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STUDY OF CORRELATION OF SERUM 25-HYDROXY-VITAMIN D LEVEL WITH ANGIOGRAPHIC SEVERITY IN CORONARY ARTERY DISEASE

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ABSTRACT

Background: Vitamin D deficiency has been increasingly recognized as a potential risk factor for cardiovascular disease. Several studies have suggested an association between low serum vitamin D levels and coronary artery disease (CAD); however, its relationship with angiographic severity remains incompletely understood.
Objectives: To evaluate the correlation between serum 25-hydroxyvitamin D [25(OH)D] levels and angiographic severity of CAD assessed using the Gensini score and to compare vitamin D levels between patients with CAD and controls.
Methods: This hospital-based case-control cross-sectional study was conducted in the Department of Cardiology, NRI Institute of Medical Sciences, Mangalagiri, India, between June 2021 and November 2022. A total of 300 participants were enrolled, including 150 patients with angiographically proven CAD and 150 controls with normal coronary angiograms. Demographic characteristics, cardiovascular risk factors, serum 25(OH)D levels, serum calcium levels, and angiographic findings were recorded. Severity of CAD was assessed using the Gensini score. Statistical analysis included Student's t-test, chi-square test, ANOVA, and Pearson correlation analysis.
Results: The mean serum vitamin D level was significantly lower among cases than controls (23.41 ± 7.40 ng/mL vs. 28.67 ± 6.38 ng/mL, $p<0.001$). Cases also had significantly lower serum calcium levels (7.92 ± 0.98 mg/dL vs. 9.05 ± 0.89 mg/dL, $p<0.001$) and significantly higher Gensini scores (35.78 ± 49.67 vs. 1.06 ± 0.52, $p<0.001$). Serum vitamin D levels declined progressively with increasing coronary artery involvement, from 27.19 ± 5.38 ng/mL in single-vessel disease to 15.58 ± 2.56 ng/mL in double-vessel disease and 13.00 ± 1.87 ng/mL in triple-vessel disease ($p<0.001$). A significant inverse correlation was observed between serum vitamin D levels and Gensini score ($r = -0.622$, $p<0.001$).
Conclusion: Serum 25-hydroxyvitamin D levels were significantly lower in patients with CAD and demonstrated a significant inverse correlation with angiographic severity assessed by the Gensini score. Vitamin D deficiency may serve as a useful marker of coronary atherosclerotic burden and CAD severity.

Keywords: *Vitamin D, Coronary artery disease, Gensini score, Coronary angiography, Cardiovascular disease.*

INTRODUCTION

Vitamin D deficiency is a common public health problem worldwide. The two principal forms of vitamin D are ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). Ergocalciferol is derived from plant sources, whereas cholecalciferol is synthesized in the skin following exposure to ultraviolet-B radiation. Vitamin D is obtained through sunlight exposure and dietary intake, including nutritional supplements [1]. The biologically active form, 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], plays an important role in several physiological processes. Serum vitamin D levels between 20–30 ng/mL are considered insufficient, while levels ≥30 ng/mL are regarded as adequate [2].

Vitamin D receptors are widely distributed in cardiomyocytes, vascular smooth muscle cells, and endothelial cells, suggesting an important role in cardiovascular health [3–5]. Growing evidence has linked vitamin D deficiency with insulin resistance, hypertension, heart failure, stroke, and other cardiovascular diseases [6–10]. Furthermore, studies have demonstrated an inverse association between sun exposure and mortality due to ischemic heart disease, highlighting a potential cardioprotective role of vitamin D [11,12]. Several mechanisms have been proposed to explain the relationship between vitamin D deficiency and coronary artery disease (CAD), including modulation of the renin–angiotensin system, regulation of blood pressure and glycemic control, improvement of vascular compliance, and anti-inflammatory effects. Vitamin D has also been associated with reduced coronary artery calcification and favorable effects on cholesterol metabolism within macrophages and foam cells [13].

Cardiovascular disease remains a leading cause of morbidity and mortality globally. Stable angina, often the earliest clinical manifestation of ischemic heart disease, affects approximately 213 individuals per 100,000 population above 30 years of age [14]. India bears a substantial burden of cardiovascular disease, with deaths increasing from 2.26 million in 1990 to 4.77 million in 2020 [15]. Given the high prevalence of vitamin D deficiency in India and the limited available evidence regarding its association with CAD severity, this study was undertaken to evaluate the correlation between serum 25-hydroxyvitamin D levels and angiographic severity of coronary artery disease.

