Original Article

Association of Serum Vitamin D level with in-hospital Outcome in Patients with Acute Myocardial infarction

Khandaker Abu Rubaiyat[1], Abdul Wadud Chowdhury[2], Mohsin Ahmed[3], Md. Gaffar Amin[4], ATM Mahfuzul Hoque[4], Kazi Nazrul Islam[4], Chowdhury Md. Kudrat E Khuda[5], A.B.M Imam Hosen[6], Md. Mozammel Haque[7]

Abstract:

Objective: Vitamin D deficiency is emerging as a new risk factor for various cardiovascular events. Several studies have been done to find out association of vitamin D level with CAD with varying results. Very few studies, however, have investigated the association between serum vitamin D levels and clinical outcomes in ACS patients thus far. The objective of this study was to assess the association between serum vitamin D levels and in-hospital complications of AMI patients in Department of Cardiology, Dhaka Medical College Hospital (DMCH), Dhaka.

Methods: This was a cross-sectional observational study. We measured serum vitamin D level in AMI (STEMI and NSTEMI) patients (n=198) admitted in Department of Cardiology, DMCH. Patients with normal vitamin D level (e”30 ng/ml) were considered as Group I and patients with low serum vitamin D level (<30 ng/ml) were considered as Group II; and in-hospital complications were evaluated.

Results: The study showed that 51% of study subjects of AMI had in-hospital complications; 71.1% patients with low vitamin D level had adverse in-hospital outcome whereas 14.3% patients with normal vitamin D level had AMI complications which was statistically significant (p<0.001). Heart failure and arrhythmias were the most frequently observed complications. The results of the study demonstrates that the association between low vitamin D level and in-hospital complications after AMI remains statistically significant (p<0.001).

Conclusions: Low serum vitamin D level is independently associated with a higher frequency of several in-hospital adverse clinical events including mortality after acute myocardial infarction (STEMI and NSTEMI). Whether low vitamin D levels represent a risk marker or a risk factor in ACS remains to be elucidated.

Keywords: *AMI, Serum vitamin D, Adverse in-hospital outcome.*

(Bangladesh Heart Journal 2022; 37(2): 89-98)

Introduction

Coronary artery disease (CAD) is one of the common causes of death and disability in developed countries, responsible for about one in every five deaths[1]. It is rapidly becoming a pandemic within the developing world as well where it involves a relatively younger population[2]. Great reduction in mortality has been achieved by improvement in myocardial revascularization techniques. However, the results are still unsatisfactory in high-risk

1. Junior Consultant, Department of Cardiology, M Abdur Rahim Medical College Hospital, Dinajpur, Bangladesh.
2. Professor & Head of the Department, Department of Cardiology, Dhaka Medical College Hospital, Dhaka, Bangladesh.
3. Associate Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
4. Assistant Professor, Department of Cardiology, Dhaka Medical College, Dhaka, Bangladesh.
5. Assistant Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.
6. Junior Consultant (Cardiology), Jhalakati Sadar Hospital, Jhalakati, Bangladesh.
7. Assistant Professor, Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.

Address of Correspondence: Dr. Khandaker Abu Rubaiyat, Junior Consultant (Cardiology), Department of Cardiology, M Abdur Rahim Medical College Hospital, Dinajpur, Bangladesh. Mobile: +8801712245870, Email: karubaiyat@yahoo.com

DOI: https://doi.org/10.3329/bhj.v37i2.63132

patients[3,4]. Therefore, more interests have been focused on the identification of new risk factors for coronary artery disease (CAD) and its prevention[5]. Calcium metabolism disorders, and especially vitamin D deficiency, represent a rising problem. Recently vitamin D has been received greater interests for its multiple effects on inflammatory system and potential role in atherothrombosis[6,7,8].

Beyond its fundamental role in bone metabolism and calcium homeostasis, vitamin D may influence several other medical conditions, including cardiovascular disease. Indeed, vitamin D receptors have been found in the myocardium as well as in vascular cells, and hypovitaminosis D, a common finding in many industrialized countries, has been independently associated with increased risk of developing acute myocardial infarction and heart failure[9]. Moreover, vitamin D deficiency has been linked to conditions such as hypertension, diabetes mellitus, metabolic syndrome, cardiac hypertrophy and chronic kidney disease that predispose to cardiovascular disease[10,11,12,13]. More importantly, vitamin D supplementation has been shown to be associated with improved survival in heart failure patients[14]. Thus, vitamin D seems to play an important role in cardiac function and in the development and progression of CAD.

