Original Research Article

A study of C-reactive protein in diabetic and non-diabetic patients with acute myocardial infarctions

Yerraguntla Shashidhar[1], Golla Vahini[2*]

[1]Assistant Professor, General Medicine, Gandhi Medical College/General Hospital, Secunderabad, Telangana, India
[2]Assistant Professor, General Medicine, Gandhi Medical College/General Hospital, Secunderabad, Telangana, India

Received: 14-11-2021 / Revised: 21-12-2021 / Accepted: 11-01-2022

Abstract

Background: In this study we wanted to determine the CRP level at the time of admission as a strong predictor of hospital mortality and morbidity in patients with Diabetes mellitus as well as in patients without Diabetes mellitus who had acute myocardial infarction. **Methods:** This is a longitudinal study, conducted among patients of acute myocardial infarction admitted in ICU in Gandhi Medical College, from January 2021 to December 2021. Foe each study patient, a detailed history was taken, he/she was examined in detail, relevant investigations like ECG changes, lipid profile, CPKMB enzyme levels, blood glucose levels (FBS/PPBS) and C-reactive protein were done, the patient was followed till discharge and all complications like arrhythmias, failure and outcome were noted. **Results**: 96% of diabetic patients were found to be having CRP level >7mg/l as compared to 80% of non-diabetic patients with acute myocardial infarction. The mean CRP in diabetic group was 51.80 mg/l as compared to 15.78mg/l in non-diabetic group which was statistically significant (p<0.001).10% of diabetic patients had mortality as compared with 4% in non-diabetic group. Diabetic patients who died in hospital presented with higher plasma levels of CRP on admission as compared to non-diabetic patients. **Conclusions:** CRP on admission is a strong predictor for hospital morbidity and mortality in both diabetic and non-diabetic patients with acute myocardial infarction. Diabetic patients presented with higher CRP levels compared with those in non-diabetic patients with acute myocardial infarction. CRP may serve as marker in predicting the hospital mortality in patients with acute myocardial infarction. It can be concluded that significant high values of CRP in diabetics may indicate a considerable damage to the vascular endothelium, which could play role in causation of cardiovascular events.

Keywords: CRP, Myocardial Infarction, Diabetes Mellitus

Introduction

Acute myocardial infarction is a complication of coronary artery disease which is fatal and cause disability due to compromised LV function. The incidence of acute myocardial infarction is difficult to judge because of varied reporting pattern of death certification or may be due to vast majority of cases die at home even before they reach the hospital without having been examined by a qualified practitioner. So acute myocardial infarction remains a leading cause of death in developed and developing countries[1]. It is estimated that the prevalence of IHD among adults in India is 96.7 per 1000 population in the urban and 27.1 percent in rural areas[2].

Acute phase response occurs secondary to inflammatory process. This response is due to by pro inflammatory cytokines which are released from the tissue by inflammatory and/or parenchymal cells. These stimulate the liver to synthesize acute phase proteins. C-Reactive Protein (CRP), being one among them, synthesized by the liver in response to factors released by adipocytes[3]. CRP is a marker for inflammation and is increased in both atherosclerosis and in coronary artery disease. They co-relate with cardiac outcomes following acute myocardial infarction.

Diabetes mellitus is identified as one major cause of mortality and morbidity with increasing incidence in developing countries than developed countries.

*Correspondence
Dr. Golla Vahini
Assistant Professor, General Medicine, Gandhi Medical College/ General Hospital, Secunderabad, Telangana, India
E-mail: vahini506@gmail.com

Today, India has largest number of diabetic subjects as compared with any given country. Currently estimated diabetic population of India is 31.7 million individuals and it is expected to reach 79.4 million by the year 2025. Diabetes mellitus is an independent risk factor for atherosclerosis. It is considered to be a state of low-grade inflammation. CRP levels have been reported to be augmented in diabetic patients[4].

Recent studies have shown CRP can predict the risk for the future myocardial infarction, stroke and coronary heart disease in healthy persons[5]. This study is aimed at determining the role of CRP in the patients with myocardial infarction and at comparing the results between diabetic and non-diabetic patients as studies have shown importance of CRP levels on admission with regard to the hospital outcome of diabetic and nondiabetic patients. The excessive risk of mortality in patients with diabetes and elevated.

CRP will require an intensification of strategies to overcome the poor prognosis.

Objectives

To determine the CRP level at the time of admission as a strong predictor of hospital mortality and morbidity in patients with Diabetes mellitus as well as in patients without Diabetes mellitus who had acute myocardial infarction.

