

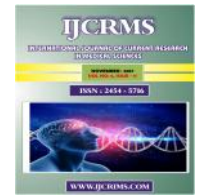


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To Study the Association of Coronary Artery Disease and Non Alcoholic Fatty Liver Disease

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Abstract

Background: Coronary artery disease (CAD) is one of the most common and devastating illness. Non alcoholic fatty liver disease (NAFLD) is well linked with metabolic syndrome and so is coronary artery disease. But CAD has been poorly linked to NAFLD in the past. Here we conducted a study to find the association of CAD and NAFLD. Risk factors of NAFLD and CAD like hypertension, diabetes mellitus, dyslipidemia and obesity were also studied.

Subject and method: It was a case control study conducted in Guru Nanak Dev Hospital attached to Government Medical College, Amritsar. Subjects were 100 diagnosed cases of CAD with age and sex matched non CAD controls.

Results: 42 subjects in case group were having fatty liver on ultrasound in comparison to 16 in controls. The mean BMI in case group was 23.85 ± 2.11 kg/m² and in control group, it was 21.78 ± 1.92 kg/m². The subjects labeled obese (BMI > 25 kg/m²) were 39 in case group and 8 in control group (p value < 0.001). Smoking was significantly higher in case group (23%) versus control group (11%), (p value < 0.001). Hypertension was higher among cases (43%) than controls (12%), (p value < 0.001). Similarly diabetes mellitus was also high among cases (40%) than controls (16%), (p value < 0.001).

Conclusion: In this study we observed that there is association of CAD to NAFLD. It was also observed that smoking, hypertension, diabetes, dyslipidemia and obesity are associated to CAD.

Keywords: CAD, NAFLD, BMI, Hypertension, dyslipidemia and obesity .

Introduction

Prevalence of nonalcoholic fatty liver disease (NAFLD) is increasing in Indian population. The aim of this study is the investigation of association between nonalcoholic fatty liverdisease (NAFLD) and coronary artery disease (CAD).Coronary artery disease is a leading cause of death worldwide. Its association with metabolic syndrome is well studied. Non alcoholic fatty liver disease (NAFLD) is also associated with metabolic syndrome and both predispose to increased risk of CAD. Association of NAFLD and CAD has not been well studied in the past. We planned this study to compare the association between NAFLD and CAD. Risk factors of NAFLD and CAD like hypertension, diabetes mellitus, dyslipidemia and obesity were also studied.

Aims and objectives

1. To study the association of coronary artery disease and nonalcoholic fatty liver disease.
2. To study the occurrence of NAFLD in CAD patients and to compare occurrence in age and sex matched controls.
3. To study the association of main risk factors (hypertension, diabetes mellitus, dyslipidemia and obesity) among cases and controls.

Materials and Methods

Study Design: Cross-sectional study.

Subjects: 100 diagnosed cases of CAD with age and sex matched non CAD controls.

A case control study was carried out in the Department of Medicine and Department of Radiodiagnosis and imaging at Guru Nanak Dev Hospital attached to Government Medical College, Amritsar from Jan 2014 to March 2015.

100 cases presenting to medical emergency, medical OPD and those admitted in various medical wards in the age group of 30-70 years with diagnosis of CAD who qualified the

inclusion criteria formed the case group. The control group consisted of equal number of age and sex matched subjects without any evidence of overt CAD and qualifying the exclusion criteria.

Inclusion Criteria

1. Old diagnosed cases of coronary artery disease
2. New ST segment elevation myocardial infarction (STEMI).
3. Non ST elevation myocardial infarction (NSTEMI) inclusive of diagnosed cases of ACS or stable angina.
4. Age 30-70 yrs of either sex.

Exclusion Criteria

1. Chronic alcohol intake 20gms/day.
2. Systemic diseases like chronic liver diseases, chronic renal diseases (serum creatinine >2mg/dl), tuberculosis, patients of collagen vascular disease and thyroid disorders.
3. Patients of cardiovascular accidents, congestive heart failure, cardiomyopathies and significant valvular heart disease.
4. History of viral hepatitis with positivity of HBsAg and /or anti-HCV antibody and significantly deranged enzymes (AST/ALT >5 of normal).
5. Patients on drugs causing fatty liver changes like- amiodarone, methotrexate, tamoxifen, antiretroviral drugs (nucleoside analogues), tetracyclines, acetaminophen and corticosteroids.

Methodology

All the patients of CAD fulfilling the inclusion criteria and not a part of exclusion criteria presenting to Department of Medicine, Guru Nanak Dev Hospital, Amritsar, were taken as case group. Age and sex matched controls were enrolled according to the exclusion criteria and who did not have CAD.Ultrasound examination was done in Department of Radiodiagnosis Government Medical College Amritsar. In addition risk factors for CAD (hypertension, diabetes mellitus, obesity and dyslipidemia) were also studied in both the groups.