Moreover, observational studies, small clinical trials, and meta-analyses indicate that vitamin D therapy may reduce cardiovascular events and mortality[14,15,16]. Although these data from apparent healthy subjects support a role of vitamin D deficiency as a new potential cardiovascular risk factor; there is still paucity of information regarding the implications of vitamin D deficiency in ACS and its possible association or causal relationship with morbidity and mortality. Clinical interest derives from the fact that vitamin D deficiency can be readily determined by blood testing and treated by supplementation. In particular, a single oral ultra-high dose of vitamin D has been shown to restore normal 25(OH) D levels within 2 days in critically ill patients, without causing adverse effects, thus providing the basis of an easy-to-administer dosing regimen for prospective intervention trials in acute cardiovascular settings[17]. Thus far, the largest study evaluating vitamin D and prognosis in ACS patients was that by Ng et al.[18]. They found an association between the lowest vitamin D quartile (<7.3 ng/mL) and long-term major adverse cardiovascular outcomes in 1259 patients. Notably, the association was predominantly with nonfatal adverse outcomes, such as re-hospitalization for ADHF (acute decompensated heart failure) or for another ACS, rather than mortality.

Very few studies, however, have investigated the association between vitamin D levels and clinical outcomes in ACS patients thus far[18,19,20]. Therefore, convincing data demonstrating the possible impact of vitamin D insufficiency or deficiency on morbidity and mortality of ACS patients are still lacking. Notably, vitamin D has been demonstrated to suppress the renin-angiotensin-aldosterone system and to affect endothelial function, inflammatory processes, platelet function, insulin resistance, and blood pressure[12,21,22,23]. All these effects are relevant during ACS, and related to patients' clinical course. Moreover, low levels of vitamin D have been associated with ventricular dysfunction and cardiac remodeling after ACS and with heart failure mortality and sudden cardiac death[8,20]. Thus, both the short and long-term outcomes of ACS patients could be significantly affected by vitamin D status.

However, there is no data on the association of serum vitamin D with in-hospital outcome of AMI in Bangladeshi population. So, we aimed to study the association of serum vitamin D level with AMI complications in our population. We analyzed serum vitamin D level in cases of newly diagnosed acute myocardial infarction patients to study this association.

The purpose of this study was to determine the clinical implications of vitamin D levels in acute MI (STEMI & NSTEMI) patients at hospital admission, and their possible association with in-hospital morbidity and mortality. Very few studies, however, have investigated the association between vitamin D levels and clinical outcomes in ACS patients thus far. Therefore, convincing data demonstrating the possible impact of vitamin D insufficiency or deficiency on morbidity and mortality of ACS patients are still lacking. No such study has been done in Bangladesh so far to investigate association between in-hospital outcome of coronary artery disease and vitamin D level. The purpose of this study was to measure vitamin D levels in AMI (STEMI & NSTEMI) patients during hospital admission and their possible association with in-hospital complications in patients with acute myocardial infarction; so that both primary and secondary preventive measures can be taken to reduce/prevent AMI complications by improving serum vitamin D level.

Methods

This observational cross-sectional study was conducted at the Department of Cardiology, Dhaka Medical College Hospital (DMCH), Dhaka between July, 2017 to June, 2018. All the newly diagnosed acute MI (STEMI & NSTEMI) patients admitted in the Department of Cardiology, DMCH within the study period fulfilling the inclusion and exclusion criteria were included in this study by convenient purposive sampling. Study subjects having previous history of myocardial infarction, heart failure, Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Graft (CABG), cardiomyopathy, any valvular heart disease, congenital heart disease; other myocardial or pericardial diseases; severe co-morbid conditions such as liver disease, thyroid disorder, renal disease, malabsorption or malignancy; who received vitamin D supplement in recent times; and unwilling to be included in the study were excluded. According to serum vitamin D level, all the study subjects were divided in two groups – patients with serum vitamin D level of 30 ng/ml or more were considered as normal group and patients with serum vitamin D level less than 30 ng/ml were considered as low vitamin D level group. Then all the patients were closely monitored till discharge or death for in-hospital complications like heart failure, cardiogenic shock, clinically significant tachy/brady-arrhythmias and AKI; and the association of serum vitamin D level with in-hospital complications of AMI was studied.

Results

One hundred & ninety-eight AMI patients admitted in the Department of Cardiology, DMCH, Dhaka fulfilling the inclusion and exclusion criteria were included in this study during the period from July, 2017 to June, 2018. Among the 198 patients, those who had normal serum vitamin D level (e˘30 ng/ml) were assigned as Group I and patients with low serum vitamin D level (<30 ng/ml) were assigned as Group II.

