

# Association between Angiographic Severity of Coronary Artery Disease and High Sensitivity C-Reactive Protein

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## Abstract

**Objectives:** To determine correlation between blood levels of high sensitivity c-reactive protein (Hs CRP) and severity of coronary artery disease (CAD) on coronary angiography measured through Gensini scoring system.

**Study type, settings and duration:** The descriptive case study was conducted at Rawalpindi institute of cardiology. The duration of study was six month.

**Patients and Methods:** Adult patients of both genders between age 25 to 60 years visiting to outpatient department of the institute and registered for coronary angiogram were included. From each of the enrolled patient about 5cc venous blood sample was collected and Hs-CRP was performed. Severity was measured through Gensini score after coronary angiography. Angiographic Gensini scores were correlated with Hs-CRP using Pearson's correlation (2-tailed). Value of  $< 0.05$  was considered statistically significant.

**Results:** Total 87 patients fulfilling the inclusion criteria were enrolled among them 81.6% (n=71) were males and 18.4% (n=16) were females. The correlation coefficient was found to be 0.043, implying that there is negligible relationship between Hs-CRP and Gensini scores at  $p=0.696$ .

**Conclusion:** There is no significant correlation between Hs-CRP and severity of CAD measured through Gensini scores on coronary angiography.

**Key words:** CRP, CAD, Gensini score.

## Introduction

The coronary artery disease (CAD) is present in highest propensity within the natives of subcontinent. Therefore it is not astonishing that CAD is now considered primary basis of death in this region.<sup>1,2</sup> Frequency in the increase of CAD in these countries is almost double when compared with developed countries.<sup>3</sup> The clinical indication are angina, myocardial infarction (MI), stroke or sudden death between 50-60 aged men and 60-70 years aged women. Patient's clinical history and diagnostics has exhibited that atherosclerosis is not

only concerned in lipid deposition but it can play a crucial part in the systemic inflammation, atherothrombotic inception and progression of disease processes.<sup>4,5</sup> Acute coronary syndromes are caused by the induction of plaque rupture that is developed by chronic inflammatory process.<sup>6</sup>

C-reactive protein (CRP) is an acute phase protein; hepatocytes mostly produce CRP with the influence of cytokines like interleukin (IL-6) and tumor necrosis factor-alpha. In blood circulation, the concentration of CRP rises up to 10,000 folds in an acute response to tissue damage and severe infection.<sup>7</sup> High sensitive CRP (hs-CRP) has been broadly used diagnostic marker for inflammation and especially for cardiovascular disease (CVD) risk.<sup>8,9</sup> In spite of an absence of specificity for the root causes of inflammation, the results from >30 epidemiologic researches have been revealed a noteworthy relationship between raised hs-CRP with primary cause of atherosclerosis, occurrence of first cardiovascular events and risk of repeated cardiovascular events in individuals already suffering from cardiac disease.<sup>10</sup> Different meta analyses have proved that hs-CRP can be used as predictor of CAD.<sup>11,12</sup> hs-CRP is considered as a nonspecific cardiac marker because it mainly increases in

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**Received:** 09 November 2016, **Accepted:** 12 September 2017,  
**Published:** 29 September 2017

### Authors Contribution

SR has done the conceptualization of project. SR and MNA did the data collection. SR, MNA and WA have done the literature search. SR and WA also did the statistical analysis. Drafting, revision and writing of the manuscript were done by SR, MNA and AMK.

many acute stage responses to any inflammation rather than directly linked in the development of atherosclerosis.<sup>13</sup>

The relationship of hs-CRP concentrations with the severity of CAD measured through Gensini score studied by different authors and they found significant correlation between them.<sup>14</sup> The Gensini score is very valuable and mainly calculated for the estimation of severity of CAD on the basis angiographic outcomes.<sup>15,16</sup>

Objective of the study was to find out correlation between blood levels of hs-CRP and severity of CAD on coronary angiography measured through Gensini scoring system.