Statistical analysis: The data was tabulated and analyzed to obtain mean \pm SD and p-value. Multiple logistic regression was applied to study the association between risk factors in both groups.

Observations and Results

Demographic Profile

In both the groups male and female ratio was same and the mean age was 53.45 years in cases group and 53.43 years in controls.

Anthropometric data

The mean BMI in case group was 23.85 ± 2.11 kg/m² and in control group it was 21.78 ± 1.92

kg/m². The subjects who were overweight (BMI>23 kg/m²) were 25 in cases group and 14 in control group (p value< 0.001). The subjects labeled obese (BMI>25 kg/m² were 39 in case group and 8 in control group (p value < 0.001).The difference in BMI was significantly higher in case group compared to control group.

Risk factor profile

History of smoking was significantly higher in case group (23%) versus control group (11%), (p value <0.001). Already diagnosed cases of hypertension were higher among cases (43%) than controls (12%), (p value <0.001). History of diabetes mellitus was also high among cases (40%) than controls (16%), (p value<0.001). (Table 1 and 2)

Table 1 Risk factor profile

Variable	Case group n (%)	Control group n (%)	p-value
smokers	23 (23%)	11 (11%)	<0.001

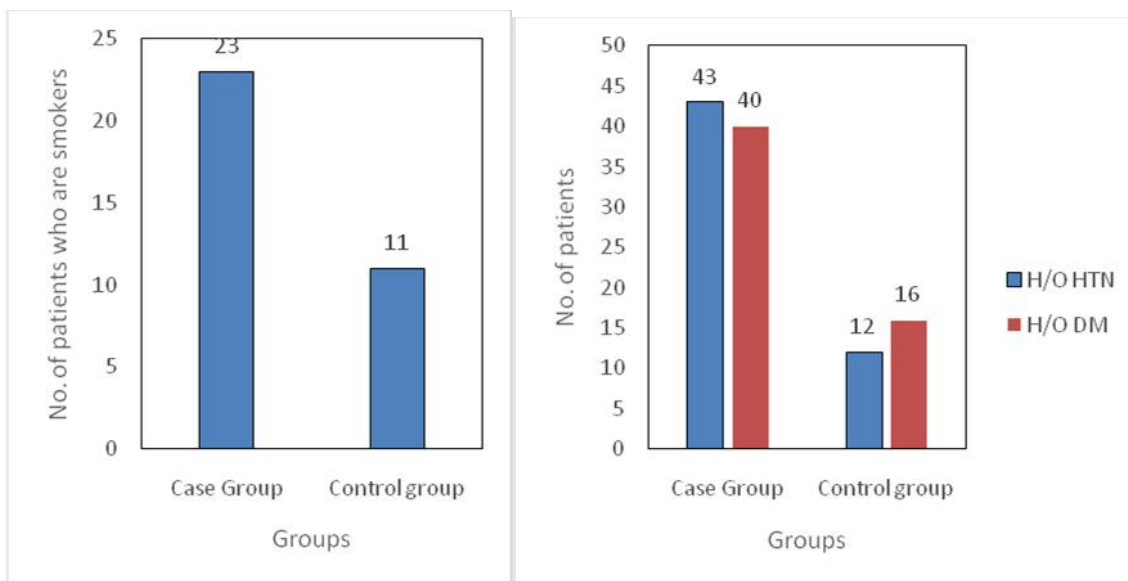


Table 2 Risk factor profile

Variable	Case group n (%)	Control group n (%)	p-value
h/o HTN	43 (43%)	12 (12%)	<0.001
h/o DM	40 (40%)	16 (16%)	<0.001

Lipid profile

The mean serum cholesterol was 215 ± 48.36 mg/dl and 163.97 ± 31.86 mg/dl in cases and controls respectively. The cholesterol value was higher among cases than controls (p value <0.001). Mean TG was 162.65 ± 38.03 mg/dl in case group and 119 ± 64.97 mg/dl in controls. HDL was comparable in both the groups 39.66 ± 7.01 mg/dl and 40.22 ± 6.44 mg/dl in cases and control groups.

Hypercholesterolemia (> 200mg/dl) was found to be 54% and 9% among cases and controls respectively (p value <0.001). Low HDL (females <50 mg/dl and <40 mg/dl in males) was most common dyslipidemia in both the groups, 70% in cases and 69% in control and TG >150 mg/dl was found in 55% of cases and 20% of controls. Dyslipidemia was significantly higher among cases than controls. (Table 3)

Table 3 Showing number of patients with dyslipidemia in both the groups

Serum lipids	Case group (%)	Control group (%)	p-value
Cholesterol >200(mg/dl)	54	9	<0.001
TG > 150(mg/dl)	55	20	<0.001
HDL< 50(mg/dl) in females &<40(mg/dl) in males	70	69	>0.05 (NS)

Fatty liver on USG

42 subjects in case group were having fatty liver on ultrasound in comparison to 16 in controls.

