RELATIONSHIP BETWEEN CORONARY ARTERY DISEASE AND SERUM VITAMIN D LEVEL IN A GROUP OF POSTMENOPAUSAL WOMEN IN IRAN

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Abstract

INTRODUCTION: Female carpet-weavers are vulnerable to vitamin D deficiency due to cultural, occupational and economic reasons. This case-control study was conducted to compare the frequency coronary artery disease (CAD) and its risk factors in relation with the serum vitamin D level in 260 female carpet-wearers and non-carpet-weavers in the villages across Isfahan Province in the centre of Iran.

METHODS: All postmenopausal women aged over 50 were matched for cultural and socioeconomic status. The participants underwent clinical examinations. Blood samples were obtained and electrocardiography was performed. When necessary, echocardiography and exercise test were also administered to diagnose heart disease. Dietary intake of vitamin D was determined by completing a semi-quantitative food frequency questionnaire. A questionnaire obtaining personal data and length of daily exposure to sunlight was also completed. The existence of CAD was determined using standardized WHO Rose questionnaire and/or the Minnesota electrocardiography coding system. Blood lipids and vitamin D levels were measured using an ELAN-2000 auto analyzer and radioimmunoassay, respectively.

RESULTS: The results showed that only the frequency percentage of myocardial infarction (MI) in non-carpet-weavers was significantly higher than in female carpet weavers ($P=0.001$). The differences of age, serum vitamin D level, blood lipids, blood pressure and other variables were not significant ($P>0.05$). Neither was there any statistical association between serum vitamin D level and CAD risk factors, however, after adjustment for confounders (age, etc.), a direct relationship was observed between abdominal obesity as measured by waist-to-hip ratio (WHR) ($WHR>1$) and serum vitamin D level ($OR=0.99$, $P>0.05$). Carpet weaving had no effect on CAD risk factors ($P>0.05$).

CONCLUSION: The findings of this study reveal no association between vitamin D and CAD. Further research is recommended into the possible relationship between CAD and vitamin D, as well as vitamin D receptor (VDR) gene polymorphisms responsible for genetic differences in vitamin D uptake by the bone.

Keywords: Vitamin D, carpet-weaver women, coronary artery disease (CAD), risk factors, postmenopause, angina pectoris, ischemia, blood lipids, blood pressure, Iran.

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Introduction

The prevalence of cardiovascular diseases (CVD) and their associated mortality, [1, 2] are increasing at alarming rates. There have been suggestions of a possible relationship between the effect of vitamin D and CVD.

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Vitamin D deficiency and high mortality due to CAD in the winter,[3] and also high mortality rates from myocardial infraction in some countries with low intake of vitamin D have led to the hypothesis of the relation between vitamin D and CAD.[4,5] An indirect link between vitamin D and CAD risk factors has also been suggested. Many studies have been done on the relationship between vitamin D and CAD risk factors in various groups, but different results have been obtained.[6-9]

In rural areas of Iran, women are major contributors to families' economy. Hence, their health has inevitable effects on the community. In small and remote villages, most women spend long hours daily in carpet weaving factories with very little sunlight in sitting position, and as in other studies[10] a high prevalence of osteomalacia has been reported among this group of women.[11] These women are also at higher risk of CAD after menopause.

We studied the relationship between vitamin D and CAD risk factors in postmenopausal women living in small remote villages of Isfahan Province (Iran).

Materials and Methods

This study was performed on 460 postmenopausal women from small remote villages of Isfahan Province who enjoyed low socioeconomic and educational levels. Nearly half of the subjects were carpet weavers and the rest were housewives. We studied women who had worked continuously in a traditional carpet-weaving factory for at least 1 year and had been exposed to sunlight for a maximum of 1 hour daily.

The women were invited by Behvarzes (rural community health workers) already briefed about the study, to attend an orientation session. The women were examined by a general physician in the rural Health House.

Rose and general questionnaires were completed for the women by the general physician. A technician conducted 12-lead electrocardiography for all of the subjects. Special cases were examined by a cardiologist at the Isfahan Cardiovascular Research Center (ICRC). When necessary, echocardiography (2D color Doppler) and/or exercise test (according to Bruce protocol) were also conducted.

Seca instruments were used to measure weight and height of women barefoot in light clothes. Waist and hip circumferences were also measured.

Blood pressure was measured on the right arm in sitting position after at least 5 minutes of rest using a random zero mercury sphygmomanometer; the average of two readings measured 5 minutes apart was recorded.

Fasting blood samples were taken from the subjects in the rural Health Houses and vitamin D and blood lipids were measured at ICRC laboratory.

Blood lipids were analyzed using an ELAN 2000 auto autonalyzer (Eppendorf, Germany), and the radioimmunoassay method was used to measure vitamin D, using kits from IDS, England (Gamma-B1, 25-dihydroxy vitamin D). A semi-quantitative food frequency questionnaire was also completed for each subject and vitamin D intake was calculated.

