

## hs-CRP- A New Risk Assessment Tool in Prehypertensive Subjects

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Prehypertension is an American medical classification for cases where a person's blood pressure is elevated above normal but not to the level considered as hypertensive, systolic 120 to 139 mm Hg and diastolic 80 to 89 mm Hg<sup>1</sup>. Prehypertension is the most important public health problem in developing countries and one of the major risk factor for cardiovascular diseases. The natural history of prehypertension starts when some combination of hereditary and environmental factors set in to the motion transient but repetitive perturbation of cardiovascular homeostasis not enough to raise the blood pressure to level defined as abnormal but enough to begin the cascade that, over many years lead to BPs that are usually elevated<sup>2</sup>. The main aim of this study was to evaluate the association between undiagnosed prehypertension and serum CRP level across the range of blood pressure categories including prehypertension i.e. 121-139/89 mm Hg. C reactive protein, a simple downstream marker of inflammation, has now emerged as a major cardiovascular risk factor. In the present study, serum hs-CRP level and lipid profile were monitored in 100 subjects with prehypertension and 100 age sex matched with normotensive controls. The level of hs-CRP in serum of cases were significantly high ( $p < 0.0001$ ) and level of HDL were significantly low ( $p < 0.0001$ ) compare to healthy controls.

**Key words:** Prehypertension, hs-CRP, Inflammation.

hs-CRP is alpha globulin with a molecular weight of approx. 110,000 to 140,000 daltons and is composed of five identical subunits which are non-covalently assembled as a cyclic pentamer. CRP is synthesized in liver and is normally present as a trace constituent. hs-CRP considered an acute phase reactant and a potential marker of inflammation<sup>3</sup>. Prehypertension is a warning sign that you may get high BP in the future. High BP increases your risk for coronary artery disease. There is no question that atherosclerotic vascular disease involve multiple inflammatory cells and elevation in hs-CRP is a marker of this inflammatory process.

### MATERIAL AND METHODS

The study consisted of 100 prehypertensive subjects who have BP between 120 to 139 and diastolic 80 to 89. Blood samples were collected from the patients attending O.P.D of medicine dept. of Gandhi Medical college Bhopal. The diagnosis of Prehypertension was established according to their blood pressure. The control group consisted of 100 healthy adults who had been matched for age sex, BMI, socio economic status, were selected for study. The study was approved by the Institutional Ethical Committee, for biomedical research.

#### Exclusion criteria

Patients with active inflammatory diseases, estrogen therapy, collagen disease arthritis and patients on long term hypolipidemic drug and antioxidants.

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### Estimation of lipid profile

Fasting lipid profile was done in all subjects serum cholesterol, HDL-C, VLDL-C were determined by CHOD-PAP method (Roche Diagnostics) Serum Triglyceride was measured by enzymatic GPO-POD method. LDL-C calculated by using Friedewald formula ( $LDL = \text{total cholesterol} - 1/5TG - HDL$ )<sup>4</sup>.

### Estimation of hs-CRP

This is a latex-enhanced turbidimetric invitro immuno assay. CRP in the sample binds to specific anti-CRP antibodies, which had been adsorbed to latex particles and agglutinates. The agglutination is detected as an absorbance change. The magnitude of the change is proportional to the concentration of CRP in the sample. The actual concentration is then detected by interpolation

from a calibration curve prepared from calibrators of known concentration<sup>5-6</sup>.

### Sample: Fresh serum (free of hemolysis)

Prepared the following calibrator dilution using normal saline as diluent. Multiply the concentration of the CRP ultra-calibrator by the corresponding factors stated in the table below to obtain the CRP ultra-concentration of each dilution.

Laboratory procedure for semi auto analyser

	Calibrator	Sample/control
CRP ultra	R1400 $\mu$ L	400 $\mu$ l
Dil. Calibrator	10 $\mu$ L	
Sample/control -	10 $\mu$ L	
CRP ultra R 2	200 $\mu$ l	200 $\mu$ L

Dilution	1	2	3	4	5	6
Calib. ( $\mu$ L)		10	10	20	50	100
Saline ( $\mu$ L)	100	150	70	60	50	
Dil. Factor	0	0.0625	0.125	0.25	0.5	0.1

Mix and read absorbance immediately (A1), and after 2 minutes (A2) of the sample addition at 578 nm.

### Limitation of study

Patients included in the present study were attended O.P.D of medicine Department. This study was subjected to 100 prehypertensive cases within 30-75 years. The laboratory of Biochemistry department is well equipped with semi auto analyser, colourimeter and spectrophotometer; hence all investigation were carried out on auto analyser and spectrophotometer. All investigation methods used in this study were standardized in our laboratory.