Minimum age of the respondent was 30 years and maximum was 73 years. Major proportion of the patients (48%) were in 50-59 years age group; whereas few patients (1%) belonged to age less than 40 years. The mean age of the study population was 52.8±6.7 years. The patients with low vitamin-D level (Group I) were more older than patients with normal vitamin-D level (Group II) (58.1±7.1 vs. 53.1±.7.4). Analysis revealed statistically highly significant (p<0.001) mean age difference between the study groups.

Table I

Age distribution of the study population (n=198)

Age group (years)	Normal 25 (OH) vitamin D level (n=70)		Low 25 (OH) vitamin D level (n=128)		Total (n=198)		p-value
	Number	%	Number	%	Number	%	
<40	2	2.9	0	0.0	2	1.0	
40 – 49	20	28.6	15	11.7	35	17.7	
50 – 59	36	51.4	59	46.1	95	48.0	
≥60	12	17.1	54	42.2	66	33.3	
Mean±SD	53.1±.7.4		58.1±7.1		56.3±7.6	**<0.001****	

Unpaired t-test was done. **means significant (p<0.05).

Out of total 198 patients, proportion of male (79.8%) was higher than female (20.2%). In Group I, 73.4% were male and 26.6% were female. In Group II, 91.4% were male and 8.6% were female. Statistically significant association was seen in term of sex among the study groups (p=0.003). Male: female ratio was 4:1. Male patients were predominant in the study.

Table II

Sex distribution of the study population (n=198)

Sex	Normal 25 (OH) vitamin D level (n=70)		Low 25 (OH) vitamin D level (n=128)		Total (n=198)		p-value
	Number	%	Number	%	Number	%	
Male	64	91.4	94	73.4	158	79.8	**0.003****
Female	6	8.6	34	26.6	40	20.2	

Chi-square test was done. **means significant (p<0.05).

On an average, female patients had lower vitamin D level than male (18.8±8.0 ng/ml vs. 26.1±10.5 ng/ml). It was statistically significant ($p<0.001$).

Table III

Comparison of vitamin D level of the study population by gender (n=198)

25 (OH) vitamin D level (ng/ml)	Male (n=158)	Female (n=40)	p-value
mean±SD	26.1±10.5	18.8±8.0	**<0.001****

Unpaired t-test was done.
**means significant ($p<0.05$).

Vitamin D levels of the study population were categorized as ≤10, 11-20, 21-29 and ≥30 ng/ml classes. Major proportion of the patients (45.5%) had vitamin-D level within 11-20 ng/ml (vitamin D deficiency). No patients were found to have severe vitamin D deficiency. Average serum vitamin D level was 24.62±10.45 ng/ml with minimum 11 ng/ml and maximum 46 ng/ml.

The presence of some established risk factors were collected by asking close ended questions and observing previous medical records. Patients with history of diagnosed diabetes mellitus and smoking were significantly higher in Group I compared to Group II with p value 0.002 and <0.001 respectively. Patients with hypertension had higher vitamin D level within 11-20 ng/ml (42.2%) but did not show any significant association ($p=0.14$).

Heart failure was significantly higher in patients having vitamin D level within 11-20 ng/ml (41.1%), followed by 26.3% within 21-29 ng/ml group and 5.7% patients had normal vitamin D level with significant association ($p<0.001$). Cardiogenic shock occurred more frequently in patients having vitamin D level within 11-20 ng/ml (17.8%) and 5.3% patients were within 21-29 ng/ml group; no patient with normal vitamin D level had cardiogenic shock with highly significant association ($p<0.001$). Six patients died who were in 11-20 ng/ml group.

Table IV

Distribution of vitamin D level in the study population (n=198)

25 (OH) vitamin-D	Number level (ng/ml)	Percentage (%)
Normal (≥30)	70	35.4
Insufficiency (21 – 29)	38	19.2
Deficiency (11 – 20)	90	45.5
Severe deficiency (≤10)	0	0.0

Table V

Distribution of the study population according to cardiovascular risk factors (n=198)

Risk Factors	25 (OH) vitamin D level (ng/ml)			Total	p-value
	≥30 (n=70) No. (%)	21 -29 (n=38) No. (%)	11 - 20 (n=90) No. (%)	(n=198) No. (%)	
Smoking	54 (77.1)	30 (78.9)	43 (47.8)	127 (64.1)	**<0.001****
Hypertension	20 (28.6)	11 (28.9)	38 (42.2)	69 (34.8)	0.14*
Diabetes mellitus	16 (22.9)	9 (23.7)	42 (46.7)	67 (33.8)	**0.002****
Dyslipidaemia	0 (0.0)	0 (0.0)	2 (2.2)	2 (1.0)	0.29*
Family history of CAD	2 (2.9)	1 (2.6)	2 (2.2)	5 (2.5)	0.96*

