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Original Article

Pattern of Non Alcoholic Fatty Liver Disease in Coronary Artery Atherosclerosis in Central India

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Introduction
Patients with NAFLD were associated with more prevalent CAD independent of other risk factors, including glycemic control and Met S components. This finding was despite factoring in the other risk factors for CAD and the components of metabolic syndrome. In patients with NAFLD, metabolic abnormalities are commonly found and vary from 33 to 100% depending on types of study and the selection criteria of NAFLD patients. The criteria of MetS by the International Diabetes Federation in 2005 considers mandatory the presence of abdominal obesity as measured by waist circumference(WC) with ethnicity specific, plus any two of other criteria, which is different from those in the ATPIII definition[(67).]
Coronary artery atherosclerosis begins at young ages and typically becomes symptomatic after middle-aged with various clinical signs including acute coronary syndrome (ACS)
Material and Methods: *The study will be conducted in the Department of Medicine and Department of Cardiology at Gandhi Medical College and Hamidia Hospital, Bhopal. The study subjects will be selected from amongst the patients who attend the Medicine OPD, Cardiology OPD and admitted in the Cardiology WARD of Hamidia Hospital, Bhopal.*
Type of Study: *Observational Cross-Sectional Study*
Inclusion Criteria
150 proven CAD patients will be included in the study
Proven CAD patients will be defined either as ECG changes or Echocardiographic findings of RWMA.
100 non CAD patients will be included in the control group. Non CAD patients will be defined on the basis of no significant cardiac history, no ECG changes and normal echocardiograph.
Exclusion Criteria
1. Documented liver disease.
2. history of alcohol intake of more than 20 gms of alcohol per day.
3. Drug history
Summary & Conclusion
The summary of the study is as follows
The study shows prevalence of NAFLD in CAD and CONTROL group is 48.66%.and 22% respectively. Prevalence of NAFLD in males is 44.56% and 22.95% & in females it is 55.17% and 20.51% respectively.
The study shows that mean BMI is higher in patients with NAFLD in both males and females as compared to that in Non NAFLD group.
The study shows that mean waist/hip is higher in patients with NAFLD in both males and females as compared to that in Non NAFLD group.
Incidence of NAFLD is more in Hypertensive CAD group as compared to that of Hypertensive Control group.
Incidence of NAFLD is more in Diabetic CAD group as compared to that of Diabetic Control group.
In our study we found that there is no positive correlation of smoking with NAFLD
Thus we conclude that prevalence of NAFLD is higher in CAD population. Further prevalence of NAFLD increases

with other CAD risk factors i.e. hypertension, DM-2, central obesity, High BMI and dyslipidemia. Thus it can be concluded that presence of NAFLD with these risk factors further increases cardiovascular morbidity as depicted by higher CRP positive patients in this group.

In our study we found that patients of NAFLD in CAD group have higher fasting blood glucose levels, more dyslipidaemia, higher SGOT/SGPT levels, more incidence of Hypertension, thus retrospectively we can conclude that patients with NAFLD with these risk factors have higher incidence of CAD and should be screened for the same.

Introduction

Coronary artery atherosclerosis begins at young ages and typically becomes symptomatic after middle-aged with various clinical signs including acute coronary syndrome (ACS) [50,51]. Previous studies have revealed a close relationship between obesity and coronary artery disease (CAD) risk factors [51-54]. Non-alcoholic fatty liver disease (NAFLD) is a clinical and pathological condition associated with abdominal obesity, Type 2 diabetes mellitus (DM), hypertension and dyslipidemia. Also, NAFLD affects as high as 14–23% of the general population, and its prevalence reaches 70–90% in obese and type 2 DM patients [55-57]. However, the associations shown until now include associations among NAFLD and CAD risk factors and subclinical atherosclerosis markers such as endothelial dysfunction and increased carotid intima-media thickness [56, 58], and NAFLD and CAD [58].

Aims and Objectives

1. Identify the prevalence of non alcoholic fatty liver disease in the non CAD patients.
2. Identify the prevalence of non alcoholic fatty liver disease in the CAD patients.
3. Find the correlation of C Reactive Protein with non alcoholic fatty liver disease.

