Original Article

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# Risk Factors and Protective Role of Vitamin C in Coronary Artery Disease: Insights from a Case-control Study

Internal Medicine Section

TILAK KUMAR KADIPAKU[1], BS GOPALA KRISHNA[2], AHAMMAD BASHA SHAIK[3]



## ABSTRACT

**Introduction:** Coronary Artery Disease (CAD) is a major global health burden, with oxidative stress playing a critical role in its pathogenesis. Vitamin C, a potent antioxidant, may offer protective effects against CAD; however, evidence from rural Indian populations remains limited.

**Aim:** To investigate the association between plasma vitamin C levels and CAD, and to assess cardiovascular risk factors contributing to CAD among patients attending a tertiary care hospital in rural Southern India.

**Materials and Methods:** A hospital-based prospective case-control study was conducted at the Department of Cardiology, Narayana Medical College, Nellore, Andhra Pradesh, India, between July 2023 and December 2024. The study included 200 participants aged ≥30 years, diagnosed with CAD via Coronary Angiography (CAG). Age- and sex-matched healthy controls were also recruited. Plasma vitamin C levels were measured using ultra-High-Performance Liquid Chromatography (u-HPLC). Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS) version 27.0 and R Studio Version 2024.12.0. Chi-square tests, paired t-tests, Odds Ratios (OR) with 95% Confidence Intervals (CIs), and logistic regression analyses were employed.

**Results:** Of the 200 participants, 100 had CAD (cases) and the remaining 100 were non CAD (controls). The overall mean age of participants was 56.94±11.70 years, with ages ranging from 30 to 83 years. The mean serum vitamin C level was significantly lower among cases (65.53±8.75 µmol/L) than in healthy controls (71.63±7.67 µmol/L; p-value <0.001). Hypertension (OR=1.84; 95% CI: 1.05-3.23; p-value=0.033) and diabetes (OR=2.01; 95% CI: 1.14-3.55; p-value=0.015) were significantly associated with CAD, while dyslipidaemia was not (OR=1.99; 95% CI: 0.95-4.22; p-value=0.066). A significant negative correlation was observed between plasma vitamin C levels and CAD severity (r-value=-0.348; p-value <0.01). In multivariate analysis, increasing age and lower vitamin C levels were found to be significant independent predictors of CAD.

**Conclusion:** Lower plasma vitamin C levels were significantly associated with CAD, supporting its potential protective role. Hypertension and diabetes emerged as major risk factors. These findings highlight the need for preventive strategies focusing on dietary antioxidants and the control of modifiable risk factors to reduce the burden of CAD.

**Keywords:** Ascorbic acid, Cardiovascular disease, Diabetes mellitus, Hypertension

## INTRODUCTION

Cardiovascular Diseases (CVD) are the primary source of mortality and morbidity worldwide. According to the World Health Organisation (WHO), in 2019, CVDs caused approximately 17.9 million deaths, accounting for 32% of all deaths globally. Among these, 85% resulted from heart attacks and strokes. Heart incidents and strokes account for four out of every five CVD fatalities, with one-third of these deaths occurring by the age of 70 years [1]. CAD accounts for eight million deaths, with atherosclerotic disease of the coronary arteries being its common cause. Major risk factors for developing CAD include tobacco use, diabetes, hypertension, dyslipidaemia and obesity. Diagnosis and management of CAD involve electrocardiograms, echocardiograms, cardiac biomarkers and coronary angiograms. CVD was reported to account for 65% of deaths in diabetic women in a Western-based population study [2]. The two most serious life-threatening CVDs are CAD and its complication, myocardial infarction, both caused by atherosclerosis. The pathophysiology of atherosclerosis involves vascular endothelial dysfunction, increased release of inflammatory cytokines, immune cell infiltration and subsequent proliferation of vascular smooth muscle cells. Traditionally, blood-borne immune cells are thought to be the source of inflammatory cells [3].

