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Correlation of Plasma 25-Hydroxy-Vitamin D Level with Angiographic Severity in Coronary Artery Disease.

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KEYWORDS

25-hydroxy-vitamin D level, angiographic severity (Gensini score), coronary artery disease

ABSTRACT:

Background: Coronary artery disease remains a major global health concern, ranking among the leading causes of mortality and contributing significantly to the global burden of disease measured in Disability-Adjusted Life Years (DALYs). In an article published in 2024, it was reported that there were 315 million prevalent cases of CAD worldwide. Vitamin D levels in the human body are influenced by a complex interplay of environmental, physiological, and health-related factors. Factors like geographic location, sunlight exposure are some of the important determinants as ultraviolet B (UVB) radiation from sunlight is required for cutaneous synthesis of vitamin D3. Along with this, skin pigmentation, dietary habits also play a significant role in the levels of Vitamin D in an individual. Additionally, comorbidities like obesity and chronic kidney disease can impair the synthesis of Vitamin D.

Objective: To study the correlation of plasma 25-hydroxy-vitamin D level with angiographic severity (Gensini score) in coronary artery disease.

Methodology: The present cross sectional observational study conducted at Department of Cardiology, Pradyumna Bal Memorial Hospital, KIMS, Bhubaneswar, Odisha. Results: The largest proportion of participants (33.3%) belonged to the 56–65 years age group, followed closely by the 66–75 years group, which constituted 31.7% of the total. The 35–45 and 46–55 age groups were less represented, making up 18.3% and 16.7% of the sample, respectively. The study population consisted of 60 participants, with a predominance of males. The Vitamin D levels of the 60 patients were categorized into six groups based on severity. Very severe Vitamin D deficiency (levels < 5 ng/ml) was observed in 1 patient (1.7%). Severe Vitamin D deficiency (5–10 ng/ml) was present in 18 patients (30.0%). Vitamin D levels between 11–30 ng/ml (Suboptimal level to Vitamin D deficiency) have the highest incidence of vessel involvement across all categories, particularly in double and triple vessel disease. In contrast, those with severe Vitamin D deficiency (≤10 ng/ml) (Severe to Very severe deficiency) also show a notable frequency of triple vessel involvement, indicating a potential link between deficiency and extensive coronary artery disease. On the other hand, individuals with sufficient Vitamin D levels (≥31 ng/ml) (Optimal level) exhibit minimal vessel involvement across all categories. This pattern suggests an inverse relationship between Vitamin D.

Conclusion: This study from Bhubaneshwar highlights a significant inverse association between serum vitamin D levels and the angiographic severity of coronary artery disease (CAD), as reflected by both the Gensini score and the degree of multivessel involvement.

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Introduction

Coronary Artery Disease (CAD), also termed ischemic heart disease, involves progressive arterial narrowing caused by atherosclerosis.[1] This constriction hampers coronary blood flow and may ultimately result in myocardial infarction.[2] Coronary artery disease remains a major global health concern, ranking among the leading causes of mortality and contributing significantly to the global burden of disease measured in Disability-Adjusted Life Years (DALYs). In an article published in 2024, it was reported that there were 315 million prevalent cases of CAD worldwide.[3]

Literature says that compared to Caucasians, East Asians are less likely to develop CAD, however, they develop CAD at an accelerated rate and at an early age.[4] Indians on the other hand exhibit the highest rates of coronary artery disease (CAD), a trend that cannot be fully attributable to established risk determinants alone.[5] Indians shows 5 to 10 folds higher chances of getting hospitalized due to coronary artery disease before the age of 40 years, when compared with other ethnic communities. Furthermore, conventional risk factors, such as hypertension, diabetes mellitus, dyslipidemia, smoking, and obesity are considered to contribute to the high prevalence of coronary artery disease (CAD) among Indians.[5] The rising trend of CAD morbidity among Indians at a younger age leads to significant public health challenges, such as, reduced productivity during prime working years, and a greater burden on healthcare systems.[5]

