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High Sensitivity C-Reactive Protein in Patients of Acute Myocardial Infarction with Type-2 Diabetes Mellitus-A Cross-Sectional Study

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Abstract

Study background: High sensitivity C-reactive protein (CRP) is an established prognostic marker in Coronary Heart Diseases (CHD); however, no Indian study has specifically addressed its prognostic role in type-2 diabetes mellitus. We evaluated the prognostic role of hs-CRP separately in diabetic and non-diabetic patients with CHD.

Aim: The aim was to assess the damage caused to the vascular endothelium in type-2 diabetes mellitus which could play a role in the causation of coronary heart disease (CHD) in these subjects.

Objectives:

1. To determine the levels of high-sensitivity C-reactive protein (hs-CRP) in subjects of acute myocardial infarction with history of type-2 diabetes mellitus.
2. To determine the levels of high-sensitivity C-reactive protein (hs-CRP) in subjects of acute myocardial infarction without history of diabetes mellitus.
3. To compare the results of the above two groups and analyze the damage caused to the vascular endothelium (hs-CRP levels) which could play a role in the causation of coronary heart disease (CHD) in these subjects.

Methods: This was a cross-sectional study which consisted of 30 patients admitted to the intensive care unit with acute myocardial infarction with type-2 diabetes mellitus and 30 patients of acute myocardial infarction who were non-diabetic. hs-CRP levels were estimated by particle enhanced immunoturbidimetric method using Statfax 3300 semi -automated analyzer after 12 hours post admission. Statistical analysis was done by unpaired *'t'* test using SPSS Package (version 11.0).

Results: Significant differences were found in hs-CRP levels between patients of acute myocardial infarction with and without type-2 diabetes mellitus, the values being higher in diabetics with acute myocardial infarction than the other group.

Conclusion: It can be concluded that significant high values of hs-CRP in diabetics may signal a considerable damage to the vascular endothelium, which could play a role in the causation of acute myocardial infarction.

Keywords: hsCRP; Coronary heart disease; Type-2 diabetes mellitus; Inflammation; Myocardial infarction

Introduction

Type-2 diabetes mellitus is a strong risk factor for Coronary Heart Disease (CHD), which in turn is the leading cause of morbidity and mortality in diabetic patients [1]. Patients with type-2 diabetes mellitus have two to four fold increased risk for CHD and more than 50% of all diabetic patients die of CHD [2]. Although the increased risk has been attributed primarily to hyperglycemia, dyslipidemia and a prothrombotic state, recent observations have focused attention on low grade inflammation in the pathogenesis of type-2 diabetes mellitus and its complications [3]. Inflammation plays an important role in all stages of the atherosclerotic process, from the onset of initial lesions to plaque progression and complications [4].

Recent studies have shown that higher concentrations of high sensitivity C-Reactive Protein (hsCRP) are associated with an increased cardiovascular risk in type-2 diabetes mellitus patients without previous history of cardiovascular disease [5-7]. Type 2 diabetic patients have increased CRP values, and inflammation has been found to be related to insulin resistance syndrome, which may partly explain the high incidence of CHD in diabetic group [8]. There are only a few studies in India reporting an association between elevated hsCRP and cardiovascular events in patients with type-2 diabetes mellitus. Hence, we aimed to assess the damage caused to the vascular endothelium in type-2 diabetes mellitus which could play a role in the causation of CHD in these subjects. So, we considered to determine the levels of hsCRP in subjects of Acute Myocardial Infarction (MI) with history of type-2 diabetes mellitus and in subjects with acute MI who were non-diabetic, and to compare the results of the two groups and analyze the damage caused to the vascular endothelium, which could have played a role in the causation of CHD in these subjects.

Material and Methods

This was a cross sectional study done between Jan 2010 and May 2011 at Hanagal Sri Kumareshwar Hospital, a tertiary care hospital at

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Bagalkot. Ethical clearance was obtained from the Institute's Ethical Clearance Committee.

60 subjects who were admitted to the intensive cardiac care unit were included for the study. Informed consent from the subjects was obtained. 30 subjects were patients suffering with acute MI with history of type-2 diabetes mellitus from past 10 years (Group A) and 30 subjects were patients suffering from acute MI, but non-diabetic (Group B). Patients with history of hypertension, previous MI, ischemic heart disease (IHD), smokers, patients with acute infections who were likely to have acute phase response and patients on drugs like salicylates and hypolipidemics were excluded from the study.