### Patients and Methods

This was a descriptive case series study performed on adult patients of both genders between age 25 to 60 years who presented to OPD of Rawalpindi institute of cardiology and were registered for coronary angiogram. Patients with cardiomyopathy, valvular heart diseases (evaluated by echocardiography) and patients who had history of chronic diseases or autoimmune disorders were excluded. The hs-CRP was estimated by using Beckman Coulter hs-CRP quantitative kit as per instructions of the manufacturer and its values were recorded in mg/L. Each patient underwent coronary angiography by the radial/femoral approach at least 4 views of the left coronary artery and 2 views of the right coronary artery were included. Stenosis Score was measured through Gensini score, it provides valuable data identified with the main part of the atherosclerotic sore and impacted by wordy procedures, for example, plaque rupture. Each of coronary vessel segments was scored according to severity of occlusion; score from one to thirty two was assigned depending on the severity of arterial stenosis. In each segment the score were added to get an overall score for the specific artery and then all arterial stenosis scores added, to get a total score indicating the severity of stenosis.

Data was entered and analyzed by using Statistical Package for Social Sciences (SPSS) version 17.0. The categorical data was articulated as in numbers and percentages; however the continuous variables were expressed as mean,  $\pm$  standard deviation (SD). Angiographic Gensini scores were correlated with hs-CRP using Pearson's correlation (2-tailed). A cut-off *p* value of  $< 0.050$  was consider as significant value.

### Results

There were 87 cases who fulfilled our selection criteria, including 81.6% (n=71) males and 18.4% (n=16) females. There were 57.5% (n=50) patients who had hypertension, 24.1% (n=21) were diabetic, 40.2% (n=35) were smokers and 42.5% (n=35) had dyslipidemia. There

is no significant difference in mean hs-CRP among both males and females ( $3.90 \pm 5.30$  vs.  $4.40 \pm 6.30$  mg/L) ( $p=0.77$ ), hypertensives and non-hypertensives ( $3.70 \pm 5.50$  vs.  $4.50 \pm 5.40$  mg/L) ( $p=0.45$ ), diabetics and non-diabetics ( $3.90 \pm 4.10$  vs.  $4.10 \pm 5.90$  mg/L) ( $p=0.910$ ), smokers and non-smokers ( $3.90 \pm 5.2$  vs.  $4.1 \pm 5.7$  mg/L) ( $p=0.89$ ) and patients who had dyslipidemia and who had not ( $3.1 \pm 3.3$  vs.  $4.7 \pm 6.6$  mg/L) ( $p=0.890$ ).

The calculated data of hs-CRP through patient's blood sample were correlated with Gensini score calculated on angiography results by assuming both variables were approximately normally distributed. Pair wise associations for set of both variables were computed and results are displayed in a matrix (Table). The quality and course of relationship between two factors was determined by calculating Pearson correlation coefficient (*r*). The correlation coefficient reported in the table was 0.043, implying that there is negligible relationship between hs-CRP and Gensini scores at  $p=0.696$  significance level (2-tailed).

**Table: Correlation between CRP and gensini score.**

Variables		CRP	Gensini Score
CRP	Pearson Correlation	1	0.043
	Sig. (2-tailed)		0.696
	N	87	87
Gensini score	Pearson Correlation	0.043	1
	Sig. (2-tailed)	0.696	
	N	87	87

### Discussion

Much debate has been found in literature whether hs-CRP is contributory factor in developing atherosclerosis. The Gensini score reveals not just the overall figure of lesions with individual scale of stenosis, but additionally the utilitarian importance of injuries as far as the zone of myocardium in question

