e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(12); 691-695

Original Research Article

A Study to Investigate the Association of CRP with Systolic and Diastolic Blood Pressure: A Case Control Study

Suman[1], Robina Shamim[2], Jyoti Priya[3], Rita Kumari[4]

[1]Tutor, Department of Physiology, Nalanda Medical College, Patna, Bihar, India

[2]Tutor, Department of Physiology, Nalanda Medical College, Patna, Bihar, India

[3]Assistant Professor, Department of Physiology, Nalanda Medical College, Patna, Bihar, India

[4]Professor and HOD, Department of Physiology, Nalanda Medical College, Patna, Bihar, India

Received: 19-10-2023 Revised: 14-11-2023 / Accepted: 22-12-2023
Corresponding Author: Dr. Robina Shamim
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to evaluate the CRP levels of hypertensive cases with respect to that of normotensive controls and to investigate the association of CRP with systolic and diastolic blood pressure.

Methods: A cross-sectional case-control study was carried out on 75 hypertensive and 75 normotensive subjects at Nalanda Medical College, Patna, Bihar, India. Both genders were included in the study. The cases were randomly sampled from the patients visiting our hospital, whereas the controls mostly belonged to our hospital staff members.

Results: The hypertensive and normotensive groups were age and sex-matched, and data represented as mean ± SD. Systolic blood pressure, diastolic blood pressure and CRP levels were all significantly higher in the hypertensive cases than the normotensive controls. CRP levels were positively correlated and significant with both systolic blood pressure and diastolic blood pressure.

Conclusion: CRP levels which are an extensively and widely used inflammatory marker may be used to detect high risk hypertensive patients and help prevent complications of hypertension such as arrhythmias and sudden cardiac death. Especially developing countries like India should realize and acknowledge its value in screening, risk prediction and prognosis of hypertension.

Keywords: CRP levels, high sensitivity-CRP, hs-CRP, systolic blood pressure, diastolic blood pressure, hypertension, hypertensive, normotensive

Introduction

A Hypertension is a commonly occurring, readily detectable disease. Arterial hypertension is a silent killer and major risk factor for atherosclerosis, coronary artery disease, stroke, kidney failure. [1,2] The prevalence of hypertension in the early twentieth century varied in India, ranging from 2-15% in Urban India and 2-8% in Rural India. In the INTERHEART and INTERSTROKE study, hypertension accounted for 17.9% and 34.6% of population attributable risk for coronary artery disease and stroke respectively. CRP appears in serum in response to a variety of inflammatory stimuli. Raised level of hs-CRP is seen with increasing with age, during an infection, inflammation, coronary artery diseases, obesity, sepsis, smoking and vasculitis. Chronic vascular inflammation plays a role in initiation and the development of essential hypertension either as pathogenic or secondary event. Inflammatory mediators such as CRP, IL-1β, IL-6, TNF–α and reactive oxygen species have been proposed to contribute essential hypertension through several mechanism including enhancement of arterial stiffness, endothelial dysfunction. [3]

Increasing evidence supports a relationship between C-reactive protein (CRP) levels and cardiovascular disease and mortality [4-6], sudden cardiac death[5] and stroke. [7] CRP is an acute phase protein that conveniently serves as an in vivo bioassay to gauge the overall degree of inflammation. Elevated CRP has also emerged as a non-traditional risk factor for adverse cardiovascular outcomes, though its contribution to predicting cardiovascular disease outcomes is less impressive after traditional risk factors have been considered. [8,9] Hypertension is associated with elevated CRP [10] and among normotensive subjects, elevated CRP predicts future risk of hypertension. [11] CRP is correlating more with systolic and pulse pressure, rather than with

diastolic blood pressure, even in treatment naive patients. This relationship may reflect underlying atherosclerosis [12] as elevated CRP also correlates with measures of arterial wave reflection and stiffness. [13] Low CRP values, along with normal BNP levels, predict the absence of left ventricular hypertrophy (LVH) among hypertensive individuals. [14]

The available data on the effect of anti-hypertensives from different classes on CRP is limited to mostly small trials. Some [15,16] but not all [17,18] studies report lower CRP values with either angitensin converting enzyme inhibitors or angiotensin receptor blockers. To date, there is only one large, community-based study reporting on the relationship between antihypertensive medication class and CRP. Recently, Palmas et al reported an association of beta-blocker use with lower CRP values, based on the baseline cohort exam from the Multi-Ethnic Study of Atherosclerosis (MESA). [19]

The aim of the present study was to evaluate the CRP levels of hypertensive cases with respect to that of normotensive controls and to investigate the association of CRP with systolic and diastolic blood pressure.