Chi Square test was done
** means significant ($p<0.05$)
*means not significant ($p>0.05$)

Table VI

Comparison of outcome variables by vitamin D level (n=198)

Outcome variables	25 (OH) vitamin D level (ng/ml)			Total (n=198)	p-value
	≥30 (n=70) No. (%)	21 - 29 (n=38) No. (%)	11 - 20 (n=90) No. (%)	No. (%)	
Heart failure	4 (5.7)	10 (26.3)	37 (41.1)	51 (25.8)	<0.001**
Cardiogenic shock	0 (0.0)	2 (5.3)	16 (17.8)	18 (9.1)	<0.001**
Arrhythmia	2 (2.9)	10 (26.3)	28 (31.1)	40 (20.2)	<0.001**
AF	0 (0.0)	4 (10.5)	8 (8.9)	12 (6.1)	
VT	0 (0.0)	4 (10.5)	6 (6.7)	10 (5.1)	
1st degree AV block	0 (0.0)	0 (0.0)	4 (4.4)	4 (2.0)	
Complete AV block	2 (2.9)	0 (0.0)	10 (11.1)	12 (6.1)	
Trifascicular block	0 (0.0)	2 (5.3)	0 (0.0)	2 (1.0)	
AKI	0 (0.0)	0 (0.0)	12 (13.3)	12 (6.1)	<0.001**
Death	0 (0.0)	0 (0.0)	6 (6.7)	6 (3.0)	0.02**

Chi Square and Fisher's Exact test were done
** means significant (p<0.05)
*means not significant (p>0.05)

Mean hospital stay was found higher in Group I compared to Group II (6.88±2.02 vs. 5.20±0.83 days) and the mean difference was statistically significant (p<0.001). The average hospital stay was 6.29±1.89 days of the study patients.

Table VII

Comparison of the study population according to hospital stay (n=198)

Hospital stay (days)	Study population		p-value
	Normal 25 (OH) vitamin D level (n=70)	Low 25 (OH) vitamin D level (n=128)	
Mean ± SD	5.20±0.83	6.88±2.02	<0.001**

Chi Square test was done
** means significant (p<0.05)

The study indicates that 68.8% patients with adverse in-hospital outcome had low vitamin D level and 8.6% patients with adverse in-hospital outcome had normal vitamin D level with significant association (p<0.001).

Table VIII

Comparison between adverse in-hospital outcomes and vitamin D level (n=198)

Adverse in-hospital outcome	Normal 25 (OH) vitamin D level (n=70) Number (%)	Low 25 (OH) vitamin D level (n=128) Number (%)	Total (n=198) Number (%)	p-value
Present	6 (8.6)	88 (68.8)	94 (47.5)	**<0.001****
Absent	64 (91.4)	40 (31.2)	104 (52.5)	

Chi Square test was done
** means significant (p<0.05)

Table IX

Multivariate logistic regression analysis of in-hospital cardiac events with confounding factors (n=198)

Variables of interest	Standardized coefficient (â)	Odds Ratio (OR)	95% CI of OR	p-value
Age>50 years	0.298	1.35	0.446 – 4.074	0.59
Female gender	-2.796	0.06	0.012-0.304	0.001
Smoking	-0.485	0.62	0.146 – 2.599	0.51
Diabetes mellitus	2.654	14.20	4.555 – 44.313	<0.001**
Low HDL-C	0.017	1.02	0.944 – 1.096	0.66
Elevated TG	0.006	1.00	0.998 – 1.014	0.13
Elevated Troponin I	0.142	1.15	1.052 – 1.263	0.002**
Presence of low vitamin D level	2.981	19.70	6.697 – 57.976	0.001**

**means significant (p<0.05)

*means not significant (p>0.05)

Multivariate logistic regression model was constructed with age >50yrs, female gender, smoking, diabetes mellitus, low HDL-C, elevated TG, elevated Troponin I and presence of low vitamin D level as independent variables and adverse in-hospital outcome as the dependent variable. The variables diabetes mellitus, elevated Troponin I and presence of low vitamin-D level were found to be significantly associated with adverse in-hospital outcomes with the ORs being 14.20, 1.15 and 19.70 respectively.

