



STUDY OF CRP, BMI AND LIPID PROFILE IN CORONARY ARTERY DISEASE

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ABSTRACT

Background: Various studies have suggested the association between low grade chronic inflammation and Coronary Artery Disease (CAD).

Aim: Present study was done to evaluate relationship between CRP, Body Mass Index (BMI), Lipid Profile in patients of CAD. In the present study BMI and serum levels of CRP, Lipid profile were compared between 100 cases of CAD and 100 age and gender matched controls. Unpaired t-test was performed to compare BMI, CRP and Lipid Profile between CAD case and control groups. Pearson correlation coefficient (r) was calculated to assess the correlation between BMI and CRP in CAD Case group, Lipid profile and CRP in CAD case group & BMI and Lipid profile in CAD case group. Both the tests were two sided. The p value <0.05 was considered as statistically significant. The p value < 0.001 was considered as highly significant and the p value > 0.05 was taken as non-significant (NS).

Results: A highly significant increase in BMI, CRP, total cholesterol (TC), triglycerides (TG) and low density lipoprotein cholesterol (LDL-c) was found in the cases as compared to that in normal controls. Significantly higher CRP level in females as compared with males was found. A highly significant decrease in High density lipoprotein cholesterol (HDL-c) was found in the cases as compared to that in normal controls. The highly significant positive correlation is found between BMI and CRP in CAD patients. The relationship between CRP and Lipid Profile is found to be non-significant in CAD patients. The relationship between BMI and Lipid Profile is found to be non-significant in CAD patients.

Conclusion: Chronic low grade inflammation and obesity is positively associated with CAD and the relationship is not independent of each other. Lipid profile is positively associated with CAD and the relationship between CAD and lipid profile is independent of CRP and BMI.

KEYWORDS : Coronary Artery Disease (CAD), Body Mass Index (BMI), C-Reactive Protein (CRP), Lipid Profile, Total Cholesterol, Triglycerides, High density lipoprotein cholesterol (HDL-c), Low density lipoprotein cholesterol (LDL-c).

INTRODUCTION:

Coronary artery disease (CAD) is the pathologic state where blood supply to the heart is compromised due to obstruction of the coronary artery that supplies oxygen and nutrients to the heart. It's root cause is atherosclerosis. The complete blockage of the coronary artery leads to heart attack.

Inflammation plays a pivotal role at all the stages of the atherosclerosis, from its initiation to the development of complications.^{1,2} Incidence and prevalence of CAD has been rising at the alarming rate. Life style modification and increased level of stress has been regarded as the most important factor behind this alarmed rise in CAD cases.

C-reactive protein activates the complement system.³ Thus CRP is a powerful inflammatory marker. There are various evidence which suggest that CRP may also directly participate in the inflammatory process of atherogenesis.^{4,5}

Obesity leads to over production of inflammatory molecules like TNF- α and IL-6 by the white adipose tissue⁶, which leads to the increased production of CRP.

This study has been carried out to know the relationship between C-Reactive Protein (CRP), body mass index (BMI), Lipid Profile and CAD. This will help us to know the chances of incidence of CAD in a apparently normal person and the preventive measures can be taken at earliest.

MATERIALS AND METHOD:

The present study was conducted in the Department of Biochemistry, Government Medical College, Nagpur with the help of Medicine Department. The study was approved by institutional Ethics Committee for research work.

Study design: Hospital based cross sectional study with Comparison Groups.

Sample size estimation: From the study of **Deveci OS et al**⁷

- SD₁ in CAD cases= 121
- SD₂ in controls= 83.2
- Difference of means of serum uric acid in two groups= 56.5
- α -Error= 5%
- β -Error= 10 %
- Power= 90%
- Minimum sample size needed for study in each arm= 72
- Sample size was calculated using MedCalc Statistical software⁸

Study population: From Oct 2013 to Sept 2015, one hundred patients with Coronary Artery Disease were studied. Coronary Artery Disease patients were acute Myocardial infarction patients admitted in the ICU of Medical College.

The criteria to select patient in our study consisted of the patients with acute myocardial infarction diagnosed by physician on the basis of the definition approved by American College of Cardiology Committee (ACC) and European Society of Cardiology (ESC). This included typical rise and gradual fall of troponin level and /or severe increase and decrease of CK-MB associated with at least one of the following parameters:

- 1) Gradual appearance of pathological Q wave on electrocardiogram strip (ECG) or
- 2) EKG changes indicating ischemia on the ECG strip (ST segment elevation)

STUDY GROUPS: The study subjects were divided into two groups.

