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Association between serum 25-hydroxyvitamin D levels and pulmonary function, among Korean adults, during 2010–2014, by sex, age, and body mass index

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ABSTRACT

Background: This study examined the association between serum 25-hydroxyvitamin D (25(OH)D) and pulmonary function, among Korean adults, from 2010 to 2014.

Methods: The data were obtained from the fifth Korea National Health and Nutrition Examination Survey (KNHANES 5), and the first and second year (2013–2014) of KNHANES 6. The study population comprised 14,378 individuals. The variable of interest was serum 25(OH)D, and the dependent variable, pulmonary function.

Results: All people with vitamin D levels below 30 ng/ml had lower lung functions, which was significant in lower forced expiratory volume in the first second (FEV1) (serum 25(OH)D < 10 ng/ml, 20 to < 30 ng/ml: P = .001, 10 to < 20 ng/ml: P = 0) and forced vital capacity (FVC) (serum 25(OH)D level < 10 ng/ml: P = .01, 10 to < 20 ng/ml: P = .001, 20 to < 30 ng/ml: P = .008). The lower the serum 25(OH)D, the lower the levels of FEV1 in men and this was significant. (serum 25(OH)D < 10 ng/ml: P = .007, 10 to < 20 ng/ml: P = .002, 20 to < 30 ng/ml: P = .007). The values of FEV1 and FVC were lower in people aged 50–69 years when vitamin D was lower than 30 ng/ml which were all significant. Among participants with BMI values < 23 kg/m^2, lower vitamin D levels were significantly associated with lower pulmonary function.

Conclusions: We found a significant association between serum 25(OH)D and pulmonary function, and this was related to sex, age and body mass index.

1. Introduction

The prevalence of vitamin D deficiency has been reported in many populations [1,2]. Vitamin D deficiency is associated with rickets [1], cardiovascular disease [3], metabolic syndrome [4], autoimmune diseases, and cancer [5], as well as all-cause mortality from cardiovascular disease, cancer and respiratory disease [6].

The major circulating form of vitamin D is 25-hydroxyvitamin D (25(OH)D), and its concentration in the serum reflects the vitamin D status [1]. Individuals with low serum 25(OH)D levels may be more susceptible to respiratory tract infection, especially if they have respiratory tract diseases, such as asthma [7]. Patients with chronic obstructive pulmonary disease (COPD) are likelier to have serum 25(OH)D deficiencies than healthy smokers [8].

The relationship between vitamin D status and pulmonary disease has also drawn attention to the relationship between vitamin D status and pulmonary function. A study in the United States of America identified a strong relationship between serum 25(OH)D and pulmonary function (forced expiratory volume in the first second [FEV1] and forced vital capacity [FVC]) [9]. In an Australian study, vitamin D deficiency resulted in impaired pulmonary function [10,11]. In a Chinese study, vitamin D deficiency was highly prevalent among asthma patients, and was associated with poor pulmonary function. There was a strong positive association between serum 25(OH)D and pulmonary

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; KNHANES, Korea National Health and Nutrition Examination Survey

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function, in Korean adults [12], using data from the Korea National Health and Nutrition Examination Survey (KNHANES 2008–2010). An analysis of medical records found that serum 25(OH)D was associated with lung function [13].

The association between serum 25(OH)D and pulmonary function, in Korea, has not been widely studied. In addition, there are no follow-up studies using national data focusing on the relationship between vitamin D status and pulmonary function. Globally, many individuals have vitamin D deficiency, and this has gained attention as the deficiency is associated with several diseases. In urban Korea, the prevalence rates of vitamin D deficiency were 59.7% and 86.5%, respectively, in men and women (2007–2010) [14]. Our study aimed to examine the association between serum 25(OH)D and pulmonary function, among Korean adults, using KNHANES data from 2010 to 2014.

2. Materials and methods

2.1. Study population

The data were obtained from KNHANES 5, and the first and second years (2013–2014) of KNHANES 6. "The KNHANES is an ongoing surveillance system in the Republic of Korea (hereafter 'Korea') that assesses the health and nutritional status of Koreans, monitors trends in health risk factors and the prevalence of major chronic diseases, and provides data for the development and evaluation of health policies and programs in Korea [15]." It is conducted by the Korea Centers for Disease Control and Prevention. The target population of the KNHANES comprises nationally representative, non-institutionalized civilians. Each survey year includes a new sample of about 10,000 individuals, aged ≥1 year. The KNHANES comprises three component surveys: a health interview, health examination and nutrition survey [15]. Among the 38,979 individuals who participated in the survey, from 2010 to 2014, we set the age range from 40 to 79 years, as pulmonary function tests were performed on those in this age bracket. We excluded participants with missing data regarding variables such as education level, income, smoking, alcohol consumption, exercise status, occupation, region, COPD diagnosis, and body mass index (BMI) values. A total of 14,378 participants were included in the analysis.

