Hs-CRP as an independent marker for cardiovascular diseases: A Correlation analysis

Dr. Vivek Kumar Jain[1], Dr. Dharmveer Sharma[2], Dr. Vidyanand Pandit[3]

[1]Associate Professor, Department of Biochemistry, Graphic Era Institute of Medical Science, Dehradun, Uttarakhand, India

[2]Professor, Department of Biochemistry, SRVS Government Medical College, Shivpuri, Madhya Pradesh, India

[3]Assistant Professor, Department of Pathology, SRVS Government Medical College, Shivpuri, Madhya Pradesh, India

Corresponsing Author: Dr. Vidyanand Pandit
Email: panditvidya@gmail.com

ABSTRACT

Introduction: The advent of high-sensitivity C-reactive protein (Hs-CRP) assays has enhanced the utility of this acute-phase reactant in forecasting initial cardiovascular events. Elevated Hs-CRP levels are partially indicative of the extent of myocardial injury and can serve as predictors of both short-term and long-term outcomes in patients experiencing acute myocardial infarction. The study aims to investigate the relationship between elevated Hs-CRP levels and various traditional risk factors, including age, sex, lifestyle, and comorbidities.

Materials and Methods: A prospective cross-sectional study involving 123 patients with traditional risk factors and pre-existing cardiovascular conditions was conducted at a tertiary care center. Hs-CRP levels were measured using immunoturbidimetric methods, and statistical correlations were performed. The statistical analysis was carried out using SPSS version 21 software.

Results: Out of 123 patients, 82 had Hs-CRP levels exceeding 3 mg/L, while 41 patients had Hs-CRP levels below 3 mg/L. A total of 36.59% of the patients were in the age group of 51–60 years, with the majority (78.05%) being male. Among the individual lifestyle factors and traditional risk factors evaluated, five parameters—sedentary lifestyle, smoking, pre-existing hypertension, diabetes mellitus, and electrocardiographic changes—were found to be statistically significant. The correlation between elevated Hs-CRP levels and cardiovascular disease was also statistically significant.

Conclusion: Hs-CRP is an independent biomarker for cardiovascular disease, with a significant positive correlation established between elevated Hs-CRP levels and major traditional risk factors such as sedentary lifestyle, smoking, hypertension, and diabetes mellitus.

Key Words: Atherosclerosis; C-Reactive Protein; Myocardial Infarction; Cardiovascular Disease

INTRODUCTION

Acute myocardial infarction (AMI) represents a critical form of ischemic heart disease and stands as a leading cause of mortality in both industrialized nations and developing countries such as India. AMI has recently emerged as a significant contributor to the rising rates of morbidity and mortality in contemporary society. Recent studies have shown encouraging outcomes in the early

detection of cardiovascular events through the use of high-sensitivity C-reactive protein (Hs-CRP). The levels of Hs-CRP may provide insight into the degree of myocardial necrosis, making it a valuable prognostic marker for myocardial infarction (MI) and other cardiovascular conditions. In addition to Hs-CRP, several other biochemical markers, including homocysteine, plasminogen activator inhibitor-1, fibrinogen, IL-1, IL-6, serum amyloid A, and tumor necrosis factor α, have been identified as useful for both diagnostic and prognostic purposes [1-3].

Elevated Hs-CRP levels have also been shown to be significant in the presence of traditional risk factors such as hypertension and diabetes mellitus, in addition to myocardial infarction. This association may be due to the link between Hs-CRP and metabolic syndromes [4,5]. The study aimed to assess the levels of high-sensitivity C-reactive protein in patients with cardiovascular events, investigate the relationship between elevated Hs-CRP levels and various conventional risk factors such as age, sex, lifestyle, and comorbidities, and establish elevated Hs-CRP levels as an independent marker for cardiovascular events.

MATERIAL AND METHODS
The study was designed as a prospective cross-sectional investigation. A total of 123 patients who met the inclusion criteria were recruited from those attending the inpatient clinics. The study was conducted over a period of two years. The study included patients with confirmed cardiovascular events and those with traditional risk factors. Patients who had acute infections or inflammatory conditions were excluded.

Blood samples were collected from all participants during their hospital stay, using plain collection tubes. Fresh serum was obtained either by allowing the blood to stand or by centrifugation, and the samples were analyzed using the semi-automated biochemistry analyzer.

Data were tabulated, and variables were analyzed using the Chi-square test and Yates' Chi-square test. A P-value of less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 21 software.

RESULTS
The study cohort comprised 123 participants (Table 1), with a majority being male (78.05%) and a minority female (21.95%). The age distribution was varied, with the largest proportion of participants falling within the 51–60 years age group (36.59%). The next most common age group was 61–70 years (26.83%), followed by 71–80 years (16.26%). Participants aged 41–50 years constituted 10.57%, while those aged 31–40 years and 21–30 years were less represented at 7.32% and 2.44%, respectively. The mean age of the participants was 47.89 years, with a standard deviation of 9.45 years.