Materials and Methods

A cross-sectional case-control study was carried out on 75 hypertensive and 75 normotensive subjects at Nalanda Medical College, Patna, Bihar, India. Both genders were included in the study. The cases were randomly sampled from the patients visiting our hospital, whereas the controls mostly belonged to our hospital staff members. Both groups were age and sex matched. Inclusion criteria: The hypertensive group consisted of those having Systolic BP (SBP) >140mm of Hg and/or Diastolic BP (DBP)> 90mm of Hg or those taking anti-hypertensive medications. All cases were on regular anti- hypertensive treatment. Even if the BP was under control due to the anti-hypertensives, they were still considered as hypertensive cases. The normotensive group consisted of those having SBP<140mmHg and DBP<90mmHg and those who were earlier neither diagnosed as hypertensive nor were under any BP lowering medications. The subjects were in the age group of 35-45 years so that to reduce coexisting diseases.

Exclusion Criteria: Smokers, alcoholics, tobacco chewers and those suffering from diabetes mellitus or any active/chronic infections, inflammations, neoplastic disorders, liver disease, thyroid disorders were excluded from the study. Also those on antibiotics, anti- inflammatory, corticosteroids, postmenopausal hormone replacement therapy and subjects with CRP > 10 mg/dl were excluded. Prior necessary approvals were obtained from the Institutional Ethical Committee. The details and purpose of the study was explained to the subjects and their doubts clarified. Further it was stated that their confidentiality would be maintained. Informed written consents were obtained from all subjects. Resting supine blood pressure was recorded using a mercury sphygmomanometer from the participants. Palpatory method (reappearance of radial pulse) was used to know the approximate systolic blood pressure. Auscultatory method provided the systolic blood pressure (phase I of Korotkoff sounds) and diastolic blood pressure (phase IV/ V of Korotkoff sounds). Three recordings with 2 minute interval were obtained and the average was considered for analysis. CRP levels were obtained by using high sensitivity CRP (hs CRP) assay kits. Statistical Package for Social Sciences (SPSS 20) was used to analyze the data. Mean±SD was used to represent continuous data. It was implied to be statistically significant for standard P<0.05. Independent Samples t-test and Pearson's correlation were used in analyzing the data.

Results

Table 1: Comparison of systolic and diastolic blood pressure and CRP levels of hypertensive cases and normotensive controls

Measured variable	Hypertensive Cases (n=75)	Normotensive Controls (n=75)	P value
Systolic BP (mm Hg)	154.16±17.93	111.9±6.64	<0.001
Diastolic BP (mm Hg)	94.76±8.72	72.4±7.83	<0.001
C-reactive protein(CRP) (mg/L)	1.52±1.08	0.74±0.16	<0.001

The hypertensive and normotensive groups were age and sex-matched, and data represented as mean ± SD. Systolic blood pressure, diastolic blood pressure and CRP levels were all significantly higher in the hypertensive cases than the normotensive controls.

Table 2: Correlation of C-reactive protein (CRP) levels with blood pressure (BP)

	Correlation coefficient (R value)	P value
Systolic BP	0.2442	<0.05
Diastolic BP	0.4337	<0.001

CRP levels were positively correlated and significant with both systolic blood pressure and diastolic blood pressure.

Discussion

Hypertension is a major health concern prevalent worldwide. It is one of the foremost significant causes of morbidity and mortality globally. It is a vital health challenge particularly in developing countries like India. [20] It has been reported that in India, one in three are inclined to develop hypertension. [21] CRP is an acute phase reactant produced by the liver consequent to stimulation by Interleukin-6. Hypertension has also been viewed as an inflammatory disorder. Inflammation propels activity of neuro-humoral factors causing non-structural cardiac abnormalities, which in turn can lead to prolonged ventricular repolarization. [22] C-reactive protein (CRP) is considered to be an index of systemic inflammation. Earlier studies have shown increased CRP levels in hypertensive patients, while other studies suggested increased CRP to increase the risk of developing hypertension. [23] Increased levels of CRP is said to cause endothelial dysfunction. It increases the production of endothelin-1 and reduces nitric oxide production resulting in vasoconstriction and consequent hypertension. [24]

The hypertensive and normotensive groups were age and sex-matched, and data represented as mean ± SD. Systolic blood pressure, diastolic blood pressure and CRP levels were all significantly higher in the hypertensive cases than the normotensive controls. CRP levels were positively correlated and significant with both systolic blood pressure and diastolic blood pressure. The critical causal role of inflammation and CRP in developing hypertension has been established.[24] IL-6 and CRP are markers for inflammation. Increased IL-6 and CRP levels lead to vascular endothelial dysfunction with decreased nitric oxide production and vasoconstriction. Moreover has pro-thrombotic and pro-atherosclerotic characteristics and influences the renin-angiotensin mechanisms. All these contribute to the pathogenesis of hypertension. [25-27]

