

Vitamin D deficiency and coronary artery disease

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BACKGROUND: Several factors such as hyperlipidemia, diabetes and hypertension have a determining role in cardiovascular disease. In recent years, the effect of vitamin D deficiency on cardiovascular disease has been emphasized. This study compares vitamin D deficiency in coronary heart disease patients with the control group. **METHODS:** In a cross-sectional study, 25-hydroxycholecalciferol level was compared in 119 individuals including 57 people with confirmed coronary heart disease and 62 healthy people. 25-hydroxyvitamin D [25(OH)D] was assessed using standard protocol. The level of 25(OH)D under 20 ng/dl was determined as cutoff point. **RESULTS:** The calculated odds ratio was 3.9 (95% confidence interval 2.6-5.5). Vitamin D deficiency significantly different between patients and the control group ($p = 0.01$). Of 37 (31%) individuals having vitamin D deficiency, 36 (97.3%) had coronary artery disease and from 57 patients with coronary artery disease 36 (63.2%) had vitamin D deficiency. **CONCLUSIONS:** Vitamin D deficiency is a relatively common disorder. Risk of cardiovascular disease in people with vitamin D deficiency is almost four times of those with normal levels of vitamin D. To confirm the casual relationship between vitamin D and cardiovascular disease, clinical trial studies are suggested.

KEYWORDS: Coronary Artery Disease, Cardiovascular Disease, Vitamin D Deficiency

BACKGROUND

Cardiovascular disease is one of the main causes of disability and death across the world.^[1] Animal studies and clinical observation in the first half of twentieth century showed the relationship between risk factors such as hypercholesterolemia with the risk of cardiovascular events. Framingham prospective study presented strong evidence for the role of such factors on coronary artery disease.^[2] The casual relation of lipid disorders to cardiovascular disease has been proved.^[3] Diabetes is a cardiac heart disease equivalent.^[4] Some of the studies have demonstrated the association between male sex, postmenopausal period, disorders of coagulation, homocystein abnormalities, and risk of coronary artery disease.^[5-8]

Previous epidemiological studies suggested that 25(OH)D deficiency or insufficiency play a role in myocardial infarction, heart failure, diabetic cardiovascular disease and peripheral vascular disease. The rate of cardiovascular complications such as death from MI or heart failure were 53% to 80% higher in individuals with vitamin D deficiency that were followed for about four to five years.^[9] Fur-

thermore, recent studies suggested that the mean serum level of 25(OH)D has a reverse association with blood pressure, diabetes, carotid atherosclerosis, microalbuminuria, stroke and decreased renal function.^[10-13] A multicenter study conducted on 5232 individuals in different parts of Iran showed that vitamin D deficiency is a common disorder. Tehran had the highest rate and Mashhad and Boushehr the lowest rate of vitamin D deficiency.^[14-18]

Given the high prevalence of vitamin D deficiency in Iran and its possible association with heart disease, the relationship between vitamin D deficiency and coronary artery disease were evaluated.

METHODS

This cross-sectional study was conducted in Isfahan from March 2010 to March 2011.

The cases were individuals over 40 years with angina pectoris that were admitted to Khorshid hospital in Isfahan, Iran. Their disease was confirmed by clinical and paraclinical methods.

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The control group was selected from the family or the friends of the patients. Their age and sex were matched and did not have any cardiovascular disease in clinical evaluation. Individuals with chronic renal disease were not entered to the study.

The sampling method was convenient non probability method and the sample size was 62 in each group. Data collection methods were checklist and questionnaire. Each individual that participated in the study was questioned by the researcher and then weight, height and blood pressure were measured according to the standard protocol and then the checklist was completed. BMI was calculated as weight/height² and individuals with a BMI over 30 were considered obese. Also a rapid assessment questionnaire for the measurement of physical activity was used. The physical activity was divided in three levels and the individuals were categorized into five levels according to their physical activity.