CAD encompasses a spectrum of conditions including stable angina, acute coronary syndrome (ACS), and silent myocardial ischemia. The majority of deaths attributed to coronary heart disease (CHD) stem from underlying coronary artery disease. Acute coronary syndrome, which nearly always presents with clinical symptoms, includes both unstable angina and myocardial infarction.[6] The development of coronary artery disease occurs through a complicated pathophysiological process. Risk factors such as hypertension, dyslipidemia, smoking and diabetes often precipitate endothelial dysfunction.[7] This in turn increases vascular permeability, allowing low-density.[7]

Vitamin D levels in the human body are influenced by a complex interplay of environmental, physiological, and health-related factors. Factors like geographic location, sunlight exposure are some of the important determinants as ultraviolet B (UVB) radiation from sunlight is required for cutaneous synthesis of vitamin D3.[8] Along with this, skin pigmentation, dietary habits also play a significant role in the levels of Vitamin D in an individual.[9,10] Additionally, comorbidities like obesity and chronic kidney disease can impair the synthesis of Vitamin D.

Objective: To study the correlation of plasma 25-hydroxy-vitamin D level with angiographic severity (Gensini score) in coronary artery disease.

Materials and methods

Type of Study: Prospective Observational Study

Design of study: Cross-sectional Study

Study Setting: Department of Cardiology, Pradyumna Bal Memorial hospital, KIMS, Bhubaneswar Odisha.

Study Period: July 2023- May 2025 (25 months)

Study Population: The study included all the pregnant ladies admitted in IPD of Department of Cardiology at Pradyumna Bal Memorial Hospital, KIMS, Bhubaneswar, Odisha.

Inclusion Criteria:

1. Age ≥ 18 years and ≤ 75 years.
2. Myocardial Infarction patients being admitted to our ICU undergoing angiography.
3. CAD patients without a history of myocardial infarction (including those with chronic stable angina and unstable angina) undergoing coronary angiography

Exclusion Criteria:

1. Known patients of Chronic Kidney Disease.
2. Patients with Hepatic failure
3. Patients with diagnosed disorders affecting the parathyroid hormone–vitamin D axis, such as hyperparathyroidism or hypoparathyroidism.
4. Patients currently receiving calcium, vitamin D, or parathyroid hormone supplementation
5. Pregnant patients
6. Patients who did not give written informed consent

Sample Size: 60

Sampling Design: Simple random sampling

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Study Parameters:

The study assessed the following parameters:

- Sociodemographic Information- Age, Gender
- Personal Characteristics:
- MI- Weight (Kg), Height (meter)
- Smoking

Co-morbidities:

- Hypertension
- Type 2 Diabetes mellitus
- Dyslipidemia

Diagnosis:

- NSTEMI: Non-ST segment elevation Myocardial infarction
- STEMI: ST segment elevation Myocardial infarction- Anterior wall MI, Inferior wall MI, Posterior wall MI
- Unstable Angina
    - NYHA (New York Health Association) classification

NYHA classification	**Interpretation**
Class I	No symptoms and no limitation in ordinary physical activity
Class II	Mild symptoms and slight limitation during ordinary activity
Class III	Noticeable limitation in activity due to symptoms, comfortable only at rest
Class IV	Unable to carry out any physical activity without discomfort

- Clinical evaluation:
    - ECG
    - ECHO
    - Diastolic dysfunction
    - Vitamin D level in ng/ml

Vitamin D (ng/ml)	**Interpretation**
< 5	Very severe Vitamin D deficiency
5-10	Severe Vitamin D deficiency
11-20	Vitamin D deficiency
21-30	Suboptimal Vitamin D level
31-50	Optimal Vitamin D level
51-70	Upper Normal

Statistical Analysis

Data collected were compiled using Microsoft Excel 2019 and statistically analyzed with SPSS version 16.0. Numerical variables were summarized using either the mean and standard deviation or the median and interquartile range, based on the distribution of the data. For normally distributed variables, results were expressed as mean ± standard deviation, whereas for non-normally distributed variables, the median and interquartile range were reported. Categorical variables were presented as frequencies and percentages, while correlations between continuous variables were assessed using appropriate statistical methods. Spearman's Rho was denoted in correlation for the variables not following normal distribution. Scatter plot was created for all evaluated correlations.

