

## ORIGINAL ARTICLE

**CORRELATION OF DIASTOLIC BLOOD PRESSURE WITH HIGH SENSITIVITY C-REACTIVE PROTEIN IN MIDDLE AGED CORONARY HEART DISEASE PATIENTS****Nadia Haleem, Musarat Zahra\*, Ayesha Naureen Awan, Sarwat Abbasi, Alruba Taimoor\*\*, Matiullah Khan\*\*\***

Department of Biochemistry, Ayub Medical College, Abbottabad, \*Department of Physiology, Gajju Khan Medical College, Swabi, \*\*Department of Physiology, \*\*\*Cardiology, Ayub Medical College, Abbottabad, Pakistan

**Background:** C-reactive protein is a plasma protein used to determine the levels of inflammation inside our body. There are low levels of C-reactive protein (CRP) in our blood but moderate to severe elevated levels can be seen in bacterial infections and any other autoimmune diseases. Hypertension is considered to be the significant risk factor in coronary heart disease (CHD). The objective of this study was to determine the correlation of high sensitivity C-reactive protein with diastolic blood pressure (DBP) in middle aged individuals with CHD. **Methods:** This was a descriptive cross-sectional study conducted among two groups, i.e., coronary heart disease (n=100) and control (n=50). Their CRP levels as well as two readings of diastolic blood pressure were taken. Data were entered and analysed on SPSS-23. **Results:** Mean diastolic blood pressure in control group was 81.60±9.87 mmHg and it was 92.15±17.14 mmHg in hypertensive patients showing significant differences ( $p<0.01$ ) between the DBP of normal and hypertensive patients. The coefficient of correlation between hs-CRP and mean DBP below 90 mmHg was 0.263 ( $p<0.001$ ), and it was 0.070 in patients with elevated DBP above 90 mmHg which was not significant ( $p>0.05$ ). **Conclusion:** There is a strong association of high sensitivity C-reactive protein with DBP in middle aged CHD patients. Elevated hs-CRP can be used as a tool for early indication/prediction of developing hypertension in future.

**Keywords:** Diastolic blood pressure, Coronary heart disease, CHD, High sensitivity C-reactive protein, Cardiovascular disease, Blood pressure

Pak J Physiol 2024;20(2):3–6, DOI: <https://doi.org/10.69656/pjp.v20i2.1650>**INTRODUCTION**

C-reactive protein, discovered by two scientists, Tillet and Francis in 1930, is a highly conserved plasma protein.<sup>1</sup> It was discovered accidentally when these two scientists were investigating and observing the serum samples of pneumococcal infected patients. They named it because this protein basically reacts with the capsular C polysaccharide of pneumococcal bacteria.<sup>1</sup> C-reactive protein is basically homo-pentameric and has a calcium binding site specific for phosphocholine (PCH). Regulation of C-reactive protein (CRP) expression mainly takes place at the transcriptional level with the principle inducer of the gene, i.e., interleukin-6 and takes place during the acute phase reaction. The topology, crystal structure and chemical composition of its ligand binding to the C-reactive protein has been determined precisely.<sup>2</sup> The native Pentameric form of C-reactive protein is considered as an acute phase reactant. Its serum expression increases in inflammatory diseases. A modified version of CRP (monomeric CRP) was identified by immunohistochemistry which gives us the significant tissue binding insoluble modified form of m-CRP.<sup>3</sup>

Synthesis of CRP primarily takes place in liver hepatocytes. It may be synthesized by smooth muscle cells, endothelial cells, adipocytes, lymphocytes and macrophages. Evidence suggests that oestrogen taken in

the form of human replacement therapy may influence and affects the level of C-reactive protein in elderly individuals. It is traditionally considered a noble marker of infection and cardiovascular events. It is evident that CRP plays a vital role in inflammatory reaction and may be involved in host response to infections, i.e., complement pathway, phagocytosis, and apoptosis, release of nitric oxide, specifically interleukin-6 and TNF- $\alpha$ .<sup>4</sup>

