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Evaluation of Vitamin D3 Level and Apo B/Apo A1 Ratio in Acute Myocardial Infarction Patients in Kerbala Province

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Abstract : Objective: The aim of study to find a possible association between acute myocardial infraction and vitamin D3, Apo A1, Apo B, and Apo B/Apo A1 ratio and other risk factors (age, body mass index and smoking).
Materials and Methods: This case-control study was conducted during the period from Nov. 2015 till Sep. 2016. Forty patients of acute myocardial infraction presented with typical chest pain to the coronary care unit in Al-Hussein Teaching Hospital/ Kerbala. Fifty persons were matched with patient as a control group.
Results: Vitamin D3 deficiency (< 30 ng/mL) were prevalent in patients compared with those considered to be sufficient in vitamin D3 (≥ 30 ng/mL) (odds ratio [OR], 33.78; 95%, confidence interval [CI], 7.28-156.73; P < 0.001). The results obtained that 25(OH) D3 was highly significant in smoker when comparison with non-smoker in patient and control group (p < 0.001, P < 0.05 respectively). The serum Apo B, Apo A1 and Apo B/Apo A1 ratio were highly significant between patient and control group (P < 0.01, P < 0.001,P < 0.001 respectively). On the other hand, vitamin D3 recorded significant decrease with increase serum troponin I in patient group (P < 0.05).
Conclusion: The present study showed a highly significant association between vitamin D3, Apo B, Apo A1 levels, Apo B/Apo A1 ratio and patients as compared with control group, and significant correlation between vitamin D3 and age, body mass index and smoking.
Keywords: Acute myocardial infarction, Vitamin D3, ApoA1, Apo B, Apo B/Apo A1 ratio.

Introduction:

Acute myocardial infarction is one of the major causes of mortality and morbidity in the world [(1)]. Acute myocardial infarction, commonly known as a heart attack, is defined as the necrosis or death of myocardial cells, occurs when blood flow stops to a part of the heart causing damage to the heart muscle [1].Traditionally, vitamin D3 has been a well-known vital nutrient for healthy bones and calcium homeostasis. However, recent researches are revealing that vitamin D3 is associated with numerous outcomes including not only rickets or osteomalacia but also in several chronic non-skeletal diseases, because the discovery that the VDR is ubiquitously expressed in almost all body cells, such as immune, vascular or myocardial cells, suggests an involvement of vitamin D3 mediated effects in several other systems [2-3]. Vitamin D3 has been shown to play a key role in CVD [4]. Disturbances in mineral metabolism are common in older adults and may adversely affect cardiovascular health [5]. Older age is associated with lower circulating levels of 25(OH)D3, impaired vitamin D3

activation within the kidney, and a rise in serum parathyroid hormone (PTH) concentrations [6]. Disturbances in vitamin D3 and PTH metabolic axes may increase cardiovascular risk through diverse pathways [7]. Vitamin D3 deficiency activates the renin angiotensin aldosterone system (RAAS), stimulates inflammatory cytokines, and promotes cardiomyocyte growth. PTH excess increases intracellular calcium in target tissues and is associated with hypertension, cardiac valve calcification, and left ventricular hypertrophy. Lower 25(OH)D3 and higher PTH levels would be associated with cardiovascular events and that associations would be strongest in the presence of both disturbances, because PTH represents an endogenous biologic marker of inadequate vitamin D stores [8].

Suboptimal vitamin D3 is thought to influence CVD risk predominantly by acting on established CVD risk factors, namely hypertension, diabetes, and inflammation [9]. Vitamin D3 also play important role in regulation atrial natriuretic peptide (ANP), its protein secreted by heart muscle cells for reducing blood pressure, It is involved in the homeostatic control of body water, sodium, potassium and fat (adipose tissue). Vitamin D3 deficiency inhibits the secretion of atrial natriuretic peptides in atrial and ventricular myocytes [10].