Fatty liver was found to be more common in case than control group.

Table 4 Showing number of subjects with fatty liver on USG

Variable	Case group (%)	Control group (%)	p-value
Total no. of subjects with fatty liver	42	16	<0.001

Anthropometric data of subjects having NAFLD

Among cases 42 subgroup of subjects had NAFLD. This subgroup of patients 23.80% (n=10) were overweight and 76.19% (n=32) was obese. None of the subjects had normal weight. Among 16 controls who had fatty liver, 37.50% (n=6) and 50% (n=8) were found to be overweight and obese respectively. Cases with NAFLD were more obese than controls.

Lipid profile of patients having NAFLD

The subgroup of subjects having fatty liver shows that mean cholesterol was higher (216 ± 51.44 mg/dl) in case group than control group (174 ± 45.50 mg/dl). Mean HDL was comparable in both the groups, 38.78 ± 6.91 mg/dl in cases and $39 \pm$

4.61 mg/dl in control sub group. Mean triglyceride level was higher in case subgroup (180.57 ± 31.94 mg/dl) than control subgroup (157 ± 60.59 mg/dl). The total cholesterol and TG were statistically high in the subgroup of NAFLD cases than control (p value <0.001).

Risk factors predisposing to NAFLD

On analysis of subjects having NAFLD in both the groups taken together, it was seen that Mean BMI was 25.34 ± 1.25 kg/m² and 21.78 ± 1.71 kg/m² in subjects with NAFLD and subjects without NAFLD respectively. Mean cholesterol was 204 ± 52.58 mg/dl and 183 ± 44.97 mg/dl in subjects with NAFLD and without NAFLD respectively. Mean TG was 174 ± 42.50 mg/dl and 127 ± 57.16 mg/dl in subjects with NAFLD and subjects without NAFLD respectively.

HDL was 38.98 ± 6.33 mg/dl and 40.33 ± 6.33 mg/dl in subjects with NAFLD and subjects without NAFLD respectively.

The subjects with higher BMI OF $>23\text{kg/m}^2$ were 94.82% and 21.83% in subgroup of NAFLD and without fatty liver respectively. History of diabetes mellitus was found in 39.65% and 23.94% in subjects with NAFLD and in subjects without NAFLD respectively. The subjects with serum cholesterol $>200\text{mg/dl}$ were 48.27% and 25.35% in subjects with NAFLD and without fatty liver respectively. Subjects with TGR $>150\text{mg/dl}$ were 67.24% and 27.46% in subgroup of NAFLD and without fatty liver respectively.

Association of CAD and NAFLD

In 100 cases of CAD, 42 had NAFLD. However among controls only 16 had NAFLD. The NAFLD was found to be higher among the cases of CAD than without CAD (p value <0.001). So it could be well said that NAFLD is associated with CAD, because of increased occurrence of it in CAD patients.

Risk factors predisposing to CAD studied using logistic regression

Risk factors predisposing to CAD were smoking, history of diabetes mellitus, history of hypertension, BMI and dyslipidemia using logistic regression analysis. (Table 5)

Table 5 Risk factors predisposing to CAD

Risk factors	p-value	Odds ratio
Smoking	<0.001	5.67
BMI ($>23\text{ kg/m}^2$)	<0.001	6.78
Serum Cholesterol ($>200\text{mg/dl}$)	<0.001	11.74
TG ($>150\text{mg/dl}$)	<0.001	10.87
Diabetes	<0.001	9.87
Hypertension	<0.001	7.65

Risk factors predisposing to NAFLD were higher BMI, dyslipidemia, diabetes but the factors which were found to be associated to NAFLD were higher BMI, raised serum cholesterol and triglyceride (p value for other factors were insignificant). Higher BMI was the most important factor which predisposes to NAFLD.

Discussion

NAFLD was earlier considered to be a benign disease but studies have shown its increasing prevalence and its association with coronary artery disease and subclinical atherosclerosis. Multicentric studies have shown that risk factors which predispose to CAD, predispose to NAFLD also. We planned to study the association of CAD with NAFLD.