Discussions

This cross-sectional observational study was carried out to find out the association of low serum vitamin D level with more in-hospital complications in patients with acute myocardial infarction. The results of our study demonstrates that low vitamin D level increases the chance of adverse in-hospital outcomes after AMI and the association between vitamin D level and in-hospital complications remains statistically significant even after adjustment for significant cardiovascular risk factors. The mean age of the study population was 52.8 ± 6.7 years ranging from 30 to 73 years and most of the patients (48%) belonged to 50-59 years of age. Male patients were predominant in the study population which were 79.8%. Female patients were 20.2%. In our study female patients had lower vitamin D level than male (Mean 26.1±10.5 ng/ml vs. 18.8±8.0 ng/ml) which was statistically significant (p<0.001). Lips, 2007 and Hagenau et al., 2009 showed women often have lower levels of 25(OH)D levels than men[24,25]. Potential causes include differences in body fat composition, inadequate dietary intake, childbearing and menopause[26]. As Bangladesh has a predominantly muslim society, the practice of purdah/borkha (a covered-up style of dress) and 'shari' are very common in women of different socio-economic classes. In addition, avoiding sun exposure predispose to a reduced endogenous synthesis of vitamin D. Among the risk factors for CAD, the frequency of smoking was higher (64.1%) whereas the frequency of hypertension (34.8%) and diabetes mellitus (33.8%) were nearer to each other. Patients with history of smoking and diabetes mellitus were significantly higher in low vitamin D level compared to normal vitamin-D level with p-value <0.001 and 0.002 respectively. Patients with hypertension had higher vitamin D level (42.2% patients were within 11-20 ng/ml range) but did not show any significant association (p=0.14). This study found smoking as the most prevalent (64.1%) risk factor for CAD. Akanda et al., (2011) also found smoking as the most prevalent (60%) risk factor among the patients of CAD of the Bangladeshi population similar to our study findings[27]. Major proportion of diabetic patients had vitamin D deficiency (46.7%); 23.7% patients with insufficiency and 22.9% patients with normal vitamin D level. Mauss et al., (2015) found that Vitamin D deficiency is associated with DM in working older adults[28].

Vitamin D insufficiency and deficiency were very common among our study population. 64.6%(128 cases) patients with AMI had vitamin D level less than 30 ng/ml, while 35.4%(70 cases) patients had normal level (≥30 ng/ml). A significant proportion (45.4%) of study population had vitamin D deficiency (less than 20 ng/ml). No patients were found as severe deficiency. Average serum vitamin D level was 24.62±10.45 ng/ml with minimum 11 ng/ml and maximum 46 ng/ml. Kumar, et al., (2016) showed that vitamin D deficiency was present in 39.5% of patients as compared to 26% in control population and insufficient vitamin D levels were present in 18% of patients as compare to 11% in control population[29]. Karur et al., (2014) in a study published in India stated that of the patients enrolled 67.5% were vitamin D deficient and 16% insufficient, for a total of 83.5% of patients with low vitamin D level[30]. Akin et al., (2012) found that 83% of the patients had vitamin D level less than 30 ng/ml[31]. Syal et al., (2012) also found in his study higher proportion (93%) of vitamin D deficiency and insufficiency, while only 7% had normal vitamin D levels[32]. The high prevalence of vitamin D deficiency is a reflection of generalized hypovitaminosis D in our country as well.

In this study, adverse in-hospital outcome was considered as the presence of any early complications of acute coronary syndrome, such as heart failure, tachy/ brady-arrhythmia, acute kidney injury, cardiogenic shock and death; occurring after the index event during hospital stay before discharge from hospital. The study showed that 51% patients had adverse in-hospital outcome; 71.1% patients with low vitamin-D level had adverse in-hospital outcome whereas 14.3% patients with normal vitamin-D level had adverse in-hospital outcome with significant association ($p<0.001$). Kumar, et al., (2016) showed that the patients with vitamin D deficiency were associated with a higher risk for several in-hospital MACEs, including mortality and it was statistically significant (p-value<0.05)[29].The study supports the close association between low vitamin D levels at hospital presentation and worse prognosis in ACS patients[29]. Indeed, patients with 25 (OH) D deficiency had a 3-fold higher mortality risk, even after adjustment for important independent variables associated with mortality in ACS[29]. In our study, heart failure was significantly higher in patients with low vitamin D level than patients with normal vitamin D level with significant association ($p<0.001$). Cardiogenic shock was observed in 9.1% patients who all had low vitamin D level; while no AMI patients with normal vitamin D level developed cardiogenic shock with highly significant association ($p<0.001$). Arrhythmia and AKI were also more frequent in AMI patients with low vitamin D level. Among the AMI patients, 6.7% patients died who all had vitamin D level in the deficient range.

