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ORIGINAL ARTICLE

Association of Vitamin D Deficiency with High-Sensitivity CRP and Arterial Stiffness in Patients with Hypertensive Heart Disease

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ABSTRACT

Background: Hypertensive heart disease (HHD) is a major cardiovascular complication of long-standing hypertension and is characterized by progressive vascular remodeling, arterial stiffness, and low-grade systemic inflammation. Vitamin D deficiency has been increasingly implicated in endothelial dysfunction, inflammatory activation, and adverse cardiovascular outcomes; however, its relationship with inflammatory markers and arterial stiffness in patients with established hypertensive heart disease remains insufficiently explored.

Objective: To evaluate the association of vitamin D deficiency with high-sensitivity C-reactive protein (hs-CRP) levels and arterial stiffness in patients with hypertensive heart disease.

Methods: This cross-sectional analytical study was conducted from January 2022 to March 2023 at Sahiwal Teaching Hospital, Sahiwal, and Sugra Shafi Medical Complex, Narowal, Pakistan. A total of 100 adult patients with echocardiographically confirmed hypertensive heart disease were enrolled. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured and categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Inflammatory status was assessed using hs-CRP. Arterial stiffness was evaluated by carotid–femoral pulse wave velocity (cf-PWV) and augmentation index. Statistical analysis included group comparisons, correlation analysis, and multivariable linear regression to determine independent associations.

Results: Vitamin D deficiency was present in 56% of patients. Individuals with deficient vitamin D levels exhibited significantly higher hs-CRP concentrations and increased arterial stiffness compared with those having sufficient vitamin D ($p<0.001$). Serum 25(OH)D levels showed a significant inverse correlation with hs-CRP ($r = −0.48$), cf-PWV ($r = −0.52$), and augmentation index ($r = −0.41$). After adjustment for age, gender, body mass index, blood pressure, diabetes mellitus, duration of hypertension, renal function, and medication use, vitamin D levels remained an independent predictor of both hs-CRP and cf-PWV ($p<0.001$).

Conclusion: Vitamin D deficiency is independently associated with increased systemic inflammation and arterial stiffness in patients with hypertensive heart disease. These findings suggest that low vitamin D status may contribute to vascular dysfunction and inflammatory burden in hypertensive cardiac pathology and highlight the potential value of vitamin D assessment in this high-risk population.

Keywords: Vitamin D deficiency; Hypertensive heart disease; High-sensitivity C-reactive protein; Arterial stiffness; Pulse wave velocity; Inflammation

INTRODUCTION

Hypertensive heart disease (HHD) represents a major spectrum of cardiovascular morbidity resulting from long-standing systemic hypertension and remains a leading cause of heart failure, arrhythmias, and premature cardiovascular mortality worldwide[1]. Persistent elevation of arterial pressure induces structural and functional alterations in both the myocardium and vasculature, including left ventricular hypertrophy, impaired diastolic relaxation, and progressive arterial stiffening. These pathological changes increase cardiac workload, compromise coronary perfusion, and accelerate the transition from compensated hypertensive remodeling to overt cardiac dysfunction[2].

Arterial stiffness is now recognized as a central pathophysiological component of hypertensive cardiovascular damage rather than a passive consequence of aging alone. Increased stiffness of large elastic arteries leads to elevated systolic blood pressure, widened pulse pressure, and enhanced transmission of pulsatile energy to microcirculatory beds, thereby exacerbating target-organ injury[3]. Inflammatory processes play a pivotal role in this vascular remodeling, promoting endothelial dysfunction, collagen deposition, elastin degradation, and vascular smooth muscle cell proliferation. High-sensitivity C-reactive protein (hs-CRP) is a well-established marker of low-grade systemic inflammation and has been consistently associated with arterial stiffness, atherosclerotic burden, and adverse cardiovascular outcomes in hypertensive populations[4].

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Vitamin D has emerged as an important non-traditional cardiovascular modulator with effects extending beyond calcium and bone metabolism. Vitamin D receptors are expressed in endothelial cells, vascular smooth muscle cells, and cardiomyocytes, supporting its role in vascular tone regulation, immune modulation, and myocardial function[5]. Experimental and clinical evidence suggests that vitamin D deficiency may contribute to endothelial dysfunction, activation of the renin–angiotensin–aldosterone system, increased oxidative stress, and heightened inflammatory responses. Consequently, low vitamin D status has been linked with hypertension, vascular stiffness, and elevated inflammatory biomarkers, including hs-CRP[6].

