HIGH SENSITIVE C-REACTIVE PROTEIN (hs-CRP) AND ITS CORRELATION WITH ANGIOGRAPHIC SEVERITY OF PATIENT WITH CORONARY ARTERY DISEASE (CAD)

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Abstract:

Background: Association between the plasma hs-CRP levels and the severity of coronary stenosis in subjects remains controversial. This cross sectional study was performed in the Department of Cardiology, Dhaka Medical College during July 2008 to December 2009, to determine whether the concentrations of hs-CRP correlate with the coronary atherosclerotic disease assessed by coronary angiography.

Methods: For this purpose, a total number of 90 consecutive patients having IHD admitted in the Dhaka Medical College Hospitals were enrolled in this study. Patients were divided into three groups according to their level of hs-CRP. Out of 90 cases, 22(24.4%) patients were in group I, in group II 33(36.7%) patients and rest 35(38.9%) were in group III according to their hs-CRP level. Severity of CAD was assessed by vessel score, stenosis score and extent score.

Result: Significant positive correlation (r=0.7409; p<0.001 r=0.6648; p<0.001 and r=0.6386; p<0.001) was found between hs-CRP and vessel score, stenosis score and hs-CRP and extent score suggesting increasing level of hs-CRP strongly suggestive of extensive coronary artery disease.

Conclusion: High level of hs-CRP strongly suggestive of extensive coronary artery disease

Key words: hs-CRP, angiogram, coronary artery disease, vessel score, stenosis score and extent score.


Introduction:

Coronary artery disease (CAD) is the end result of the accumulation of atheromatous plaques within the walls of the coronary arteries that supply the myocardium.¹

CAD is the largest single cause of death in the UK and many parts of the world. Each year there are approximately 60 deaths per 100,000. Sudden cardiac death is a prominent feature of CAD. One in every six coronary attacks was found to present with sudden death as the first, last, and only symptom.²

In USA, among adults age 20 and older, the total number of coronary heart disease (CHD) in 2006 was 16,800,000 (about 8,700,000 men and 8,100,000 women). CHD caused about one of every five deaths in the United States in 2005. It is the largest single killer of American males and females.³

National data on incidence and mortality of coronary heart disease are few in Bangladesh. The prevalence of coronary heart disease was estimated as 3.3/1000 in 1976 and 17.2/1000 in 1986 indicating 5 folds in the disease in 10 years.⁴,⁵

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Traditionally there are some conventional risk factors like age, male sex, positive family history, hypertension, smoking, hyperlipidaemia, metabolic syndrome, diabetes, lack of exercise, obesity, and some emerging risk factors, like C-Reactive Protein, Homocysteine, Fibrinogen.6

Less than 50% of the CAD can be ascribed to traditional risk factors and rests are unexplained.7 CRP has emerged as the most exquisitely sensitive systemic marker of inflammation and a powerful predictive marker of future cardiovascular risk. Role for inflammation has become well established over the past decade or more in theories describing the atherosclerotic disease process.8

A body of evidence now suggests that atherosclerosis represents a chronic inflammatory response to vascular injury caused by a variety of agents that activate or injure endothelium and promote lipoprotein infiltration, retention, and modification, combined with inflammatory cell entry, retention and activation.9

So, from a pathological viewpoint, all stages, i.e., initiation, growth, and complication of the atherosclerotic plaque might be considered to be an inflammatory response to injury.10,11 C-reactive protein (CRP) is one of the acute phase proteins that increase during systemic inflammation.12 Several prospective studies recently showed that plasma high sensitive C-reactive protein (hs-CRP) levels, a more sensitive CRP test, are a powerful predictor of future myocardial infarction and cardiac death among apparently healthy individuals.13

However, the association between the plasma hs-CRP levels and the severity of coronary stenosis in subjects remains controversial. Some studies previously demonstrated such associations whereas other could not found it.14,15

This study was performed to determine whether the concentrations of hs-CRP correlate with the coronary atherosclerotic disease assessed by coronary angiography.

**Objectives:**

**General Objective:**
1. To correlate the levels of hs-CRP with angiographic severity of coronary artery stenosis in patients with IHD admitted for CAG in DMCH.

**Specific objectives:**
1. To correlate the levels of hs-CRP with vessel score.
2. To correlate the levels of hs-CRP with stenosis score.
3. To correlate the levels of hs-CRP with extent score.

**Materials and Methods:**
This cross sectional study was done in the department of cardiology, Dhaka Medical College during July 2008 to, December 2009. hs-CRP test was done in immunology department of BSMMU.

CAG was done in the cath-lab of the Department of Cardiology, Dhaka Medical College Hospital.

**Inclusion criteria**
All patients of IHD admitted for CAG in department of cardiology DMCH.

**Exclusion criteria**
1. Patient with past CABG
2. Patient with PTCA
3. Patient with valvular heart disease.
4. Patient with hepatic dysfunction.
5. Patient with a major non-cardiovascular disease.
6. Patient with collagen vascular disease.
7. Any systemic infection.
8. Unwilling to give consent.

