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High-Sensitivity C-Reactive Protein as a Sensitive Indicator for Early Assessment of Inflammatory Factors in Hypertension

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ABSTRACT

Inflammation stands as an established pivotal factor in the pathogenesis of hypertension. C-reactive protein (CRP) is a recognized indicator of vascular inflammation linked to the development of hypertension. High-sensitivity CRP (hs-CRP) is a highly responsive marker for evaluating inflammatory changes even before the elevation of conventional CRP. The primary objective of this investigation was to discern the stage at which inflammation initiates in relation to the progression of hypertension, utilizing CRP and hs-CRP as biomarkers. This study employed a cross-sectional design, involving a cohort of 158 participants, categorized into three groups: Normotensive (n = 56), pre-hypertensive (n = 56) and hypertensive (n = 56) individuals. The classification of blood pressure was conducted in accordance with the Joint National Committee (JNC) guidelines. The analysis of hs-CRP was carried out employing the enzyme-linked immunosorbent assay (ELISA) method. A substantial disparity in hs-CRP levels was observed between the normotensive and hypertensive groups. Furthermore, a robust association was identified between hypertension, CRP and hs-CRP. High-sensitivity CRP emerges as a highly sensitive marker for the early assessment of inflammatory components in the context of hypertension.

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Key Words
C-reactive protein, hypertension, inflammation

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INTRODUCTION

The estimation suggests that approximately 1 billion adults worldwide suffer from hypertension, with 333 million residing in economically developed nations and 639 million in economically developing countries[1]. Research has indicated that hypertension is closely linked to an inflammatory state[2]. Essential hypertension exhibits various inflammatory markers, including C-reactive protein (CRP)-a well-established marker for hypertension-as well as vascular cell adhesion molecule and inter-cellular adhesion molecule[3]. Limited evidence currently supports the association between high-sensitivity CRP (hs-CRP) levels and blood pressure indices[4].

High-sensitivity CRP (hs-CRP) is primarily synthesized in hepatocytes, which are stimulated by interleukin-6 (IL-6) and tumor necrosis factor (TNF), both recognized biomarkers of systemic inflammation. Therefore, hs-CRP may serve as an early indicator of hypertension[5,6].

There has been a scarcity of studies establishing a clear link between hs-CRP and hypertension. This study aims to investigate the relationship between hs-CRP and CRP in hypertensive, pre-hypertensive and normotensive individuals. The study has three specific objectives. Firstly, it aims to investigate the levels of CRP in individuals with varying blood pressure statuses, including hypertension, pre-hypertension and normal blood pressure. Secondly, the study seeks to assess the correlation between blood pressure and inflammatory markers, specifically CRP and high-sensitivity C-reactive protein (hs-CRP). Lastly, the research will delve into the association between CRP and hs-CRP values within subgroups of hypertensive, pre-hypertensive and normotensive individuals, shedding light on potential links between these inflammatory markers and different blood pressure categories.

MATERIALS AND METHODS

In this case-control study, the study's sample size comprised 156 subjects, evenly divided into three groups: 52 hypertensive, 52 pre-hypertensive and 52 normotensive individuals. Among the hypertensive group, participants were further categorized into two subgroups-recently diagnosed hypertensive and those with a history of antihypertensive medication for either 2 years or less. Selection of subjects adhered to specific inclusion and exclusion criteria. Hypertension was defined as systolic blood pressure exceeding 140 mmHg and diastolic blood pressure exceeding 90 mmHg[7]. Subjects within the age range of 25-60 years were included, encompassing individuals with a history of hypertension and those recently diagnosed and undergoing medical treatment for hypertension. Excluded from the study were subjects with chronic medical conditions other than hypertension, pregnant or menstruating women and individuals with infections within the past 3 months, those with obesity, smokers and regular alcohol consumers. During the examination, participants were required to rest for 10 min with their arm exposed and supported against a chair. Ideally, they should not have consumed caffeine within 30 min before testing. Blood pressure measurements were recorded twice, with a 2 min interval between readings, using a standard mercury sphygmomanometer.

Classification of CRP and hs-CRP values is as follows:

- **CRP range:** <5 mg L^{-1} (Normal), 5-10 mg L^{-1} (Mild) and >20 mg L^{-1} (Severe)
- **hs-CRP range:** <0.5 mg L^{-1} (Normal), 0.5-1.0 mg L^{-1} (Mild), 1-5 mg L^{-1} (Moderate) and >5 mg L^{-1} (severe)

Statistical methods employed in the study included the presentation of summary statistics with mean, standard deviation and standard error for quantitative data. Parametric tests, such as independent samples t-test and one-way analysis of variance, were utilized. Additionally, association and correlation analyses were conducted to explore the relationships between the study parameters.

