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ORIGINAL ARTICLE

Vitamin D Levels Assessment in Relation to Coronary MDCT Angiographic Findings

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ABSTRACT

Background: Although vitamin D has a major role at the skeletal mineralization, it has been implicated at cardio vascular system, owing to **abundance** of its receptor there. Atherosclerosis is the most presenting symptom of the cardio-vascular system that warrants the urge to detect the effect of vitamin D serum level changes in progression of the atherosclerosis. Objective is to assess the correlation between vitamin D level and coronary artery findings using MDCT. **Methods:** Two hundred and Fifty patients were included in our study, all of them underwent MDCT for coronary artery angiography, and then the findings were compared with vitamin D serum levels. **Results:** 4 % of all examined patients (n=10) had vitamin D deficiency, 44 % (n=110) had insufficient levels of vitamin D, 52 % have sufficient vitamin D level (n=130). There is significant positive correlation between Lab. vitamin D levels and coronary artery calcium score (CACS) with P<0.005. **Conclusions:** Vitamin D levels play significant role in modifying the risk of coronary artery involvement.

Keywords: MDCT, vitamin D, CAD.

INTRODUCTION

It is projected that coronary artery diseases (CAD) will be the leading cause of death in developing countries by the year 2025 [1]. In Egypt, according to WHO statistics, the mortality rates secondary to CAD is rapidly rising [2].

Vitamin D deficiency is prevalent in most parts of the world. Vitamin D exists in two forms: Ergocalciferol (D2) and cholecalciferol (D3) [3].

According to Vit. D serum level; It is considered Vit. D deficiency if it's less than 10 ng/ml, insufficient level if it's between 10-30 ng/ml , sufficient level if it's between 31-100 ng/ml, and toxic level if it is higher than 100 ng/ml [4].

Although vitamin D is traditionally associated with bone health because of its crucial role in bone and mineral metabolism [5], different non skeletal functions have been proposed for this critical vitamin. Recently, a much broader role has been implicated for this unique vitamin, owing to the presence of its receptor in different tissues, including cardiovascular organs. Atherosclerosis, as a hallmark of cardiovascular disorders, is a complex process that can progress for decades before presentation [6].

However, there's still remains insufficient evidence owing to controversial reports in the literature both in favor of [7] and against [8] this concept. However, genetic polymorphism of the vitamin D receptor could modify its role [9]. Thus, differences in ethnicity, life style and

geographic conditions could potentially change its effects.

Although coronary angiography is considered to be the gold standard method for the evaluation of coronary artery disease and its management, it is invasive. The noninvasive techniques, such as coronary CT angiography (CCTA), have been developed and are considered as important diagnostic tools for identifying patients with CAD, especially symptomatic patients . CCTA is also important in determining coronary artery calcium score (CACS) as well as determining the best management for patients with CAD. In addition to its advantages, CCTA has some limitations, including exposure to high doses of radiation and low sensitivity and specificity due to blooming artifacts caused mainly by the calcification of vessels (10 Sun Z)

The aim of this study is to assess the correlation between vitamin D level and coronary artery findings using MDCT.

METHODS

2.1. Patients

Two hundred and Fifty patients were included in our study that was held at the period from January 2017 to March 2019. They were 175 males (70%) and 75 females (30%), their age ranged from 42 to 69 years. The protocol for the CT exam and a Zagazig University Institutional Review Board (IRB) approved consent form was used in our study. Patients signed a printed informed consent and asked also to fill a written survey including demographic and clinical data.

The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration Helsinki) for studies involving humans.

All examined patients were referred to us from the cardiology outpatient clinics, Zagazig University hospitals.

The inclusion criteria included patients clinically suspicious of coronary artery disease, typical chest pain and those with abnormal stress ECG.

Patients with renal insufficiency presented with arrhythmia or underwent coronary stenting or bypass graft were excluded. Those regularly taking vitamin D were excluded as well.

All patients were subjected to the following:

A) Full clinical history including personal history (age, sex, occupation, residency and special habits as smoking).

B) Patients were asked to perform blood sampling for analysis of serum level of 25-hydroxyvitamin D (25(OH)D), that was measured using high-performance liquid chromatography.

