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"HIGH-SENSITIVITY C-REACTIVE PROTEIN AS AN EARLY BIOMARKER OF SUBCLINICAL INFLAMMATION IN INDIVIDUALS WITH A FAMILY HISTORY OF HYPERTENSION"

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Abstract

Background: Hypertension is a major modifiable risk factor for cardiovascular disease. A positive family history of hypertension is an established predictor of its development in the offspring of hypertensive parents. High-sensitivity C-reactive protein (hs-CRP) is a widely studied biomarker for cardiovascular disease risk prediction. The high-sensitivity assay can detect CRP within a range of 0.01–10 mg/L, enabling the assessment of low-grade systemic inflammation even in the absence of overt inflammatory or immunologic disorders.

Aim: To evaluate hs-CRP as an early biomarker of endothelial dysfunction and future hypertension risk in young, healthy adults with a family history of hypertension.

Methods: A total of 140 participants aged 18–30 years were included. The study comprised 70 cases—offspring of hypertensive parents (OHTPs)—and 70 controls—offspring of normotensive parents (ONHTPs). Anthropometric variables and hs-CRP levels were recorded and analysed using appropriate statistical methods.

Results: The mean hs-CRP level was significantly higher in OHTPs compared with ONHTPs ($p < 0.001$). No significant differences were observed between the groups with respect to age and body mass index.

Conclusion: Elevated hs-CRP levels in normotensive offspring of hypertensive parents suggest the presence of subclinical inflammation and early endothelial dysfunction, which may contribute to the future development of hypertension. Identifying such biomarkers may aid in risk stratification and early preventive strategies.

Keywords: Hypertension, hs-CRP, Offspring, Endothelial dysfunction, Subclinical inflammation.

Background

Hypertension is a major risk factor for cardiovascular disease, and a positive family history represents an important non-modifiable determinant of its development. Approximately 30% of blood pressure variability is attributable to genetic factors, ranging from 25% in pedigree studies

to 65% in twin studies [1,2]. Genetic predisposition involves mechanisms such as altered sodium handling [3] and increased oxidative stress [4,5], both of which contribute to vascular dysfunction.
Hypertension is now widely recognized as an inflammatory disease, highly mediated by angiotensin II. Angiotensin II promotes vascular inflammation by increasing endothelial permeability, stimulating leukocyte adhesion, enhancing VEGF-driven vascular proliferation, and inducing endothelin-mediated vascular stiffening [6,7]. These processes result in vascular remodelling, arterial stiffness, and progressive hypertension [8,9,10].
C-reactive protein (CRP), a pentraxin family acute-phase protein synthesized in the liver under the regulation of interleukin-6, is a well-established marker of systemic inflammation [11,12]. In healthy individuals, CRP levels are generally below 5 mg/L, whereas higher values are associated with infection, tissue injury, or necrosis [13,14]. The development of high-sensitivity assays (hs-CRP) has enabled the detection of low-grade inflammation in the range of 0.01–10 mg/L [15], making hs-CRP a widely studied biomarker for cardiovascular disease risk prediction [16].
Endothelial dysfunction is a key mechanism linking inflammation with hypertension. It is characterized by impaired vasodilation, vascular remodelling, and a shift toward a pro-inflammatory and pro-thrombotic state [17]. CRP itself interferes with nitric oxide and prostacyclin activity, further impairing endothelial function and promoting atherosclerosis [18]. Chronic low-grade inflammation, therefore, may contribute to both the initiation and progression of hypertension and cardiovascular disease.
In **2003** the **Centers for Disease Control and Prevention (CDC)** and **The American Heart Association (AHA)** recommended patient stratification into three groups in cardiovascular disease risk assessment (Table 1):

hs-CRP Level	**Risk of Development of CVD**
<1 mg/L	Low Risk
1-3 mg/L	Intermediate Risk
>3 mg/L	High Risk
Table 1: hs-CRP Risk Stratification	

Hs-CRP has been observed to predict the development of cardiovascular disease independently of established risk factors, and these studies has added to the growing body of evidence of low-grade inflammation in the pathogenesis of cardiovascular disease [19]

Materials and Method

The study design was a case-control study. The study was conducted in the Department of Physiology, Government Medical College Kota, Kota, Rajasthan after approval from the Institutional Ethical Committee *[No.F.3()Acad/Ethicalclearance/Batch2021/2022/62]*

The Study groups

The study was conducted on a total of 70 normotensive participants aged 18–30 years. The study groups were defined as **A. *Case group* -** Having a family history of hypertension; **B. *Control group* -** Having no family history of hypertension.
The subjects were recruited after applying the criteria for exclusion and inclusion. After the selection of subjects informed written consent was obtained and then data were collected.
Inclusion criteria: Healthy young adults between the age group of 18-30 years, of both sexes with family history of hypertension.
Exclusion criteria: Endocrine disorders, recent infections, cardiorespiratory disorders, medications affecting central and autonomic nervous system.
Aim of the Study: To determine the role of using hs-CRP as a biomarker for the early detection of endothelial dysfunction and prediction of future development of hypertension in young healthy adults with family history of hypertension.

