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Clinical Profile of Patients with 30 Days Myocardial Infarction and HS-CRP Levels.

Vamsi Krishna kamana[1]*, Nawal Shabbar[2], Umesh Pai M[2], and Ravella Keerthika Chowdary[3].

[1]KMC, Manipal, Udupi, Karnataka, India.
[2]CVT, SOHAS, Manipal hospital, Udupi, Karnataka, India.
[3]NIMS, Punjagutta, Hyderabad, Telangana, India.

ABSTRACT

High sensitive- C Reactive Protein (Hs-CRP) evaluates vascular inflammation. Relatively high levels of Hs-CRP predicts of an increased risk of a future heart attack, stroke, sudden cardiac death, and/or peripheral arterial disease. In patients with Post myocardial infarction (MI) the role of serum CRP is not well known. The study was planned to analyze the clinical profile of patients with history of MI and raised Hs- CRP levels. This is a single centre, non-randomized, observational study, done on 155 post MI 30 days patients. Documentation of MI atleast 30 days prior to enrolment should be done by medical history of clinical symptoms consistent with myocardial ischemia, elevation of cardiac biomarkers or the development of pathological Q waves regardless of symptoms. Out of 155 subjects 131 were males and 24 females. The mean age was 56.03 yrs. Maximum had anterior wall MI, followed inferior wall MI and MI with bundle branch blocks. A total of 108 patients have normal LVEF i.e. EF>50% and 47 patients are having LV dysfunction I.e., EF<50%. The EF of 155 subjects was not statistically correlated with Hs-CRP levels (p 0.436). There are maximum numbers of subjects with DM and Hypertension with Hs-CRP levels < 1 mg/dl. Measurement of Hs-CRP during follow-up after 30 days of MI may be useful in evaluating the success and guiding the intensity of treatment with statins and other preventive interventions.

Keywords: Acute coronary syndromes, Atheroma, Myocardial Infarction, Statins, C reactive protein

Corresponding author

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INTRODUCTION

Inflammation is established as an important contributor to atherogenesis and acute atherothrombosis. [1] Several studies have shown that C-reactive protein (CRP), an acute-phase reactant that is synthesized and secreted in the liver 6 h after an acute inflammatory stimulus, takes part directly in the atherosclerotic process and represents one of the most important predictors of vascular death in several clinical settings. [2-4] High-sensitivity measurement of C-reactive protein (hs-CRP) is the most extensively studied marker and is associated with the risk of adverse cardiovascular outcomes in apparently healthy individuals and in patients with established coronary artery disease. It detects low concentrations of C-reactive protein to help/predict a healthy person's risk of cardiovascular disease. Relatively high levels of hs-CRP predicts of an increased risk of a future heart attack, stroke, sudden cardiac death, and/or peripheral arterial disease. The American Heart Association and U.S. Centres for Disease Control and Prevention have defined risk groups as follows: Low risk: less than 1.0 mg/L, Intermediate risk: 1.0 to 3.0 mg/L, High risk: above 3.0 mg/L it is well known that myocardial necrosis is an established cause of the acute-phase response. [5] In patients with ST-elevation myocardial infarction (STEMI) undergoing Primary Percutaneous coronary interventions (PCI), the prognostic role of serum C-reactive protein is not well known. [6-8]

Increased CRP levels may portend the vulnerability of an atherosclerotic plaque and also contribute to plaque disruption. [9] Systemic inflammation has been shown in angiographic, angioscopic and intravascular ultrasound (IVUS) studies to predispose the individual to multifocal plaque disruption and the development of acute coronary syndromes (ACS). [9-11] Moreover, it has been suggested that CRP may not only be a marker of generalized inflammation but directly and actively participates in both atherogenesis. [12-13] and atheromatous plaque disruption. [14] When the patients were allocated to early intensive statin therapy, they were more likely to achieve hs-CRP levels <1 mg/L at 30 days and at 4 months. [16-17] CRP levels can also predict future cardiovascular events independently of CAD severity and correlate with number of angiographically complex coronary artery stenosis in patients with ACS. Hs-CRP was also significantly higher in patients with ACS compared to CSA and correlated with number of complex angiographic stenosis. Hs-CRP was also increased in patients with NYHA functional class III or IV compared to those in class I or II. [18-27] Thus, CRP levels are proven to be the marker of atheromatous plaque vulnerability and CAD activity. [28-35]

The study “Clinical Relevance of C-Reactive Protein During Follow-Up of Patients With Acute Coronary Syndromes in the Aggrastat-to-Zocor Trial”(David A. Morrow et al 2006) was conducted to analyze if elevated levels of high-sensitivity C-reactive protein (hs-CRP) are associated with higher risk of adverse outcomes in patients at risk for or with established coronary artery disease. This study showed that this risk may be modified with statin therapy.