Diastolic blood pressure is defined as disappearance of the fifth Korotkoff sound, or by the fourth sound if the fifth sound is persistent.<sup>5</sup> Increased blood pressure is a well-known and well-established cause of coronary artery disease and the risk be reduced by lowering the levels of blood pressure.<sup>6,7</sup> Elevated tangential fluid stress at arterial endothelial surface is the most important source of coronary collateral circulation. Most of the coronary circulation occurs in diastole.<sup>8</sup>

Cardiovascular diseases, including ischemic heart disease and stroke are the leading cause of premature mortality and morbidity.<sup>9</sup> According to a study conducted in Pakistan, Bangladesh, and India, the South Asia has the highest number of mortality and disability-adjusted life years among major geographic regions of the world.<sup>10</sup> Studies have shown that elevated levels of high sensitivity C-reactive protein (hs-CRP) are associated with increased inflammation, which can

contribute to development and progression of CHD.<sup>11,12</sup>

Inflammation within the arterial walls can lead to atherosclerosis, a condition characterized by the build-up of plaque that can restrict blood flow to the heart. Monitoring hs-CRP levels can provide valuable insights into the inflammatory processes underlying cardiovascular diseases.<sup>13,14</sup>

Diastolic blood pressure is an essential component of overall blood pressure regulation and cardiovascular function.<sup>15,16</sup> High diastolic blood pressure level of  $\geq 90$  mmHg can indicate increased resistance in the arteries, which can strain the heart and increase the risk of heart disease.<sup>17</sup> The 2017 American College of Cardiology/American Heart Association guidelines has also highlighted the significance of isolated diastolic hypertension (IDH) as a risk factor for cardiovascular disease (CVD) particularly for myocardial infarction and CVD death.<sup>18</sup>

Understanding how diastolic blood pressure interacts with hs-CRP levels in middle-aged patients with coronary heart disease can offer valuable information on the combined impact of inflammation and blood pressure on cardiovascular health outcomes.

By exploring the intricate relationship between diastolic blood pressure and hs-CRP this specific demographic study aimed to uncover potential mechanisms linking inflammation, blood pressure regulation, and coronary heart disease. This deeper understanding can pave the way for more targeted interventions and personalized treatment strategies to improve outcomes for middle-aged patients with coronary heart disease.

## MATERIAL AND METHODS

This cross-sectional study was carried out at Ayub Medical Complex, Abbottabad. The research data was collected and analysed using the Pearson product moment correlation on SPSS-23. Tests were done in a well-equipped laboratory of Biochemistry Department of Ayub Medical College Abbottabad in Aug–Dec 2022. Sample size (n=150) was determined using online OpenEpi (OpenEpi.com) sample size calculator with the formula ( $n=4PQ/25$ ) where ‘n’ is the sample size to be calculated, P=expected percentage of the variable and  $q=(100-p)$ . One hundred cases of coronary heart disease and 50 control healthy middle-aged individuals of age group 40–60 years, including both males and females were included. Relationship of two biochemical parameters, i.e., diastolic blood pressure with high-sensitivity C-reactive protein was considered and studied thoroughly in the form of scatter diagram. This study received clearance from the hospital ethical review committee.

Measurements of systolic and diastolic blood pressures in both control and individuals having coronary events were taken with standardized methods,

using a mercury sphygmomanometer and a standard arm cuff. Blood pressure values were reported in millimetres of mercury. Before going through the process, all subjects under study were relaxed mentally and physically. At least two readings were taken at interval of 10 minutes and their mean was recorded.

The serum high-sensitivity C-reactive protein was determined by two CLIA strip reader (model-4100) using the immunoenzymometric chemiluminescence assay. The blood specimen of 5 ml from every subject was collected in a plain vacutainer tube. High-speed centrifugation was done in the centrifuge machine to get serum which was refrigerated at 2–8 °C for at least five days. Serum C-reactive protein levels analysis was done on samples. The sensitive assaying methodologies were done routinely. Patient and control specimens and calibrator were added and mixed to streptavidin coated well. Enzymes labelled antibodies were added to biotinylated monoclonal antibodies. Mixed them well and reaction between CRP antibodies and native CRP took place. The complex united with streptavidin coated well. After completion of conjugation period, the enzyme CRP antibody bound conjugate detached from unbound enzyme. The enzyme activity was quantified with a suitable substrate to produce light.