Table 1: Demographic parameters of study participants

Parameter	n (%)
Age Group (Years)	
21–30	3 (2.44)
31–40	9 (7.32)

41–50	13 (10.57)
51–60	45 (36.59)
61–70	33 (26.83)
71–80	20 (16.26)
Mean ± SD	47.89 ± 9.45
Gender	
Male	96 (78.05)
Female	27 (21.95)

Table 2 illustrates the relationship between hs-CRP levels and various cardiovascular disease risk factors. Out of 123 patients, 82 had Hs-CRP levels exceeding 3 mg/L, while 41 patients had Hs-CRP levels below 3 mg/L. A notable correlation is observed between a sedentary lifestyle and elevated hs-CRP levels, with 54% of participants with hs-CRP > 3 mg/L having a sedentary lifestyle compared to only 12% in those with hs-CRP < 3 mg/L, yielding a p-value of <0.05, indicating statistical significance. Smoking also shows a strong association, with 50% of individuals with hs-CRP > 3 mg/L being smokers, compared to 11% in the lower hs-CRP group, although the p-value was not provided.

Hypertension, diabetes mellitus, and a positive family history of cardiovascular disease also demonstrate associations with elevated hs-CRP levels, though the differences were less pronounced. Specifically, 48% of those with hs-CRP > 3 mg/L had hypertension versus 7% with hs-CRP < 3 mg/L; 28% with hs-CRP > 3 mg/L had diabetes mellitus compared to 2% in the lower hs-CRP group; and 25% with hs-CRP > 3 mg/L had a positive family history versus 10% with hs-CRP < 3 mg/L. Notably, positive ECG findings were present in 55% of participants with high hs-CRP levels compared to 2% with low hs-CRP levels, although the p-value for this association was not specified. Similarly, elevated Troponin I levels were observed in 49% of those with high hs-CRP, compared to only 1% in the lower hs-CRP group.

Table 2: Correlation between hs-CRP and cardiovascular disease risk factors

Risk Factor	Hs-CRP < 3 mg/L (%)	Hs-CRP > 3 mg/L (%)	P Value
Sedentary Lifestyle	12	54	
Smoking	11	50	
Hypertension	7	48	
Diabetes Mellitus	2	28	<0.05
Positive Family History	10	25	
Positive ECG Findings	2	55	
Elevated Trop I	1	49	

Overall, these findings suggest that higher hs-CRP levels are associated with several cardiovascular risk factors, particularly a sedentary lifestyle and positive ECG findings, highlighting the potential role of hs-CRP as a marker for cardiovascular risk.

DISCUSSION
When comparing the distribution of high-sensitivity C-reactive protein (hs-CRP) levels with findings from other studies, the current research demonstrates that 33.33% of participants had hs-

CRP levels below 3 mg/L, while 66.67% exhibited levels above 3 mg/L. In comparison, studies conducted by Berk et al. [6], Gaud [7], and De Beer et al. [8] reported that 64.31%, 62.02%, and 60.20% of participants, respectively, had hs-CRP levels exceeding 3 mg/L. The mean age of patients in the present study is approximately 47.89 years, with a standard deviation of 9.45 years. In contrast, Rashidinejad et al. [9] observed a mean patient age of 60 years with a deviation of 11 years, and Chaithra et al. [10] reported a mean age of 54 years with a deviation of 12 years.

The current research also indicates a male predominance, with 78.05% of cardiovascular event patients being male. Similarly, the Framingham Heart Study [11] and Chaithra et al. [10] found male preponderance at 65% and 72%, respectively. Furthermore, this study reveals that 71.72% of smokers had elevated hs-CRP levels, while only 28.28% had hs-CRP levels below 3 mg/L. Comparable findings were reported by Danesh et al. [12], Saito et al. [13], and Ridker et al. [14], where 64.34%, 65.77%, and 68.81% of smokers, respectively, had hs-CRP levels exceeding 3 mg/L. A significant association was also observed between high hs-CRP levels and pre-existing hypertension, with 75.19% of hypertensive patients exhibiting hs-CRP levels above 3 mg/L, consistent with findings from Saito et al. [13] and Ridker et al. [14].