C) All patients with suspicion of CAD (250 cases in our study) underwent MDCT coronary angiography, using Philips Ingenuity core 128 ™ (v3.5.7.25001, Philips healthcare systems, Netherlands) at radiology department, Zagazig University Hospital.

Patients were classified into four main groups according to the serum level of vitamin D as follows: Vitamin D deficiency (<10 ng/mL), insufficient level of vitamin D (10–30 ng/mL), sufficient level of vitamin D (31–100 ng/mL), and toxic level of vitamin D (>100 ng/mL).

2.2. Method of MDCT exam

Patient preparation

Patients were asked to fast 4-6 hours prior to the examination.

Beta Blockers: to reduce the heart rate (below 65 bpm), oral administration of a beta blocker (unless contraindicated, we used concor 5 mg) 1 hour before CT scanning was applied. The onset of action of is approximately 30 min.

Breath-hold Training : to improve the temporal resolution, patients were practiced to take deep breath then hold it for about 20 seconds in order to reduce the heart rate, as well as during the actual scan to reduce respiration motion artifact.

Positioning and ECG

The patients are asked to lie in a supine position on the CT table with elevation of the arms above the head. We put the three electrodes of the ECG leads along the right clavicle represents the right arm, along the left clavicle represents the left arm and the third one

inferior to nipple represents the lower limb. The electrodes are not included within the scan field to avoid artifacts.

Contrast Agent

Through 18 G cannula into the ante-cubital vein of the right upper limb the intra venous contrast was injected according to the patient weight we adjusted the contrast agent injection rate (usually 5-6 ml/sec) & the required amount of contrast (1-1.5 ml/kg, mean about 100 ml for an 80 kg body weight). First we inject contrast agent, then saline chaser (50 ml by the same flow rate of contrast injection) simultaneously, using a dual-syringe injector.

Nitroglycerin

Sublingual nitroglycerin administration was routine at all exams. Its action starts within ten to twenty seconds after its administration, and its effect lasts for ten to thirty minutes.

Planning the Scan

The scan range applied was started from the level of aortic knob down to the diaphragmatic copula to secure the vicinity of the inferior & posterior heart surface.

Starting the Scan

We used the following parameters: Detector collimation 16 x 0.75 mm, tube voltage 120-140 kV and tube current 600- 800mA, based upon the body mass index. Pitch of 0.2-0.3, rotation time 0.42 seconds, reconstruction slice width 0.6 mm and increment 0.5 mm.

First we apply a non contrast series to calculate the calcium score (using the Agatson's score)

We applied the bolus tracking technique. Simply it monitors contrast arrival and trigger the scan so long the pre-determined threshold achieved (180 HU). We put the ROI (region of interest) at the descending thoracic aorta just below the level of tracheal bifurcation. There is delay time of 6 seconds between the contrast arrival to the determined threshold and triggering the scan. We used a retrospective ECG gated coronary scan.

Image processing & reconstruction

All scans were reviewed and processed by two radiologists who are competent at cardiac imaging. Images were reconstructed at 0, 30, 35, 40, 50, 70, 75, 80, 85 & 90 of the R–R interval of the cardiac cycle. The images were then post-processed using the Philips Extended intellispace™ portal Workstation. Multiple reformations multi-planner reformation (MPR), curved planar reformation (CPR), maximum intensity projection (MIP), and volume rendering (VR) to delineate the coronary arteries, cardiac and extra cardiac changes.

Using the Agatston scoring method (Smart Score software). The coronary artery calcium score (CACS) was measured and recorded for each patient. Patients were classified into five groups depending on their scores as follows: normal (CACS =0), minimal (CACS =1–10), mild (CACS =11–100), moderate (CACS =101–400), and severe (CACS >400). This follow Rumberger's guidelines (11).

The presence and the degree of Coronary artery stenosis were measured as the ratio of the luminal diameter of the most stenotic segment over that of the unaffected distal portion, and the ratio is considered as significant stenosis if it was 50% or more. Accordingly, patients were categorized into five groups: normal (no plaque), non-significant (presence of plaque with <50% stenosis), single-vessel disorder where there was a significant plaque in one of the major coronary arteries, double-vessel disorder where there was a significant plaque in two of the major coronary arteries, and triple-vessel disorder where there was a significant plaque in three major coronary arteries. We also classified patients into 2 main groups, the "negative for CAD" group (include normal and non-significant CAD affection) and "positive for CAD" (include patients with SVD, DVD, and TVD).

