e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(5); 657-663

Original Research Article

The Role of Hs-C Reactive Protein & Correlation of Serum Zinc & Magnesium in Essential Hypertension as a Cardiovascular Risk Marker

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Received: 01-02-2026 / Revised: 15-03-2026 / Accepted: 21-04-2026
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Conflict of interest: Nil

Abstract

Introduction: Hypertension affects over a billion of people globally and is a major contributor to cardiovascular diseases such as heart disease, stroke, and kidney failure. Essential hypertension, influenced by genetic and environmental factors, is associated with chronic inflammation, where high-sensitivity C-reactive protein (hs-CRP) serves as a key marker. The minerals zinc and magnesium are crucial for blood pressure regulation. This study examines the relationship between hs-CRP, zinc, and magnesium levels in essential hypertension and their implications for cardiovascular risk.

Methodology: A total of 170 participants, including 85 newly diagnosed hypertensive patients and 85 normotensive controls, were evaluated. Serum hs-CRP was measured using the turbidimetry method, magnesium by the colorimetric method, and zinc via inductively coupled plasma mass spectrometry (ICP-MS). Statistical analysis was performed using SPSS (version 21.0).

Results: Hypertensive individuals had significantly higher systolic (151.14 ± 9.86 mmHg) and diastolic (94.51 ± 8.21 mmHg) blood pressure compared to controls ($p < 0.001$). hs-CRP levels were significantly elevated in hypertensive participants (4.67 ± 4.74 mg/L) versus controls (1.71 ± 2.28 mg/L; $p < 0.001$). Serum magnesium levels were lower in hypertensive individuals (1.94 ± 0.35 mg/dL; $p < 0.001$), while no significant difference in serum zinc levels was observed ($p = 0.36$). A negative correlation was found between serum magnesium and blood pressure, but no correlation with zinc was evident.

Conclusion: Elevated hs-CRP levels and magnesium deficiency are critical markers in essential hypertension. Monitoring these biomarkers could enhance hypertension management and reduce cardiovascular risks.

Keywords: Hypertension, Zinc, Magnesium, hs-CRP.

DOI: 10.25258/ijcpr.18.5.102

Introduction

Hypertension is one of the most prevalent non-communicable diseases worldwide and represents a major contributor to global morbidity and mortality. It affects more than one billion individuals and is responsible for nearly 9–10 million deaths annually due to its strong association with cardiovascular, cerebrovascular, and renal complications. Persistent elevation of blood pressure significantly increases the risk of coronary heart disease, heart failure, stroke, chronic kidney disease, and peripheral vascular disease. Because it often remains asymptomatic until target organ damage occurs, hypertension is widely recognized as a "silent killer," necessitating early detection and effective risk stratification. [1]

Blood Pressure classification in adults

Table 1: Latest guideline by American Heart Association. DS-16580 8/20. [2]

Blood pressure category	Systolic (mmHg)		Diastolic (mmHg)
Normal	<120	And	<80
Elevated	120-129	And	<80
Hypertension			
Stage -1	130-139	Or	80-89
Stage -2	≥ 140	Or	≥90
Hypertensive Crisis	>180	&/or	>120

Based on American heart association guidelines, adult blood pressure is classified into normal, elevated, stage 1 hypertension, stage 2 hypertension, and hypertensive crisis. While most patients are diagnosed with primary (essential) hypertension, nearly 5–20% have identifiable secondary causes. Essential hypertension, which accounts for approximately 80–95% of cases, is multifactorial in origin and results from complex interactions between genetic predisposition and environmental influences such as obesity, sedentary lifestyle, excess salt intake, and psychosocial stress. Increased peripheral vascular resistance, altered renin–angiotensin–aldosterone system activity, sympathetic overactivity, and endothelial dysfunction play key roles in its pathophysiology. [3] Obesity and metabolic syndrome have emerged as important determinants of hypertension. Central adiposity is strongly correlated with insulin resistance, dyslipidaemia, and chronic low-grade inflammation, all of which contribute to vascular injury and atherosclerosis. Traditional cardiovascular risk assessment tools, including lipid profile alone, may not adequately identify individuals at risk, highlighting the need for additional biomarkers that reflect underlying inflammatory processes. [4]

