DOI: https://doi.org/10.3329/cardio.v13i2.52973

Original Article

Vitamin D Status and Acute Coronary Syndrome – A Single-Centre Study

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Key Words : *Vitamin D, Acute Coronary Syndrome, Bangladesh, IHD.*

Abstract:

Background: *Vitamin D are needed for normal functioning of cardiovascular system, and its deficiency has been linked to different cardiovascular disorders, including hypertension. However, the relationship between vitamin D deficiency and ischaemic heart disease is not yet clear. The present study was intended to find out the association between serum vitamin D level and acute coronary syndrome (ACS).*

Methods: *The cross-sectional analytical study was carried out in a tertiary care hospital of Dhaka, Bangladesh. Fifty-one consecutive ACS patients admitted into the Department of Cardiology of the hospital were considered as the cases and 51 apparently healthy subjects were considered as the controls. The exposure and outcome variables were serum vitamin D and ACS respectively. Vitamin D insufficiency and deficiency were defined as serum 25(OH) D <30-20 ng/ml and <20 ng/ml, respectively. Severe vitamin D deficiency was defined as serum 25(OH) D <10 ng/ml.*

Results: *Hypovitaminosis D was prevalent in both cases and controls; however, the mean serum 25(OH) D was significantly lower in the former than the latter (14.2 ± 5.9 ng/ml vs. 18.2 ± 6.3 ng/ml, respectively; p <0.001). Vitamin D insufficiency and moderate deficiency (serum 25(OH) D <20-10 ng/ml) did not differ significantly between the groups, but severe deficiency (<10 ng/ml) was significantly more common in patients with ACS compared to the healthy controls. The risk of having moderate and severe vitamin D deficiency was 1.9-fold (95% CI = 0.8 – 4.7) and 22.8-fold (2.9 – 180.4) higher for ACS patients than for healthy subjects (p = 0.173 and p <0.001, respectively).*

Conclusion: *Vitamin D deficiency is more common in patients with ACS compared to those without ACS. However, the independent association between vitamin D deficiency and ACS needs further evaluation.*

(Cardiovasc j 2021; 13(2): 183-188)

Introduction:

Coronary artery disease (CAD) is a major cause of morbidity and mortality worldwide. It accounts for >9 million deaths in 2016 according to the World Health Organization (WHO) estimates.[1] The exact prevalence of CAD in Bangladesh is not known. Only a limited number of small-scale epidemiological studies are available. According to a review by Islam et al., the estimated prevalence of CAD in Bangladesh is 4-6%.[2] On the other hand, vitamin D deficiency is also widely prevalent; almost half of the world's population has got vitamin D deficiency.[3-5] Data regarding vitamin D status in Bangladesh are scarce, however, hypovitaminosis D appears to be highly prevalent here.[6,7] The link between vitamin D deficiency and CAD has been a concern because vitamin D was found to be associated with the normal functioning of multiple systems of the body, including the cardiovascular system. Low circulating vitamin D level was observed in patients with a history of myocardial infarction in patients with type 2 diabetes mellitus.[8] Also, severe vitamin D deficiency was associated with an increased risk

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of acute myocardial infarction even after adjustment for other risk factors in a case-control study involving Indian population.[9] In a large prospective study, hypovitaminosis D was associated with an increased risk of CAD, myocardial infarction, and early death during 9 years of follow-up.[10] On the contrary, vitamin D deficiency was not found to be associated with increased risk of adverse outcomes including cardiovascular ones over 5 years after control for comorbidities in older women,[11] cardiovascular mortality in older adults,[12] or even risk of cardiovascular disease (CVD).[13] Also, Jarrah et al. did not find any association between vitamin D deficiency and the incidence or the reoccurrence of coronary artery stenosis.[14] So, the relationship between vitamin D status and CAD is still a matter of ongoing debate, and this merits further investigation. In Bangladesh, both hypovitaminosis D and CAD are common, and an association may exist between these two public health problems, i.e., hypovitaminosis D and CAD. On other hand hypovitaminosis D is an easily preventable as well as treatable condition. So, in case an association between hypovitaminosis D and CAD is found in Bangladeshi population, simple preventive and curative measures can be beneficial to the overall prevention and management of CAD.

Methods:

The present cross-sectional study was carried out in the Department of Cardiology, Sir Salimullah Medical College & Mitford Hospital (SSMC & MH), Dhaka, Bangladesh over a period of 1 year from April 2016 to March 2017. All ACS patients presenting at the Department of Cardiology of SSMC & MH were considered as case (group 1) and apparently healthy subjects (friends, peers or relatives of the ACS patients) were the control (group 2). Patients with valvular heart disease, cardiomyopathy, congenital heart disease, renal disease or ischaemic heart disease were excluded. Study variables including age, sex, education, smoking status, life-style, usage of antihyperlipidemic, antidiabetic and antihypertensive drugs were interrogated using a semi structured questionnaire. Weight, height, body mass index (BMI) and blood pressure were measured and recorded. For vitamin D assay, 3 ml blood was obtained, centrifuged and assayed by chemiluminescence immunoassay. Vitamin D insufficiency was considered as 25-hydroxyvitamin D (25(OH)D) levels between e"10 to <30 ng/ml and severe deficiency was defined as 25(OH)D level <10 ng/ml.[15] Data were processed and analyzed using Statistical Package for Social Sciences (SPSS) software. The p values <0.05 were considered as significant.