The ApoB and ApoAI are the two major apolipoproteins involved in lipid transport and independent predictors of CVD in the general population. The ApoB/ApoAI ratio indicates the balance between atherogenic and anti-atherogenic particles, the higher the value, the higher is the cardiovascular risk. It may be a better marker of the CVD risk than conventional lipid measurements[11-12-13]. Previous reports have shown that ApoB/ApoAI ratio for men and women respectively <0, 7 and <0, 6 is associated with low risk for CVD. The advantage of calculating this index is that the concentration of apolipoproteins do not change after the meal and do not change in different times of day. In addition, with regard to the tests performed after AMI have occurred there is no matter how much time has elapsed since the in the blood collection[14].

The aim of the study to find a possible association between smokers and non-smokers of acute myocardial infraction patients with vitamin D3, Apo A1, Apo B, and ApoB/Apo A1 ratio and other risk factors (age and body mass index) in Kerbala province.

Experimental:

This case-control study was conducted during the period from Nov. 2015 till Sep. 2016. Forty male patients of acute myocardial infraction had been selected from coronary care unit (CCU) in AL-Hussein Teaching Hospital /AL-Hussein Medical City- Kerbala Health Directorate / Holy Kerbala - Iraq.The diagnosis was based on the clinical history, electrocardiography and troponin I.The (mean ± SD) of age is (53.35 ± 8.70) ranged between 35 to 70 years old. Fifty male individuals as control were matched with patients group in their age and body mass index and the (mean ± SD) of age is (52.72 ± 8.74) and ranged between 40 to 72 years old. Approvals of the study program was taken from the administration of Al-Hussein General Hospital, and from the patients and the controls groups.

Serum 25(OH)D3, Apo A1, Apo B, troponin I, random blood sugar (RBS), urea and creatinine. Serum 25(OH)D3 and troponin I levels were measured using Auto Immunoassay Analyzer [MAGLUMI CLIA (chemiluminescence immunoassay)]. Serum Apo A1, Apo B, urea, creatinine and random blood sugar were measured using Auto Analyzer Biochemistry (Cormay).

Statistical analysis

Statistical analysis was done by Statistical Package for the Social Sciences(SPSS 21). Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables (Age, BMI, glucose, Apo A1, Apo B, Apo B/A1 ratio, urea, creatinine, troponin I and 25(OH) D3). Independent samples student t-test,Chi square, Fisher's exact test, correlation coefficient (r) test were used to compare, assess and describe the association between the different studied variables; P values < 0.05 were considered to indicate statistical significance and highly significant if it is <0.01.

Results:

The characteristics of population of this study are presented in Table 1.

Table (1) Association between patient and control groups in all biomarkers

Parameters	Mean± SD		P. value
	Control (N=50)	patient (N=40)	
25(OH)D3 , (ng/ml)	35.15 ± 11.79	16.59 ± 4.54	< 0.001**
Apo B , (mg/dl)	98.05 ± 37.73	128.05 ± 42.13	0.001**
Apo A1 , (mg/dl)	144.49 ± 28.16	113.89 ± 28.39	< 0.001**
Apo B/A1 ratio	0.68 ± 0.21	1.19± 0.50	< 0.001**
Troponin I , (pg/ml)	6.37 ± 1.78	241.19 ± 140.79	< 0.001**
Urea , (mg/dl)	30.34 ± 5.86	34.20 ± 4.85	0.001**
Creatinine , (mg/dl)	0.91 ± 0.17	0.96 ± 0.19	0.16
Random B. Sugar, (mg/dl)	108.40 ± 13.15	108.62 ± 13.59	0.94

**High Significant association p< 0.01.

There was highly significant between patient and control groups when classified vitamin D3 levels to sufficiency (≥ 30) and deficiency (< 30), the results shown in table 2.

