

## Original Article

# C-Reactive protein in hypertension as a cardiovascular risk factor: A prospective observational study

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## Abstract

**Background and objective :** C-reactive protein (CRP) is a well-known inflammatory biomarker and is associated with cardiovascular risk. Our objective was to see whether it is also associated with hypertension and its complications.

**Methodology :** This prospective observational study was carried out in general outpatient department (OPD) of a tertiary level hospital on a total of 112 patients, among them 71 were hypertensive and 41 were normotensive. Baseline CRP was measured in all subjects and followed them up to six months to see any association between the level of CRP and hypertensive complications.

**Results :** It is found that mean CRP was 2.923 ( $\pm$  0.294) in hypertensive subjects and 1.058 ( $\pm$  0.330) in normotensive subjects. No association is found between level of CRP and hypertensive complications.

**Conclusion :** CRP is raised in hypertension. But it is not established that its level can predict the complication of hypertension.

**Key words:** C-reactive protein (CRP), Hypertension.

## Introduction:

C-reactive protein (CRP) is a nonspecific acute phase reactant and an integral part of the innate immune system. It is produced and synthesized in the liver in response to inflammatory cytokines.<sup>1,2</sup> Since its discovery in 1930 it is widely used as an inflammatory marker, and for last few years it is also considered that it has a strong role in the pathogenesis of many chronic inflammatory conditions as well, for example, atherosclerosis.<sup>3-7</sup>

As cardiovascular diseases are now considered as a consequence of chronic inflammatory process, CRP is widely used to predict the risk of developing complications.<sup>8,9</sup> As

cardiovascular complication is common in many individuals without having conventional risk factors (eg, obesity, family history, hyperlipidemia), role of CRP is increasingly evaluated for screening these individuals.<sup>10,11</sup>

Hypertension is one of the cardiovascular diseases responsible for much morbidity and mortality throughout the world<sup>10-13</sup> and has been proven to be a consequence of chronic inflammation of the arterial wall.<sup>11,13</sup> So it can be assumed that CRP has an association with hypertension, though it is still controversial whether hypertension is the result of raised CRP.<sup>4-6,9,10</sup>

Considering these alarming findings, we did a prospective observational study with the purpose of determining whether hypertensive patients have higher CRP than normotensive patients, and whether CRP levels in hypertensive patients can predict the complications.

## Materials and Methods

This prospective observational study was carried out in a tertiary level hospital on outpatient basis with the primary objective of finding any relation between CRP and hypertension, and secondary objective of finding predictive value of CRP in hypertensive complications. We included all the ambulant adult patients (above 18 years of age) of both sex having hypertension and normotension attending in the general outpatient department (OPD) for one month. We excluded known cases of ischemic heart disease (IHD), diagnosed case of any infectious and inflammatory condition (eg, fever due to any cause, urinary infection, symptomatic arthritis, etc), psychiatric patients, those who had uncontrolled diabetes mellitus (DM) (HbA1c > 7.0%) and those who were unwilling to participate in the study. The

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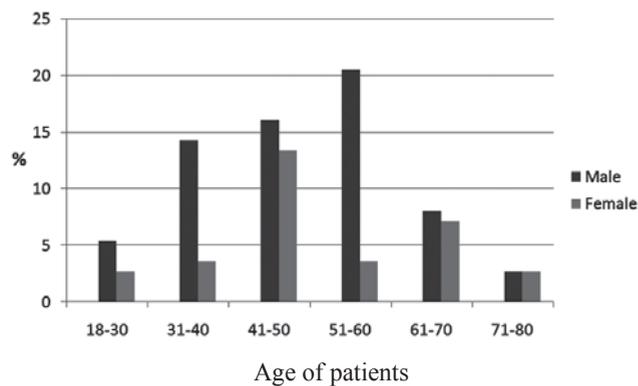
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objective of the study was discussed in details with the patients or their attendants before their decision to enroll themselves into the study and written consent was taken. Subject's age, gender, medical and clinical history were collected before conduction of study. Hypertension was diagnosed by manually measuring blood pressure with aneroid sphygmomanometer on the spot along with collecting data of previous three months from their medical record books. Hypertension was considered when either systolic blood pressure (SBP) was more than 120 mmHg or diastolic blood pressure (DBP) was more than 80 mmHg, or both. Clinical examination was done and baseline CRP was sent. CRP was measured in BN ProSpec by Nephelometry and was expressed as mg/L. Normal range is less than 6 mg/L. Data were collected in a pre-designed structured data collection sheets. Both hypertensive and normotensive groups were followed up after six months. By this period, we properly gave management to the hypertensive patients. After six months, ECG was done in every patient of both groups to identify left ventricular hypertrophy (LVH) and ischemic heart disease (IHD). Specific investigations (chest X-ray, troponin-I, echocardiogram) were done only in those who complained about angina or features of heart failure (dyspnea or cough on lying). All the relevant collected data were compiled on a master chart first & then organized by using scientific calculated and standard statistical formulas, percentage was calculated to find out the proportion of the findings. Data entry and analysis were done using SPSS for windows version 22.0. Output of data and graphical representation was done using Microsoft Office chart and Microsoft-Word. *p*-value was considered as significant when it was <0.05. The results were presented in tables, figures, diagrams etc.