Results:

The baseline characteristics including sex, lifestyle, BMI, hyperlipidaemia, family history of CAD, and serum lipid profile did not differ significantly between the groups. However, group 1 patients were older than group 2 patients (p <0.001). Smoking, hypertension and diabetes mellitus were more common in group 1 than in group 2. Also, fasting blood sugar and serum creatinine were significantly higher in group 1 than in group 2 (p < 0.05). (Table I).

All patients of group 1 were deficient in serum 25(OH)D (<30 ng/dl), compared to 94.1% of the group 2. The mean 25(OH)D level was significantly lower in group 1 than in group 2 (14.2 ± 5.9 ng/ml vs. 18.2 ± 6.3 ng/ml, respectively; p <0.001). (Table II) Vitamin D insufficiency i.e., 25(OH)D <30 to e"20 ng/ml was numerically more common in group 1 than in group 2, however, the difference was not statistically significant (p =0.129). Moderate vitamin D deficiency i.e., 25(OH)D <20 to e"10 ng/ml was also numerically more common in group 1 than in group 2, however, again the difference was not statistically significant (p =0.173). On the other hand, severe vitamin D deficiency i.e., 25(OH)D <10 ng/dl was significantly commoner in group 1 than in group 2 (p <0.001). The risk of having moderate and severe vitamin D deficiency was 1.9-fold (95% CI = 0.8 - 4.7) and 22.8-fold (2.9 - 180.4) higher for group 1 than for group 2 (p = 0.173 and p < 0.001, respectively). (Table III)

A step-wise regression model was done to find the independent predictors of ACS. The model, which included 5 predictor variables (emerged as significant predictors in univariate analysis), was first subjected to model-fit test. Hosmer and Lemeshow goodness-of-fit test demonstrated that the model was a good fit model (chi-square = 13.5, p = 0.095) which could correctly predict the outcome (ACS) in 82.4% of the subjects included in the study and was equally capable of predicting both case and control. (Table IV)

On multivariate analyses, diabetes and hypertension emerged as independent predictors of ACS with odds of happening the outcome (ACS) being 6.1 (95% CI = 1.5-24.0) and 3.0 (95% CI = 0.9-9.3), respectively. (Table V)

Table-I

Comparison of baseline characteristics between groups (N=102).

Trait	Group 1n=51	Group 2n=51	p value
Age (years)#	52.7 ± 11.0	42.6 ± 13.2	< 0.001
Sex*			
Male	41(80.4)	39(76.5)	0.630
Female	10(19.6)	12(23.5)	
Life style*			
Active	31(60.8)	38(74.5)	0.138
Sedentary	20(39.2)	13(25.5)	
BMI* (kg/m^2)	3(5.9)	1(2.0)	
< 25	25(49.0)	27(53.0)	0.692
e" 25	26(51.0)	24(47.0)	0.500
Smoking*			
Current	22(43.1)	6(11.8)	0.001
Past	9(17.6)	8(15.7)	
Never	20(39.2)	37(72.5)	
DM*	18(35.3)	4(7.8)	0.001
Hypertension*	25(49.0)	11(21.6)	0.004
Hyperlipidemia*	24(47.1)	21(41.2)	0.550
Family history of CAD*	10(19.6)	25(24.5)	0.250
Serum cholesterol (mg/dl)#	171.7 ± 41.9	179.7 ± 36.9	0.312
Serum LDL (mg/dl)#	105.2 ± 39.4	108.2 ± 28.4	0.764
Serum HDL (mg/dl)#	37.7 ± 5.7	39.7 ± 8.8	0.201
Serum TG (mg/dl)#	155.3 ± 67.9	171.3 ± 100.7	0.349
FBS (mg/dl)#	6.8 ± 3.2	5.5 ± 1.3	0.006
Serum creatinine (mg/dl)#	1.0 ± 0.2	0.9 ± 0.2	0.039

Figures in the parentheses indicate corresponding percentage

*Data were analyzed using chi square (χ^2) test.

#Data was analyzed using unpaired t-test and were presented as mean ± SD.

Table-II

Distribution of study subjects by mean serum 25(OH) D.

Serum 25(OH) D (ng/ml)	Group		p value
	Group I(n = 51)	Group II(n = 51)	
Serum 25(OH) D	14.2 ± 5.9	18.2 ± 6.3	0.001

#Data were analyzed using Student's t-test and were presented as mean ± SD.

Table-III

Distribution of study subjects by severity of vitamin D deficiency (N=102).

Serum 25(OH)D (ng/ml)*	Group		p value	Odds Ratio
	Group 1(n = 51)	Group 2(n = 51)		(95% CI of OR)
<30 (Insufficiency)	51(100.0)	48(94.1)	0.129	Not computable
<20 (Moderate deficiency)	41(80.4)	32(68.6)	0.173	1.9(0.8-4.7)
<10 (Severe deficiency)	16(31.4)	1(2.0)	< 0.001	22.8(2.9-180.4)

Figures within the parentheses indicate corresponding percentage

*Data were analyzed using chi square (χ^2) test.