## RESULTS

Mean diastolic blood pressure in control group was  $81.60 \pm 9.87$  mmHg and it was  $92.15 \pm 17.14$  mmHg in hypertensive patients showing significant differences ( $p < 0.01$ ) between the DBP of normal and hypertensive patients (Table-1).

The coefficient of correlation between hs-CRP and mean DBP below 90 mmHg was 0.263 ( $p < 0.001$ ), and it was 0.070 in patients with elevated DBP above 90 mmHg which was not significant ( $p > 0.05$ ) (Table-2).

**Table-1: Mean Diastolic Blood Pressure of study groups**

Variables	Patients (n=100)	Controls (n=50)	P
DBP-1 (mm Hg)	96.95±17.87	82.20±12.00	<0.01
DPB-2 (mm Hg)	89.41±13.40	81.30±7.88	<0.01
Mean DPB (mm Hg)	92.14±17.14	81.60±9.87	<0.01

**Table-2: Correlation of CRP with diastolic blood pressure in coronary artery disease and controls**

Y axis vs X-axis	Coefficient of correlation	p
CRP vs Mean DBP (below 90 mmHg)	0.263	<0.001
CRP vs Mean DBP (above 90 mmHg)	0.070	0.622

## DISCUSSION

Our study confirms a significant association between hs-CRP and DBP in coronary heart disease patients. Hypertension is a known risk factor for coronary pathologies in association with the inflammatory processes that are involved in the pathogenesis of CHD.

C-reactive protein is commonly used as acute phase marker in these coronary events. Previous studies confirm the association between hs-CRP and the increased risk of CHD in middle aged and elderly individuals with hyperuricaemia.<sup>19</sup> Liu Y *et al*<sup>20</sup> also confirmed the correlation amongst high sensitivity C-reactive protein and the seriousness of CAD. It was also proved that high sensitivity-CRP is a biomarker in hypertensive patients.<sup>20</sup> The correlation between hs-CRP and age is not clear, while hypertension and age are interrelated as evidenced by the study which determines the relationship between hs-CRP and age, body mass index and blood pressure in middle aged individuals. The study shows a positive correlation among high sensitivity-CRP, blood pressure including both systolic and diastolic blood pressure and body mass index but no relationship was found between age and high sensitivity CRP levels.<sup>21</sup>

Decreased nitric acid production in the endothelial cells may cause increased interleukin levels of CRP which leads to increased production of endothelin and causes vasoconstriction. Hence, hypertension along with inflammatory processes may lead to more dangerous left ventricular hypertrophy which results in sudden cardiac death.<sup>22</sup>

Bautista *et al*<sup>23</sup> assessed circulating CRP levels in 300 patients of  $\geq 30$  years age and concluded that the prevalence of hypertension was 46% in their cases. They concluded that adjusted and unadjusted prevalence of hypertension was 58.7% in the highest quartile of CRP and 34.7% in the lowest quartile of CRP. At 95% confidence interval (CI) the prevalence was found to be 1.14, 1.58, and 0.82 ( $p=0.442$ ). They suggested for the first time that CRP level is an independent risk factor for the development of hypertension. As this was a cross sectional study, their finding might be confirmed by a prospective cohort study to be helpful in elucidating the role of CRP in the diagnosis, prediction, and management of hypertension.<sup>23</sup>

Chuang SY *et al*<sup>24</sup> suggested that CRP predicts systolic blood pressure (SBP) and pulse pressure (PP) but not diastolic blood pressure. They concluded that inflammation was related to future systolic blood pressure and associated with cardiovascular events and mortality. They did not find significant association with DBP. They enrolled 2,113 subjects in his study, mostly non-diabetic adults having normal blood pressure. During the follow-up period of a median of 3 years, about 145 participants developed hypertension suggesting that CRP is predictive of hypertension having association with PP and SBP, but not with DBP.<sup>24</sup>

In another study, Bautista *et al*<sup>25</sup> evaluated association between CRP and hypertension in 904 healthy participants aged 39–50 years. This was basically a case-control study with inclusion criteria of