A: Control subjects (n=100)

One hundred normal subjects without CAD

B: CAD Cases (n=100)

One hundred newly diagnosed CAD patients.

INCLUSION CRITERIA:

- One hundred newly diagnosed cases of acute myocardial infarction more than or equal to twenty years of age admitted in the ICU of Medical College Hospital.

EXCLUSION CRITERIA:

- Patients with inflammatory diseases like gout, rheumatoid arthritis, inflammatory bowel disease, renal disease, hypothyroidism, diabetes, anaemia, stroke, malignancy, bacterial infections and smokers were excluded from the study.

CLINICAL DATA RECORDING

After explaining all details, informed consent was taken from each subject for participation in this study. History and examination of patient was recorded on preformed questionnaire which included detailed history and clinical examination.

BODY MASS INDEX (BMI):

The body mass index was calculated by the formula, weight in kilograms divided by square of height in meters.

BMI=Weight in kg/ (Height in m²)

Normal BMI is 18.5- 24.99 kg/m²; Overweight was defined as BMI ≥ 25. Obesity was defined as BMI > 30.

SPECIMEN COLLECTION AND PRESERVATION:

Blood samples were collected from peripheral veins of case and control subjects under aseptic conditions. Enrolment was voluntary, and written consent was obtained from each participant. Fasting blood samples were taken. After one hour of collection samples were centrifuged; serum of a subject were separately taken in the new tubes. Serum CRP, Lipid profile were estimated on XL300 - Erba Mannheim – A Fully Automatic Random Access Clinical Chemistry Analyzer. Serum was preserved at 2-8 degree Celsius.

PARAMETERS WERE ESTIMATED WITH FOLLOWING METHODS:

S.No	PARAMETERS	METHOD
1	C Reactive Protein	CRP Latex Turbidimetry 9
2	Total Cholesterol	Enzymatic method - Cholesterol esterase, cholesterol oxidase and peroxidase.10
3	Triglyceride	Enzymatic method- Glycerol phosphate oxidase and peroxidase; End point.11
4	HDL-C	Direct HDL-C Colorimetric (End Point)12
5	LDL-C	LDL-C Direct Enzymatic colorimetric, liquid Method13

STATISTICAL ANALYSIS

- BMI, CRP and Lipid Profile were presented as mean ± SD .
- Statistical data was recorded on Microsoft Excel program.
- Unpaired t-test was performed to compare BMI, CRP and Lipid Profile between CAD case and control groups.
- Pearson correlation coefficient (r) was calculated to assess the correlation between BMI and CRP in CAD Case group, Lipid profile and CRP in CAD case group & BMI and Lipid profile in CAD case group.
- Both the tests were two sided. p value <0.05 was considered as statistically significant. The p value < 0.001 was considered as highly significant and the p value > 0.05 was taken as non-significant (NS).
- Statistical software Microsoft Excel was used for statistical analysis.
- The p value calculator downloaded from www.socscistatistics.com was used for calculating p value for Pearson's correlation.

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RESULTS AND DISCUSSION:

Study Design: Hospital based Cross Sectional Comparative Study between Two Groups one was the CAD Patients Group and the other was the Control Group with subjects without CAD.

Table- 1: Distribution of CRP, BMI and Lipid Profile in CAD patients and controls without CAD

PARAMETERS	CONTROLS (Mean ± SD)	CASES (Mean±SD)	P-VALUE
CRP levels in both males and females (mg/L)	2.62 ± 0.59	17.66 ± 6.41	< 0.001
CRP levels in males (mg/L)	2.72 ± 0.55	16.97 ± 6.95	< 0.001
CRP levels in female (mg/L)	2.43 ± 0.64	19.06 ± 4.95	< 0.001
BMI (kg/m ²)	25.13 ± 2.01	29.02 ± 2.82	< 0.001
Total Cholesterol (mg/dl)	168.44 ± 10.3	177.84±24.46	< 0.001
Triglyceride (mg/dl)	122.98± 17.10	155.06± 40.53	< 0.001
HDL-C (mg/dl)	48.75 ± 5.7	39.72 ± 3.82	< 0.001
LDL-C (mg/dl)	95.06 ± 7.06	107.46± 22.02	< 0.001

