



**ORIGINAL RESEARCH PAPER**

**Gastroenterology**

**PREVALENCE OF NON ALCOHOLIC FATTY LIVER DISEASE IN THE NON CAD,CAD PATIENTS AND CORRELATION OF C REACTIVE PROTEIN WITH NON ALCOHOLIC FATTY LIVER DISEASE.**

**KEY WORDS:** acute coronary syndrome (ACS), Non-alcoholic fatty liver disease (NAFLD), cad (coronary artery disease)

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**ABSTRACT**

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). Patients with NAFLD were associated with more prevalent CAD independent of other risk factors, including glycemic control and Met S components (61,62). This finding was despite factoring in the other risk factors for CAD and the components of metabolic syndrome (63). 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 (57,61,64). Central obesity, high triglyceride levels and hypertension are the major abnormal metabolic syndrome criteria in patients with NAFLD. Metabolic syndrome (MetS) components including central obesity, hypertension, hypertriglyceridemia, decreased high density lipoprotein cholesterol (HDL-C) and impaired glucose test or type 2 diabetes mellitus (DM) are commonly found in NAFLD (65). MetS is defined by the presence of three or more of these metabolic abnormalities by the 2001 National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) criteria (66) and was modified by the International Diabetes Federation in 2005 as shown in Table 2 (67,68). The criteria of MetS by the International Diabetes Federation in 2005 (68) 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). Non-alcoholic fatty liver disease (NAFLD) affects upto a third of the population worldwide and may confer increased cardiometabolic risk with consequent adverse cardiovascular outcomes independent of traditional cardiovascular risk factors and the metabolic syndromes. It is characterized almost universally by insulin resistance and is strongly associated with type 2 diabetes and obesity. Non alcoholic fatty liver disease is a marker of pathological ectopic fat accumulation combined with a low grade chronic inflammatory state. This results in several deleterious pathophysiological processes including in abnormal glucose, fatty acid and lipoprotein metabolism, increased oxidative stress, deranged adipokine profile, hypercoagulability endothelial dysfunction and accelerated progression of atherosclerosis. This ultimately leads to a dysfunctional cardiometabolic phenotype with cardiovascular mortality representing the main mode of premature death in NAFLD. So, in this study we are trying to find out the prevalence of non alcoholic fatty liver disease in CAD patients and correlation of C reactive protein with NAFLD group of CAD population and Control population.

**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.

**DISCUSSION**

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 1<sup>st</sup> November 2011 to 1<sup>st</sup> 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<sup>117</sup> et al found that prevalence of CAD was 60.5% in DM II with NAFLD and 45.2% in DM II with Non NAFLD. Akash Shukla<sup>118</sup> et al found that NAFLD patients tends to have higher calcium scores on CT

coronary angiography and higher prevalence of CAD on angiography. Targher<sup>119</sup> et al found that the prevalence of CAD in NAFLD patients as 26.6% versus 18.3% in Non NAFLD group. Hamaguchi et al<sup>174</sup> 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<sup>2</sup> and 24.95kg/m<sup>2</sup> 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<sup>120</sup> found the same results. A K Agrawal<sup>117</sup> et al found that mean BMI is 27.5kg/m<sup>2</sup> & 25.3kg/m<sup>2</sup>, mean Waist/Hip is 0.97 & 0.93 in NAFLD and Non NAFLD population of DM II. Mahmut A et al<sup>121</sup> 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<sup>122</sup> found prevalence of NAFLD as 49.5% in hypertensive participants of 50-75 years age group. A K Agrawal et al<sup>117</sup> found the prevalence of NAFLD as 57.2% in DM II patients and prevalence of

CAD as 60.5% in diabetics. Mantovani A et al<sup>123</sup> 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<sup>124</sup> found the prevalence of metabolic syndrome and NAFLD to be 24% and 14.8% respectively in non alcoholic North Indian men. Mishra et al<sup>124</sup> found prevalence of NAFLD (54.5%) was significantly higher in patients with DM II as compared to those with pre diabetes.

In smokers of CAD and control population, prevalence of NAFLD is 43.63% and 22.22% respectively which is not significant with a p value of 0.39. Hamabe et al<sup>125</sup> found cigarette smoking as an independent risk factor for onset of NAFLD. Zein Co et al<sup>126</sup> found that smoking was associated with advanced liver fibrosis in NAFLD patients. A K Agrawal et al<sup>117</sup> found prevalence of CAD is significantly higher in NAFLD smokers group. Manopriya T<sup>120</sup> et al also found the same relation. In our study we did not find significant correlation of smoking with NAFLD which may be due to small sample size in our study.

On further analysis we observed that fasting blood sugar (fbs) values are in higher range in CAD with NAFLD than in control population. Mean FBS value is 103.36mg and 92.13mg in CAD and controlled population respectively with a significant p value of 0.0017. Bajaj et al<sup>127</sup> found that the mean FBS value in NAFLD group of general population 96.39mg. Prashanth et al<sup>128</sup> found a high prevalence of NAFLD in DM II which increased with multiple component of metabolic syndrome. A. K Agarwal et al<sup>117</sup> found mean FBS as 161.3mg and 168.88mg in NAFLD and non NAFLD of DM II population. Mohan et al<sup>129</sup> found that the prevalence of NAFLD (54.5%) was significantly higher in patients with diabetes compared to those with pre diabetes (IGT or IFG) (33%), isolated IGT (32.4%), isolated IFG (27.3%) and normal glucose tolerance (NGT) (22.5%).

Serum transaminases (SGOT and SGPT) values are significantly raised in NAFLD group of CAD population than in control population. Mean SGOT and SGPT values are 37.55 IU & 55.71 IU and 24.22 IU & 26.63 IU in NAFLD population of CAD & control group respectively, which is significant with p value of 0.001 & 0.0024 respectively. Manopriya T et al<sup>120</sup> also found similar results. A. K Agarwal et al<sup>117</sup> observed that SGPT is more than SGOT in NAFLD of CAD population.

Correlation of HDL, LDL & TG's are found to be significant in NAFLD of CAD and control group. Mean HDL value is 40.58mg & 44.59mg in NAFLD group of CAD and control population with a significant p value of 0.0035, for LDL mean value is 120.78mg & 103.45mg respectively with a significant p value of 0.0001 and for TG's mean value is 162.16mg & 133.22mg respectively with a highly significant p value of 0.0002. Manopriya et al<sup>120</sup> also found similar results. A.K Agarwal<sup>117</sup> found similar results for HDL and TG but LDL mean value is 102.7mg in NAFLD in comparison to 117.8mg of non NAFLD in diabetic population.

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<sup>120</sup> found higher CRP level in NAFLD with CAD group than in NAFLD group. Nicholas D et al<sup>130</sup> & Ramon Arroyo et al<sup>131</sup> 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 :

1. 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.
2. 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.
3. 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.
4. Incidence of NAFLD is more in Hypertensive CAD group as compared to that of Hypertensive Control group.
5. Incidence of NAFLD is more in Diabetic CAD group as compared to that of Diabetic Control group.
6. In our study we found that there is no positive correlation of smoking with NAFLD
7. Fasting Blood sugar levels were found to be on higher side of normal in NAFLD group of CAD patients as compared to control population.
8. 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.
9. 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.
10. 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.
11. Serum SGOT and SGPT levels were found to be significantly elevated in NAFLD group of CAD population as compared to control population.
12. 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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