2.2. Variables

The measurement of serum 25(OH)D–the variable of interest–was conducted using participants' blood samples. The blood samples were obtained by venipuncture, refrigerated immediately, and transported to a central testing institute, and were analyzed within 24 h after transportation. Serum 25(OH)D concentrations were measured using a gamma-counter (1470 Wizard; Perkin-Elmer, Turku, Finland) with a 25-hydroxyvitamin D 125I RIA kit (DiaSorin Inc., Stillwater, MN, USA). At serum 25(OH)D concentrations of 8.6, 22.7, 33.0, and 49.0 ng/ml (21.5, 56.8, 82.5, and 122.5 nmol/l), the inter-assay coefficients of variation were 11.7%, 10.5%, 8.6%, and 12.5%, respectively, and the intra-assay coefficients of variation were 9.4%, 8.2%, 9.1%, and 11.0%, respectively. The KNHANES participates in the Vitamin D Standardization Program, so the measurement of 25(OH)D was standardized using the recently developed reference procedure of the National Institute of Standards and Technology–Ghent University [16]. We categorized the participants into four groups, by their vitamin D values [12].

The dependent variable– pulmonary function–was measured by clinical technicians, using dry rolling seal spirometers (Model 2130; SensorMedics, Yorba Linda, CA, USA), following the American Thoracic Society/European Respiratory Society criteria for the standardization of pulmonary function tests [17]. Spirometric data were obtained on-site, and transferred to an internet review center where the information was carefully examined and compared against the metrics for acceptability, reproducibility and quality control. A principal investigator validated and stored the data in a Korea Centers for Disease Control and Prevention repository management system.

The independent variables included sex, age, BMI, education level, income, smoking, alcohol consumption and exercise status, occupation, region, and COPD diagnosis. Age was divided as 40–49, 50–59, 60–69 and 70–79 years. BMI was divided into < 23, 23 to < 25 and ≥ 25 kg/m^2. Education level was divided into primary, secondary, upper secondary, and tertiary. Income was divided into lowest, lower-middle, upper-middle, and highest. Smoking status was divided into current, ex-smoker, and never. Alcohol consumption was divided as no and yes. Exercise status was divided as no, middle and high. Occupation was divided into white, pink, blue and others. Region was divided into rural and urban. COPD diagnosis was divided into no and yes.

2.3. Statistical analysis

The data analysis was conducted using multiple regression in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). The data were analyzed over the entire population, and then stratified by serum 25(OH)D level. Results with a P value < .05 were considered statistically significant.

3. Results

Table 1 shows the baseline patient characteristics. Of the 14,378 participants, 4559 (31.71%) had serum 25(OH)D levels < 10 ng/mL, 6325 (43.99%) were in the 10 to < 20 ng/mL group, 3004 (20.89%) in the 20 to < 30 ng/mL group, and only 490 (3.41%) in the group with levels > 30 ng/mL. The FEV1 and FVC values were higher in men than in women, and the FEV1/FVC values were in the normal range in both sexs. Older age was associated with more impaired FEV1, FVC and FEV1/FVC values. Individuals with normal BMI values had higher pulmonary function than those with abnormal BMI values. Individuals diagnosed with COPD had worse pulmonary function. All the variables had significant associations with FEV1, FVC and FEV1/FVC, except for COPD diagnosis (with FVC), income, and alcohol consumption (with FEV1/FVC).

Table 2 shows the results obtained through the examination of the association between pulmonary function (FEV1, FVC and FEV1/FVC) and each variable. All participants with vitamin D levels < 30 ng/mL had lower pulmonary function, with significant differences in FEV1 (serum 25(OH)D level < 10 ng/ml: β -0.066, P = .001, 10 to < 20 ng/ml: β -0.071, P = 0, 20 to < 30 ng/ml: β -0.068, P = .001) and FVC values (serum 25(OH)D level < 10 ng/ml: β -0.062, P = .01, 10 to < 20 ng/ml: β -0.077, P = .001, 20 to < 30 ng/ml: β -0.065, P = .008). Men had significantly higher FEV1 and FVC values but significantly lower FEV1/FVC values (P < .0001). Lower age was associated with significantly better pulmonary function (P < .0001). Individuals with a BMI < 23 or ≥ 25 kg/m^2 had lower FEV1 (P = .001) and FVC values (BMI ≥ 25 kg/m^2: P < .0001), and the association was significant, except for BMI values < 23 kg/m^2 and FVC (P = .467).

Table 3 shows the results of the subgroup analyses of the associations between serum 25(OH)D and FEV1, FVC and FEV1/FVC. Lower serum 25(OH)D levels were associated with lower levels of FEV1 and FVC in both sexes; however, only the relationship between vitamin D and FEV1 values in men was significant (serum 25(OH)D level < 10 ng/ml: P = .007, 10 to < 20 ng/ml: P = .002, 20 to < 30 ng/ml: P = .007). The FEV1/FVC values showed a tendency to decrease when the serum 25(OH)D levels were < 30 ng/mL in only men (serum 25(OH)D level < 10 ng/ml: β -0.007, P = .111, 10 to < 20 ng/ml: β -0.005, P = .0255, 20 to < 30 ng/ml: β -0.009, P = .048). The FEV1, FVC and FEV1/FVC values were lower in those aged 50–69 years, when the vitamin D levels were < 30 ng/mL; all these associations were significant, except for the relationship between age 50–59 years and the FEV1/FVC value. However, there was no correlation between age 40–49 years and over 70 years, and the FEV1, FVC and FEV1/FVC