

Qualitative assay of C-reactive proteins in acute coronary syndromes

Jayaprakash Appajigol¹ and A.G. Srinivasmurthy²

¹Department of General Medicine, KLE University's JN Medical College, KLES Dr. Prabhakar Kore Hospital & MRC, Belgaum- 590010, Karnataka, India

² Department of General Medicine, Shree Siddhartha Medical College, Tumkur, Karnataka, India.

Abstract

Introduction: Acute coronary syndromes (ACS) are the major causes of mortality in coronary care units. Inflammation plays an important role in ACS. C-reactive protein (CRP) is one of the inflammatory markers, which plays a key role in the pathogenesis. This study aimed at assessing C-reactive protein levels in acute coronary syndromes, and determining its significance in prognosis.

Methods: Fifty patients admitted with the diagnosis of ACS were included in the study. Qualitative C - reactive protein assay was done at the time of admission. Patients were followed up for the complications till discharge.

Results: Age group between 41 to 70 years constituted 40 (80%) patients. Out of 50 patients with acute coronary syndromes 36 patients had elevated CRP. Thirty patients (83.33%) of them met with complications. Of the 14 patients with low CRP only two (14.28%) patients met with the complications.

Conclusions: Qualitative plasma CRP estimation gives valuable prognostic information in acute coronary syndromes.

Keywords: Acute coronary syndromes, Inflammation, hypertension, diabetes

INTRODUCTION

Cardiovascular disease is the most common cause of mortality worldwide. Earlier thought as the disease of the developed world, it is recognized that more cardiovascular deaths occur in developing world^[1]. The prevalence of cardiovascular diseases in India has doubled in rural areas in the last decade. In urban areas it has increased from 1% in 1960 to 9.7% in 1995^[2].

Asian Indians either living in their own country or elsewhere have much higher incidence of coronary artery diseases as compared to all other ethnic groups. Coronary artery diseases among Asian Indians has been found to be more aggressive, diffuse and associated with serious complications and increasing mortality at a younger age^[3]. The classically defined risk factors for atherosclerotic arterial disease are hyperlipidemia, hypertension, diabetes mellitus and cigarette smoking. In ethnic Asian Indians the insulin resistance syndrome, metabolic syndrome X, lipoprotein (a), atherogenic dyslipidemic phenotype and some newer emerging risk factors (homocysteine, tPA, PAI-1, Fibrinogen, factor VII, infections and inflammations.) may be more relevant^[4]. An underlying genetic susceptibility associated with a modest abnormality in lipids and life style factors make coronary artery diseases assume a malignant course in Asian Indians.

Pathologic data have focused particular attention on the fibrous cap at the edge of the atheromatous lesion or shoulder region, where inflammatory cells accumulate and plaque rupture most frequently occurs. Macrophage and T- cells have been shown to

dominate at the site of plaque compromise^[5]. Laboratory and clinical data demonstrate the participation of inflammatory processes at every stage of athero-thrombosis.

In concert with laboratory data, prospective clinical studies have evaluated several acute phase proteins, cytokines and inter-cellular adhesion molecules as potential novel markers for cardiovascular risk assessment. CRP has several characteristics that render this inflammatory marker particularly attractive for this purpose. CRP is well described as a marker of systemic inflammation and is documented to raise several hundred folds in response to acute injury, infection, or other inflammatory stimuli. Its concentrations remain stable over long periods in the absence of new stimuli and depend entirely on the rate of hepatic production, rather than factors influencing protein clearance.

METHODOLOGY

Source of Data

Fifty patients of acute coronary syndromes (ST Elevation Acute myocardial Infarction or Unstable angina/Non ST Elevation Myocardial Infarction) admitted to ICCU of Sree Siddhartha Medical College, Hospital and who gave written informed consent were the subjects. Diagnosis of Acute coronary syndromes was made by history, physical examination and electrocardiogram.

Patients with stable angina, infectious diseases, neoplastic diseases, recent major trauma, recent major surgery, patients on immunosuppressive drugs, osteoarthritis, rheumatoid arthritis, psoriatic arthritis, gout, immunological disorders, patients on Statins, Fibrates, Niacin, Aspirin, patients taking estrogen or progesterone pills were excluded from the study.

