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Vitamin D status and its association with cardiometabolic risk factors in Korean adults based on a 2008-2010 Korean National Health and Nutrition Examination Survey

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Abstract

Recent studies suggest that vitamin D deficiency and cardiometabolic disorders are becoming increasingly more prevalent across multiple populations. However, there is a lack of comprehensive data for Korean adults. We investigated the vitamin D status, the prevalence of vitamin D deficiency and its association with metabolic syndrome (MS) risk in Korean adults aged 20 years or older. The study subjects (n = 18,305) were individuals who participated in the Korean National Health Examination and Nutrition Survey (KNHANES) in 2008-2010. Vitamin D status (25-hydroxyvitamin D [25(OH)D]) was categorized as < 20, 21-29, and ≥ 30 ng/mL, which are the cut-off points for deficiency, insufficiency and normal limits. A wide variety of cardiometabolic risk factors were compared according to the vitamin D status. Vitamin D deficiency was found in 53.9% of men and 70.5% of women. Mean BMI, systolic BP, HbA1c and low density lipoprotein cholesterol (LDL-C) were highest in the vitamin D deficiency group in both genders. Further, the MS was most prevalent in the vitamin D deficiency group in both genders (12.3%, $P = 0.002$ in men and 9.2%, $P < 0.001$ in women). Compared to the vitamin D normal group, the adjusted odds ratio (ORs) (95% confidence interval [95% CI]) for MS in the vitamin D deficiency group were 1.46 (1.05-2.02) in men and 1.60 (1.21-2.11) in women, after adjusting for confounding variables. In conclusion, Vitamin D deficiency is a very common health problem in Korean adults and is independently associated with the increasing risk of MS.

Key Words: Vitamin D, prevalence, metabolic syndrome, cardiovascular disease, Korean National Health and Nutrition Examination Survey

Introduction

Cardiometabolic disorders, including cardiovascular disease (CVD), type 2 diabetes mellitus (DM) and metabolic syndrome (MS), are major causes of morbidity and mortality worldwide [1,2]. Hypertension (HTN), dyslipidemia, central obesity and glycemic dysregulations are the known risk factors for CVD [2]. MS represents the clustering of these risk factors, which together lead to an increased risk of developing CVD and DM [3] Thus, early identification of the associated risk factors for CVD and MS is important from the public health perspective.

As more and more people live in cities spending a majority of their time indoors, people hardly get enough sunlight exposure for adequate cutaneous production of vitamin D. Thus, vitamin D deficiency has become a major health concern in the modern society. In recent studies, it is estimated that between 30% and 50% of the general population have vitamin D deficiency [4,5]. In Korea, vitamin D deficiency is also very common. In an international epidemiologic study that investigated the vitamin D status among postmenopausal osteoporotic women, including 101 Koreans, the mean serum 25-hydroxyvitamin D [25(OH)D] level of the Korean participants was 17.6 ng/mL, which was the lowest among 18 countries. Moreover, the prevalence of 25(OH)D less than 30 ng/mL was the highest in Korea with a rate of 92.1% [6].

Vitamin D is known to play an important role in bone and mineral homeostasis, and has also been linked with multiple pathophysiological mechanisms. The vitamin D binding receptor is not only expressed in tissues involved in calcium homeostasis, but is also found in more than 36 other tissue types [7]. Further, vitamin D has more recently been implicated in a number of additional pathological processes. These processes include cancer, multiple sclerosis, psoriasis and inflammatory response [8,9].

There is also a growing evidence to support the link between abnormal levels of vitamin D and CVD and MS [4,10]. However, there is a paucity of data that measure the effects of vitamin D status on the cardiometabolic risk factors in the Korean population. Thus, we investigated the vitamin D status, the prevalence of vitamin D deficiency, its association with MS risk and surrogate CVD risk factors, such as inflammatory markers, using the representative data for Korean men and women over 19 years of age (aged 20-87 years) who participated in the Korean National Health Examination and Nutrition Survey (KNHANES) in 2008-2010.