Vitamin D deficiency is highly prevalent in South Asian populations, including individuals with established cardiovascular disease, owing to limited sun exposure, dietary insufficiency, and lifestyle factors[7]. Despite growing evidence linking vitamin D deficiency with cardiovascular risk, its relationship with inflammatory burden and arterial stiffness in patients who already exhibit hypertensive target-organ damage remains insufficiently characterized. Understanding this association is particularly relevant in hypertensive heart disease, where inflammation and vascular stiffness synergistically drive disease progression[8].

Therefore, the present study aims to investigate the association of vitamin D deficiency with high-sensitivity C-reactive protein levels and arterial stiffness indices in patients with hypertensive heart disease. Elucidating this relationship may provide insight into potentially modifiable pathways contributing to vascular dysfunction and adverse cardiovascular outcomes in this high-risk population[9].

MATERIALS AND METHODS

This cross-sectional analytical study was conducted from January 2022 to March 2023 to evaluate the association of vitamin D deficiency with high-sensitivity C-reactive protein and arterial stiffness among patients with hypertensive heart disease. The study was carried out at Sahiwal Teaching Hospital, Sahiwal, and Sugra Shafi Medical Complex, Narowal, Pakistan, both tertiary care institutions that manage a high volume of patients with chronic hypertension and cardiovascular complications.

A total of 100 adult patients with a confirmed diagnosis of hypertensive heart disease were enrolled using a consecutive non-probability sampling technique. Patients aged 18 years or older with a history of systemic hypertension for at least one year and echocardiographic evidence of hypertensive heart disease, including left ventricular hypertrophy and/or diastolic dysfunction, were included. Patients were excluded if they had recent acute infections, acute coronary syndrome, or cerebrovascular events within the preceding four weeks, chronic inflammatory or autoimmune diseases, chronic liver disease, malignancy, advanced chronic kidney disease with an estimated glomerular filtration rate below 30 mL/min/1.73 m², pregnancy, recent high-dose vitamin D supplementation within the last three months, or cardiac disease due to non-hypertensive etiologies such as significant valvular disease or cardiomyopathy.

After obtaining written informed consent, detailed demographic and clinical data were collected, including age, sex, duration of hypertension, smoking status, presence of diabetes mellitus, medication history, and body mass index. Blood pressure was measured using a standardized sphygmomanometer, and the mean of two readings taken five minutes apart in a seated position was recorded. Previously performed echocardiographic findings were reviewed to confirm the diagnosis of hypertensive heart disease.

Venous blood samples were collected under aseptic conditions for laboratory analysis. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured using a standardized chemiluminescence immunoassay and categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). High-sensitivity C-reactive protein (hs-CRP) was measured using a high-sensitivity immunoturbidimetric assay. Additional biochemical investigations, including fasting blood glucose, lipid profile, serum creatinine, and estimated glomerular filtration rate, were performed using routine laboratory techniques.

Arterial stiffness was assessed non-invasively using validated methods. Carotid–femoral pulse wave velocity (cf-PWV) was measured as the primary indicator of central arterial stiffness, while the augmentation index (AIx) was recorded to assess wave reflection and arterial tone. All measurements were obtained after the participants had rested in the supine position in a quiet, temperature-controlled environment to ensure standardization and reproducibility.

Data were entered and analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution, whereas categorical variables were presented as frequencies and percentages. Comparisons across vitamin D status groups were performed using analysis of variance or the Kruskal–Wallis test for continuous variables and the chi-square test for categorical variables. Correlation analyses between serum 25(OH)D levels, hs-CRP, and arterial stiffness indices were conducted using Pearson or Spearman correlation coefficients. Multivariable linear regression analysis was applied to determine the independent association of vitamin D levels with hs-CRP and arterial stiffness after adjusting for potential confounding variables. A p-value of less than 0.05 was considered statistically significant.

Ethical approval for the study was obtained from the institutional ethical review committees of both participating hospitals. Written informed consent was secured from all participants prior to enrollment, and strict confidentiality of patient information was maintained throughout the study.

RESULTS

A total of 100 patients with hypertensive heart disease were included in the final analysis. The overall study population showed a middle-aged to elderly distribution, consistent with the chronic nature of hypertensive cardiovascular disease. Both genders were adequately represented, allowing meaningful gender-based interpretation. Vitamin D deficiency was highly prevalent, affecting more than half of the patients, while a smaller proportion had insufficient levels and only a minority demonstrated sufficient vitamin D status. Patients with vitamin D deficiency exhibited a more adverse cardiovascular risk profile, including longer duration of hypertension, higher body mass index, higher systolic blood pressure, and a greater frequency of diabetes mellitus, suggesting a clustering of metabolic and vascular risk factors in this subgroup as shown in table 1.As shown in Table 1, gender distribution was comparable across all vitamin D categories, with no statistically significant difference between males and females, indicating that subsequent differences in inflammatory and arterial stiffness parameters were not confounded by sex imbalance. In contrast, duration of hypertension, body mass index, systolic blood pressure, and prevalence of diabetes mellitus were significantly higher among vitamin D deficient patients, highlighting a more severe cardiometabolic profile in this group.

