HIGH SENSITIVE C - REACTIVE PROTEIN AND ITS ASSOCIATION WITH BLOOD PRESSURE – A HOSPITAL BASED STUDY

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Abstract: Background and Objectives: Although some traditional risk factors such as drinking alcohol, being overweight, a diet high in salt and genetic factors are confirmed risk factors of hypertension, its etiology and pathogenesis are not fully understood. Therefore this study was conducted to find out if there is any association of hsCRP (a marker of inflammation) with blood pressure. **Materials and Method:** This hospital based case control study included a total of 209 subjects (108 = cases, 101 = control) aged 30 years and above. The hsCRP test was performed by using BioCheck high sensitivity C-reactive protein enzyme immunoassay test kit. Statistical analyses included Independent-Samples T Test, Chi-square test and Spearman's correlation coefficients. **Result:** hsCRP was significantly correlated with both systolic blood pressure and diastolic blood pressure ($p<0.005$). **Conclusion:** Increased hsCRP was significantly associated with hypertension suggesting a role of inflammation in the development of hypertension and thus estimation of serum hsCRP can be used as a risk assessment tool for prediction of hypertension.

Key Words: Body Mass Index (BMI), High sensitive C-reactive protein (hsCRP), Hypertension (HTN)

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Introduction:

Hypertension is one of the major killer diseases in the world. Blood pressure levels, the rate of age-related blood pressure increase, and the prevalence of hypertension vary among countries and among subpopulations within a country. One in three adults worldwide, according to the report of the World Health Statistics, 2012[1], has raised blood pressure – a condition that causes around half of all deaths from stroke and heart disease. In India, 23.10% men and 22.60% women over 25 years old suffer from hypertension[2]. The picture in North-Eastern states shows that 30.1% in tea garden community, 11.8% in Assamese community and 2.04% in Mizo community suffer from raised blood pressure[3]. In Assam, the overall prevalence of hypertension was found to be 33.3%[4] and the prevalence of hypertension in the urban dwellers of Dibrugarh town in Upper Assam was found to be 27.9%[5].

Hypertension is a multifactorial trait that results from the net effect of environmental and genetic factors. Basic data suggest that increasing levels of blood pressure may stimulate a proinflammatory response and that endothelial inflammation may also herald the changes in arterial wall that characterize the hypertensive state[6]. Inflammatory processes are now recognized to play a fundamental role in atherogenesis. Attention has thus focused on whether circulating markers of inflammation can provide a new method to improve cardiovascular risk prediction.

CRP is one of the acute-phase proteins, the serum or plasma levels of which rise during general, nonspecific response to a wide variety of diseases. hsC-reactive protein's predictive power for vascular risk detection is more than that of CRP. Hence, hsCRP has evolved as the most robust and reproducible marker of vascular inflammation and is considered the prototypic downstream marker of inflammation.

High sensitive C-reactive protein is well standardized and it has limits of detection as low as 0.02 mg/dl[7, 8]. As a risk assessment tool, it has several good points - it is very stable, with very little difference in values between fresh or frozen plasma and has a long half –life of up to 20 hours[9]. It normally circulates at very low levels, but acute inflammatory processes induce marked hepatic synthesis of hsCRP, which can induce a 100-fold serum increase[10].

Hence the present study was undertaken to find out the association of serum hsCRP level across the range of blood pressures according to JNC 7 classification[11] and the influence of other specific

risk factors of hypertension viz. BMI, smoking and alcohol consumption on serum hsCRP level.

Materials and methods:

