

Evaluation of C- reactive protein as Risk factor in Coronary Heart Disease

MOHAMMAD FAISAL KHAN¹, ALIA SARFRAZ², MEHREEN LASHARI³, MUHAMMAD NAZIR AWAN⁴, TEHMINA GUL⁵, ABID ALI KHAN⁶

¹Associate Professor of Bio-Chemistry, Multan Medical & Dental College Multan.

²Senior Lecturer, Forensic Medicine Department, Islamabad Medical and Dental College Islamabad

³Demonstrator Bio-Chemistry Bolan Medical College Quetta

⁴Associate Professor Anesthesia Islamic International Medical College Rawalpindi

⁵Gynecologist THQ Hospital Mankera

⁶Anesthetist THQ Hospital Mankera

Correspondence to: Dr. Mohammad Faisal Khan, Cell: 03215667305, Email: mohsfaisalkhan2020@gmail.com

ABSTRACT

Objective: To determine the role of CRP in determining the extent and severity of coronary artery disease (CAD).

Methods: This descriptive cross sectional study was conducted in the cardiology department of MMDC and Ibna-Siena Hospital Multan. The samples were collected from January-2020 to October-2020. A total of 100 patients were included in analysis. Patients with diagnosis of acute myocardial infarction who had undergone coronary angiography for the diagnosis and determination of severity of CAD were included in the study. Patients having hs-CRP ≥ 8.4 mg/L were labelled as having elevated levels.

Results: Mean age was 55.8 ± 9.7 years. There were 26% female and 74% male patients. In patients with raised hs-CRP levels, 57 (89.1%) patients had $>70\%$ stenosis, while in patients with normal hs-CRP levels, 15 (41.7%) patients had $>70\%$ stenosis (p-value 0.0002). Regarding number of diseased vessels, 44 (68.8%) patients with raised hs-CRP had MVD, and only 12 (33.3%) patients with normal hs-CRP had MVD (p-value 0.001).

Conclusion: High sensitivity CRP is a valuable test for predicting the extent and severity of CAD.

INTRODUCTION

Coronary artery disease (CAD) is the major public health concern. In US, it account for up-to 40% of all cause deaths each year.¹ CAD occurs most commonly as a manifestation of atherosclerosis. CAD occurs either as a results of complete or incomplete thrombus formation or due to rupture of atheromatous plaque.² Studies have reported that inflammation plays a very vital role in the pathogenesis of atherosclerosis.³

C-reactive protein (CRP) is an important marker of chronic inflammation.⁴ CRP is a cheaper, and readily available marker for early detection of inflammation. CRP levels begin rising within 4 to 6 hours after tissue injury and the levels can increase up-to several hundred times within 24 to 48 hours. CRP half-life is <24 hours.⁵ Observational studies have reported a linear association between raised CRP levels and the risk of CAD.⁶ CRP binds to low density lipoproteins, therefore it has been suggested that prolonged increase in CRP levels can predict the presence of CAD.^{7,8}

In 2002, the expert panel recommended to use high sensitivity CRP (hs-CRP) levels in routine for assessment and prevention of CAD especially in patients having 10 to 20% risk factors of CAD for >10 years.⁹ In this study we evaluated the role of CRP in determining the extent and severity of CAD.

METHODS

This descriptive comparative study was conducted in the cardiology department of MMDC and Ibna-Siena Hospital Multan. The samples were collected from January-2020 to October-2020. A total of 100 patients were included in analysis. Approval of study was obtained from hospital authority. Informed consent was signed by each patient.

Patients with diagnosis of acute myocardial infarction who had undergone coronary angiography for the diagnosis and determination of severity of CAD were included in the study. While patients having hematologic disorders such as leukemia, other chronic infections such as pulmonary tuberculosis, and those with chronic kidney disease were excluded from study. Venous blood samples were obtained from each patient during the hospital stay, and hs-CRP levels were measured. Patients having hs-CRP ≥ 8.4 mg/L were labelled as having elevated levels.

