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Original Article

Association of Serum Vitamin D Level with Angiographic Severity of Coronary Artery Disease in Patients of Acute Myocardial Infarction

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Key Words : *Coronary Artery Diseases, vitamin D, Vessel score, Gensini score, Bangladesh.*

Abstract

Background: *Besides conventional risk factors, a novel risk factor hypovitaminosis D may play unique role in the development of coronary artery disease. Evidences suggest that people with low serum vitamin D level is associated with risk of acute MI even after adjusting for the known risk factors. This study was conducted to find out the association between serum vitamin D Level and angiographic severity of coronary artery disease in patients of acute myocardial infarction.*

Methods: *One hundred and four patients of acute myocardial infarction undergoing coronary angiography in DMCH during May 2017 to April 2018 were the study population. The population were divided into 2 groups based on their serum vitamin D level; normal vitamin D (>30 ng/ml) and low vitamin D (d"30 ng/ml). Low vitamin D level again divided into 3 groups; insufficient (vitamin D 21 to 30 ng/ml), deficient (Vitamin D 10-20 ng/ml) and severely deficient having vitamin D <10 ng/ml. Coronary angiogram was done during index hospitalization. The severity of the coronary artery disease was assessed by vessel score and Gensini score. After calculation of Gensini score, 36 points was chosen as an appropriate cut-off value and patients were divided into two groups; those with a Gensini score d"36 points was considered as having absent or mild coronary artery disease and those with a Gensini score >36 points was considered as having moderate to severe coronary artery disease. Association between serum vitamin D Level and angiographic severity of CAD was looked for.*

Results: *Seventy seven (74.0%) of study population had vitamin D level d" 30 ng/ml, while 27(26.0%) patients had normal level. There was no significant association between common cardiovascular risk factors with vitamin D level. Double or triple-vessel CAD were more frequent in those with vitamin D levels d"30 ng/ml as compared to those with normal vitamin D levels (>30 ng/ml) (P<0.05). Majority (48.1%) of patients had double vessel disease (DVD). Among them 4(8%) patients had normal serum vitamin D levels (>30 ng/ml) and 46 (92%) patients had low vitamin D (d"30 ng/ml). Mean Gensini score was found 20.8±5.1 in normal vitamin D (>30 ng/ml) and 48.3±13.3 in low vitamin D (d"30 ng/ml) (p<0.05). Moderate to severe CAD (Gensini score >36) was found in 54.1% of patients with vitamin D insufficiency (21-30 ng/dl) and 83.3% of patients with vitamin D deficiency (10-20 ng/dl) (p<0.05). Moderate negative correlation (r= -0.641; p=0.001) was found between Gensini score and serum vitamin D level of patients with acute myocardial infarction.*

Conclusion: *Low serum vitamin D level is associated with increasing severity of coronary artery disease, docsumented angiographically among patients of acute myocardial infarction. Low serum vitamin D levels may be an emerging, independent, and potentially modiûable cardiovascular risk factor.*

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Introduction:

Coronary artery disease (CAD) is an important medical and public health issue and the leading cause of death throughout the world. Though vitamin D has been traditionally associated with bone health, adequate levels are also important for optimal cardiovascular function. The quest to identify new predictors of cardiovascular disease has focused the attention on vitamin D, given its association with various established risk factors

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for CAD, including hypertension, diabetes, obesity, metabolic syndrome and congestive heart failure.[1-2] Vitamin D deficiency is a highly prevalent condition in the general population and in patients with coronary artery disease.[3]

Most experts define vitamin D deficiency as a calcidiol level of <20 ng/mL and insufficiency as 21–29 ng/mL. Vitamin D is sufficient if >30 ng/mL.[4] Zittermann et al. found a vitamin D level of 30–35 ng/L as the best choice for risk reduction in cardiovascular mortality.[5]