Results

Table 1: Distribution of study participants according to Age (N=60)

Age (in years)	**Number**	**Percentage**	**Descriptive statistics**
35-45	11	18.3	**Median [IQR (25-75)] =** 58.0 (50.5-67.0)
46-55	10	16.7	
56-65	20	33.3	
66-75	19	31.7	

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			Minimum = 38 **Maximum = 73**
Total	**60**	**100.0**	

Table 1 shows the study sample comprised of 60 individuals, categorized into four age groups. The largest proportion of participants (33.3%) belonged to the 56–65 years age group, followed closely by the 66–75 years group, which constituted 31.7% of the total. The 35–45 and 46–55 age groups were less represented, making up 18.3% and 16.7% of the sample, respectively. The overall median age of the participants was 58 years, with an interquartile range (IQR) of 50.5 to 67.0 years, indicating that half of the participants were within this age range. The youngest participant was 38 years old, while the oldest was 73 years, reflecting a moderately wide age distribution in the study population.

Table 2: Distribution of study participants according to Gender (N=60)

Gender	Number	Percentage
Female	20	33.3
Male	40	66.7
Total	**60**	**100.0**

Table 1.2 shows the distribution of study participants according to Gender**.** The study population consisted of 60 participants, with a predominance of males. Of the total, 40 participants (66.7%) were male, while 20 participants (33.3%) were female. This indicates a male-to-female ratio of approximately 2:1, highlighting a gender disparity in the sample with a higher representation of male participants.

Table 3: Distribution of study participants according to Diagnosis (N=60)

Diagnosis	Number	Percentage
'Anterior wall Myocardial Infarction'	20	33.3
'Inferior wall Myocardial 'Infarction	10	16.7
'Posterior wall Myocardial Infarction'	1	1.6
'Non ST elevation Myocardial Infarction'	19	31.7
'Unstable Angina'	10	16.7
Total	**60**	**100.0**

Table 3 shows that in the study cohort of 60 patients, the most common diagnosis was Anterior Wall Myocardial Infarction (AWMI), accounting for 33.3% (n = 20) of cases. This was followed closely by Non-ST Elevation Myocardial Infarction (NSTEMI) at 31.7% (n = 19). Inferior Wall Myocardial Infarction (IWMI) and Unstable Angina (UA) were each observed in 16.7% (n = 10) of the participants. Posterior Wall Myocardial Infarction (PWMI) was the least frequent diagnosis, reported in only 1.6% (n = 1). These findings indicate that AWMI and NSTEMI were the predominant acute coronary syndromes in this population, suggesting a high burden of significant ischemic cardiac events.

Table 4: Distribution of study participants according to Vitamin D level (N=60)

Vitamin D (ng/ml)	**Number**	**Percentage**	**Descriptive statistics**
< 5 *(Very severe Vitamin D deficiency)*	1	1.7	
5-10 *(Severe Vitamin D*	18	30.0	**Median [IQR (25-**

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deficiency)			**75)] =**
11-20 *(Vitamin D deficiency)*	22	36.7	18.0 (9.0-22.8) **Minimum=** 4.92
21-30 *(Suboptimal Vitamin D level)*	15	25.0	**Maximum=** 56.0
31-50 *(Optimal Vitamin D level)*	2	3.3	
51-70 *(Upper Normal)*	2	3.3	
Total	**60**	**100.0**	

Table 4 illustrates the Distribution of study participants according to Vitamin D level. The Vitamin D levels of the 60 patients were categorized into six groups based on severity. Very severe Vitamin D deficiency (levels < 5 ng/ml) was observed in 1 patient (1.7%). Severe Vitamin D deficiency (5–10 ng/ml) was present in 18 patients (30.0%). Vitamin D deficiency (11–20 ng/ml) was the most common category, affecting 22 patients (36.7%). Suboptimal Vitamin D levels (21– 30 ng/ml) were seen in 15 patients (25.0%). Only a small number of patients had optimal Vitamin D levels (31–50 ng/ml) and upper normal levels (51–70 ng/ml), with 2 patients (3.3%) in each category. The median Vitamin D level was 18.0 ng/ml with an interquartile range of 9.0 to 22.8 ng/ml, ranging from a minimum of 4.92 ng/ml to a maximum of 56.0 ng/ml. This indicates a high prevalence of Vitamin D deficiency among the patients studied.