SPSS package (version 10) was used for statistical analysis of the data. Independent t test, logistic regression and correlation analysis tests were used.

Results

Mean age, serum vitamin D level and CAD risk factors in the studied population are been presented in Table 1.

TABLE 1. Mean value of CAD risk factors among studied population

Factors	Mean ± SD
Total cholesterol (mg/dl)	228.4±38.4
Triglycerides (mg/dl)	216.6±89.5
LDL-cholesterol (mg/dl)	144.7±35.9
HDL- cholesterol (mg/dl)	40.1±20.5
BMI*(Kg/m2)	25.4±4.5
Age (yr)	55.5±4.5
Systolic blood pressure (mmHg)	131.9±23.8
Diastolic blood pressure (mmHg)	86.4±27.5
Education (yr)	3.0±1.7
WHR**	2.4±9.5

*BMI: Body mass index
**WHR: Waist to hip ratio

Table 2 shows the relation between vitamin D and some of the CAD risk factors in the studied population. There was no significant relation between these risk factors and vitamin D (P>0.05).

According to the data in Table 3, age was the only significant difference between female carpet weavers and non-carpet weavers (52.9±7.6 years in the case group vs. 59.0±7.5 years in the control group, P=0.000).

No significant association was found between vitamin D levels and CAD risk factors in carpet weavers and non-carpet weavers (Table 4). Further analysis of the data revealed a significant relationship between physical activity and the level of serum vitamin D (r = -0.16, P<0.05).

TABLE 2. The relationship of CAD risk factors and vitamin D after the adjusting for age and other risk factors

Risk factors	Adj OR+	95% CI	P*
CAD (coronary artery disease)	1.00	0.99, 1.007	0.48
Hypercholesterolemia	1.002	0.99, 1.008	0.62
Hypertriglyceridemia	0.99	0.00, 1.003	0.99
High LDL cholesterol	1.00	0.99, 1.003	0.93
Low HDL cholesterol	1.00	0.99, 1.006	0.40
Hypertension	0.99	0.99, 1.003	0.57
BMI** ≥ 25	0.99	0.99, 1.004	0.75
WHR*** ≥ 1	0.99	0.99, 1.005	0.70

* Logistic regression
** BMI: Body mass index
*** WHR: Waist to hip ratio
+ Adjusted Odd's Ratio

TABLE 3. Basic characteristics among carpet-weaver and non carpet-weaver women in Iran, 2000

Factors	Carpet-weavers Mean ± SD	Non Carpet-weavers Mean ± SD	95%CI	P*
Vitamin D (pmol/1)	137.9±67.1	148.7±116.6	(-37.2,15.7)	0.42
Total cholesterol (mg/dl)	234.6±43.3	234.3±45.9	(-11.6,12.2)	0.37
Triglycerides (mg/dl)	233.6±124.6	215.3±103.0	(-12.1,48.4)	0.24
LDL-cholesterol (mg/dl)	149±39.7	149.0±43.1	(-11.2,11.4)	0.99
HDL- cholesterol (mg/dl)	39.8±8.7	41.8±9.5	(-4.5,0.4)	0.10
Age (yr)	52.9±7.6	59.0±7.5	(-7.9,-4.3)	0.00
Systolic blood pressure (mmHg)	129.2±21.2	132.3±21.8	(-8.4,2.3)	0.26
Diastolic blood pressure (mmHg)	84.8±14.4	86.0±15.2	(-4.8,2.5)	0.51
Education (yr)	3.0±1.3	3.0±2.8	(-25.9,25.9)	1.0
BMI** (Kg/m2)	25.4±6.3	25.7±6.0	(-1.8,1.3)	0.67
WHR***	0.93±0.12	1.4±5.5	(-1.5,0.52)	0.34

*P value of independent t test
** BMI: Body mass index
*** WHR: Waist to hip ratio

TABLE 4. The relationship of vitamin D and some risk factors of coronary artery disease in carpet-weaver and non carpet-weaver women

Factors	Carpet weavers			Non-carpet weavers		
	B	95% CI	P	B	95% CI	P
Total cholesterol (mg/dl)	-0.05	-0.19,0.10	0.50	-0.003	-0.14,0.14	0.97
Triglycerides (mg/dl)	-0.02	-0.68,0.18	0.25	-0.13	-0.47,0.21	0.44
LDL-cholesterol (mg/dl)	-0.02	-0.15,0.12	0.80	0.02	-0.12,0.17	0.76
HDL- cholesterol (mg/dl)	0.004	-0.02,0.04	0.78	-0.01	-0.03,0.02	0.48
BMI* (Kg/m2)	-0.003	-0.25,0.02	0.77	-0.001	-0.21,0.02	0.90
WHR**	-0.0001	-0.0005,0.0002	0.40	-0.01	-0.03,0.01	0.24
Systolic blood pressure (mmHg)	-0.01	-0.08,0.06	0.71	0.01	-0.05,0.08	0.74
Diastolic blood pressure (mmHg)	-0.001	-0.05,0.05	0.96	0.01	-0.03,0.05	0.65
Smoking	0.014	-0.72,80.7	0.91	-0.11	-5.41,1.95	0.34

* BMI: Body mass index
** WHR: Waist to hip ratio

Vitamin D intake was not significantly different between the two groups, and none of the subjects were taking vitamin D supplements.