Collected information was compiled in SPSS v25 statistical software. Chi-square test was applied to determine the association of elevated CRP levels with severity of CAD. P-value ≤ 0.05 was taken as significant association.

RESULTS

Mean age was 55.8 ± 9.7 years. There were 26% female and 74% male patients. Regarding co-morbidities, 39% patients were smokers, 48% were diabetic, 56% hypertensive and 33% patients were having positive family history. Severe CAD was diagnosed in 72% patients. Out of 100, 56% patients had multi-vessel disease. Elevated hs-CRP were diagnosed in 64% patients [Table 1].

A strong association was found between raised hs-CRP and CAD severity. In patients with raised hs-CRP levels, 57 (89.1%) patients had $>70\%$ stenosis, while in patients with normal hs-CRP levels, 15 (41.7%) patients had $>70\%$ stenosis (p-value 0.0002). Regarding number of diseased vessels, 44 (68.8%) patients with raised hs-CRP had MVD, and only 12 (33.3%) patients with normal hs-CRP had MVD (p-value 0.001) [Table 2].

Table 1. Baseline Study Variables.

Age	55.8±9.7
Female Gender	26 (26%)
BMI (Kg/m ²)	27.6±4.3
Smoking history	39 (39%)
Diabetes Mellitus	48 (48%)
Hypertension	56 (56%)
Family History	33 (33%)
Severity of CAD	
50-70% Stenosis	28 (28%)
>70% Stenosis	72 (72%)
Number of Diseased Vessels	
Single Vessel Disease	44 (44%)
Multi-vessel Disease	56 (56%)
HS-CRP Levels	
Normal	36 (36%)
Elevated	64 (64%)

Table 2. Association of Elevated hs-CRP Levels with CAD Severity.

	Raised hs-CRP (N=64)	Normal hs-CRP (N=36)	P-value
<i>CAD Severity</i>			
50-70% Stenosis	07 (10.9%)	21 (58.3%)	0.0002
>70% Stenosis	57 (89.1%)	15 (41.7%)	
<i>Number of Diseased Vessels</i>			
SVD	20 (31.2%)	24 (66.7%)	0.001
MVD	44 (68.8%)	12 (33.3%)	

DISCUSSION

Inflammation play a pivot role in whole atherosclerosis process. Inflammatory mediators also play a pivot role in CAD, by playing their role in stimulation of atheroma formation, destabilization of plaques, thrombus formation and in thrombo-embolic events.^{10, 11} Role of CRP levels for AMI prognosis has been well documented and studies have reported that CRP is a useful predictor for estimating future events in CAD patients.^{12, 13}

In present study, we found that CAD severity including number of involved vessels and extent of disease was higher in raised hs-CRP level patients. A recent trial by Bouzidi et al. reported similar results, they reported >70% stenosis in 53.0% patients with raised hs-CRP group versus in 47% patients in normal group. MVD was found in 61.4% patients with raised hs-CRP and in only 38.6% patients in normal CRP group.¹⁴

The MRFIT trial was one of the preliminary epidemiological trials who reported association of CRP levels and presence and severity of CAD. This trials studied various bio-chemical markers such as CRP, Serum albumin, glycoproteins for predicting the risk and severity of CAD in a case-control manner. In 17 years follow-up, they reported a strong association between CRP and CAD severity and events.¹⁵ Masood et al. used Gensini score as a marker of CAD severity and determined its association with CRP levels. The Gensini score was significantly higher in elevated CRP group, 78.7±41.0 versus 28.9±7.9 in normal to mildly elevated CRP level group.¹⁶

Tanveer et al. determined the relation of hs-CRP levels with CAD severity and the authors were failed to find any association. However, the hs-CRP values were higher in DVD and TVD patients in comparison to SVD patients.¹⁷

The present study was a single center and enrolled patients were limited in numbers, which make this study unable to present whole Pakistani population. Moreover we measured hs-CRP as stat test, kinetic measurement of CRP can help to get more information regarding the association of CRP levels with CAD severity.