Statistical Analysis

The findings of CT imaging studies were evaluated and correlated to the serum vitamin D levels. Quantitative variables and qualitative variables were expressed as mean $\pm$ standard deviation and proportions were expressed as percentages. Sensitivity, specificity and diagnostic accuracy were calculated. All data manipulation and analysis were performed

using the 20th version of SPSS (Statistical Package for Social Sciences).

RESULTS

This study included 250 patients; all of them have clinical suspicion of coronary artery disease (CAD). Most of them (79.2 %) presented by chest pain (n= 198). The mean age was 55.5 ± 2.5 years (range 42-69 years). 70% (n=175) were males, 30% were females (n=75). 80 % (n= 200) were smokers. 15.2 % (n=38) had a positive family history of CAD in first-degree relatives (Table 1).

Regarding our MDCT findings; we found 54 patients (21.6 %) had normal CTA, 82 patients (32.8%) had non-significant findings; 11.2% (n=28) had single-vessel disease (SVD); 9.6% (n=24) had double-vessel disease (DVD); and 24.8% (n=62) had triple-vessel disease (TVD).

The patients were divided into two groups: group 1 "negative for CAD" (n=136, 54.4%) and group 2 "positive for CAD" (n=114, 45.6%). Group 2 comprised more males and more smokers (P=0.005). Those with negative family history were more prevalent in negative CAD group 2. By using the Agatson's score for coronary arterial calcium load calculation burden, We found that the mean calcium score in our examined patients was 382.45 ± 47.5. Patient were classified into 5 groups according to Ca scoring. 21 patients had normal Ca score representing 8.4 %, 16 patients had minimal Ca score representing 6.4 %, 49 patients had mild Ca score representing 19.6 %, 77 patients had moderate Ca score representing 30.8 % and lastly 87 patients had severe Ca score representing 34.8 % (table 2). As expected, the mean calcium score increased in patients with severe coronary artery diseases (P<0.001), and the results of this work showed significant negative correlation between serum vitamin D levels and coronary artery calcium score (CACS) with P<0.005 (Fig 1). The mean vitamin D serum level was 25.3±5.2 ng/dL. Regarding the vitamin D serum levels, 10 patients (4%) had vitamin D deficiency, 110 patients (44 %) had insufficient levels of vitamin D, 130 patients (52%) had sufficient vitamin D level and No cases presented by toxic levels. The mean serum vitamin D level declined remarkably (P<0.005) as the severity of CAD increased (from normal to non-significant status, to single-, double- and triple-vessel stenosis in an ascending manner). The mean value of vitamin D level in blood in the "positive group that had CAD" was 20.1 ng/mL, a value that was significantly lower than that (29.7 ng/mL) in the "negative group for CAD" (P<0.001). The odds ratios for smoker males and calcium score were 3.2 (P=0.001), 3.5 (P=0.001) and 1.02 (P<0.001), respectively. According to this analysis, vitamin D levels play a significant role in modifying the risk of coronary artery affection (fig. 2).

Table 1. sex and age groups among the study participants.

Age group.	Male patient	Female patient	total
40 -<50 year	52	9	61 (24.4%)
50-<-60 year	56	21	77 (30.8%)
>60 year	67	45	112(44.8%)
total	**175 (70%)**	**75(30%)**	**250**

Table 2. Serum vitamin D level and coronary artery calcium scoring in cases with different severity of coronary artery disease.