TABLE 1 Basic Characteristics Of Males With Nafld

	Normal (N = 63)	CAD Patients with NAFLD (N = 69)	P
Age (years)	47.7 ± 3.6	48.1 ± 14.6	0.982
Weight kg	66.1 ± 7.8	79 ± 11.9	<0.0001
BMI (kg/m^2)	22.7 ± 2.4	27.8 ± 3.4	<0.0001
Waist-to-hip ratio (cm/cm),	0.87 ± 0.04	0.94 ± 0.04	<0.0001
Body fat mass (kg)	12.5 ± 3.4	21.3 ± 6.3	<0.0001
Systolic blood pressure (mmHg)	113.6 ± 13.4	127.9 ± 16.2	<0.0001
Diastolic blood pressure (mmHg)	69.6 ± 11.4	78.8 ± 11.8	0.002
Triglyceride (mg/dl)	123.6 ± 63.9	181.8 ± 92.1	0.004
HDL cholesterol (mg/dl)	47.1 ± 9.1	41.0 ± 7.9	0.005
HOMA	1.49 ± 0.71	3.04 ± 1.6	<0.0001
Uric acid (mg/dl)	5.6 ± 1.2	7.4 ± 1.7	0.05
ALT (IU/I)	20.7 ± 9.3	42.9 ± 29.1,	<0.0001
AST (IU/I)	19.7 ± 4.3	28.4 ± 14.2	<0.001
AST/ALT ratio	>1	<1	
CRP (mg/l)	3.72 ± 2.11	8.48 ± 2.75	<0.01
PAI-I ng%	3.6 ± 1.2	7.9 ± 2.3	<0.01
TNF- α pg/ml%	6.66 ± 0.26	8.92 ± 0.44	<0.05
Adiponectin (ug/ml)	6.2 ± 3.4	4.5 ± 2.8	<0.05

TABLE 2 Basic Characteristics of Females with NAFLD

	Normal (N = 61)	CAD patients with NAFLD (N = 76)	*P*
Age (years)	47.1 ± 11.5	55.6 ± 8.5	-
Weight kg	55.8 ± 6.4	67.2 ± 8.9	<0.0001
BMI (kg/m^2)	22.6 ± 2.5	27.1 ± 2.9	<0.0001
Waist-to-hip ratio (cm/cm),	0.87 ± 0.05	0.94 ± 0.05	<0.0001
Body fat mass (kg)	16.3 ± 4.3	23.7 ± 4.3	<0.0001
Systolic blood pressure (mmHg)	116.8 ± 16.7	124.7 ± 13.6	0.0008
Diastolic blood pressure (mmHg)	71.5 ± 11.6	76.7 ± 10.4	0.015
Triglyceride (mg/dl)	98.7 ± 53.7	150.0 ± 73.2	<0.0001
HDL cholesterol (mg/dl)	57.2 ± 11.4	47.8 ± 9.0	<0.0001
HOMA	1.46 ± 0.8	2.56 ± 1.1	<0.0001
Uric acid (mg/dl)	4.55 ± 2.40	7.55 ± 2055	<0.001
ALT (IU/I)	16.6 ± 6.8	68.0 ± 19.7	<0.0001
AST (IU/I)	20.0 ± 5.9	45.0 ± 10.7	<0.001
AST/ALT ratio	-	<1	-
CRP (mg/l)	3.22 ± 1.11	7.80 ± 2.75	<0.01
PAI – I ng%	3.80 ± 1.2	6.90+2.3	<0.01
TNF- α pg/ml%	6.86+0.26	8.92+0.44	<0.05
Adiponectin (ug/ml	10.6 ± 4.8	7.2 ± 3.5	<0.0001

Mahmut A et al. [(0121)] study group consisted of 355 patients [253 (71.3%) male, 102 (28.7%) female; mean age: 57.5±11.4 years].Study group consisted of patients who underwent coronary angiography for various reasons such as ACS, chest pain and/or positive effort test or abnormal nuclear imaging. Hepatic ultrasound examinations were performed shortly before the patients were discharged. Of 355 patients in the study group, 265 (74.6%) had ACS, 50 (14.1%) had stable angina, 40 (11.3%) had atypical angina or atypical chest pain. Of 265 patients with ACS, 132 (49.8%) had unstable angina, 78 (29.4%) had non-Q wave myocardial infarction (MI), 55 (20.8%) had ST-elevation MI. A total of 169 (47.6%) patients were obese and 109 (30.7%) had metabolic syndrome.

