Al-Azhar International Medical Journal

Volume 4 | Issue 12 Article 27

2023
Section: Cardiology

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How to Cite This Article

Ghander, Sherif Hussein Nasr; Zaid, Ahmed Abo; Khalil, Essam Ahmed; Ahmed, Mohamed Abdelhady Abo; and Mohamed, Yasser Radwan (2023) "Association of Vitamin D Status with Severity of Acute Coronary Syndrome," *Al-Azhar International Medical Journal*: Vol. 4: Iss. 12, Article 27.
DOI: https://doi.org/10.58675/2682-339X.2139

ORIGINAL ARTICLE

Association of Vitamin D Status With the Severity of Acute Coronary Syndrome

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Abstract

Background: **Due to the existence of its receptor in cardiomyocytes, vitamin D deficiency influences alterations in these cells. People who have low levels of 25OHD in their blood are more likely to get an acute myocardial infarction (MI).**

Aim: **To assess the level of vitamin D (concentrations of 25OHD in serum) in people having acute coronary syndrome (ACS) and its relationship to the extent of the condition.**

Patients and methods: **This cross-sectional work was performed on 50 individuals. The age of the patients, who were diagnosed with ACS ranged from 32 to 82 years. All patients were subjected to left ventricular function [estimated ejection fraction (EF) using either echocardiography or left ventriculography), 12-lead ECG, or 25OHD in serum.**

Results: **Of the cases, 66 % were diagnosed with STEMI by the ECG; 34 % of the cases were non-STEMI; 18 % had anterior non-STEMI; 12 % had inferior non-STEMI; and 4 % of them had lateral STEMI. Regarding ECHO EF, it ranges between 38 and 65 % while the mean ECHO EF was 51.94 $\pm$ 7.03. Of the cases, 26 % had creatine-kinase-myoglobin binding (CKMB), while 44 % of them had + CKMB; 20 % of them had ++ CKMB; and 10 % of them had +++ CKMB. Regarding vitamin D level, there was a negative medium correlation among vessel number, SYNTAX score, and vitamin D ($r = -0.585$, $r = -0.589$, respectively, $P < 0.001$).**

Conclusions: **Deficiency of vitamin D showed a higher prevalence rate among ACS patients, a medium negative correlation among vessel number, SYNTAX score, and vitamin D.**

Keywords: Acute coronary syndrome, Serum 25OHD concentration, Vitamin D

1. Introduction

The most important reason for mortality worldwide for both men and women is acute coronary syndrome (ACS). According to estimates from the WHO, ischemic heart disease caused 13.2 % of all fatalities globally in 2012.[1]

ACSs can present as a variety of clinical findings that include acute myocardial infarction (MI), sudden cardiac arrest, or unstable angina, typically brought on by coronary obstruction caused by an atherosclerotic plaque breakdown, erosion, fissuring, or a combination thereof with superimposed intracoronary (IC) thrombosis.[2]

In addition to being a vitamin that is soluble in fat, vitamin D is also considered a prohormone. Although vitamin D's traditional role was long believed to be to improve the intestinal absorption of calcium for healthy bones, its importance in maintaining health extends to many different types of cells across the body, which include cardiomyocytes, smooth muscle of the vessels, and endothelium. As a consequence of the existence of its receptor in cardiomyocytes, vitamin D works on the renin–angiotensin–aldosterone path and causes alterations in these cells, this explains how vitamin D directly impacts the cardiovascular system.[3]

Accepted 30 July 2023.
Available online 2 February 2024

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https://doi.org/10.58675/2682-339X.2139

Decreased levels of 25OHD in the serum are correlated with a high risk of acute MI.[4]

The function of endothelial cells is directly impacted by vitamin D deficiency, which results in more unstable plaques.[5] Vascular homeostasis is crucially maintained by the endothelium, and risk factors for disease of the cardiovascular system encourage the occurrence of endothelial dysfunction by impairing vasodilation that is dependent on the endothelium and proinflammatory or procoagulant endothelial activities. The European Society of Cardiology's suggested global descriptions of MI, the finding of the increase and/or decrease of troponin correlated with no less than one of the variables as follows: ischemic symptoms, ECG alterations suggestive of newly occurring ischemia, signs of new myocardial viability loss, or new regional wall motion abnormalities, and autopsy or angiography for the detection of IC thrombus. In addition to decreasing hypertension and enhancing cholesterol management, appropriate serum levels of 25OHD may also reduce the risk of MI and mortality from cardiovascular diseases, so it could enhance cardiovascular outcomes, according to emerging research.[5,6]

The purpose of this work was to assess the status of vitamin D (serum 25OHD concentrations) in ACS patients and its relationship to disease severity.