In present study no significant association between mean hs-CRP levels and the severity of CAD as evaluated by the Gensini score could be found. In a similar type of study conducted by Masood et al, the mean angiographic Gensini scores demonstrated a rising pattern from low-grade to high- grade hs-CRP risk groups ( $p < 0.001$ ).<sup>14</sup> Serum values of hs-CRP demonstrated noteworthy relationship with individual angiographic Gensini scores by Pearson's correlation ( $p < 0.001$ ) in high risk group. The difference in the results from this study may be attributed to difference in data analysis methodology. They categorized the data in low, moderate and in higher risk groups on the grounds of estimated hs-CRP values. However, no such categorization was carried out in this study. We tried to assess the overall

relationship between two variables. The essential element in such an examination is to acquire a suitable study sample size which permits exact assessment of the effect sizes. In a study, when there is need to categorized the data in low, moderate and high risk groups then the sample size should be high enough to exactly measure the relationship, that is by all accounts insufficient in their investigation.

No direct affiliation between severity of CAD and hs-CRP concentration has been reported. While the outcomes from various epidemiologic examinations have uncovered an essential connection between raised serum/plasma values of hs-CRP and the pervasiveness of basic atherosclerotic vascular disease, the hazard of recurring cardiovascular events among patients with build-up disease, and the rate of first cardiovascular events among individuals not known to have atherosclerosis. At the point when considered alone or in mix with conventional cardiovascular risk factors, raised hs-CRP values have been related with a higher risk of future cardiovascular events.<sup>17-19</sup>

Several large population-based studies assessing hs-CRP in unselected asymptomatic populaces have demonstrated that in apparently healthy people, the baseline values of hs-CRP forecast the long-term risk of a first incidence of MI, ischemic stroke, hypertension, peripheral vascular disease, sudden cardiac death.<sup>20-22</sup> Increased serum hs-CRP is also linked with recognized risk factors and associates with the occurrence of traditional cardiovascular risk factors (e.g, elder age, diabetes, smoking, hypertension and dyslipidemia) and it may reveal influences of these risk factors to vascular inflammation. The relationship between hs-CRP and cardiovascular risk persists after adjustment for age, blood pressure, diabetes, smoking and lipid levels.<sup>22-26</sup> Baseline serum hs-CRP measurements also seem to forecast cardiovascular risk in older adults (i.e, those over 65 years).<sup>27-29</sup>

Several research studies have established that, serum hs-CRP provides additional information to global risk measurement using traditional risk of cardiovascular events and may be considered as an independent risk marker.<sup>30,31</sup> In addition, several meta-analyses have revealed a significant association between baseline hs-CRP and subsequent coronary heart disease or cardiovascular events.<sup>11,12,32</sup>

In summary, hs-CRP may be considered as a inflammatory marker for clinical practice and values should be reported in mg/L. hs-CRP can be helpful as an independent biomarker for the prognosis in individuals with stable coronary heart disease or an ACS, however, there is at present insufficient evidence to recommend it as a predictor of severity of CAD and as a determinant factor in the application of specific therapies for acute management of ACS or for secondary prevention. Notwithstanding the reliable epidemiological association

with risk, there is, at exhibit, no recognized part for routine estimation of hs-CRP in patients with built-up cardiovascular disease.

In our study we measure hs-CRP levels in patients of stable angina being booked for coronary angiography from outpatient department. Most of these patients were already on treatment including statins that is an important component of their treatment. Statins exhibit pleiotropic effect on many components of atherosclerosis including determinants of plaque thrombogenicity such as plaque inflammation and proliferation and have some anti inflammatory effects and may alter Hs-CRP levels in OPD patients already taking treatment, hence Hs-CRP levels may be lower than expected in such patients.

Another important limitation expected in our study is about the quantification of angiographic findings that is limited to visual interpretation of attending cardiologist and this may not give accurate atherosclerosis burden. Intravascular ultrasound can give actual atherosclerotic burden by visualizing the intramural atherosclerosis. But due to logistic and expertise constraints IVUS is not being done routinely in every case even in best centre's.

**Conflict of interest:** None declared.

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