A venous blood sample was collected from each subject 12 hours post admission. Serum was separated and hsCRP concentration was measured by Particle Enhanced Immunoturbidimetric method (Euro Diagnostic Systems, Chennai) using Stat fax 3300 semi automated analyzer. Statistical analysis was performed using SPSS package version 11.0 by unpaired '*t*' test.

Results

In this cross-sectional study, the mean age (in years) of the subjects in Group A (patients suffering with acute MI with history of type-2 diabetes mellitus) was 65 ± 9.9 years and that in Group B (patients suffering from acute MI, but non-diabetic) was 62.93 ± 11.4 years (Table 1) (Figure 1).

The mean hsCRP (in mg/L) among Group A subjects was 7.71 ± 1.9 and among Group B subjects was 6.3 ± 1.81. There was a statistically significant difference among both the groups with p value being 0.005 (Table 2) (Figure 2).

There were 16 male and 14 female subjects in Group A, whereas 17 male and 13 female subjects in Group B. When the results were analyzed gender-wise, the mean hsCRP values among male and female subjects in Group A were 8.17 ± 2.2 and 7.19 ± 1.42 respectively, which was not statistically significant (p=0.17). The hsCRP values among male and female subjects in Group B were 6.39 ± 1.7 and 6.19 ± 1.9 respectively, which was again not statistically significant (p=0.776) (Table 3) (Figure 3).

Group	Mean age	*t*	p	Significance
A (n=30)	65 ± 9.9	0.74	0.458	Not significant
B (n=30)	62.93 ± 11.4			

Table 1: Mean age of the subjects in both the groups.

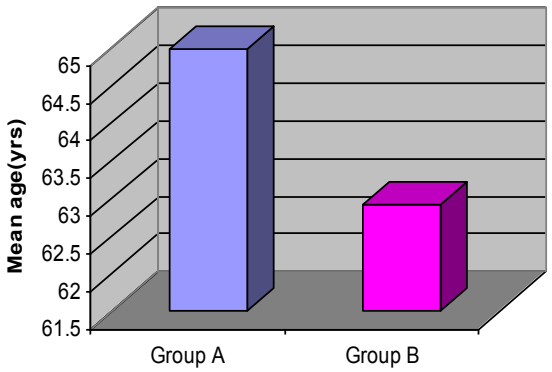


Figure 1: Mean age of the subjects in both the groups.

Group	hsCRP (mg/L)	*t*	p	Significance
A (n=30)	7.71 ± 1.9	2.89	0.005	Significant
B (n=30)	6.30 ± 1.81			

Table 2: hsCRP levels of the subjects in both the groups.

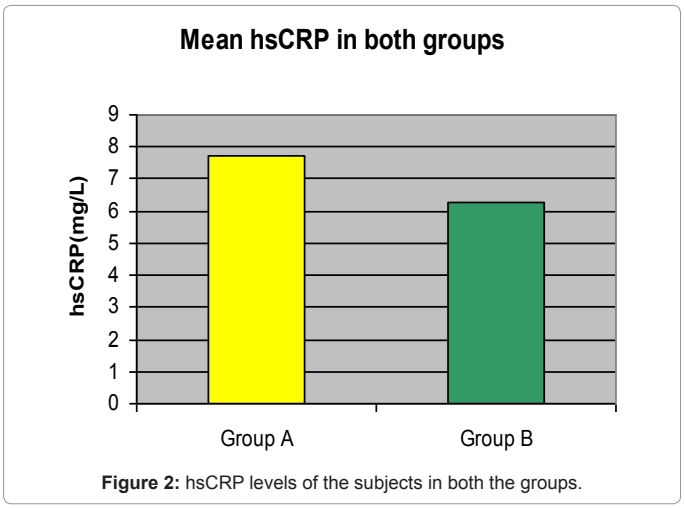


Figure 2: hsCRP levels of the subjects in both the groups.

Group	Gender	hsCRP	*t*	p	Significance
A	Males (n=16)	8.17 ± 2.2	1.407	0.17	Not significant
	Females (n=14)	7.19 ± 1.42			
B	Males (n=17)	6.39 ± 1.7	0.288	0.776	Not significant
	Females (n=13)	6.19 ± 1.9			

Table 3: hsCRP levels of the subjects in both the groups analyzed gender-wise.