Heart failure was the most frequently observed adverse in-hospital outcome among the ACS patients (25.8% patients). Only 5.7% patients with normal vitamin D level developed heart failure whereas 41.1% patients with vitamin D deficiency and 26.3% patients with vitamin D insufficiency developed heart failure with significant association ($p<0.001$). Gotsman et al., (2012) found that the percentage of patients with vitamin D deficiency was higher in patients with HF compared with the control group ($p<0.00001$); only 8.8% of the HF patients had optimal vitamin D levels[14]. Pilz et al., (2008) also showed that vitamin D was negatively correlated with N-terminal pro-B-type natriuretic peptide and was inversely associated with higher New York Heart Association classes and impaired left ventricular function[8]. The major potential mechanisms that may explain a direct protective effect of vitamin D against heart failure include effects on myocardial contractile function, regulation of natriuretic hormone secretion, effects on extracellular matrix remodeling, reduced left ventricular hypertrophy and the regulation of inflammatory cytokines[33,34]. Indirectly, vitamin D can also affect cardiac function by altering parathyroid hormone and serum calcium levels. The initial evidence in humans came from dialysis patients. In patients with uremic cardiomyopathy, treatment with 1-alfa hydroxyl cholecalciferol 1g per day for 6 weeks produced a decrease in plasma parathyroid concentration and an increase in fractional fiber shortening on M-mode echocardiography ($p<0.025$)[35].

Arrhythmia was observed in 20.2% AMI patients in this study. AF(6.1%), VT(5.1%), First degree AV block(2%), Trifascicular block(1%) and Complete AV block(6.1%) were noted among the arrhythmias. All the arrhythmias developed more frequently in patients with vitamin D deficiency except trifascicular block which more frequently developed in patients with vitamin D insufficiency. In a recent report, the correction of vitamin D deficiency and hypocalcemia resulted in control of incessant ventricular tachycardia and cardiomyopathy[36]. A rare case of fetal atrial flutter was reported in vitamin D–resistant rickets[37]. In an animal study, rats fed a vitamin D–deficient diet for 12 weeks developed significant QT-interval shortening despite normal serum calcium levels compared to normal rats[38]. These findings suggest a possible role for vitamin D deficiency as a causal factor for arrhythmia and the need for further exploration.

The patients who developed cardiogenic shock, all had low vitamin D level; none with normal vitamin D level developed cardiogenic shock with highly significant association ($p<0.001$). 17.8% patients with vitamin D deficiency developed this adverse outcome while it was present in 5.3% patients with vitamin D insufficiency. The association of low vitamin D level with cardiogenic shock due to AMI needs to be further evaluated.

Death occurred in 3% of AMI patients as a consequence of adverse outcome andall those patients had vitamin D level in deficient range while no death occurred in AMI patients with normal vitamin D level which was statistically significant (p<0.02). There are studies that have shown an association between vitamin D intake and death due to CAD. An example is a cohort study that provided evidence that inadequate amounts of vitamin D in the body may predict a higher risk of coronary heart disease death[39]. Ginde, et al., (2009) also showed that serum vitamin D levels had an independent, inverse association with cardiovascular disease and all-cause mortality in non-institutionalized older adults, a group at high risk for all-cause mortality[6].

Conclusion

The results of the study demonstrates that the association between low vitamin D level and in-hospital complications after AMI remains statistically significant (p<0.001). Low serum vitamin D level is independently associated with a higher frequency of several in-hospital adverse clinical events including mortality after AMI. Whether low vitamin D levels represent a risk marker or a risk factor in ACS remains to be elucidated.

Limitations of the study

Although the result of this study supports the hypothesis, there are some facts to be considered which might have affected the result of the current study. It was a single center study. The number of study population was relatively small. Sampling method was non-randomized, so there was risk of selection bias. The data were only hypothesis generating as they did not provide evidence to support a causal relationship and they require confirmation in suitably designed clinical trials. Many factors that affect vitamin D status (eg, latitude, season, sunlight exposure, skin color, dietary vitamin D intake, serum albumin, serum calcium etc.) were not taken into account in the study and might have influenced, at least in part, the results. The Parathyroid Hormone (PTH) level was not assessed and thereby we could not determine whether the association between vitamin D status and cardiovascular risk was mediated in part by secondary hyperparathyroidism.

Recommendations

The results of the present study suggest that low vitamin D level is a risk factor for developing adverse outcome following AMI. The correction of vitamin D deficiency and maintenance of an optimal status may be a promising approach for acute treatment and secondary prevention of AMI complications that requires confirmation in interventional trials with vitamin D supplementation. Further clinical and experimental studies may be warranted to validate the findings, to investigate the mechanisms underlying increased cardiovascular risk and to determine whether correction of vitamin D deficiency could contribute to the prevention of cardiovascular disease.

