Original research article

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CORRELATION OF C-REACTIVE PROTEIN WITH ARTERIAL HYPERTENSION IN PATIENTS OF UDAIPUR DISTRICT

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ABSTRACT:

Background: Higher levels of C-reactive protein (CRP), an inflammatory marker, measured easily in laboratory, for which clinical cut off value is recommended, prospectively associated with an increased risk of atherosclerosis so associated with arterial hypertension (AH) and coronary artery disease (CAD). Present study was conducted to examine whether CRP act as a marker or mediator for low grade systemic inflammation in vascular system, was associated with arterial hypertension. **Material and Methods:** One hundred fifty cases of AH attending Pacific medical college and hospital, Udaipur were included in the study and their various investigations were carried out to exclude the other co-morbid diseases in all cases. No follow- up CRP levels was observed. **Results:** We found about 42.67 % (64/150) cases of AH were having elevated CRP levels. In CRP positive group 79.69% (51) were male and 20.31% (13) were female indicating male preponderance. **Conclusions:** CRP levels are associated with future development of AH and CAD, due to inflammatory conditions related to atherosclerosis concluded in our study.

KEYWORDS: CRP, arterial hypertension, atherosclerosis, inflammation, rennin angiotensin system (RAS).

INTRODUCTION:

Inflammation has been hypothesized as an etiology for the development of atherosclerosis, which in future leads to the development of hypertension. **(1)**

Elevations in plasma inflammatory markers among individuals with elevated blood pressure (BP) had been found in various studies. **(2, 3)**

Higher levels of C-reactive protein (CRP), an inflammatory marker, measured easily in laboratory, for which clinical cut off value is recommended, prospectively associated with an increased risk of atherosclerosis so associated with arterial hypertension (AH) and coronary artery disease (CAD). **(4,5)**

However, the relationship of other inflammatory markers in spite of CRP remains untouched for identifying the risk of developing arterial hypertension. Elevated levels of CRP and of cytokines were associated with a series of

indicators of endothelial dysfunction which finally leads to atherosclerosis.

Low grade inflammation localized in vascular tissue leads to the initiation and progression of atherosclerosis as increased expression and plasma concentrations of inflammatory markers and mediators is present.

Various epidemiological studies shown that high-sensitivity CRP (hsCRP) is a powerful tool for interpretation of ischemic cardiovascular events in patients with angina. Also, hsCRP levels were correlated well with systolic blood pressure (BP), pulse pressure, and arterial hypertension. **(6)**

Routine measurement of HS-CRP along with cholesterol as a screening tool for AH and cardiovascular disease is not a widely accepted recommendation and its practical implication remains controversial.

That's why increase in blood pressure (BP) and high level of CRP have additional predictive value for atherosclerosis and act as independent risk factor for cardiovascular disease.

The activation of the rennin angiotensin system (RAS), involved in the path physiology of hypertension and result for the future development of CAD, **(7)** as angiotensin II is also a pro-inflammatory mediator. **(8, 9)**

Present study was conducted to examine whether CRP act as a marker or mediator for low grade systemic inflammation in vascular system, was associated with arterial hypertension.

MATERIAL AND METHODS

One hundred fifty cases of arterial hypertension (newly diagnosed) attending the OPD and IPD, Department of Medicine, Pacific medical college and hospital, Udaipur a tertiary care hospital, were randomly included in study with criteria for exclusion were diabetes mellitus, high sodium intake, lack of physical activity, kidney disease, Smoking, alcohol abuse, and stress which are considered to be a risk factor for arterial hypertension.

Diagnoses of these cases of hypertension were made on the basis of criteria of Seventh report of the Joint National Committee on Prevention, Detection, Evaluation and treatment of High blood pressure (JNC-7).

Routine investigations with blood sugar, lipid profile, BMI, and BP monitoring were carried out.

Qualitative estimation of CRP in vitro was done by diagnostic commercial reagent kit (Span Diagnostic Ltd.) in human serum by qualitative and semi-quantitative rapid latex slide test. No follow- up CRP levels was observed.

RESULT

Out of 150 patients whose data were collected, 103 were male and 47 were female. A patient age was ranging from 21 years to 79 years and mean age was 52 years.

In present study raised CRP levels were observed in 42.67 % (64/150) patients and normal CRP levels were observed in 57.33% (86/150) patients.

In 64 patients CRP positive group 79.69% (51) were male and 20.31% (13) were female indicating male preponderance. Simultaneously CBC, blood sugar, urea, creatinine and lipid profile was also carried out to exclude the other co-morbid diseases in all cases.

Table 1: Characteristic of Study Subjects

Crietaria	Value (range)
Number (M/F)	150 (103/47)
Age (y)	52.0 ± 10.9
Body mass index (kg/m2)	25.7 ± 4.2
Waist-to-hip ratio	0.81 ± 0.07
Sub scapular-to-triceps ratio	1.35 ± 0.58
Systolic blood pressure (mm Hg)	124.7 ± 18.1
Diastolic blood pressure (mm Hg)	80.1 ± 12.0
Triglyceride (mmol/L)	1.2 (1.1, 1.5)
HDL cholesterol (mmol/L)	1.37 ± 0.32
LDL cholesterol (mmol/L)	3.61 ± 1.01
Fasting plasma glucose (mmol/L)	4.6 ± 0.6
2-h plasma glucose (mmol/L)	4.7 ± 1.0

Table 2: Characteristics of Subjects with Low and High titre of C - reactive protein

