Study of vitamin D level in acute coronary syndrome

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Abstract

Background: Vitamin D (Vit. D) insufficiency is thought to play a role in the prognosis of some cardiovascular diseases (CVDs) and other comorbidities such as Diabetes millets (DM), chronic kidney disease (CKD), obesity, and hypertension. In heart failure (HF) cases, Vit. D supplementation is associated with bettered survival. Furthermore, Vit. D supplementation decreased mortality rates in critical medical situations, such as end-stage renal disease (ESRD) and coronary artery disease (CAD).

Objectives: The current study aimed to assess Vit. D levels in cases present with the acute coronary syndrome (ACS).

Patients and Methods: 60 ACS patients and 30 healthy individuals were recruited for the current study. All participants passed a clinical-based cross-sectionalstudy, at SohagUniversity hospital within six months (From March to September 2019 for vit. D levels and other laboratory measures.

Results: In this study,16.6 % of ACS cases were Vit. D deficient, compared to 10% of control. 45%of ACS cases were Vit. D inadequate, compared to26.6% of control (*P= 0.001*).

Conclusion: Since Vit. D insufficiency is a potentially modifiable threat factor in CVDs patients, hence a persistent need to consider in diagnosis and treatment. ACS patients with estimated Vit. D deficiency or insufficiency should be advised with Vit. D supplementations. Vit. D issues should be bandied with the family members from a moment's perspective.

Keywords: Vit. D; acute coronary syndrome; Sohag University Hospital.

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Introduction

Vit. D or its blood-circulating form (25- hydroxyVit. D (25 (OH) D) is one of the factors necessary for the regulation and preservation of serious medical situations such as calcium homeostasis, bone metabolism, hypertension, and different CVDs **(Khazai et al., 2008).** Indeed, Vit. D receptors are located in all cells of the body, particularly, in the myocardium, vascular smooth muscle cell, and immune cells **(Milazzo et al., 2017).** The deficiencies in Vit. D (HypovitaminosisD) is an important risk factor for the development of acute myocardial infarction (AMI) and HF, which had been reported worldwide (**Naghavi et al., 2003**).

Vit. D insufficiency is directly related to the prognosis of critical medical situations, such as Diabetes millets (DM), chronic kidney disease (CKD), end-stage renal disease (ESRD), hypertension, and other heart and vesicular diseases (**Makki et al., 2015**). More importantly, in HF and ESRD cases, the supplementation of Vit. D was reported to decrease the mortality and incidence rates associated with these disorders (**Busa et al., 2020; Makki et al., 2015**).

Recently, deficiencies of Vit. D blood levels were suggested to be associated with the prognosis of ACS(**De Metrio et al., 2015**). Multiple studies correlated the low serum levels of Vit. D and increased hospitalization rates and the need for intensive care in ACS patients, according to long-term results and follow-up (**Vacek et al., 2012; Makki et al., 2015**). However, studies about the direct impact of Vit. D deficiency or insufficiency in the mortality rates of ACS cases is limited (**De Metrio et al., 2015**).

Moreover, different reports revealed the negative relationship between the serum levels of Vit. D and the renin-angiotensin system, which subsequently affects blood pressure regulation, insulin resistance, platelet characteristics, and endothelial function (**Jia et al., 2022**). All these factors are considered during ACS diagnosis and treatment (**Siadat et al., 2012**). Besides, the abnormal serum levels of Vit. D is associated with other ACS co-morbidities such as left ventricular dysfunction (LVD), ventricular remodeling, HF, and sudden cardiac death (SCD) (**De Metrio et al., 2015**). Therefore, both the short- and long-term issues of ACS cases could be significantly affected by Vit. D status(**KneževićPraveček et al., 2017**).

The current study aimed to assess Vit. D levels in ACS cases attending Sohag University Hospital, Sohag, Egypt.

Patients and methods

Subjects

The study was approved by the ethics board of the Faculty of Medicine, Sohag University, Sohag, Egypt. Written consents were obtained from all participants.The study included 60 patients admitted to Sohag University Hospital presented by ACS and 30 persons as a control. All participants underwent a cross-sectional clinical-based study within six months (From March to September 2019).