Data Collection:

Blood sample and Anthropometric variables-

Anthropometric variables were obtained for all participants.

Blood sample collected in proper aseptic condition and Collected blood sample transported to laboratory in ice cube container on same day and Hs-CRP-levels measured by fully automated Immuno turbidimetry method.

Result:

S. No.	Group	Parameter	Mean ± SD	p-value	Statistical Significance
1	Case Group	Female	34 (48.6%)	0.8	Not Significant
		Male	36 (51.4%)		
	Control Group	Female	32 (45.7%)		
		Male	38 (54.3%)		
2	Case Group	Age	22.8 ± 2.5	0.21	Not Significant
	Control Group	Age	22.2 ± 3.1		
3	Case Group	BMI	21.9 ± 3.6	0.61	Not Significant
	Control Group	BMI	21.6 ± 3.5		
4	Case Group	hs-CRP	2 ± 0.9	0.000001	Significant
	Control Group	hs-CRP	1.1 ± 0.6		

Table 2: Statistical Analysis of Demographic and Biochemical Parameters in Case vs. Control Groups

A total of 70 participants were included in the study, comprising 34 (48.6%) females and 36 (51.4%) males in the case group, while the control group consisted of 32 (45.7%) females and 38 (54.3%) males.

The mean age of participants in the case group was 22.8 ± 2.5 years, compared to 22.2 ± 3.1 years in the control group. The difference in age between the two groups was statistically insignificant ($p = 0.21$).

The mean body mass index (BMI) in the case group was 21.9 ± 3.6 kg/m², while in the control group it was 21.6 ± 3.5 kg/m². Independent t-test analysis revealed no significant difference between the two groups with respect to BMI ($p = 0.6146$).

In contrast, the mean hs-CRP level in the case group was 2.0 ± 0.9 mg/L, whereas in the control group it was 1.1 ± 0.6 mg/L. This difference was found to be highly significant ($p < 0.0000001$), indicating that hs-CRP levels were markedly elevated in the case group compared to controls.

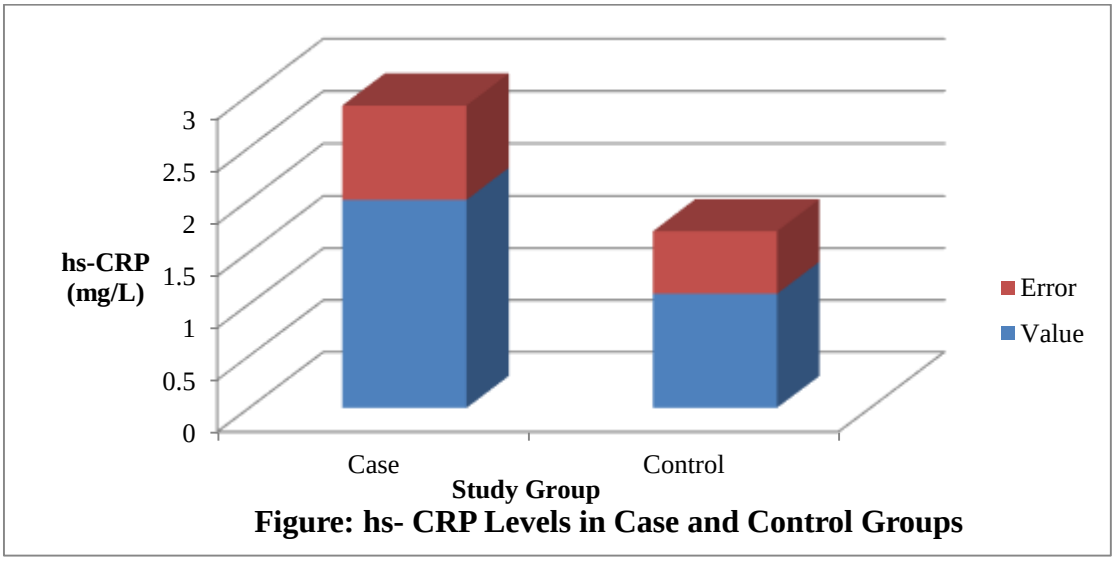

Figure: hs- CRP Levels in Case and Control Groups

Discussion

Previous studies have highlighted a bidirectional relationship between obesity and depression. Luppino et al. [20] reported that the elevated BMI levels and depression are linked through several mechanisms, including systemic inflammation. Interestingly, obesity and depression were also found to be inversely correlated in certain contexts. Furthermore, neuroendocrine abnormalities in patients with depression may contribute to weight gain and increased BMI [21].