Detailed history, clinical examination and laboratory tests were the tools used to exclude these conditions.

Apart from routine blood investigations electrocardiography and echocardiography was done in all patients. All patients were followed up and observed for the development of complications.

Received: Oct 11, 2012; Revised: Nov 22, 2012; Accepted: Dec 23, 2012.

*Corresponding Author

Jayaprakash Appajigol

Department of General Medicine, KLE University's JN Medical College, KLES Dr. Prabhakar Kore Hospital & MRC, Belgaum- 590010, Karnataka, India

Tel: +91-831-2473777; Fax: +91-831-247073

Email: jayaprakashappajigol@gmail.com

Procedure for Performing C-reactive protein Assay

The C reactive protein assay was performed by the rapid slide agglutination test for the direct detection and semi-quantitation of C-reactive protein. The presence of agglutination indicates that the content of CRP in the sample equal to or greater than 0.6 mg/dL. Homogenous suspension of fluid (without agglutination) indicates a CRP level lower than 0.6 mg/dL.

RESULTS

Age distribution

Maximum incidence of acute coronary syndrome was observed in age group between 41 to 50 years, accounting for 16 (32%) patients. Age group between 41 to 70 years constituted 40 (80%) patients. Youngest was 30 years old and suffered STEMI. Oldest was 90 years female, who had UA/NSTEMI.

Table 1. Distribution of acute coronary syndromes among different Age groups and sex

Age Groups In years	STEMI		UA/NSTEMI		Total
	Males	Females	Males	Females	
30-40	5	0	1	0	6
41-50	13	0	2	1	16
51-60	8	1	1	1	11
61-70	4	1	3	5	13
71-80	2	0	1	0	3
81-90	0	0	0	1	1
Total	32	2	8	8	50

Sex Distribution

In this study of the 50 patients we observed, 40(80%) patients were males and 10(20%) female patients. There were 34 STEMI patients; of these 32 were males and 2 females. And of 16 UA/NSTEMI, 8 each were from male and female group. Mean age of incidence in males was 52.2 years and that for females 64.2 years.

Symptoms

Chest pain was the most common symptom accounting for 45(90%) patients, followed by sweating in 32(64%), Breathlessness in 18(36%), Vomiting in 11(22%) and Giddiness in 5(10%) patients.

Risk Factors

In this study the most common risk factor was Smoking, account for 35(70%) patients followed by Diabetes and dyslipidemias. It is noted that out of 40 male patients who suffered acute coronary syndromes, 35(87.5%) were smokers. Thus smoking was strongly associated with ischemic heart diseases. Diabetes mellitus (32%) and lipid abnormalities (50%) were the next common risk factors observed. Triglycerides were high and HDL was low in 15 (30%) patients each. LDL was high in 10 (20%) patients. Five (10%) patients had raised total cholesterol.

Classification of Acute Coronary Syndromes

Out of 50 patients with acute coronary syndromes, 34 patients had STEMI and 16 patients had UA/NSTEMI.

Types of ST elevation MI

Out of the 34 patients of STEMI, fifteen (44%) had extensive anterior wall MI followed by 10 (29.4%) patients having antero-septal involvement. Antero-lateral wall and inferior wall involvement was

seen in 2 (5.9%) and 7 (20.6%) patients respectively.

Reperfusion Therapies Performed

In our hospital pharmacological reperfusion was performed to eligible patients with Streptokinase 1.5 million units. So we had 34 patients with STEMI. Only 15 patients were eligible for Streptokinase therapy, and one patient was not thrombolysed due to financial constraints. Chest pain of more than 12 hrs and formed Q waves (14 patients) was the most common cause to withhold thrombolysis followed by Hypotension (5 patients).