Clinical, laboratory and angiographic findings in patients undergoing coronary angiography

	Coronary Artery Disease			
Parameters	Present	Absent		*p
	(n=250)	(n=105)		
Age, years	58.7±10.9	54.8±12.1		0.004
Men gender, n(%)	196 (78.4)	57(54.3)		0.0001
Diabetes mellitus, n(%)	42 (16.8)	9	(8.6)	0.044

Dyslipidemia, n(%)	200 (80.0)	50	(47.6)	0.0001
Hypertension, n(%)	56 (22.4)	18	(17.1)	0.26
Smoking, n(%)	168 (67.2)	41	(39.0)	0.0001
Prior MI, n(%)	97 (38.8)	0 (0)		0.0001
Body mass index, kg/m^2	29.1±4.6	28.7±4.6		0.51
Obesity, n(%)	122 (48.8)	47	(44.8)	0.48
Metabolic syndrome, n(%)	77 (30.8)	32	(30.5)	0.95
Total cholesterol, mg/dL	195.2±52.1	194.1±46.7		0.85
LDL cholesterol, mg/dL	132.0±40.9	133.0±36.4		0.82
HDL cholesterol, mg/dL	42.1±8.2	44.8±9.5		0.007
Triglycerides, mg/Dl	191±130	188±144		0.83
AST, U/L	44.0±74.1	28.2±22.7		0.033
ALT, U/L	28.7±16.9	25.2±12.9		0.059
GGT, U/L	36.5±27.2	27.2±11.5		0.001
Fatty liver, n(%)	93 (37.2)	22	(21.0)	0.003
Gensini score	68.7±44.5	1.3±2.9		0.0001
Anti-lipid drugs, n(%)	117 (46.8)	21 (20)		0.0001
Other drugs, n(%)	156 (62.4)	38	(36.2)	0.0001

MATERIAL AND METHODS

The study will be conducted in the Department of Medicine and Department of Cardiology at Gandhi Medical College and Hamidia Hospital, Bhopal. The study subjects will be selected from amongst the patients who attend the Medicine OPD, Cardiology OPD and admitted in the Cardiology WARD of Hamidia Hospital, Bhopal.

Type of Study

Observational Cross-Sectional Study

Inclusion Criteria

150 proven CAD patients will be included in the study

Proven CAD patients will be defined either as ECG changes or Echocardiographic findings of RWMA.

100 non CAD patients will be included in the control group. Non CAD patients will be defined on the basis of no significant cardiac history, no ECG changes and normal echocardiograph.

Exclusion Criteria

1. Documented liver disease.
2. history of alcohol intake of more than 20 gms of alcohol per day.
3. Drug history

Methods

From both the study and the control group baseline demographic data will be collected and a detailed physical examination will be performed.

ECG of every patient included in the study will be taken and will be interpreted as follows

MI will be defined by the presence of one of the following criteria:

1. Elevation of the origin of the ST segment at its junction (J point) with the QRS complex of:

a) >/=0.10mV in two or more limb leads or precordial leads V4 to V6, or

b) >/=.20mV in two or more precordial leads V1 to V3.

MI in LBBB will be defined by the presence of one of the following criteria

1.ST segment elevation >/=1mm and concordant with a predominantly negatively QRS complex.

UNSTABLE ANGINA will be defined by a combination of two diagnostic criteria in at least one ECG lead

1. ST depression of >/=1mm(0,10mV) at the J point.

Interpretion of USG ABDOMEN

NAFLD pts shows the presence of fatty liver on ultrasonography.

STUDY ANALYSIS

Baseline characteristics of the study participants expressed in mean ± SD and percentage. Student's 't' test used to analyze differences in baseline characteristics between the study group and the control group. Chi-square test used to analyze the association between Non Alcoholic Fatty Liver Disease and Coronary Artery Disease.

Degree of freedom was calculated and hence p value was obtained.

P value <0.05 was significant

P value <0.01 was very significant

P value <0.001 was highly significant

P value >0.05 was insignificant.

OBSERVATION

TABLE NO. 1 Prevalence of Non Alcoholic Fatty Liver Disease in CAD and Control Population

NAFLD	CAD	
	Present	Not Present
Present	73	22
Not Present	77	78
Total	150	100
Percentage of patients with NAFLD	48.66	22

Table 1 shows that out of total 150 CAD patients 73 (48.66%) has NON ALCOHOLIC FATTY LIVER DISEASE as compared to CONTROL population in which only 22 patients(22%) out of 100 has NON ALCOHOLIC FATTY LIVER DISEASE with a p value of less than .0001 which is statistically highly significant.