The history of hypertension was 43% in case group and 12% in control group. History of

diabetes was 40% in case group and 16% in control group, the association of hypertension and diabetes with CAD has been well studied. Tewari et al¹ showed that diabetes predisposes to premature coronary artery disease. Diabetes is a known conventional risk factor for CAD as mentioned by Goel et al.²

Smoking was major risk factor being present in 23% and 11% of cases and controls. Smoking is already known to be dominant conventional risk factor for CAD.³ Obesity was more prevalent in CAD group compared to controls. In our study it was found that 25% and 39% were overweight and obese among cases compared to 14% overweight and 8% obese in control group. Obesity increases the risk of CAD. This is in consonance with previous studies done on CAD patients.⁴

As regards the issue of dyslipidemia, elevated cholesterol was seen in 54% of cases and 9% of controls. Prevalence of hypertriglyceridemia was 55% in case group and only 20% in control group. Raised TG increases risk of CAD.

Fatty liver was diagnosed on the basis of USG. It is characterized by increased echotexture of liver compared to kidney, attenuation of USG beams and blurring of liver margins.⁵⁻⁷ In current study 42% and 16% of cases and controls respectively had fatty liver. Previous studies have shown that prevalence of NAFLD in normal population is around 20-30% which increases with diabetes and CAD to around 60-70%⁸. Sombat et al⁹ showed that NAFLD is strongly associated with CAD.

In subgroup of subjects with fatty liver, obesity was found in 76.19% and 50% in subgroup with fatty liver among cases and controls respectively. This is in accordance with previous studies which have shown that increasing BMI predisposes to NAFLD.¹⁰

Similarly dyslipidemia in the form of serum cholesterol 200 mg /dl was found in 57% and 25%, cases and controls subgroup with fatty liver respectively. Higher TG 150 mg/dl was seen in 71.42% among cases and 50% in control subgroup having fatty liver. Low HDL was 69% among cases and 87% among controls. This is also in accordance with previous studies showing raised serum cholesterol and raised TG among fatty liver subgroup.¹¹

In the subgroup of subjects with fatty liver we observed that diabetes mellitus was seen in 42.85% and 31.25% in case and control subgroup with fatty liver respectively. This is in accordance with studies done so far, showing diabetes is associated with NAFLD.¹²

In this study, we observed that risk factors predisposing to NAFLD were higher BMI and dyslipidemia. Studies done so far also show similar risk factors.¹³⁻¹⁴ Obesity prevalence in patients with NAFLD varies from 30% -100% and prevalence of hyperlipidemia varies from 20%-90%. In our study, we found higher BMI >23 kg/m² in 94.82% subjects, Dyslipidemia was

found in 67.24% subjects due to raised TG, in 77.5% due to low HDL and in 48.27% subjects due to raised cholesterol in subjects of NAFLD in both the groups. Previous studies have also shown that NAFLD is a risk factor for atherosclerosis and CAD. We have also found that NAFLD was seen more in patients of CAD. Thus it can be said that NAFLD is associated with CAD

Summary

The present study was done to evaluate the association of CAD with NAFLD. This was a case- control and age- sex matched cross sectional study which included 100 subjects of CAD and equal number of non-CAD. The age of the subjects varied from 30 years to 70 years.

- Presence of obesity was significantly higher in case group. Among cases we observed that 25% and 39% were overweight and obese respectively. However 14% and 8% were overweight and obese respectively in control group.
- Smoking was most prevalent in case group. In our study we observed that 23% and 11% were smokers in case and control group respectively.
- Among cases 40% patients were diabetic. However among controls 16% were diabetic.
- Low HDL cholesterol was observed as the most prevalent component of dyslipidemia being present in 70% of cases and in 69% of control group
- The mean total cholesterol was higher in case group than controls. Elevated total cholesterol (>200 mg/dl) was found in 54% patients of case group and 9% in control group. Hypercholesterolemia was found more in CAD group.
- Elevated triglyceride (>150 mg/dl) was present in 55% of cases and 20% of control group. Triglycerides were higher in patients having fatty liver. The mean TGR was higher in case group compared to controls.
- In case group, 42% of patients had fatty liver. However only 16% of the subjects in the control group had fatty liver.

- Fatty liver was significantly associated with obesity and dyslipidemia and both of these increased the risk of NAFLD.
- Risk factors for CAD were smoking, higher BMI, raised triglyceride, raised serum cholesterol, diabetes and hypertension.
- In present study NAFLD was found to be associated to cases of CAD

Conclusion

In the case control, cross sectional and age sex matched study we observed that there is association of CAD to NAFLD. It was also observed that smoking, hypertension, diabetes, dyslipidemia and obesity are associated with CAD.

The subjects having NAFLD were found to have higher BMI, total cholesterol, and TG. The obesity, diabetes and dyslipidemia were associated to NAFLD.

It is time to reflect and stop eating fat containing and fried fast foods to avoid NAFLD and to save our vital and precious hearts from CAD.

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Conflict of interest: None declared

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