SBP  $\geq 140$  mmHg and DBP  $\geq 90$  mmHg (120 cases and 784 controls). Their subjects in the highest CRP quartile were 2.35 times more likely to develop hypertension than those in the lowest quartile ( $p=0.03$ ). They concluded that there was consistent independent association between serum CRP and elevated BP.<sup>25</sup>

Liu HH *et al*<sup>26</sup> presumed the combined effects of high sensitivity CRP and hypertension on coronary severity and cardiovascular outcomes. There were 7,325 participants in their study with angina-like chest pain, and had undergone coronary angiography, 4,291 were stable participant with newly diagnosed coronary heart disease, and all were followed for occurrence of coronary events. They found that cardiovascular event risk was significantly increased in participants with high CRP and hypertension ( $p<0.05$ ).<sup>26</sup>

Chen B *et al*<sup>27</sup> explored the association between hs-CRP and hypertension in Chinese adults. In that prospective cohort study, adult participants who had no hypertension in 2009 were followed up to 2015. Their study revealed a weak positive correlation between CRP and future incidence of hypertension.<sup>27</sup>

## CONCLUSION

There is a strong association of C-reactive protein with DBP in middle aged coronary heart disease patients. Hypertensive people, especially with increased DBP, have elevated serum CRP which can be used as a tool for early indication/prediction of developing hypertension in future.

## REFERENCES

1. Plebani M. Why C-reactive protein is one of the most requested tests in clinical laboratories? *Clin Chem Lab Med* 2023;61(9):1540–5.
2. Miura D, Motohashi S, Goto A, Kimura H, Tsugawa W, Sode K, *et al*. Rapid and convenient single-chain variable fragment-employed electrochemical c-reactive protein detection system. *Int J Mol Sci* 2024;25(5):2859.
3. Slevin M, Matou-Nasri S, Turu M, Luque A, Rovira N, Badimon L, *et al*. Modified C-reactive protein is expressed by stroke neovessels and is a potent activator of angiogenesis in vitro. *Brain Pathol* 2010;20(1):151–65.
4. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. *Front Immunol* 2018;9:754.
5. Daskalopoulou SS, Rabi DM, Schiffrin EL, Feldman RD, Padwal RS, Tremblay G, Khan NA; Hypertension Canada. Hypertension Guidelines in the United States and Canada: Are we getting closer? *Hypertension* 2018;71(6):976–8.
6. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, *et al*. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet* 2016;387(10022):957–67.
7. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, *et al*. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013;34(28):2159–219.
8. Shu W, Jing J, Fu LC, Min JT, Bo YX, Ying Z, *et al*. The relationship between diastolic pressure and coronary collateral