Despite adequate sunshine suboptimal vitamin D status is common among women in many Southeast Asian countries, including India and Pakistan. In Bangladesh serum 25(OH)D <37.7nmol/l was seen in 50% of those in low income groups (median 36.7nmol/l) compared to 38% of high income groups median (43.5nmol/L). Prevalence of low 25(OH) D increased in lactating women. Vitamin D insufficiency was common (80%) regardless of age, lifestyle and clothing in study from Dhaka. Concealing clothing may negatively affect the vitamin D status of many Bangladeshi women as well, since the vast majority of Bangladesh's population is Muslim and a covered style of dress (*Sari*) is common among Muslim Bangladeshi women.[6]

Activated vitamin D may influence cellular growth, proliferation and apoptosis, oxidative stress, membrane transport, matrix homeostasis, cell adhesion, and immune system functions and may regulate a large number of genes and healthy aging.[7,8] Vitamin D deficiency stimulates systemic and vascular inflammation, enabling atherogenesis.[9] On the other hand, hypertension is also associated with lack of vitamin D, due to activation of the Renin Angiotensin Aldosterone (RAA) system, enabling endothelial dysfunction, the first step in plaque formation.[10] Vitamin D deficiency was associated with vascular stiffness, which is a known predictor of cardiovascular morbidity and mortality and a marker of subclinical atherosclerosis. A strong association was found between vitamin D deficiency and slow coronary flow, endothelial dysfunction and subclinical atherosclerosis, in patients with normal or near-normal coronary arteries at coronary angiography.[11] Lower serum vitamin D was associated with the metabolic syndrome and its components, especially HDL cholesterol concentration.[12]

Poor vitamin D status was associated with cardiovascular and overall mortality, despite unconvincing results of vitamin D supplementation on mortality.[13-15] Vitamin D deficiency was associated with coronary heart disease and myocardial infarction and was found in a high proportion of patients with myocardial infarction.[16] It has been shown that a reduction of vitamin D levels lower than 30 ng/ml may increase the risk for coronary artery disease.[17]

Vitamin D status is prognostic for major post infarction adverse events, such as heart failure hospitalizations, recurrent acute myocardial infarction, death or restenosis after percutaneous coronary intervention.[10] A significant, moderate association was found between circulating vitamin D concentration and the risk of all-cause mortality, especially deaths due to coronary disease. The severity of coronary artery stenosis, assessed according to the Gensini score, a validated measure of the angiographic severity of coronary heart disease, was associated with vitamin D deficiency.[18]

We aimed to investigate whether serum 25-hydroxyvitamin D was associated with severity of coronary artery involvement.

Methods:

Cross sectional study was conducted in the Department of Cardiology, DMCH, Dhaka, Bangladesh from January 2017 to Dec 2017. The newly diagnosed acute myocardial infarction patients who had undergone coronary angiography were included in the study. Patients with CKD, hepatic impairment, malignancy, and other cardiac diseases, history of taking steroid, calcium, Vit. D and anticonvulsants were excluded from the study.

Detailed history, physical examination, relevant investigations were done after enrolling them in the study. All the subjects were evaluated for demographic profile (Age and Sex); risk factors for coronary artery disease like diabetes, hypertension, dyslipidemia, smoking, obesity and family history of premature coronary artery disease. A fasting blood sample was collected within 24 hours of admission to the hospital.

Serum vitamin D was measured by chemiluminescence immunoassay on blood samples collected and stored at -70^{0}c in the biochemistry laboratory of BSMMU or a private hospital. Then the study subjects were divided into 2 groups based on their serum vitamin D level; normal vitamin D (>30 ng/ml) and low vitamin D (d"30 ng/ml). Low serum vitamin D level again divided into 3 groups; insufficient (vitamin D 21 to 30 ng/ml), deficient (Vitamin D 10-20 ng/ml) and severely deficient having vitamin D <10 ng/ml. Coronary angiogram was done. Angiographic severity of coronary artery disease among the study population was assessed through Vessel Score and Gensini Score. After calculation of Gensini score, 36 points was chosen as an appropriate cut-off value (Sun and Lü,2011) and patients were divided into two groups; those with a Gensini score ≤36 points was considered as having absent or mild coronary artery disease and those with a Gensini score >36 points was considered as having moderate to severe coronary artery disease. Association between serum vitamin D Level and angiographic severity of CAD were looked for.