TABLE NO. 2 Sex Wise Distribution of NAFLD in CAD and Control Population Male Sex Distribution

NAFLD	CAD	
	Present	Not Present
Present	41	14
Not Present	51	47
Total	92	61
Percentage of patients with NAFLD	44.56	22.95

Table 2 shows that out of total 92 male CAD patients 41(44.56%) has NON ALCOHOLIC FATTY LIVER DISEASE as compared to control population in which 14 males(22.95%) out of 61 has NON ALCOHOLIC FATTY LIVER DISEASE with a p value of .0106 which is statistically significant.

TABLE NO 3 Female Sex Distribution

NAFLD	CAD	
	Present	Not Present
Present	32	8
Not Present	26	31
Total	58	39
Percentage of patients with NAFLD	55.17	20.51

Table 3 shows that out of total 58 female CAD patients 32(55.17%) has NON ALCOHOLIC FATTY LIVER DISEASE as compared to CONTROL population in which 8 females (20.51%) out of 39 has NON ALCOHOLIC FATTY LIVER DISEASE with a p value of .0014 which is statistically significant.

TABLE NO. 4 Comparison between Male and Female NAFLD Percentage in CAD and Control Population

CAD	NAFLD	
	Males	Females
Present	44.56	55.17
Not Present	22	20.51

Table 4 shows that prevalence of male NAFLD % is less than female NAFLD% in CAD patients as compared to CONTROL population in which male NAFLD% is more than female NAFLD%.

TABLE NO 5 Comparison of BMI in NAFLD Patients in CAD and Control Population

BMI(kg/m^2)	CAD present	CAD Not Present
<25	2	15
25-30	65	7
>30	6	0
Total	73	22

It has been observed that as BMI increases chances of NON ALCOHOLIC FATTY LIVER DISEASE also increases as 71 NAFLD patients of CAD population have BMI >25 as compared to 7 NAFLD patients of CONTROL population.

Similarly mean BMI of NAFLD in CAD patients is 27.83 as compared to mean BMI of 24.95 in NAFLD of control population with a p value of less than .0001 which is statistically highly significant.

DISCUSSSION

The present study included 150 coronary artery disease(CAD) patients and 100 control patients matched in terms of age, sex, hypertension, type 2 diabetes mellitus and smoking from 1st November 2011 to 1st December 2012 attending cardiology OPD , medicine OPD, and admitted in cardiology ward and medicine ward of Hamidia Hospital, Bhopal.

Out of these 150 CAD patients (92 males & 58 females) and 100 control patients (61 males & 39 females) ranging from 30-96 years age group, prevalence of NAFLD was observed as 48.66% with 44.56% in males, 55.17% in females of CAD population and 22%in Control population with 22.95% in males ,20.51% in females which is statistically significant with a p value<.0001, p=.0106 in males and p=.0014 in females respectively.

In this study we find out that the prevalence of NAFLD in CAD patients is statistically higher than the control patients. Earlier , studies found that the prevalence of CAD in NAFLD is significantly higher than in Non NAFLD population. A K Agrawal[117] et al found that prevalence of CAD was 60.5% in DM ll with NAFLD and 45.2% in DM ll with Non NAFLD. Akash Shukla[118] et al found that NAFLD patients tends to have higher calcium scores on CT coronary angiography and higher prevalence of CAD on angiography. Targher[119] et al found that the prevalence of CAD in NAFLD patients as 26.6% versus 18.3% in Non NAFLD group. Hamaguchi et al[74] found the prevalence of CAD as 2.2% in NAFLD versus 0.3% in Non NAFLD group. Prevalence of NAFLD based on ultrasonography was 18.9% in general Indian population.

On further analysis we observed that mean BMI and mean Waist/Hip is on higher side in NAFLD patients of CAD group than control population. Mean BMI is 27.83kg/m^2 and 24.95kg/m^2 in NAFLD population of CAD and control group respectively with a highly significant p value of .0001. Mean Waist/Hip of males is 0.949 & 0.892 with a significant p value of .0011 and mean Waist/Hip of females is 0.945 & 0.890 with a significant p value of .0001 in NAFLD population of CAD and control group respectively. Manopriya T et al [120]found the same results. A K Agrawal[117] et al found that mean BMI is 27.5kg/m^2& 25.3kg/m^2, mean Waist/Hip is 0.97 & 0.93 in NAFLD and Non NAFLD population of DM II. Mahmut A et al[121] found that in a CAD population 37.2% have fatty liver and 48.8% have obesity.

