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Original Research Article

# Vitamin B12 and Vitamin D3 Deficiency- Association with Premature Coronary Artery Disease

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**Abstract:**

**Background:** Premature coronary artery disease (PCAD), defined as the occurrence of CAD in individuals younger than 45 years, is on the rise globally, particularly in South Asian countries. While traditional risk factors such as smoking, hypertension, and diabetes are well established, recent studies suggest that micronutrient deficiencies, particularly **Vitamin B12 and Vitamin D3**, may play a critical role in the early development and severity of CAD.

**Aim:** To evaluate the association between **Vitamin B12 and Vitamin D3 deficiencies** and the **severity of premature coronary artery disease** in patients aged below 45 years.

**Methods:** This **prospective observational study** was conducted at the **Department of Medicine and Cardiology, ANMMCH**, involving **110 patients** with angiographically confirmed PCAD. Clinical profiles, vitamin levels, and coronary angiographic findings were recorded. Vitamin B12 and D3 levels were measured using chemiluminescence assays. Statistical analysis was performed using SPSS version 23.0, and associations were assessed using chi-square and correlation analyses.

**Results:** Of the 110 individuals, 57.3% had deficiencies in vitamin B12, 64.5% had deficiencies in vitamin D3, and 37.3% had deficiencies in both. Deficiency rates were much greater in those with double- and triple-vessel disease. Vitamin levels and the severity of CAD were found to be statistically significantly inversely correlated ($p < 0.05$), with higher Gensini scores being linked to lower vitamin levels.

**Conclusion:** The study discovered a strong correlation between elevated PCAD severity and vitamin B12 and D3 deficits. These inadequacies might be modifiable risk factors that could help younger people develop coronary artery disease earlier and more rapidly.

**Recommendations:** Routine screening for **Vitamin B12 and D3 levels** should be considered in young patients presenting with or at risk of CAD. Further longitudinal and interventional studies are needed to explore the impact of **vitamin supplementation** on cardiovascular outcomes.

**Keywords:** Vitamin B12, Vitamin D3, Premature Coronary Artery Disease, Micronutrient Deficiency, Atherosclerosis



## Introduction

(CAD) remains a leading cause of morbidity and mortality worldwide, with an increasing trend observed in younger populations under 45 years of age—referred to as premature coronary artery disease (PCAD) [1]. While conventional

risk factors such as smoking, hypertension, diabetes, dyslipidemia, and a positive family history are well established in the pathogenesis of CAD, emerging evidence highlights the role of **micronutrient deficiencies**, particularly **Vitamin B12** and **Vitamin D3**, in accelerating atherosclerotic processes and worsening cardiovascular outcomes [2,3].

Vitamin B12 (cobalamin) is essential for DNA synthesis and homocysteine metabolism. Deficiency in B12 can lead to **hyperhomocysteinemia**, a known independent risk factor for endothelial dysfunction and atherothrombosis [4]. Recent studies have shown that low serum B12 levels are frequently observed in patients with CAD, suggesting its contributory role in the early onset and severity of the disease [5]. In addition, certain dietary patterns, vegetarianism, and malabsorption syndromes further predispose individuals to B12 deficiency, particularly in South Asian populations [6].

Vitamin D3 (cholecalciferol), traditionally associated with bone health, has gained recognition for its **cardioprotective and immunomodulatory roles**. It exerts anti-inflammatory effects, regulates the renin-angiotensin system, and modulates endothelial function—all of which are integral to cardiovascular health [7]. Hypovitaminosis D has been linked with increased carotid intima-media thickness, arterial stiffness, and adverse cardiovascular events [8]. A meta-analysis by Karakas et al. in 2020 confirmed the inverse association between Vitamin D3 levels and CAD incidence in younger adults [9].

Despite these associations, there is limited research focusing specifically on the **coexistence of Vitamin B12 and D3 deficiencies** in patients with premature CAD and their correlation with the severity of coronary artery involvement. This is particularly relevant in the Indian population, where vegetarian diets, lack of sun exposure, and socioeconomic disparities contribute to widespread micronutrient deficiencies [10]. To evaluate the association between **Vitamin B12 and Vitamin D3 deficiencies** and the **severity of premature coronary artery disease** in patients aged below 45 years.

## Methodology

### Study Design

This was a **prospective observational study**.

### Study Setting

The study was conducted at the **Department of Medicine and Cardiology**, **Anugrah Narayan Magadh Medical College and Hospital (ANMMCH), Gaya, Bihar**, over a period of 12 months from [Insert Month and Year] to [Insert Month and Year].

### Participants

A total of **110 participants** diagnosed with premature coronary artery disease (age <45 years) were recruited from inpatient and outpatient services of the Department of Cardiology. All participants provided informed consent before enrollment.