The CAD is a condition in which a waxy substance called plaque builds up on the inner walls of the coronary arteries, reducing the supply of oxygen-rich blood to the heart muscle [4]. CAD remains the leading cause of mortality in developing countries. Notably, recent evidence indicates a substantial rise in CAD prevalence among South Asians, estimated at approximately 39% between 1990 and 2019 [5-7]. Although this population has a lower Body Mass Index (BMI) and Waist Circumference (WC), CAD manifests at a much younger age and with greater severity compared to other groups [8]. In India, the incidence of CAD has been increasing over the last 30 years, while a decreasing trend has been noted in Western populations [9]. Reports have revealed that Asian Indians have three to four times higher CAD risk than white Americans, 20 times higher than Japanese individuals, and six times higher than Chinese individuals [9-11].

Traditionally, major risk factors such as diabetes mellitus, hypertension, smoking and dyslipidaemia do not entirely explain the increased prevalence of CAD in younger age groups. These atherosclerotic changes are attributed to urbanisation, lifestyle modifications, obesity and poor dietary habits [12]. Diabetic women have lost their former protection against CAD [2,12]. CAD includes stable angina, unstable angina, ST-elevation Myocardial Infarction (MI) and non-ST elevation MI [13,14].

Vitamin C (L-ascorbic acid) is a water-soluble micronutrient that stimulates immune function, is commonly referred to as a natural antioxidant and possesses powerful antioxidant properties [15]. It is a safe and effective antioxidant, and it is hypothesised that vitamin C deficiency may lead to CAD [15]. Certain studies have suggested

that there is no significant relationship between vitamin C levels and CAD [4,14,16]; however, vitamin C plays a protective role in the development and progression of atherosclerosis, primarily through its antioxidant properties. Animal experimental studies have also suggested that dietary antioxidants, particularly ascorbate—the most biologically active form of vitamin C—may help mitigate vascular damage and inhibit the progression of atherosclerotic disease [17,18].

Currently, statins are extensively used in the treatment of CAD, but they can have side-effects with long-term usage [19]. Hence, further studies are needed to estimate vitamin C levels. The current research aimed to investigate the potential role of vitamin C as a future alternative therapy for patients with CAD.

## MATERIALS AND METHODS

The prospective case-control study was conducted after obtaining local ethical clearance (Ref. No: NMC/IEC/09/2019), and data were collected between July 2023 and December 2024 at the Department of Cardiology, Narayana Medical College, Nellore, Andhra Pradesh, India. Written and oral informed consent was obtained from the patients after explaining the nature of the study in English and Telugu.

**Sample size:** The sample size calculation was performed using G*Power software version 3.1.9.7. According to previous literature [14], the effect size (d) was taken as 0.3, the power of the study (1-β) was set at 0.8, and the significance level (α) was fixed at 0.05 with a two-tailed t-test. The required sample size was 90 for each group. To account for potential loss to follow-up and confounding factors, the final sample size was adjusted to 100 participants in each group.

**Inclusion and Exclusion criteria:** Participants were included and excluded based on the following criteria:

**Inclusion criteria:**

**Cases (CAD):** The participants more than 30 years of age presented with a diagnosis of CAD based on CAG.

**Controls (Non CAD):** Age- and sex-matched healthy controls were recruited. Controls were selected from individuals attending routine health checkups or outpatient services who had no history of CVD and were matched to cases by age and sex to minimise confounding factors. All controls underwent clinical evaluations and basic laboratory tests to confirm the absence of CAD or other major co-morbidities.

**Exclusion criteria:** Patients aged under 30 years, those without a CAD diagnosis based on CAG, individuals with Chronic Renal Failure (CRF), and those with severe systemic illnesses and participants who were unwilling to provide consent were excluded from the study.