		Coronary artery disease cases : number (%)				
		normal	**Non significant**	**Single vessel**	**double vessels**	**triple vessels**
Vit D level	**Mean±SD (ng/ml)**	**31.6±18.3**	**28.5±15.3**	**24.2±11.4**	**19.6±7.5**	**18.6±7.2**
	Deficinecy	**0(0)**	**1(1.2%)**	**2(7.1%)**	**1(4.2%)**	**6(9.7%)**
	insufficiency	**22(40.7%)**	**21(25.6%)**	**15(53.6%)**	**16(66.6%)**	**36 (58.1%)**
	sufficiency	**32(59.3%)**	**60(73.2%)**	**11(39.3%)**	**7(29.2)**	**20(32.2%)**
Calcium scoring	**Mean±SD**	**14.8±11**	**168.9±21**	**368.76±112**	**815.9±112**	**823.5±83**
	Normal	**12 (22.2%)**	**6 (7.3%)**	**2 (7.1%)**	**1(4.2%)**	**0 (0%)**
	Minimal	**9 (16.7%)**	**5 (6.1%)**	**1(3.6%)**	**1 (4.2%)**	**0(0%)**
	Mild	**21 (38.9%)**	**18 (22%)**	**6 (21.4%)**	**2 (8.3%)**	**2 (3.2%)**
	Moderate	**8 (14.8)**	**38 (46.3%)**	**7 (25%)**	**8 (33.3 %)**	**16 (25.8%)**
	Severe	**4 (7.4%)**	**15 (18.3%)**	**12 (42.9%)**	**12 (50%)**	**44 (71%)**

Table 3. Patients groups according to MDCT findings.

		Number of cases	**Percentage**
Negative CAD group	Normal CTA	54	21.6%
	Non significant findings	82	32.8%
Positive CAD group	Single vessel disease	28	11.2%
	Double vessels disease	**24**	**9.6%**
	Triple vessels disease	**62**	**24.8%**

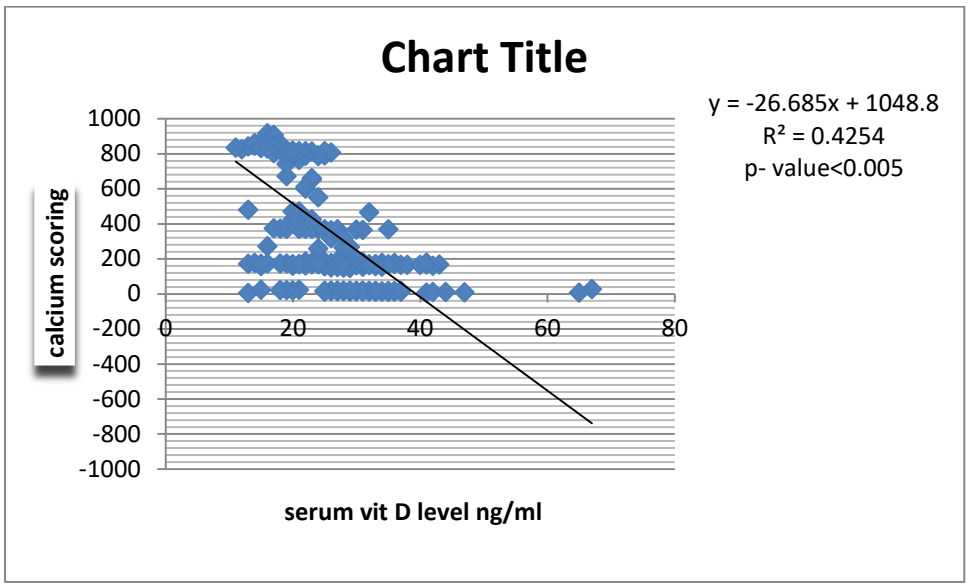

Figure 1. Spearman correlation between serum levels of vitamin D and the coronary artery calcium score.