Criteria	Low CRP	High CRP	P
Number (M/F)	86 (52/34)	64 (51/13)	0.39
Age (y)	54.9 ± 10.6	61.1 ± 9.6	0.003
Body mass index (kg/m2)	24.1 ± 3.8	27.6 ± 4.1	0.001
Waist-to-hip ratio	0.82 ± 0.06	0.88 ± 0.08	0.001
Sub scapular-to-triceps ratio	1.14 ± 0.48	1.42 ± 0.61	0.003
Systolic blood pressure (mm Hg)	118.5 ± 15.1	130.1 ± 18.7	0.001
Diastolic blood pressure (mm Hg)	76.7 ± 11.0	83.3 ± 10.8	0.009
Triglyceride (mmol/L)	1.1 (0.9, 1.58)	1.36 (1.13, 1.91)	0.027
HDL cholesterol (mmol/L)	1.41 ± 0.32	1.35 ± 0.32	0.17
Fasting plasma glucose (mmol/L)	4.4 ± 0.3	4.9 ± 0.4	0.39

Variables are presented as mean ± SD, or as median (inter-quartile range) for variables

DISCUSSION

The prognostic significance of raised levels of C-reactive protein in patients with hypertension, as concentrations of CRP in healthy subjects predicted the incidence of CHD and suggests that inflammation play a role in the initiation of atherosclerosis as well as in occurrence of an acute event.

Synthesis of CRP is predominantly under the control of IL-6, 10 which originate largely from activated leukocytes, in the vessel wall or at the site of infection or inflammation. **(11)**

C-reactive protein levels were higher among people who were physically inactive, **(12, 13, 14, 15) having** critical cardio respiratory fitness, **(16, 17)** and were more obese. 18C-reactive protein level correlates well with the presence and extent of the metabolic syndrome, **(15, 19, 20)** subclinical atherosclerosis, **(21)** and with the increased intensity of atherosclerosis. **(22, 23)**

Relationships of CRP levels with BMI, triglycerides, HDL, glucose etc. have been noted previously as in other studies. **(24, 25)**

Cholesterol lowering medications (statins) have been found to lower the CRP levels in individuals with high cholesterol. However the fall of CRP levels may occur even without significant improvement in cholesterol levels. Earlier researchers have observed that the patients with high LDL have better clinical outcomes in patients with low CRP than those with higher levels.

The use of aspirin in healthy individuals does not reduce CRP levels significantly but in patients with cardiovascular disease and elevated CRP, the reduction of cardiovascular risk and CRP levels was noted effectively after aspirin.

Inflammation has been hypothesized to play a role in development of hypertension and studies suggest higher CRP levels among individuals who were hypertensive were noted. **(2, 3, 17, 26, 27, 28)** In present study similar findings were observed that 42.67 % case were having raised levels of CRP Interestingly incidence of raised levels of CRP was very high in male as compare to female (in CRP positive group 79.69% were male & 20.31% were female). Higher levels of CRP may increases blood pressure by reducing nitric oxide (NO) production in the endothelial cells.**(29-32)** CRP may act as a pro-atherosclerotic factor by up regulating angiotensin type 1 receptor expression **(33)** Inflammation has been shown to correlate with endothelial dysfunction **(34)** rennin-angiotensin systems. **(35)** as a result it has been hypothesized that arterial hypertension may be in part an in inflammatory disorder.

To reduce the burden of cardiovascular morbidity and mortality Arterial BP must be regulated. Indeed, arterial hypertension contributes to increase the morbidity and mortality in combination with other risk factors such as obesity, diabetes mellitus and dyslipidaemia. JNC-7, WHO-ISH and other national and international guidelines suggested various different non-pharmacological (weight loss, exercise and Mediterranean-style diet) and pharmacological guidelines to control BP and to reduce vascular inflammation in patients with hypertension, in order to reduce cardiovascular events and to improve outcome in randomized clinical trials. **(36, 37)**

Antagonism of the RAS can improve the cardiovascular outcomes by reducing vascular inflammation and remodelling, beyond BP control.

If CRP screening is performed, then two separate testing need to be done (at an interval of 2 weeks) to assess the risk. Any therapy which lowers CRP level, lower the cardiovascular risk factors.

The current study had several limitations. First, sample collections must be large for further study, second; only qualitative and semi-quantitative assessment of CRP was done. The value of CRP level is in the range of 3-5 mg/l for

assessing inflammation while hsCRP test able to measure down to 0.3 mg/l which is more beneficial in risk assessment for vascular disease. Third, no base line and post treatment status of CRP levels were carried out to assess the risk. However, it has been shown that single CRP measurements provide important information for risk prediction only. Fourth, it is not correlated with the severity of hypertension. However our study showed CRP is an important marker in diagnosis, prognosis and medical management of hypertensive diseases.

CONCLUSIONS

Hypertension may be considered a disease associated with low-grade inflammation of the cardiovascular system. Non pharmacological (weight loss, exercise and Mediterranean-style diet) and pharmacological approaches to control high BP may reduce vascular inflammation independently of BP reduction, resulting in reduced cardiovascular events in randomized control clinical trials. Among other antihypertensive agents, ARBs have shown more potent anti-inflammatory properties unrelated to BP-lowering effect as a result of direct antagonism of angiotensin II. Although reducing BP is the primary goal, reduction of low-grade inflammation in hypertension may be an interesting and important target in order to reduce the cardiovascular morbidity and mortality.

Drugs which contain anti-hypertensive as well as anti-inflammatory properties may prove to be a novel anti-hypertensive drug in future.

In the present study approximately 42.67% cases were having raised levels of CRP in Hypertension cases with male preponderance having markedly higher incidence of raised levels of CRP. As a result we concluded that association of inflammation in the development of AH and CAD, the mechanisms of these require further evaluation to reduce the cardiovascular morbidity and mortality.

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