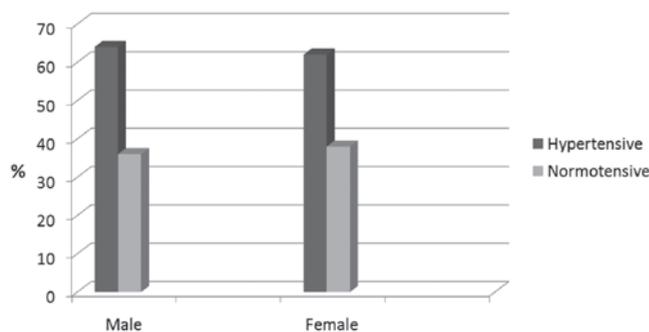
**Results**

Our total study population was 112, among them 66.9% (n=75) were male and 33.0% (n=37) were female. Most of the male subjects were in 51 – 60 years of age and the female were in 41 -50 years (Figure 1). Among 75 of male subjects, 64% were hypertensive, and among 37 females 62% were hypertensive (Figure 2). Mean CRP level in normotensive group was 1.058 mg/L ( $\pm$  0.330) and in hypertensive group was 2.923 mg/L ( $\pm$  0.294) (Figure 3).

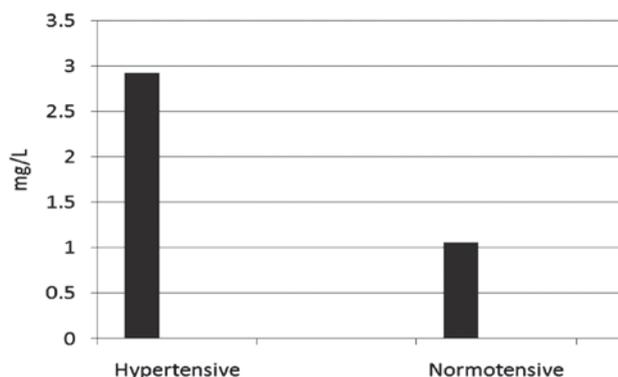
Those who developed LVH (n=75, 50.70%), their baseline CRP was 2.897 mg/L ( $\pm$ 0.308). Those who developed heart failure (HF) (n=2, 2.81%), their mean CRP was 3.100 mg/L ( $\pm$ 0.141). Those who developed angina pectoris (n=14, 19.71%), their mean CRP was 3.050 mg/L ( $\pm$ 0.240) (Figure 4). However, no significant difference in CRP level [2.909 mg/L ( $\pm$ 0.224)] was observed in those hypertensive patients (n=22, 30.98%) who did not develop any form of complication. We did not get any association between age or sex and level of CRP.



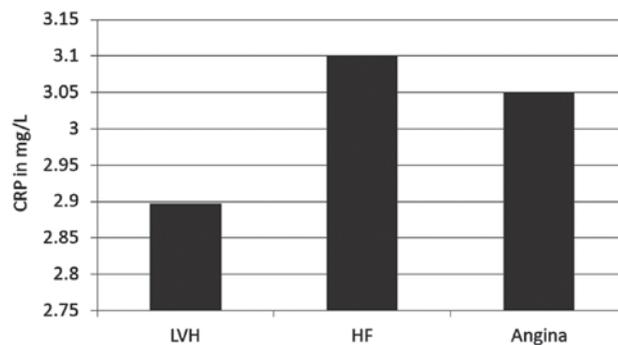
**Fig 1**



**Fig 2**



**Fig 3**



**Fig 4**

## Discussion

In our study we got two major findings: First, hypertension is associated with higher CRP level. Second, raised CRP level is not associated with hypertensive complications. We also have some secondary findings: Frequency of hypertension is more in male than in female, but female developed hypertension earlier than male (Figure 1).

It is already proven in many epidemiological studies that atherosclerosis is an inflammatory process and may lead to hypertension and other cardiovascular diseases.<sup>3-11</sup> So there was assumption that hypertensive individuals should have higher CRP. Like other studies<sup>10,14-16</sup> we also got the same findings: Hypertensive subjects have higher CRP than those of normotensive subjects. There are many studies carried out to find the correlation whether higher level of CRP may lead to hypertensive complications, but it still remains controversial. High CRP was found to be associated particularly with IHD.<sup>3,16-18</sup> However, a recent study (n = 476) showed that high CRP is associated with resistant hypertension and thus has worse cardiovascular prognosis.<sup>19</sup> We have not found any significant association between high CRP with hypertensive complications. Many hypertensive subjects in our study have not developed any hypertensive complications though they have high CRP similar to those who developed complications.

Our secondary findings have similarity with other studies: Male has higher frequency of hypertension than female.<sup>20,21</sup> But, those large epidemiological studies showed that most female has developed hypertension in around fifth and sixth decade. We found that most female has hypertension in their fourth decade (Figure 1). This is likely because of our single center-based study with referral bias.

We have some limitations in our study. First, this is a single center-based observational study which has much referral biasness. Second, IHD remains silent in many elderly diabetic patients, and this can easily elevate level of CRP. It is common that many patients have concomitant hypertension, DM and IHD. And CRP can be raised more due to DM and IHD.<sup>14</sup> As we excluded IHD only by symptom and ECG findings, there was high chance of missing many true cases of IHD.

Still, our study has several strengths. First, this is a much larger study in our country comparing CRP in both hypertensive and normotensive subjects. Second, we followed the hypertensive group for at least six months. Third, we excluded all diabetic patients whose HbA<sub>1c</sub> is more than 7.0% to minimize the error in measuring CRP.

However, due to the important limitations mentioned above, much larger population based studies are needed to detect whether level of CRP is truly associated with hypertensive complications, and thus we can predict in advance to prevent those morbidity and mortality.

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