All statistical analysis was performed using the statistical package for social science (SPSS) program, version 22 for Windows. The significance of the results as determined in 95.0% confidence interval and a value of p <0.05 were consider to be statistically significant. Linear regression was done.

Results:

This cross-sectional study was conducted with a total of 104 newly diagnosed acute myocardial infarction patients. Association between serum vitamin D Level and angiographic severity of CAD were looked for.

Maximum number of study population was found in the age group 50-59 years in low serum vitamin D group. Mean age was found 51.3±9.3 years in low serum vitamin D group and 52.8±8.8 years in normal serum vitamin D group (p>0.05) (Table I). Female patients had lower vitamin D level than male (Mean 24.69±10.88 ng/ml vs. 25.17±10.79 ng/ml) (p>0.05) (Table I). Seventy seven (74.0%) of study population had vitamin D level ≤30 ng/ml, while 27(26.0%) patients had normal level (>30 ng/ml). Among the low vitamin D group, majority (35.6%) of patients had insufficient vitamin D level (21 to 30 ng/ml). Mean serum vitamin D level was 24.9±10.8 ng/ml with range from 7.0 to 60.1 ng/ml (Table II). Table III shows smoker, hypertension, diabetes mellitus, dyslipidemia, family history of premature CAD and alcohol intake were not statistically significant (p>0.05) between normal and low vitamin D level. Table IV shows smoker, hypertension, diabetes mellitus, dyslipidemia, family history of premature CAD and alcohol intake were not statistically significant (p>0.05) when compared with low serum vitamin D level.

Double and triple vessel CAD were more frequent in patients with low vitamin D levels (d"30 ng/ml) as compared to those with normal vitamin D levels (>30 ng/ml). The difference was statistically significant (p<0.05) between two groups (Table V). Double vessel disease (DVD) was found in 22(59.5%) patients having insufficient vitamin D (21-30 ng/ml) and in 24(66.7%) patients having deficient vitamin D (10-20 ng/ml). Triple vessel disease (TVD) was 100% among those with severely deficient vitamin D level. The difference was statistically significant (p<0.05) when compared with low serum vitamin D level (Table VI). Table VII shows mean Gensini score was found 20.8±5.1 in persons having normal vitamin D (>30 ng/ml) and the score was 48.3±13.3 in those having low vitamin D level (≤30 ng/ml). The mean Gensini score was statistically significant (p<0.05) between two groups.

Table VIII shows mean Gensini score was increasing with the decrease of serum vitamin D level. The highest mean Gensini score (68.8±11.7) was found in persons having severely deficient vitamin D (<10 ng/ml). The mean Gensini score was statistically significant (p<0.05) among three groups.

Multivariate Logistic regression analysis of Angiographic Severity of Coronary Artery Disease in Patients of Acute Myocardial Infarction shows that a subject with vitamin D (d"30 ng/ml) vs. (>30 ng/ml) had 3.633 (95% CI 1.264 to 7.443) times increase in odds having acute myocardial infarction. Which was statistically significant (p>0.05) (Table-IX).

Scatter diagram (Figure 1)) shows moderate negative correlation (r= -0.641; p=0.001) between Gensini score and serum vitamin D level of the study population.

Table-I

Age and gender distribution of the study population (N=104).

