PREOPERATIVE C-REACTIVE PROTEIN LEVELS AND POSTOPERATIVE COMPLICATIONS OF CARDIOVASCULAR SURGERY

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ABSTRACT:

OBJECTIVE: To determine the correlation between preoperative C reactive protein (CRP) and postoperative complication of elective cardiac surgery including systemic inflammatory response syndrome, atrial fibrillation, acute kidney injury, wound infection, shock and death.

MATERIAL AND METHOD: This prospective observational study was conducted in Punjab Institute of Cardiology, Lahore. Patients undergoing cardiovascular surgery from September 2012 to January 2013 were included. CRP levels were measured in all patients in the morning on the day of surgery. Patients were categorized as Group A (CRP < 2 mg/dl) and Group B (CRP > 2 mg/dl) and were followed for occurrence of postoperative complications till their stay in the hospital.

RESULTS: Out of 149 patients [104 (70%) males and 45 (30%) females] studied; 97 (65.1%) patients had CRP < 2 mg/dl (Group A) and 52 (34.9%) had CRP > 2 mg/dl (Group B). Mean age in Group A was 43.6±13.2 years and in Group B it was 48.9±13.4 years. Overall incidence of death was 3.35 % (n = 5) in our study. Overall systemic inflammatory response syndrome (SIRS) was noted in 81 (54.4 %); 34 (65.4%) from Group B and 47 (48.5%) from group A (p= 0.048). Acute renal failure developed in 26 (50%) patients in group B versus 28 (28.9%) in group A (p= 0.011). Wound infection was observed in 13 (25%) patients in high CRP group and 11 (11.3%) in low CRP group (p= 0.031). Statistically significant difference was not noted in both the groups in terms of atrial fibrillation and shock. The death rate was also similar in both the groups.

CONCLUSION: Elevated preoperative CRP levels can predict postoperative complications like SIRS, acute renal failure and wound infection after elective cardiac surgery.

KEY WORDS: C Reactive Proteins, Cardiovascular Surgery, Postoperative Complications.

INTRODUCTION

C-reactive protein (CRP) is an acute phase reactant which is derived from liver. It increases in response to inflammation and contributes to host defense system against a variety of antigens. Its value as a risk predictor has been investigated in patients with arteriosclerosis and consequent clinical states.[1] Identification of factors related to an increased risk of postoperative complications allows risk stratification and helps in preoperatively optimization of the clinical status of patients. Multiple scoring methods have been developed for patients undergoing cardiac surgery. Although not used in routine practice, serum levels of CRP before coronary angioplasty is reported to be superior as a predictor of acute

complications and clinical restenosis as compared to clinical presentation and other risk factors.[2]

Inflammatory reaction plays a pivotal role in the development of postoperative morbidity and mortality. Accordingly, the preoperative inflammatory status of the patient will significantly affect the degree of systemic inflammation and the postoperative outcome.[3] Among inflammatory biomarkers, C-reactive protein (CRP) is the one most widely used. However, its predictive role and clinical application in patients undergoing cardiac surgery remains controversial.[4]

The present study is done to see frequency of postoperative complications after elective cardiac surgery (mainly for coronary artery disease, valvular heart disease and congenital heart disease) in patients with normal and raised CRP levels. Postoperative complications of interest (endpoints) were systemic inflammatory response syndrome (SIRS), arrhythmias, acute kidney injury, wound infection, shock and death.

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MATERIAL AND METHODS

This prospective, observational study was conducted at Punjab Institute of Cardiology, Lahore, Pakistan. After informed consent, patients were selected using non- probability sampling technique over a period of 5 months (2012-13). Demographics like age and gender were noted. The effect modifiers like Diabetes Mellitus, hypertension, smoking, dyslipidemia and family history of coronary artery disease were also recorded. Baseline investigations like Hematocrit, white blood cell count, platelet count, aPTT, Urea and Creatinine were recorded. Patients with previous cardiac surgery, diagnosed cases of infective endocarditis, clinical or laboratory markers of active infection or those who needed an emergency surgery e.g., aortic dissection thrombosed prosthetic valve etc, were excluded.