### Study Procedure

A detailed medical history was recorded and a comprehensive clinical examination was conducted, with specific emphasis on common symptoms of CVD. Blood samples were acidified with a chelator and perchloric acid prior to analysis. A rapid and reliable u-HPLC method was employed to determine vitamin C levels. Serum was separated from whole blood and acidified with a chelating agent and perchloric acid to stabilise ascorbic acid. A rapid and straightforward Reverse-Phase HPLC (RP-HPLC) method was developed and validated to accurately quantify vitamin C. The analysis was performed using the Hitachi D-2000 Elite HPLC system equipped with a gradient pump. Separation was achieved on a C18 column, and detection was carried out using a UV-Visible detector.

## STATISTICAL ANALYSIS

The collected data were entered into MS Excel and analysed using IBM SPSS Version 27.0 and R Studio Version 2024.12.0. Categorical data were presented as frequencies and percentages, with associations between case and control groups assessed using the Chi-square test. Continuous data were expressed as mean and standard deviation and mean differences between case and control groups were compared using the paired Student's t-test. Logistic regression analysis was used to identify prognostic risk factors for cases. A p-value <0.05 was considered statistically significant.

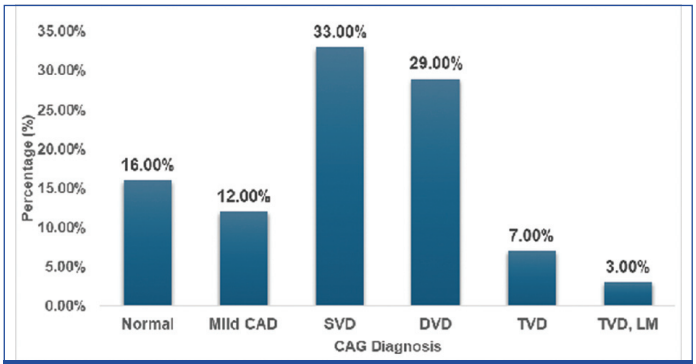
## RESULTS

Among a total of 200 participants, 100 (50.0%) had CAD (cases), while the remaining 100 (50.0%) were non CAD (controls). The overall mean age was 56.94±11.70 years, ranging from 30 to 83 years. [Table/Fig-1] shows that age (p-value=0.042), hypertension (p-value=0.033), and diabetes mellitus (p-value=0.015) were significantly associated with CAD; however, sex (p-value=0.198) and dyslipidaemia (p-value=0.066) were not significantly associated with CAD. This suggests that traditional risk factors contribute to CAD risk, but their effects may be influenced by other variables.

| Variables | CAD severity | | | p-value | Odds Ratio (OR) | |
|---|---|---|---|---|---|---|
| | Cases (n=100) | Controls (n=100) | Total (n=200) | | Crude OR | Adjusted OR |
| **Age group (years)** | | | | | | |
| 30-40 | 10 (10.0%) | 9 (9.0%) | 19 (9.5%) | 0.042* | 1 | 1 |
| 41-50 | 14 (14.0%) | 29 (29.0%) | 43 (21.5%) | | 2.30 (0.76-6.94) | 0.43 (0.14-1.31) |
| 51-60 | 30 (30.0%) | 31 (31.0%) | 61 (30.5%) | | 1.15 (0.41-3.22) | 0.87 (0.31-2.44) |
| >60 | 46 (46.0%) | 31 (31.0%) | 77 (38.5%) | | 0.75 (0.28-2.05) | 1.34 (0.49-3.66) |
| **Sex** | | | | | | |
| Male | 38 (38.0%) | 47 (47.0%) | 85 (42.5%) | 0.198 | 1 | 1 |
| Female | 62 (62.0%) | 53 (53.0%) | 115 (57.5%) | | 0.69 (0.39-1.21) | 0.66 (0.37-1.18) |
| **Hypertension** | | | | | | |
| Yes | 53 (53.0%) | 38 (38.0%) | 91 (45.5%) | 0.033* | 1 | 1 |
| No | 47 (47.0%) | 62 (62.0%) | 109 (54.5%) | | 1.84 (1.05-3.23) | 1.07 (0.54-2.15) |
| **Diabetes mellitus** | | | | | | |
| Yes | 52 (52.0%) | 35 (35.0%) | 87 (43.5%) | 0.015* | 1 | 1 |
| No | 48 (48.0%) | 65 (65.0%) | 113 (56.5%) | | 2.01 (1.14-3.55) | 1.86 (0.94-3.67) |
| **Dyslipidaemia** | | | | | | |
| Yes | 23 (23.0%) | 13 (13.0%) | 36 (18.0%) | 0.066 | 1 | 1 |
| No | 77 (77.0%) | 87 (87.0%) | 164 (82.0%) | | 1.99 (0.95-4.22) | 1.48 (0.69-3.17) |