Age (years)	Normal vitamin D (>30 ng/ml) (n=27)		Low vitamin D (≤30 ng/ml) (n=77)		p value
	n	%	n	%	
<40		3	11.1	11	14.3
40-49	6	22.2	18	23.4	
50-59	9	33.3	28	36.4	
>60	9	33.3	20	26.0	
Mean±SD	52.8 ±8.8		51.3±9.3		0.467^{ns}
Range (min-max)	(37-65)		(32-68)		
Male	19 (27.1%)		51 (72.9%)		0.832
Female	08 (23.5%)		26 (76.5%)		

Table-II

Distribution of the study population by serum vitamin D level (N=104)

Serum vitamin D level	Frequency	Percentage
Normal (vitamin D >30 ng/ml)	27	26.0
Low (vitamin D ≤30 ng/ml)		
Insufficient (vitamin D 21 to 30 ng/ml)	37	35.6
Deficient (vitamin D 10-20 ng/ml)	36	34.6
Severely deficient (vitamin D <10 ng/ml)	4	3.8
Mean±SD	24.9±10.8	
Range (min-max)	7.0-60.1	

Table-III

Cardiovascular risk factors profile of study subjects (N=104).

Risk factors	Normal vitamin D (>30 ng/ml) (n=27)		Low vitamin D (≤30 ng/ml) (n=77)		p value
	n	%	n	%	
Smoking	18	66.7	48	62.3	0.387^{ns}
Hypertension	14	51.9	42	54.5	0.809^{ns}
Diabetes mellitus	12	44.4	49	63.6	0.081^{ns}
Dyslipidemia	10	37.0	40	51.9	0.182^{ns}
Family history of premature CAD	11	40.7	32	41.6	0.941^{ns}
Alcohol intake	2	7.4	2	2.6	0.276^{ns}

Table-IV

Association of cardiovascular risk factors with low serum vitamin D group (N=77).

Risk factors	Insufficient (vitamin D 21 to 30 ng/ml) (n=37)		Deficient (vitamin D 10-20 ng/ml) (n=36)		Severely deficient (vitamin D <10 ng/ml) (n=4)		p value
	n	%	n	%	n	%	
Smoking	24	64.9	23	63.9	1	25.0	0.284^{ns}
Hypertension	20	54.1	20	55.6	2	50.0	0.974^{ns}
Diabetes mellitus	23	62.2	23	63.9	3	75.0	0.879^{ns}
Dyslipidemia	18	48.6	19	52.8	3	75.0	0.600^{ns}
Family history of premature CAD	16	43.2	14	38.9	2	50.0	0.875^{ns}
Alcohol intake	1	2.7	1	2.8	0	0.0	0.945^{ns}

Table-V

Association of vessel score with serum vitamin D level of the study population (N=104).

Vessel score	Normal vitamin D (>30 ng/ml) (n=27)		Low vitamin D (≤30 ng/ml) (n=77)		p value
	n	%	n	%	
None	10	37.0	1	1.3	
SVD	13	48.1	19	24.7	0.001^{s}
DVD	4	14.8	46	59.7	
TVD	0	0.0	11	14.3	

SVD- Single vessel disease, DVD- Double vessel disease, TVD- Triple vessel disease

Table-VI

Association of vessel score with low serum vitamin D group (N=77).

Vessel score	Insufficient (vitamin D 21 to 30 ng/ml) (n=37)		Deficient (vitamin D 10-20 ng/ml) (n=36)		Severely deficient (vitamin D <10 ng/ml) (n=4)		p value
	n	%	n	%	n	%	
None	1	2.7	0	0.0	0	0.0	
SVD	12	32.4	7	19.4	0	0.0	0.001^{s}
DVD	22	59.5	24	66.7	0	0.0	
TVD	2	5.4	5	13.9	4	100.0	

SVD- Single vessel disease, DVD- Double vessel disease, TVD- Triple vessel disease

Table-VII

Association of Gensini score with serum vitamin D level (N=104).

Gensini score	Normal vitamin D (>30 ng/ml) (n=27)		Low vitamin D (≤30 ng/ml) (n=77)		p value
	n	%	n	%	
≤36	26	96.3	23	29.9	
>36	1	3.7	54	70.1	
Mean±SD	20.8	±5.1	48.3	±13.3	0.001^{s}
Range (min-max)	16.0	-32.0	16.0	-84.0	

Table-VIII

Association of Gensini score with low serum vitamin D level (N=77).