Measurement of CRP was carried out by using Latex Agglutination technique. Samples were collected in the morning before surgery. Patients were categorized into two groups: **Group A** having CRP level < 2 mg/dl and **group B** with CRP levels > 2 mg/dl. Postoperatively, all patients were followed for complications especially systemic inflammatory response syndrome (SIRS), arrhythmias, acute kidney injury, wound infection, shock and death. SIRS was diagnosed if two or more of the following were present[5]: temperature above 38 °C or below 36 °C, tachycardia (HR > 90/min), tachypnea (RR > 20/min) with hypocapnia (PCO_2 < 32 mmHg) and alterations in white blood cell count (WBC > 12,000/mm³ or < 4,000/mm³). Postoperative AF was diagnosed by telemetry or electrocardiogram, if it persisted for more than an hour or required electrical or pharmacological cardioversion, in the absence of other causes like electrolyte abnormalities, use of adrenergic drugs or thyrotoxicosis, during hospitalization. The criteria of the Acute Kidney Injury Network were used to define renal failure (RF) [6]: an acute reduction of the renal function (within 48 hours) diagnosed by an absolute increase of > 0.3 mg/dl in serum Creatinine level, or higher than 50% (1.5 times) rise with regard to basal value, or reduction in urine output to < 0.5 ml/kg/h for more than 6 hours.

Vasoplegic shock was defined as: mean arterial pressure < 50 mmHg or systolic blood pressure (systolic BP) < 80 mm Hg and CVP <5 mm Hg.

STASTISTICAL ANALYSIS

All the data were analyzed by SPSS (Statistical Package for Social Sciences) Version 18.0 for Windows. Continuous variables were presented as mean ± standard deviation. Categorical variables were presented as frequencies, percentages and graphs. For qualitative variables, association of the post-operative complications with pre operative CRP levels in cardiovascular surgery patients was determined by Chi-square test while for quantitative variables independent sample t-test was applied. P-value < 0.05 was considered significant. All tests were applied two tailed.

RESULTS

A total of 149 patients [104 (69.80%) male and 45 (30.20%) females] were studied. Among them, 97 (65.1%) patients had CRP <2 mg/dl (Group A) and 52 (34.9%) had CRP > 2 mg/dl (Group B). Mean age of study population was 45.4 years. Patients in Group B were older as compared to those in Group A, mean age being 48.88±13.4 and 43.6±13.2 years respectively (p=0.045). There was no significant difference in both groups regarding gender, weight and height. Prevalence of Diabetes Mellitus, hypertension, smoking, dyslipidemia and presence of family history of ischemic heart disease was similar in both groups (Table 1). Use of beta blockers, aspirin, and joint diseases was similar in both groups. Previous myocardial infarction and fever within last two weeks was significantly associated with raised CRP levels (p= 0.018 and 0.012 respectively). Overall incidence of death was 3.35 % (n = 5) in our study; 3 patients were from Group B and 2 from Group A.

SIRS was noted in 81 (54.4 %) patients, 34 (65.4%) were from Group B and 47 (48.5%) from Group A (p 0.048). Fifty four patients (36.2%) developed acute renal failure; 26(50%) from high CRP Group versus 28(28.9%) from normal CRP Group (p=0.011). Wound infection was observed in 24 (16%) patients out of whom 13 had raised pre- op CRP levels (p= 0.031). The prevalence of atrial fibrillation and shock was similar in both groups (Table 2).

DISCUSSION

Our single centre observational data revealed that elevated preoperative CRP levels can predict postoperative complications like SIRS, acute renal failure, shock and wound infection after elective cardiac surgery.

Identification of factors related to an increased risk of postoperative complications allows risk stratification and helps in preoperatively optimization of the clinical status patients. Multiple scoring

Table 1: Baseline Characteristics of the Study Population.

Variable		CRP levels (mg/dL)		P-value
		Group A <2 n=97	Group B ≥2 n=52	
Gender	Male	66 (68%)	38 (73.1%)	0.523
	Female	31 (32%)	14 (26.9%)	
Age (years)		43.6±13.2	48.88±13.4	0.045
Height (Cm)		157.3±17.8	160.5±14.5	0.101
Weight (Kg)		65.6±15.7	66.2±12.4	0.315
Diabetes mellitus		31(32.0%)	19 (36.5%)	0.573
Hypertension		56(57.7%)	28(53.8%)	0.648
Smoking		32(33%)	24(46.2%)	0.114
Dyslipidemia		24(24.7%)	15(26.2%)	0.587
Family history		40(41.2%)	24(46.2%)	0.563
Previous acute MI		23(23.7%)	22(42.3%)	0.018
Fever at least 2 weeks		16(16.5%)	18(34.6%)	0.012
Known joint disease		24(24.7%)	14(26.9%)	0.771
Operation type	CABG	67(69.1%)	36(69.2%)	
	Valvular	24(24.7%)	15(28.8%)	0.466
	Congenital	6(6.2%)	1(1.9%)	
Use of Aspirin		35(36.1%)	25(48.1%)	0.155
Use of Beta-blockers		33(34%)	15(28.8%)	0.518

Table 2: Primary final events according to preoperative levels of CRP.