**[Table/Fig-1]:** Association of demographic variables and risk factors with CAG-diagnosed Coronary Artery Disease (CAD) patients.
*p<0.05 – Statistically Significant

Among the cases, 12.0% had Non-ST-Elevation Myocardial Infarction (NSTEMI), 70.0% had ST-Elevation Myocardial Infarction (STEMI) {Anterior Wall Myocardial Infarction (AWMI) 35.0%, Inferior Wall Myocardial Infarction (IWMI) 34.0%, and Posterior Wall Myocardial Infarction (PWMI) 1.0%}, and 18.0% had unstable angina. Based on CAG diagnosis, 12 (12.0%) cases had mild CAD, 33 (33.0%) cases had Single-Vessel Disease (SVD), 29 (29.0%) cases had Double-Vessel Disease (DVD), 7 (7.0%) cases had Triple-Vessel Disease (TVD), 3 (3.0%) cases had both TVD and Left Main (LM) disease, and 16 (16.0%) cases had normal epicardial coronaries, as graphically shown in [Table/Fig-2].




**[Table/Fig-2]:** Distribution of patients according to CAG diagnosis (n=100).

[Table/Fig-3] indicated that plasma vitamin C levels were significantly lower in CAD cases compared to controls (p-value <0.001), suggesting a potential protective role of vitamin C. Although the mean age was higher in CAD cases, the difference was not statistically significant (p-value=0.052).

| Variables | Cases (n=100) | Controls (n=100) | Paired t-test | | |
|---|---|---|---|---|---|
| | Mean±Std Dev | Mean±Std Dev | Mean Diff. | t-value | p-value |
| Age (years) | 58.54±11.59 | 55.33±11.65 | 3.21 | 1.953 | 0.052 |
| Plasma vitamin C levels (µmol/L) | 65.53±8.75 | 71.63±7.67 | -6.104 | -5.248 | <0.001* |

**[Table/Fig-3]:** Comparison of mean differences of age (years), and plasma Vitamin C concentration levels (µmol/L) in CAG-diagnosed Coronary Artery Disease (CAD) patients.
*p-value <0.001 -Statistically Significant

[Table/Fig-4] presents the univariate and multivariate logistic regression results for risk factors associated with CAD. Increasing age was a significant independent predictor, with each additional year increasing the odds of CAD by 4% (Adjusted Odds Ratio [AOR]=1.04; 95% Confidence Interval [CI]: 1.01-1.08; p-value=0.021). Higher serum vitamin C levels showed a protective effect, reducing CAD odds by about 3% per unit increase (AOR=0.97; 95% CI: 0.95-0.99; p-value=0.006). While diabetes showed a statistically significant association with CAD in the univariate model (Odds Ratio [OR]=1.54; 95% CI: 1.01-2.36; p-value=0.046), this association lost significance after adjusting for other factors (AOR=1.32; 95% CI: 0.59–2.89; p-value=0.494), indicating potential confounding. Similarly, dyslipidaemia exhibited a borderline association in the univariate analysis (OR=1.80; 95% CI: 0.96–3.38; p-value=0.068) but was not significant in the multivariate model (AOR=1.37; 95% CI: 0.62–3.02; p-value=0.440). Hypertension and sex were not significantly associated with CAD in either model, suggesting they were not independent risk factors in this population. A significant negative correlation was observed between plasma vitamin C levels and CAD severity (r-value=-0.348; p-value <0.01).