Gensini score	Insufficient (vitamin D 21 to 30 ng/ml) (n=37)		Deficient (vitamin D 10-20 ng/ml) (n=36)		Severely deficient (vitamin D <10 ng/ml) (n=4)		p value
	n	%	n	%	n	%	
≤36	17	45.9	6	16.7	0	0.0	
>36	20	54.1	30	83.3	4	100.0	
Mean±SD	31.9	±9.9	51.4	±10.5	68.8	±11.7	0.001[s]
Range (min-max)	16.0	-56.0	16.0	-68.0	56.0	-84.0	

Table-IX

Multivariate Logistic regression analysis of Angiographic Severity of Coronary Artery Disease in Patients of Acute Myocardial Infarction.

	Adjusted OR	95% CI		p Value
		Lower	Upper	
Smoking	1.084	0.430	2.730	0.864[ns]
Hypertension	1.160	0.482	2.795	0.740[ns]
Diabetes mellitus	0.889	0.549	1.467	0.724[ns]
Dyslipidemia	0.950	0.778	1.189	0.622[ns]
Family history of premature CAD	0.601	0.145	2.490	0.483[ns]
Alcohol intake	0.975	0.952	1.189	0.171[ns]
Low vitamin D (≤30 ng/ml)	3.633	1.264	7.443	0.037[s]

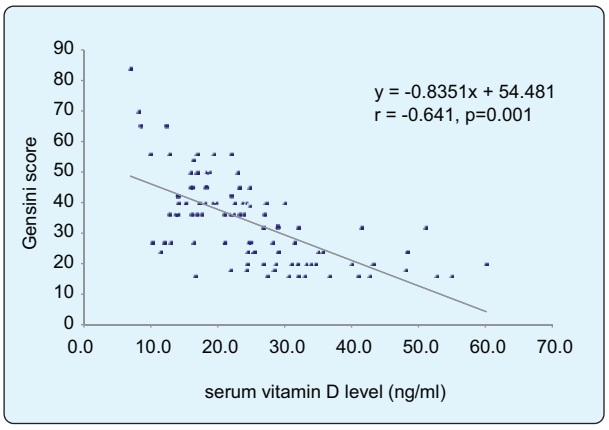

Fig.-1: *Scatter diagram shows moderate negative correlation (r= -0.641; p=0.001) between Gensini score and serum vitamin D level of the study population.*

Discussion:

The results of our study demonstrates that vitamin D deficiency increases the chance of coronary artery disease and the association between angiographic severity of CAD and vitamin D deficiency remains significant even after adjustment for significant cardiovascular risk factors such as diabetes, high blood cholesterol and low HDL level.

Average age of the patients was similar in other studies conducted with acute MI in Bangladesh.[19] Male patients were predominant in the study population which were 67.3%. Female patients were 32.7%. In almost all studies related to coronary artery disease (CAD) similar male preponderance was found. In the low socioeconomic background of our country females are given less attention and access for them to the health care facilities is limited. This financial and socio-cultural factor might have contributed for this male predominance.

In this study, majority of patients were male in vitamin D level >30 ng/ml, 24(64.9%) in 21-30 ng/ml, 25(69.4%) in 10-20 ng/ml and 2(50.0%) in <10 ng/ml. (p>0.05). other studies have also showed women often have lower levels of 25(OH) D levels than men.[20,21] Potential causes include differences in body fat composition, inadequate dietary intake, childbearing and menopause.[22]

Vitamin D insufficiency and deficiency were very common among our study population. In a similar study by Akin, et al., 83% of the patients had vitamin D level less than 30 ng/mL which is similar to our findings.[18] But Syal, et al., also found in his study higher proportion (93%) of vitamin D deficiency and insufficiency, while only 7% had normal vitamin D levels.[23] The high prevalence of vitamin D deficiency is a reflection of generalized hypovitaminosis D in our country as well.

Among the cardiovascular risk factors we found there was no significant association with vitamin D level. Mauss et al.,[24] found that Vitamin D deficiency is associated with prevalent DM in working older adults. Chaudhuri et al.,[25] found deficiency of 25-hydroxyvitamin D was independently associated with dyslipidemia in Indian subjects.