Complications

Left ventricular failure was the most common complication seen in 15(30%) patients, followed by Cardiogenic shock 6(12%), Atrioventricular block 5(10%), and one patient had LBBB. Out of 50 patients, 5(10%) patients had Ventricular Tachycardia/ Ventricular Fibrillation and died. Thus 32(64%) patients suffered from complications where as 18(36%) patients did not have any complications. Of the 5 patients with AV blocks, 3 patients had 2:1 Second-degree AV block, one patient had Wenke Bach phenomenon, and other had complete heart block.

C reactive Protein Levels at admission

According to semi-quantitative method of assay of C reactive proteins estimation, a level, equal to or more than 0.6 mg/dL is detected as positive. A level below 0.6 mg/dL is denoted as negative. In our study 36(72%) patients had C reactive protein levels detectable (i.e., equal to or more than 0.5 mg/dL). The following table shows elevated C reactive Protein levels and their relation to complications.

Table 2. CRP in patients with and without complications

C Reactive Protein Levels	Acute coronary syndromes with Complication	Acute coronary syndromes without Complication	Total
< 0.6 mg/dL	2	12	14
≥ 0.6 mg/dL	30	6	36
Total	32	18	50

At one degree of freedom p value is highly significant (p<0.01). This indicates that, the patients with high serum C Reactive Level at admission are prone for going in to complications. And levels were low in patients who did not undergo complications.

Other Investigations

Erythrocyte Sedimentation Rate

As ESR is also a marker of inflammation it may also be raised in acute coronary syndromes. In this study, ESR was raised in 32(64%) patients, which include 26 males and 6 females (normal values: Males= 0-17mm after 1 hr; Females= 1-25mm after 1 hr).

Total Leukocyte Counts

Leukocytosis is seen in the setting of acute coronary syndrome, but we observed raised leukocyte counts only in 15(30%) patients.

Random Blood Glucose

Raised blood glucose levels were found in 16 (32%) patients who were known diabetes mellitus patients. Diabetes mellitus is one of the risk factor for ischemic heart disease and is considered as ischemic heart disease equivalent.

DISCUSSION

It is known fact that mean age of development of ACS in Indian subcontinent is a decade earlier than western population. In our study mean age of patients was 58.21 years. In studies by Suleiman *et al.*,^[6] and Foussas *et al.*,^[7] ACS was seen in seventh decade. Sex distribution in our study was comparable to the previous studies with males constituting 80% of the patients.

Risk Factors

In our study smoking was the most common risk factor, found in 35 (70%) patients.

In Foussas *et al.*,^[7] study, smoking was observed in 57% of patients. In Suleiman *et al.*,^[6] study, smoking was observed in 40% of patients. Yusuf *et al.*,^[8] study, 65.19% of patients were smokers.

Lipid Abnormalities

In our study 25 (50%) patients had dyslipidemias. Most common lipid abnormalities were high triglycerides and low HDL levels. In Foussas *et al.*,^[7] study 64.6% of patients had lipid abnormalities. And in Suleiman *et al.*,^[6] study 41% of patients had dyslipidemias.

Diabetes Mellitus

In our study 16 (32%) patients had diabetes as the risk factor. In Foussas *et al.*,^[7] study Diabetes mellitus was seen in 31% of patients and Suleiman *et al.*,^[6] study diabetes was present in 30% of patients.

Hypertension

In our study 7 (14%) patients had hypertension. But hypertension was seen more frequently in Foussas *et al.*,^[7] study (51%) and Suleiman *et al.*, (6) study (53%). In "INTER HEART" study by Yusuf *et al.*,^[8] hypertension was seen in only 19.3% of patients, if only South Asian population is considered.

Type of Myocardial Infarction

In our study 34 (68%) patients had ST segment Elevation Myocardial infarction. Almost similar number of patients had ST segment Elevation Myocardial infarction in Suleiman *et al.*,^[6] study.

Reperfusion Therapy

In this study only 14 (41%) patients with STEMI underwent reperfusion therapy in the form of pharmacological thrombolysis with streptokinase. It is comparable to 32% of patients thrombolysed in Suleiman *et al.*,^[6] study.

