

## STUDY OF RELATIONSHIP BETWEEN SERUM LEVELS OF HS-CRP AND THE SEVERITY & COMPLEXITY OF CORONARY ARTERY STENOSIS IN PATIENTS WITH UNSTABLE ANGINA

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### Abstract

**Background:** High sensitive C-reactive protein inflammatory biomarker is one of the best informative markers of prognosis and severity of CAD particularly in ACS that has been studied. **Materials and Methods:** This study included 36 patients with clinically diagnosed unstable angina with hs-Troponin negative, of which 10 hs-Troponin patients act as controls. Hs-CRP levels were measured in patients before angiography by ELISA method, were compared between the groups and its correlation with severity and complexity of coronary lesions was evaluated. **Result:** Out of 36 patients, 22 patients (61.1%) were documented to have complex coronary lesion, while 14 patients (38.9%) was found to have simple lesion. Hs-CRP levels were elevated in 28 patients (77.8%) and serum levels not elevated in 8 patients (22.2%). Presence of complex coronary lesion significantly correlated with serum levels of hs-CRP ( $p = 0.04$ ). A significant relationship between serum hs-CRP levels and hs-troponin assays was not seen ( $p > 0.9$ ). **Conclusion:** We found that hs-CRP levels correlate well with angiographic severity and complexity in unstable angina patients. The findings suggest that higher the hs-CRP levels more the number of vessels involved. The hs-CRP values elevation was much higher in Hs-troponin positive patients than in Hs-troponin negative patients.

## INTRODUCTION

CAD is the common form of cardiovascular disease with a prevalence of 6.9% in men and 6% in women. The prevalence of risk factors may differ among population. The study of the factors influencing atherosclerosis are variable. Inflammation is the key initiator of plaque formation and plays a role in plaque instability, plaque rupture and endothelial denudation. Plaque erosion and plaque rupture plays a key role in stimulation of ACS. Risk factors include diabetes mellitus, hypertension, smoking, sedentary and stressful life style, obesity, lack of consumption of fruits and vegetables and non modifiable risk factors like age, race, genetics, ethnicity, sex, family history of CAD.<sup>[1-5]</sup>

High sensitive CRP, a marker of systemic inflammation, rises as a result of injury, infection and to inflammatory stimuli. Serum hs-CRP remains

elevated for long time even in the absence of stimuli. hs-CRP increases thrombogenicity and vascular vulnerability through stimulation of endothelin plasminogen activator inhibitor,<sup>[1]</sup> increased expression of cell adhesion molecules, downregulates endothelial nitric oxide production and abnormal LDL uptake by macrophages.<sup>[6-8]</sup>

Most studies tried to correlate serum hs-CRP levels and severity study, less data are available regarding relationship between hs-CRP, the activation of plaque, the incidence of unstable angina. Multiple studies have shown the association of hs-CRP and the adverse cardiac events in patients with previously stable CAD. In patients recovering from ACS, measures to reduce the LDL (<70mg/dl) but with hs-CRP >2mg/l shown to have recurrent ischemic events.<sup>[9]</sup>

Hence, the goal is to reduce both the lipid levels and hs-CRP levels together. hs-CRP levels should be an

additive tool along with serum lipid measurements in patients with unstable angina. The aim of this study was to correlate the serum levels of hs-CRP to the severity and complexity of coronary artery lesions in patients with unstable angina diagnosed clinically.<sup>[10]</sup>

## MATERIALS AND METHODS

This is a hospital based prospective observational study, was conducted in the Department of Cardiology, Government Rajaji Hospital, Madurai for a total period of 1 year for around 36 patients. All patients with clinical history suggestive of anginal pain (nature, site, radiation, aggravated by stress or emotion, relieved by rest or nitrates) with or without risk factors for CAD and with or without ST segment and t wave changes in ECG, with or without regional wall motion abnormalities on Echo, and patients with hs-Troponin negative and positive patients are enrolled in this study.

Patients with chronic medical illness, infective endocarditis or sepsis; History of chronic diseases known to cause inflammation like connective tissue disorders, infiltrative disorders, muscle dystrophies or systemic malignancies; chronic cardiomyopathy of any cause in whom ejection fraction was below 35% (calculated by modified Simpson method); Presence of severe anemia, coagulopathy, end stage renal disease (ESRD), dyselectrolyemia or thyroid disorders; any surgery done within 3 months of unstable angina, and patients on immunosuppressant drugs were actively excluded from this study.