MATERIALS AND METHODS

This hospital-based case-control cross-sectional study was conducted in the Department of Cardiology, NRI Institute of Medical Sciences, Mangalagiri, Andhra Pradesh, India, over a period of 18 months from June 2021 to November 2022. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants before enrolment.

The sample size was calculated using the prevalence of coronary artery disease among the urban Indian population reported by Gupta et al. [31]. Using the formula $N = Z^2PQ/E^2$, with a prevalence of 13.2%, confidence level of 95%, and absolute error of 4%, the minimum required sample size was estimated to be 276. To compensate for possible exclusions and incomplete data, a total of 300 participants were included in the study. Among 388 patients screened during the study period, 300 fulfilled the eligibility criteria and were enrolled. All enrolled participants completed the study and had complete clinical and laboratory data available for analysis.

The study population consisted of patients aged 30–70 years presenting with chest pain and diagnosed with coronary artery disease, including ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, chronic stable angina, and unstable angina. Diagnoses were established according to the American College of Cardiology and American Heart Association (ACC/AHA) guidelines [32]. Subjects with normal coronary angiographic findings served as controls. Pregnant and lactating women, patients with renal, hepatic, or cardiac failure, those receiving vitamin D supplementation, patients with osteoporosis, and those with incomplete clinical data were excluded from the study. Participants were recruited using a convenience sampling technique.

A total of 300 subjects were included and categorized into two groups: cases (n=150), comprising patients with abnormal coronary angiographic findings consistent with CAD, and controls (n=150), comprising subjects with normal coronary angiographic findings. Demographic and clinical characteristics including age, sex, diabetes mellitus, hypertension, body mass index, smoking status, alcohol consumption, and low-density lipoprotein cholesterol levels were recorded for all participants.

All participants underwent detailed clinical evaluation, standard 12-lead electrocardiography, echocardiography, and coronary angiography. Serum 25-hydroxyvitamin D and serum calcium levels were measured using standard laboratory methods. The severity of coronary artery disease was assessed angiographically using the Gensini scoring system. Data regarding angiographic findings, type of CAD, and associated cardiovascular risk factors were systematically recorded and analysed.

Statistical analysis was performed using appropriate statistical methods. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were presented as frequencies and percentages. Comparisons between two groups were performed using the independent samples t-test, while comparisons among multiple groups were carried out using one-way analysis of variance (ANOVA). Associations between categorical variables were assessed using the chi-square test. Pearson correlation analysis was used to determine the relationship between serum 25-hydroxyvitamin D levels and Gensini score. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 300 participants were enrolled in the study, comprising 150 cases with angiographically proven coronary artery disease (CAD) and 150 controls with normal coronary angiograms. The majority of participants were aged above 50 years (70.0%), while 30.0% were below 50 years of age. The mean age was significantly higher among cases compared to controls (56.08 ±7.06 years vs. 54.17 ±8.60 years; p=0.036).

NSTEMI was the most common clinical presentation, accounting for 106 (35.3%) patients, followed by chronic stable angina in 90 (30.0%), STEMI in 71 (23.7%), and unstable angina in 33 (11.0%) patients.

Table 1. Baseline Characteristics of Study Participants

Variable	Cases (n=150)	Controls (n=150)	Total (n=300)
Age (years), mean ± SD	56.08 ± 7.06	54.17 ± 8.60	55.12 ± 7.91
Male sex, n (%)	105 (70.0)	78 (52.0)	183 (61.0)
Female sex, n (%)	45 (30.0)	72 (48.0)	117 (39.0)
Diabetes mellitus, n (%)	43 (28.7)	19 (12.7)	62 (20.7)
Hypertension, n (%)	37 (24.7)	14 (9.3)	51 (17.0)
Smoking, n (%)	45 (30.0)	18 (12.0)	63 (21.0)
Alcohol consumption, n (%)	31 (20.7)	12 (8.0)	43 (14.3)
BMI (kg/m²), mean ± SD*	27.59 ± 4.74	25.73 ± 3.39	—
LDL cholesterol (mg/dL), mean ± SD	160.17 ± 24.33	127.71 ± 14.90	—

*BMI data available for 149 participants in each group.

Cases were older and had a higher prevalence of male sex, diabetes mellitus, hypertension, smoking, alcohol consumption, higher BMI, and elevated LDL cholesterol levels compared with controls.