## DISCUSSION

CAD is a leading cause of mortality and morbidity in adult populations worldwide. Elevated oxidative stress and deficiencies in antioxidant protection play significant roles in endothelial function and influence the progression of atherosclerosis. Several animal models and human studies support the oxidative stress theory in atherosclerosis [3,17,18]. Oxidative stress is a well-documented contributor to the progression of CAD, primarily due to its role in endothelial dysfunction, inflammation and lipid oxidation. Vitamin C, a powerful water-soluble antioxidant, is essential for reducing oxidative stress by neutralising Reactive Oxygen Species (ROS) and improving endothelial function [20].

The observed decrease in vitamin C levels in CAD patients supports the hypothesis that insufficient antioxidant defense mechanisms may play a role in disease progression. This aligns with previous studies that indicate a linear relationship between dietary vitamin C intake and cardiovascular health, emphasising that individuals with higher plasma vitamin C levels exhibited a lower prevalence of CAD [21,22]. Vitamin C is the most vital dietary antioxidant and ecological studies suggest that low vitamin C intake is associated with higher rates of CVD [23]. Further research, a meta-analysis by Guan Y et al., assessed randomised controlled trials and concluded that while vitamin C supplementation alone may not significantly reduce cardiovascular events, its combined effect with other antioxidants may offer protective benefits [24]. A study by Yuan S et al., proposed that oxidative stress in CAD accelerates vitamin C utilisation, leading to lower circulating levels [25].

In the present study, the mean age of participants was higher among cases (58.54±11.59 years) compared to controls (55.33±11.65 years); however, this difference was not statistically significant (p-value=0.042). Heitzer T et al., reported a significantly higher mean age in the CAD group (63±7 years) compared to the non CAD group (59±9 years), with a statistically significant association (p-value=0.01) [26]. Conversely, Torkzaban A et al., observed a mean age of 58.5±8.1 years in the CAD group and 56.2±8.5 years in the non CAD group, with no significant difference (p-value=0.20) [27]. Thus, present study findings align with those of Torkzaban A et al., while differing from those of Heitzer T et al., [26,27].

| Variables | Univariate analysis | | | | Multivariate analysis | | | |
|---|---|---|---|---|---|---|---|---|
| | Estimate | Odds Ratio (OR) | 95% CI | p-value | Estimate | Odds Ratio (OR) | 95% CI | p-value |
| Age (years) | 0.001 | 1.00 | 0.97-1.01 | 0.696 | 0.041 | 1.04 | 1.01-1.08 | 0.021* |
| Sex (Males Vs Females) | -0.213 | 0.81 | 0.53-1.24 | 0.330 | -0.379 | 0.68 | 0.38-1.24 | 0.210 |
| Hypertension (Yes Vs No) | 0.329 | 1.39 | 0.93-2.08 | 0.108 | -0.244 | 0.78 | 0.34-1.82 | 0.571 |
| Diabetes (Yes Vs No) | 0.434 | 1.54 | 1.01-2.36 | 0.046* | 0.274 | 1.32 | 0.59-2.89 | 0.494 |
| Dyslipidaemia (Yes Vs No) | 0.598 | 1.80 | 0.96-3.38 | 0.068 | 0.312 | 1.37 | 0.62-3.02 | 0.440 |
| Plasma Vitamin C levels (µmol/L) | -0.001 | 0.99 | 0.99-1.01 | 0.533 | -0.033 | 0.97 | 0.95-0.99 | 0.006* |

**[Table/Fig-4]:** Univariate and multivariate binary logistic regression analysis for cases.
*p-value <0.05 – Statistically Significant

In this study, females constituted a greater proportion than males in both the case group (62.0% vs. 38.0%) and the control group (53.0% vs. 47.0%). However, the association between sex and CAD was not statistically significant (p-value=0.198). Heitzer T et al., reported that males comprised 80% of both CAD and non CAD groups [26]. Similarly, Torkzaban A et al., observed that males accounted for 61.4% in the CAD group and 59.1% in the non CAD group, with no significant association between sex and CAD (p-value=0.83) [27]. Therefore, the findings of present study are consistent with those reported by Torkzaban A et al., [27].