Inflammation has been increasingly recognized as a pivotal mechanism in the development and progression of atherosclerosis. High-sensitivity C-reactive protein (hs-CRP), an acute phase reactant synthesized by the liver, has gained considerable attention as a sensitive and reliable marker of systemic inflammation. Elevated hs-CRP levels are associated with endothelial dysfunction, plaque instability, and enhanced thrombogenesis, thereby predicting future cardiovascular events independent of conventional risk factors. Measurement of hs-CRP using high-sensitivity assays enables detection of low-grade inflammation and may provide additional prognostic value in patients with essential hypertension. [5,6]

In addition to inflammatory markers, micronutrients such as zinc and magnesium have been implicated in blood pressure regulation. Zinc, an essential trace element and cofactor for numerous enzymes, plays an important role in antioxidant defense mechanisms, immune function, and cellular metabolism. Zinc deficiency has been associated with increased oxidative stress, enhanced renal sodium retention, and vascular dysfunction, which may contribute to the development of hypertension. Similarly, magnesium is a critical intracellular cation involved in vascular tone regulation, electrolyte transport, ATP-dependent enzymatic reactions, and smooth muscle relaxation. Alterations in magnesium levels can influence cardiac excitability and vascular reactivity, thereby affecting blood pressure homeostasis. [7,8,9,10]

Considering the growing evidence linking inflammation and micronutrient imbalance with cardiovascular risk, evaluating hs-CRP, serum zinc, and magnesium levels may provide valuable insights into the pathophysiology of essential hypertension. Therefore, the present study aims to assess the role of hs-CRP as an inflammatory cardiovascular risk marker and to determine its correlation with serum zinc and magnesium levels in patients with essential hypertension, thereby contributing to improved risk assessment and preventive strategies.

Materials and Methods

The present study was designed as a cross-sectional analytical study to evaluate the association of high-sensitivity C-reactive protein (hs-CRP), serum zinc, and serum magnesium levels with essential hypertension. The study was carried out in the Clinical Biochemistry Laboratory and the Multidisciplinary Research Unit (MDRU) of M.B. Government Hospital, which is attached to R.N.T. Medical College, Udaipur, and Rajasthan, India. The hospital is a tertiary care teaching centre catering to urban and rural populations, thereby providing a representative patient base.

Prior to commencement, approval was obtained from the Institutional Ethical Committee. All procedures adhered to ethical standards in accordance with the Declaration of Helsinki. Written informed consent was obtained from each participant after explaining the purpose and protocol of the study.

Study Population and Sample Size

A total of 170 participants were included in the study (Sample size was calculated based on prevalence reported by Jinkook Lee et al. [32] in 2022). Participants were divided into two groups:

- Group I (Control): 85 normotensive healthy subjects
- Group II (Cases): 85 newly diagnosed patients with essential hypertension

The sample size was calculated based on previously published prevalence data indicating that approximately 45–50% of the middle-aged Indian population is hypertensive. Considering a confidence level of 95% and adequate statistical power, the calculated sample size was deemed sufficient to detect significant biochemical differences between the two groups.

Inclusion Criteria

Participants fulfilling the following criteria were enrolled:

1. Age between 30 and 60 years
2. For control group: clinically healthy individuals with normal blood pressure
3. For study group: newly diagnosed cases of essential hypertension

Exclusion Criteria

To minimize confounding variables, the following individuals were excluded:

- Diabetes mellitus
- Chronic inflammatory or autoimmune diseases
- Acute infections or sepsis
- Stroke or cardiovascular events
- Recent trauma
- Gout
- Chronic renal or hepatic disease
- Patients on lipid-lowering drugs, probenecid, or anti-inflammatory medications
- Critically ill or hospitalized patients

Selection of Participants: Hypertensive patients were recruited from the Medicine Outpatient Department (OPD). Diagnosis of essential hypertension was made based on repeated blood pressure measurements and clinical assessment. Controls were selected from healthy attendants, hospital staff, and relatives of patients, provided they satisfied eligibility criteria and demonstrated normal blood pressure values.

All participants underwent detailed clinical history taking, physical examination, and baseline investigations before inclusion.

Blood Pressure Measurement: Blood pressure was measured using a calibrated mercury sphygmomanometer. Measurements were taken in a quiet environment after the participant had rested for at least five minutes in a sitting posture. The cuff was applied to the right upper arm at heart level. Two readings were recorded five minutes apart, and the average value was considered for analysis.

