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STUDY OF VARIABLES IN UNSTABLE ANGINA WITH EMPHASIS ON C-REACTIVE PROTEIN

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ABSTRACT: OBJECTIVES: Prevalence rates of coronary artery disease are reported to be very high in Asian Indians. Traditional risk factors alone fail to explain the high rates of coronary disease in Indians. Acute phase reactants C-reactive protein in Indian subjects with unstable angina were evaluated and compare them with suitable control to test the hypothesis that a relationship exists between acute phase reactants and unstable angina. **METHODOLOGY:** 50 cases unstable angina and 50 suitable cases enrolled for the study. Unstable angina had significantly increased level of CRP compare to control group (p=0.01098).**RESULTS:** Statistically significant difference was found between case and control group in TLC (p=0.0037) and ESR (p=0.0368), TLC and ESR being more in case group as compare to control group. C- reactive protein was significantly correlated with TLC and ESR in case group and TLC and ESR in control group. C reactive protein, TLC and ESR in case group while no correlation was observed with any variable in control group. **CONCLUSION:** The present study concludes that a relationship exists between acute phase reactant studied and unstable angina. **KEYWORDS:** Unstable angina, C - reactive protein, Clinical Outcome.

INTRODUCTION: Cardiovascular disease is the commonest cause of death globally. Also Asian Indians have the highest morbidity and mortality of coronary artery disease (CAD) in the whole world.[1, 2]. Ischemic heart disease is no longer a disease of the western world and no longer a disease of only affluent population as believed earlier. It is also increasingly common in younger age groups in Asian indians[3] and people belonging to all social-economic strata are being affected. Conventional risk factors alone fail to explain these rates of CAD.

The immediate precipitating event of the atherosclerotic plaque responsible for that critical degree of ischemia in unstable angina has been shown in numerous studies[4,5] with the rupture of the fibrous cap of the atherosclerotic plaque with subsequent exposure of the underlying lipid core to blood. This initiates platelet aggregation, thrombosis and vasospasm. Inflammation may contribute to weakening of the atherosclerotic plaque and lead to its rupture and subsequent event.

Recent research focuses on the possible role of inflammation in CAD. For this purpose various markers of inflammation are being studied quantitatively and qualitatively. These include acute phase recants such as C-reactive protein (CRP).

Acute phase reactants are proteins in the plasma whose levels increase during acute inflammatory states secondary to certain types of tissue damage. Acute phase reactants are believed to play a role in inflammation. Change in acute phase proteins are a general response to inflammation. CRP is a very sensitive marker of inflammation. The complement system functions is most disease states in producing inflammation and damage. In this study we report on the relationship between acute phase of reactants CRP and unstable angina.

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MATERIAL AND METHODS: The study was under taken at BRIMS Teaching Hospital, Bidar. The patients were taken from medicine emergency, General Medicine ward and cardiology wards including intensive coronary care unit. A total eight subjects were selected which included 50 cases and 50 controls. Detailed history, general physical examination and relevant investigations helped in selection of cases and controls who were further investigated for the study.

Conditions known to be associated with raised acute phase proteins were a basis of exclusion. 50 cases of unstable angina formed the case group. Criteria for unstable angina were solely based on history, physical examination, ECG, finding and values of cardiac enzymes. The control group included 40 age and sex matched healthy subjects. The baseline investigations performed in each subject were ECG, complete hemogram, ESR, Blood urea, Blood Sugar, Liver function test with serum protein and lipid profile.

Those enrolled for the study had further blood samples taken by venepuncture which was assayed for CRP. CRP was analyzed by quantitative enzyme immunoassay.

STATISTICAL ANALYSIS: The various parameters of the study were analyzed statistically in both cases and controls. The statistical significance of the difference between means was estimated using 't' test. Difference was labeled statistically significance if p-value came out to be <0.05. Covariate analysis was used to adjust for the confounding factors. Correlations of the acute phase reactants CRP with the other variable was estimated.

OBSERVATIONS: The clinical and biochemical characteristics of the study group are shown in table 1.

Cases and controls were found to be matched for age, sex, smoking, fasting blood sugar, cholesterol, HDL, cholesterol and LDL Cholesterol. Triglyceride level was found to be significantly higher in case group (p=0.0006) as compared to the control group. There is no significant difference for the rest of the lipid profile. LTC and ESR were also found to be higher in case group as compared to the control group, the difference being statistically significant p=0.0037 and 0.0368 respectively.

Level of CRP was found to be 7.49±6.2mg/l in controls and 10.91±5.53mg/l in cases. Thus it is significantly higher in case reports compared to control group (p=0.01098) thereby favoring the hypothesis that CRP has a relation with unstable angina.