Table (2) Comparison between vitamin D3 in patient and Control Groups

		Case type	
		Patient	**Control**
25(OH)D3 Category	**< 30**	38	18
		95.0%	36.0%
	≥ 30	2	32
		5.0%	64.0%
P. value		<0.001**	
Total		40	50
		100%	100%

**High Significant correlation p< 0.01.

The odds ratio of this study of risk myocardial infraction was 33.78 (95% confidence interval 7.28–156.73; P < 0.001).

Table 3. Present the correlation between vitamin D3 and the age in two groups, it was significant in control group as shown in figure 1, and the correlation between vitamin D3 and BMI it also significant in control group as shown in figure 2.

Table (3) Correlation between vitamin D3 and the age, BMI in patient and control groups

Case type		N	Mean ± SD		r	P. value
			25(OH)D3 (ng/ml)	**Age, (year)**		
Age	**Patient**	40	16.59 ± 4.54	53.35 ± 8.70	-0.22	0.13
	Control	50	35.15 ± 11.79	52.72 ± 8.74	-0.47	0.001**
			25(OH)D3 (ng/ml)	**BMI(kg/m^2)**		
BMI	**Patient**	40	16.59 ± 4.54	28.41 ± 2.41	-0.03	0.81
	Control	50	35.15 ± 11.79	29.55 ± 2.01	-0.42	0.002**

**Highly Significant correlation p<0.01.

A significant association was shown between smokers and non-smokers in patient group ($p < 0.001$). Additionally it was shown significant association shown between smokers and non-smokers in control group ($p < 0.05$), as shown in table 4.

Table (4)Comparison between vitamin D3 and smoking in patients and control groups

Parameter	Case type	Smokers	N	Mean ± SD	P. value
25(OH)D3 (ng/ml)	Patient	Positive	25	14.29 ± 2.52	< 0.001**
		Negative	15	20.44 ± 4.61	
	Control	Positive	16	29.88 ± 4.76	0.029*
		Negative	34	37.63 ± 13.28	

*Significant association p< 0.05, **High Significant association p< 0.01.

The results were shown significant correlation between vitamin D3 and troponin I in patient group, ($p < 0.05$, $r = -0.33$) as shown in figure 1, and no significant associated between vitamin D3 and troponin I in control group, ($p = 0.39$, $r = -0.12$).

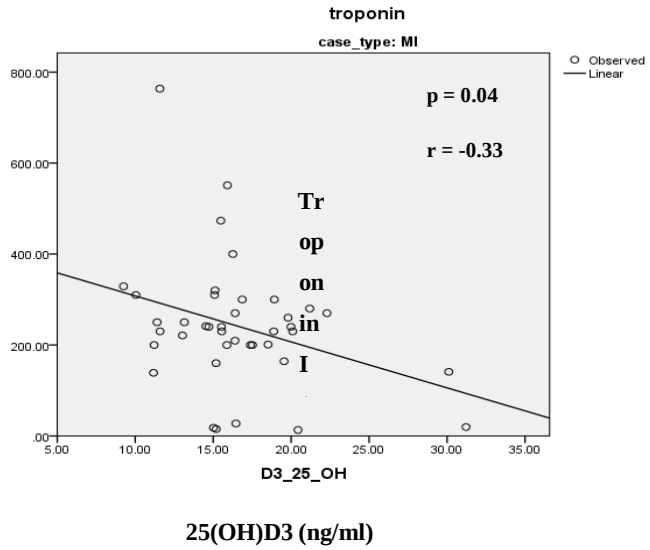

Figure (1) Correlation between vitamin D3 and troponin I in patient group.

