



## Study of Biomarkers for Assessing Risk Factors for Coronary Artery Disease in North Indians

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### ABSTRACT

*Our Study is a case control study and was carried out to study the risk factors for coronary artery disease in North Indians. The diagnosis of coronary artery disease was based on correlation of clinical, biochemical, electrocardiography, echocardiography, treadmill testing and coronary angiography findings. The study comprised 100 cases of coronary artery disease (acute coronary syndrome and chronic coronary artery disease) and 100 controls in a tertiary care hospital of North India. The subjects were evaluated for total plasma homocysteine, insulin, C-reactive protein (CRP), lipoprotein fibrinogen and anti-chlamydial antibodies. Male to female ratio was 10:1 in study group with similar predominance of males in controls. Mean age of the cases was 46 years (range 25-59 years) and that of controls was 44 years (range 23-56 years). 64% cases had acute coronary syndrome and 34% had chronic coronary artery disease. In the coronary artery disease population, 76% cases had hyperhomocysteinemia, 9% hyperinsulinaemia, 11% abnormal CRP values, 23% abnormal lipoprotein A levels, 40% IgG anti-chlamydial anti-bodies and only 11% had Ig M anti-chlamydial antibodies. In the control population, 72% had hyperhomocysteinemia and 6% hyperinsulinaemia while 23 % and 9% controls had IgG and IgM anti chlamydial antibodies respectively. In control group 19% cases had abnormal lipoprotein A levels and only 2% had abnormal C reactive protein values. Significant correlation of CAD was seen with CRP values and Ig G anti-chlamydial antibodies. Both the study group and controls had higher homocysteine levels. High C reactive protein levels and Ig G anti-chlamydial antibodies are associated with coronary artery disease. Insulin, lipoprotein A, fibrinogen, IgM anti-chlamydial antibodies and higher levels of total plasma homocysteine have no significant association with coronary artery disease.*

**KEYWORDS :** Risk factors; Coronary artery disease, CRP, Homocysteine.

### Introduction: -

The risk factors for CAD are broadly classified as Modifiable and Non-Modifiable risk factors. Modifiable risk factors include Hypertension, Diabetes Mellitus, Dyslipidaemia, Obesity, Smoking, Habitual Physical Inactivity & Stress. Non- Modifiable risk factors include Age, Sex, Race, and Family History for CAD. The present study was undertaken to evaluate the same in the two subsets of CAD patients viz. acute coronary syndrome (ACS) and chronic CAD.

### Material and Methods

The study was carried out in our tertiary care hospitals over a period of one year, involving a total of 100 cases (both ACS and chronic CAD). Equal number of controls were enrolled from those found normal on evaluation for CAD or admitted for management of unrelated disabilities. History, physical examination, electrocardiography (ECG), chest radiograph, haemogram and metabolic profile were done in all cases. Echocardiography and treadmill test (TMT) were done as indicated. Coronary arteriography (CART) was done in suspected cases of acute coronary syndromes. The grading of CAD was based on standard criteria of American Heart Association. Patients with renal disease, liver disease, diabetes mellitus, respiratory or heart failure, and those on drugs influencing glucose or lipid metabolism were **excluded**. Plasma total homocysteine (tHcy), lipoprotein A [Lp (a)], C reactive protein (CRP) and insulin levels were measured. Anti-chlamydial antibodies were determined by enzyme-linked immunosorbent assay (ELISA) technique. Fibrinogen was estimated by clot assay method (Spin React SA kit). Student's 't' test was used to compare continuous variables. One way analysis of variance (ANOVA) was used for comparison between the subgroups. Categorical variables were compared using Chi square test.

### Discussion

We found a strong association between plasma total homocysteine (tHcy) levels and overall mortality in patients with angiographically confirmed CAD but a causal relationship has not been proven between tHcy and mortality. Conflicting reports exist about association of tHcy with CAD. The present study found no correlation of CAD with tHcy, though it shows higher levels of tHcy in Indian population. This may be due to genetic differences and/or nutritional deficiencies of Vit B12, folic acid and Vit B6. We found IgG anti-chlamydial antibody in a significant number of patients of CAD suggesting a link between

the two. Lp (a) has been implicated in pathogenesis of CAD as it increases the risk of thrombosis and atherosclerosis by competing with plasminogen for cell surface binding, thereby reducing the formation of endogenous tissue plasminogen activator. In contrast to the study by Vasisht et al [23], this study found no association between Lp(a) and CAD. Psycho-social factors such as stress, type A personality, depression and hostility have emerged as significant risk factors for CAD. They probably act via neuro - endocrine mechanisms, vaso-spasm and non-compliance with therapy.

### Prevalence of emerging risk factors for CAD

Variables	ACS (% of cases)	Chronic CAD (% of cases)	'p' value
tHcy(>15µmol/L)	51	24	>0.05
Insulin (>25mU/L)	9	0	>0.05
CRP (>8 ig/mL)	5	6	>0.05
Lp(a) (>30mg/dL)	18	7	>0.05
Fibrinogen (>350mg/dL)	14	7	>0.05
Anti-chlamydial IgG	28	12	>0.05
Anti-chlamydial IgM	5	6	>0.05

### Results

The mean age of the patients was 46 years (range 25-59) and that of controls 44 years (range 23-56). Male: female ratio was 10:1 in study group with similar predominance in controls. The subjects were a mix of middle and upper middle socio-economic strata. 64% cases had ACS and the rest chronic CAD. 60%, 20% and 12% cases had single, double and triple-vessel disease respectively. In 8% cases CART was non-contributory. Mean tHcy values were significantly higher in study group than controls (34.14µ mol/L vs 24.85µmol/L) though the proportions having abnormal tHcy did not differ significantly 76% vs 72% (p>0.05). The insulin levels did not differ significantly in study group and controls (p> 0.05). Abnormal CRP values were seen in 11% cases and 2% controls (p< 0.05). The CRP levels did not correlate with the extent of disease. Lp (a) values were abnormal in 23% cases and 19% controls (p> 0.05). Higher levels of Lp (a) were associated with multiple vessel disease. 21% cases and 12% controls had abnormal fi-

brinogen values ( $p > 0.05$ ). Their levels did not correlate with extent of disease. The Ig G anti- chlamydial antibodies levels were significantly higher in study group whereas no difference was seen for Ig M anti-chlamydial antibodies.

### Conclusion

The present study showed no significant difference in fasting insulin levels in CAD cases and controls in contrast to the findings of Misra et al [11]. Our study documented raised levels of CRP which have been directly correlated with incidence of coronary events, suggesting the presence of an inflammatory process in unstable CAD. Persistent inflammation in atherosclerotic coronary artery related probably to infection, oxidised lipid, free radicals or products of renin-angiotensin system (RAS) is considered an important factor for CAD. We found an association between coronary artery disease and raised levels of serum CRP and Ig G anti-chlamydial antibodies.

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