Table 2. Comparison of Serum Vitamin D, Serum Calcium and Gensini Score Between Cases and Controls

Parameter	Cases (n=150) Mean ± SD	Controls (n=150) Mean ± SD	p-value
Serum Vitamin D (ng/mL)	23.41 ± 7.40	28.67 ± 6.38	<0.001
Serum Calcium (mg/dL)	7.92 ± 0.98	9.05 ± 0.89	<0.001
Gensini Score	35.78 ± 49.67	1.06 ± 0.52	<0.001

Patients with CAD had significantly lower serum vitamin D and serum calcium levels and significantly higher Gensini scores than controls.

Coronary angiography revealed normal coronary arteries in 150 (50.0%) participants. Among CAD patients, single-vessel disease was present in 104 (34.7%), double-vessel disease in 33 (11.0%), and triple-vessel disease in 13 (4.3%) participants.

Table 3. Serum Vitamin D Levels According to Coronary Angiographic Severity

Angiographic Findings	n	Mean Vitamin D (ng/mL) ± SD
Normal coronary arteries	150	28.67 ± 6.38
Single-vessel disease	104	27.19 ± 5.38
Double-vessel disease	33	15.58 ± 2.56
Triple-vessel disease	13	13.00 ± 1.87

ANOVA: $F = 74.30$, $p < 0.001$

A significant decline in serum vitamin D levels was observed with increasing severity of coronary artery involvement, with the lowest levels seen among patients with triple-vessel disease.

Table 4. Correlation Between Serum Vitamin D Levels and Gensini Score

Parameter	Value
Pearson correlation coefficient (r)	-0.622
Covariance	-179.741
Test statistic	-13.711
p-value	1.651×10^{-33}

Pearson correlation analysis demonstrated a significant moderate negative correlation between serum vitamin D levels and Gensini score, indicating that lower vitamin D levels were associated with greater angiographic severity of coronary artery disease.

The mean serum vitamin D levels among patients with chronic stable angina, NSTEMI, STEMI, and unstable angina were 25.54 ±6.92 ng/mL, 26.42 ±7.75 ng/mL, 26.31 ±6.47 ng/mL, and 25.61 ±9.28 ng/mL, respectively, with no statistically significant difference between the groups (ANOVA p=0.830). Similarly, mean Gensini scores were 20.34 ±41.70, 17.89 ±39.65, 11.95 ±24.65, and 28.83 ±52.66, respectively, and the differences were not statistically significant (ANOVA p=0.214).

DISCUSSION

The present study evaluated the relationship between serum 25-hydroxyvitamin D [25(OH)D] levels and angiographic severity of coronary artery disease (CAD) using the Gensini scoring system. The principal findings were that patients with CAD had significantly lower serum vitamin D levels than controls, vitamin D levels progressively declined with increasing coronary vessel involvement, and serum vitamin D levels demonstrated a significant inverse correlation with Gensini score. These findings suggest that vitamin D deficiency is associated not only with the presence of CAD but also with the extent and severity of coronary atherosclerosis.

In the present study, CAD patients had significantly lower serum vitamin D levels compared with controls (23.41 ±7.40 ng/mL vs. 28.67 ±6.38 ng/mL, p<0.001). Similar observations were reported by Siadat et al. [16], who demonstrated a significantly higher prevalence of vitamin D deficiency among CAD patients compared with healthy controls. Likewise, Mokadem et al. [17] reported that nearly three-fourths of patients undergoing coronary angiography had vitamin D deficiency and that lower vitamin D levels were associated with more advanced coronary disease. Mathew et al. [18] also observed a significant association between reduced vitamin D levels and the severity of coronary artery disease in Indian patients undergoing coronary angiography. These findings collectively support the hypothesis that vitamin D deficiency is closely linked to coronary atherosclerosis.

The biological mechanisms underlying this association are multifactorial. Vitamin D receptors are present in endothelial cells, vascular smooth muscle cells, and cardiomyocytes [3–5]. Deficiency of vitamin D has been associated with endothelial dysfunction, activation of the renin–angiotensin–aldosterone system, increased oxidative stress, insulin resistance, and systemic inflammation [6–10,13]. These mechanisms may accelerate atherosclerotic plaque formation and progression, ultimately increasing the burden of coronary artery disease.