In this study, 48.1% patients had double vessel disease (DVD). Among them 14.8% patients had serum normal vitamin D and 59.7% patients had low vitamin D. The mean Gensini score was statistically significant when compared with vitamin D level. Moderate negative correlation between Gensini score and serum vitamin D level of patients with acute myocardial infarction. Syal, et al.,[23] found vitamin D deficiency had higher frequency of double- or triple-vessel CAD (53% vs. 38%) and higher mean number of coronary vessels involved (1.78 vs. 1.24).

Conclusion:

This study demonstrates that serum vitamin D levels are inversely associated with angiographic severity of coronary artery disease in patients with acute MI. Our results suggest that low vitamin D levels may be an emerging and independent cardiovascular risk factor. The findings of this study may motivate future larger trials to determine whether vitamin D interventions prevent the development of Cardiovascular diseases.

Conflict of Interest - None.

References:

1. Holick MF. Vitamin D deficiency. New England Journal of Medicine. 2007;357(3):266-281. doi:10.1056/nejmra070553
2. Zittermann A. Vitamin D and disease prevention with special reference to cardiovascular disease. Progress in Biophysics and Molecular Biology. 2006;92(1):39-48. doi:10.1016/j.pbiomolbio.2006.02.001
3. Norman AW, Bouillon R, Whiting SJ, Vieth R, Lips P. 13th workshop consensus for vitamin D nutritional guidelines. The Journal of Steroid Biochemistry and Molecular Biology. 2007;103(3-5):204-205. doi:10.1016/j.jsbmb.2006.12.071
4. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. The American Journal of Clinical Nutrition. 2004;80(6). doi:10.1093/ajcn/80.6.1678s
5. Wang L, Ma J, Manson JAE, Buring JE, Gaziano JM, Sesso HD. A prospective study of plasma vitamin D metabolites, vitamin D receptor gene polymorphisms, and risk of hypertension in men. European Journal of Nutrition. 2012;52(7):1771-1779. doi:10.1007/s00394-012-0480-8
6. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. The American Journal of Clinical Nutrition. 2000;72(2):472-475. doi:10.1093/ajcn/72.2.472
7. Atiq M, Suria A, Nizami SQ, Ahmed I. Maternal vitamin-D deficiency in Pakistan. Acta Obstetricia et Gynecologica Scandinavica. 1998;77(10):970-973. doi:10.1034/j.1600-0412.1998.771004.x
8. Islam AKMM, Majumder AAS. Coronary artery disease in Bangladesh: A Review. Indian Heart Journal. 2013;65(4):424-435. doi:10.1016/j.ihj.2013.06.004
9. Islam MZ, Akhtaruzzaman M, Lamberg-Allardt C. Hypovitaminosis D is common in both veiled and nonveiled Bangladeshi women. Asia Pac J Clin Nutr. 2006;15(1):81-87.
10. Islam MZ, Lamberg-Allardt C, Kärkkäinen M, Outila T, Salamatullah Q, Shamim AA. Vitamin D deficiency: a concern in premenopausal Bangladeshi women of two socio-economic groups in rural and urban region. Eur J Clin Nutr. 2002;56(1):51-56. doi:10.1038/sj.ejcn.1601284
11. Chowdhury R, Kunutsor S, Vitezova A, et al. Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies. BMJ. 2014; 348: g1903. Published 2014 Apr 1. doi:10.1136/bmj.g1903
12. Norman PE, Powell JT. Vitamin D and cardiovascular disease. Circ Res. 2014; 114(2):379-393. doi:10.1161/CIRCRESAHA.113.301241
13. Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor? J Am Coll Cardiol. 2008; 52(24):1949-1956. doi:10.1016/j.jacc.2008.08.050
14. Kunadian V, Ford GA, Bawamia B, Qiu W, Manson JE. Vitamin D deficiency and coronary artery disease: a review of the evidence. Am Heart J. 2014;167(3):283-291. doi:10.1016/j.ahj.2013.11.012