2. Patients and methods

This cross-sectional work was performed on 50 individuals. Age ranged from 32 to 82 years diagnosed with ACS from February 2022 to February 2023.

The work was done following receiving permission from the Ethics Committee Al-Azhar University Hospitals, Cairo, Egypt. The patient provided written permission after being fully briefed.

Criteria of exclusion were heart failure, aggressive cancer, chronic renal disease, patients with vitamin D and/or calcium supplements, and hepatic diseases.

Each participant received complete history taking, history of ACS, thorough physical examination, risk stratification using risk score from the worldwide registration of ACSs, function of the left ventricle [estimated ejection fraction (EF) using either echocardiography or left ventriculography], 12-lead ECG, data analysis, serum urea, and estimated glomerular filtration rate $= 186 \times (\text{creat}/88.4)-1.154 \times (\text{age})-0.203 \times (0.742$ if female), fasting blood glucose, cardiac markers (creatine phosphokinase-MB, troponin), and serum 25OHD.

Stenosis of more than 70 % in the main coronary artery or more than 50 % within the trunk of the left coronary artery designates a lesion as serious. The extent of coronary artery disease (CAD) is defined by the GINSINI or SYNTAX scores.

The existence of no more than two of the following:

Ischemic symptoms, an indicative ECG, and increased cardiac biomarkers are necessary for the diagnosis of acute MI. A new left bundle branch block or presumed new pathologic Q waves are among the ECG features indicative of ACS. In addition, ST elevation is more than or equal to 0.1 mV in two or more adjacent leads of limb and/or more than or equal to 0.2 mV in leads of the chest.

Without the rise in cardiac biomarkers, symptoms of ischemia were used to identify unstable angina, and an abnormal ECG may also be indicative of ischemia.

The ultrahigh-performance liquid chromatography system with a tandem mass detector system, which was composed of a Waters Quattro Premier XE tandem mass spectrometer (Waters Corporation, Milford, Massachusetts, USA), was used to analyze the blood concentrations of vitamin D, which included D2, 25OHD, and 1,25OH2D. This analysis was carried out to determine whether or not the vitamin D levels were within the normal range.

According to the United States Endocrine Society (USES) guidelines, (OH)D deficiencies were identified as serum levels of lower than 20 ng/ml and 25(OH)D inadequacy as levels of between 20 and 29.99 ng/ml, whereas normal values were above 30 ng/ml.

2.1. Coronary angiography

Using conventional diagnostic catheters through the access of a femoral or radial artery, it was conducted on all of the participants. It uses dye contrasts and radiograph to identify obstructions in the coronaries, which are often brought on by plaques caused by atherosclerosis.

The circumflex, anterior descending branches, and right coronary artery were the three main epicardial coronaries that received a score of 1 for stenosis of more than 70 %. A two-vessel disease was additionally regarded as when the left major coronary artery's stenosis was more than or equal to 50 % and scored at two points. The score was determined by adding together all the points, which may represent a single, two, or three vessels in CAD.

Based on the most recent guidelines from the European Society of Cardiology, a rise in markers of myocardial necrosis, particularly troponin, and no less than one of the following criteria: signs or symptoms of ischemic myocardium, alterations in

the ECG that indicate recent ischemia, development of pathological Q waves, demonstration from imaging researches of a recent lack of functional myocardium or a newly segmented disruption in the motion of the wall of the heart, or a thrombi in the coronaries.