References

1. Lloyd-Jones D, Adams R, Carnethon M, Simone GD, Ferguson TB, Flegal K, et al. Heart disease and stroke statistics—2009 update: A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2009;119(3):e21-181.
2. Omran AR. Changing patterns of health and disease during the process of national development. Chicago: Rand McNally. 1979; 157:10-3.
3. Luca GD, Bellandi F, Huber K, Noc M, Petronio AS, Arntz HR, et al. Early glycoprotein IIb-IIIa inhibitors in primary angioplasty-abciximab long-term results (EGYPT-ALT) cooperation: Individual patient’s data meta-analysis. Journal of Thrombosis and Haemostasis:JTH. 2011;9(12):2361–70.
4. Luca GD, Cassetti E and Marino P. Percutaneous coronary intervention-related time delay, patient’s risk profile, and survival benefits of primary angioplasty vs lytic therapy in ST-segment elevation myocardial infarction. The American Journal of Emergency Medicine. 2009;27(6):712–19.
5. Luca GD, Santagostino M, Secco GG, Cassetti E, Giuliani L, Franchi E, et al. Mean platelet volume and the extent of coronary artery disease: Results from a large prospective study. Atherosclerosis. 2009;206(1):292–97.
6. Ginde AA, Scragg R, Schwartz RS and Camargo CA. Prospective study of serum 25-hydroxyvitamin D level, cardiovascular disease mortality, and all-cause mortality in older U.S. adults. Journal of the American Geriatrics Society. 2009;57(9):1595–1603.
7. Giovannucci E, Liu Y, Hollis BW and Rimm EB. 25-hydroxyvitamin D and risk of myocardial infarction in men: A prospective study. Archives of Internal Medicine. 2008;168(11):1174–80.
8. Pilz S, März W, Wellnitz B, Seelhorst U, Fahrleitner-Pammer A, Dimai HP, et al. Association of vitamin D deficiency with heart failure and sudden cardiac death in a large cross-sectional study of patients

referred for coronary angiography. The Journal of Clinical Endocrinology and Metabolism. 2008;93(10):3927–35.

9. Lavie CJ, Lee JH and Milani RV. Vitamin D and cardiovascular disease will it live up to its hype?. Journal of the American College of Cardiology. 2011;58(15):1547–56.

10. González EA, Sachdeva A, Oliver DA and Martin KJ. Vitamin D insufficiency and deficiency in chronic kidney disease. A single center observational study. American Journal of Nephrology. 2004;24(5): 503–10.

11. Holick MF. Vitamin D deficiency. The New England Journal of Medicine. 2007;357(3):266–81.

12. Pittas AG, Lau J, Hu FB and Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. The Journal of Clinical Endocrinology and Metabolism. 2007;92(6):2017–29.

13. Saleh FN, Schirme H, Sundsfjord J and Jorde R. Parathyroid hormone and left ventricular hypertrophy. European heart journal. 2003; 24(22):2054–60.

14. Gotsman I, Shauer A, Zwas DR, Hellman Y, Keren A, Lotan C, et al. Vitamin D deficiency is a predictor of reduced survival in patients with heart failure; vitamin D supplementation improves outcome. European Journal of Heart Failure. 2012;14(4): 357–66.

15. Autier P and Gandini S. Vitamin D supplementation and total mortality: A meta-analysis of randomized controlled trials. Archives of Internal Medicine. 2007;167(16):1730–37.

16. Teng M, Wolf M, Ofsthun MN, Lazarus JM, Hernán MA, Camargo CA, et al. Activated injectable vitamin D and hemodialysis survival: A historical cohort study. Journal of the American Society of Nephrology : JASN. 2005;16(4):1115–25.

17. Amrein K, Sourij H, Wagner G, Holl A, Pieber TR, Smolle KH, et al. Short-term effects of high-dose oral vitamin D3 in critically ill vitamin D deficient patients: A randomized, double-blind, placebo-controlled pilot study. Critical Care (London, England). 2011;15(2):R104.

18. Ng LL, Sandhu JK, Squire IB, Davies JE and Jones DJL. Vitamin D and prognosis in acute myocardial infarction. International Journal of Cardiology. 2013;168(3):2341–46.

19. Correia LCL, Sodré F, Garcia G, Sabino M, Brito M, Kalil F, et al. Relation of severe deficiency of vitamin D to cardiovascular mortality during acute coronary syndromes. The American Journal of Cardiology. 2013;111(3):324–27.