In the present study, no significant differences were observed between genders, or ages of case and control subjects. Similarly, BMI values did not differ significantly between the two groups, indicating that BMI may not be a distinguishing factor in our study.

Our findings on hs-CRP are consistent with previous literature. Nyandak et al. [22] reported a correlation between the severity of coronary stenosis and hs-CRP levels, emphasizing the role of inflammation not only as an acute trigger for plaque rupture but also as a chronic driver of atherosclerosis. Our observation of significantly elevated hs-CRP levels in OHTPs compared with controls reinforces the notion that low-grade systemic inflammation is a pivotal early pathophysiological change, linking familial predisposition to heightened cardiovascular risk

hs-CRP has also been recognized as a prognostic biomarker in patients without evidence of myocyte necrosis. Studies have shown that elevated hs-CRP levels in the stable phase after acute cardiovascular events hold prognostic value for future outcomes [23]. Our findings underscore the prognostic significance of elevated hs-CRP levels, which were positively associated with individuals in the case group and with a family history of hypertension.

The association of hs-CRP with metabolic and cardiovascular risk factors has been reported in multiple studies. Soriano-Guillen et al. [24] found hs-CRP to be positively correlated with BMI, systolic blood pressure (SBP), and diastolic blood pressure (DBP), though not with serum lipids. Similarly, other research has shown that BMI, triglycerides, and HDL cholesterol levels influence hs-CRP variability, and that elevated hs-CRP is predictive of future hypertension [25]. Experimental studies suggest that elevated blood pressure may itself stimulate a pro-inflammatory response, leading to endothelial inflammation and subsequent structural changes in the arterial wall [26]. Tatasciore et al. [27] and Abramson et al. [28] also demonstrated a significant relationship between hs-CRP levels and blood pressure variability, even in healthy, normotensive adults. These findings underscore the potential role of inflammation in driving hemodynamic instability and long-term vascular risk.

Our study adds to the growing body of evidence that hs-CRP is a significant biomarker of cardiovascular risk. While BMI and demographic parameters were not significantly different between groups, the elevation of hs-CRP in cases highlights its value as an early indicator of vascular inflammation and potential target for risk stratification.

Limitations and Future Directions

The present study has some limitations. First, the sample size was relatively small, which may limit the generalizability of our findings. Second, we did not assess other potential confounding factors such as dietary habits, physical activity, socioeconomic status, or medication use, all of which may influence hs-CRP levels. Moreover, incorporating additional inflammatory biomarkers and advanced imaging modalities may provide a more comprehensive understanding of the role of inflammation in cardiovascular disease progression.

Conclusion

We conclude the statistically insignificant differences between age, gender, and BMI in OHTPs and ONHTPs strengthens the comparability of our findings.

Elevated hs-CRP in OHTPs may indicate a contributory role of inflammation in the early development of hypertension and cardiovascular risk. hs-CRP may a valuable biomarker for future outcomes. Future large studies should further investigate whether hs-CRP can be applied as a reliable screening tool.

Conflict of Interest

There are no conflicts of interest.

References:

