

The Relationship between Oxidative Stress, Vitamin D3 and its Cardiac Troponin in Acute Coronary Syndrome Patients

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Abstract: **Background:** One of the world's leading causes of morbidity and death is still acute coronary syndrome. Although vitamin D3 deficiency and oxidative stress have been linked to cardiovascular disease separately, little is known about how they work together to modulate cardiac injury. **Objective:** To look into how vitamin D3 modulates oxidative stress pathways and how it relates to elevated cardiac troponin in myocardial infarction patients. **Methodology:** This comparative study was conducted at Department of Cardiology, Mansoura University, Egypt from 15th November 2024 to 14th May 2025 vide letter No. MS.24.10.2958 dated 2nd November 2024. Two hundred people participated in a prospective study have 100 controls and 100 acute coronary syndrome patients (33 ST-elevation myocardial infarction, 33 non-ST-elevation myocardial infarction and 34 unstable angina). Measurements were made of cardiac troponin I, serum 25-hydroxyvitamin D3, and oxidative stress indicators such as glutathione, superoxide dismutase, and malondialdehyde. **Results:** When compared to controls, acute coronary syndrome patients showed noticeably higher levels of oxidative stress. ST-elevation myocardial infarction patients had the highest malondialdehyde levels (84.19 ± 21.86 vs. 7.05 ± 1.45 mmol/L in controls, $p < 0.001$). Compared to 16.0% of controls, 78.8% of ST-elevation myocardial infarction, 48.5% of non-ST-elevation myocardial infarction, and 23.5% of unstable angina patients had vitamin D3 deficiency (< 20 ng/mL) ($p < 0.001$). Oxidative stress markers and vitamin D3 levels showed strong correlations ($r = -0.65$ with malondialdehyde, $r = 0.72$ with glutathione sulfhydryl, $p < 0.001$). Oxidative stress indicators and vitamin D3 levels together accounted for 76% of the variation in the severity of cardiac injury, according to multiple regression analysis ($R^2 = 0.76$, $p < 0.001$). **Conclusions:** Vitamin D3 deficiency appears to change oxidative stress pathways in acute coronary syndrome patients, aggravating cardiac damage. The protective role of vitamin D3 supplementation in the management of cardiovascular disease is suggested by the inverse relationship observed between oxidative stress markers and vitamin D3 status.

Keywords: Myocardial infarction, Vitamin D3, Oxidative stress, Troponin, Acute coronary syndrome

INTRODUCTION

Acute myocardial ischemia is the hallmark of acute coronary syndrome (ACS), which also includes unstable angina, non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).¹ ACS continues to be a major cause of cardiovascular morbidity and mortality worldwide, even with notable advancements in diagnosis and treatment techniques.²

The pathophysiology of cardiovascular disease is significantly impacted by oxidative stress, which is defined as an imbalance between the generation of reactive oxygen species (ROS) and antioxidant defense mechanisms.³

Plaque instability, endothelial dysfunction, and myocardial injury are all influenced by elevated oxidative stress during acute coronary events.⁴ Important markers of oxidative stress include glutathione (GSH) and superoxide dismutase (SOD), as

well as malondialdehyde (MDA), a byproduct of lipid peroxidation.⁵

Historically known for its function in bone metabolism and calcium homeostasis, vitamin D3 has become a multipurpose hormone with important cardiovascular implications.⁶ Through a variety of molecular pathways, vitamin D3 demonstrates anti-inflammatory, antioxidant, and cardioprotective qualities in addition to its traditional

uses.⁷ Serum 25-hydroxyvitamin D levels and the risk of cardiovascular disease have been shown to be inversely correlated in epidemiological studies.⁸

According to recent mechanistic research, vitamin D3 may activate the nuclear factor erythroid 2-related factor 2 (Nrf2) antioxidant response pathway which in turn may modulate oxidative stress pathways.⁹ Furthermore, in a number of disease states, vitamin D3 deficiency has been linked to increased oxidative stress and the production of pro-inflammatory cytokines.¹⁰

The exact way that vitamin D3 alters oxidative stress pathways in the context of an acute myocardial infarction is still unknown.¹¹ Furthermore, a thorough analysis is required to ascertain the connection between oxidative stress indicators, vitamin D3 status, and the level of cardiac injury as demonstrated by troponin elevation.¹²

The connection between oxidative stress and myocardial injury¹³, as well as between vitamin D3 deficiency and cardiovascular outcomes.^{14,15} Nevertheless, there is still little integrated evaluation of these pathways in the context of acute coronary syndrome.¹⁶

The purpose of this research is to clarify how vitamin D3 modulates oxidative stress pathways and investigate how it relates to elevated cardiac troponin levels in myocardial infarction patients and to identify possible therapeutic targets for the management of ACS and offer insights into the pathophysiological mechanisms underlying vitamin D3's cardioprotective effects by integrating multiple biomarker assessments.