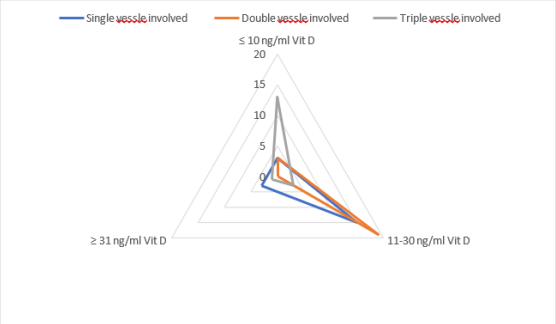

Figure 1: Spider chart showing No. of vessels involved across Vitamin D levels (N=60)

The triangular radar chart displays the relationship between serum Vitamin D levels and the number of coronary vessels involved (single, double, and triple). It shows that patients with Vitamin D levels between 11–30 ng/ml (Suboptimal level to Vitamin D deficiency) have the highest incidence of vessel involvement across all categories, particularly in double and triple vessel disease. In contrast, those with severe Vitamin D deficiency (≤10 ng/ml) (Severe to Very severe deficiency) also show a notable frequency of triple vessel involvement, indicating a potential link between deficiency and extensive coronary artery disease. On the other hand, individuals with sufficient Vitamin D levels (≥31 ng/ml) (Optimal level) exhibit minimal vessel involvement across all categories. This pattern suggests an inverse relationship between Vitamin D.

Discussion

In recent years, the association between serum vitamin D levels and the angiographic severity of coronary artery disease (CAD) has attracted growing research attention. Emerging data indicate that lower vitamin D levels may correlate with increased atherosclerotic burden and more extensive coronary involvement, as reflected in angiographic scoring systems like the Gensini score. Against this backdrop, the present study was undertaken at a tertiary care center in Bhubaneswar to investigate the relationship between serum vitamin D levels and the angiographic severity of CAD.

Socio-demographic particulars:

This study evaluated a total of 60 participants. The average age of the study participants was 58 years, with an interquartile range of 50.5 to 67.0 years. The highest proportion of participants (20, 33.3%) were in the 56–65

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years age group. Age was not found to be associated with Vitamin D levels in the multivariable model. This study demonstrated a predominance of male participants, with 40 out of the total 60 (66.7%) being male. The male to female ratio was 2:1. Among the male, the largest proportion belonged to the age group of 56 to 65 years. Whereas, among females the largest proportion belonged to the age group of 56 to 75 years. Gender showed no association with vitamin D level in the regression model.

Similar to this, a study by Rehman et al. (2023)[11] stated no significant association of age and gender with vitamin D level. The mean age in this study was slightly lower at 52.8 ± 8.8 years; the majority of participants in the study were male. Another study by Sahni et al. (2024) [12] stated a median age of 56.5 years in its study participants with a dominance of male. The study showed no significant association with of Vitamin D level with Age and Gender. The consistent findings denote that other factors are more likely to impact vitamin D status in this population.

Patient particulars:

In this study of 60 study participants, ST-elevation myocardial infarction (STEMI) was the predominant presentation, seen in 31 cases (51.6%). Among these, anterior wall infarction was most common, followed by inferior (10 cases, 32.3%) and posterior wall infarctions (1 case, 3.2%). Non-ST-elevation myocardial infarction (NSTEMI) occurred in 19 participants (31.7%), while unstable angina was reported in 10 participants (16.7%).