20. Khalili H, Talasaz AH and Salarifar M. Serum vitamin D concentration status and its correlation with early biomarkers of remodeling following acute myocardial infarction. Clinical Research in Cardiology : Official Journal of the German Cardiac Society. 2012;101(5):321–27.

21. Li YC. Vitamin D regulation of the renin-angiotensin system. Journal of Cellular Biochemistry. 2003;88(2):327–31.

22. Ortega A, Pérez de Prada MT, Mateos-Cáceres PJ, Ramos MP, González-Armengol JJ, González DCJM, et al. Effect of parathyroid-hormone-related protein on human platelet activation. Clinical Science (London, England : 1979). 2007;113(7): 319–27.

23. Schleithoff SS, Zittermann A, Tenderich G, Berthold HK, Stehle P and Koerfer R. Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: A double-blind, randomized, placebo-controlled trial. The American Journal of Clinical Nutrition. 2006;83(4):754–59.

24. Lips P. Vitamin D status and nutrition in Europe and Asia. The Journal of Steroid Biochemistry and Molecular Biology. 2007;103(3):620–25.

25. Hagenau T, Vest R, Gissel TN, Poulsen CS, Erlandsen M, Mosekilde L, et al. Global vitamin D levels in relation to age, gender, skin pigmentation and latitude: An ecologic meta-regression analysis. Osteoporosis International : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2009;20(1):133–40.

26. Dijkstra SH, van Beek A, Janssen JW, Vleeschouwer LHMD, Huysman WA and van den Akker ELT. High prevalence of vitamin D deficiency in newborn infants of high-risk mothers. Archives of Disease in Childhood. 2007;92(9):750–53.

27. Akanda MAK, Ali SY, Islam A, Rahman MM, Parveen A, Kabir MK, et al. Demographic Profile, Clinical Presentation & Angiographic Findings in 637 Patients with Coronary Heart Disease. Faridpur Medical College Journal. 2011;6(2):82-5.

28. Mauss D, Jarczok MN, Hoffmann K, Thomas GN and Fischer JE. Association of vitamin D levels with type 2 diabetes in older working adults. International Journal of Medical Sciences. 2015;12(5):362–68.

29. Kumar S, Saxena P. To evaluate the role of vitamin D level as a prognostic marker and its relation to in-hospital complications in patients with acute coronary syndrome. International Journal of Advances in Medicine. 2016;3(4):976-81.

30. Karur S, Veerappa V and Nanjappa MC. Study of vitamin D deficiency prevalence in acute myocardial infarction. International Journal of Cardiology. Heart & Vessels. 2014;3:57–9.

31. Akin F, Ayça B, Köse N, Duran M, Sari M, Uysal OK, et al. Serum vitamin D levels are independently associated with severity of coronary artery disease. Journal of Investigative Medicine : the Official Publication of the American Federation for Clinical Research. 2012;60(6):869–73.

32. Syal SK, Kapoor A, Bhatia E, Sinha A, Kumar S, Tewari S, et al. Vitamin D deficiency, coronary artery disease, and endothelial dysfunction: Observations from a coronary angiographic study in Indian patients. The Journal of Invasive Cardiology. 2012;24(8):385–89.

33. Tishkoff DX, Nibbelink KA, Holmberg KH, Dandu L and Simpson RU. Functional vitamin D receptor (VDR) in the t-tubules of cardiac myocytes: VDR knockout cardiomyocyte contractility. Endocrinology. 2008;149(2):558–64.

34. Weishaar RE, Kim SN, Saunders DE and Simpson RU. Involvement of vitamin D3 with cardiovascular function. III. Effects on physical and morphological properties. The American Journal of Physiology. 1990;258:E134-42.

35. McGonigle RJ, Fowler MB, Timmis AB, Weston MJ and Parsons V. Uremic cardiomyopathy: Potential role of vitamin D and parathyroid hormone. Nephron. 1984;36(2):94–100.

36. Chavan CB, Sharada K, Rao HB, Narsimhan C. Hypocalcemia as a cause of reversible cardiomyopathy with ventricular tachycardia. Ann Intern Med. 2007;146:541–42.

37. Vintzileos AM, Neckles S, Campbell WA, Andreoli JW, Nochimson DJ, Kaplan BM. Three fetal ponderal indexes in normal pregnancy. Obstet Gynecol. 1985;65(6):807– 11.

38. Sood S, Reghunandanan R, Reghunandanan V, Gopinathan K, Sood AK. Effect of vitamin D deficiency on electrocardiogram of rats. Indian J Exp Biol. 1995;33(1):61–3.

39. Melamed ML, Michos ED, Post W and Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. Archives of Internal Medicine. 2008;168(15):1629–37.