MATERIAL AND METHODS

Two hundred people participated in a prospective case-control study: 100 healthy controls and 100 acute coronary syndrome patients (33 ST-elevation myocardial infarction, 33 non-ST-elevation myocardial infarction and 34 unstable angina). All patients age range 18–80 years, symptoms appear six hours after presentation, capacity to give informed consent, no history of cardiovascular disease, normal lipid profile

RESULTS AND OBSERVATIONS:

The clinical features and baseline demographics was shown in Table 1. The age and gender distributions of the groups did not differ significantly ($p>0.05$). However, compared to controls, ACS patients had significantly higher rates of conventional cardiovascular risk factors like smoking, diabetes mellitus, and hypertension ($p<0.001$). Age ($p=0.12$) and gender distribution ($p=0.89$) did not significantly differ between groups. The average age of STEMI patients were 58.2 ± 8.4 years, with 63.6% of them being male, whereas the average age of controls was 60.1 ± 8.2 years, with 58% of them being males. Comparability between study groups is guaranteed by the balanced demographic profile (Fig. 1). Traditional cardiovascular risk factor prevalence in each study group ($p<0.001$ for all comparisons compared to controls). Compared to controls (12%, 25%, and 8%, respectively), the highest prevalence of smoking (54.5%), hypertension (66.7%), and diabetes mellitus (45.5%) were found in STEMI patients. The severity of ACS is correlated with the steady rise in risk factor burden (Fig. 2).

and ECG, no long-term conditions influencing the metabolism of vitamin D or oxidative stress were included. Chronic liver or kidney disease; active cancer; taking vitamin D supplements within six months; being pregnant or nursing; and endocrine conditions that impact the metabolism of calcium phosphate were excluded.

Clinical presentation, echocardiographic parameters, ECG results, cardiovascular risk factors, and demographics were all methodically documented. Venous blood samples were taken from controls during routine visits and from ACS patients within 6 hours of the onset of symptoms. After an hour of processing, the samples were kept at -80°C until analysis. Oxidative stress markers: The thiobarbituric acid reactive substances assay is used to measure malondialdehyde. Superoxide dismutase: Assay for enzymatic activity. The colorimetric assay for glutathione: Vitamin D3: Chemiluminescent immunoassay measurement of serum 25-hydroxyvitamin D. Cardiac markers: High-sensitivity assays for Troponin I and CK-MB. Blood sugar levels, lipid profiles, and additional biochemical indicators. The data was entered and analyzed through SPSS-27. According to distribution normality (Shapiro-Wilk test) was applied. A one-way ANOVA or the Kruskal-Wallis test, as appropriate, was used for between-group comparisons. After that, post-hoc analysis was conducted using the Bonferroni correction. Pearson's or Spearman's correlation coefficients were used to evaluate correlations. A p-value of less than 0.05 was considered significant.

STEMI patients had the most unfavorable metabolic profile, with dyslipidemia and glucose intolerance showing progressive worsening in correlation with the severity of ACS (Table 2). The most significant increase was seen in MDA levels, which were almost twelve times higher in STEMI patients than in controls ($F=234.7$, $p<0.001$). This biomarker had the largest effect size among all those measured (Table 3).

Concentrations of serum malondialdehyde as a gauge of lipid peroxidation in each study group. MDA levels were significantly higher in STEMI patients (84.19 ± 21.86 mmol/L), almost 12 times higher than in controls (7.05 ± 1.45 mmol/L, $p<0.001$). The increasing oxidative stress severity that correlates with the clinical presentation of ACS is indicated by this progressive elevation (STEMI > NSTEMI > UA > Controls) [Fig. 3].