RESULTS

Figure 1 displays the distribution of CRP and hs-CRP in normotensive, pre-hypertensive and hypertensive individuals. Table 1 reveals an association between blood pressure grades, with hs-CRP exhibiting a robust correlation. The Chi-square statistic indicates

Table 1: Correlation between CRP, hs-CRP and hypertension

	Controls		Pre-HTN		HTN		Recently diagnosed HTN		
CRP	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	p-value
Negative	53	94.64	53	94.64	26	89.66	17	62.96	<0.05
Mild	3	5.36	3	5.36	2	6.90	7	25.93	
Severe	0	0.00	0	0.00	1	3.45	3	11.11	
hs-CRP									
Negative	49	87.50	41	73.21	11	37.93	11	40.74	<0.05
Mild	4	7.14	4	7.14	1	3.45	3	11.11	
Moderate	0	0.00	7	12.50	11	37.93	6	22.22	
Severe	3	5.36	4	7.14	6	20.69	7	25.93	

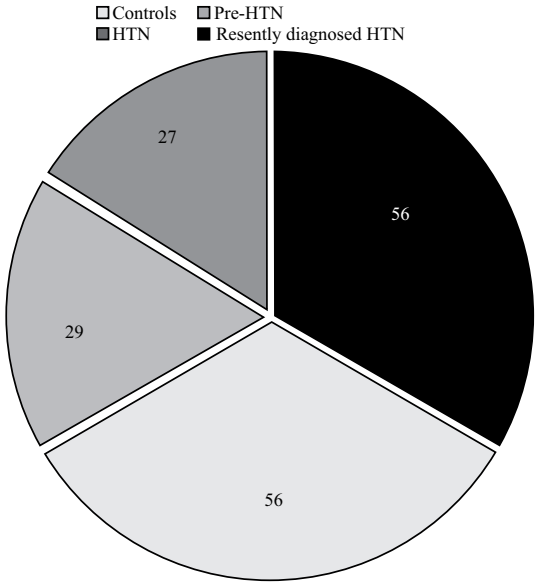

Fig. 1: Distribution of hypertensives, pre-hypertensive and normotensives

a significant association, with a p<0.05. This association is most prominent in recently diagnosed hypertensive patients, followed by prehypertensive individuals and established hypertensive patients.

DISCUSSIONS

The Framingham Heart Study demonstrated a consistent increase in the incidence of hypertension across the age spectrum, from 30-84 years old. This rise in blood pressure with age is primarily attributed to the stiffening of large arteries due to arteriosclerosis. This arterial stiffness results in increased reflection of pressure waves from arterioles back to the heart during their propagation. With advancing age, several physiological changes occur, including reduced baroreceptor sensitivity, heightened response to sympathetic stimulation, altered sodium metabolism and changes in the interplay between renin and aldosterone systems[8].

Additionally, certain studies propose that hypertension triggers various proinflammatory stimuli within the blood vessel walls, leading to the release of proinflammatory cytokines like IL-6, tumor necrosis factor-α and CRP as part of a defensive response. Inflammation, in turn, hampers endothelium-dependent vasodilation mediated by vasodilators such as adenosine and nitric oxide, consequently elevating blood pressure. This phenomenon has been corroborated in studies involving patients with coronary heart disease, where increased CRP levels were found to impair endothelial vasodilation, leading to vasoconstriction, leukocyte adhesion, platelet activation, oxidation and eventually thrombus formation. These mechanisms could also occur in individuals with hypertension[1,6].

The study also observed a linear increase in blood pressure with rising BMI, consistent with findings in a study by Dua *et al*.[9]. Notably, hs-CRP serves as an exceptionally sensitive marker of inflammation, detecting inflammation at a very fine scale even before CRP can identify it[10,11]. CRP, in addition to hs-CRP, demonstrates a strong association with a similar trend across four groups of subjects in the study, as indicated by a p<0.05. These findings align with those of Giles *et al*.[7].

The study's strengths lie in the recognition of hs-CRP and CRP as established markers of inflammatory components in hypertensive and prehypertensive individuals. These markers can aid in identifying individuals at risk and guide lifestyle modifications to prevent the onset of hypertension. However, it's important to note that hs-CRP and CRP testing can be relatively costly, making them less accessible for individuals with low socioeconomic status. Future research could consider conducting studies with larger sample sizes to further establish and refine the associations observed in this study.

CONCLUSION

High-sensitivity C-reactive protein (hs-CRP) stands as a perceptive and responsive marker, capable of detecting low-grade inflammation even before traditional CRP can identify it. Additional research is warranted to establish cost-effective parameters for the early assessment of inflammatory changes in pre-hypertensive individuals.

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