15. Oz F, Cizgici AY, Oflaz H, et al. Impact of vitamin D insufficiency on the epicardial coronary flow velocity and endothelial function. Coronary Artery Disease. 2013; 24(5):392-397. doi:10.1097/mca.0b013e328362b2c8

16. Maki KC, Rubin MR, Wong LG, et al. Serum 25-hydroxyvitamin D is independently associated with high-density lipoprotein cholesterol and the metabolic syndrome in men and women. Journal of Clinical Lipidology. 2009; 3(4):289-296. doi:10.1016/j.jacl.2009.07.003

17. Zittermann A, Prokop S. The role of vitamin D for cardiovascular disease and overall mortality. Sunlight, Vitamin D and Skin Cancer. 2014:106-119. doi:10.1007/978-1-4939-0437-2_6

18. Wang TJ, Pencina MJ, Booth SL, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation. 2008;117(4):503-511. doi:10.1161/CIRCULATIONAHA.107.706127

19. Wang L, Ma J, Manson JE, Buring JE, Gaziano JM, Sesso HD. A prospective study of plasma vitamin D metabolites, vitamin D receptor gene polymorphisms, and risk of hypertension in men. Eur J Nutr. 2013;52(7):1771-1779. doi:10.1007/s00394-012-0480-8

20. Goleniewska BM, Kacprzak M, Zielinska M. Vitamin D level and extent of coronary stenotic lesions in patients with first acute myocardial infarction. Cardiology Journal. 2013. doi:10.5603/cj.a2013.0048

21. Arad Y, Spadaro LA, Roth M, et al. Serum concentration of calcium, 1,25 vitamin D and parathyroid hormone are not correlated with coronary calcifications. An electron beam computed tomography study. Coron Artery Dis. 1998;9(8):513-518. doi:10.1097/00019501-199809080-00007

22. Goleniewska BM, Kacprzak M, Zielinska M. Vitamin D level and extent of coronary stenotic lesions in patients with first acute myocardial infarction. Cardiology Journal. 2013. doi:10.5603/cj.a2013.0048

23. Pilz S, Gaksch M, O'Hartaigh B, Tomaschitz A, März W. The role of vitamin D deficiency in cardiovascular disease: where do we stand in 2013?. Arch Toxicol. 2013;87(12):2083-2103. doi:10.1007/s00204-013-1152-z

24. Lips P. Vitamin D status and nutrition in Europe and Asia. J Steroid Biochem Mol Biol. 2007;103(3-5):620-625. doi:10.1016/j.jsbmb.2006.12.076

25. Hagenau T, Vest R, Gissel TN, et al. Global vitamin D levels in relation to age, gender, skin pigmentation and latitude: an ecologic meta-regression analysis. Osteoporos Int. 2009;20(1):133-140. doi:10.1007/s00198-008-0626-y

26. Dijkstra SH, van Beek A, Janssen JW, de Vleeschouwer LH, Huysman WA, van den Akker EL. High prevalence of vitamin D deficiency in newborn infants of high-risk mothers [published correction appears in Arch Dis Child. 2007 Nov;92(11):1049]. Arch Dis Child. 2007;92(9):750-753. doi:10.1136/adc.2006.105577

27. Syal SK, Kapoor A, Bhatia E, et al. Vitamin D deficiency, coronary artery disease, and endothelial dysfunction: observations from a coronary angiographic study in Indian patients. J Invasive Cardiol. 2012;24(8):385-389.

28. Mauss D, Jarczok MN, Hoffmann K, Thomas GN, Fischer JE. Association of Vitamin D levels with type 2 diabetes in older working adults. International Journal of Medical Sciences. 2015;12(5):362-368. doi:10.7150/ijms.10540

29. Chaudhuri JR, Mridula KR, Anamika A, et al. Deficiency of 25-hydroxyvitamin d and dyslipidemia in Indian subjects. J Lipids. 2013;2013:623420. doi:10.1155/2013/623420