Hypertension leads to cardiovascular autonomic imbalances. The autonomic imbalance in hypertension affects the inflammatory modulatory process thereby increasing the CRP levels. [28] CRP being an inflammatory marker causes adverse autonomic tone disparity, especially by increasing the sympathetic tone and also by causing changes in the calcium and/or potassium conductance. [29] And inflammation and CRP may release neuro-endocrine factors causing non-structural cardiac modifications It has also been recommended that drugs lowering CRP be developed and used to prevent and treat at-risk hypertensive patients. However there have been objections to this that CRP may be in confounding associations with other factors. A previous study has also shown the dietary fiber benefits in lowering inflammatory cytokines and thus CRP levels. [30]

Beta blockers and diuretics have already shown to affect the CRP levels. [31] CRP levels may be altered by BP lowering drugs and the number of and combination of these drugs. Future studies should study the role played by CRP in the pathogenesis of arteriosclerosis since coronary heart disease and cerebrovascular disease contribute to significant morbidity and mortality. Likewise interleukin 6 (IL-6) may be studied along with CRP levels. Similar studies should also be done in type 2 diabetes and metabolic syndrome patients.

Conclusion

CRP levels which are an extensively and widely used inflammatory marker may be used to detect high risk hypertensive patients and help prevent complications of hypertension such as arrhythmias and sudden cardiac death. Especially developing countries like India should realize and acknowledge its value in screening, risk prediction and prognosis of hypertension.

References

1. Fuster V. Lewis A. Conner Memorial Lecture. Mechanisms leading to myocardial infarction: insights from studies of vascular biology. Circulation. 1994 Oct;90(4):2126-46.
2. Joensuu T, Salonen R, Winblad I, Korpela H, Salonen JT. Determinants of femoral and carotid artery atherosclerosis. J Intern Med. 19 94 Jul;236(1):79-84.
3. Boos CJ, Lip GY. Is hypertension an inflamm atory process? Curr Pharm Des. 2006; 12(13): 1623-35.
4. Ridker PM, Hennekens CH, Buring JE, Rifai N. C-reactive protein and other markers of inflammation in the prediction of cardiov-ascular disease in women. New Engl J Med. 20 00;342(12):836–843.
5. Albert CM, Ma J, Rifai N, Stampfer MJ, Ridker PM. Prospective study of C-reactive protein, homocysteine, and plasma lipid levels as predictors of sudden cardiac death. Circul-ation. 2002;105(22):2595–2599.
6. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, Joshipura K, et al. Inflammatory markers and the risk of coronary heart disease in men and women. New Engl J Med. 2004;51(25):2599–2610.
7. Ford ES, Giles WH. Serum C-reactive protein and self-reported stroke: findings from the Third National Health and Nutrition Examination Survey. Arterioscl Thromb Vasc Biol. 2000;20(4):1052–1056.
8. Shlipak MG, Fried LF, Cushman M, Manolio TA, Peterson D, Stehman-Breen C, et al.