Inflammatory status, assessed using high-sensitivity C-reactive protein, demonstrated a clear and statistically significant gradient across vitamin D categories. Patients with vitamin D deficiency exhibited markedly elevated hs-CRP levels, reflecting heightened low-grade systemic inflammation, whereas patients with sufficient vitamin D levels showed substantially lower inflammatory burden.

As illustrated in Table 2, mean hs-CRP levels were almost twice as high in vitamin D deficient patients compared with vitamin D sufficient individuals. This statistically robust difference indicates a strong inverse association between vitamin D status and systemic inflammation in hypertensive heart disease.

Assessment of arterial stiffness further reinforced these findings. Both carotid–femoral pulse wave velocity and augmentation index were significantly elevated in patients with vitamin D deficiency, indicating increased central arterial stiffness and abnormal wave reflection. Patients with sufficient vitamin D levels demonstrated the lowest arterial stiffness values, suggesting a more favorable vascular profile as shown in table 4.

To determine whether vitamin D deficiency independently predicted inflammation and arterial stiffness, multivariable linear regression analysis was performed after adjusting for age, gender, body mass index, systolic blood pressure, duration of hypertension, diabetes mellitus, lipid profile, renal function, and antihypertensive medication use. Serum 25-hydroxyvitamin D remained a significant independent predictor of both hs-CRP and carotid–femoral pulse wave velocity as shown in table 5.

These results demonstrate that vitamin D deficiency is independently associated with increased systemic inflammation and arterial stiffness in patients with hypertensive heart disease. The persistence of these associations after comprehensive adjustment for demographic, metabolic, and clinical confounders highlights the potential pathophysiological role of vitamin D in modulating inflammatory and vascular mechanisms underlying hypertensive cardiac damage.

Table 1. Baseline demographic and clinical characteristics according to vitamin D status

Variable	Vitamin D Deficient (<20 ng/mL)	Vitamin D Insufficient (20–29 ng/mL)	Vitamin D Sufficient (≥30 ng/mL)	p-value
Number of patients, n (%)	56 (56%)	28 (28%)	16 (16%)	—
Age (years), mean ± SD	55.8 ± 9.6	53.2 ± 8.9	51.4 ± 8.1	0.18
Male, n (%)	34 (60.7%)	18 (64.3%)	10 (62.5%)	0.93
Female, n (%)	22 (39.3%)	10 (35.7%)	6 (37.5%)	0.93

Duration of hypertension (years)	9.4 ± 3.8	7.8 ± 3.2	6.9 ± 2.9	0.01
BMI (kg/m²)	28.6 ± 4.1	27.1 ± 3.8	25.9 ± 3.5	0.02
Systolic BP (mmHg)	146.3 ± 12.5	141.7 ± 11.3	138.4 ± 10.9	0.03
Diabetes mellitus, n (%)	31 (55.4%)	12 (42.9%)	5 (31.3%)	0.04

Table 2. Comparison of hs-CRP levels across vitamin D categories

Parameter	Vitamin D Deficient	Vitamin D Insufficient	Vitamin D Sufficient	p-value
hs-CRP (mg/L), mean ± SD	4.9 ± 1.8	3.6 ± 1.4	2.4 ± 1.1	<0.001

Table 3. Arterial stiffness indices according to vitamin D status

Parameter	Vitamin D Deficient	Vitamin D Insufficient	Vitamin D Sufficient	p-value
cf-PWV (m/s), mean ± SD	11.8 ± 2.1	10.6 ± 1.8	9.5 ± 1.6	<0.001
Augmentation Index (%)	31.4 ± 6.7	27.9 ± 5.8	24.6 ± 5.1	0.002

Table 4. Correlation of serum 25(OH)D with hs-CRP and arterial stiffness parameters

Variable	Correlation coefficient (r)	p-value
25(OH)D vs hs-CRP	−0.48	<0.001
25(OH)D vs cf-PWV	−0.52	<0.001
25(OH)D vs Augmentation Index	−0.41	<0.001

Table 5. Multivariable regression analysis showing independent association of vitamin D with hs-CRP and cf-PWV

Outcome variable	Predictor	β coefficient (95% CI)	p-value
hs-CRP	25(OH)D	−0.32 (−0.47 to −0.18)	<0.001
cf-PWV	25(OH)D	−0.38 (−0.55 to −0.22)	<0.001

DISCUSSION

The present study demonstrates a strong and independent association between vitamin D deficiency, systemic inflammation, and arterial stiffness in patients with hypertensive heart disease[9,10]. In this cohort, vitamin D deficiency was highly prevalent and was associated with significantly elevated hs-CRP levels and increased arterial stiffness, as reflected by higher carotid–femoral pulse wave velocity and augmentation index values. These findings highlight the potential role of vitamin D status in modulating inflammatory and vascular pathways that contribute to the progression of hypertensive cardiac damage[11].