Exclusion criteria

All CKD patients with serum Creatinine ≥ 2mg/dl were excluded. Patients with valvularheart diseases, congenital heart diseases, liver cirrhosis, or alcoholic liver disease were excluded, as well. Also, those subscribed with calcium or Vit. D supplementation, corticosteroids, and Rifampicin were not included. Particular medical situations of pregnancy, lactation, abnormal calcium levels (Normal reference range – 9 to 11 mg/dl), diabetic, and hypertensive patients were excluded from the study, as well.

Methodology

All participants underwent the following methodological plan:

- Thorough medical history included the first complaint of the typical chest pain, its nature, degree, and if it was increased with exertion. Besides, any other symptoms such as excessive sweating and breathlessness.
- Clinical characteristics included smoking, alcohol consumption, hypertension, DM, and a family history of ischemic heart disease (IHD)were recorded.
- A thorough clinical examination was carried out in each case with special reference to pulse, blood pressure, cardiovascular, and respiratory examination for the presence of murmur, crepitations, and an S3 gallop.
- During hospitalization, the patients underwentthe followinglaboratory investigations:

1. For each participant, the venous blood sample was collected in an EDTA tube for CBC and HbA1C, and in plain tubes to get serum for estimation of blood urea, fasting, lipid profile, liver function tests, pregnancy test, total calcium, Creatine Kinase MB (CKMP), Troponin-T (TnT), and 2-hour postprandial blood glucose. The serum samples were collected by direct centrifugation of coagulated blood to determine the serum creatinine and Vit. D levels by radioimmunoassay, were deficient, insufficient, and normal Vit. D levels were considered at 0-15 ng/ml, 16-30 ng/ml, and ≥31 ng/ml, respectively. No special preparations of the individual were necessary before specimen collection.
2. The levels of complete blood count, fasting (FBS) & postprandial blood glucose, blood urea, serum creatinine, liver function tests, lipid profile, pregnancy test, HbA1C, total calcium, Creatine Kinase MB (CKMP), and Troponin-T (TnT) were measured.
3. Radiological investigations includingchest x-ray, ECG, and echowere done.

Statistical analysis

The collected data were analyzed using STATA v. 14.2 (College Station, TX, United States). Skewness and Kurtosis normality tests were used to determine data distribution. The statistical correlation between Vit. D serum level and ACS ratio were analyzed by the Multiple stepwise regression analysis. The quantitative and qualitative data were analyzed by student t-test and Chi-square test, respectively. Pearson’s correlation analysis was used to find the relation between different variables. Graphs were produced by using Excel or STATA program.

Results

Demographic and clinical characteristics of the study population

The study included 90 participants (60 patients and 30 healthy-apparent individuals as control). The mean age of the study group was 51.5±9.93 years. 61participants were males (68.9%) versus 29 females (31.1 %). A comparison of Life Style factors revealed that 50% (30 cases) of cases were active smokers compared to 13.3 % (four cases) of controls. About 25% (15 cases) of patients were nonsmokers compared to 70% (21 cases) of control. 25% (15 cases) of patients were ex-smokers compared to 16.6% (5 cases) of control (**Table 1**).

Table 1. Demographic data of the study population.

Variables		**Patients**	**Control**	**Total**
Number		60 (66.7%)	30 (33.3%)	90
Age (Mean±SD) of all particibants		***51.5±9.93***		
Gender	**Male**	41 (76.75%)	20 (32.25%)	61
	Female	19 (64.3%)	10 (35.7%)	29
Smoking	**Non-smokers**	15 (25%)	21 (70%)	37
	Active smokers	30 (50%)	4 (13.3%)	34
	Ex-smokers	15 (25%)	5 (16.6%)	20

SD: Standard Deviation.

Of the 60 patients, six had ST-elevation myocardial infarction (STEMI), three had non-ST elevation myocardial infarction (NSTEMI), and 51 had unstable angina. Four male(6.7%) and two female patients had STEMI, while two male and one female patients had NSTEMI. Unstable Angina was reported in 35 male and 16 female patients.Analysis of the patient's lipid profile revealed that 70% of ACS cases were diagnosed with hyperlipidemia, unlike the control group(**Table 2**).