**Statistical analysis:**
For all statistical analyses, SPSS version 16.0 was used. For all statistical tests, p<0.05 was considered as statistically significant. Continuous variables were presented as mean ± SD and numerical variables were presented as proportions. Continuous variables were compared through the ANOVA test, categorical variable by chi-square test, and correlation coefficient was done where applicable.
Observation and Results:

### Table I

**hs-CRP distribution of the study patients (n=90).**

<table>
<thead>
<tr>
<th>hs CRP</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I: &lt;1.0 mg/L</td>
<td>22</td>
<td>24.4%</td>
</tr>
<tr>
<td>Group II: 1.0 – 3.0 mg/L</td>
<td>33</td>
<td>36.7%</td>
</tr>
<tr>
<td>Group III: &gt;3.0 mg/L</td>
<td>35</td>
<td>38.9%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>90</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Table-I shows distribution of hs-CRP levels among the study patients. A total of 90 cases were included in the study the age ranged from 20 to 72 years. Among them 73 patients were male and rest are female.

Patients were divided into three groups according to their level of hs-CRP. The level of hs-CRP <1.0 mg/L was consider as group I, 1.0 mg/L to 3.0 mg/L group II and >3.0 mg/L group III. Out of 90 cases 22(24.4%) belong to group I, 33(36.7%) was group II and rest 35(38.9%) was group III.

### Table II

**Major risk factors status of the study patients (n=90)**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Group I (n=22)</th>
<th>Group II (n=33)</th>
<th>Group III (n=35)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Present</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Present</td>
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<tr>
<td>Absent</td>
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<tr>
<td>DM</td>
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<tr>
<td>Present</td>
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<tr>
<td>Absent</td>
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<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
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<tr>
<td>Absent</td>
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<tr>
<td>F/H IHD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Group I= <1.0 mg/L; Group II= 1.0 – 3.0 mg/L; Group III= >3.0 mg/L; NS= not significant

### Table III

**Distribution of patients by vessel score (n=90)**

<table>
<thead>
<tr>
<th>Vessel score</th>
<th>Group I (n=22)</th>
<th>Group II (n=33)</th>
<th>Group III (n=35)</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>18</td>
<td>81.8</td>
<td>4</td>
<td>12.1</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>9.1</td>
<td>16</td>
<td>48.5</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>4.5</td>
<td>10</td>
<td>30.3</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>4.5</td>
<td>3</td>
<td>9.1</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>0.3</td>
<td>±0.8</td>
<td>1.4</td>
<td>±0.8</td>
</tr>
<tr>
<td>Range (min-max)</td>
<td>0</td>
<td>-3</td>
<td>0</td>
<td>-3</td>
</tr>
</tbody>
</table>
Table II shows distribution of major risk factors among study patients. Regarding the smoking status it was found that 9(40.9%) in group I, 22(66.7%) in group II and 21(60.0%) in group III were smokers. No significant (p>0.05) difference was found among three groups in chi square test.

Hypertension was found in 13(59.1%) in group I, 19(57.6%) in group II and 23(65.7%) in group III. No significant (p<0.05) difference was found among three groups in chi square test. The results are shown in the table II.

Diabetes mellitus was found 3(13.6%) in group I, 13(39.4%) in group II and 12(34.3%) in group III. No significant (p>0.05) difference was found among three in chi square test. The results are shown in the table II.

Family history of IHD was found 6(27.3%), 7(21.2%) and 11(31.4%) in group I, group II and group II respectively. No significant (p>0.05) difference was found among three groups in chi square test. The results are shown in the table II.

Dyslipidemia was found in 13(59.1%) in group I, 21(63.6%) in group II and 21(60.0%) in group III. No significant (p>0.05) difference was found among three groups in chi square test. The results are shown in the table II.

Table –III shows distribution of patients by vessel score. More than eighty (81.8%) had vessel score ‘0’ in group I, in group II majority (48.5%) had vessel score 1 and in group III most (65.7%) had vessel score 3. The mean (±SD) vessel score was 0.3±0.8, 1.4±0.8 and 2.4±0.9 in group I, group II and group III respectively. The vessel score difference was statistically significant (p<0.05) among three groups in ANOVA test.

Table IV shows Distribution of patients by stenosis and extent score (n=90).

<table>
<thead>
<tr>
<th></th>
<th>Group I(n=22)</th>
<th>Group II(n=33)</th>
<th>Group III (n=35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenosis score</td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.2 ±7.4</td>
<td>23.5 ±18.9</td>
<td>38.3 ±26.5</td>
<td>0.001S</td>
</tr>
<tr>
<td>Range (min-max)</td>
<td>(0 -24)</td>
<td>(0 -72)</td>
<td>(0 -112)</td>
<td></td>
</tr>
<tr>
<td>Extent score</td>
<td>8.9 ±18.0</td>
<td>36.1 ±16.9</td>
<td>51.2 ±16.6</td>
<td>0.001S</td>
</tr>
<tr>
<td>Range (min-max)</td>
<td>(0 -60)</td>
<td>(0 -80)</td>
<td>(0 -80)</td>
<td></td>
</tr>
</tbody>
</table>

Group I= <1.0 mg/L, Group II= 1.0 – 3.0 mg/L, Group III= >3.0 mg/L, NS= not significant

Correlation between hs CRP with vessel score (n=90).