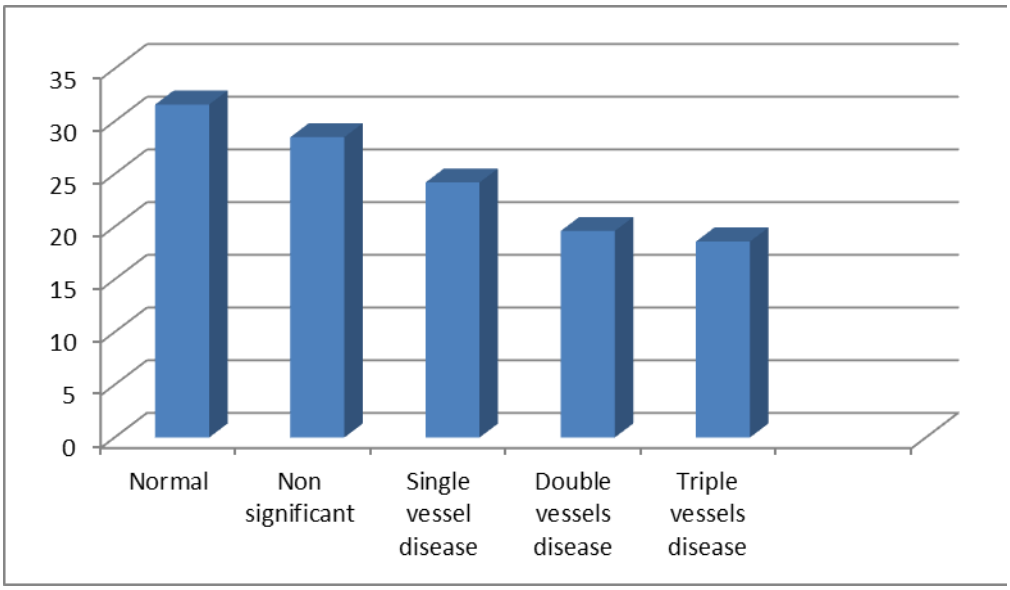

Fig. 2. Bar chart: Relation between vitamin D level and the severity of coronary artery disease. (Vertical bar: Mean vit D in ng/ml).

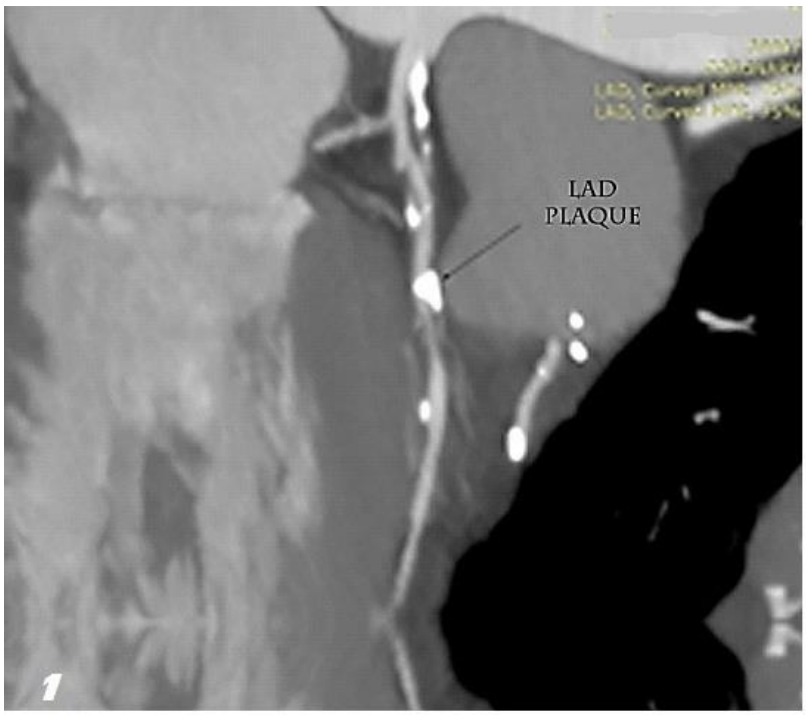

Fig. 3. Case no. 1 A heavy smoker 55 years old male presented with chest pain. CT coronary angiography multiplanar reformatted (MPR) image shows extensive calcified plaques (non ulcerating) along the whole length of the left anterior descending artery (LAD), of variable length & exerting different significant lesions of different grades of stenosis, the worst is at its mid portion (black arrow). His Calcium score= 645 and Vitamin D level= 12ng/dl (Insufficient).

Fig. 4. Case no. 2, A 40 years old female who was referred for atypical chest pain & equivocal stress ECG result. CT coronary angiography multiplanar reformatted (MPR) image shows small calcified plaque at the left anterior descending artery (LAD), at the level of the 1st diagnoal artery of very small length= 2 mm & exerting non significant stenosis (black arrow). Her Calcium score= 45 and Vitamin D level= 22 ng/dl (Sufficient).