Table 2: Clinical characteristics of the patient group.

	Male (n=41)	**Female (n=19)**	**Total (n=60)**
STEMI	4 (9.8%)	2 (10.5%)	6 (10%)
NSTEMI	2 (4.9%)	1 (5.3%)	3 (5%)
Unstable angina	35 (85.3%)	16 (84.2%)	51 (85%)
Hyperlipidemia	42 (70%)		

The mean serum Vit. D level in ACS patients was 27.61 ng/ml and 33.73 ng/ml in controls, which represented a statistically significant difference (*P=0.004*). In this study, 16.6% of ACS patients were Vit. D deficient as compared to 10% of control. 45% of ACS patients were Vit. D insufficient, as compared to 26.6 % of controls (*P=0.001*) (**Table 3** and **Fig.1**).

Table 3: Comparison of Serum Level of Vit. D in the study population.

Vit. D levels (ng/dl)	Patients		Control	Total	Mean ±SD	*P-value*
	Unstable Angina	MI				
Deficient (<15 ng/dl)	10	0	3	13	11±1.1	0.001*
Insufficient (16-30ng/dl)	24	3	8	35	26±7.3	0.001*
Sufficient (>30ng/dl)	17	6	19	42	39±6.9	0.001*
Total	51	9	30	90		

* Significant at *P<0.05*. SD: Standard Deviation.

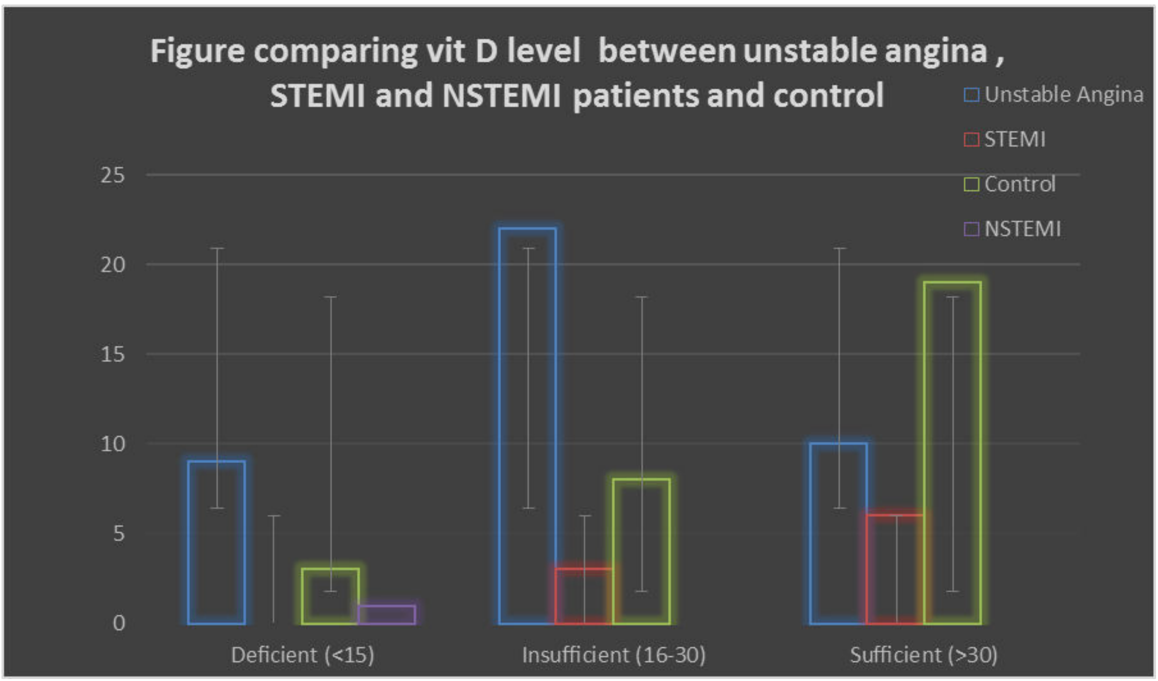

Fig.1: Ratio between Vit D level in Unstable Angina & STEMI and NSTEMI patients.