Discussion

Although non-carpet-weavers enjoyed greater exposure to sunlight, their serum vitamin D levels were not significantly different from those of carpet weavers. This can be explained by the women's cover, which blocks exposure to UV. The two groups had similar dietary vitamin D intakes.

There is no relationship between serum vitamin D level and blood lipids in Iranian rural postmenopausal women. Vitamin D3 is used extensively in the prevention of osteoporosis in postmenopausal women, but the effect of the vitamin on serum lipids has not been clearly shown.[12] It seems that a reduction of vitamin D, a fat-soluble vitamin, may have destructive effects on lipid metabolism.[13] Other studies have shown a negative effect of the vitamin on the blood lipid profile through increasing LDL-C serum level.[7,8]

The investigators are of the opinion that vitamin D3 may exhibit an in vivo anti-oxidant property in the liver, being more effective than vitamin E.[14] Bondar et al. showed that the presence of vitamin D3 in lipids can influence the delayed phase behavior of lipids and at the same time have a definite effect on the function of lipids and blood vessel walls.[15]

Based on the literature, it can be concluded that dietary vitamin D has undesirable effects on the blood lipid profile, while vitamin D synthesized under the skin under the influence of sunlight has no such undesirable effects. Our findings also showed that dietary vitamin D intake of the subjects is negligible and its main source is the sunlight.

Reports in the literature during the past decade have showed that vitamin D probably has a role in blood pressure regulation.[9] Also, serum calcium relates positively and highly significantly to blood pressure.[16] However, a study on this subject in postmenopausal women[17] revealed no statistically significant association between serum vitamin D and blood pressure. Kristal-Bonen could not find any association between calcitriol and blood pressure in postmenopausal hypertensive and normotensive women.[9] It is said that the serum levels of 1,25-dihydroxy- vitamin D in postmenopausal women are not different from that in premenopausal women.[18] There is evidence that before the age of 75 years, age has no appreciable reducing effect on 25-hydroxy, 1,25- dihydroxy or 24,25-dihydroxy forms of the vitamin.[19] Therefore, other factors and mechanisms related to menopause must be involved. Several mechanisms in connection with the effect of calcitriol on blood pressure are likely at play. For example, it is known that parathyroid hormone (PTH) plays a part in the regulation of blood pressure,[9,18,20-22] and that there are receptors on the parathyroid gland for calcitriol.[23] Calcitriol prevents excretion of PTH in vitro,[24] which means that it may have an indirect effect on blood pressure through reducing circulating levels of PTH.[21] Kristal-Bonen, however, found no association between PTH and blood pressure[9] (we did not measure PTH in the present study). Some investigators believe that calcitriol is a hypertensive agent and that dietary calcium supplements may bring about a reduction in blood pressure through reducing calcitriol levels.[13, 25]

Some investigators have reported lesions in the aorta and coronary arteries in animals fed cholesterol and vitamin D2. High blood levels of these 2 compounds led to accumulation of calcium and lesions resulting from cholesterol accumulation in the vessels. Such lesions were not observed in mice fed only cholesterol.[26,27] According to Beckman et al. report, limiting dietary calcium and increasing vitamin D3 causes a reduced effect of PTH on 25-0H-D-lα-hydroxylase, thereby increasing excretion of 1,25-dihydroxy vitamin D.[28]

Low physical activity is a CVD risk factor. The inverse relationship between the level of physical activity and the serum vitamin D levels in our study may be due to the enhanced resorption of bone calcium caused by physical activity,[29] hence the reduction of serum vitamin D level. Jarvinen et al. reported that irrespective of the VDR genotype, physical activity may be beneficial for the bones in postmenopausal women.[30]

We conclude that except for physical activity which had an inverse relationship with serum vitamin D level, none of the other CAD risk factors showed any association with the vitamin in postmenopausal women of remote small rural areas of Iran. Therefore, the high prevalence of CAD risk factors[31] in Iranian women cannot be related to vitamin D.

We recommend studies to investigate any possible relationship between CAD and vitamin D as related to VDR polymorphisms and VDR genotypes in the Iranian women.

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