Systolic blood pressure corresponded to the first Korotkoff sound (Phase I), while diastolic blood pressure corresponded to the disappearance of sounds (Phase V). Blood pressure was expressed in millimeters of mercury (mmHg). [12]

Sample Collection and Handling: After overnight fasting of 8–10 hours, approximately 5–7 mL of venous blood was collected from each participant using aseptic precautions.

- 2 mL in EDTA vial for complete blood count
- Remaining blood in plain clot activator tube for biochemical tests

Samples were allowed to clot for one hour and centrifuged at 3500 rpm for 10 minutes. Serum was separated carefully to avoid hemolysis and transferred to metal-free polypropylene tubes. Serum aliquots were analyzed immediately or stored at −20°C until further analysis. [11]

Laboratory Investigations: All biochemical parameters were analyzed using automated analyzers to ensure accuracy and reproducibility.

Routine Biochemical Tests

The following tests were performed in all participants:

- Fasting blood glucose
- Lipid profile (Total cholesterol, triglycerides, HDL, LDL, VLDL)
- Kidney function tests (urea, creatinine, uric acid, electrolytes)
- Liver function tests (bilirubin, AST, ALT, total protein)
- Complete blood count

Analyses were performed on the Cobas Pro integrated clinical chemistry system manufactured by Roche Diagnostics.

Estimation of hs-CRP: Serum hs-CRP levels were measured by particle-enhanced immunoturbidimetric assay using latex particles coated with monoclonal anti-CRP antibodies. The antigen-antibody reaction produces turbidity proportional to CRP concentration.

The reaction mixture was analyzed photometrically at 546 nm, and results were automatically calculated and expressed in mg/L. Internal quality controls were run daily to ensure assay precision and reliability. [25]

Estimation of Serum Magnesium: Serum magnesium was measured by a colorimetric endpoint method using xylidyl blue dye. Magnesium ions form a colored complex with the dye, and the intensity of color is directly proportional to magnesium concentration.

Absorbance was read at 510 nm. Results were expressed in mg/dL. Hemolyzed samples were excluded due to possible interference. [26]

Estimation of Serum Zinc: Serum zinc levels were determined using inductively coupled plasma mass spectrometry (ICP-MS), a highly sensitive and specific technique for trace element analysis. Measurements were performed on the Agilent 7850 ICP-MS system from Agilent Technologies. [27] Results were expressed in µg/dL. Strict contamination control measures were maintained throughout processing. [27]

Quality Control Measures: Standard operating procedures were followed for all laboratory analyses. Calibration of instruments was performed regularly. Internal and external quality controls were run daily. All assays were conducted by trained personnel to minimize analytical errors.

Statistical Analysis: Data were compiled and analyzed using Statistical Package for Social Sciences (SPSS) software version 21.0. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as percentages.

Comparisons between two groups were made using Student's independent t-test. Analysis of variance (ANOVA) was used for multiple comparisons. Chi-square test was applied for categorical variables. Correlation analysis was performed to assess relationships between hs-CRP, zinc, magnesium, and blood pressure. A p-value < 0.05 was considered statistically significant with a 95% confidence interval.

Results: The research involved a total of 170 participants, comprising 85 newly diagnosed hypertension patients and 85 normotensive individuals serving as controls.

All 170 participants were of age from 30 to 60 years with mean age of 47.45±8.28 years.

Mean age of hypertensive group- 48.94 ± 8.35 years and mean age of normotensive group- 45.97±8.01 years.

Blood pressure distribution

- The mean systolic and diastolic blood pressure of 170 participants were 132.28±21.19 mmHg and 88±16.5 mmHg respectively.
- The mean systolic and diastolic blood pressure in hypertensive (cases) group were 151.14±9.86 mmHg and 94.51±8.21 mmHg respectively.
- The mean systolic and diastolic blood pressure in normotensive (controls)
- Group were 113.41±9.27 mmHg and 69.20±5.17 respectively.
- The mean systolic blood pressure and diastolic blood pressure of both hypertensive (cases) and normotensive (controls) groups indicates significantly higher systolic and diastolic blood pressure compared to the control group with p-value <0.001.