- circulation in patients with stable angina pectoris and chronic total occlusion. *Am J Hypertens* 2013;26(5):630–5.
9. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, *et al*. Global burden of cardiovascular diseases and risk factors, 1990–2019: Update from the GBD 2019 study. *J Am Coll Cardiol* 2020;76(25):2982–3021.
  10. Crea F. The burden of cardiovascular risk factors: a global perspective. *Eur Heart J* 2022;43(30):2817–20.
  11. Gao Y, Wang M, Wang R, Jiang J, Hu Y, Wang W, *et al*. The predictive value of the hs-CRP/HDL-C ratio, an inflammation-lipid composite marker, for cardiovascular disease in middle-aged and elderly people: evidence from a large national cohort study. *Lipids Health Dis* 2024;23(1):66.
  12. Aziz D, Imdad KM, Afraa Z. Association of high sensitivity c-reactive protein (Hs-CRP) with poor glycaemic control and coronary heart disease in type 2 diabetes mellitus. *Res J Pharm Technol* 2023;16(1):193–9.
  13. Guo X, Ma L. Inflammation in coronary artery disease-clinical implications of novel HDL-cholesterol-related inflammatory parameters as predictors. *Coron Artery Dis* 2023;34(1):66–77.
  14. Attiq A, Afzal S, Ahmad W, Kandeel M. Hegemony of inflammation in atherosclerosis and coronary artery disease. *Eur J Pharmacol* 2024;176338.
  15. Mohammadnia N, Opstal TSJ, El Messaoudi S, Bax WA, Cornel JH. An update on inflammation in atherosclerosis: how to effectively treat residual risk. *Clin Ther* 2023;45(11):1055–9.
  16. Akimova NS, Shvarts YG, Mikhel ND, Kiselev AR, Ledvanova TY, Konshina LE, *et al*. The severity of chronic heart failure and the parameters of daily blood pressure profile in patients with coronary heart disease. *Explor Med* 2024;5(1):101–11.
  17. Civieri G, Kerkhof PLM, Montisci R, Iliceto S, Tona F. Sex differences in diagnostic modalities of coronary artery disease: Evidence from coronary microcirculation. *Atherosclerosis* 2023;384:117276.
  18. Yano Y, Kim HC, Lee H, Azahar N, Ahmed S, Kitaoka K, *et al*. Isolated diastolic hypertension and risk of cardiovascular disease: controversies in hypertension-pro side of the argument. *Hypertension* 2022;79(8):1563–70.
  19. Xie M, Xie D, Yang Y, Zhang Y, Li K, Zhou B, *et al*. Association of high-sensitivity C-reactive protein in middle-aged and elderly Chinese people with hyperuricaemia and risk of coronary heart disease: a cross-sectional study. *BMJ Open* 2019;9(10):e028351.
  20. Liu Y, Jia SD, Yao Y, Tang XF, Xu N, Jiang L, *et al*. Impact of high-sensitivity C-reactive protein on coronary artery disease severity and outcomes in patients undergoing percutaneous coronary intervention. *J Cardiol* 2020;75(1):60–5.
  21. Zhao H, Lu Y, Niu J, Bian H, Kuang X. Age-independent association between high-sensitivity C-reactive protein and blood pressure in middle aged adults. *Vojnosani Pregl* 2023;80(11):915–20.
  22. Kurl S, Jae SY, Voutilainen A, Mäkikallio T, Laukkanen JA. Joint effect of blood pressure and C-reactive protein and the risk of sudden cardiac death: A prospective cohort study. *Int J Cardiol* 2021;326:184–8.
  23. Bautista LE, López-Jaramillo P, Vera LM, Casas JP, Otero AP, Guaracao AI. Is C-reactive protein an independent risk factor for essential hypertension? *J Hypertens* 2001;19(5):857–61.
  24. Chuang SY, Hsu PF, Chang HY, Bai CH, Yeh WT, Pan HW. C-reactive protein predicts systolic blood pressure and pulse pressure but not diastolic blood pressure: the cardiovascular disease risk factors two-township study. *Am J Hypertens* 2013;26(5):657–64.
  25. Bautista LE, Atwood JE, O'Malley PG, Taylor AJ. Association of C-reactive protein and hypertension in healthy middle aged men and women. *Coron Artery Dis* 2004;15(6):331–6.
  26. Liu HH, Cao YX, Sun D, Jin JL, Zhang HW, Guo YL, *et al*. High sensitivity C-reactive protein and hypertension: combined effects on coronary severity and cardiovascular outcomes. *Hypertens Res* 2019;42(11):1783–93.
  27. Chen B, Cui Y, Lei M, Xu W, Yan Q, Zhang X, *et al*. C-reactive protein levels in relation to incidence of hypertension in Chinese adults: longitudinal analysis from the China health and nutrition survey. *Int J Hypertens* 2021;2021:Article ID 3326349.

### Address for Correspondence:

**Dr. Alruba Taimoor**, Assistant Professor, Department of Physiology, Ayub Medical College, Abbottabad, Pakistan.  
Cell: +92-323-9841515  
Email: medicolodhi@outlook.com

Received: 20 Mar 2024

Reviewed: 13 Apr 2024

Accepted: 24 Apr 2024

### Contribution of Authors:

**NH:** Substantial contributions to the conception and deigning of work, analysis and data interpretation

**MZ:** Drafting of work, revising critically for important intellectual contents

**ANA:** final approval of version to be published

**SA:** Agreement to be accountable for all accepts of the work ensuring that question related accuracy

**AT:** Drafting the work and reviewing critically and proofreading

**MK:** Drafting the work and reviewing critically and proofreading

**Conflict of interest:** It is declared by the authors that there is no conflict of interest regarding the publication of this article.

**Funding:** Didn't receive any financial support.