Instead of decreasing, SOD activity paradoxically increased, indicating compensatory upregulation in response to oxidative stress. SOD activity was 2.5 times higher in STEMI patients than in controls (8.24 ± 2.91 vs. 3.23 ± 0.93 U/mL, $p<0.001$). On the other hand, GSH levels gradually decreased in proportion to the severity of ACS, suggesting that non-enzymatic antioxidant

reserves had been depleted. GSH levels were 35% lower in STEMI patients than in controls (30.03 ± 8.01 vs. 45.97 ± 5.68 U/L, $p < 0.001$). The patterns of antioxidant enzyme activity are contrasting. ACS patients exhibit compensatory upregulation of SOD activity (blue line), with STEMI exhibiting 2.5 times higher activity (8.24 ± 2.91 U/mL) than controls (3.23 ± 0.93 U/mL, $p < 0.001$). On the other hand, glutathione levels (red line) show progressive depletion; STEMI patients have 35% lower GSH levels (30.03 ± 8.01 U/L) than controls (45.97 ± 5.68 U/L, $p < 0.001$), which suggests that non-enzymatic antioxidant reserves have been depleted (Fig. 4).

The prevalence of vitamin D3 deficiency rose sharply as the severity of ACS increased ($\chi^2 = 31.2$, $p < 0.001$). Patients with STEMI had the highest deficiency rate (78.8%), which was almost five times higher than that of controls (16.0%) [Table 4].

Troponin I positivity rates ($\chi^2 = 12.8$, $p < 0.01$) showed the anticipated gradient across the ACS spectrum. Similar

trends were seen in the elevation of CK-MB, with STEMI patients showing levels that were almost 50 times higher than those of controls (Table 5).

All of the main biomarker categories showed strong correlations with one another, confirming the integrated pathophysiological model. MDA and CK-MB showed the strongest positive correlation ($r = 0.81$), whereas MDA and vitamin D3 showed the strongest negative correlation ($r = -0.65$) [Table 6]. To find independent predictors of the severity of cardiac injury, multiple linear regression analysis was conducted using CK-MB as the dependent variable. Although females in the STEMI group had slightly higher rates of vitamin D3 deficiency (83.3% vs. 76.2%, $p = 0.56$, not significant), male and female patients displayed similar patterns of biomarker changes. Although the general trends were the same across age groups, patients over 60 years of age displayed more noticeable oxidative stress markers and lower vitamin D3 levels than younger patients (Table 7).

Table 1: Clinical features and baseline demographics

Parameter	STEMI (n=33)	NSTEMI (n=33)	UA (n=34)	Controls (n=100)	p-value
Age (years)	58.2±8.4	62.1±9.1	59.8±7.8	60.1±8.2	0.12
Male gender	21 (63.6%)	19 (57.6%)	20 (58.8%)	58 (58%)	0.89
Smoking	18 (54.5%)	15 (45.5%)	12 (35.3%)	12 (12%)	<0.001
Hypertension	22 (66.7%)	20 (60.6%)	18 (52.9%)	25 (25%)	<0.001
Diabetes mellitus	15 (45.5%)	12 (36.4%)	8 (23.5%)	8 (8%)	<0.001

Table 2: Comparison of metabolic and lipid profiles

Parameter	STEMI (n=33)	NSTEMI (n=33)	UA (n=34)	Controls (n=100)	p-value
Total Cholesterol (mg/dL)	206.45±33.10	197.53±38.61	185.69±32.91	171.62±26.97	<0.001
Triglycerides (mg/dL)	229.24±30.32	190.39±34.10	168.17±30.49	123.21±26.39	<0.001
HDL-C (mg/dL)	35.21±5.30	40.28±7.42	45.37±6.30	49.55±8.46	<0.001
LDL-C (mg/dL)	124.64±17.38	108.30±21.71	94.08±17.41	88.27±13.79	<0.001
Fasting Glucose (mg/dL)	127.99±13.76	117.33±18.34	107.58±13.76	88.96±9.04	<0.001
Random Glucose (mg/dL)	179.27±25.95	159.12±31.13	139.72±20.51	110.33±14.23	<0.001

Table 3: Oxidative stress indicators by study group applying ANOVA test

Parameter	STEMI (n=33)	NSTEMI (n=33)	UA (n=34)	Controls (n=100)	p-value
MDA (mmol/L)	84.19±21.86***	52.51±13.12***	35.03±8.21***	7.05±1.45	<0.001
SOD (U/mL)	8.24±2.91***	6.16±1.94***	5.00±1.66***	3.23±0.93	<0.001
GSH (U/L)	30.03±8.01***	35.03±6.01***	37.67±4.87***	45.97±5.68	<0.001