* p<0.05 is considered significant; SD – Standard deviation

The mean level of C-reactive protein in both males and females taken together in control group is 2.62 ± 0.59 mg/L and in case group is 17.66 ± 6.41 mg/L with p value < 0.001. The CRP levels are significantly higher in CAD cases compared with normal controls. Arroyo et al¹⁴, N. Yilmaz et al¹⁵ and Suman B Sharma et al¹⁶ have reported significantly higher CRP level in CAD patients than in normal controls. The main biological function of CRP is the nonspecific defence against the infectious agents and removal of apoptotic and necrotic cells. As, myocardial tissue necrosis is associated with myocardial infarction which, may lead to the increased level of CRP. CRP directly participate in the inflammatory process of atherosclerosis & localizes in atherosclerotic plaque^{4,5}. C-reactive protein also increases the production of matrix metalloproteinase (MMP) thus, makes the plaque vulnerable for rupture and hence may lead to acute myocardial infarction.¹⁷⁻¹⁹ Prothrombotic state generated by CRP is due to tissue factor release from mononuclear cells.^{20,21} CRP promotes endothelial, and smooth muscle cells proliferation.²²

The mean level of C-reactive protein in males in case group is 16.97 ± 6.95 mg/L and in females in case group is 19.06 ± 4.95 mg/L. The mean CRP levels are slightly higher in females as compared to that in males in CAD cases. Significantly higher CRP level in females as compared with males have been reported by Ross Arena et al.²³

The mean value of BMI in control group was 25.13 ± 2.01 Kg/m² and in case group was 29.02 ± 2.82 Kg/m². A highly significant increase in BMI was found in the cases as compared to that in normal controls. Obesity, leads to hyperlipidemia and inflammation²⁴, hence increases the possibility of rupture for atheromatous plaque. Obesity has been related with an increased expression of tissue factor,²⁵ enhanced platelet activation,²⁶ and elevated plasminogen activator inhibitor-1 (PAI-1),²⁷ and thus, affect the initiation and progression of intraluminal thrombosis after coronary plaque rupture. Also, obesity may be related with cardiac hypertrophy²⁸ and

may impair coronary flow reserve, increasing the chances for myocardial ischemia.

The mean level of total cholesterol in control group was 168.44 ± 10.3 mg/dl and in case group was 177.84 ± 24.46 mg/dl. A highly significant increase in total cholesterol level was found in the cases as compared to that in normal controls. The mean levels were within normal reference range in both cases and controls.

The mean level of triglyceride in control group was 122.98 ± 17.10 mg/dl and in case group was 155.06 ± 40.53 mg/dl. A highly significant increase in triglyceride level was found in the cases as compared to that in normal controls. The mean levels were within normal reference range in both cases and controls.

The mean level of HDL-C in control group was 48.75 ± 5.7 mg/dl and in case group was 39.72 ± 3.82 mg/dl. A highly significant decrease in HDL-C level was found in the cases as compared to that in normal controls. The mean levels were within normal reference range in both cases and controls.

The mean level of LDL-C in control group was 95.06 ± 7.06 mg/dl and in case group was 107.46 ± 22.02 mg/dl. A highly significant increase in LDL-C level was found in the cases as compared to that in normal controls. The mean levels were within normal reference range in both cases and controls.

Raised level of serum cholesterol is one of the main modifiable risk factors for CAD²⁹. LDLc is a causal factor for atherosclerosis and its enhanced value increases the morbidity & mortality.^{30,31,32}

Reduced levels of HDLc, is correlated with the increase in the intimal coat of arteries in young individuals^{33,34,35}.

An associated between TG levels and obesity, was shown by Valverde et al.³⁶, in a study with obese infants, with a prevalence of 35% for high concentration of TG. The inhibition of lipoprotein lipase activity as reported by Navab et al³⁷ leads to decreased lipoprotein clearance. Balci³⁸ has reported that the free fatty acids mobilization due to increase in the adrenergic mediated lipolysis of the adipocytes under the stressful conditions like AMI and hepatic secretion of very low density lipoprotein also increases the TG levels. Thus, both the increase in lipoprotein production and decrease in lipoprotein clearance causes elevated levels of TG.

Table -2 : The Pearson Correlation coefficient between BMI and CRP in CAD cases:

Pearson correlation coefficient between BMI and CRP	Value of Pearson correlation coefficient (r)	P value
Between BMI and CRP	0.674	< 0.001

* p<0.05 is considered significant

BMI and CRP in CAD case group was found to be positively correlated (r=0.674), with p- value < 0.001 that means, the correlation is highly significant.

Obesity leads to overproduction of inflammatory molecules like TNF- α and IL-6 by the white adipose tissue⁶, which leads to the increased production of CRP.