Discussion:

In recent years, an increased attention focused on vitamin D3 due to its effects on several organs such as cardiovascular system, in addition its important role in the mineralization of bone. Most studies observed that low vitamin D3 levels were associated with a high risk of CVD. Interest in the role of vitamin D3 in CVD came from animal studies. In general, increasing observational evidence supports an association between low vitamin D3 levels and CVD [15]. The results of this study showed that concentration of vitamin D3 was highly significant in patient group as compared with normal control group. The presented data in agreement with previous study in United State. It has been prospectively analyzed a large database from medical records to identify the prevalence of vitamin D3 deficiency and the relation of vitamin D levels to incident and prevalent cardiovascular risk factors and diseases, including mortality. The database included 41,504 patient records with a one minimum of measured vitamin D3 level. The prevalence of vitamin D3 deficiency (≤30 ng/ml) was 63.6%, with only minor differences by age or gender. The vitamin D3 levels were highly significant (invers associated) with myocardial infarction, coronary artery disease, heart failure, and stroke (all $p < 0.0001$). These observations indicate that there is a strong support to the hypothesis that vitamin D3 might play a primary role in cardiovascular risk factors and disease [16].

Other study in Iraq showed (when they give supplementation of vitamin D3) they no significant effect of short term treatment with 5000 IU of vitamin D3 on the outcome of myocardial infarction. The database consisted of 44 patient with acute ST-segment elevation myocardial infarction [17].

The odds ratio of this study of risk myocardial infraction events was about 34 times higher in men with vitamin D3 levels< 30 ng/ml compared with those with levels ≥ 30 ng/ml (95% confidence interval 7.28–156.73; P < 0.001), This result agree with Wang *et al.*, which concluded that vitamin D deficiency is associated with incident CVD [18]. Our results are in agreement with the case-control study in India with 120 consecutive cases of first incident acute myocardial infarction and 120 gender and age matched healthy controls, the results showed that Vitamin D3 deficiency [vitamin D3 < 30 ng/ml] was highly prevalent in cases and controls (98.3% and 95.8% respectively). Multivariate logistic regression analysis revealed severe vitamin D3 deficiency [vitamin D3 < 10 ng/ml] was associated with a risk of myocardial infraction with an odds ratio of 4.5 (95% confidence interval 2.2–9.2) [19].

Results of this study showed that vitamin D3 deficiency was significant higher with age in control group, this result agreement with a previous study, which indicates that the odds for vitamin D3 deficiency increased with age [20]. Older adults are at increased risk of developing vitamin D3 insufficiency, age related changes in the skin, renal function, gut absorption, and sunlight exposure may adversely impact upon formation of vitamin D3 metabolites. The aging process is linked with change in the skin that lead to less efficient conversion 7-dehydrocholesterol to cholecalciferol. Furthermore, the amount of 7-dehydrocholesterol in the skin is also decrease in older compared with younger subjects [21-22].

There are several studies to evaluate the relationship between BMI and vitamin D3, the existence of inverse association was observed between vitamin D3 and the obesity [2-23]. In this study it was noticed that there a significant inverse association between vitamin D3 and BMI in control group, increase of BMI leading to decrease vitamin D3, people who are obese, a (BMI ≥ 30) is associated with lower serum vitamin D3 levels compared with non-obese individuals; people who are obese may need larger than usual intakes of vitamin D3 to achieve vitamin D3 levels comparable to those of normal weight. Obesity does not affect skin's capacity to synthesize vitamin D3, but greater amounts of subcutaneous fat sequester more of the vitamin and alter its release into the circulation [24].

Some other studies indicate that the significant associated between vitamin D3 and smokers, where the smoking associated with decrease vitamin D3, as shown in this study.In this study among adults, it was observed lower vitamin D3 levels and higher prevalence of vitamin D3 insufficiency and deficiency in the adults male subjects with AMI in smokers rather than nonsmoker, similar results have been seen in many other studies [25-26]. Soldin *et al*, found an adverse effect of smoking on the synthesis of steroid hormones, including vitamin D3. The exact mechanisms of the effect of smoking on vitamin D3 metabolisms is still unclear [27].