***p<0.001 vs Controls (Post-Hoc Tukey test)

Table 4: Distribution of vitamin D3 status

Group	Mean ± SD (ng/mL)	Deficiency <20 ng/mL	Insufficiency 20-30 ng/mL	Sufficiency >30 ng/mL
STEMI	15.79±6.25***	26 (78.8%)	5 (15.2%)	2 (6.1%)
NSTEMI	20.79±6.25***	16 (48.5%)	13 (39.4%)	4 (12.1%)
UA	22.49±4.87*	8 (23.5%)	24 (70.6%)	2 (5.9%)
Controls	24.97±4.85	16 (16.0%)	69 (69.0%)	15 (15.0%)

***p<0.001, *p<0.05 vs. Controls

Table 5: Cardiac injury markers

Parameter	STEMI (n=33)	NSTEMI (n=33)	UA (n=34)	Controls (n=100)	p-value
Troponin I positive	24 (72.7%)	14 (42.4%)	10 (29.4%)	0 (0%)	<0.001
CK-MB (U/L)	974.93±639.38***	343.73±159.84***	42.71±10.57***	20.12±5.31	<0.001

***p<0.001 vs. Control

Table 6: Correlation matrix of key variables

Variables	Pearson r	95% CI	p-value
MDA vs SOD	0.78	0.71-0.84	<0.001
MDA vs Vitamin D3	-0.65	-0.73 to -0.55	<0.001
SOD vs Vitamin D3	-0.58	-0.67 to -0.47	<0.001
GSH vs Vitamin D3	0.72	0.64-0.79	<0.001
MDA vs CK-MB	0.81	0.75-0.86	<0.001
Vitamin D3 vs Troponin I	-0.54	-0.64 to -0.42	<0.001

Table 7: Multiple linear regression results (dependent variable: CK-MB)

Variable	β Coefficient	Standard Error	t-value	p-value	95% CI
MDA	8.45	1.23	6.87	<0.001	6.03-10.87
Vitamin D3	-15.34	3.45	-4.45	<0.001	-22.12 to -8.56
SOD	12.67	4.21	3.01	0.003	4.37-20.97
GSH	-8.92	2.87	-3.11	0.002	-14.58 to -3.26
Age	2.34	1.45	1.61	0.109	-0.53 to 5.21
Gender	45.67	28.34	1.61	0.109	-10.34 to 101.68

Model Statistics: F = 78.4, R² = 0.76, Adjusted R² = 0.74, p < 0.001 76% of the variation in cardiac injury severity was explained by the final model

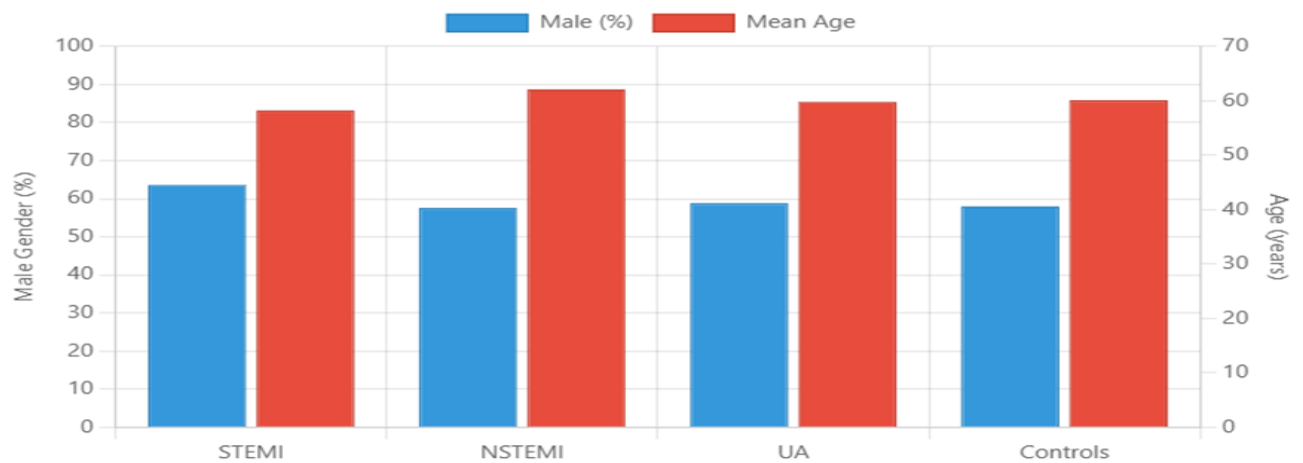


Fig. 1: Group by group patient demographics study participants' demographics in each of the four groups.

