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Prognostic importance of high-sensitivity C-reactive protein (hs-CRP) for in-stent restenosis and 6-month major adverse cardiac events following percutaneous coronary intervention (PCI)

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ABSTRACT

There is controversy regarding the prognostic role of high-sensitivity C-reactive protein (hs-CRP) in predicting re-stenosis and major adverse cardiac events (MACE) in patients who undergo percutaneous coronary intervention (PCI) and stenting. To determine relationship between serum hs-CRP level and in-stent restenosis and 6-month MACE in patients who had underwent PCI and stenting. In this cohort study, 55 patients who presented to Imam Ali hospital for PCI and stenting were recruited consecutively. Serum hs-CRP level was measured upon admission to hospital and once again 24 hours after stenting. Six months later, the patients were followed by phone call and those who experienced acute coronary syndrome or with positive exercise tolerance test underwent coronary angiography. Upon presentation, only three patients (5.5%) had elevated levels of hs-CRP, but 24 hours after PCI, 45% had elevated serum hs-CRP levels. Six-month MACE (major adverse cardiac events) occurrence was 52.7%. Five patients (9%) developed restenosis of which mild stenosis (stenosis of 30-49%) was seen in 1.8%, moderate stenosis (50-74%) was seen in 1.8%, and severe stenosis (>75% stenosis) was detected in 5.4%. Diabetes mellitus (DM) was the only risk factor, which showed significant association with restenosis. There was a significant association between high LDL level and 6-month MACE ($P= 0.001$). All patients with in-stent restenosis experienced MACE. In addition, 66% of patients with elevated hs-CRP level experienced in-stent restenosis. There was a significant association between primary serum hs-CRP level and in-stent restenosis ($P= 0.01$). There was also a significant relationship between primary hs-CRP serum level and 6-month MACE ($P= 0.02$). PCI patients who have DM and abnormal LDL level are more likely to experience in-stent restenosis and consequent adverse events. These events are predictable through hs-CRP measurement after stenting.

Key words: hs-CRP, PCI, MACE

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1. INTRODUCTION

Currently, acute coronary syndrome (ACS) is the most common cause of death worldwide. One of the most beneficial therapeutic interventions applied in ACS patients in percutaneous coronary intervention (PCI). This intervention has replaced coronary bypass surgery in many patients. Since PCI is a costly treatment, numerous studies have been done to study its factors, which affect efficiency and failure rate of this

method. Inflammatory markers have been mentioned extensively as important predisposing factors in development and progression of coronary arteries atherosclerosis. Studies have demonstrated association between elevated inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP) and coronary atherosclerosis. It is assumed that inflammatory markers play role in atheroma formation and its expansion. There are studies which have pointed out to the prognostic role of

hs-CRP in predicting mortality in patients with ACS or congestive heart failure (CHF). However, there is controversy in terms of prognostic value of hs-CRP in predicting restenosis and related adverse cardiac events in patients who undergo PCI. In this study, we intended to determine the association between serum hs-CRP level and the severity of in-stent restenosis and major adverse cardiac events (MACE) in a 6-month follow up of patients who underwent PCI.

2. MATERIALS AND METHODS

In this cohort study, 55 patients (30 males and 25 females) with age range of 27-74 years who participated to our medical center due to ACS and underwent PCI and stenting were included consecutively. Patients with these conditions can have an increase in CRP level such as infectious diseases, rheumatologic diseases, malignancies, and inflammatory diseases were excluded. Upon presentation, the required data were gathered through interview and medical records. Serum hs-CRP level was measured (normal was defined as hs-CRP level less than 2 mg/L). Once again, 24 hours after stenting, serum hs-CRP level was measured. According to the second hs-CRP measurement, the patients were divided into normal hs-CRP or abnormal hs-CRP groups. In 6-month follow-up, the patients who experienced ACS underwent coronary angiography. Other patients who did not have ACS underwent exercise tolerance test (ETT). Those who had abnormal ETT underwent coronary angiography. MACE were also documented and compared between the two groups of patients with normal and abnormal hs-CRP levels. The data were analyzed using Stata statistical software. Descriptive indices including frequency, percentage, mean, and its standard deviation were used to express data. To compare categorical variables between the two groups, the Chi-squared test was used. To compare continuous variables, the t-test was applied. To assess the association between hs-CRP level and in-stent restenosis and MACE, logistic regression was used. Significance level was set at 0.05.