Several mechanisms proposed to explain the relation between vitamin D3 deficiency and CVD is that chronic vitamin D3 deficiency causes secondary hyperparathyroidism, acting through pathogenic pathways associated with PTH excess: increased pancreatic cell dysfunction and insulin resistance, predisposing to the metabolic syndrome and diabetes; increasing blood pressure (by activation of the renin angiotensin system), and leading to left ventricular hypertrophy (with subsequent apoptosis and fibrosis); and stimulation of systemic and vascular inflammation, augmenting atherogenesis [(16-18)]. Other studies suggest that parathyroid hormone has a proinflammatory effect, stimulating vascular smooth muscle cells to release cytokines [28]. Known risk factors for CVD, including smoking, obesity, advanced age and inactivity (reduced sun exposure), are associated with lower vitamin D3, which make the dissection of the causal role of low vitamin D3 status in CVD difficult. Finally, recent evidence has suggested that vitamin D3 may be a negative acute phase reactant; so, chronic disease may lead to low vitamin D3 even in the presymptomatic phases of CVD [29].

Studies revealed the relationship between apolipoprotein (B and A1) and cardiovascular disease, which is considered a strong indicator to detect the risk of cardiovascular disease [30]. In this study it was observed a highly significant associated between AMI and ApoB, ApoA1 and ApoB/Apo A1 ratio, it was found the significant associated between ApoB and AMI when compared with control group, the greater Apo B the likelihood of increased risk of AMI, this is in line with other study [31], and it was the inversely significant associated between ApoA1 and AMI when compared with control group, decrease ApoA1 leading to increase the risk of ischemic heart disease, this is agree with another study [32], and disagree with study done by [31-33], there was no significant associated between ApoA1 and cardiovascular disease. ApoB/ApoA1 ratios were designed to associate higher values with increased risk of acute myocardial infarction and lower values with reduced risk [34].

In this study the association between vitamin D3 and traditional biomarkers of AMI was examined and found that it was inversely associated with troponin I, it is in agreement with other study [35], but not with ApoB, ApoA1, ApoB/ApoA1 ratio, this result was in agreement with other study, previous research was observed that no significant associated between vitamin D3 and (ApoB, ApoA1)[36]. While another study showed counterproductive, it was concluded that Vitamin D3 supplementation among children could improve ApoB levels [37]. The mechanistic link between vitamin D3 and lipid metabolism remains poorly understood, vitamin D3 has been proposed to modulate the transcription activity of a group of genes known to be involved in lipid metabolism. In addition, it suggested that vitamin D3 may upregulate lipoprotein lipase activity in adipocytes, and this will decreased circulating triglyceride levels [36].

Conclusions:

According to the findings of the current study, it can be concluded that there was a highly significant association for level of vitamin D3 between patient and control groups. There was highly prevalent for level of low vitamin D3 among patients. There was a significant inverse correlation between vitamin D3 level and the ages in control group and there was a significant inverse correlation between vitamin D3 level and obesity. There was a significant association between vitamin D3 level and the smoking. There was a significant correlation between ApoB, ApoA1 levels and ApoB/ApoA1 ratio with each of acute myocardial infarction and control groups. No significant effect of vitamin D3 on ApoB, ApoA1 levels and ApoB/ApoA1 ratio. There was a significant inverse correlation between vitamin D3 level and troponin I concentration in patient group.

References:

1. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Third universal definition of myocardial infarction. Circulation. 2012 Oct 16;126(16):2020-35.
2. Kienreich K, Tomaschitz A, Verheyen N, Pieber T, Gaksch M, Grübler MR, Pilz S. Vitamin D and cardiovascular disease. Nutrients. 2013 Jul 31;5(8):3005-21.
3. Kwon HJ. Vitamin D receptor signaling is required for heart development in zebrafish embryo. Biochemical and biophysical research communications. 2016 Feb 12;470(3):575-8.
4. Norman PE, Powell JT. Vitamin D and cardiovascular disease. Circulation research. 2014 Jan 17;114(2):379-93.
5. Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. Endocrine reviews. 2001 Aug 1;22(4):477-501.
6. Kamycheva E, Sundsfjord J, Jorde R. Serum parathyroid hormone level is associated with body mass index. The 5th Tromso study. European Journal of Endocrinology. 2004 Aug 1;151(2):167-72.
7. Holick MF. Vitamin D deficiency. New England Journal of Medicine. 2007 Jul 19;357(3):266-81.
8. Kestenbaum B, Katz R, de Boer I, Hoofnagle A, Sarnak MJ, Shlipak MG, Jenny NS, Siscovick DS. Vitamin D, parathyroid hormone, and cardiovascular events among older adults. Journal of the American College of Cardiology. 2011 Sep 27;58(14):1433-41.
9. Lutsey PL, Michos ED. Vitamin D, calcium, and atherosclerotic risk: evidence from serum levels and supplementation studies. Current atherosclerosis reports. 2013 Jan 1;15(1):1-8.
10. Pilz S, Tomaschitz A. Role of vitamin D in arterial hypertension. Expert review of cardiovascular therapy. 2010 Nov 1;8(11):1599-608.
11. Lamprea-Montealegre JA, Sharrett AR, Matsushita K, Selvin E, Szklo M, Astor BC. Chronic kidney disease, lipids and apolipoproteins, and coronary heart disease: The ARIC Study. Atherosclerosis. 2014 May 31;234(1):42-6.
12. Jing F, Mao Y, Guo J, Zhang Z, Li Y, Ye Z, Ding Y, Wang J, Jin M, Chen K. The value of Apolipoprotein B/Apolipoprotein A1 ratio for metabolic syndrome diagnosis in a Chinese population: a cross-sectional study. Lipids in health and disease. 2014 May 14;13(1):1.
13. Walldius G. The apoB/apoA-I ratio is a strong predictor of cardiovascular risk. lipoproteins in health and diseases. 2012:95-148.
14. Walldius G, Jungner I. The apoB/apoA-I ratio: a strong, new risk factor for cardiovascular disease and a target for lipid-lowering therapy–a review of the evidence. Journal of internal medicine. 2006 May 1;259(5):493-519.

