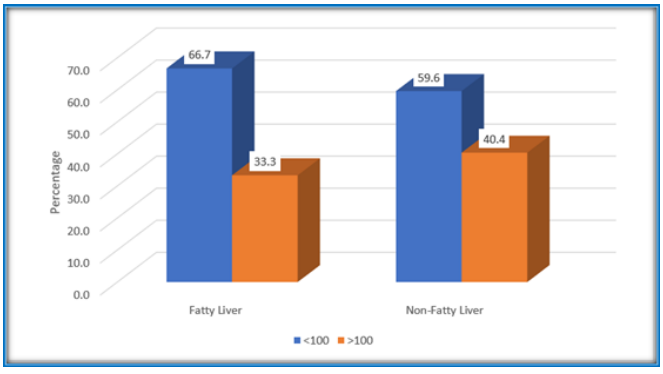

Figure 6: Graphical representation of Study participants according to LDL levels

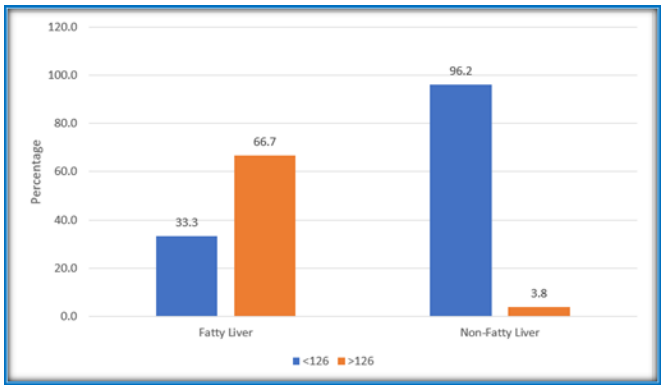

Figure 7: Graphical representation of Study participants according to Fasting Blood Glucose levels

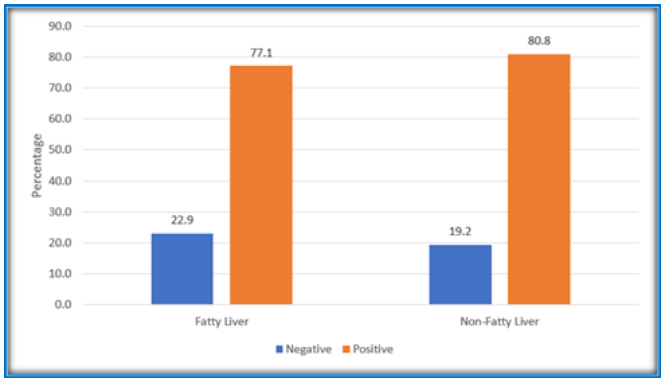

Figure 8: Graphical representation of Study participants according to Trop-I

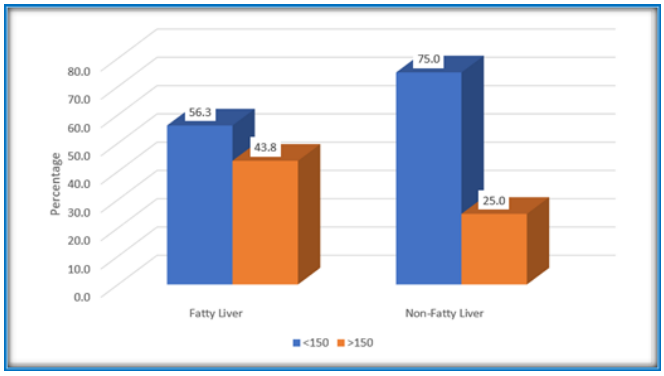

Figure 9: Graphical representation of Study participants according to Triglycerides levels

Discussion

Majority of study subjects (79%) were males and 21% were females. Both males and females had similar proportion of fatty liver cases.

56 years was the mean age of subjects and majority of subjects (55%) were in 40 – 60 years age group. Highest proportion of subjects (29%) were in 51-60 years of age and lowest (9%) in above 70 years of age. There was similar age distribution in both the groups. Similar to our study, 69.6% patients of NAFLD were between 40-60 years and 21.7% were above 60 years as reported by Zafar et al.[3] The mean age of subjects in a study done by Agarwal et al 52 and Chen et al 70 was 59 years and 53 years, similar to ours.

Chest pain was the commonest presenting symptom preceding breathlessness and sweating. In the fatty liver group, a high proportion of subjects had history of Type-II DM (31% vs 4%) and Hypertension (18% vs 11%) in comparison to normal liver group.

The mean BMI of study participants in the present study was 29.5 kg/m2. In fatty liver group, higher proportion of subjects had BMI higher than 27.8 (93.8%) than the non-fatty liver subjects (55.8%). This comparison was significant statistically ($p< 0.001$).

Chan et al also reported similar findings in his study.[13]

In fatty liver group, higher proportion of subjects had fasting blood glucose levels > 126 (66.7%) than the non-fatty liver subjects (3.8%). This was significant statistically with p value of less than 0.001).

In fatty liver subjects, higher proportion of subjects had total cholesterol levels higher than 200 (14.6%) than the non-fatty liver subjects (1.9%). This comparison was statistically significant ($p< 0.05$).

In group with non-fatty liver, greater proportion of subjects had LDL levels higher than 100 (40.4%) than the fatty liver group (33.3%). In group with fatty liver, higher proportion of subjects had Triglycerides levels > 200 (43.8%) than the normal liver group (25%). Zafar et al.[3] reported high Triglyceride levels in 58.7% of subjects. Although, the mean total cholesterol and LDL were similar in both the groups.[14]

it was found that 37.5% subjects had mild grade of NAFLD whereas 43.8% had moderate grade and 18.7% had severe grade of NAFLD. Montemezzo et al,[9] reported NAFLD in 55.2% of subjects with 23.6% with grade III disease similar to our study.

Conclusion

Over the last few years, significant data has emerged demonstrating a significant relationship between NAFLD and an elevated CVD risk in those with or without MetS. NAFLD is considered to be a risk factor for poor CVD outcomes, such as death and morbidity from major vascular events. Increased surveillance and early treatment can benefit NAFLD subjects. Despite data associating NAFLD to an elevated risk of CVD, the predictive relevance of NAFLD in CHD risk stratification remains unknown. To see if adding NAFLD to the already known risk score methods improve cardiovascular disease risk prediction, larger follow-up studies are needed. Furthermore, it is unclear whether NAFLD's prognostic value in the progress of CVD is applicable only to non-alcoholic steatohepatitis or is also linked with simple steatosis. Finally, further studies are required to understand whether genes involved in NAFLD carry the similar risk for CVD as NAFLD associated with MetS.

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