These findings align with regional and international data showing STEMI as the most common acute coronary syndrome (ACS) presentation. For example, the North-Eastern India ACS registry reported STEMI in approximately 72.4% of patients, compared to NSTEMI/unstable angina in 27.6% (89-91). South Indian data demonstrated ST-segment elevation myocardial infarction (STEMI) in 37% of cases, compared to non-STEMI at 31% and unstable angina at 32% further supporting STEMI predominance in Indian populations.[13]

Clinical interpretation:

In this study, very severe Vitamin D deficiency was seen in only 1 (1.7%) participant. Severe Vitamin D deficiency was seen in 18 (30.0%) participants and Vitamin D deficiency was seen in 22 (36.7%) participants. Whereas, Sub-optimal to optimal levels of 20 ng/ml and above were noted in only 17 (28.3%) participants. Interestingly, the women in this study had a higher level of Vitamin D as compared to men.

Among those with Vitamin D level of ≥ 31 ng/ml STEMI and Unstable Angina was noted and among those with 11 to 30 ng/ml of Vitamin D level STEMI (21, 67.7%) was noted in majority, followed by NSTEMI (10, 52.6%) and Unstable Angina (6,60.0%). Among those with ≤ 10 ng/ml STEMI (8, 25.8%) was noted in majority, followed by NSTEMI (9, 47.4%%) and Unstable Angina (2, 20.0%). It was also noted that, lower levels of Vitamin D showed more number of vessel involvement. [12]

In this study, severe vitamin D deficiency was notably common: 1.7% of participants exhibited very severe deficiency (<10 ng/mL), 30% had severe deficiency, and 36.7% were deficient (11–20 ng/mL). Only 28.3% had suboptimal-to-optimal levels (≥20 ng/mL). Interestingly, women in the study had higher vitamin D levels compared to men, contrasting with other literature reporting lower levels in females. This gender difference could stem from population-specific factors such as lifestyle, dietary habits, sun exposure, or genetic variables.

Among participants with higher vitamin D levels (≥31 ng/mL), acute coronary syndromes presented as both STEMI and unstable angina. In contrast, those with intermediate levels (11– 30 ng/mL) showed predominantly STEMI (67.7%), followed by NSTEMI (52.6%) and unstable angina (60%). In participants with very low levels (≤10 ng/mL), STEMI still predominated (25.8%), although NSTEMI (47.4%) was also common. A notable trend emerged: lower vitamin D levels were associated with multivessel coronary involvement.

Angiography and Gensini score: In this study, coronary angiography (CAG) revealed significant atherosclerotic burden among the participants, with varying degrees of vessel involvement. The most common finding was Double Vessel Disease (DVD), seen in 21 participants (35.0%), followed by Single Vessel Disease (SVD) in 18 (30.0%) cases. A subset of these (3 cases; 5.0%) had SVD with complete (100%) occlusion, indicating a more severe localized pathology. Triple Vessel Disease (TVD) was identified in 12 participants (20.0%), and in an additional 3 participants (5.0%), TVD was accompanied by total occlusion in one or more arteries, representing

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advanced coronary involvement. A small number of patients had complex presentations such as TVD with Left Main Coronary Artery (LMCA) involvement (1.7%) and TVD + LMCA + 100% cut off (1.7%), which are associated with high-risk clinical scenarios and typically warrant more aggressive therapeutic strategies. Notably, no participants in the study had a normal angiogram, reinforcing the study population's significant clinical load of coronary artery disease. These findings reflect the expected angiographic patterns in patients with acute coronary syndromes and are in line with existing literature highlighting the high prevalence of multivessel involvement, especially among those with more severe or recurrent ischemic events. CAG findings showed no significant association with Vitamin D level.

Conclusion

This study from Bhubaneshwar highlights a significant inverse association between serum vitamin D levels and the angiographic severity of coronary artery disease (CAD), as reflected by both the Gensini score and the degree of multivessel involvement. The high prevalence of severe vitamin D deficiency observed in the study population, along with its strong link to advanced coronary lesions, underscores the importance of evaluating vitamin D status in CAD patients. These findings support the consideration of vitamin D supplementation as a complementary approach to potentially slow coronary atherosclerosis progression, especially in the Indian context where vitamin D deficiency is widespread.

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