2.2. The SYNTAX score

The SYNTAX score which was created by the team at the Thoraxcenter, Erasmus Medical Center, the Netherlands, led by the senior investigator Professor Patrick Serruys, was used to assess the complexities of CADs. It was developed from the sum of the person's scores for each distinct lesion, which was identified as more than or equal to 50 % obstructing the lumen in vessels more than or equal to 1.5 mm. It was estimated using specialized software for each patient. There are three tertiles for the SYNTAX score: lower (≤22), middle (23–32), and high (>33). The SYNTAX score is the total of the points given to every lesion seen in the coronary tree that has a diameter reduction of more than 50 % in arteries with a diameter bigger than 1.5 mm. The AHA categorization divides the coronary tree into 16 parts. Having values that range from 3.5 for the proximal left anterior descending artery (LAD) to 5.0 for the left main and 0.5 for lesser branches, every segment gets a score of 1 or 2 based on the existence of illness. This score then gets weighted according to a chart. One point is awarded for each of the following: a side-branch more than 1.5 diameter, a bridging collateral image, a blunt stump, branches of 3 months, and initial segment observable beyond the whole occlusion. One sick segment receives three points, two unhealthy segments receive four points, three unhealthy segments receive five points, and four diseased segments receive six points for trifurcations. One point is awarded for bifurcation lesions of kinds A, B, and C; two points are awarded for those of types D, E, F, and G; and one point is awarded for angulations of more than 70°. If there is an aorto-ostial lesion, you will get one point, two points for severely tortuous vessels, one point for lesions longer than 20 mm, two points for substantial calcification, one point for thrombus, and one point for widespread disease or minor vessel involvement for each segment. Lesions that are scored as a single lesion include those that are separated by no more than three reference vessel diameters.

2.3. Statistical analysis

SPSS (Statistical Package for the Social Sciences), version 25 (IBM Inc., Chicago, Illinois, USA) was used for the statistical evaluation. Shapiro–Wilk normality tests and histograms were used to analyze the distribution of quantitative data and determine whether parametric or nonparametric statistical testing was appropriate. Age is one example of a parametric variable that was represented as mean and SD. The Kruskal–Wallis test was used to evaluate nonparametric variables, which were reported as median and interquartile range. Categorical characteristics, such as sex, were statistically examined using the χ^2 test and presented as frequency and percentage.

3. Results

The demographic data and risk factors are presented in Table 1.

The majority of the cases (78 %) were class I in KILLIP score, the mean SYNTAX score was 18.56 ± 6.60, and the median of the vessels was 2.0 (Table 2).

In Table 3, the ECHO EF, renal function, and other vital signs are presented. The median vitamin D was 12 ng/ml.

A negative medium association existed among the vessels number, SYNTAX score, and vitamin D, *P* value less than 0.001 (Table 4).

4. Discussion

The aberrant blood levels of vitamin D are linked to additional ACS comorbidities like left ventricle dysfunction, remodeling of ventricles, HF, and sudden cardiac death.

Therefore, levels of vitamin D may have a major impact on both the long-term and short-term problems associated with patients with ACS.[7,8]

In this study, 66 % of the cases were diagnosed with STEMI by the ECG, 42 % of them had anterior

Table 1. Distribution of the examined cases based on demographic information (N = 50).

Parameters	*n* (%)
Sex	
Male	44 (88)
Female	6 (12)
Age (years)	
≤50	13 (26)
>50	37 (74)
Dyslipidemia	35 (70)
DM	25 (50)
HTN	29 (58)
Smoking	36 (72)
IHD	17 (34)
Family history	18 (36)

DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease.

Table 2. Distribution of the examined cases based on KILLIP, GRACE score, ECG admission, SYNTAX, creatine kinase-myocardial band and troponin, thrombus burden, and vessels (N = 50).