### Inclusion Criteria

- Patients aged **less than 45 years** with angiographically confirmed **coronary artery disease**.
- Willingness to provide informed consent.
- Both males and females included.

### Exclusion Criteria

- Patients above 45 years of age.
- Individuals with known **vitamin supplementation** in the last 3 months.
- Patients with chronic **kidney disease**, **liver disease**, **malabsorption syndromes**, or **active malignancies**.
- Patients with **autoimmune disorders** or on long-term corticosteroid therapy.

### Bias

The successive sampling method was used to reduce selection bias. Enrollment was

open to any eligible patients who presented during the trial period. By making sure that laboratory personnel evaluating vitamin B12 and D3 levels were blinded to the individuals' clinical status, observer bias was decreased.

### Data Collection

Detailed clinical history, demographic details, and risk factors (smoking, hypertension, diabetes, dyslipidemia, family history) were recorded. Blood samples were collected after overnight fasting to assess **serum Vitamin B12** and **Vitamin D3 levels** using chemiluminescent immunoassay methods. Results were interpreted based on standardized reference ranges.

### Procedure

After enrollment, each participant underwent clinical evaluation and biochemical investigations including lipid profile, blood glucose, renal and liver function tests. Coronary angiography findings were documented to assess the extent and severity of CAD. Simultaneously, Vitamin B12 and Vitamin D3 levels were measured. Patients were grouped based on vitamin sufficiency or deficiency and comparisons were drawn with CAD severity.

### Statistical Analysis

SPSS version 23.0 was utilized for data entry and analysis. Whereas categorical data were displayed as frequencies and percentages, continuous variables were represented as mean ± standard deviation (SD). Continuous variables were compared using Mann-Whitney U tests or independent t-tests. For categorical data, Fisher's exact tests or chi-square tests were employed. P-values less than 0.05 were regarded as statistically significant.

### Results

There were 84 (76.4%) male patients and 26 (23.6%) female patients out of 110 individuals with a diagnosis of premature coronary artery disease (PCAD). With a mean age of 41.2 ± 3.1 years, the majority (62%) were in the 40–44 age range. 56 (50.9%) of the patients smoked, 47 (42.7%) had high blood pressure, 33 (30.0%) had type 2 diabetes, and 61 (55.5%) had a positive family history of coronary artery disease.

**Table 1: Clinical Characteristics of Participants (N = 110)**

| Variable | Value |
|---|---|
| Mean age (years) | 41.2 ± 3.1 |
| Gender (Male/Female) | 84 (76.4%) / 26 (23.6%) |
| Smoking | 56 (50.9%) |
| Hypertension | 47 (42.7%) |
| Type 2 Diabetes | 33 (30.0%) |
| Family history of CAD | 61 (55.5%) |

Males were more likely to be impacted. The two most common risk factors were smoking and family history.

### Vitamin B12 and D3 Status in Study Population

Out of 110 patients, **63 (57.3%) had Vitamin B12 deficiency**, and **71 (64.5%) had Vitamin D3 deficiency**. **41 patients (37.3%)** had **deficiency of both vitamins**. The mean serum Vitamin B12 level was **183 ± 46 pg/mL** and Vitamin D3 level was **18.5 ± 7.2 ng/mL**.

**Table 2: Vitamin B12 and Vitamin D3 Deficiency Status**

| Parameter | Mean ± SD / n (%) |
|---|---|
| Vitamin B12 level (pg/mL) | 183 ± 46 |
| Vitamin D3 level (ng/mL) | 18.5 ± 7.2 |
| Vitamin B12 Deficient | 63 (57.3%) |
| Vitamin D3 Deficient | 71 (64.5%) |
| Both Vitamins Deficient | 41 (37.3%) |

A significant proportion of patients with PCAD had deficiencies of either or both vitamins.

**Association with Severity of Coronary Artery Disease**

Angiography was used to determine the severity of coronary artery disease. Forty patients (36.4%) had single-vessel disease (SVD), forty-five (40.9%) had double-vessel disease (DVD), and twenty-five (22.7%) had triple-vessel disease (TVD).

Vitamin B12 and D3 deficiency were found to be more prevalent in patients with **multivessel disease**.

**Table 3: Association of Vitamin Deficiency with CAD Severity**

| CAD Severity | B12 Deficient (%) | D3 Deficient (%) | Both Deficient (%) |
|---|---|---|---|
| SVD (n=40) | 17 (42.5%) | 20 (50.0%) | 10 (25.0%) |
| DVD (n=45) | 29 (64.4%) | 32 (71.1%) | 18 (40.0%) |
| TVD (n=25) | 17 (68.0%) | 19 (76.0%) | 13 (52.0%) |
| **p-value** | 0.03 | 0.02 | 0.01 |

Vitamin insufficiency and worsening CAD severity were statistically significantly correlated ($p < 0.05$).