Materials and methods

This is a longitudinal study, conducted among patients of acute myocardial infarction admitted in ICU in Gandhi Medical College, from January 2021 to November 2021. Foe each study patient, a detailed history was taken, he/she was examined in detail,relevant investigations like ECG changes, lipid profile, CPKMB enzyme

levels, blood glucose levels (FBS/PPBS) and C-reactive protein were done, the patient was followed till discharge and all complications like arrhythmias, failure and outcome were noted.

Inclusion Criteria

- Patients of any age who are admitted in ICU in Gandhi Medical Cllege from January 2021 to December 2021.
- The non-ST segment elevation MI, ST segment elevation MI are selected on basis of history, examination and relevant investigations (WHO criteria).
- Patient was considered to be diabetic if patient was informed of the diagnosis earlier or was on prescribed anti-diabetic treatment (ADA criteria).

Exclusion Criteria

Patients with renal failure, inflammatory bowel disease, non-cardiac chest pain, recent infections, immunologic disorder, known or suspected neoplastic disease, major trauma, surgery, burns or re-infarction were excluded from the study.

Sample Size Calculation

With Anticipated Mean Difference of CRP between the two study groups as 1.3 and Anticipated SD as 1.8, the minimum sample size per group is 50 with 90% power and 5% level of significance.

By using the formula:

$$n = \frac{(Z_\alpha + Z_\beta)^2\ 2\ SD}{MD^2}$$

Where Z= Z statistic at a level of significance

MD= Anticipated mean difference

SD= Anticipated Standard deviation

A total of 100 patients were included in the study and out of which 50 subjects were non-diabetic and 50 were diabetic.

These patients have been divided into two groups

Group A: Diabetic patients

Group B: Nondiabetic patients

Statistical Methods

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

Results

The youngest patient was aged 26 years and eldest patient being 88 years. The maximum number of patients between age group 51-70 years. In diabetic group 42% of patients were in the age group of 61-70 years and 36% of patients in non-diabetic were in the age group of 51-60 years. Out of 100 patients 71 were male and 29 patients were female. In diabetic group 66% were males and in diabetic group 76% were males.

Table 1. Distribution of Symptoms Between Group A & B

Symptoms	Group A		Group B		Total		P Value
	N	%	N	%	N	%	
Chest pain	34	68	36	72	70	70	0.663
Breathlessness	18	36	20	40	38	38	0.680
Sweating	38	76	29	58	67	67	0.056
Others	24	48	15	30	39	39	0.065

Chest pain is the commonest symptom occurring in 70(70%) patients, followed by Sweating in 67(67%), and breathlessness in 38(38%) patients of acute myocardial infarction.In this study the most common non modifiable risk factor is male sex accounting for 71 of all cases followed by age >60 years (42%). The common modifiable risk factor other than diabetes is dyslipidemia noted in 72(72%) patients followed by smoking (46%) and hypertension (27%). Among diabetics 42 patients had dyslipidemia(84%) while 30patients in non-diabetic group had dyslipidemia (60%).Left ventricular dysfunction was the most common complication seen in 34(34%) patients, followed by conduction blocks in 20(20%) patients, arrhythmias in 6 patients, cardiogenic shock in 3 patients and death in 7 patients.

Table 2.Distribution of Complications between Group A & B

Complications	Group A		Group B		Total		P Value
	N	%	N	%	N	%	
LV Dysfunction	22	44	12	24	34	34	0.035*
Shock	2	4	1	2	3	3	0.558
Conduction Block	14	28	6	12	20	20	0.046*
Arrhythmias	5	10	1	2	6	6	0.092
Death	5	10	2	4	7	7	0.240
Note: * significant at 5% level of significance (p<0.05)							

C-reactive protein levels at admission

In our study CRP level of 7mg/l is taken as cut off value.

Table 3.Distribution of CRP Level between Group A & B

CRP Level	Group A		Group B		Total		P Value
	N	%	N	%	N	%	
<7	2	4	10	20	12	12	0.014*
>7	48	96	40	80	88	88	
Total	50	100	50	100	100	100	
Note: * significant at 5% level of significance (p<0.05)							

Among the study groups 88 (88%) patients had CRP of more than 7mg/l, and 12(12%) patients had CRP of less than 7mg/l.

Table 4.Mean CRP Level between Group A & B

	Group A		Group B		P Value
	Mean	SD	Mean	SD	
Mean CRP (mg/l)	51.80	34.71	15.78	12.67	<0.001*
Note: * significant at 5% level of significance (p<0.05)					

In our study group, 96% of diabetic patients were found to be having CRP level >7mg/l as compared to 80% of non-diabetic patients in acute myocardial infarction. The mean CRP in diabetic group was 51.80 mg/l as compared to 15.78mg/l in non-diabetic group which was statistically significant(p<0.001)

On applying appropriate statistical test there was significant correlation between CRP level and diabetes in patients with acute myocardial infarction.