After obtaining written consent from the participants (according to the declaration of Helsinki), a 2.5 cc blood sample were taken from each individual after 8 hours of fasting and collected in a plastic tube and were kept in -20°C in the laboratory freezer. Then, the levels of 25(OH)D in the serum of each sample was determined. The level of fasting blood sugar and cholesterol was also measured. Cholesterol levels of more than 240 mg/dl was considered high.^[13] Serum levels of 25(OH)D less than 20 ng/ml was defined as deficient, 21-29 ng/ml as inadequate and 30ng/ml or more was defined as optimal.^[12]

Data analysis was performed by SPSS statistical package version 19 (SPSS Inc., Chicago, IL, USA). Independent t-test, chi-square test and logistic regression were used. P-value < 0.05 was considered statistically significant.

RESULTS

The patient group and their control did not show significant difference in terms of sex ($p > 0.05$). Distribution of vitamin D deficiency among men and women also showed no significant difference ($p > 0.05$). Among the participants, 30 (81%) of individuals with vitamin D deficiency had primary school education. Distribution of educational level was different between patients and the control group. Among 57 patients, 44 (86%) had primary school education, 6 (10.5%) had secondary school education and 2 (3.5%) had college education. In the control group 6.5% had collage edu-

cation and 33.9% had primary school education ($p < 0.05$, $df = 2$, $\chi^2 = 34$).

Smokers were 15 (26.3%) in the patients group and 10 (16.1%) in the control group ($p < 0.05$, $\chi^2 = 6.9$, $df = 2$). Of the people with vitamin D deficiency, 32% were smokers and 10% were past smokers. In individuals with normal vitamin D, 15% were smokers and non of them were past smokers ($p < 0.05$). Of the patients, 7 (12.3%) were obese but in the control group, none of the participants were obese ($p < 0.05$).

The number of people that had a high cholesterol level or used antilipid drugs were 39 (68.4%) and 18 (29%) in the patients and the control group, respectively. The anthropometric and biochemical variables of the studied individuals are presented in table 1. Of the control group, 16 (25%) of the individuals used antihypertensive drugs while in the patients this was 57.9% ($p < 0.05$). The use of antidiabetic drugs in the patients and the control group were 38.6% and 19.6%, respectively ($p < 0.05$).

The odds ratio was estimated for the patients and it was 3.9 (95%CI: 2.6-5.5). Comparison of vitamin D deficiency in patients and the control group showed statistically significant difference ($p < 0.01$, $df = 1$, $\chi^2 = 52.5$). Of 37 (31%) individuals having vitamin D deficiency, 36 (97.3%) had coronary artery disease and from 57 patients with coronary artery disease, 36 (63.2%) had vitamin D deficiency.

The comparison of vitamin D deficiency in the patient and control groups is presented in figure 1. Frequency of vitamin D deficiency was 45 times more than the control group.

DISCUSSION

The results of this study showed that there is a close relationship between serum vitamin D and cardiovascular disease. Coronary artery disease is more prevalent in individuals with vitamin D deficiency than those with normal levels of vitamin D.

The present study showed that the chance of having coronary artery disease in patients with vitamin D deficiency is nearly four times than the people with normal levels of vitamin D.

In a research conducted by Thomas on the survivors of the Framingham study, the risk of cardiovascular disease was estimated 1.62.^[19,20] The findings of both of the

| | Group | mean | SD | P-value |
|---------------------------------|---------|-------|------|-----------------|
| Age (years) | Patient | 58.7 | 10.8 | NS ^f |
| | Control | 60.5 | 9.6 | |
| Systolic blood pressure (mmHg) | Patient | 135. | 23.1 | S |
| | Control | 125.6 | 15.6 | |
| Diastolic blood pressure (mmHg) | Patient | 81.2 | 8. | NS |
| | Control | 80.6 | 8.6 | |
| Physical activity | Patient | 2.7 | 1.3 | S ^{tt} |
| | Control | 3.2 | .68 | |
| Fasting blood sugar (mg/dl) | Patient | 125.9 | 62.6 | S [†] |
| | Control | 104.6 | 30.7 | |
| Vitamin D (ng/ml) | Patient | 58.7 | 39.6 | S ^{tt} |
| | Control | 79.9 | 18.9 | |