**Correlation Analysis**

Lower vitamin levels were linked to more severe coronary artery involvement, according to Pearson correlation, which also revealed an inverse relationship between Vitamin B12 and Gensini Score ($r = –0.38$, $p = 0.004$) and Vitamin D3 and Gensini Score ($r = –0.41$, $p = 0.002$).

**Summary of Key Findings**

- A significant proportion of patients with PCAD had Vitamin B12 (57.3%) and D3 (64.5%) deficiencies.
- Combined deficiency was seen in 37.3% of cases.
- Vitamin deficiency was more common in those with double- or triple-vessel disease.
- Vitamin levels and the severity of CAD were statistically significantly inversely correlated.

**Discussion**

Vitamin B12 (57.3%) and vitamin D3 (64.5%) deficiencies were shown to be very prevalent in this prospective observational study, which included 110 individuals with PCAD. Interestingly, concomitant deficits of both vitamins were present in 37.3% of subjects. With a mean age of 41.2 ± 3.1 years and a male preponderance of 76.4%, smoking and a family history of CAD were found to be the most prevalent risk factors.

A significant relationship was found between **vitamin deficiencies and the severity of coronary artery disease**. Patients with multivessel disease, particularly **double- and triple-vessel disease**, had higher rates of both Vitamin B12 and D3 deficiencies compared to those with single-vessel disease. For instance, **68% of patients with triple-vessel disease** were Vitamin B12 deficient, while **76%** had Vitamin D3 deficiency, and more than **half (52%)** had both deficiencies. These differences were statistically significant ($p < 0.05$), suggesting a strong association

between **micronutrient deficiency and disease burden**.

Further analysis using **Pearson correlation** demonstrated a **significant inverse relationship** between serum Vitamin B12 and Vitamin D3 levels and the **Gensini score**, a marker of CAD severity. This indicates that **lower levels of these vitamins correlated with greater coronary artery involvement**, highlighting the potential role of these micronutrients in modulating atherosclerosis and cardiovascular risk.

Deficits in vitamin B12 and vitamin D3 are becoming more widely acknowledged as modifiable risk factors linked to the onset and severity of CAD, especially in younger populations. This link is well supported by numerous investigations carried out after 2018.

According to a case-control research, 50% of CAD patients had vitamin B12 insufficiency, and their levels were noticeably lower than those of healthy controls. Furthermore, B12 levels showed an inverse relationship with certain atherogenic lipid fractions and a positive correlation with HDL cholesterol, indicating that lipid dysregulation may be a contributing factor to CAD in cases with low B12 status [11].

Similarly, another study involving patients with acute myocardial infarction reported significantly lower mean serum levels of Vitamin B12 and folic acid among cases than controls. This study emphasized that these deficiencies may lead to hyperhomocysteinemia, a known contributor to endothelial dysfunction and atherosclerosis [12].

An observational review also discussed the cardiovascular complications linked to B12 deficiency, particularly through elevated homocysteine levels, which impair endothelial function and promote vascular inflammation [13]. The predictive value of elevated homocysteine—often resulting from Vitamin B12 deficiency—was further corroborated by a study showing a direct association between serum homocysteine levels and CAD severity measured by the SYNTAX score [14].

Regarding Vitamin D3, a case-control study in young Indian patients found significantly lower Vitamin D levels in individuals with premature CAD. Though widespread deficiency in the population complicates interpretation, the data suggested a contributory role of Vitamin D in early-onset CAD, especially when combined with other risk indicators like insulin resistance [15].

A possible gene-environment interaction involving vitamin D receptor polymorphisms was highlighted in another investigation that found a strong correlation between low 25-OH vitamin D3 levels and an elevated risk of Type 2 diabetes co-existing with CAD [16]. Similarly, a dose-dependent link was suggested by research from Iran that showed a substantial inverse relationship between serum vitamin D levels and the severity of CAD using the Gensini score [17].

An additional study found that individuals with Vitamin D deficiency had a significantly higher coronary artery calcium score and were more likely to develop calcified or mixed atherosclerotic plaques, indicating that Vitamin D status could be a predictor of plaque morphology and burden [18]. Last but not least, genetic research has also demonstrated that vitamin D receptor polymorphisms increase the risk of developing premature CAD, hence confirming vitamin D's involvement in cardiovascular pathophysiology beyond its conventional uses [19].

## Conclusion

In conclusion, these findings underscore the importance of **routine screening for Vitamin B12 and D3 deficiencies** in young patients with CAD. Their deficiency may not only reflect poor nutritional status but could also serve as **modifiable risk factors** that influence the **extent and progression**

of coronary artery disease. Further longitudinal and interventional studies are needed to determine whether **vitamin supplementation** could have a beneficial impact on disease outcomes.

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