The measured serum concentration of hs-CRP at 30 days (n=3813) and 4 months in patients with non–ST-elevation or ST-elevation acute coronary syndrome were randomly assigned to an early intensive versus delayed conservative simvastatin strategy in the Aggrastat-to-Zocor Trial. Patients with hs-CRP >3 mg/L at 30 days had significantly higher 2-year mortality rates than those with hs-CRP 1 to 3 mg/L or hs-CRP <1 mg/L (6.1% versus 3.7% versus 1.6%, P<0.0001). Results were similar with hs-CRP measured at 4 months. After adjusting for age, gender, diabetes, smoking, cardiovascular history, index event, lipid levels, and randomly assigned treatment, patients with hs-CRP >3 mg/L were at more than 3-fold higher risk of death (HR, 3.7; 95% CI, 1.9 to 7.2) compared with those with hs-CRP <1 mg/L. “Average” levels of hs-CRP (1 to 3 mg/L) were also associated with increased risk compared with those with hs-CRP <1 mg/L (HR, 2.3; 95% CI, 1.2 to 4.6). Patients allocated to early intensive statin therapy were more likely to achieve hs-CRP levels <1 mg/L at 30 days (P=0.028) and 4 months (P<0.0001). [16-17]

It was concluded that achieved levels of hs-CRP at 30 days and 4 months after acute coronary syndrome are independently associated with long-term survival. Patients treated with more aggressive statin therapy are more likely to achieve lower levels of hs-CRP

The study “C-reactive protein elevation and disease activity in patients with coronary artery disease” (Ramón Arroyo-Espliguero et al 2004) was conducted, at St. George’s Hospital Medical School, Cranmer Terrace, London to assess (a) whether C-reactive protein (CRP) is an independent predictor of future cardiovascular events after adjustment for coronary artery disease (CAD) severity and (b) if CRP levels correlate with number of angiographically complex coronary artery stenosis.

In this study 825 consecutive angina patients (mean age 63±10 years, 74% men), 700 with chronic stable angina (CSA) and 125 with acute coronary syndromes without ST-segment elevation (ACS). The composite endpoint of non-fatal acute myocardial infarction, hospital admission with class IIIb unstable angina and cardiac death was assessed at one year follow-up. Hs-CRP level was higher in CSA patients with the combined end-point after adjustment for number of diseased coronary arteries. Hs-CRP was also significantly higher in patients with ACS compared to CSA and correlated with number of complex angiographic stenosis. Hs-CRP was also increased in patients with NYHA functional class III or IV compared to those in class I or II. [18-27]

It was concluded that CRP levels predict future cardiovascular events independently of CAD severity and correlate with number of angiographically complex coronary artery stenosis in patients with ACS. Thus, CRP levels are a marker of atheromatous plaque vulnerability and CAD activity. [28-35]

Hence this is a small study planned to analyze the clinical profile of patients with history of MI or after 30 days of acute MI and risk stratification of patients based on their hs-CRP levels.

MATERIALS AND METHODS

Type of study: A single centre observational study.

Methods: Fasting blood samples were obtained from patients for hs-CRP at least 1 month after MI on stable medication and then analyze the clinical profile with demographics of high risk, intermediate risk and low risk patients based on hs-CRP levels.

STUDY CRITERIA

Inclusion criteria: Written informed consent. Male/Female of non child bearing potential with age>18yrs, documented spontaneous MI at least 30 days prior to randomisation. (A) Cases of acute MI, requiring documentation of a rise &/ or fall of cardiac biomarkers or evidence of myocardial ischemia by at least one of the following: Symptoms of ischemia, ECG changes indicative of new ischemia, Development of pathological Q waves, Imaging evidence of new loss of viable myocardium or new RWMA. (B) Prior MI: requires documentation on any one of the following: Development of new pathological Q waves with or without symptoms, Pathological findings of a healed or healing MI, Imaging evidence of a region of loss of viable myocardium that is thin and fails to contract, in the absence of a non – ischemic cause, Patients with MI resulting from PCI or CABG will not be eligible

Exclusion criteria: Pregnant or lactating women, Women of child bearing potential unless they are post menopausal and not of child bearing potential. H/ o alcohol and / or substance abuse that could interfere with the conduct of trial, History of ongoing or recurrent or chronic Infectious disease and any of the following conditions:

- Planned PCI/CABG or any other major surgical procedures
- Major non cardiac surgical or endoscopic procedure within 6 months
- Multivessel CABG surgery within the past 3 years
- Symptomatic patients with NYHA Class IV heart failure
- Uncontrolled hypertension
- Uncontrolled diabetes with nephrotic syndrome or e GFR < 30 ml/ min/1.73 m^2 per MDRD formula or kidney transplant
- Known active or recurrent hepatic disorder
- Prior malignancy (cancer) other than basal cell skin carcinoma

Data analysis: All data will be entered in Microsoft excel sheet and Statistical analysis was done by Statistical Package for the Social Science (SPSS) version 16.