A detailed history including presenting symptoms, past history, family history of CAD or other relevant history, history of atherosclerotic risk factors and drug history was taken from all patients. Complete physical examination including CVS, CNS, ABDOMEN, RESPIRATORY system was then performed. Base line investigations including electrocardiogram (ECG), complete blood count, kidney function tests, liver function tests, serum electrolytes, lipid profile, fasting blood sugar, hs-CRP levels, hs-troponin and quantitative troponin were obtained. Echocardiography for regional wall motion abnormalities, diastolic dysfunction and to assess left ventricular function was also done in all the cases. Serum hs-CRP levels were measured by ELISA method. Serum levels of hs-Troponin was measured by rapid card method whereas serum quantitative measurement was done by chemo luminescent assay method separately. Coronary angiography (CAG) was performed via either trans-radial or trans-femoral approach. The angiograms were assessed by two independent interventional cardiologists who were blinded to the clinical details of the patients. The lesion was quantified by QCA method. Multiple angiogram views are taken to assess the complexity and severity of coronary lesions.

Coronary artery disease is defined as the presence of any degree of narrowing in at least one of major coronary arteries [left anterior descending (LAD), left circumflex (LCx), right coronary artery (RCA)]

or their branches. Significant CAD was defined as >50% diameter stenosis in any of these major vessels, while <50% diameter stenosis was stratified as non-significant CAD. CAD was categorized as single vessel disease (SVD), double vessel disease (DVD), or triple vessel disease (TVD) according to number of major branches involvement. Complex lesions include bifurcation lesions, calcified lesions, ostial lesions, left main disease and chronic total occlusions.

Statistical analysis was performed by SPSS software package (version 22.0, SPSS Inc, Chicago, Illinois, USA). All continuous variables were expressed as mean and SD, and categorical variables were reported as frequency and percentages. Group comparisons were performed with Student t-test or crosstabs. The Chi-square test or Fisher exact test was used for categorical variables. A p-value of <0.05 was considered statistically significant.

## RESULTS

During the study period of 1 year, a total of 36 patients with symptomatic Unstable angina with troponin negative patients irrespective of ECG and echo changes along with troponin positive patients as control were enrolled in the study. The mean age of our patients was 51.6 years with patients ranging from 36 to 75 years. Majority of the patients belonged to 46-55 years age group (38.9%). Out of 36 patients, 12 were males and 24 were females. Hs troponin are negative in 25 patients whereas Hs troponin was positive in around 11 patients. Out of 36 patients, 22 patients (61.1%) were documented to have complex coronary lesion while 14 patients (38.9%) were found to have simple coronary lesion.

Association between hs-CRP level and complex lesion was found to be statistically significant (p value 0.04) while the association between hs-CRP levels in Hs-troponin negative patients (study group) vs Hs-troponin positive patients (control) was not statistically significant. Hs-CRP levels were elevated in 28 patients (77.8%), and it is not elevated in 8 patients (22.2%). In terms of the number of vessels involved, 12 patients had single vessel disease (SVD), 5 patients had double vessel disease (DVD) and 12 patient had triple vessel disease (TVD), 7 patients have normal coronaries, 4 patients have left main disease, 1 patient has GRAFT vessel disease. Among all 22 patients with complex disease (61.1%), CHRONIC total occlusion was seen in 3 patients, Bifurcation lesion was seen in 4 patients, OSTIAL lesion was seen in 8 patients, 7 patients are found to have CALCIFIC type C lesion. Among all 14 patients with non complex lesion (38.9%), 2 patients had ectatic coronaries, 1 patient had non obstructive CAD, 1 patient had anomalous origin of LCX from right coronary sinus, remaining were found to have normal coronaries. Of 11 patients who had hs-Troponin elevation, their quantitative troponin is

significantly elevated. 12 patients in our study group were active smokers.

With respect to clinical symptoms, majority presented with angina. Among the risk factors for CAD, large group of patients presented with Diabetes followed by hypertension and obesity, smoking. The statistical association between hs-CRP levels and complex lesion in angiography was found to be statistically significant. Among patients with abnormal CAG, 61.1% patients had complex coronary lesion such as chronic total occlusion, true bifurcation lesion, calcific type C lesion, ostial lesion, left main disease were found. Of these 38.9% patients with non-complex lesions, normal coronaries, ectatic coronaries, non-obstructive CAD, anomalous coronary artery were seen.