CRP levels on admission were higher in diabetic patients than in non-diabetic patients with median value of CRP in diabetic patients 51.80mg/dl as compared to 15.78mg/dl in non-diabetic patients with acute myocardial infarction.

Table 5: Proportion OF Complications by CRP Level in Group A and B

		Yes		No
	N	%	N	%
<7	0	0	2	8.3
>7	26	100	22	91.7
Total	26	100	24	100.0
Proportion OF Complications by CRP Level in Group A				
Note: Proportion of complications was significant at 5% level of significance (p<0.05) (z test of proportion)				
CRP Level		**Complications**		
		Yes		**No**
	N	**%**	**N**	**%**
<7	8	22.2	2	14.3
>7	28	77.8	12	85.7
Total	36	100.0	14	100.0
Proportion of Complications by CRP Level in Group B				
Note: Proportion of complications was significant at 5% level of significance (p<0.05) (z test of proportion)				

The diabetic patients with higher CRP level had high incidence of mortality and morbidity as compared to non-diabetic patients. Diabetic patients who died in the hospital presented with higher plasma CRP levels on admission as compared to non-diabetic patients.

Discussion

In this study CRP levels were classified in two groups <7mg/l and >7mg/l. Out of 100 subjects, 88 patients(88%) had CRP of more than 7mg/l, and 12 patients(12%) had CRP of less than 7 mg/l. In our study group, 96% of diabetic patients were found to be having CRP level >7mg/l as compared to 80% of non-diabetic patients in acute myocardial infarction.

Similar study done by Kushner et al[6] showed that myocardial infarction results in rapid exponential increase in serum concentration of CRP, and this increase usually begins within few hours after chest pain, and that its magnitude is related to the degree of tissue injury. The study done by De Beer FC[7] et al found that all individuals with infarction or raised CPKMB levels showed a rise in CRP concentration. Thompson et al found that the concentrations of CRP were on an average 20.2% hiogher in the patients who had coronary events than in those without such events, after adjustment for other risk factors and higher levels predict poor outcomes in patients with coronary artery disease[8].Liuzzo et al[9] showed that in 31 patients with severe unstable angina and no evidence of myocardial necrosis, as documented by the absence of increased cardiac enzymes, hs-CRP concentration >3mg/l were associated with an increased incidence of recurrent angina, coronary revascularization, MI and cardiovascular death.

In a similar study, Ferreiros et al[10] concluded that the prognostic value of CRP measured at discharge was better than that determined at admission in predicting adverse outcome at 90 days.

Data from the thrombolysis in myocardial infarction 11A, a study of unstable angina and non Q wave MI, showed that markedly increased hs-CRP(15.5mg/l) at admission was a predictor of 14 day mortality in that population.

Similar results were found in studies conducted by Nikfardjam et al[8], Dibra et al[11], Voulgari et al[10] and Lim et al[12].

In this study CRP levels on admission were higher in diabetic patients than in non-diabetic patients with median value of CRP in diabetic patients 51.80mg/dl as compared to 15.78mg/dl in non-diabetic patients with acute myocardial infarction which was statistically significant(p<0.001)

The diabetic patients with higher CRP level had high incidence of mortality and morbidity as compared to non-diabetic patients. Left ventricular dysfunction was the most common complication seen in 34(34%) patients, followed by conduction blocks in 20(20%) patients, arrhythmias in 6 patients, cardiogenic shock in 3 patients and death in 7 patients.

Diabetic patients who died in the hospital presented with higher plasma CRP levels on admission as compared to non-diabetic patients.

Table 6. HS-CRP Level and ODDS Ratios for Post MI Complications

Study	HS-CRP level	RR/OR	95% CI
OKeskins et al	>2.0 mg% (once at admission within 6-12hrs)	1.024 for recurrent cardiac events within 30days	1.002 to1.047
Suleiman et al[13]	>2.23 mg% (once at admission) within 12 -24hrs	3.0 for 30 d mortality andheart failure	1.3 to 7.2
Anzai et al	>20 mg% (peak)	4.72 for cardiac rupture& one year cardiac death	1.6 to 13.6
Zebracks et al	CRP levels, at predischarge	Not associated with death or recurrent cardiacevents	1.93 to 6.3
Helsinki Heart Study	≥ 3 mg% (once at admission) within 6 to12hrs	5.2 for post MI complications during hospital course	2.2 to 13.7