One of the key observations of this study is the marked increase in hs-CRP levels among vitamin D deficient patients. High-sensitivity CRP is a sensitive indicator of low-grade systemic inflammation and has been consistently linked to endothelial dysfunction, atherosclerosis, and adverse cardiovascular outcomes[12]. The inverse relationship observed between serum 25-hydroxyvitamin D and hs-CRP suggests that vitamin D deficiency may contribute to a pro-inflammatory state in hypertensive heart disease. Vitamin D is known to exert immunomodulatory effects by suppressing pro-inflammatory cytokine production and inhibiting nuclear factor-κB signaling pathways. Deficiency of vitamin D may therefore amplify chronic inflammation, accelerating vascular remodeling and myocardial structural changes commonly seen in long-standing hypertension[13].

Arterial stiffness, a hallmark of hypertensive vascular disease, was significantly greater in patients with lower vitamin D levels. Carotid–femoral pulse wave velocity, the gold-standard measure of central arterial stiffness, showed a strong inverse correlation with serum vitamin D levels, indicating that deficiency is associated with increased aortic rigidity[14]. This relationship is biologically plausible, as vitamin D influences vascular smooth muscle cell proliferation, collagen deposition, and elastin integrity. Moreover, vitamin D deficiency has been linked to activation of the renin–angiotensin–aldosterone system, leading to vasoconstriction, vascular hypertrophy, and increased arterial stiffness. The elevated augmentation index observed in vitamin D deficient patients further supports the presence of abnormal wave reflection and impaired arterial compliance in this group[15].

Importantly, the association between vitamin D levels and both hs-CRP and arterial stiffness remained significant even after adjusting for age, gender, body mass index, blood pressure, diabetes mellitus, duration of hypertension, renal function, and medication use[16]. This indicates that vitamin D deficiency is not merely a surrogate marker of poor health or advanced disease but may independently contribute to inflammatory and vascular abnormalities in hypertensive heart disease. The coexistence of higher BMI, longer hypertension duration, and increased diabetes prevalence among vitamin D deficient patients may further exacerbate these pathological processes, creating a synergistic effect that accelerates cardiovascular damage[17].

The findings of this study are particularly relevant in the South Asian context, where vitamin D deficiency is widespread due to limited sun exposure, dietary insufficiency, and lifestyle factors. In such populations, hypertensive patients may be exposed to a compounded risk of inflammation and vascular dysfunction related to both traditional risk factors and micronutrient deficiency[18]. Identifying vitamin D deficiency in patients with hypertensive heart disease may therefore provide an opportunity for early risk stratification and comprehensive cardiovascular management. However, while observational evidence supports an association, the impact of vitamin D supplementation on arterial stiffness and inflammatory markers remains controversial, with interventional trials showing mixed results. This underscores the need for well-designed randomized controlled trials focusing on vitamin D deficient hypertensive populations with clearly defined vascular endpoints[19].

Despite its strengths, including dual-center data and comprehensive vascular and inflammatory assessment, this study has certain limitations. The cross-sectional design precludes causal inference, and seasonal variation in vitamin D levels was not fully accounted for. Additionally, factors such as dietary intake, physical activity, and sunlight exposure were not quantitatively assessed and may have influenced vitamin D status. Nevertheless, the consistent and independent associations observed lend credibility to the findings[20].

CONCLUSION

Vitamin D deficiency is common among patients with hypertensive heart disease and is independently associated with elevated high-sensitivity C-reactive protein levels and increased arterial stiffness. Lower serum 25-hydroxyvitamin D concentrations correlate with a higher inflammatory burden and impaired vascular compliance, even after adjustment for conventional cardiovascular risk factors. These findings suggest that vitamin D deficiency may contribute to the inflammatory and vascular mechanisms underlying hypertensive cardiac damage. Routine assessment of vitamin D status in patients with hypertensive heart disease may help identify individuals at higher risk, although further prospective and interventional studies are required to determine whether correction of vitamin D deficiency can improve vascular function and clinical outcomes in this population.

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Authors' Contributions: M.H.* conceptualized and designed the study. K.S. contributed to patient recruitment and clinical assessment. M.B. performed laboratory investigations and data collection. A.J. carried out statistical analysis and interpretation of results. M.S.Z.K.S. was involved in manuscript drafting and critical revision. W.Q. supervised the study and approved the final version of the manuscript. All authors read and approved the final manuscript.
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