Research Article

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Association of C-reactive protein and arterial hypertension

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ABSTRACT

Background: Emerging evidence links inflammation to atherosclerosis. Although some study have suggested the role of inflammation in patients with arterial hypertension and coronary artery disease cases. Higher levels of C-reactive protein (CRP), a common, easily measured inflammatory marker for which clinical cut points have been recommended, have been prospectively associated with an increased risk of hypertension. However, the relationship of other inflammatory markers, other than CRP, with the risk of developing hypertension remains largely untested. The activation of the renin-angiotensin system (RAS) is primarily involved in the pathophysiology of hypertension and the development of CVD. In addition to its effect on BP, angiotensin II is also a proinflammatory mediator. Antagonism of the RAS may improve cardiovascular outcomes beyond BP control, by reducing vascular inflammation and remodeling. It is over all contribution in AH and CVD far from being understand. Present study aimed to examine whether CRP a marker and systemic inflammation, are associated with AH.

Methods: One hundred cases of AH attending Jhalawar Medical College and Hospital, Jhalawar were included in the study and their CRP levels and lipid profile and other routine investigations were carried out by suitable standard methods.

Results: We found about 48 % cases of AH were having elevated CRP levels.

Conclusions: CRP levels are associated with future development of AH, which suggest AH due to atherosclerosis is in part of inflammatory disease concluded in present study.

Keywords: C-reactive protein (CRP), Arterial hypertension (AH), Cardio Vascular Disease (CAD), Hypertension (HT), Renin-angiotensin system (RAS)

INTRODUCTION

Inflammation has been hypothesized to play a role in the development of hypertension. ^{1,2} Cross-sectional evidence demonstrates elevations in plasma inflammatory markers among individuals with elevated blood pressure (BP). ²⁻⁶ Higher levels of C-reactive protein (CRP), a common, easily measured inflammatory marker for which clinical cut points have been recommended, ⁷ have been prospectively associated with an increased risk of hypertension. ⁸⁻¹⁰ However, the relationship of other inflammatory markers, other than CRP, with the risk of developing hypertension remain largely untested.

Low grade inflammation localized in vascular tissue is increasingly recognized as an important contributor to the pathophysiology of hypertension, 11 to the initiation and progression of atherosclerosis and the development of cardiovascular disease (CVD). 12,13 Patients with CVD present increased expression and plasma concentrations of inflammatory markers and mediators. Among them, C-reactive protein (CRP) has been demonstrated as an independent risk factor for the development of hypertension. 14,15 And has been associated with increased risk of diabetes and CVD. Numerous epidemiological studies have shown that plasma levels of high-sensitivity CRP (hsCRP) are a powerful predictor of ischemic

cardiovascular events in patients with stable or unstable angina. Furthermore, hsCRP levels have been shown to correlate with systolic blood pressure (BP), pulse pressure, and incident hypertension. 16 Thus CRP and high BP in combination have additional predictive value for cardiovascular outcomes, as they contribute as independent determinants of cardiovascular risk. The activation of the renin-angiotensin system (RAS) is primarily involved in the pathophysiology hypertension and the development of CVD.¹⁷ In addition to its effect on BP, angiotensin II is also a proinflammatory mediator. 18,19 Antagonism of the RAS may improve cardiovascular outcomes beyond BP control, by reducing vascular inflammation and remodeling. In this study we will discuss the role of CRP as marker and /or mediator of low-grade inflammation in the vasculature of hypertensive patients.

METHODS

One hundred cases of arterial hypertension (Newly diagnosed) attending Jhalawar Medical College and Hospital Jhalawar a tertiary care center were randomly included in study with criteria for exclusion were Diabetes mellitus, CRF, Smoking which are considered as a risk factor for arterial hypertension, Diagnosis of these cases as a hypertension were JNC-7 criteria. Routine investigations along with blood sugar, lipid profile, urea, creatinine were carried out Estimation of CRP were done in OPD in as well as in IPD in hypertensive cases. Qualitative estimation of CRP was done by diagnostic commercial reagent kit method for the in vitro detection of CRP in human serum by qualitative and semi-quantitative rapid latex slide test. No follow- up CRP levels was observed.

RESULTS

Out of 100 patients whose data were collected, 72 were male and 28 were female. A patient age was ranging from 30 years to 82 years and mean age was 59 years. In present study raised CRP levels were observed in 48% patients (48 cases) and normal CRP levels were observed in 52% patients (52 cases). In 48 patients CRP positive group 42 were male and 6 were female. Simultaneously CBC, blood sugar, urea, creatinine and lipid profile was also carried out to exclude the other co-morbid diseases in all cases.