1. Corvol P, Jeunemaitre X, Charru A, Soubrier F. Can the genetic factors influence the treatment of systemic hypertension? The case of the renin-angiotensin-aldosterone system. Am J Cardiol. 1992;70(12):14D–20D. doi:10.1016/0002-9149(92)90267-3.
2. Carretero OA, Oparil S. Essential hypertension. Part I: definition and etiology. Circulation. 2000;101(3):329–335. doi:10.1161/01.CIR.101.3.329.
3. Simsolo RB, Romo MM, Rabinovich L, Bonanno M, Grunfeld B. Family history of essential hypertension versus obesity as risk factors for hypertension in adolescents. Am J Hypertens. 1999;12(3):260–263. doi:10.1016/S0895-7061(98)00253-2.
4. Williams RR, Hunt SC, Hopkins PN, Hasstedt SJ, Wu LL, Lalouel JM. Tabulations and expectations regarding the genetics of human hypertension. Kidney Int Suppl. 1994;44:S57–S64.
5. Münzel T, Gori T, Bruno RM, Taddei S. Is oxidative stress a therapeutic target in cardiovascular disease? Eur Heart J. 2010;31(22):2741–2748. doi:10.1093/eurheartj/ehq396.
6. Hage FG, Oparil S, Xing D, Chen YF, McCrory MA, Szalai AJ. C-reactive protein–mediated vascular injury requires complement. Arterioscler Thromb Vasc Biol. 2010;30(6):1189–1195. doi:10.1161/ATVBAHA.110.205120.
7. Harrison DG, Guzik TJ, Lob HE, et al. Inflammation, immunity, and hypertension. Hypertension. 2011;57(2):132–140. doi:10.1161/HYPERTENSIONAHA.110.163576.
8. Boos CJ, Lip GY. Elevated high-sensitivity C-reactive protein, large arterial stiffness and atherosclerosis: a relationship between inflammation and hypertension? J Hum Hypertens. 2005;19(7):511–513. doi:10.1038/sj.jhh.1001864.
9. Kusche-Vihrog K, Urbanova K, Blanqué A, et al. C-reactive protein makes human endothelium stiff and tight. Hypertension. 2011;57(2):231–237. doi:10.1161/ HYPERTENSIONAHA.110.163444.
10. Smith GD, Lawlor DA, Harbord R, et al. Association of C-reactive protein with blood pressure and hypertension: life course confounding and mendelian randomization tests of causality. Arterioscler Thromb Vasc Biol. 2005;25(5):1051–1056. doi:10.1161/01. ATV. 0000160351.95181.d0.
11. Kushner I, Samols D. Oswald Avery and the pneumococcus. Pharos Alpha Omega Alpha Honor Med Soc. 2011;74(1):14–18.
12. Francis T, Tillett WS. Studies on the somatic C polysaccharide of pneumococcus: I. cutaneous and serological reactions in pneumonia. J Exp Med. 1937;65(1):59–73. doi:10.1084/jem.65.1.59.
13. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med. 1999;340(6):448–454. doi:10.1056/NEJM199902113400607.
14. Trayhurn P. Endocrine and signalling role of adipose tissue: new perspectives on fat. Acta Physiol Scand. 2005;184(4):285–293. doi:10.1111/j.1365-201X.2005.01468.x.
15. Roberts WL. CDC/AHA Workshop on markers of inflammation and cardiovascular disease: application to clinical and public health practice: laboratory tests available to assess inflammation—performance and standardization: a background paper. Circulation. 2004;110(25):e572–e576. doi:10.1161/01.CIR.0000148983.92011.5E.
16. Wang CH, Li SH, Weisel RD, et al. C-reactive protein upregulates angiotensin type 1 receptors in vascular smooth muscle. Circulation. 2003;107(13):1783–1790. doi:10.1161/01.CIR.0000058460.40405.17.
17. Savoia C, D'Agostino M, Lauri F, Volpe M. Angiotensin type 2 receptor in hypertensive cardiovascular disease. Curr Opin Nephrol Hypertens. 2011;20(2):125–132. doi:10.1097/MNH.0b013e3283437fcd.

18. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med. 1999;340(6):448–454. doi:10.1056/NEJM199902113400607.
19. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N Engl J Med. 2002;347(20):1557–1565. doi:10.1056/NEJMoa021993.
20. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry. 2010;67(3):220–229. doi:10.1001/archgenpsychiatry.2010.2.
21. Faith MS, Matz PE, Jorge MA. Obesity–depression associations in the population. J Psychosom Res. 2002;53(4):935–942. doi:10.1016/S0022-3999(02)00308-2.
22. Nyandak T, Gogna A, Bansal S, Deb M. High sensitive C-reactive protein (Hs-CRP) and its correlation with angiographic severity of coronary artery disease (CAD). J Indian Acad Clin Med. 2007;8(3):217–221.
23. Blake GJ, Ridker PM. Inflammatory biomarkers and cardiovascular risk prediction. J Intern Med. 2002;252(4):283–294. doi:10.1046/j.1365-2796.2002.01021.x.
24. Soriano-Guillen L, Hernández-García B, Pita J, Domínguez-Garrido N, del Río-Amacho G, Rovira A. High-sensitivity C-reactive protein is a good marker of cardiovascular risk in obese children and adolescents. Eur J Endocrinol. 2008;159(1):R1–R4. doi:10.1530/EJE-08-0092.
25. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. JAMA. 2003;290(22):2945–2951. doi:10.1001/ jama. 290.22.2945.
26. Intengan HD, Schiffrin EL. Vascular remodeling in hypertension: roles of apoptosis, inflammation, and fibrosis. Hypertension. 2001;38(3):581–587. doi:10.1161/hy09t1.096249.
27. Tatasciore A, Zimarino M, Renda G, Zurro M, Soccio M, Prontera C, et al. Awake blood pressure variability, inflammatory markers and target organ damage in newly diagnosed hypertension. Hypertens Res. 2008;31(12):2137–2146. doi:10.1291/hypres.31.2137.
28. Abramson JL, Lewis C, Murrah NV, Anderson GT, Vaccarino V. Relation of C-reactive protein and tumor necrosis factor-α to ambulatory blood pressure variability in healthy adults. Am J Cardiol. 2006;98(5):649–652. doi:10.1016/j.amjcard.2006.03.049.