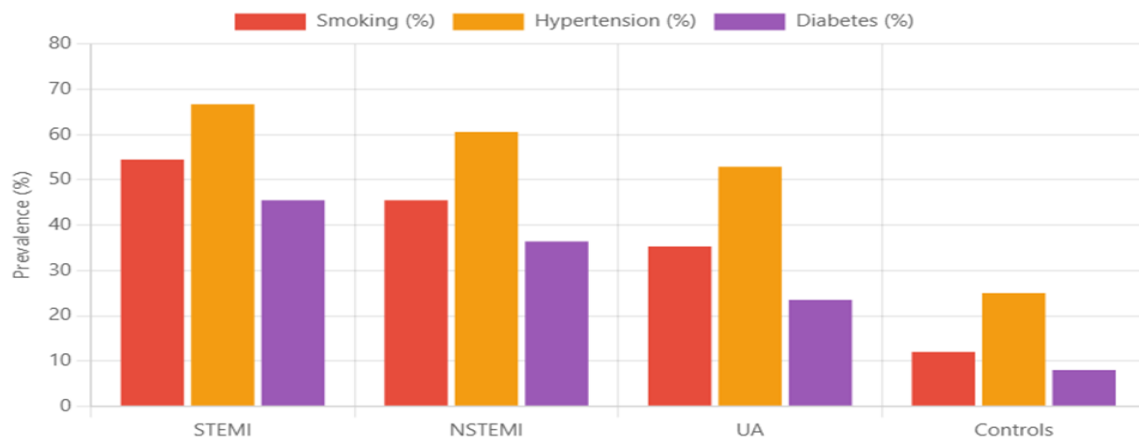


Fig. 2: Distribution of cardiovascular risk factors

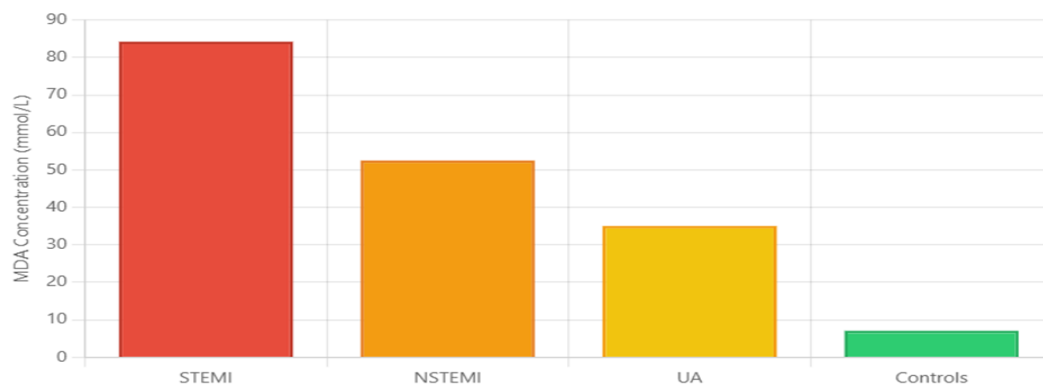


Fig. 3: Malondialdehyde (MDA) levels by group

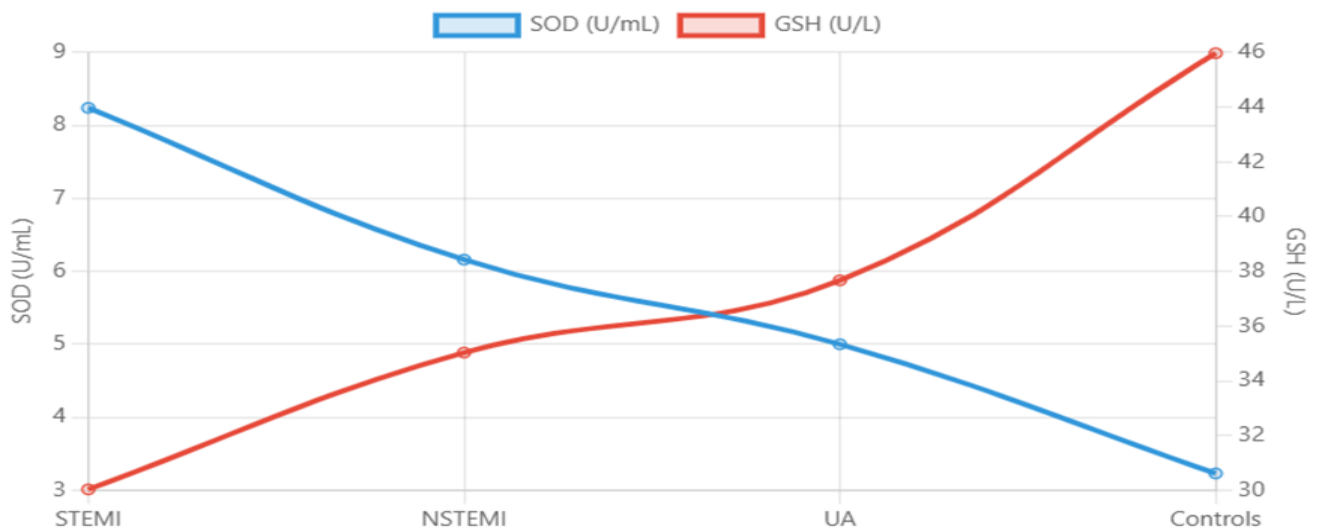


Fig. 4: Activity of antioxidant enzymes (SOD & GSH)

DISCUSSION

Vitamin D3's antioxidant qualities in the cardiovascular context are strongly supported by the observed inverse relationship between vitamin D3 and MDA levels ($r=-0.65$, $p<0.001$). According to this relationship, a vitamin D3 deficiency may make acute coronary events more likely to cause membrane damage and increased lipid peroxidation. There are several ways that vitamin D3 influences oxidative stress.¹⁷ Additionally, vitamin D3 inhibits NADPH oxidase activity, which is the main source of vascular ROS production.¹⁸

Glutathione levels and vitamin D3 have a positive correlation ($r=0.72$, $p<0.001$), which further supports vitamin D3's function in preserving cellular antioxidant capacity. The most prevalent intracellular antioxidant, glutathione, is essential for preventing oxidative damage and seems to be preserved when vitamin D3 levels are sufficient.¹⁹

Instead of depletion, the unexpected increase in SOD in ACS patients is a compensatory reaction to extreme oxidative stress. This result is consistent with new research that indicates adaptive upregulation of antioxidant enzymes is triggered by acute coronary events.²⁰ The simultaneous increase in MDA, however, suggests that this compensatory reaction is not enough to stop oxidative damage. This interpretation is supported by the strong positive correlation between MDA and SOD ($r=0.78$, $p<0.001$), which indicates that the degree of oxidative stress determines the proportionate induction of antioxidant enzymes. This pattern suggests that rather than just increasing antioxidant capacity, therapeutic approaches should concentrate on preventing the production of oxidative stress.²¹

Potential clinical applications are suggested by the integrated biomarker model that accounts for 76% of the variance in cardiac injury. Assessment of vitamin