CONCLUSION

High sensitivity CRP is a valuable test for predicting the extant and severity of CAD.

REFERENCES

- Preventza O, Critsinelis A, Simpson K, Olive JK, LeMaire SA, Cornwell LD, et al. Sex, Racial, and Ethnic Disparities in US Cardiovascular Trials in More Than 230,000 Patients. *Ann Thorac Surg.* 2020; Inpress.
- Christiansen MK. Early-onset coronary artery disease clinical and hereditary aspects. *Dan Med J.* 2017;64(9):B5406.
- Kasikara C, Doran AC, Cai B, Tabas I. The role of non-resolving inflammation in atherosclerosis. *J Clin Invest.* 2018;128(7):2713-23.
- Sproston NR, Ashworth JJ. Role of C-Reactive Protein at Sites of Inflammation and Infection. *Front Immunol.* 2018;9:754.
- Armani A, Becker RC. The biology, utilization, and attenuation of C-reactive protein in cardiovascular disease: part I. *Am Heart J.* 2005;149(6):971-6.
- Chandrasekara S. C-reactive protein: An inflammatory marker with specific role in physiology, pathology, and diagnosis. *Int J Rheumat Clin Immunol.* 2014;2(S1):SR3.
- Badimon L, Peña E, Arderiu G, Padró T, Slevin M, Vilahur G, et al. C-reactive protein in atherothrombosis and angiogenesis. *Front Immunol.* 2018;9:430.
- Wensley F, Gao P, Burgess S, Kaptoge S, Di Angelantonio E, Shah T, et al. Association between C reactive protein and coronary heart disease: mendelian randomisation analysis based on individual participant data. *BMJ.* 2011;342:d548.
- Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon III RO, Criqui M, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: a statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation.* 2003;107(3):499-511.
- Sara JDS, Prasad M, Zhang M, Lennon RJ, Herrmann J, Lerman LO, et al. High-sensitivity C-reactive protein is an independent marker of abnormal coronary vasoreactivity in patients with non-obstructive coronary artery disease. *Am Heart J.* 2017;190:1-11.
- Vuković-Dejanović V, Bogavac-Stanojević N, Spasić S, Spasojević-Kalimanovska V, Kalimanovska-Oštrić D, Topalović M, et al. Association of Serum Pentraxin-3 and High-Sensitivity C-Reactive Protein with the Extent of Coronary Stenosis in Patients Undergoing Coronary Angiography. *J Med Biochem.* 2015;34(4):440-9.
- James SK, Armstrong P, Barnathan E, Califf R, Lindahl B, Siegbahn A, et al. Troponin and C-reactive protein have different relations to subsequent mortality and myocardial infarction after acute coronary syndrome: a GUSTO-IV substudy. *J Am Coll Cardiol.* 2003;41(6):916-24.
- Vaucher J, Marques-Vidal P, Waeber G, Vollenweider P. Cytokines and hs-CRP levels in individuals treated with low-dose aspirin for cardiovascular prevention: a population-based study (CoLaus Study). *Cytokine.* 2014;66(2):95-100.
- Bouzidi N, Messaoud MB, Maatouk F, Gamra H, Ferchichi S. Relationship between high sensitivity C-reactive protein and angiographic severity of coronary artery disease. *J Geriatr Cardiol.* 2020;17(5):256-63.
- Kuller LH, Tracy RP, Shaten J, Meilahn EN. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study. Multiple Risk Factor Intervention Trial. *Am J Epidemiol.* 1996;144(6):537-47.
- Masood A, Jafar SS, Akram Z. Serum high sensitivity C-reactive protein levels and the severity of coronary atherosclerosis assessed by angiographic gensini score. *J Pak Med Assoc.* 2011;61(4):325-7.
- Tanveer S, Banu S, Jabir NR, Khan MS, Ashraf GM, Manjunath NC, et al. Clinical and angiographic correlation of high-sensitivity C-reactive protein with acute ST elevation myocardial infarction. *Exp Ther Med.* 2016;12(6):4089-98.