The mean Aspartate aminotransferase (AST) levels in ACS patients and control were 60.36 and 33 U/L, respectively (*P=0.05*). The mean total calcium levels had insignificant difference between ACS patients (8.95 mg/dL) control (9.06 mg/dL**)** (*P=0.637*). The mean CKMP had significantly higher levels in ACS patients (63.98 IU/L) as compared to the control (24.36 IU/L) (*P=0.023*). The mean Troponin level in ACS patients was 10.4 ng/ml as compared to (4.07 ng/ml) in controls, which represented a statistically insignificant difference (*P=0.27*)(**Table 4**).

Table 4: Comparison of Serum Level of AST, Total Calcium, CKMP, and Troponin in the study population.

Variable	Type	Mean	Std. Error	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound	*P-Value*
AST (U/L)	**Case**	60.367	8.230	44.01	76.723	0.05*
	Control	33.033	11.640	9.902	56.165	
Total Calcium (mg/dL)	**Case**	8.950	0.142	8.667	9.233	0.637
	Control	9.067	0.201	8.667	9.466	
CKMP (IU/L)	**Case**	63.983	8.379	42.320	78.647	0.03*
	Control	24.367	10.435	3.629	45.104	
Troponin (ng/ml)	**Case**	10.411	3.222	4.007	16.815	0.37
	Control	4.078	4.557	-4.978	13.135	

* Significant at $P<0.05$.

Five ACS patients reported HF, and four (80%) had Vit. D insufficiency ($P< 0.001$), while one patient had normal Vit. D level. Furthermore, two cases had hypotension accompanied by Vit. D deficiency ($P<0.001$). Six patients had Arrhythmia, however, four of them had normal Vit. D (66.6%), and two hada deficiency.

Discussion

Vit. D deficiency is a prevalent medical condition, which affects the health of all ethnicities, both genders, and at any age **(Sanghera et al., 2017).** Statistically, about 50% of the world population suffers from Vit. D deficiency (**Nair et al., 2012**). In addition to the reported role of Vit. D in calcium homeostasis (**Bouillon and Suda, 2014**), it's considered an important risk factor for the prognosis of CAD (**Raljević et al., 2021**). Clinical investigations suggested an association between Vit. D low levels and AMI, which was responsible for the elevated morbidity and mortality percentages (**GBD 2013 Mortality and Causes of Death Collaborators, 2015**; **Aleksova et al., 2015**).

The current study assessed the relationship between different concentrations of the serum Vit. D and ACS patients were admitted to Sohag university hospital, Egypt. As noticed, ACS patients had higher ages>50 years. This is in agreement with the global burden towards providing sufficient health care resources, better management, and evidenced-based medications against the risk of ACS in old age (**Jha et al., 2005**). ACS-age-related issues might be due to a time factor, as the higher prevalence of elderly ACS cases was, notably, reported with delayed diagnosis, late presentation, and limited diagnostic electrocardiograms (***Simms* et al., *2012***). Furthermore, increased mortality rates among elderly ACS cases might be due to underestimated diagnoses resulting from either limited cardiologist advice, limited medical equipment, cognitive/psychological impairment, insufficient guidelines about ACS management in the older population, or other medical complications such as disability and comorbidity (**Collinson et al., 2005; Simms et al., 2012**). The targeted health care improvements of ACS patients at advanced ages might increase the required outcomes in the treatment and management of ACS, however, it might be affected by other non-modifiable factors related to age such as immunity problems (**Avezum et al., 2005**).