### Statistical Analysis

All the data were analyzed by using the

SPSS version 10.0. shows the demographic and clinical characteristics of patients and normal healthy controls. Among 100 prehypertensive cases, 70 were males and 30 were females. There are 35 prehypertensive patients with obesity and only 10 controls were obese. Diabetic prehypertensive cases had mean age  $61.2 \pm$  years. Non diabetic prehypertensive cases had mean age  $65.0 \pm 14.10$  years and controls had mean age  $65 \pm 14.63$  years.

Table 2 shows the biochemical characteristics of subjects and normal healthy controls. Blood lipid parameters- total cholesterol, Triglyceride, LDL, were significantly ( $p < 0.001$ ) more increased and HDL was significantly ( $p < 0.001$ )

**Table 1.**

Variables	Control (n=100)	Cases (n=100)	
		DM	NDM
Age (years)	$65 \pm 14.63$	$61.2 \pm 14.63$	$63.1 \pm 14.10$
Sex (male/female)	40/10	30/15	40/15
Body mass index	$22.54 \pm 1.99$	$25.5 \pm 1.50$	$24.7 \pm 1.65$
Diastolic blood pressure (mm Hg)	$75.56 \pm 5.48$	$95.12 \pm 4.37$	$87.12 \pm 5.1$
Systolic blood pressure (mm Hg)	$120.38 \pm 8.69$	$137.21 \pm 4.60$	$130.10 \pm 3$

**Table 2.**

Parameter	Control	Cases(n=100)	
	(n=100)	DM(n=45)	NDM(n=55)
Cholesterol(mg/dl)	104.42±48.42	164.76±77.52	160.45±72.21
Triglycerides(mg/dl)	68.86±19.46	139.99±64.17	132.78±62.78
LDL cholesterol(mg/dl)	68.66±28.96	109.98±52.69	103.92±54.78
HDL cholesterol(mg/dl)	78.96±30.42	34.41±11.38	32.40±9.67
VLDLcholesterol(mg/dl)	22.12±6.12	31.64±18.63	30.63±14.67

**Table 3.**

Parameter	Control	Cases
hs-CRP(mg/l)	1.893±0.74	5.93±2.05

more decreased in cases compared to controls.

Table 3 shows serum hs-CRP activity was significantly high ( $p < 0.001$ ) as compared with control group.

## DISCUSSION

The global burden possess by cardiovascular disease due to rising incidence of known risk factors like dyslipidemia, elevated high sensitive CRP in prehypertensive subjects. This study sought to examine the possible alteration in the level of hs-CRP, lipid profile and the interaction among these parameters in prehypertensive subjects. Young prehypertensive have high level of markers of inflammation compared with controls. More importantly impaired arterial stiffness is significantly associated with the marker of inflammation in patients with prehypertension. Hs-CRP is an independent marker of inflammation<sup>7</sup>.

Hypertension is one of the major risk factor for atherosclerosis. If blood pressure is not controlled in prehypertensive subjects, it will lead to hypertension. Atherosclerosis progress slowly after deposition of oxidized LDL and finally lead to formation of plaque which results in heart stroke and myocardial infarction.

## CONCLUSION

Estimation of hs-CRP proved to be very useful in prehypertensive subjects. In present study

there is elevated level of hs-CRP in prehypertensive subjects i.e between 3 to 5mg/l. This increase in hs-CRP activity play a central role in atherosclerotic process.

Prospective epidemiological studies have shown that hs-CRP measurement is a strong predictor of hypertension and myocardial infarction, peripheral vascular disease and sudden cardiac death without a history of heart disease. LDL was found to be increased in prehypertensive patients<sup>8</sup>. Numerous studies have established that when the total cholesterol and LDL cholesterol, increased HDL concentration have been shown to be protective for cardiovascular diseases in both epidemiological and clinical trial studies, Because atherosclerotic process begins at an early age and can take decades to clinically manifest itself, the measurement of plasma lipids is valuable means to identify individuals at risk for coronary artery disease<sup>9</sup>.

Elevated hs-CRP appeared to be predictive for the development of future hypertension in apparently normotensive individuals, which suggests that inflammation may play an integral part in the development of hypertension, occurring either as a primary or secondary and also increase risk for cardiovascular disease. The observed elevation in hs-CRP in subjects who subsequently go on to develop hypertension is particularly relevant and create options for potential primary prevention strategies. Weight loss, exercise, yoga and other healthy lifestyle changes can often control prehypertension — and set the stage for a lifetime of better health.

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