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Original Research Article

Association between serum 25-hydroxyvitamin D concentrations and prevalence of metabolic syndrome

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ABSTRACT

Purpose: There is now good evidence that 25-hydroxyvitamin D (25OHD) status may have an important impact on the development and progression of cardiovascular disease. Because of the potential involvement of vitamin D deficiency in blood pressure control and immune responses, we aimed to investigate whether there was a relationship between 25OHD status and the prevalence of metabolic syndrome in an Iranian population.
Material/methods: The study was carried out on a sample of 846 subjects [357(42.19%) males and 489(57.80%) females], derived from MASHAD STUDY. Serum 25OHD levels were measured using a competitive electroluminescence protein binding assay. Anthropometric indices were measured using standard protocols.
Results: Serum 25OHD was 12.7 (6.8–18.4) ng/ml in the metabolic syndrome (MetS) group and 14.1 (8.8–19.0) ng/ml in the group without metabolic syndrome ($P = 0.43$). The frequency of vitamin D deficiency was 80.7% and 79.0% in subjects with or without metabolic syndrome in Iranian population.
Conclusions: We found no significant difference in serum 25OHD concentrations between individuals with or without MetS and no significant linear relationship between serum 25OHD and several CVD risk factors.

1. Introduction

Vitamin D (25-hydroxyvitamin D or 25OHD) has an essential role in calcium homeostasis and the maintenance of bone health [1–3]. There is now good evidence that 25OHD status may have an important impact on other conditions including: cancer [4,5], blood pressure via the modulation of renin synthesis [6,7]; and the development and progression of cardiovascular disease [8,9]. Furthermore, vitamin D deficiency has been reported to have a significant role in the pathogenesis of type 1 and 2 diabetes [10,11], multiple sclerosis and other autoimmune disease [12].

Vitamin D deficiency is common [13], and given its potential roles, it may contribute to cardiovascular risk.

Metabolic syndrome (MetS), or syndrome X was first described by Kylin in the 1920s as a clustering of hypertension, hyperglycemia and gout [14]. More recent criteria for metabolic syndrome have placed greater emphasis on central adiposity and insulin resistance, dyslipidemia, and elevated blood pressure. Metabolic syndrome has also been reported to be associated with other cardiovascular risk factors including a pro-inflammatory and prothrombotic state [15,16]. Individuals with MetS are therefore at a substantially increased risk of cardiovascular disease and the

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morbidity and mortality related to these conditions [17–19]. The prevalence of MetS is >21% in many Westernized populations and its prevalence is rising in many developing countries [20,21].

Because of the potential role of vitamin D deficiency in blood pressure control and immune responses, we aimed to investigate whether there was a relation between 25OHD status and the prevalence of metabolic syndrome in an Iranian population.

2. Material and methods

2.1. Study population

The study was carried out on a sample of 846 subjects [357(42.19%) males and 489(57.80%) females], derived from the MASHAD STUDY and was obtained using a stratified-cluster sampling method [22]. Pregnant and breast-feeding women, patients who had systemic disease, and patients taking any drug (including patients with dyslipidemia taking lipid lowering agents) were excluded from the study. Prior to taking part in the study, subjects did not receive any treatment that may have affected 25OHD status, or its measurement (any medication or vitamin D supplements), and were unaffected by any condition that may have affected 25OHD status (overt liver, or kidney disease, or malabsorption). Each subject gave informed written consent to participate in the study, which was approved by the Mashhad University of Medical Science Ethics Committee with an ID number 89707.

2.2. Anthropometric and other measurements

For each patient, height, weight, systolic and diastolic blood pressure were measured using previously described standard methods. Body mass index (BMI) was calculated as weight divided by height squared (m^2). All of these parameters were measured by an investigator using standardized methods at the beginning of the study. Systolic and diastolic blood pressure were measured twice and the average were reported for each. BMI >30 kg/m^2 was used to define obesity and a BMI between 25 and 30 kg/m^2 considered as overweight.

2.3. Physical activity level

Physical activity level was evaluated using a standard questionnaire [23], which was coded using the Human Energy Requirement [24]. According to the physical activity level values, subjects were classified to extremely inactive (PAL <1.40), sedentary (1.40–1.69), moderately active (1.70–1.99), vigorously active (2.00–2.40) or extremely active (>2.40) subgroups.