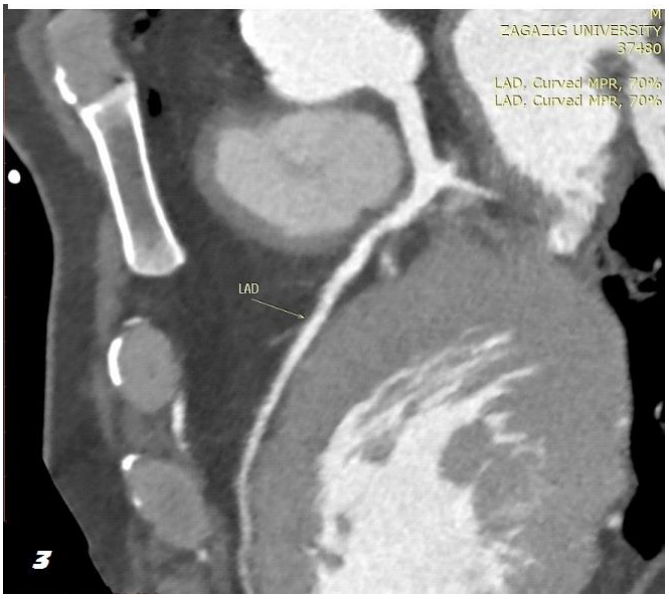

Fig.5. Case no. 3, A 35 years old female who was referred for chest tightness & equivocal stress ECG result. CT coronary angiography multiplanar reformatted (MPR) image shows patent lumen of the whole length left anterior descending artery (LAD), no plaques nor stenosis noted (Green arrow). Her Calcium score= 0 and Vitamin D level= 29 ng/dl (Sufficient).

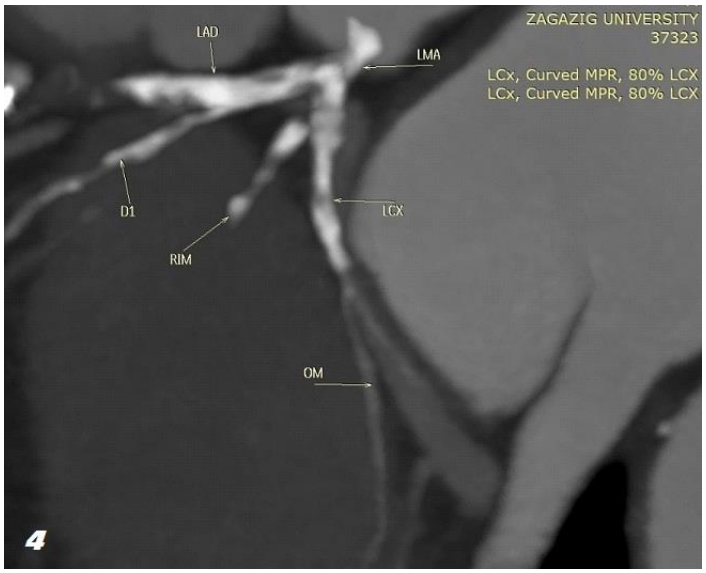

Fig. 6. Case no. 4, A heavy smoker 62 years old male presented with chest pain. Echocardiography shows extensive myocardial infarction (MI) with low ejection fraction (EF)= 35 %. CT coronary angiography multiplanar reformatted (MPR) image shows extensive calcified plaques (non ulcerating) along the whole length of the left main coronary artery (LMA), left anterior descending artery (LAD), 1st diagonal branch, ramus intermedius variant and left circumflex artery (LCX) with non-opacified distal circulation including obtuse marginal (OM) branch of the LCX (green arrows). His Calcium score= 1035 and Vitamin D level= 9 ng/dl (Deficient).

DISCUSSION

Vitamin D deficiency is an important worldwide health problem that affects many developing countries [12].

Vitamin D is a hormone precursor. Its mature form is 1,25-Dihydroxyvitamin D and it helps in regulation of mineral haemostasis [13].

Most of the tissues have its receptors including heart muscle. Vitamin D plays an important roles in muscle and immune system physiology and in the process of inflammation and cell proliferation [14].