An important observation of the present study was the progressive decline in serum vitamin D levels with increasing angiographic severity. Patients with triple-vessel disease had the lowest mean vitamin D levels (13.00 ±1.87 ng/mL), followed by those with double-vessel disease (15.58 ±2.56 ng/mL) and single-vessel disease (27.19 ±5.38 ng/mL). Similar findings were reported by Ewelina A et al. [19], who demonstrated significantly lower vitamin D levels among patients with one-, two-, and three-vessel disease compared with those without significant coronary lesions. Mokadem et al. [17] also reported a significant association between vitamin D deficiency and the number of affected coronary vessels. These consistent observations across different populations suggest that vitamin D status may reflect the overall atherosclerotic burden.

The most important finding of the present study was the significant inverse correlation between serum vitamin D levels and Gensini score ($r = -0.622$, $p<0.001$). The Gensini score is a validated measure of angiographic disease severity that incorporates both the degree of luminal stenosis and the anatomical significance of the affected coronary segment [20,21]. The observed correlation indicates that lower vitamin D levels were associated with more severe coronary artery stenosis. Similar inverse associations between vitamin D levels and angiographic severity have been reported by Mokadem et al. [17] and Mathew et al. [18]. These findings reinforce the potential utility of serum vitamin D as a marker of CAD severity.

The present study also identified a significantly higher prevalence of conventional cardiovascular risk factors among CAD patients. Diabetes mellitus, hypertension, smoking, alcohol consumption, increased BMI, and elevated LDL cholesterol levels were significantly more common among cases than controls. Comparable findings were reported by Siadat et al. [16], who observed significantly higher rates of diabetes, hypercholesterolemia, obesity, and smoking among CAD patients. The coexistence of vitamin D deficiency with these established cardiovascular risk factors suggests that hypovitaminosis D may contribute to cardiovascular risk through multiple interconnected pathways.

Interestingly, no significant differences in serum vitamin D levels were observed among patients with chronic stable angina, NSTEMI, STEMI, and unstable angina. Similar findings have been reported in some studies, indicating that vitamin D levels may be more closely related to the overall extent of atherosclerosis than to the specific clinical presentation of CAD. The absence of significant differences in Gensini scores among diagnostic categories in the present study further supports this observation.

The strengths of the present study include angiographic confirmation of CAD, assessment of disease severity using the validated Gensini scoring system, inclusion of a well-defined control group, and an adequate sample size. However, certain limitations should be acknowledged. The study was conducted at a single tertiary-care centre, limiting the generalizability of the findings. The cross-sectional design precludes establishment of a causal relationship between vitamin D deficiency

and CAD severity. In addition, vitamin D levels were measured only once and seasonal variations in vitamin D status were not assessed.

Overall, the findings of the present study demonstrate a significant inverse relationship between serum vitamin D levels and angiographic severity of coronary artery disease. The consistency of these findings with previous studies supports the hypothesis that vitamin D deficiency may contribute to the development and progression of coronary atherosclerosis. Further prospective multicentric studies are required to determine whether correction of vitamin D deficiency can influence cardiovascular outcomes and reduce the burden of coronary artery disease.

CONCLUSION

The present study demonstrated a significant association between serum 25-hydroxyvitamin D levels and the severity of coronary artery disease. Patients with angiographically proven CAD had significantly lower serum vitamin D levels and serum calcium levels compared with individuals having normal coronary angiograms. A progressive decline in vitamin D levels was observed with increasing coronary vessel involvement, and a significant moderate inverse correlation was identified between serum vitamin D levels and Gensini score. These findings suggest that lower vitamin D concentrations are associated with greater angiographic severity and a higher burden of coronary atherosclerosis. Traditional cardiovascular risk factors such as diabetes mellitus, hypertension, smoking, alcohol consumption, increased body mass index, and elevated LDL cholesterol were also more prevalent among CAD patients. The results indicate that vitamin D deficiency may be a useful biomarker for identifying patients at risk of severe coronary artery disease. Further prospective multicentric studies are required to establish causality and evaluate the potential benefits of vitamin D supplementation in cardiovascular risk reduction.

DECLARATIONS

Funding: None.

Conflict of Interest: The authors declare no conflict of interest.

Ethical Approval: The study was approved by the Institutional Ethics Committee of NRI Institute of Medical Sciences, Mangalagiri.

Informed Consent: Written informed consent was obtained from all participants prior to enrolment.

Availability of Data and Materials: Data are available from the corresponding author upon reasonable request.

Authors 'Contributions: All authors contributed to study conception, data collection, analysis, manuscript preparation, and approved the final manuscript.

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