2.4. Blood sampling and biochemical analyses

Blood samples were collected from each subject after a 12 h fast. Serum was separated following centrifugation at 2500 rpm for 15 min at room temperature, and then stored at −20 °C prior to analysis routine biochemical analysis comprising total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, fasting blood glucose (FBG) and high-sensitivity C-reactive protein (Hs-CRP) were measured for all patients using routine analytical methods. Diabetes mellitus was defined using a FBG ≥126 mg/dl, or receiving treatment with an oral hypoglycemic agents or insulin treatment. MetS was defined using the International Diabetes Federation (IDF, 2006) criteria, if three of the following five criteria were met: (1) abdominal obesity: waist circumference >94 cm in men and >80 cm in women; (2) hypertriglyceridemia: ≥150 mg/dl or specific treatment; (3) low levels of HDL-C: <40 mg/dl in men and <50 mg/dl in women or specific treatment; (4) high blood pressure (HBP): ≥130/85 mmHg or specific treatment; (5) high fasting glucose: ≥100 mg/dl or treatment with anti-diabetic drugs. Hypertension was diagnosed in individuals with a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg, or a prior diagnosis of hypertension based on their past medical history and used anti-hypertensive drugs [20].

Kits supplied by Roche Diagnostics were used for measurement of serum levels of blood urea nitrogen (BUN) (Reference Number: 1400029, Roche Diagnostics, Mannheim, Germany) and creatinine (Reference Number: 1400009, Roche Diagnostics, Mannheim, Germany) by routine methods. Serum calcium (Reference Number: 1400007) and phosphate (Reference Number: 1500027) levels were determined by Pars Azmun kits, Karaj, Iran. All biochemical measurements were performed using an auto-analyzer (BT-3000, USA).

2.5. 25OHD measurement

Serum 25OHD levels were measured using a competitive electroluminescence protein binding assay (Roche Diagnostics vitamin D total assay kit; Reference Number: 06506780160, Roche Diagnostics, Mannheim, Germany) on a Cobas e411 analyzer [25]. Serum 25OHD was measured with an intra-assay precision CV of 6.65%. Vitamin D insufficiency and deficiency were defined as a serum 25OHD of 20–30 ng/ml and <20 ng/ml, respectively [26].

2.6. Statistical analysis

Data were analyzed using SPSS 20 software. Data were assessed for normality using the Kolomogorov–Smirnov test, and were expressed as means ± SD (for normally distributed data) or median and interquartile range (for non-normally distributed data). For group comparisons, *t*-tests and chi-square tests were used for quantitative and qualitative variables using a Bonferonni correction for multiple comparisons. Data that were not normally distributed were analyzed using the non-parametric tests. A two-sided *p*-value of <0.05 was considered as statistically significant. A multivariate analysis model was used to examine the associations between MetS and its components such as HDL-C, waist circumference, hypertension, fasting blood glucose, TG and also calcium and phosphate level with 25OHD concentration after correction for age, sex and smoking as potential confounding factors with a value of $P < 0.05$ in the univariate analysis. The variables in the multivariate analysis model were analyzed as enter method.

3. Results

3.1. Association between serum 25OHD concentrations and metabolic syndrome

Correlation analysis was performed by Spearman's analysis. Correlation between serum 25OHD level and metabolic syndrome components was not significant in all subjects. The greatest correlation identified was between serum 25OHD levels and triglyceride levels in the MetS and obese groups {*r* (Spearman correlation coefficient): 0.364, $P = 0.007$ and $r = 0.119$, $P = 0.043$, respectively} (Fig. 1).

There was no significant difference in serum 25OHD concentrations between men and women. There were significant differences in anthropometric and biochemical data between the groups with and without metabolic syndrome as may be expected (Table 1). However, there were no significant differences in 25OHD, BUN, creatinine, calcium, phosphate and physical activity levels between the MetS and healthy groups ($P > 0.05$). Serum 25OHD was 12.7(6.8–18.4) ng/ml in the MetS group and