Table -3 : The Pearson Correlation coefficient between Lipid Profile and BMI in CAD cases

Pearson correlation coefficient between BMI and Lipid profile	Value of Pearson correlation coefficient (r)	P value
TOTAL CHOLESTEROL	-0.023	0.82
TRIGLYCERIDES	-0.049	0.62
HDL-C	0.111	0.27
LDL-C	-0.012	0.90

* p<0.05 is considered significant

BMI and Total cholesterol in CAD case group was found to be negatively correlated (r = -0.023), with p = 0.82 that means, the correlation is not significant.

BMI and Triglycerides in CAD case group was found to be negatively correlated (r = -0.049), with p = 0.62 that means, the correlation is not significant.

BMI and HDL-C in CAD case group was found to be positively correlated (r = +0.111), with p = 0.27 that means, the correlation is not significant.

BMI and LDL-C in CAD case group was found to be negatively correlated (r = -0.012), with p = 0.9 that means, the correlation is not significant.

The Diaphane Collaborative Study Group in France have reported that the risk of overall mortality has decreased with increasing BMI among hemodialysis patients³⁹. This has been called as "obesity paradox". Later on, many studies have shown that obesity paradox is associated with other clinical conditions like diabetes⁴⁰, hypertension⁴¹, and heart failure⁴². But there are differences in opinion about the association of BMI with mortality in CAD patients. Various studies have reported positive associations⁴³, inverse associations⁴⁴, J-shaped associations⁴⁵, or no associations⁴⁶.

Table -4: The Pearson Correlation coefficient between Lipid Profile and CRP in CAD cases

Pearson correlation coefficient between CRP and Lipid Profile	Value of Pearson correlation coefficient (r)	P value
TOTAL CHOLESTEROL	-0.0478	0.64
TRIGLYCERIDES	-0.032	0.75
HDL-C	0.023	0.81
LDL-C	-0.063	0.53

* p<0.05 is considered significant

CRP and Total cholesterol in CAD case group was found to be negatively correlated (r = -0.047), with p = 0.6423 that means, the correlation is not significant.

Bjorck et al. (1957)⁴⁷ have reported that serum cholesterol levels decreased during MI. Another study done by Khan et al⁴⁸ have shown significantly decreased level of TC in AMI patients. This decline in TC level is either due to inflammatory response, or it may be due to increased utilization of cholesterol in tissue repair and hormonal synthesis (Correia et al., 2004⁴⁹)

CRP and Triglycerides in CAD case group was found to be negatively correlated (r = -0.032), with p = 0.7519 that means, the correlation is not significant. Tsompanidi et al⁵⁰, Nigam⁵¹ and Pitt et al⁵² have reported an increased level of TG after AMI.

CRP and HDL-C in CAD case group was found to be positively correlated (r=0.0239), with p = 0.8134 that means, the correlation is not significant. In AMI, inflammation leads to changes in both the size and the function of the HDL reported by Ansell et al⁵³. Inflammation decreases the level of HDL by increasing the activity of endothelial lipase and soluble phospholipase A2 and replacing the apolipoprotein A1 in the HDL with serum amyloid A.

CRP and LDL-C in CAD case group was found to be negatively correlated (r = -0.063), with p = 0.5334 that means, the correlation is not significant.

Though during acute phase reaction, LDL synthesis is increased, the LDL level decreases due to upregulated LDLR activity as reported by Balci³⁸. Also, LDL particle size is smaller in patients with AMI as compared to normal subjects.

Summary and Conclusions:

This study entitled 'STUDY OF CRP, BMI AND LIPID PROFILE IN CORONARY ARTERY DISEASE' was a hospital based cross sectional study with comparison groups, conducted in the Department of Biochemistry at tertiary health care centre with the help of Medicine Department during the period of two years.

The Study population consisted of one hundred newly diagnosed CAD patients as case group and one hundred normal subjects as control group. Both the groups were comparable with each other for age and sex. The study was carried out to evaluate the relationship between CRP and CAD, Lipid Profile and CAD, BMI and CAD, Lipid Profile and CRP in CAD, BMI and CRP in CAD, Lipid Profile and BMI in CAD. The concentrations of total cholesterol, triglyceride, HDL-C and LDL-C were estimated from the serum samples of both the cases and controls by colorimetric methods. The serum CRP levels were measured by Latex Turbidimetry.

CONCLUSIONS:

In the present study, we have following findings -

1. The mean CRP level is significantly higher in CAD cases compared with normal controls.
2. The mean CRP level is slightly higher in females as compared with males in CAD cases.
3. The mean BMI level is significantly higher in CAD cases compared with normal controls.
4. The highly significant positive correlation is found between BMI and CRP in CAD patients.
5. The relationship between BMI and Lipid Profile is found to be non significant in CAD patients.
6. The relationship between CRP and Lipid Profile is found to be non significant in CAD patients.

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