The study conducted by W Otter et al[14] also showed high CRP levels in diabetic patients with acute myocardial infarction with median value of 8mg/l in diabetic as compared to 6mg/l in non-diabetic.In Munich myocardial infarction registry the combined presence of diabetes and CRP levels in the two upper quintiles showed that mortality was 6 to 7 fold higher as compared to diabetic with low CRP[14].In a study done by Dombal A[15] et al the mean hs CRP value in diabetic patients with acute myocardial infarction was 7.71mg/l as compared to 6.30mg/l in non-diabetic patients. The United Kingdom prospective diabetes study(UKPDS) showed that by maintaining intensive glycemic control, there was 16% reduction in the risk of myocardial infasrction,I t also showed thsat control of other cardiovascular risk factors in diabetics was of benefit in preventing adverse macrovascular outcomes.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. In patients with type 2 diabetes who had acute coronary syndrome, CRP seemed to be an independent predictor for cardiovascular death. Several studies have found that diabetes doesnot significantly affect the prognostic value of hs-CRP in population

studies but such data in patients with acute coronary syndrome are lacking[16].

Conclusion

The present study results demonstrated that CRP on admission is a strong predictor for hospital morbidity and mortality in both diabetic and non-diabetic patients with acute myocardial infarction.Diabetic patients presented with higher CRP levels compared with those in non-diabetic patients with acute myocardial infarction.CRP may serve as marker in predicting the hospital mortality in patients with acute myocardial infarction. It can be concluded that significant high values of CRP in diabetics may indicate a considerable damage to the vascular endothelium,which could play role in causation of cardiovascular events.

Limitations of the Study

1. The sample size was small
2. The severity of diabetes was not considered
3. The extent of infarction was not considered.
4. The role of thrombolysis was not highlighted
5. Other risk factors of CVD also played a role in the cardiac events

References

1. Dev BP, Siddarth NS, Dilip RK. ST elevation myocardial infarction. In: Shah SN, ed. API textbook of medicine. 8th edn. 2008: p. 520
2. WHO. Health situation in the South East Asia Region 1998-2000. New Delhi 2002.
3. Lau DC, Dhillon B, Yan H. Adipokines: molecular links between obesity and atherosclerosis. Am J Physiol Heart Circ Physiol 2005;288(5):H2031-41.
4. Pai JK, Pischon T, Ma J. Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med 2004;351(25):2599-610.
5. Kuller LH, Tarcy RP, Shaten J. 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.
6. Kushner I. Control of acute phase response. Demonstration of C-reactive protein synthesis by hepatocytes during acute inflammation in rabbit. J Exp Med 1978;148(2):466-77.
7. De Beer FC, Hind CR, Fox KM. Measurement of serum C-reactive protein in myocardial ischemia and infarction. Br Heart J 1982;47(3):239-43.
8. Nikfardjam M, Schreiber W. The association between C-reactive protein on admission and mortality in patients with acute myocardial infarction. J Intern Med 2000;247(3):341-5.
9. Liuzzo G, Biasucci LM, Gallimore JR. The prognostic value of C-reactive protein and serum amyloid a protein in severe unstable angina. N Engl J Med 1994;331(7):417-24.
10. Voulgari F, Cummins P, Gardecki T. Serum levels of acute phase and cardiac proteins after myocardial infarction, surgery, and infection. Br Heart J 1982;48(4):352-6.
11. Dibra A, Mehilli J, Schwaiger M. predictive value of basal C-reactive protein levels for myocardial salvage in patients with acute myocardial infarction is dependent on the type of reperfusion treatment. Eur Heart J 2003;24(12):1128-33.
12. Lim SY, Jeong MH, BaeEH. Predictive factors of major adverse cardiac events in acute myocardial infarction patients complicated by cardiogenic shock undergoing primary percutaneous coronary intervention. Circ J 2005;69(2):154-8.
13. Suleiman M, Aronson D, Reisner SA. Admission C-reactive protein levels and 30-day mortality in patients with acute myocardial infarction. Am J Med 2003;115(9):695-701.
14. Otter W, Winter M, Doering W. C-reactive protein in diabetic and non-diabetic patients with acute myocardial infarction. Diabetes Care 2007;30(12):3080-2.
15. Dambal A,Herur A. High sensitivity C-reactive protein in patients of acute myocardial infarction with type-2 diabetes mellitus-a cross-sectional study. Open Access Scientific Reports 2012;12:1-4.
16. Thompson SG, Kienast J, Pyke SD. Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study Group. N Engl J Med 1995;332(10):635-41.

Conflict of Interest: Nil Source of support: Nil