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Subjects and Methods

Study population

This study was based on data obtained from the 2008-2010 KNHANES, a nationally-representative survey conducted by the Korean Ministry of Health and Welfare. The survey's target population included non-institutionalized civilians over one year of age in Korea. Sampling units consisted of households selected through a stratified, multistage, probability-sampling design, based on geographic area, sex and age group using household registries. Participants completed four parts of a questionnaire that consisted of a health interview, a health behavior, a health examination and a nutrition survey. After excluding 7,664 individuals younger than 20 years of age, 21,571 subjects were used for the current study. Subjects who had not fasted for at least 12 hours prior to blood sampling, subjects with a triglyceride level exceeding 400 mg/dL and subjects with any missing data for the blood vitamin D measurements (serum 25(OH)D levels) and the MS component of the survey were excluded (n = 1,936). Those who had not performed a whole body dual energy X-ray absorptionmetry (DXA) scan were also excluded (n = 1,247). After the exclusion of individuals with liver cirrhosis or other chronic liver or renal diseases (n = 83), 18,305 subjects (aged 20-87 years: 7,957 men, 10,348 women) were included in our final analysis. The study protocol was approved by the Institutional Review Board of Soonchunhyang University College of Medicine (IRB No.2013~042).

Data collection

For the 2008-2010 KNHANES, citizens were informed that they had been randomly selected as a household to voluntarily participate in a nationally representative survey conducted by the Korean Ministry of Health and Welfare, and that they had the right to refuse to participate in accordance with the National Health Enhancement Act, supported by the National Statistics Law of Korea. All study participants provided written informed consent. The Korean Centers for Disease Control and Prevention also obtained written informed consent to use blood samples from the participants for further analysis. The health examination, which was performed in 2008-2010, included a medical disease history, a physical examination, a questionnarie about health-related behaviors, anthropometric, biochemical measurements and DXA. Physical examinations were performed by trained medical staff following the standardized procedures. Participants were asked about lifestyle behaviors, including cigarette smoking, alcohol consumption and physical activity. Participants were categorized as either nonsmokers or current smokers. Regular alcoholic consumption was considered as two or more drinks per week. All subjects were instructed to record their daily engagement in moderate or vigorous activity during the previous 7-day period. Regular exercise was defined as follows: subjects who were engaged in moderate intensity exercise $\geq$ 5 times/week or in vigorous intensity exercise $\geq$ 3 times/week. Completed questionnaires were reviewed by trained staff and were entered into a database. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, with the subject wearing light indoor clothing without shoes. Waist circumference (WC) was measured at the narrowest point between the lower border of the rib cage and the iliac crest. Body mass index (BMI) was calculated as the ratio of weight (kg)/height squared (m^2). Blood pressure (BP) was measured after the subject had rested for five minutes in a sitting position. BP was measured in the right arm using a standard mercury sphygmomanometer (Baumanometer, USA). Two systolic blood pressure (SBP) and diastolic blood pressure (DBP) readings were recorded at 5-min intervals and averaged for analysis. After a 12 hours overnight fast, blood samples were obtained from the antecubital vein. Samples were immediately sent to a central certified laboratory and the plasma was separated by centrifugation. Fasting plasma glucose, total cholesterol (TC), triglycerides (TG) and high density lipoprotein cholesterol (HDL-C) levels were measured using a Hitachi 700-110 Chemistry Analyzer (Hitachi, Tokyo, Japan). Fasting insulin levels were measured by immunoradiometric assay (Biosource, Belgium) using a ɣ-counter (1470 Wizard; PerikinElmer, Turku, Finland). HbA1c was measured by high performance liquid chromatography (HLC-723G7, Tosch, Japan). White blood cell (WBC) counts were quantified by an automated blood cell counter (ADIVA 120, Bayer, NY, USA). Serum ferritin levels were measured by immunoradiometric assay (DiaSorin Inc., Stillwater, MN, USA) using a ɣ-counter. The DXA scan was performed for each subject to measure total body fat mass (kg) and total body fat percentage (%) using fan-beam technology (Lunar Corp., Madison, WI). Plasma low density lipoprotein cholesterol (LDL-C) values were estimated using the following formula: TC (mg/dL) - HDL-C (mg/dL) - TG (mg/dL)/5 [11]. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the following formula: [fasting plasma glucose (mg/dL) × fasting insulin (µIU/mL)/18]/22.5 [12].