The short-term mortality after ACS is directly proportional to gender type in STEMI cases (**Siabani et al., 2020**). A meta-analysis including >136,000 patients from 11 randomized clinical trials of ACS showed that women with STEMI had worse 30-day outcomes than men, but women with NSTEMI or unstable angina had better outcomes (**Berger et al., 2009**). Another study revealed that, despite the improvement in the gender-mortality relationship in hospitalized ACS after clinical adjustment, the effect was limited in STEMI cases (10.2% versus 5.5%; $P < 0.0001$) (**Jneid et al., 2008**), which is still unexplained in ACS short-term prognosis. However, in contrast to these findings, a previous old study denied any existence of gender-based differences in long-term mortality (**Johansson et al., 1984**), which is compared to multiple recent studies that report the variability of the crude death rates between genders at the baseline clinical factors. In accordance, a previous review compared almost 40 studies in the last 50 years and concluded that the death rate due to MI among females is more non-adjustable than in males (**Bucholz et al., 2014**). However, another cohort study in the Netherlands suggested that the long-term mortality rates were not constant in the terms of gender type, at baseline clinical factors (**Koek et al., 2006**).

The VIRGO study (2015) indicated that youthful women (aged< 55 years) with STEMI entered reperfusion remedy less constantly and were more likely to have reperfusion detainments than also aged men (**D'Onofrio et al., 2015**). More lately, **Goleniewska et al. (2014)** assessed 130 cases with ST-elevation myocardial infarction, linked Vit. D levels as independent predictors of multivessel CAD at multiple accretive logistic retrogression and ACS. Still, data from the combined National Health and Nutrition Examination Survey (NHANES) 2001 to 2006, a population-grounded cross-sectional study, and the NHANES III cohort, a population-grounded cohort study, showed that the associations of serum 25 (OH) D with mortality, particularly due to CVD and colorectal cancer, were modified by magnesium input. The antipode associations were primarily present among those with magnesium input above the standard (**Deng et al., 2013**). Likewise, in an analysis of NHANES III 1988 – 1994, low Vit. D was associated with CVD and CVD risk factors, including DM, obesity, and hypertriglyceridemia (**Kendrick et al., 2009).** In a prospective nested case-control study between 1993 and 1999 of 225 American men (Health Professionals Follow-Up Study), low Vit. D was associated with an advanced threat of MI in comparison with sufficient 25 (OH) D after multivariate adaptation (**Giovannucci et al., 2008**).

One of the major parameters is the lipid profile. Analysis of the patient's lipid profile revealed that 70% of ACS cases were diagnosed with hyperlipidemia, unlike the control group. revealed that the lipid profile of a high percentage had at least one alteration in lipid levels, revealing different values from those reported by the patients with a history of dyslipidemia at the time of admission. **Pitt et al. (2008)** revealed that the abnormal lipid profile with, at least, one higher value of Total Cholesterol (TC), HDL, or LDL levels, is usually related to a history of dyslipidemia. That might be explained by the international guidelines for the prevention of CVDs by determining only TC and LDL- C levels (**Reiner *et al.,* 2011**). On the contrary, the underestimation of dyslipidemia might threaten the development of CVDs such as MI (**Emerging Risk Factors Collaboration et al., 2009**). Besides, a previous study reported low HDL and LDL levels in 68.6% and 80%, respectively, of CAD cases, which might be due to the strong inverse association between HDL levels and ACS rates (**Assmann et al., 1996**). Similarly, another study reported LDL levels < 100 mg/ dL and HDL levels < 40 mg/ dL in 50% of the CAD cases at the admission time (**Sachdeva et al., 2009**). These findings have clinical applicability to the compliances in cases with a stable IHD, in which the decreased HDL values were associated with increased mortality of MI among cases treated with a statin (**Pintó et al., 2010**). An epidemiological study reported a significant reduction in TC, HDL, and LDL levels in ACS patients suffered from obesity, Insulin resistance, or DM (**Ormazabal et al., 2018**)

A better knowledge of the lipid profile in cases with ACS allows for relating some types of dyslipidemia and for acclimatizing specific treatment. In agreement with this study, a study report in 1978 examined Vit. D levels in 75 cases with stable angina, 53 cases with AMI, and 409 healthy subjects, and it set up that Vit. D levels were significantly lower in cases with angina or AMI than in controls (**Lund et al., 1978**). In 1990, a case-control study showed that AMI cases had lower Vit. D levels than controls and this difference was more pronounced in the downtime-spring period (**Scragg et al., 1990**). In 1739 Framingham seed Studied healthy actors, the rates of major cardiovascular events were 50 and 80 advanced in those with Vit. D insufficiency and insufficiency, independently (**Wang et al., 2008**). Eventually, in a large meta-analysis study conducted with 1825 men, the low Vit. D levels were considered a risk factor for AMI, indeed after controlling for other cardiovascular threat factors, which showed an acclimated pooled relative threat according to Vit. D levels (**Wang et al., 2012**). Therefore, there's growing substantiation suggesting that, Vit. D insufficiency represents a new threat factor for AMI. This study set up a statistically significant positive association between active smoking and ACS.