| Variables	CRP levels (mg/dL)		P-value
	Group A <2 n=97	Group B ≥2 n=52	
SIRS	47(48.5%)	34(65.4%)	0.048
Acute Renal Failure	28(28.9%)	26(50%)	0.011
Atrial Fibrillation	12(12.4%)	11(21.2%)	0.157
Shock	26(26.8%)	21(40.3%)	0.089
Wound Infection	11(11.3%)	13(25.0%)	0.031
Death	2(2.1%)	3(5.8%)	0.343

methods have been developed for patients undergoing cardiac surgery. These systems are complex and dynamic nature of surgical and anesthesiologic management with wide variety of extracardiac comorbidities make these scoring systems difficult to use. There is a need for some simple and practical predictors which can accurately predict postoperative outcomes and be applied conveniently in day to day practice. Few scoring systems have been shown to be good predictors of outcome after cardiac surgery as they suffer a certain degree of inaccuracy in predicting the individual's risk of postoperative death.[7,8] During last few decades, CRP has emerged as an important predictor of cardiovascular events in healthy subjects and in those with known coronary artery disease. It predicts short and long term outcomes after percutaneous coronary intervention[9] and after peripheral vascular surgery[10]. Gaudino et al[4] showed in a series of 113 patients that those with preoperative levels of CRP > 0.5

mg/dl did not have an increased risk to develop postoperative adverse events. Kangasniemi et al[11] retro-spectively analyzed 843 patients after coronary surgery, and observed no impact of preoperative CRP level of 1 mg/dl or higher on early postoperative outcome, however, they observed its adverse influence on long-term overall survival (mean follow-up of 12 years). Cappabianca et al.[12] showed increased in-hospital and 3-year all cause mortality in a heterogeneous patient population with preoperative CRP levels > 5 mg/l undergoing cardiac surgery including CABG. Biancari and colleagues [3] reported that a preoperative CRP level of 1 mg/dl or more was an independent risk factor for postoperative mortality in 764 CABG patients. The present study was conducted to assess the association of high levels of CRP with post cardiac surgery complications like SIRS, acute renal failure, atrial fibrillation, shock, wound infection and death.

AHA/ACC classifies SIRS as a frequent postoperative complication of cardiac surgery[5]. The state of underlying inflammation which is not identified by routine clinical parameters and laboratory investigations may influence this significant complication.[3,4] Among inflammatory biomarkers, CRP is the most widely used.[5] Our study showed significant relation of high CRP to postoperative development of SIRS. Atrial fibrillation is common postoperatively in cardiac surgery patients.[5] Elevated basal levels of CRP may identify high risk patients.[13,14] In present study postoperative atrial fibrillation is not associated with high levels of CRP and this contrary finding can possibly due to limited samples size.

Acute renal failure is strongly related to preop-

Fig 1: Frequency CRP Groups with respect to SIRS.
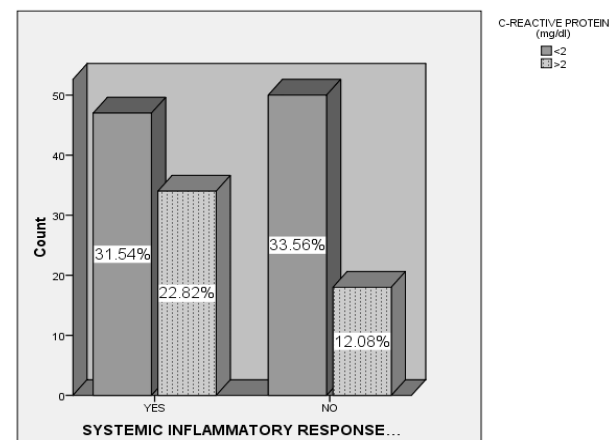
erative high CRP levels as shown in past studies. Kim et al.[15] proved an association between pre-operative levels of CRP and renal dysfunction in the postoperative period.

Tjörvi et al.[16] demonstrated the role of high CRP in post cardiac surgery mortality at levels $\geq$ 3 mg/dl. Our study failed to reproduce this relation; it might be due to small sample size and low short term mortality. Silvina et al.[17] demonstrated the significance of CRP in predicting shock postoperatively, in our study the shock was more common in paitents with rasied CRP levels althaugh statistically significant difference was not seen between the two groups. Wound infection can also be predicted by preoperative underlying inflammatory states as evident by raised levels of serum CRP, our study supports this hypothesis.

CONCLUSION

Elevated preoperative CRP levels can predict post operative complications like systemic inflammatory response, acute renal failure, shock and wound infection in patients undergoing elective cardiac surgery.

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