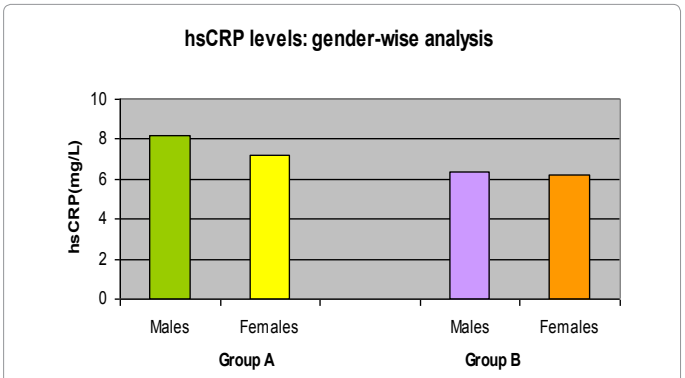


Figure 3: Gender-wise analysis of hsCRP levels of the subjects in both the groups.

Discussion

As per the American Heart Association recommendations, hsCRP levels below 1 mg/L is considered as low risk, between 1-3 mg / L, as average risk and above 3 mg/L is considered as high risk for CHD [9] (Table 4).

In the present study, subjects in both the groups had hsCRP more than 3 mg/L (high risk for CHD). Subjects of both groups were matched for their age and gender. There was no statistical difference.

As per the results, the hsCRP levels were significantly high in subjects with type-2 diabetes mellitus suffering with acute myocardial

hsCRP levels	Risk for CHD
<1 mg/L	low
1-3 mg/L	average
>3 mg/L	high

Table 4: American Heart Association Criteria.

infarction in comparison with subjects who were non diabetic suffering from acute myocardial infarction. This is in accordance with studies done by Sanchez et al. [10] and Biasucci et al. [11].

The significant difference in hsCRP can be attributed to low grade inflammation in the pathogenesis of type-2 diabetes mellitus [3]. Studies in non diabetic patients [12] and in subjects with impaired glucose tolerance or impaired fasting glucose [5] have confirmed that high concentrations of inflammatory markers predict the development of type-2 diabetes mellitus and are closely linked to insulin resistance.

hsCRP behaves as an inflammatory marker by activating complement pathway [13], induces adhesion molecule expression by human endothelial cells [14], recruitment of monocytes into the arterial walls [15], enhances the entry of LDL particles into macrophages [16], and induces plasminogen activator inhibitor-1 expression [17]. All these processes result in vascular endothelial injury [18].

The Hoorn study showed an association between CRP and cardiovascular mortality in patients with type-2 diabetes, but the association was not independent of other CHD risk factors [7]. In patients with type-2 diabetes who had acute coronary syndrome, CRP seemed to be an independent predictor for cardiovascular death [10]. In the Honolulu Heart Program, the association with elevated CRP and MI was weaker in diabetic than in non-diabetic men [19]. It is possible that other CHD risk factors typical for patients with type-2 diabetes like high triglyceride level, low HDL cholesterol level, hypertension and hyperglycemia per se partially masks the role of hs-CRP as a risk factor for CHD in this population. In non-diabetic subjects, increased level of hs-CRP seems to be a strong risk factor in apparently healthy individuals [20-22], but it also seems to predict future outcomes in patients with established CHD [23]. Several studies have found that diabetes does not significantly affect the prognostic value of hsCRP in population studies but such data in patients with acute coronary syndrome are lacking [24,25]. Because diabetes is associated with higher risk, the additional risk carried by hsCRP may not become apparent unless the inflammatory component related to the disease is very prominent.

Hence, the our study indicates that significant high values of hsCRP in diabetics could be due to vascular endothelial damage, which in turn could have led to acute MI.

Conclusion

It can be concluded that significant high values of hsCRP in diabetics may signal a considerable damage to the vascular endothelium, which could play a role in the causation of CHD.

The limitations of the present study were –

1. The sample size was small.
2. The severity of diabetes was not considered.
3. The extent of infarction was not considered.

All these limitations and also assessing the prognosis of these subjects depending upon the hsCRP levels would be considered in our future endeavor, which would be continuation of the present study.

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