Measurement of serum 25(OH)D

For measurements of serum 25(OH)D levels, the blood samples of individual subjects were collected during the survey. Blood samples were properly processed, immediately refrigerated and transported in cold storage to the Central Testing Institute in Seoul, Korea. Blood samples were analyzed within 24 hours after transportation. Serum 25(OH)D levels were measured using a ɣ-counter (1470 Wizard, Perkin-Elmer Finland) with a RIA (DiaSorin, Still Water, MN). The interassay coefficients of variation were 11.7%, 10.5%, 8.6% and 12.5% at 8.6, 22.7, 33.0 and 49.0 ng/mL, respectively.

Diagnostic criteria of vitamin D deficiency and vitamin D insufficiency

To categorize the serum 25(OH)D levels in our sample population, we used the cutoffs reported in a review published by Holick and Chen in 2008 [13]. Vitamin D deficiency was considered as < 20 ng/mL (50 nmol/L); a level of 21-29 ng/mL (52-72 nmol/L) was considered to indicate vitamin D insufficiency, whereas a level of 30 ng/mL (> 75 nmol/L) or greater was considered normal (sufficient or optimum).

Definition of MS

The definition for MS and its components were based on the National Cholesterol Education Program Adult Treatment Panel III guidelines, and we used the ethnicity-specific values for WC based on data from the World Health Organization and the Korean Society for the Study of Obesity [14]. MS was thus defined by the presence of three or more of the following risk factors: central obesity (WC ≥ 90 cm for men, and ≥ 80 cm for women); SBP ≥ 130 mmHg and DBP ≥ 85 mmHg; fasting glucose levels ≥ 100 mg/dL; TG levels ≥ 150 mg/dL; and low HDL-C levels (< 40 mg/dL for men, and < 50 mg/dL for women). Subjects who reported taking antihypertensive or antidiabetes medications were considered to have elevated BP or high fasting glucose levels.

Statistical analysis

All data on the continuous variables were presented as mean ± standard errors (SEs). Data from the National Census from the Korea National Statistical Office were used to define the standard population. Statistical estimates were weighted to represent the total population of Korea. In order to represent the entire Korean adults without biased estimates, sampling weights were used to account for the complex sampling. Clinical and biochemical characteristics of the study population were compared according to the vitamin D status using a one-way analysis of variance (ANOVA) test for continuous variables and the chi-square test for categorical variables. Serum 25(OH)D levels were calculated according to the number of metabolic risk factors. The prevalence of MS was compared according to the vitamin D status. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for MS were calculated using multiple logistic regression analyses after

Table 1. Characteristics according to vitamin D status in men[1)]