In this study, 90% of patients with pre-existing diabetes mellitus showed elevated hs-CRP levels. Similar results were found in studies by Saito et al. [13], Ridker et al. [14], Ford et al. [15], Freeman et al. [16], and Patel et al. [17], with 72.80%, 70.92%, 70.24%, 69.32%, and 68.44% of diabetic patients, respectively, exhibiting high hs-CRP levels. This research is among the few that investigate hs-CRP as an independent marker of cardiovascular events. Limited data from Framingham studies have suggested that hs-CRP, alongside other cardiac biomarkers such as Troponin I and Troponin T, is valuable for diagnosing and predicting outcomes in acute myocardial infarction (AMI) [11]. Additionally, hs-CRP holds prognostic value in patients without overt myocyte necrosis and remains significant during the stable phase following acute cardiovascular events [17,18].

While the present study underscores the importance of hs-CRP as a biomarker for cardiovascular events, further research involving a larger sample size is necessary to establish its precise significance. Limitations of this study include the absence of detailed clinical histories and the inability to conduct long-term follow-up, which was not feasible within the study's timeframe.

CONCLUSION
This cross-sectional study involved patients diagnosed with cardiovascular disease and individuals with established risk factors for cardiovascular events. The study revealed statistically significant elevated levels of high-sensitivity C-reactive protein (Hs-CRP) in patients with cardiovascular conditions. Consequently, Hs-CRP can be considered an independent biomarker for cardiovascular disease. A positive correlation was identified between elevated Hs-CRP levels and major traditional risk factors, including a sedentary lifestyle, smoking, hypertension, and diabetes mellitus.

REFERENCES

1. Van der Wal AC, Becker AE, van der Loos CM, Das PK. Site of intimal rupture or erosion of thrombosed coronary atherosclerotic plaques is characterized by an inflammatory process irrespective of the dominant plaque morphology. Circulation. 1994;89:36-44.
2. Pandya DB, Bhetariya B, Koitiya N. High-sensitivity C-reactive protein as a biomarker of cardiovascular events. Natl J Physiol Pharm Pharmacol. 2024;14(2):210-212.
3. Ross R. Cell biology of atherosclerosis. Annu Rev Physiol. 1995;57:791-804.
4. Berk BC, Weintraub WS, Alexander RW. Elevation of C-reactive protein in "active" coronary artery disease. Am J Cardiol. 1990;65:168-72.
5. Kuller LH, Tracy RP, Shaten J, Meilahn EN. 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;144:537-47.
6. Berk BC, Weintraub WS, Alexander RW. Elevation of C-reactive protein in "active" coronary artery disease. Am J Cardiol. 1990;65:168–72.
7. Gaud VA. Kothivale Thesis. Kanpur University, Estimation of hs-CRP Levels in ACS, a Cross Sectional Study; 2002.
8. De Beer FC, Hind CR, Fox KM, Allan RM, Maseri A, Pepys MB. Measurement of serum C-reactive protein concentration in myocardial ischaemia and infarction. Br Heart J. 1998;47:239-43.
9. Rashidinejad H, Hosseini SM, Moazenzadeh M, Azimzadeh BS, Mirzaeipour F, Fakhreddini K, et al. Relationship between serum level of high-sensitive C-reactive protein and extension of myocardial involvement in patients with acute myocardial infarction. Rom J Intern Med. 2012;50:211-5.
10. Chaithra SP, Harsha MM. High sensitive C-reactive protein in acute MI and its correlation with one year mortality. J Evol Med Dent Sci. 2013;29:5293-99.
11. Framingham Heart Study: A Project of National Heart, Lung and Blood Institute and Boston University. Available from: https://www.framinghamheartstudy.org [Last accessed on 2023 May 28].
12. Danesh J, Muir J, Wong YK, Ward M, Gallimore JR, Pepys MB. Risk factors for coronary heart disease and acute-phase proteins. A population-based study. Eur Heart J. 1999;20:954-9.
13. Saito M, Ishimitsu T, Minami J, Ono H, Ohrui M, Matsuoka H, et al. Relations of plasma high-sensitivity C-reactive protein to traditional cardiovascular risk factors. Atherosclerosis. 2003;167:73-90.
14. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Plasma concentration of C-reactive protein and risk of developing peripheral vascular disease. Circulation. 1998;97:425-8.
15. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: Findings from the third National Health and Nutrition Examination Survey. JAMA. 2002;287:356-9.
16. Freeman DJ, Norrie J, Caslake MJ, Gaw A, Ford I, Lowe GD, et al. C-reactive protein is an independent predictor of risk for the development of diabetes in the West of Scotland Coronary Prevention Study. Diabetes. 2002;51:1596-600.
17. Patel VB, Robbins MA, Topol EJ. C-reactive protein: A 'golden marker' for inflammation and coronary artery disease. Cleve Clin J Med. 2001;68:521-4, 527-34.

18. Blake GJ, Ridker PM. Inflammatory biomarkers and cardiovascular risk prediction. J Intern Med. 2002;252:283-94.