Cardiovascular mortality risk in chronic kidney disease: comparison of traditional and novel risk factors. JAMA. 2005;293(14):1737–1745.
9. Wang TJ, Gona P, Larson MG, Tofler GH, Levy D, Newton-Cheh, et al. Multiple biomarkers for the prediction of first major cardiovascular events and death. New Engl J Med. 2006;355(25):2631–2639.
10. Bautista LE, Lopez-Jaramillo P, Vera LM, Casas JP, Otero AP, Guaracao AI. Is C-reactive protein an independent risk factor for essential hypertension? J Hypertension. 2001; 19:857–861.
11. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. JAMA. 2003;290(22):2945–2951.
12. Schillaci G, Pirro M, Gemelli F, Pasqualini L, Vaudo G, Marchesi S, et al. Increased C-reactive protein concentrations in never-treated hypertension: the role of systolic and pulse pressures. J Hypertension. 2003;21(10):1841–1846. [PubMed] [Google Scholar]
13. Kullo IJ, Seward JB, Bailey KR, Bielak LF, Grossardt BR, Sheedy PF, 2nd., et al. C-reactive protein is related to arterial wave reflection and stiffness in asymptomatic subjects from the community. Am J of Hypertens. 2005;18(8):1123–1129.
14. Conen D, Zeller A, Pfisterer M, Martina B. Usefulness of B-type natriuretic peptide and C-reactive protein in predicting the presence or absence of left ventricular hypertrophy in patients with systemic hypertension. Am J Card. 2006;97(2):249–252.
15. Manabe S, Okura T, Watanabe S, Fukuoka T, Higaki J. Effects of angiotensin II receptor blockade with valsartan on pro-inflammatory cytokines in patients with essential hypertension. J Cardiovasc Pharm. 2005;46 (6):735–739.
16. Amar J, Ruidavets JB, Peyrieux JC, Mallion JM, Ferrieres J, Safar ME, et al. C-reactive protein elevation predicts pulse pressure reduction in hypertensive subjects. Hypertension. 2005;46(1):151–155.
17. Fliser D, Buchholz K, Haller H. For the European trial on olmesartan and pravastatin in inflammation and atherosclerosis (EUTOPIA) Investigators. Antiinflammatory effects of angiotensin II subtype 1 receptor blockade in hypertensive patients with microinflammation. Circulation. 2004;110:1103–1107.
18. Schram MT, van Ittersum FJ, Spoelstra-de Man A, van Dijk RA, Schalkwijk CG, Ijzerman RG, et al. Aggressive antihypertensive therapy based on hydrochlorothiazide, candesartan or lisinopril as initial choice in hypertensive type II diabetic individuals: effects on albumin excretion, endothelial function and inflammation in a double-blind, randomized clinical trial. J Hum Hypertens. 2005;19:429–437.
19. Palmas W, Ma S, Psaty B, Goff DC Jr, Darwin C, Barr RG. Antihypertensive medications and C-reactive protein in the multi-ethnic study of atherosclerosis. Am J Hypertens. 2007 Mar;20 (3):233-41.
20. Solanki JD, Gadhavi BP, Makwana AH, Mehta HB, Shah CJ, Gokhale PA. Early screening of hypertension and cardiac dysautonomia in each hypertensive is needed-inference from a study of QTc interval in Gujarat, India. International Journal of Preventive Medicine. 2018;9.
21. Solanki JD, Gadhavi BP, Makwana AH, Mehta HB, Shah CJ, Gokhale PA. QTc interval in young Gujarati hypertensives: Effect of disease, antihypertensive monotherapy, and coexisting risk factors. Journal of Pharmac-ology and Pharmacotherapeutics. 2016 Dec;7 (4):165-70.
22. Lazzerini PE, Acampa M, Capecchi PL, Hammoud M, Maffei S, Bisogno S, Barreca C, Galeazzi M, Laghi-Pasini F. Association between high sensitivity C-reactive protein, heart rate variability and corrected QT interval in patients with chronic inflammatory arthritis. European journal of internal medicine. 2013 Jun 1;24(4):368-74.
23. Smith GD. Association of C-reactive problem with blood pressure and hypertension-Life course confounding and Mendelian randomization tests of causality (vol 25, pg 1051,2005). ARTERIOSCLEROSIS THRO - MBOSIS AND VASCULAR BIOLOGY. 2005 Aug 1;25(8):E129-.
24. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. Jama. 2003 Dec 10;290(22):2945-51.
25. Verma S, Wang CH, Li SH, Dumont AS, Fedak PW, Badiwala MV, Dhillon B, Weisel RD, Li RK, Mickle DA, Stewart DJ. A self-fulfilling prophecy: C-reactive protein attenuates nitric oxide production and inhibits angiogenesis. Circulation. 2002 Aug 20;106 (8):913-9.
26. Venugopal SK, Devaraj S, Yuhanna I, Shaul P, Jialal I. Demonstration that C-reactive protein decreases eNOS expression and bioactivity in human aortic endothelial cells. Circulation. 2002 Sep 17;106(12):1439-41.
27. Verma S, Li SH, Badiwala MV, Weisel RD, Fedak PW, Li RK, Dhillon B, Mickle DA. Endothelin antagonism and interleukin-6 inhibition attenuate the proatherogenic effects of C-reactive protein. Circulation. 2002 Apr 23 ;105(16):1890-6.
28. Medenwald D, Kors JA, Loppnow H, Thiery J, Kluttig A, Nuding S, Tiller D, Greiser KH, Werdan K, Haerting J. Inflammation and prolonged QT time: results from the

Cardiovascular Disease, Living and Ageing in Halle (CARLA) study. PloS one. 2014 Apr 25 ;9(4):e95994.
29. Rohde LE, Hennekens CH, Ridker PM. Survey of C-reactive protein and cardiovascular risk factors in apparently healthy men. The American journal of cardiology. 1999 Nov 1; 84(9):1018-22.
30. King DE, Mainous III AG, Egan BM, Woolson RF, Geesey ME. Fiber and C-reactive protein in diabetes, hypertension, and obesity. Diabetes care. 2005 Jun 1;28(6):1487-9.
31. Chang KT, Shu HS, Chu CY, Lee WH, Hsu PC, Su HM, Lin TH, Voon WC, Lai WT, Sheu SH. Association between C-reactive protein, corrected QT interval and presence of QT prolongation in hypertensive patients. The Kaohsiung Journal of Medical Sciences. 2014 Jun 1;30(6):310-5.