Characteristics	Total (n = 7,957)	Vitamin D deficiency (n = 4,295)	Vitamin D insufficiency (n = 2,854)	Normal (n = 808)	P[2)]
Age (yrs)	43.5 ± 0.3	41.1 ± 0.32	46.1 ± 0.4	49.9 ± 0.7	< 0.001
Current smoking	3,514 (44.2)	2,035 (47.4)	1,141 (40.0)	338 (41.8)	< 0.001
Alcohol drinking	3,120 (39.2)	1,542 (35.9)	1,174 (41.1)	404 (50.0)	< 0.001
Regular exercise[3)]	2,256 (28.4)	1,090 (25.4)	891 (31.2)	275 (34.0)	< 0.001
Anthropometric index					
BMI (kg/m^2)	24.1 ± 0.05	24.1 ± 0.07	24.1 ± 0.06	23.7 ± 0.10	0.009
WC (cm)	84.3 ± 0.30	84.4 ± 0.21	84.3 ± 0.49	84.2 ± 0.40	0.900
Total body fat mass (kg)	14.8 ± 0.12	15.2 ± 0.20	14.3 ± 0.20	13.2 ± 0.30	< 0.001
Total body fat percentage (%)	224 ± 0.15	23.0 ± 0.20	21.9 ± 0.20	20.9 ± 0.30	< 0.001
Blood pressure					
SBP (mmHg)	118.9 ± 0.49	119.6 ± 0.60	118.5 ± 0.38	117.0 ± 0.30	< 0.001
DBP (mmHg)	93.4 ± 1.03	95.7 ± 1.40	91.6 ± 0.60	87.7 ± 0.60	0.096
Glucose tolerance index					
Fasting glucose (mg/dL)	98.9 ± 0.30	99.1 ± 0.51	98.8 ± 0.70	97.8 ± 0.41	0.116
Fasting insulin (µIU/mL)	10.1 ± 0.10	10.5 ± 0.13	9.7 ± 0.13	8.9 ± 0.20	< 0.001
HOMR-IR	2.5 ± 0.03	2.6 ± 0.04	2.4 ± 0.05	2.2 ± 0.06	< 0.001
HbA1c (%)	7.3 ± 0.07	7.4 ± 0.1	7.2 ± 0.1	6.9 ± 0.1	0.006
Lipid profile					
TC (mg/dL)	186.8 ± 0.5	187.6 ± 0.8	186.0 ± 1.5	185.6 ± 0.7	0.107
TG (mg/dL)	122.7 (81.1-188.6)	123.5 (82.1-190.5)	122.3 (79.0-177.9)	120.1 (80.5-187.2)	0.007
HDL-C (mg/dL)	49.5 ± 0.2	49.2 ± 0.23	49.9 ± 0.3	50.3 ± 0.5	0.019
LDL-C (mg/dL)	106.2 ± 0.5	107.0 ± 0.8	105.8 ± 1.5	103.8 ± 0.6	0.003
Inflammatory index					
WBC count (cells/µL)	6.6 ± 0.02	6.6 ± 0.03	6.5 ± 0.04	6.4 ± 0.06	< 0.001
Ferritin (ng/mL)	99.1 (65.1-152.3)	99.4(64.7-151.5)	99.1(65.9-155.4)	98.1(65.2-152.6)	0.822

BMI, Body mass index; WC, Waist circumference; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; HOMA-IR, Homeostasis model assessment of insulin resistance; TC, Total cholesterol; TG, Triglyceride; HDL-C, High density lipoprotein cholesterol; LDL-C, Low density lipoprotein cholesterol; WBC, White blood cell.

1) Values are presented as means ± standard errors, median (inter-quartile range), or number (%).

2) Calculated by complex samples general linear model ANOVA or χ^2-test.

3) Defined as vigorous intensity exercise ≥ 3/week or moderate intensity exercise ≥ 5/week.

adjusting for confounding variables, according to the vitamin D status. All analyses were conducted using the SAS statistical software (version 9.1; SAS Institute Inc., Cary, NC, USA). Finally, all statistical tests were two-sided and the results with a P-value < 0.05 were considered statistically significant.

Results

Clinical and biochemical characteristics according to vitamin D status in the study population

The clinical and biochemical characteristics according to vitamin D status and gender are presented in Tables 1 and 2. There were 7,957 men (mean age 43.5 ± 0.3 years) and 10,348 women (mean age 45.4 ± 0.3 years) involved in the study. The mean serum 25(OH)D levels were 19.5 ± 0.2 mg/dL for men and 16.9 ± 0.2 mg/dL for women. Vitamin D deficiency was found in 53.9% of men and 70.5% of women, whereas vitamin D insufficiency was found in 35.9% of men and 24.5% of women. The percentage of current smokers was significantly higher in the vitamin D deficiency group than in any other group for both genders. Subjects in the vitamin D deficiency group were less likely to exercise regularly than those in any other group for both genders. For anthropometric indices, the vitamin D group showed a higher BMI than any other group for both genders. Mean values of total body fat mass and fat percentage were highest in the vitamin D deficiency group in men, and the mean values of WC was highest in the vitamin D deficiency group in women. In the metabolic profiles, SBP, HbA1c and LDL-C were highest in the vitamin D deficiency group in both genders, whereas the mean values of HDL-C were lowest in the vitamin D deficiency group. Mean values of fasting insulin, HOMA-IR and TG were highest in the vitamin D deficiency group in men, and the mean values of DBP, fasting glucose and TC were highest in the vitamin D deficiency group in women. For inflammatory markers, WBC counts were highest in the vitamin D deficiency group in men and ferritin levels were highest in the vitamin D deficiency group in women.