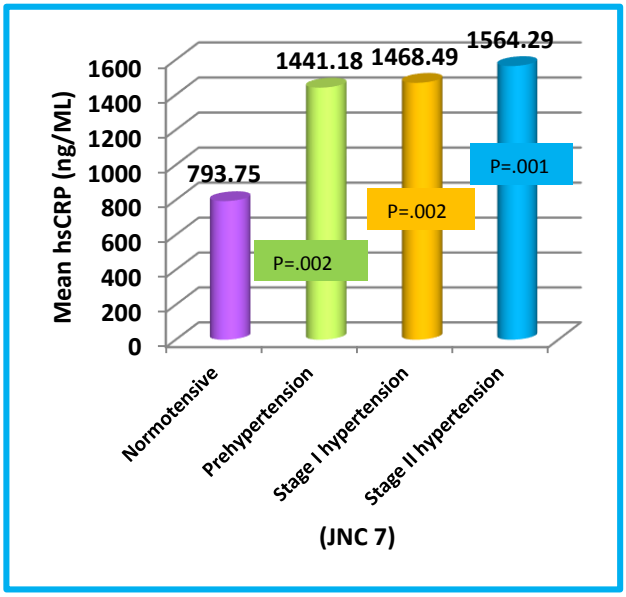
This hospital based case control study was carried out in Assam Medical College and Hospital, Dibrugarh, for a period of 1 year after obtaining approvals of the institutional review board. A total of 209 subjects aged 30 years and above, participated in the study. All the consecutive cases attending the medicine department with a - systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg and/or were on antihypertensive drugs were included into the hypertensive group (108 cases). Subjects who had any chronic inflammatory disease, collagen vascular disease (rheumatoid arthritis, osteoarthritis), cardiovascular disease(e.g. myocardial infarction, coronary artery disease, complications of hypertension etc.), renal disease, hepatic disease, autoimmune disease, any systemic infection (tuberculosis), diabetes, stroke, malignancy were excluded from the study. 101 apparently healthy, age and sex matched individuals, without any evidence of disease were included in the normotensive group (control). Blood pressure was recorded in the right arm in sitting position by using a standard mercury sphygmomanometer with appropriate cuff sizes, after the participants had been sitting for at least 10 minutes. Three readings were taken at an interval of at least 5 minutes and the average of three readings was considered as the blood pressure of the individual. Weight was measured using platform balance. Height was measured with an anthropometric rod. Body mass index (BMI) was computed as the ratio of weight to the square of height (kg/m^2). Cigarette smokers were defined as those who had a few puffs to more than one packet daily for one year or more[12]. Alcohol consumption was defined as habitual drinkers who consumed alcohol daily[13]. The hsCRP test was performed by using BioCheck high sensitivity C-reactive protein enzyme immunoassay test kit. Statistical analyses included Independent-Samples T Test, Chi-square test and Spearman's correlation coefficients. P-values <0.05 were considered as significant.

Results:

Table1: Showing mean hsCRP levels in cases and controls:

	Control Mean ± SE (ng/ml)	Cases Mean ± SE (ng/ml)	P value
hsCRP	1078.96 ± 91.12	1638.43 ± 107.55	0.000

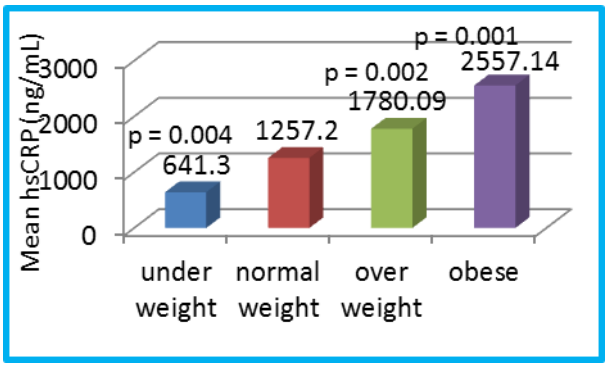
Figure1: Comparison of Mean hsCRP levels in patients with different grades of hypertension (JNC 7) with controls:



**p values were determined on comparison with normotensive group*

The above figure shows a graded association between the blood pressure range as categorized by JNC 7 and serum hsCRP levels. When compared with the hsCRP levels in control subjects (793.75ng/ml), the most significant difference was found in patients with stage II hypertension (1564.29 ng/ml) (p=0.001) followed by prehypertension (1441.18 ng/ml) (p=0.002) and stage I hypertension (1468.49 ng/ml) (p=0.002).

Figure2: hsCRP levels according to BMI classification



*p-value was determined on comparison with the normal BMI

The above figure shows that obese subjects had more elevated hsCRP levels (2557.14 ng/ml). When compared with the normal BMI subjects, the underweight, overweight and obese subjects showed a statistically significant relationship (p=0.004, p=0.002 and p=0.001 respectively).

Table2: Comparison of mean hsCRP levels according to smoking habit

Smoking History	Control Mean ± SE	Cases Mean ± SE	P value
Never	1050 ±115.13	1696.15 ±167.54	0.001
Smoked previously but quit	856.67 ±244.80	1773.44 ±268.76	0.018
Rare	1407.5 ±281.54	1225 ±360.93	0.691
Few puffs to more than one pack daily	1254.55 ±248.38	1580.47 ±181.42	0.347

hsCRP in ng/ml

The table shows that those subjects who had no history of smoking or those who quitted smoking had a significant relationship (p<0.05) whereas those subjects who had a smoking history in the present day were not significantly related (p>0.05).