Parameters	N = 50
KILLIP	
I	39 (78)
II	11 (22)
GRACE score	
Low	23 (46)
Intermediate	19 (38)
High	8 (16)
ECG admission	
STEMI	33 (66)
STEMI	
Anterior	21 (42)
Inferior	11 (22)
STD inferior lateral	1 (2)
Non-STEMI	17 (34)
Non-STEMI	
Anterior	9 (18)
Inferior	6 (12)
Lateral	2 (4)
SYNTAX score (Median = 17.50)	
Low (<22)	34 (68)
Intermediate (23–32)	16 (32)
High (>33)	0
CKMB	
−	13 (26)
+	22 (44)
++	10 (20)
+++	5 (10)
Troponin	
−	2 (4)
+	15 (30)
++	12 (24)
+++	21 (42)
Thrombus burden	
No	31 (62)
Yes	19 (38)
Vessels	
LAD	36 (72)
CX	24 (48)
RCA	22 (44)
OM	8 (16)
D	2 (4)
RAMUS	4 (8)
Number of vessels (median = 2)	
1	17 (34)
2	23 (46)
3	7 (14)
4	3 (6)

Data are presented as *n* (%).
CKMB, creatine kinase-myocardial band; CX, circumflex artery; ECHO, echocardiogram; EF, ejection fraction; LAD, left anterior descending artery; OM, obtuse marginal; RCA, right coronary artery.

STEMI, 22 % had inferior STEMI, and only 2 % had STD inferior lateral STEMI. Moreover, 34 % were non-STEMI by the ECG, 18 % had anterior non-STEMI, 12 % had inferior non-STEMI, and only 4 % had lateral STEMI. Regarding ECHO EF, it ranges between 38 and 65 %. In their work by Chew *et al.*[9]

Table 3. Descriptive analysis of the examined cases based on ECHO EF, renal function, vitamin D, and laboratory data (%).

	N = 50
ECHO EF (%) (mean ± SD)	51.94 ± 7.03
Renal function (mean ± SD)	
Urea	38.94 ± 14.23
Creatinine	0.95 ± 0.24
Vitamin D (ng/ml) median	12.0
Heart rate (mean ± SD)	81.18 ± 12.21
Systolic (mean ± SD)	125.80 ± 17.80

Table 4. Correlation between vitamin D (ng/ml) with severity (N = 50).

	Vitamin D (ng/ml)	
	r_s	*P*
Number of vessels	−0.585*	<0.001*
SYNTAX score	−0.589*	<0.001*

r_s: Spearman coefficient.
*: Statistically significant at $P \leq 0.05$.

they discovered that the LVEF increased from the baseline EF at the time of diagnosis of AMI to 2–8 weeks after AMI by 25–37.5 %. According to Samman Tahhan et al.'s[10] findings, levels of hsTnI were found in nearly all participants (99.9 %) and remained lower in those without severe native CAD when compared with people with 1-, 2-, or 3-vessel CAD.

According to this study's findings, the mean level of vitamin D was 17.63 ± 14.06, which is consistent with many epidemiological and observational studies.[11,12] Safaie et al. (2018)[13] observed that patients with acute MI had a greater prevalence of vitamin D lack and insufficiency. The inverse correlation between levels of 25OHD and the occurrence of acute MI was shown in prior case–control research.

In additionally, according to Ismail *et al.*[14] vitamin D2, D3, and 1,25(OH)2D levels were substantially reduced in ACS patients when compared with controls. In addition, a considerable increase existed in the prevalence of 25OHD deficit in our cohort among patients with ACS (91.4 %) in comparison to the control group (14 %).

In addition, results from research carried out by Chen et al.[15] and Danik and Manson,[16] and the Framingham Offspring prospective study revealed a strong association between deficiencies in vitamin D levels and the risk of coronary heart disease.

According to Mathew *et al.*[17] individuals with deficiency of vitamin D had more severe CAD than individuals with normal vitamin D levels.

In research by Beska *et al.*[18] 66 % of the individuals who first reported having a history of an MI were in the low group of vitamin D in serum. Prior MI was twice as likely to occur among individuals with baseline blood levels of vitamin D of less than

29.5 nmol/l (95 % confidence interval 1.10–3.60, $P = 0.02$). In addition, individuals with the lowest levels of blood vitamin D had a significantly higher probability of developing congestive heart failure at baseline, with individuals in the lowest category bearing 62.5 % of the burden of congestive heart failure in the research population.