Comparisons of cardiovascular risk factors according to MS status and gender

Table 3 shows the comparison of cardiovascular risk factors

Table 2. Characteristics according to vitamin D status in women[1)]

Characteristics	Total (n = 10,348)	Vitamin D deficiency (n = 7,292)	Vitamin D insufficiency (n = 2,532)	Normal (n = 524)	P[2)]
Age (yrs)	45.4 ± 0.3	43.8 ± 0.3	49.0 ± 0.5	53.7 ± 0.9	< 0.001
Current smoking	603 (5.8)	451 (6.3)	123 (4.9)	29 (5.5)	0.427
Alcohol drinking	943 (9.1)	637 (8.7)	260 (10.3)	46 (8.8)	0.123
Regular exercise[3)]	2,555 (24.7)	1,675 (22.9)	708 (27.9)	172 (32.8)	< 0.001
Anthropometric index					
BMI (kg/m^2)	23.4 ± 0.15	23.5 ± 0.10	23.3 ± 0.10	23.1 ± 0.20	< 0.001
WC (cm)	79.4 ± 0.5	79.6 ± 0.6	79.2 ± 0.3	77.3 ± 0.2	< 0.001
Total body fat mass (kg)	18.2 ± 0.10	18.2 ± 0.12	18.1 ± 0.18	17.5 ± 0.30	0.079
Total body fat percentage (%)	34.3 ± 0.10	34.4 ± 0.16	34.2 ± 0.20	33.6 ± 0.40	0.134
Blood pressure					
SBP (mmHg)	117.3 ± 0.2	118.3 ± 0.1	115.5 ± 0.5	112.8 ± 0.3	< 0.001
DBP (mmHg)	90.1 ± 0.8	91.3 ± 0.6	88.1 ± 0.8	83.6 ± 0.4	< 0.001
Glucose tolerance index					
Fasting glucose (mg/dL)	96.9 ± 0.7	97.3 ± 0.9	96.4 ± 0.5	94.7 ± 0.3	0.005
Fasting insulin (μIU/mL)	10.0 ± 0.08	10.1 ± 0.1	9.9 ± 0.2	9.7 ± 0.2	0.186
HOMR-IR	2.4 ± 0.03	2.4 ± 0.05	2.4 ± 0.03	2.4 ± 0.1	0.789
HbA1c (%)	7.4 ± 0.01	7.4 ± 0.10	7.4 ± 0.08	6.9 ± 0.1	0.002
Lipid profile					
TC (mg/dL)	190.4 ± 0.7	190.9 ± 0.9	190.4 ± 0.2	184.8 ± 0.5	< 0.001
TG (mg/dL)	94.0 (67.2-132.5)	95.4 (68.6-136.7)	91.6 (63.6-138.1)	87.0 (60.8-131.5)	0.201
HDL-C (mg/dL)	54.3 ± 0.2	53.8 ± 0.6	55.4 ± 0.3	55.6 ± 0.2	0.016
LDL-C (mg/dL)	108.1 ± 0.4	114.1 ± 0.9	112.8 ± 0.7	107.2 ± 0.5	< 0.001
Inflammatory index					
WBC count (cells/μL)	5.8 ± 0.10	5.8 ± 0.02	5.8 ± 0.02	5.7 ± 0.04	0.680
Ferritin (ng/mL)	44.3 (27.4-69.7)	46.5 (24.5-76.1)	40.6 (21.5-67.2)	32.2 (16.1-55.9)	< 0.001

BMI, Body mass index; WC, Waist circumference; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; HOMA-IR, Homeostasis model assessment of insulin resistance; TC, Total cholesterol; TG, Triglyceride; HDL-C, High density lipoprotein cholesterol; LDL-C, Low density lipoprotein cholesterol; WBC, White blood cell.