Table-IV

Hosmer and Lemeshow test for model fit.

Step	Chi-square	df	Sig.	Strength of Prediction
1	13.513	8	0.095	82.4%

Table-V

Regression analysis of predictors of ACS.

Variable of interest	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI of OR)	p value	Odds ratio (95% CI of OR)	p value
Age (year)	-	< 0.001	0.9(0.8-0.9)	0.123
Smoking	4.1(1.7 - 9.4)	0.001	0.26(0.09-0.7)	0.114
DM	6.4(1.9 - 20.6)	0.001	6.1(1.5-24.0)	0.009
Hypertension	3.4(1.4 - 8.2)	0.004	3.0(0.9-9.3)	0.041
Serum 25(OH)D <10 ng/ml	22.8(2.9-180.4)	< 0.001	0.3(0.03-0.26)	0.202

Discussion:

In the present study, vitamin D deficiency was found both in cases with ACS and controls without ACS. However, the situation was significantly worse in the former than in the latter group (mean 25(OH)D 14.2 ± 5.9 ng/ml vs. 18.2 ± 6.3 ng/ml, respectively). In a case-control study conducted at All India Institute of Medical Sciences, New Delhi, India involving 120 consecutive cases of first incident acute myocardial infarction (AMI) and 120 healthy controls, vitamin D deficiency (25(OH)D <30 ng/ml) was highly prevalent in both groups (98.3% and 95.8%, respectively) with median levels lower in cases (6 ng/ml and 11.1 ng/ml, respectively; p <0.001).[16] Similarly, vitamin D level was significantly lower in patients with CAD compared with the healthy controls (18.2±10.9 vs. 28.8±21 ng/ml) in another more recent study from India.[17] In this study, the prevalence of vitamin D deficiency was 81.4% vs. 57.7% in case and control group. Hypovitaminosis D was observed in 70·4% of 1484 patients undergoing elective coronary angiography (CAG) in a cross-sectional study.[9] In a retrospective, single-center study, out of 1,311 patients with chest pain undergoing CAG, 23% patients had normal 25(OH)D levels (>30 ng/ml), 42% had 25(OH)D deficiency (<20 ng/ml) and 35% had 25(OH)D insufficiency (<30 ng/ml).[18] So, hypovitaminosis D was even worse in our study. Also, an inverse relationship was found between the percentage of coronary artery occlusion and serum 25(OH)D concentrations.[18] In a prospective study of 139 patients, vitamin D deficiency defined as 25(OH)D <14 ng/ml was present in 72.7% of the patients who presented with AMI.[19] Mean 25(OH)D level was 14.8 ± 9.1 ng/ml — similar to our finding of 14.2 ± 5.9 ng/ml — in a prospective study involving 100 consecutive Indian patients undergoing CAG for suspected CAD. Nearly one-third (36%) patients were severely deficient of 25(OH)D <10 ng/ml, and only 7% had optimal level of vitamin D. Also, patients with lower 25(OH)D had higher prevalence of double- or triple-vessel CAD and diffuse CAD. Endothelial dysfunction as assessed by brachial artery flow-mediated dilation was also more frequently observed in those with low 25(OH)D levels.[20] A cross-sectional multi-centre study demonstrated that 25(OH)D <30 ng/ml were present in almost all patients with AMI. Of the 239 enrolled patients, 179 (75%) had low 25(OH)D (d”20 ng/ml) and 50 (21%) had 25(OH)D in the range of 20 to <30 ng/ml.[21] We did univariate and multivariate analyses to see whether vitamin D deficiency is an independent predictor of ACS or not. In univariate analysis, moderate and severe vitamin D deficiency differed significantly between the groups (p= 0.045 and <0.001, respectively). When multivariate analysis was done, hypertension and diabetes were found to be independent predictors of ACS, but vitamin D deficiency was not. Deficiency of vitamin D was found to be independently associated with AMI[16],

and CAD[17] after adjusting the conventional risk factors in Indian population. Beyond Indian Subcontinent, also in Western population, independent association was found between vitamin D deficiency and the extent of CAD[9], and significant coronary stenosis[22]. This lack of independent association in the present study may be due to overall high prevalence of vitamin D deficiency in both cases and controls in our population, or might be due to the small sample size of the present study.

The limitations of the study include failure to match the cases and controls rigorously. Also, the sample size was relatively small, and this was a single-centre study. The strength of the study lies in the fact that it included 'all-comers' with ACS admitted in a hospital entertaining patient from all over the country.

Conclusion:

Vitamin D deficiency is prevalent in patients with ACS and apparently healthy controls. All grades of deficiency are more common in patients with ACS compared to those without ACS. However, the independent association between vitamin D deficiency and ACS needs further evaluation by future well-designed studies. Whether vitamin D supplementation has got any role in primary or secondary prevention of CAD in South Asian population may be studied as well.

Conflict of Interest - None.

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