In this study, Only 10 patients (4%) had vitamin D deficiency (<10 ng/mL), 44 % (n=110) had insufficient levels of vitamin D (10-20 ng/mL), and 52 % (n=130) have sufficient vitamin D level (20-100 ng/mL). No cases presented by toxic levels.

We divided the patients into two main groups: group 1 "negative for CAD" (n=136, 54.4%) and group 2 "positive for CAD" (n=114, 45.6%).

We found that smoker males are significantly more dominant into group II than group I (P=0.005). Negative family history was more prevalent in group I (Negative CAD), but such difference was non-significant (P=0.1).

In our study, the mean calcium score among participants was 382.45 ± 47.5 and the patients were classified as normal, minimal, mild, moderate and severe calcium scores.

We found that the mean calcium score was significantly higher in patients with severe CAD (P<0.001).This was in agreement with Moradi M et al [15]. Also Almasi et al evaluated the value of CACS for predicting the presence and severity of CAD among 202 patients. Their findings confirmed the association between CACS and CAD occurrence as well as its severity [16, 17].

In our study the mean vitamin D serum level was 25.3±5.2 ng/dL.

We found significant negative correlation between serum vitamin D levels and coronary artery calcium score (CACS) with P=0.005.

Conversely, the mean CACS was significantly higher in patients with vitamin D deficiency comparing with those who had sufficient or insufficient vitamin D level (P<0.001).

This was in agreement with Moradi and Foroutanfar, who found a significant relationship between increased CACS and the severity of vitamin D abnormalities (deficiency or insufficiency)[18].

In our study there was significant relation between the deficiency of vitamin D and the severity of CAD, as the mean serum vitamin D level in the first group "positive for CAD" was 20.1 ng/mL, which was significantly lower than its value (29.7 ng/mL) in the second group "negative for CAD" (P<0.001).

Mahdavi et al also found a considerably high prevalence of vitamin D deficiency in patients with acute coronary syndrome [19].

This was in agreement with Moradi and Foroutanfar who found that the serum vitamin D level in the "positive for CAD" group was 20.98 ng/mL, a value that was significantly lower than that (30.47 ng/mL) in the "negative for CAD" group (P<0.001) [19]. This relation can be explained by the relation of CACS and plaque burden of the coronary arteries.

However, these results are contrary to those of Ho et al [20] , we thought that this disparity was found because of the differences in both geographic location and ethnicity, as well as a lower CAD prevalence and the lack of female participants.

Vitamin D receptors can be found in most tissues including heart muscle. It has some important roles in maintaining normal function of muscles and controlling the inflammatory process and immune system [21].

Another explanation of the relation of vitamin D deficiency and CAD can be the vitamin D deficiency associated abnormalities such as metabolic syndrome, obesity, insulin resistance, diabetes, hypertension and hyperlipidemia, which all have significant relationship with cardiovascular abnormalities [6,20,22,23].

The pathophysiology of these relationships between vitamin D and cardiovascular disorders can be explained by the role of vitamin D in regulating the renin-angiotensin

axis by suppressing the expression of renin gene. So vitamin D deficiency may be associated with hyperactivity of the renin-angiotensin aldosterone system with subsequent cardiovascular abnormalities [24].

Vitamin D affects the modulation of smooth muscle cell proliferation, as well as inflammation, and thrombosis. Vitamin D deficiency can lead to 2ry hyperparathyroidism with subsequent myocyte hypertrophy and vascular remodeling [25].

Also vitamin D deficiency can lead to inflammation of epicardial adipose tissue, which has a role in the pathogenesis of CAD. [26].

Also it inhibits vascular calcification, improves endothelial function and has anti-atherosclerotic effects. In addition, vitamin D is a coronary artery disease risk factor modulator [27].

There are some limitations of this study. We only had single vitamin D level report of each patient and could not follow its level during long period of time. CAD is chronic disease and requires long duration to develop. Another limitation is the seasonal variation of vitamin D which may affect the result.

CONCLUSION

Serum Vitamin D level plays an important non negligible role in assessing the risk of coronary artery affection.

Recommendation:

it is advised that people with risk of coronary artery disease either due to family history and other risk factor undergo regular follow up of serum vitamin D level to avoid vid D deficiency which can be another risk factor. It those people, vitamin D level should be kept normal by medication of healthy diet.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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