Among the cases in this study, 45.5% had hypertension, 43.5% had diabetes mellitus, and 18.0% had dyslipidaemia. In comparison, Bhalli AM et al., reported that 37% had hypertension, 25.2% had diabetes, and 56.29% had dyslipidaemia [28]. Heitzer T et al., found that in the CAD group, 40% had hypertension and 22% had diabetes, while in the non CAD group, 38% had hypertension and 20% had diabetes [26]. These results suggest that present study demonstrates a comparable prevalence of hypertension and diabetes, although the frequency of dyslipidaemia was lower.

In this study, the majority of cases presented with STEMI (70.0%), followed by unstable angina (18.0%) and NSTEMI (12.0%). Among the STEMI cases, AWMI was seen in 35.0%, IWMI in 34.0%, and PWMI in 1.0%. Similarly, Bhalli AM et al., reported 71.1% with STEMI, 8.9% with NSTEMI, and 20% with unstable angina, indicating that the distribution of clinical presentations in our study is largely in agreement with theirs [28].

Based on CAG findings in this study, 12.0% of cases had mild CAD, 33.0% had SVD, 29.0% had Double-Vessel Disease (DVD), 7.0% had TVD, 3.0% had both TVD and LM disease and 16.0% had normal epicardial coronaries. In comparison, Heitzer T et al., reported that among CAD patients, 38% had SVD, 33% had DVD, and 29% had TVD [26]. These findings show a similar distribution pattern, particularly in SVD and DVD involvement.

Using the u-HPLC method for vitamin C estimation in this study provided a reliable and precise measurement of plasma vitamin C concentrations. This methodological strength enhances the validity of the findings and supports the potential role of vitamin C as a modifiable risk factor for CAD. Given its safety, affordability, and widespread availability, vitamin C supplementation or dietary optimisation could be a viable preventive or adjunctive strategy in CAD management. However, while the study establishes an association between lower vitamin C levels and CAD, it does not establish causation. Further longitudinal and interventional studies are necessary to determine whether vitamin C supplementation can effectively diminish CAD incidence or severity.

Vitamin C plays a significant role in many aspects of vascular function, including the onset and progression of atherosclerotic CVD. A deficiency in vitamin C has been linked to several health conditions, such as CVD, atherosclerosis, diabetes and hypertension [22,29]. Research has also explored the connection between dietary habits and heart disease risk in individuals with diabetes. Additionally, high vitamin C supplementation has been associated with an improved risk of CVD-related mortality in postmenopausal women with hypertension and diabetes [30,31].

In the present study, plasma vitamin C concentrations were significantly lower in patients with CAD compared to controls (65.53±8.75 µmol/L vs. 71.63±7.67 µmol/L; p-value <0.001). This suggests a possible inverse relationship between vitamin C levels and CAD. These findings align with those of Torkzaban A et al., who also reported lower plasma vitamin C levels in CAD patients (59.8±19.1 µmol/L) than in non CAD individuals (71.8±18.6 µmol/L), although their results approached but did not reach statistical significance (p-value=0.052) [27]. The consistency in trends across studies reinforces the hypothesis that reduced antioxidant status, as indicated by lower vitamin C levels, may play a role in the pathophysiology of CAD.

Conversely, Riemersma RA et al., found no significant association between plasma vitamin C levels and acute myocardial infarction, regardless of smoking status [32]. Such contradictory findings highlight the complex interplay between antioxidants and cardiovascular risk, which may be influenced by underlying inflammation, dietary patterns, genetic predispositions and other unmeasured confounders.