Table 2: Comparison of level of hs-CRP in both Groups.

hs-CRP (mg/L)	Hypertensive (Cases)	Normotensive (Controls)	p-value
	4.67±4.74	1.71±2.28	<0.001 (HS)

- The mean value of hs-CRP level in hypertensive group: 4.67±4.74 mg/L and in normotensive group: 1.71±2.28 mg/L.
- The mean value of hs-CRP level in hypertensive group is significantly higher in comparison with normotensive group (p<0.001).
- The mean value of hs-CRP level of female participants in hypertensive group: 4.70 ± 5.38 mg/L and in female participants in normotensive group: 1.60 ± 2.13 mg/L.
- The mean value of hs-CRP level in male participants of hypertensive group: 4.65 ± 4.12 mg/L and in male participants of normotensive group: 1.81 ± 2.43 mg/L.
- The mean value of hs-CRP level of Female participants and male participants in hypertensive group is higher in comparison with female and male participants of normotensive group (p<0.001).

Table 3: Comparison of level of serum Mg in both the Groups.

Serum Mg (mg/dL)	Hypertensive (Cases)	Normotensive (Controls)	p-value
	1.94±0.35	2.08±0.19	<0.001 (HS)

- The mean value of Serum Mg level in hypertensive group: 1.94±0.35 mg/dL and in normotensive group: 2.08±0.19 mg/dL.
- The difference of mean value of Serum Mg level between hypertensive (cases) and normotensive (controls) group is significant (p<0.001).
- The mean value of Serum Mg level of female participants in hypertensive group: 1.93 ± 0.39 mg/dL and in female participant of normotensive group: 2.07 ± 0.18 mg/dL.
- The mean value of Serum Mg level in male participants of hypertensive group: 1.95 ± 0.33 mg/dL and in male participants of normotensive group: 2.09 ± 0.20 mg/dL.
- The mean value of Serum Mg level of Female participants of hypertensive group showed significant difference with female participants of normotensive group (p=0.003).
- The mean value of Serum Mg level of male participants in hypertensive group showed significant difference with male participants of normotensive group (p=0.001).

Table 4: Comparison of level of serum Zn in both Groups.

Serum Zn (µg/dL)	Hypertensive (Cases)	Normotensive (Controls)	p-value
	97.87±44.02	104.46±50.07	0.36 (NS)

- The mean value of Serum Zn level in hypertensive group: 97.87±44.02 µg/dL and in normotensive group: 104.46±50.07 µg/dL.
- The mean value of Serum Zn level in hypertensive (cases) group showed no significant relation with normotensive (controls) group (p=0.36).
- The mean value of Serum Zn level in female participants of hypertensive group: 105.34 ± 45.18 µg/dL and in female participants of normotensive group: 101.13 ± 53.52 µg/dL.
- The mean value of Serum Zn level in male participants of hypertensive group: 90.91 ± 42.23 µg/dL and in male participants of normotensive group 107.42 ± 47.20 µg/dL.
- The mean value of Serum Zn level in female participants of hypertensive group showed no significant relation with female participants of normotensive group (p=0.580).
- The mean value of serum Zn level in male participants of hypertensive group showed difference with male participants of normotensive group.

Table 5: Correlation between Serum Mg and Zn in hypertensive participants.

Hypertensive Group	Total Participants	Mean of Serum Mg (mg/dL)	Mean of Serum Zn (µg/dL)	Pearson correlation coefficient (r)
	85	1.94±0.35	97.87±44.02	0.044

Pearson correlation coefficient (r) 0.044 (positive correlation) observed between serum Mg & serum Zn in the hypertensive participants.

Table 6: Correlation of serum Mg level with blood pressure in hypertensive participants.

Variables	Mean	Pearson correlation coefficient (r) with Mg
Systole (mmHg)	151.14±9.86	-0.464**
Diastole (mmHg)	94.51±8.21	-0.242*

****. Correlation is significant at the 0.01 level (2-tailed), * correlation is significant at the 0.05 level (2-tailed).**

- Pearson correlation coefficient (r) -0.464 (Significantly negative) observed between serum Mg and systolic blood pressure.
- Pearson correlation coefficient (r) -0.242 (Significantly negative) observed between serum Mg and diastolic blood pressure.

Table 7: Correlation of Serum Zn level with blood pressure in hypertensive participants.