Of all the 36 patients, all patients were underwent therapy based on CAG. 12 patients with either normal coronaries or non-obstructive CAD underwent Optimal medical therapy alone, 12 patients with

either Single or double vessel disease underwent PCI. Of all patients with triple vessel disease and left main disease, only 2 patients underwent CABG. Remaining 10 patients with Triple vessel disease was not willing for CABG and on optimal medical therapy and followup. One left main stenting was done in our study.

Of all the 36 patients, hs-CRP levels were elevated in 28 of patients and not elevated in 8 patients, hs-CRP elevation in patients with complex coronary lesion is statistically significant ( $p < 0.04$ ). Then, hs-CRP levels was elevated in all 11 HS-troponin positive patients and quantitative troponin was also significantly elevated, hs-CRP levels were elevated in 17 hs-Troponin negative patients and not elevated in 8 hs-Troponin negative patients, and the association of hs-CRP levels with regard to hs-troponin levels was not statistically significant ( $p$  value- 0.9).

**Table 1: Distribution of patients based on age.**

Age class	Number of patients (%)
36 -45	6 (16.7%)
46-55	14 (38.9%)
56-65	12 (33.3%)
66-75	4 (11.1%)
Total	36 (100%)

**Table 2: Distribution of patients based on gender**

Gender	Number of patients (%)
Male	12(33.3%)
Female	24(66.7%)
Total	36(100%)

**Table 3: Distribution of patients based on diagnosis**

Diagnosis	Number of patients (%)
CAD/ACS/UA	35(97.2%)
CAD/ACS/UA/NON ISCHEMIC DCM	1 (2.8%)
Total	36 (100%)

**Table 4: Distribution of patients on level of hs CRP**

Hs CRP level	Number of patients (%)
Elevated	28 (77.8%)
Not elevated	8 (22.2%)
Total	36(100%)

**Table 5: Distribution of patients on angiographic findings**

Angiographic findings	Number of patients (%)
Complex lesion	22 (61.1%)
Non complex lesion	14 (38.9%)
Total	36 (100%)

**Table 6: Association between hs CRP level and angiographic findings**

Hs CRP level	Angiographic findings		P value
	Complex lesion	Non complex lesion	
Elevated	19	9	0.04( significant)
Not elevated	3	5	
	22	14	

**Table 7: Association between hs CRP level and angiographic findings**

Hs CRP level	Troponin		P value
	positive	negative	
Elevated	11	17	0.9
Not elevated	0	8	
	22	14	

## DISCUSSION

Our study showed hs-CRP levels elevated in 77.8% of patients, of which 61.1% of patients have complex coronary lesion, and serum levels of hs-CRP and complex coronary lesions are strongly positively correlated.

Most of the patients belonged to the 46-55 years age group. The number of female participants was slightly more than male participants while most studies used only male participants. Seyedian et al study showed angiographic severity by Gensini score and also they compared hs-CRP levels in patients with stable and unstable angina, however in our study we compared hs-CRP in unstable angina patients with hs-Troponin patients to hs-Troponin positive patients

Aditya sharma et al,<sup>[11]</sup> showed double vessel disease involvement was most common while our study showed TVD disease was more commonly associated with hs-CRP elevation. Similar to Tibaut et al study, there is positive correlation between hs-CRP in unstable angina patients and severity of lesion, in addition our study also showed positive correlation with complexity of coronary lesion.

Of all the patients, hs-CRP levels were elevated in 28 patients, not elevated in 8 patients. hs-CRP levels were elevated in all troponin positive patients and quantitative troponin was significantly elevated. hs-CRP levels were elevated in 17 hs-Troponin negative patients and not elevated in 8 hs-Troponin negative patients. Only, the association of hs-CRP levels with complexity and severity of the lesion is statistically significant.<sup>[12]</sup>

## CONCLUSION

Serum levels of hs-CRP is used to predict and prognosticate complex coronary artery lesion and plan management strategy as the elevated serum levels of hs-CRP correlate well with angiographic severity and complexity. It could be argued that all these patients should undergo a serum hs-CRP levels before invasive angiogram. Diagnosis and appropriate management of complex lesions particularly in Unstable angina is likely to improve

the long term prognosis of these patients, and help in appropriate measures.

### Limitations

The present study had some important limitations. This was single center study and with a small sample size. The control group is also small. Therefore, extrapolation of these results to general population requires further validation from the larger prospective multi-centre studies. The association of hs-CRP in perioperative UA needs to be studied further.

Long term follow up needs to be done to quantify the prognostic benefit like MACCE and other composite endpoints from revascularization in these patient groups.

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