Research has indicated that heart disease risk may vary based on plasma vitamin C levels, even within the normal range. Additionally, some studies suggest that consuming vitamin C in amounts exceeding the minimum required to prevent deficiency may offer potential cardiovascular benefits. Moser M and Chun O, reported that vitamin C deficiency has been linked to an increased risk of CVD-related mortality [20]. Furthermore, vitamin C may contribute to slight enhancements in endothelial function and lipid profiles, especially in individuals with low plasma vitamin C levels.

The biological plausibility of vitamin C in cardiovascular protection stems from its antioxidant properties, which help neutralise free radicals and reduce oxidative stress—a key mechanism in the development of atherosclerosis [33]. Vitamin C also supports endothelial function and inhibits Low-Density Lipoprotein (LDL) oxidation, both of which are relevant to cardiovascular health [34]. However, given the observational design of this study, causality cannot be established, and vitamin C deficiency may reflect a broader pattern of poor dietary intake or systemic inflammation rather than being an independent risk factor.

Observational studies have consistently shown an inverse relationship between vitamin C levels and the risk of CAD. This study aimed to assess and compare plasma vitamin C levels in CAD patients and healthy individuals, emphasising its potential role in CAD development. The results indicated a significant reduction in plasma vitamin C levels among CAD patients compared to the healthy control group, suggesting a link between lower vitamin C levels and increased oxidative stress in CAD. Previous research has also suggested that vitamin C supplementation may help reduce the risk of CVD [14,20,35,36].

From a public health perspective, these findings underscore the potential value of ensuring adequate dietary intake of vitamin C, particularly in populations at risk of CAD. If future longitudinal or interventional studies confirm a protective role for vitamin C, dietary guidelines and community-based nutritional interventions could serve as cost-effective strategies to support cardiovascular health. However, routine supplementation should be approached with caution until definitive evidence from randomised controlled trials is available [37].

### Limitation(s)

This study had several limitations. First, its single-centre, hospital-based, case-control design restricts the generalisability of the findings and limits causal inferences between plasma vitamin C levels and CAD. Second, plasma vitamin C concentrations were measured only once and were not adjusted for recent dietary intake, supplement use, or lifestyle factors such as smoking and physical activity, which may have introduced residual confounding. Additionally, other oxidative stress markers were not assessed, limiting a more comprehensive evaluation of antioxidant status. The modest sample size and reliance on self-reported risk factors may have further impacted the robustness of the findings due to potential recall bias. Future studies should include larger, multicentre cohorts with longitudinal follow-up and incorporate dietary assessments, lifestyle variables and biochemical markers to better understand the role of vitamin C in cardiovascular health.

## CONCLUSION(S)

In this case-control study, lower plasma vitamin C levels and older age were independently related to CAD, supporting the hypothesis of an association between oxidative stress, micronutrient status,

and CAD risk. However, causality cannot be inferred based on the observational nature of the study. Although the results add evidence in the field of antioxidants and CVD, they do not warrant clinical recommendations for vitamin C supplementation. Additional longitudinal and interventional research is needed. Efforts should be reinforced on lifestyle modification, early screening, and control of conventional risk factors to reduce the burden of CAD.

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**PARTICULARS OF CONTRIBUTORS:**
1. Assistant Professor, Department of Cardiology, Narayana Medical College, Nellore, Andhra Pradesh, India.
2. Professor, Department of Emergency Medicine, Narayana Medical College, Nellore, Andhra Pradesh, India.
3. Assistant Professor, Department of Community Medicine, Manipal Tata Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Ahammad Basha Shaik,
Assistant Professor, Department of Community Medicine, Manipal Tata Medical College, Manipal Academy of Higher Education, Manipal-576104, Karnataka, India.
E-mail: ahammad.basha@manipal.edu



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