Variables	Mean	Pearson correlation coefficient (r) with Zn
Systole (mmHg)	151.14±9.86	-0.069
Diastole (mmHg)	94.51±8.21	-0.077

- Pearson correlation coefficient (r) -0.069 (negative correlation) observed between serum Zn and systolic blood pressure.
- Pearson correlation coefficient (r) -0.077 (negative correlation) observed between serum Zn and diastolic blood pressure.

Discussion

The present study evaluates the role of high-sensitivity C-reactive protein (hs-CRP) and its association with serum zinc and magnesium levels in essential hypertension, aiming to identify potential cardiovascular risk markers. Chronic inflammation, micronutrient imbalance, and endothelial dysfunction are well-recognized contributors to hypertension pathogenesis. Elevated hs-CRP reflects systemic inflammation, while magnesium and zinc influence vascular tone and oxidative stress mechanisms. [17,30,31] A total of 170 participants were included, comprising 85 hypertensive cases and 85 normotensive controls. As expected, systolic and diastolic blood pressures were significantly higher in hypertensive individuals (p<0.001), consistent with previous findings by Tiwari et al. [22] and Sur et al. [23]. Gender distribution in our study demonstrated a higher prevalence of hypertension among males in younger age groups, which equalized with advancing age. This trend aligns with epidemiological data from National Health and Nutrition Examination Survey (NHANES) [28] and findings by Mohanty et al., [29] indicating increased prevalence among females after menopause due to hormonal changes.

Our study revealed significantly elevated hs-CRP levels in hypertensive participants, with 51% showing levels >3 mg/L compared to 19% in controls (p<0.001). These findings support the role of inflammation in hypertension and are consistent with studies by Sung et al. [14] and Sudjaroen et al., [15] who demonstrated a positive association between hs-CRP and blood pressure. Elevated hs-CRP contributes to endothelial dysfunction and vascular stiffness, thereby increasing blood pressure. [17] However, Bisaria et al. [18] reported no significant association, highlighting variability across populations.

Serum magnesium levels were significantly lower in hypertensive individuals, showing a negative correlation with both systolic and diastolic blood pressure ($p<0.001$). Magnesium plays a critical role in vascular relaxation and acts as a natural calcium channel blocker. [30] These findings are consistent with Rekha et al. [16] and Sezgin et al., [19] who also reported an inverse relationship between magnesium levels and blood pressure.

Additionally, Verma et al. [20] demonstrated that magnesium supplementation can significantly reduce systolic blood pressure. In contrast, Huitrón-Bravo et al. [21] found no association with dietary magnesium intake, suggesting potential differences between serum levels and intake-based assessments.

In contrast, serum zinc levels did not show a significant overall difference between hypertensive and normotensive groups ($p=0.36$), although a significant difference was observed among males ($p=0.017$). A negative correlation between zinc and blood pressure was noted. These findings are consistent with Bergomi et al., [13] who also reported no significant difference but observed an inverse relationship with blood pressure. However, conflicting evidence exists, as Tiwari et al. [22] reported lower zinc levels in hypertensive patients, while Taneja et al. [24] and Kunutsor et al. reported positive associations.

Overall, this study highlights the significant role of hs-CRP and magnesium in hypertension, while the role of zinc remains complex and possibly influenced by gender and other factors. These findings support the integration of inflammatory and micronutrient markers in hypertension risk assessment and emphasize the need for personalized management strategies.

Conclusion

Our study underscores the importance of high-sensitivity C-reactive protein (hs-CRP), serum zinc, and magnesium levels in the context of essential hypertension, revealing valuable insights into the multifaceted interactions between these biomarkers and hypertension. The investigation involved 170 participants, divided equally into hypertensive cases and normotensive controls, and examined the significance of these cardiovascular risk markers.

The study provides compelling evidence for the significance of monitoring hs-CRP, magnesium, and zinc levels in hypertensive patients. Elevated hs-CRP levels can serve as a marker for inflammation and cardiovascular risk, while magnesium deficiency appears to be a modifiable risk factor for hypertension. The gender-specific findings related to zinc suggest the need for personalized approaches in managing hypertension. Furthermore, the relationship between lipid profiles and hypertension underlines the importance of integrated cardiovascular risk management.

Our study contributes to a deeper understanding of the biochemical markers associated with hypertension and their potential implications for improving hypertension management and reducing associated morbidity. Future research should continue to explore these relationships and their practical applications in clinical settings.

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