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RESULTS

A total of 155 subjects were taken out of which 131 were males and 24 females. The mean age of subjects was 56.03 yrs. (TABLE 1)

Table 1: Relationship between gender with Age and with various risk factors of CAD

Age groups	Gender		Total
	Males	**Females**	
20-30	3	0	3
30-40	10	2	12
40-50	21	1	22
>50	97	21	118
Total	131	24	155
Non-smokers	123	24	147
Smokers	8	0	8
Total	131	24	155
Hs-CRP level (mg/L)			
<1	61	16	77
1-3	41	5	46
>3	29	3	32
Total	131	24	155
LV ejection fraction (LVEF in %)			
>50%	90	18	108
<50%	41	6	47
Total	131	24	155

It is seen that maximum number of patients are having anterior wall MI, followed by patients with inferior wall MI, MI with bundle branch blocks, left ventricular hypertrophy, heart blocks and atrial fibrillation. (TABLE 2)

Table 2: ECG changes with frequencies and percentages

ECG	Frequencies	Percentages
Normal	16	10.3
IWMI	40	25.8
AWMI	51	32.9
MI+ Others	37	23.9
Others (BBB, LVH, AF, HB)	11	7.1
Total	155	100

It shows that 36% of patients have hypertension, 29% have diabetes mellitus and 16 % have both hypertension and diabetes and most of them have Hs-CRP levels < 1mg/dl. Most of the subjects have Normal Left ventricular Ejection fraction (LVEF >50%). (TABLE 3)

Table 3: shows relationship between hs-CRP levels and LV EF, DM, HTN, DM+HTN, ECG changes.

Hs-CRP levels (mg/L)	LV EF		Total
	<50%	**>50%**	
<1	24	53	77
1-3	14	32	46
>3	9	23	32
Total	47	108	155
	ECG Non- MI(LBBB)	**ECG MI**	
<1	35	42	77
1-3	19	27	46
>3	10	22	32
Total	64	91	155
	Diabetes mellitus(DM)		
	No	**Yes**	

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<1	53	24	77
1-3	36	10	46
>3	21	11	32
Total	110	45	155
	Hypertension (HTN)		
	No	**Yes**	
<1	49	28	77
1-3	32	14	46
>3	18	14	32
Total	99	56	155
Hs-CRP levels	DM+ HTN combined	Percentages (%)	
<1	12	48	
1-3	6	24	
>3	7	28	
Total	25	100	

32 patients have hs-CRP levels >3g/L despite using >3 medications which included a statin. This shows that these patients have a risk of future cardiovascular disease. (TABLE 4)

Table 4: Shows relationship between the number of medications used and hs-CRP levels.

Hs-CRP levels (mg/ l)	No. of medications					Total
	2	**3**	**4**	**5**	**6**	
<1	2	10	27	24	14	77
1-3	2	6	15	13	10	46
>3	0	5	12	10	5	32
Total	4	21	54	47	29	155

DISCUSSION

This study was aimed at determining the clinical profile of patients with the history of MI and hs-CRP levels. Several studies have shown that C-reactive protein takes part directly in the atherosclerotic process and represents one of the most important predictors of vascular death.

In our centre a total number of 155 patients had the serum level of hs-CRP determined at 30 days after PCI during the period of 2012-2013.This study contains majority of male patients and a few females. The mean age of the subjects is 56.03. Most of our patients were older i.e. age >50 years, more likely to be males, and some have a history of smoking, hypertension, diabetes, and pre existing atherosclerotic vascular disease. Most of the Post MI 30 days patients have hs-CRP value of <1g/L with normal ejection fraction, i.e LVEF>50% and had a history of hypertension, diabetes and smoking. This study did not show any statistical significance between the hs-CRP levels and clinical risk factors. Some patients despite statin medication have hs-CRP levels>3g/L. In such patients more follow up and close monitoring is required to prevent the risk of a future heart attack, stroke, sudden cardiac death, and/or peripheral arterial disease.

The study by Benjamin M. Scirica, David A. Morrow [8] in 3225 patients with ACS, the hs-CRP levels were measured after 30days of PCI /revascularization and the achieved levels of hs-CRP in the study were independently associated with subsequent clinical outcome. Their findings provide evidence that the achieved level of Hs-CRP during follow-up after PCI is a strong independent predictor of subsequent outcomes in patients treated initially with or without a statin. Their observations have raised the hypothesis that CRP is a causal agent in atherothrombosis rather than merely a marker of other underlying inflammatory processes.

Since this study does not need any statistical significance between hs-CRP levels and dose of statin treatment in Post MI patients, we assume that high doses of statin will help to decrease the hs-CRP levels and thus decrease chances of future coronary artery disease.

Further study needs to be continued on 30 days post MI patients for more information and data on hs-CRP concentration role in cardiac events/ coronary artery disease with relation to dose of statin therapy on longer follow up basis.

CONCLUSION

- Achieved levels of hs-CRP after 30 days of MI does not correlate with type of MI or Left ventricular function.
- Achieved levels of hs-CRP after 30 days of MI are not affected by the clinical risk factors because of multiple medications but the long-term survival needs to be further evaluated in follow up.
- Measurement of hs-CRP during follow-up after 30 days of MI may be useful in evaluating the success and guiding the intensity of treatment with statins and other preventive interventions that reduce inflammation.

Declaration: As a corresponding author on behalf of all the authors i declare that the manuscript is original and is not published or communicated for publication elsewhere either in part or full.

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