3. RESULTS AND DISCUSSION

Seventeen patients had diabetes mellitus (DM), 22 had elevated serum LDL level, 27 cases had hypertension, and 17 were current cigarette smokers. Left anterior descending (LAD) artery was the most common involved coronary artery (60%) followed by left circumflex artery (22%) and right coronary artery (RCA) in 18% of patients. At first hs-CRP measurement, only 3 cases had elevated hs-CRP level (5.5%), but after 24 hours 45% of patients had elevated hs-CRP level. During follow-up, no mortality occurred, but 29 patients experienced ACS in the form of unstable angina (28 cases) and ST-elevation myocardial infarction (STEMI) which occurred in one patient. This yielded 6-month MACE of 52.7%. About 23% had abnormal ETT. Five patients (9%) developed restenosis, of which mild stenosis (stenosis of 30-49%) was seen in 1.8%,

moderate stenosis (50-74%) was seen in 1.8%, and severe stenosis (>75% stenosis) was detected in 5.4%. As shown in Table 1, only DM had significant association with occurrence of in-stent restenosis. In-stent restenosis occurred in 80% of patients with DM, but in non-diabetics, it was reported in only 20% of cases. Regarding 6-month MACE, no significant relationship was found between this outcome and gender (P= 0.39), age (P= 0.14), DM (P= 0.27), hypertension (P= 0.60), and smoking (P= 0.70). However, a significant association was found between 6-month MACE and elevated serum LDL level (P= 0.001).

Table 1. Association between stent re-stenosis and its risk factors

Variable		Mild Stenosis	Moderate Stenosis	Severe Stenosis	*P value
Gender	Male	1 (1.82%)	0	1 (1.82%)	0.56
	Female	0	1 (1.82%)	2 (3.64%)	
Serum LDL level	Norma l	0	11 (20%)	11 (20%)	0.37
	High	11 (20%)	0	22 (40%)	
Diabet es mellitu s	Yes	11 (20%)	11 (20%)	22 (40%)	0.04
	No	0	0	11 (20%)	
Hypert ension	Yes	11 (20%)	11 (20%)	11 (20%)	0.70
	No	0	0	22 (40%)	
Smoki ng	Yes	0	0	11 (20%)	0.80
	No	11 (20%)	11 (20%)	22 (40%)	

*P=0.001

All patients with in-stent restenosis experienced 6-month MACE. In addition, 66% of patients with elevated hs-CRP experienced restenosis. The relationship between serum hs-CRP level and in-stent restenosis was significant (P= 0.01). Likewise, a significant relationship was found between serum hs-CRP level and 6-month MACE (P= 0.02). The obtained findings suggest that hs-CRP was predictive for in-stent restenosis and 6-month MACE in patients who underwent PCI and stenting. Gach et al. also reported a similar finding that elevated hs-CRP level after stenting was predictive for MACE. We found that the second measurement of hs-CRP after PCI was more predictive for adverse events than primary hs-CRP measurement. In another study, Gottsauner et al. Showed that CRP level after stenting was higher in patients who developed restenosis at a 6 month follow up compared to those who did not develop re-stenosis. Furthermore, CRP level was associated with stenosis severity; in more severe cases of stenosis, CRP level was higher. Kim et al. in a study on 67 patients who received stenting (46 drug-eluting stents and 21 non-drug eluting stents) showed that CRP level was lower in drug-eluting stent group than other group. Buffon et al. reported that early complications following angioplasty occurred in 22% of patients with elevated hs-

CRP level, but none of the patients with normal hs-CRP level experienced early complications of angioplasty. They also followed stent stenosis at 1 year period. Stent stenosis occurred in 63% of patients with elevated hs-CRP level compared to just 27% of those with normal hs-CRP level. Significant relationship between stent re-stenosis as well as MACE and serum hs-CRP level could be affected by other cardiovascular diseases risk factors such as dyslipidemia and diabetes. The effective role of these risk factors was demonstrated in this study.

4. CONCLUSION

Patients who undergo stenting, especially those with dyslipidemia and diabetes are more susceptible to stent restenosis and its consequent complications. These events can be predicted by measuring serum hs-CRP level especially after stenting.

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AUTHORS CONTRIBUTION

This work was carried out in collaboration between all authors.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

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