Erythrocyte Sedimentation Rate

In our study 32 (64%) patients had increased ESR. Similar rise was described by Hersberg *et al.*,^[9]

C Reactive Protein Levels

We have studied 50 patients with acute coronary syndromes. In this study 36 (72%) patients had raised levels (≥ 0.6mg/dl). And 30 (60%) patients who had raised levels met with complications.

Comparison to Other Studies

Foussas *et al.*, studied 1,846 patients with acute coronary syndromes and showed that, elevated plasma CRP levels confer a significantly increased risk of future fatal or non- fatal ischemic complications^[7]. Suleiman *et al.*, concluded that, plasma CRP levels obtained within 12-24 hours of symptom onset is an independent marker of 30 day mortality and the development of heart failure in patients with acute myocardial infarction^[5]. Bhagat *et al.*, compared 44 unstable angina patients with 40 age and sex matched healthy controls. They concluded that, the plasma CRP is an independent predictor of adverse cardiac outcomes in severe unstable angina, in short term follow-up and hence is useful for risk stratification of these patients^[10]. Pietila^[11] showed that, high serum CRP concentrations

in acute myocardial infarction patients treated with thrombolytic drugs predict increased mortality up to 6 months following the myocardial infarction. Tomada *et al.*, [12] studied a total of 234 patients with acute myocardial infarction, and concluded that CRP levels within 6 hours after the onset of symptoms reflect the vulnerability of culprit coronary lesions and predict adverse coronary events after primary angioplasty. Comparing with these studies, in our study also increased levels of plasma C Reactive Protein was associated with more adverse events.

CONCLUSIONS

Qualitative plasma CRP is a simple low cost test easily available. Estimation of CRP can be adopted as a routine test in coronary units as it gives a valuable prognostic information.

REFERENCES

- [1] Reddy Srinath K, Salim Yusuf. 1998. Emerging epidemic of cardiovascular disease in developing countries. *Circulation*, 97:596-601.
- [2] Gupta R, Gupta V P. 1996. Meta-analysis of coronary heart disease prevalence in India. *Indian Heart Journal*. 48:241-5.
- [3] Milan Gupta, Narendra Singh, Subodh Verma. 2006. South Asians and Cardiovascular Risk. What Clinicians Should Know. *Circulation*. 113:924-929.
- [4] RP Tracy, 1999. disease, Inflammation markers and coronary heart, *Curr Opin Lipidol*. 10(5):435-41.
- [5] Ridker M Paul, Marrow A David, 2003. "Prevention of cardiovascular diseases, C reactive protein, inflammation and coronary risk", *Cardiology clinics*.
- [6] Suleiman M, Aronson D, Reisner SA, Kapeliovich MR, Markiewicz W, Levy Y *et al.*, 2003. Admission C reactive protein levels and 30-day mortality in patients with acute myocardial infarction. *Am Jr of Med*,115: 695-701.
- [7] Foussas SG, Zairis MN, Lyras AG, Patsourakos NG, Tsirimpis VG, Katsaros K *et al.*, 2005. Early prognostic usefulness of C reactive protein added to thrombolysis in myocardial infarction risk score in acute coronary syndromes, *Am. J. Car*, 96: 533-537.
- [8] Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F *et al.*, 1963. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study). *Am Heart J*, 65: 749-757.
- [9] Hershberg PI, Wells RE and Mc Gandy RB, 1972. "Hematocrit and prognosis in patients with acute myocardial infarction". *JAMA* 219: 855.
- [10] Bhagat S, Gaiha M, Sharma VK, Anuradha S, 2003. A comparative evaluation of C-reactive protein as a short term prognostic marker in sever unstable angina- A preliminary study. *JAPI*, 51: 349.
- [11] Pietila KO, Harmonen AP, Jokinity J, Pasternack AI, 1996. Serum C reactive protein concentration in acute myocardial infarction and its relationship to mortality during 24 months of follow-up in patients under thrombolytic treatment. *Eur Heart J*, 17:134.
- [12] Tomada H, Aoki N, 2000. Prognostic value of C reactive protein levels within six hours after the onset of acute myocardial infarction. *Am Heart J*, 140:324-328.