Table3: Comparison of mean hsCRP levels according to alcohol intake

Alcohol intake	Control Mean±SE	Cases Mean±SE	P value
No history of consumption	1038.24 ±115.36	1737.98 ±166.46	0.001
No history of consumption in last 6 months	925 ±75.00	1475 ±413.07	0.426
1 to 2 times per month	1192.39 ±200.65	1615.74 ±204.34	0.149
Habitual drinker	1137.5 ±205.34	1428 ±214.36	0.395

hsCRP in ng/ml

The above table shows a significant result in non-consumers of alcohol (p=0.001). When a history of alcohol consumption is positive the results were statistically insignificant (p>0.05).

Table4: Spearman's correlation coefficients and statistical significance between serum hsCRP level and systolic and diastolic blood pressure

Parameter	Variable	Spearman's correlation coefficients	P value
SBP	hsCRP	0.193	0.005
DBP	hsCRP	0.165	0.017

In this bivariate analysis, hsCRP was significantly correlated with both systolic blood pressure and diastolic blood pressure (p<0.05).

Discussion:

Although some traditional risk factors such as drinking alcohol, being overweight, a diet high in salt and genetic factors are confirmed risk factors of hypertension, its etiology and pathogenesis are not fully understood. Those traditional risk factors only explain part of the etiology of hypertension. Some hypertensive individuals are not at the risk of above factors, therefore other factors should be considered in research of hypertension. In recent years, interesting research was focused on the relationship between inflammation and hypertension.

Some prospective studies[14, 15] showed that baseline CRP concentrations predict the risk of stroke and more strongly that of myocardial infarction. CRP was detected in the atherosclerotic plaques and that it might contribute to atherogenesis and a procoagulant state[16, 17]. Recently, CRP has also been found to correlate with hypertension[6, 18, 19].

The present study shows that increased levels of hsCRP are associated with hypertension and risk of hypertension increases with increasing level of hsCRP. Despite the fact that the blood pressure was measured at only one point of time, a significant correlation between C - reactive protein and systolic and diastolic blood pressure were found. This finding is in accordance with other cross sectional studies[20, 21]. Thus the current study provides evidence for a critical role of inflammation in the development of hypertension.

Fatty people have higher blood pressures than thin people. Obesity and weight gain are strong, independent risk factors for hypertension. In the United States, it has been estimated that 60% of hypertensives are >20% overweight[22]. Obesity plays an important role in inflammation. Obesity itself promotes inflammation and potentiates atherogenesis independent of effects on insulin resistance or lipoproteins. A possible mechanism which links obesity to inflammation may be the production of several cytokines by the adipose tissue. For example, IL-6 (interleukin-6) production by adipocytes is the main hepatic stimulus for CRP synthesis[23]. In a study carried out by Iikay Tugba Unek et al (2010) concluded that obese patients showed a significant increase of hsCRP and sCD40L (soluble cluster of differentiation 40 ligand) levels compared with normal weight subjects, which might contribute to the known proinflammatory milieu found in these patients[24].

The present study substantiates earlier findings of a close association between hsCRP and some traditional risk factors of hypertension including cigarette smoking and alcohol consumption[25, 26, 27]. In the present study, Table 2 shows a comparison of mean hsCRP levels between cases and controls on the basis of the various categories of smoking habit. In the non-smokers there was a significant relationship between the cases and controls but in the smokers the relationship was insignificant which shows that smoking increases the level of hsCRP. Also, the study indicates a pro-inflammatory effect of alcohol consumption in the study population.

Conclusion:

- hsCRP increased as blood pressure category increased
- hsCRP showed a stepwise increase as BMI increased
- Classical risk factors like smoking cigarette and alcohol consumption increased the hsCRP level

Study reveals significant association between increasing hsCRP level and hypertension and thus estimation of serum hsCRP can be used as a risk assessment tool for prediction of hypertension. Also, it alerts the clinician of an ongoing inflammatory reaction in the body. However, one should be very cautious to draw any firm conclusion from this study as it was undertaken for a short span of one year's time with limited number of cases. It was a hospital based case-control study, which does not claim a study of the population at large of this locality. A third lacuna could have been that blood pressure measurement was a point data collection and therefore, a final conclusion could not be made that there is a causal relationship between increased hsCRP and hypertension. Further study should be focused on cohort study on relationship between hsCRP level and hypertension.

Acknowledgement:

We offer our sincere gratitude to Regional Medical Research Center, NE Region (ICMR), Dibrugarh, for allowing us to carry out the laboratory works. We are thankful to the Principal cum chief superintendent Assam Medical College and Hospital, Dibrugarh for kindly allowing us to publish the hospital records.

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Disclosure: No conflicts of interest, financial, or otherwise are declared by authors