It has been observed on further analysis that the prevalence of NAFLD is high in both, the hypertensive group and the diabetic group. The prevalence of NAFLD is 51.72% versus 20% in hypertensive group of CAD and control population respectively with a significant p value of .005.The prevalence of NAFLD is 58.33% versus 15.2% in diabetic group of CAD and control group respectively with a significant p value of .02.Lopez Surez et al[122] found prevalence of NAFLD as 49.5% in hypertensive participants

of 50-75 years age group. A K Agrawal et al[117] found the prevalence of NAFLD as 57.2% in DM ll patients and prevalence of CAD as 60.5% in diabetics. Mantovani A et al[123] found that prevalence of left ventricular hypertrophy was markedly higher among hypertensive diabetic patients than those without this disease(82% versus 18%). Mishra et al[124] found the prevalence of metabolic syndrome and NAFLD to be 24% and 14.8% respectively in non alcoholic North Indian men. Mishra et al[124] found prevalence of NAFLD (54.5%) was significantly higher in patients with DM ll as compared to those with pre diabetes.

Similarly it has been observed that NAFLD group of CAD population has significantly reduced HDL and significantly elevated triglyceride as compared to non-NAFLD group of CAD population. Mean HDL values were 40.58mg/dl and 43.35mg/dl in NAFLD and non-NAFLD group respectively which is significantly lower (p-0.0011). Mean triglyceride values were 162.16mg/dl and 130.06 respectively which is significantly higher (p<0.0001). However LDL was not found to be significantly lower in NAFLD group with a mean values of 120.78mg/dl vs. 116.68mg/dl (p-0.136).

It is been observed that 61.9 % of CRP +ve patients have NAFLD in CAD population as compared to 31.81% of control population. Manopriya T et al(120) found higher CRP level in NAFLD with CAD group than in NAFLD group. Nicholas D et al(130)& Ramon Arroyo et al(131)found increased chances of CAD with C reactive protein.

SUMMARY & CONCLUSION

The study was undertaken in Department of Medicine and Cardiology, Gandhi Medical College and associated Hamidia Hospital, Bhopal. 150 Coronary Artery Disease (CAD) patients and 100 control patients matched in terms of age, sex, hypertension, type 2 diabetes mellitus and smoking were studied with aim to observe the prevalence of Non Alcoholic Fatty Liver Disease (NAFLD) and to correlate NAFLD with various coronary artery disease risk factors. Correlation of C-Reactive Protein in CAD and control population with NAFLD was also observed.

The summary of the study is as follows

The study shows prevalence of NAFLD in CAD and CONTROL group is 48.66%.and 22% respectively. Prevalence of NAFLD in males is 44.56% and 22.95% & in females it is 55.17% and 20.51% respectively.

The study shows that mean BMI is higher in patients with NAFLD in both males and females as compared to that in Non NAFLD group.

The study shows that mean waist/hip is higher in patients with NAFLD in both males and females as compared to that in Non NAFLD group.

Incidence of NAFLD is more in Hypertensive CAD group as compared to that of Hypertensive Control group.

Incidence of NAFLD is more in Diabetic CAD group as compared to that of Diabetic Control group.

In our study we found that there is no positive correlation of smoking with NAFLD

Fasting Blood sugar levels were found to be on higher side of normal in NAFLD group of CAD patients as compared to control population.

Serum HDL levels were found to be significantly reduced in NAFLD group of CAD population as compared to control population and non-NAFLD group of CAD population.

Serum Triglyceride levels were found to be significantly elevated in NAFLD group of CAD population as compared to control population and non-NAFLD group of CAD population.

Serum LDL levels were found to be significantly elevated in NAFLD group of CAD population as compared to control population but this elevation was not found to be significant in non NAFLD group of CAD population.

Serum SGOT and SGPT levels were found to be significantly elevated in NAFLD group of CAD population as compared to control population.

Incidence of NAFLD was more in CRP positive CAD group as compared to that of CRP positive Control group.

Thus we conclude that prevalence of NAFLD is higher in CAD population. Further prevalence of NAFLD increases with other CAD risk factors i.e. hypertension, DM-2, central obesity, High BMI and dyslipidemia. Thus it can be concluded that presence of NAFLD with these risk factors further increases cardiovascular morbidity as depicted by higher CRP positive patients in this group.

In our study we found that patients of NAFLD in CAD group have higher fasting blood glucose levels, more dyslipidaemia, higher SGOT/SGPT levels, more incidence of Hypertension, thus retrospectively we can conclude that patients with NAFLD with these risk factors have higher incidence of CAD and should be screened for the same.

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