D3 may improve risk stratification in patients with ACS, especially when paired with indicators of oxidative stress. The progression of vitamin D3 deficiency from unstable angina to STEMI (23.5% to 78.8%) raises the possibility that vitamin D3 status could be used as a predictor of outcome. Moreover, possible therapeutic interventions are supported by the mechanistic insights. Supplementing with vitamin D3 may alter oxidative stress pathways and lessen the severity of cardiac injury, especially in patients who are deficient.²²

Our results are consistent with epidemiological research showing that populations lacking vitamin D3 have a higher risk of cardiovascular disease.⁸ Nonetheless, this research offers mechanistic understanding of the modulation of the oxidative stress pathway that might be responsible for these correlations. Recent metabolomic research in ACS patients is in line with the biomarker patterns that were observed.²³

Our STEMI cohort had 78.8% prevalence of vitamin D3 deficiency, which is higher than some Western populations have reported but in line with research from comparable geographic areas.¹⁵ This highlights the significance of local vitamin D3 measurements and possible supplementation plans.

The clinical data pertaining to vitamin D supplementation in cardiovascular disease is still debatable, despite the robust correlations found in our investigation. Vitamin D supplementation has not consistently improved cardiovascular outcomes, according to a number of randomized controlled trials.²⁴ These disparities show that although mechanistic and observational research points to vitamin D3's protective function, there is still a lack of conclusive causal evidence from interventional trials. Our results should therefore be regarded as hypothesis-

generating, highlighting the necessity of focused studies in high-risk, vitamin D-deficient populations.

CONCLUSION

A progressive deficiency of vitamin D3 is associated with the severity of ACS; oxidative stress markers and vitamin D3 levels have a strong inverse relationship; compensatory but insufficient upregulation of antioxidant enzymes; and an integrated predictive model that explains 76% of the variance in cardiac injury.

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