Parameters	Case group (with Unstable angina)	Control group (Healthy subjects)	p-value
Age Years	57.10±10.48	58.50±14.041	0.06140
Males	82.5%	67.5%	0.124
Smokers	52.5%	60%	0.505
Fasting blood sugar (mg/dl)	89.025±34.808	80.275±9.386	0.129
Serum cholesterol (mg/dl)	175.03±53.65	171.55±56.88	0.7794
HDL – Cholesterol (mg/dl)	40.45±21.37	44.95±12.91	0.2577
LDL- Cholesterol (mg/dl)	92.64±57.56	100.17±47.34	0.5253
Triglycerides (mg/dl)	205.68±127.91	126.70±57.20	0.0006*
TLC (per mm³)	7555±1513.35	6670±1103.19	0.0037*
ESR(mm/hour)	9.80±3.29	8.20±3.244	0.368*

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CRP (mg/l)	10.91±5.53	7.49±6.21	0.01098*
Diabetics	15%	0%	0.01*
Hypertensive's	17.5%	0%	0.005*
*Statistically Significant			
Table 1: Compares of clinical and Biochemical characteristics in case Group and control group			

Dependent variable	Mean square effect	Mean Square error	F (dfL, 12, 1, 68)	p-value
TLC	11307400	1857587	6.087121	0.016140
ESR	49	12	4.103050	0.046733
CRP	198.64	31.28	6.349518	0.014095
Table 2: Comparison Acute Phase Reactions between Controls and cases after adjusting for confounding Factors by Covariate Analysis				

Variable	TLC	ESR	CRP
TLC	1.00	0.90*	0.75*
ESR	0.90*	1.00	0.68*
CRP	0.75	0.68*	1.00
Statistical significant			
Table 3: Correlation of Acute phase Reactant with Each other in the Control Group			

Variable	TLC	ESR	CRP
TLC	1.00	0.91*	0.55*
ESR	0.91*	1.00	0.57*
CRP	0.55*	0.57*	1.00
Statistical significant			
Table 4: Correlation of Acute Phase Reactions with each other in the case group			

Table 2 compares the acute phase reactants between controls and cases after adjusting for confounding factors. Covariate analysis was performed adjusting for age, sex, smoking fasting blood sugar, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, diabetes and hypertension.

Thus, it is seen that even after adjusting, ESR, CRP and TLC are significantly different in controls and cases.

Correlation of the acute phase reactant with each other in the two groups, controls and cases are depicted in table 3 and table 4 respectively.

Thus it is observed that there is statistically significant correlation of the three variables TLC, ESR and CRP in both groups with the other three variables only in the case group.

DISCUSSION: For many years in fact as early as the mid twentieth century, the presence of inflammation in CAD has been appreciated. It is only recently being understood that traditional

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factors do not explain it all, and the role of inflammation in the causation of unstable angina is being pursued with new vigor. To this end, acute phase reactant like CRP, serum amyloid protein, leukocyte count ESR have recently been studied in unstable angina.

Various studies have shown a rise in these acute reactant in unstable angina. A meta-analysis by Danesh et al[6] showed that the baseline values of four acute phase reactants CRP, serum amyloid protein, leucocyte count and albumin are associated with one another as well as with the future risk of coronary heart disease. These data support the idea that there are some underlying processes related to inflammation that are relevant to CAD.

A study by Berk et al[7] found CRP level significantly elevated in unstable angina as compared to the control group with no ischemic illness. Another study by Abdelmouttaleb et al[8] in 142 patients with coronary disease (group 1), 37 patients with normal angiograms (group 2) and 37 control healthy subjects (group 3) found higher level of CRP in patients with unstable angina and previous myocardial infraction than in patients with stable symptoms and group 2 and group 3.

In this study also, we attempted to test the hypothesis that a relationship exists between acute phase reactant and unstable angina especially CRP. All factors known to cause a rise in acute phase proteins were a basis for exclusion from the study group.

The results of the present study showed increased level of CRP to be associated with the syndrome of unstable angina (p=0.0037) and ESR (p=0.0368). TLC and ESR being more in unstable angina as compared to healthy subjects.

According to Gaither and Frank[10] the finding of normal serum level of complement does not preclude the participation of complement in tissue injury. This the present study does not rule out the role of complement in unstable angina. Of further interest is the association of the 3 variables CRP, ESR and TLC with each other in the case group.

One major limitation of this study was that due to ethical, logistic and socio-economic constraints, coronary angiography could not be performed in all the study subjects, hence the diagnosis of unstable angina was only clinical and the control group which was considered healthy may have subjects with abnormal coronary vessel. This might explain elevated CRP values in some subject of control group.

Nevertheless all the findings of the study do suggest a relationship between acute phase reactant and unstable angina and encourage the studies probing the role of inflammation in the causation of unstable angina.

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