According to research by Brøndum-Jacobsen *et al.*[19] those who had decreased vitamin D levels had a multivariable modified risk that was elevated by 40 % for ischemic cardiovascular diseases, 64 % for MI, 57 % for premature mortality, and 81 % for fatal ischemic heart disease or MI.

However, other studies have been unable to demonstrate a causal link between death from coronary heart disease and decreased vitamin D levels. For instance, no substantial correlation existed between vitamin D and fatalities from CAD following a median follow-up of 27 years, according to information from the MINI-Finland Health Survey of 6219 males and females more than 30 years old, who did not suffer from cardiovascular disease (HR: 0.91; 95 % confidence interval 0.70–1.18; $P = 0.20$).[20]

A relatively high supplementary vitamin D dosage (2000 IU) failed to lower the composite outcome of main cardiovascular events in a large, randomized vitamin D and OmegA-3 Trial (VITAL) for primary prevention.[21]

Our research revealed a medium-negative connection ($r = -0.585$) between the vessels number and vitamin D and a negative medium connection ($r = -0.589$, $P = 0.001$) among the SYNTAX score and vitamin D.

This is consistent with Syal et al.'s[22] findings that individuals with low levels of 25OHD had a considerably greater frequency of double-vessel and triple-vessel CAD than did patients with normal levels and that 25OHD deficiency was linked with greater severe CAD on coronary angiography.

In contrast, with reference to the findings of the coronary angiography, Ismail et al.[14] could not discover a statistically substantial distinction in the vitamin D level among one-vessel and three-vessel illnesses. Notably, they do not have any ACS individuals who have 25OHD values within the ideal range. Therefore, all of the individuals fell into the 25OHD-deficient and inadequate groups.

Furthermore, Shor et al.[23] demonstrated that levels of 25OHD in the serum less than 20 ng/ml are indicators of major coronary lesions, despite the fact that they found no correlation between the arteries number that were damaged and did not distinguish among individuals with T2DM and those without T2DM.

According to Goleniewska et al.'s[24] analysis of individuals with ACS with extremely low blood 25OHD concentration, ranging from 6 to 17 ng/ml (the lowest to higher quartile), there was no correlation between the severity of lesions of coronaries and serum 25OHD levels. This concurs with Kamal et al.'s[25] findings that postmenopausal women with decreased levels of serum vitamin D had more severe coronary atherosclerosis. Individuals with more severe atherosclerosis coronaries exhibited considerably lower 25OHD concentrations. According to Mathew *et al.*[17] there is a substantial association between the occurrence of serious CAD and decreased vitamin D levels that have been assessed. Their research also found a greater incidence of coronary artery calcification, which suggests that people with VDD had more plaque in their arteries. Verdoia et al.'s[26] investigation of women of different ages highlighted the link between deficiencies in vitamin D levels and both the prevalence of CAD and the extent of atherosclerosis of coronaries. It is interesting to note that individuals who took 0.5 μg of calcitriol daily for 6 months had much less coronary artery inflammation and, as a result, significantly lower SYNTAX scores.[27] The beneficial impact of vitamin D administration on cardiovascular outcomes was not, however, supported by large cohort studies.[28] Case–control research on the US population demonstrated a positive link between reduced levels of vitamin D and the occurrence of CVDs; however, this impact was different. Together, the majority of research indicated that vitamin D protects against cardiovascular diseases.[29]

4.1. Limitations

The sample size was relatively small, and encountered cost limitations; it could not prove causation but demonstrated a statistical association.

4.2. Conclusions

Vitamin D deficiency showed a higher prevalence rate among ACS patients. Moreover, vitamin D level showed a medium negative correlation between the number of vessels, SYNTAX score, and vitamin D.

Authors' contribution

Sherif H.N. Ghander: idea formulation, data collection, analysis, and writing. Ahmed A.A. Zaid: supervision, writing, and revision. Essam A. Khalil: supervision, writing, and revision. Mohamed A.A. Ahmed: data collection, supervision, writing, and revision. Yasser R. Mohamed: idea formulation, supervision, writing, and revision.

Conflicts of interest

There are no conflicts of interest.

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