f: non-significant, †: significant at 0.05 level, ‡: significant at 0.001 level

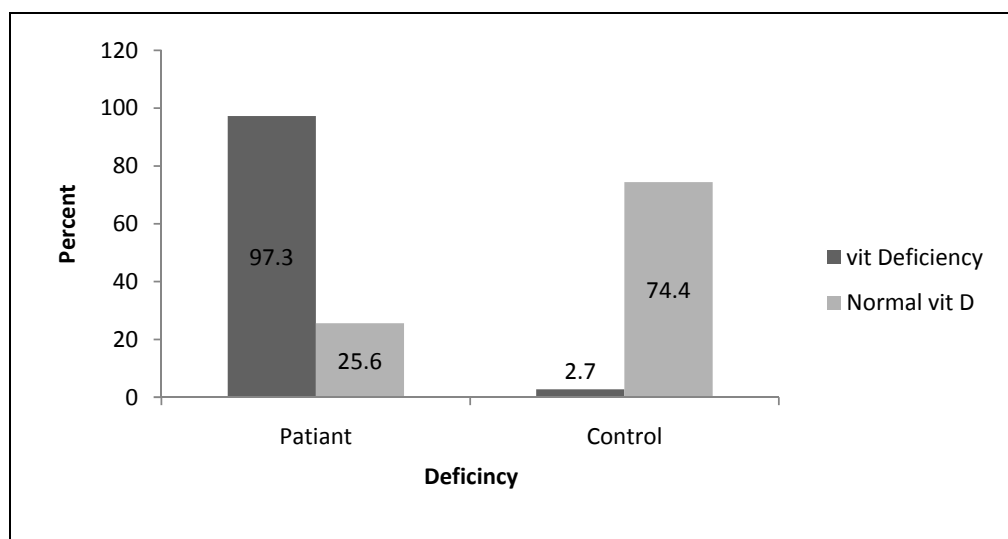


Figure 1. The prevalence of vitamin D deficiency in the patient and control group

studies suggested that vitamin D deficiency can be associated with a high risk of cardiovascular disease. Our study revealed that vitamin D deficiency is relatively common and about one third of the studied subjects and two third of the patients were vitamin D deficient. In the survivors of the Framingham study, the prevalence of vitamin D deficiency was reported 28%.^[19] However, in this study blood levels of less than 20 ng/dl was considered as cutoff point and it is expected that in lower cutoff points the sensitivity of the test is higher. It seems that in Isfahan, vitamin D deficiency is prevalent and this is probably due to lifestyle and nutrition.

Several mechanisms may explain the association between vitamin D and cardiovascular disease. Decholecalciferol regulates renin-angiotensin axis through the suppression of the rennin gene. Changes of 25-hydroxycholecalciferol causes changes in the smooth

muscle of the vascular wall and also inflammation and thrombosis and that could explain cardiovascular complications.^[21,22]

Our study demonstrated that individuals with vitamin D deficiency had lower educational levels and the percentage of smoking in this group was higher than the group with normal levels of vitamin D. A study conducted in Finland and Denmark also confirmed the above findings. The percentage of smoking in people with vitamin D deficiency was more than normal people.

In Thomas study smoking in people with vitamin D deficiency was higher than normal subjects (17% vs. 12%).^[19,23]

In conclusion, vitamin D deficiency is a relatively common disorder. Risk of cardiovascular disease in

people with vitamin D deficiency was almost four times of those with normal levels of vitamin D. To confirm the casual relationship between vitamin D and cardiovascular disease, clinical trial studies are suggested.

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