DISCUSSION

The CRP is a marker of systemic inflammation that has been associated with an increased risk of incident M.I. and stroke^{20,21} and AH. Several reports available in literature to show the high association of C - reactive protein levels with different cardiovascular event. For example, c-reactive protein levels were higher among people who were physically inactive,^{22–25} had worse cardio respiratory fitness,^{26,27} and were more obese.²⁸ c-reactive protein levels were also associated with the

presence and extent of the metabolic syndrome, ²⁹⁻³¹ with the presence of subclinical atherosclerosis, 32 and with the progression of atherosclerosis. 33,34 inflammation has been hypothesized to play a role in development of hypertension and cross sectional evidence suggest higher CRP levels among those individuals who were hypertensive. ³⁵⁻⁴⁰ In present study similar findings were observed that 48 % 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 87.5% were male & 12.5% were female). Higher levels of CRP may increases blood pressure by reducing nitric oxide production in endothelial cells. 41-44 CRP may also functions as a proatherosclerotic factor by up regulating angiotensin type 1 receptor expression.⁴⁵ Inflammation has been shown to correlate with endothelial dysfunction 46 and relate to the renninangiotensin system. 47 As a result it has been hypothesized that arterial hypertension may be in part an in inflammatory disorder.

However clinical data linking inflammation with incident arterial hypertension are scarce. 48 some experts recommend routine measurement of HSCRP along with cholesterol measurement as a screening tool for AH and cardiovascular disease. However, this is not a widely accepted recommendation and its practice remains controversial. However, if CRP screening is performed, then two separate measurements need to be done (ideally done 2 weeks apart) with the average of the measurements used to assess risk. Any therapy to lower CRP levels focuses on lowering the cardiovascular risk factors. Cholesterol lowering medications (statins) have been linked to lowering of CRP levels in individuals with high cholesterol. The fall of CRP levels may occur even without significant improvement in cholesterol levels. Earlier researcher have observed the patients with high LDL cholesterol levels, those with low HSCRP have better clinical outcomes than those with higher levels The use of aspirin in healthy individuals was not shown to reduce CRP levels significantly. However, in patients with cardiovascular disease and elevated CRP, the reduction of cardiovascular risk and CRP levels was noted after aspirin. In terms of cardiovascular disease, lower levels of c-reactive protein may be associated with lower overall risk of disease and a better outlook for the patient. The anti-hypertensive drugs which exert their pharmacological effect by antagonism of RAS have improved cardiovascular out comes beyond BP control by reducing vascular inflammation and remodeling.

Arterial BP control is critical to reduce the burden of cardiovascular morbidity and mortality. Indeed, arterial hypertension contributes to increase the latter in combination with other cardiovascular risk factors (such as obesity, diabetes and dyslipidaemia). JNC-VII and WHO-ISH and other national and international guidelines have suggested different non-pharmacological and pharmacological approaches to reduce BP in hypertensive patients. Since hypertension is a pro-inflammatory

condition, non-pharmacological (weight loss, exercise and Mediterranean-style diet) and pharmacological therapeutic intervention to control BP have also been proposed to reduce vascular inflammation in patients with hypertension, in order to achieve a reduction of cardiovascular events and improved outcomes in randomized clinical trials.

The current study had several limitations. First, sample collections were inadequate and needs large sample collections for further study, second; only qualitative assessment of CRP was done. Traditionally, CRP levels have been measured with in the 3-5mg/l range in assessing for inflammation. High sensitivity CRP (HSCRP) tests able to measure down to 0.3mg/l which is necessary in risk assessment for vascular disease are available. Third, no base line and post treatment status of CRP levels were carried out. However, it has been shown that single CRP measurements provide important information for risk prediction⁵¹. Fourth, 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 that contributes to cardiovascular disease. Non pharmacological and pharmacological approaches to control high BP may decrease vascular inflammation independently of BP reduction in patients with hypertension, resulting in reduced cardiovascular events in randomized clinical trials. Among other antihypertensive agents, ARBs have shown more potent anti-inflammatory properties unrelated to BP-lowering effect of this class of drugs, but more probably the result of a direct antagonism of the pro-inflammatory effects induced by angiotensin II. Thus, although reducing BP is the primary goal in order to decrease cardiovascular events in hypertensive patients, reduction of low-grade inflammation in hypertension may be an interesting and important target in order to reduce the cardiovascular morbidity and mortality associated with hypertension. So the drug which will contain antihypertensive as well as anti-inflammatory properties may prove a novel anti-hypertensive drug in future to prevent the cardiovascular morbidity and mortality associated with hypertension. Non-pharmacological (weight loss, exercise and Mediterranean-style diet) to control BP can be proposed to reduce vascular inflammation in patients with hypertension, in order to achieve a reduction of cardiovascular events and improved outcomes. In the present study approximately 48% cases were having raised levels of CRP in Hypertension cases and as compare to female, males were having markedly higher incidence of raised levels of CRP in hypertension cases, As a result of these studies we concluded that association of inflammation in the development of AH and CAD, the

mechanisms of this effect are uncertain and require further evaluation.

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Institutional Ethics Committee

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