

CRP levels in hypertensive and normotensive subjects: A comparative study

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Abstract

Background: Hypertension is the foremost leading cause of morbidity and mortality especially in developing countries such as India. CRP is an acute phase reactant and a measure of systemic inflammation. Some consider hypertension to be an inflammatory disorder. CRP which is a widely used parameter may be used in screening of hypertensive patients. **Objectives:** To evaluate the CRP levels of hypertensive cases with respect to that of normotensive controls. Further to investigate the association of CRP with systolic and diastolic blood pressure. **Materials and Methods:** 50 hypertensive cases and 50 normotensive controls in the age group of 35-45 years were the subjects. Resting blood pressure was recorded in the supine position. Three records with 2 minute interval in between each were obtained and the average was considered for data analysis. A single measurement of CRP levels was obtained using high sensitivity CRP (hs-CRP) kits. **Results:** The CRP levels were significantly higher in the hypertensive group when compared with the normotensive controls. Further CRP was found to have a positive and significant correlation with both systolic and diastolic blood pressure. **Discussion:** The autonomic dysfunction in hypertension influences the inflammatory modulatory processes and increases the CRP levels. CRP levels lead to endothelial dysfunction thereby reducing nitric oxide production and causing vasoconstriction. Further has pro-thrombotic and atherosclerotic properties and also releases neuro-endocrine factors causing non-structural cardiac modifications. **Conclusion:** Especially developing countries like India could use CRP levels which is an extensively used biomarker, for risk prediction and prognosis of hypertensive patients.

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

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INTRODUCTION

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.¹ It has been reported that in India, one in three are inclined to develop hypertension.² 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.³ 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.⁴ 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.⁵ High sensitivity CRP (hs CRP) assays are able to detect lower plasma CRP concentrations even in the absence of acute infection or inflammation. Since CRP is a widely used biomarker, the present study advocates its use in hypertensive screening and risk prediction. Few studies have used CRP to detect the first coronary heart event.⁶ The present study investigates the CRP levels among

hypertensive cases and normotensive controls,⁷ by this means appreciating the screening and prognostic value of this marker.⁸ Further the present study explores the correlation of CRP with blood pressure. The relationship between this marker and blood pressure has not been adequately clarified^{9,10} and there is a dearth of information especially in hypertensive patients of south India. It is imperative to study hypertension due to increased cardiovascular deaths.

AIM AND OBJECTIVES

AIM

To assess the CRP levels among hypertensive and normotensive subjects.

OBJECTIVES

1. To compare the CRP levels of hypertensive cases and normotensive controls.
2. To explore the correlation of CRP levels with systolic and diastolic blood pressure.

MATERIALS AND METHODS

A cross-sectional case-control study was carried out on 50 hypertensive and 50 normotensive subjects. 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=50)	Normotensive Controls (n=50)	P value
Systolic BP (mm Hg)	156.12±18.99	113.8±6.55	<0.001*
Diastolic BP (mm Hg)	93.72±9.78	73.2±7.97	<0.001*
C-reactive protein(CRP) (mg/L)	1.54±1.07	0.73±0.18	<0.001*

*P<0.05=statistically significant

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

	Correlation coefficient (R value)	P value
Systolic BP	0.2331	<0.05*
Diastolic BP	0.4231	<0.001*

*P<0.05=statistically significant

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 1) CRP levels were positively correlated and significant with both systolic blood pressure and diastolic blood pressure. (Table 2)

DISCUSSION

The present study revealed a statistically significant difference for CRP level among hypertensive cases and normotensives controls. CRP was positively correlated with SBP, DBP. The P value obtained from the R value showed a significant relationship for CRP with both SBP and DBP. The results with respect to CRP and hypertension were in contrast to an earlier study that reported no correlation between CRP and DBP.¹¹ Our findings were similar to a study showing significant positive correlation of CRP with both SBP and DBP.¹² Several other studies also reported positive correlation between CRP and SBP.^{13,14,15} The critical causal role of inflammation and CRP in developing hypertension has been established.⁵ 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.^{16,17,18,19,20} It has been proven that CRP increases Plasminogen activator inhibitor-1 (PAL-1) levels and PAL-1 has been found to be prominently high in hypertensive patients.^{19,21} Thus all these link inflammatory mechanisms with development of hypertension. Thus the vasoconstrictor, thrombotic and atherosclerotic properties of CRP play a vital role in the development of hypertension.²² Hypertension leads to cardiovascular autonomic imbalances. The autonomic imbalance in hypertension affects the inflammatory modulatory process thereby increasing the CRP levels.²³ 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.^{3,24} 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.²⁵ Thus increasing dietary fiber intake can also be recommended to hypertensive patients as well as those at risk of developing hypertension. The following are the limitations of the present study. The causality and reverse causality of CRP and hypertension cannot be investigated since this is a cross-sectional study. Hypertension has several confounding factors which needs further investigation. CRP is known to change over the duration of hypertension, but

we just used a single baseline measurement of CRP. Beta blockers and diuretics have already shown to affect the CRP levels.²⁶ 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.

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