15. Christakos S, Dhawan P, Verstuyf A, Verlinden L, Carmeliet G. Vitamin D: metabolism, molecular mechanism of action, and pleiotropic effects. Physiological reviews. 2016 Jan 1;96(1):365-408.
16. Anderson JL, May HT, Horne BD, Bair TL, Hall NL, Carlquist JF, Lappé DL, Muhlestein JB, Group IH. Relation of vitamin D deficiency to cardiovascular risk factors, disease status, and incident events in a general healthcare population. The American journal of cardiology. 2010 Oct 1;106(7):963-8.
17. Anwer S, Mohammed A. Effect of Vitamin D3 on Adhesion Molecules and Inflammatory Markers in Patients with Acute ST Segment Elevation Myocardial Infarction.2007 1:85:62-4.
18. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, Benjamin EJ, D'Agostino RB, Wolf M, Vasan RS. Vitamin D deficiency and risk of cardiovascular disease. Circulation. 2008 Jan 29;117(4):503-11.
19. Roy A, Lakshmy R, Tarik M, Tandon N, Reddy KS, Prabhakaran D. Independent association of severe vitamin D deficiency as a risk of acute myocardial infarction in Indians. Indian heart journal. 2015 Feb 28;67(1):27-32.
20. Daly RM, Gagnon C, Lu ZX, Magliano DJ, Dunstan DW, Sikaris KA, Zimmet PZ, Ebeling PR, Shaw JE. Prevalence of vitamin D deficiency and its determinants in Australian adults aged 25 years and older: a national, population-based study. Clinical endocrinology. 2012 Jul 1;77(1):26-35.
21. Cranney C, Horsely T, O'Donnell S. Effectiveness and safety of vitamin D. Evidence report/technology assessment no. 158. AHRQ publication no. 07-E013.
22. Gloth FM, Tobin JD. Vitamin D deficiency in older people. Journal of the American Geriatrics Society. 1995 Jul 1;43(7):822-8.
23. Earthman CP, Beckman LM, Masodkar K, Sibley SD. The link between obesity and low circulating 25-hydroxyvitamin D concentrations: considerations and implications. International journal of obesity. 2012 Mar 1;36(3):387-96.
24. Malone M. Recommended nutritional supplements for bariatric surgery patients. Annals of Pharmacotherapy. 2008 Dec 1;42(12):1851-8.
25. Ab Hameed Raina MS, Shah ZA, Changal KH, Raina MA, Bhat FA. Association of low levels of vitamin D with chronic stable angina: A prospective case-control study. North American journal of medical sciences. 2016 Mar;8(3):143.
26. Kühn T, Kaaks R, Teucher B, Hirche F, Dierkes J, Weikert C, Katzke V, Boeing H, Stangl GI, Buijsse B. Dietary, lifestyle, and genetic determinants of vitamin D status: a cross-sectional analysis from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Germany study. European journal of nutrition. 2014 Apr 1;53(3):731-41.
27. Soldin OP, Makambi KH, Soldin SJ, O'Mara DM. Steroid hormone levels associated with passive and active smoking. Steroids. 2011 Jun 30;76(7):653-9.
28. Martín-Ventura JL, Ortego M, Esbrit P, Hernández-Presa MA, Ortega L, Egido J. Possible role of parathyroid hormone–related protein as a proinflammatory cytokine in atherosclerosis. Stroke. 2003 Jul 1;34(7):1783-9.
29. Ford JA, MacLennan GS, Avenell A, Bolland M, Grey A, Witham M, RECORD Trial Group. Cardiovascular disease and vitamin D supplementation: trial analysis, systematic review, and meta-analysis. The American journal of clinical nutrition. 2014 Sep 1;100(3):746-55.
30. Khadem-Ansari MH, Rasmi Y, Rahimi-Pour A, Jafarzadeh M. The association between serum apolipoprotein AI and apolipoprotein B and the severity of angiographical coronary artery disease. Singapore medical journal. 2009 Jun 1;50(6):610.
31. Tamang HK, Timilsina U, Singh KP, Shrestha S, Raman RK, Panta P, Karna P, Khadka L, Dahal C. Apo B/Apo AI ratio is statistically a better predictor of cardiovascular disease (CVD) than conventional lipid profile: a study from Kathmandu Valley, Nepal. J Clin Diagn Res. 2014 Feb 1;8:34-6.
32. Manson JE, Bassuk SS. Biomarkers of cardiovascular disease risk in women. Metabolism. 2015 Mar 31;64(3):S33-9.
33. Mashayekhi NR, Sadrnia S, Chehrei A, Javaheri J. The correlation between serum apoA1 and B and coronary artery disease as well as its severity. International cardiovascular research journal. 2014 Jan;8(1):1.
34. McQueen MJ, Hawken S, Wang X, Ounpuu S, Sniderman A, Probstfield J, Steyn K, Sanderson JE, Hasani M, Volkova E, Kazmi K. Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. The Lancet. 2008 Jul 25;372(9634):224-33.

35. Michos ED, Selvin E, Misialek JR, McEvoy JW, Ndumele CE, Folsom AR, Gross MD, Ballantyne CM, Lutsey PL. Vitamin D Deficiency is Associated With Increased Risk of Subclinical Myocardial Damage in Younger but not Older Adults: The Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2015 Nov 10;132(Suppl 3):A13670.
36. García-Bailo B. Plasma vitamin D and biomarkers of cardiometabolic disease risk in adult Canadians, 2007–2009. Preventing chronic disease. 2013;10.
37. Hirschler V, Maccallini G, Sanchez M, Claudio G, Molinari C, Figueroa M, Arnada C, Hidalgo M. Improvement of Apolipoprotein B in Argentine Indigenous School Children after Vitamin D Supplementation. Cardiovascular & Hematological Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Cardiovascular & Hematological Agents). 2015 Aug 1;13(2):137-45.

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