Hs CRP was expressed in mg/L and vessel score ranges from 0 to 3 depending on the number of vessel involve. Significant positive correlations were found between hs-CRP and vessel score. The values of Pearson’s correlation coefficient was 0.7409 which is highly significant (p<0.001). Therefore, there was linear positive correlation between hs-CRP and vessel score (Fig. 1).
Correlation between hs CRP with stenosis score (n=90).
Hs CRP was expressed in mg/L and stenosis score ranges from 0 to 112. Significant positive correlations were found between hs-CRP and stenosis score.

The values of Pearson’s correlation coefficient was 0.6648 which is highly significant (p<0.001). Therefore, there was linear positive correlation between hs-CRP and stenosis score (Fig. 2).

Discussion
This cross sectional study was carried out with an aim to correlate the levels of hs-CRP with angiographic severity of coronary artery stenosis in patients with IHD admitted for CAG in DMCH and to correlate the levels of hs-CRP with vessel score, stenosis score and extent score.

A total of 90 patients with IHD age ranging from 20 to 70 years were included in the study, who were admitted for CAG in the department of Cardiology, Dhaka Medical College during July 2008 to December 2009.

The patients were divided into three groups according to their level of hs-CRP, which were <1.0 mg/L was considered as group I, hs-CRP range from 1.0 to 3.0 mg/L considered as group II and >3.0 mg/L considered as group III. According to hs-CRP level 22(24.4%) cases were in group I, 33(36.7%) cases group II and rest 35(38.9%) cases group III.

Danesh et al.15 reported that in general, CRP concentrations increase among smokers with increased cigarette consumption.16 Regarding the smoking status it was found in this current study that 40.9%, 66.7% and 60.0% was smoker in group I, group II and group III respectively.

Koenig et al.16 have shown in their series 50.0 percent of the patients were hypertensive which is a little inferior to the present study, where the current study observed that hypertensive was 59.1% in group I, 57.6% in group II and 65.7% in group III. Hypertensive patients was comparatively higher in group III but no significant (p>0.05) difference was found among three group.

In the present study, diabetes mellitus was higher in group II and group III with compared to group I, but no significant (p>0.05) difference was found among three groups. Diabetes mellitus observed in the present study are in higher with Koenig et al.

The family history of IHD and dyslipidemia were almost parallel among three groups, which were not statistically significant (p>0.05)
difference among three groups. Nearly one third of the patient had family history of IHD and two third had dyslipidemia of the study patients in the current study.

In this current series it was observed that the mean (±SD) vessel score was 0.3±0.8 in group I, 1.4±0.8 in group II and 2.4±0.9 in group III. More than a eighty (81.8%) had no vessel score in group I, majority (48.5%) of the patients in group II patients had vessel score 1 and most (65.7%) of the patients in group III had vessel score 3. The mean vessel score difference was significantly (p<0.05) higher in group III with compared to others two groups. Similarly, the mean stenosis score and extent score were significantly (p<0.05) higher in group III with compared to others two groups. Where the mean (±SD) stenosis score was observed in this current study was 3.2±7.4 in group I patients, 23.5±18.9 in group II patients and 38.3±26.5 in group III patients. The mean (±SD) extent score was 8.9±18.0 in group I, 36.1±16.9 in group II and 51.2±16.6 in group III.

In this present study a significant (p<0.001) positive correlation coefficient (r=0.7409) was found between hs-CRP and vessel score, which indicates that there was linear positive correlation between hs-CRP and vessel score. Similarly, significant (p<0.001) positive correlation coefficient (r=0.6648 and r=0.6386) were found between hs-CRP with stenosis score and hs-CRP and extent score. Nyandak et al.17 who have observed in their studies, Spearman’s correlation coefficient between hs-CRP and angiographic stenosis score was r = 0.316 (p<0.004) and hs-CRP with angiographic extent score was r = 0.338 (p<0.005).18 Higher hs-CRP levels were associated with higher stenosis and extent score in CAD patients, which are consistent with the present study results.

So, hs-CRP is a single cardiovascular risk factor and increases CRP concentration within reference limit are associated with future cardiovascular events. Elevated level of CRP can predict the coronary atherosclerotic disease burden.

**Conclusion:**

Significant positive correlation was observed between the extent of coronary artery disease and hs-CRP levels. Similarly hs-CRP levels were found to be higher in patients with higher degree of angiographic stenosis. This shows that hs-CRP levels have a positive correlation with the disease burden in CAD patients. hs-CRP is a single cardiovascular risk factor and are associated with severity of disease. Increases CRP concentration within reference limit are associated with future cardiovascular events. Elevated level of CRP can predict the coronary atherosclerotic disease burden.

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