A comparison of life factors revealed that 50% (30 cases) of cases were active smokers compared to 4 cases (13.3%) of controls, and about 15 cases (25%) were nonsmokers compared to 21 cases (70%) of control were nonsmokers. 15 cases (25%) were ex-smokers compared to 5 cases (16.6%) of control. These results did not reveal any connections between ACS and different Serum levels of (Hemoglobin, Creatinine, ALT, Total Calcium, and Troponin), while there was a significant relationship between ACS and Serum levels of AST and CKMP ($P<0.05$). In a German prospective study in 2008, subjects with low Vit. D levels had a two-fold increase in CVDs compared to cases with high levels of 25 (OH) D (**Dobnig et al., 2008**). In a cohort study conducted on cases with a history of IHD, no correlations were observed between the position of Vit. D and the circumstance of secondary CVDs. This effect varied with a case-control study conducted on the US population that set up a positive correlation between low Vit. D levels and the presence of CVDs. Taken together, the utmost of the studies suggested that, Vit. D defended against CVDs (**Grandi *et al.,* 2010**). thus, the association between the low position of Vit. D and the history of taking cardiovascular agents observed in this study might be attributed to the link between low Vit. D levels and an advanced frequency of CVD in these circumstances.

In the evaluation of the elders in this study, the association between HF and Obesity was significant in both bivariate and multivariate analyses, with revealed a concordance with other studies (**Kenchaiah et al., 2002**).

Obesity is considered a threat factor for HF. Besides, it's directly related to Vit. D insufficiency, and subsequently, HF prognosis (**Piepoli et al., 2016**). Previous studies demonstrated that HF mortality is obesity-independent, although, its role in HF prognosis (**Jessup et al., 2009**). A previous study showed a strong association between cardiac arrhythmia and increased threat of HF in the older population, which was suggested to be due to the higher incidence of supraventricular tachyarrhythmia and Atrial Fibrillation (AF) in long-term HF cases, which further increases the risk of HF and HF-mortality (**Patel et al., 2014; Singh et al., 2002**). A previous study correlated ventricular arrhythmias with left ventricular dysfunction, independently of SCD (**Ipek et al., 2016**). All these factors, along with HF, might increase the mortality rates of hospitalized AMI elder patients (**Stevens and Levin, 2013**).

Conclusion

CAD remains the leading cause of death in developed countries despite significant progress in primary forestallment and treatment strategies. Aged cases are at a particularly high threat of poor issues following ACS and impaired nutrition, including low Vit. D levels play a part. The extra-skeletal benefits of Vit. D, in particular, its part in maintaining a healthy cardiovascular system is entering increased attention. Longitudinal studies have demonstrated increased cardiovascular mortality and morbidity associated with Vit. D insufficiency. Low Vit. D levels have been linked to inflammation, advanced CAD calcium scores, bloodied endothelial function, and increased vascular stiffness. still, so far, many randomized controlled trials have delved into the implicit benefits of Vit. D supplementation in precluding cardiovascular events, and utmost available trials have tested low boluses of supplementation in fairly low-threat populations. Whether Vit. D supplementation will be salutary among cases with CAD including high-threat aged cases presenting with ACS. In the current study, we observed an inverse association between ACS and Vit. D insufficiency. Since Vit. D insufficiency is a potentially adjustable threat factor people with cardiovascular threat factors should be screened and treated consequently. Cases admitted with ACS should be estimated for Vit. D insufficiency and consequently supplementations should be recommended.

Conflict of interest: All authors declare no conflict of interest.

Ethical approval: The study was approved by the ethics board of the Faculty of Medicine, Sohag University, Sohag, Egypt. Written consent was obtained from all participants.

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