1) Values are presented as means ± standard errors, median (inter-quartile range), or number (%).

2) Calculated by complex samples general linear model ANOVA or χ^2-test.

3) Defined as vigorous intensity exercise ≥ 3/week or moderate intensity exercise ≥ 5/week.

Table 3. Comparisons of cardiovascular risk factors according to MS status and gender[1)]

Characteristics	Men (n = 7,957)			Women (n = 10,348)		
	No MS (n = 6,126)	MS (n = 1,831)	$P^{2)}$	No MS (n = 8,890)	MS (n = 1,458)	$P^{2)}$
Age (yrs)	42.3 ± 0.31	48.0 ± 0.38	< 0.001	43.5 ± 0.27	59.0 ± 0.45	< 0.001
Current smoking	2695 (43.9)	793 (43.3)	0.927	515 (5.8)	83 (5.7)	0.941
Alcohol drinking	2339 (38.1)	759 (41.5)	< 0.001	814 (9.2)	123 (8.4)	0.467
Regular exercise[3)]	1770 (28.9)	474 (25.9)	0.009	2165 (24.4)	376 (25.8)	0.373
Anthropometric index						
BMI (kg/m^2)	23.4 ± 0.05	26.4 ± 0.09	< 0.001	22.7 ± 0.05	26.2 ± 0.11	< 0.001
WC (cm)	82.3 ± 0.37	91.8 ± 0.23	< 0.001	76.3 ± 0.17	88.8 ± 0.24	< 0.001
Total body fat mass (kg)	13.8 ± 0.13	18.5 ± 0.19	< 0.001	17.8 ± 0.11	21.7 ± 0.23	< 0.001
Total body fat percentage (%)	21.6 ± 0.16	25.8 ± 0.19	< 0.001	33.9 ± 0.15	37.4 ± 0.23	< 0.001
Blood pressure						
SBP (mmHg)	115.6 ± 0.26	125.2 ± 0.47	< 0.001	111.1 ± 0.23	132.1 ± 0.60	< 0.001
DBP (mmHg)	86.8 ± 0.40	99.5 ± 0.62	< 0.001	82.6 ± 0.35	100.8 ± 0.92	< 0.001
Glucose tolerance index						
Fasting glucose (mg/dL)	94.4 ± 0.29	112.7 ± 0.81	< 0.001	91.7 ± 0.18	119.9 ± 1.24	< 0.001
Fasting insulin (μIU/mL)	9.3 ± 0.09	12.8 ± 0.26	< 0.001	9.5 ± 0.07	13.6 ± 0.36	< 0.001
HOMR-IR	2.2 ± 0.03	3.6 ± 0.09	< 0.001	2.2 ± 0.02	4.2 ± 0.15	< 0.001
HbA1c (%)	7.3 ± 0.14	7.3 ± 0.07	0.473	7.1 ± 0.09	7.6 ± 0.08	< 0.001
Lipid profile						
TC (mg/dL)	184.0 ± 0.59	194.6 ± 0.97	< 0.001	183.4 ± 0.48	207.2 ± 1.25	< 0.001
TG (mg/dL)	106.1 (73.9-147.3)	212.9 (165.7-296.0)	< 0.001	82.2 (59.0-117.2)	181.4 (150.8-244.6)	< 0.001
HDL-C (mg/dL)	51.8 ± 0.19	41.1 ± 0.25	< 0.001	56.4 ± 0.18	48.7 ± 0.45	< 0.001
LDL-C (mg/dL)	100.7 ± 0.11	106.2 ± 0.54	< 0.001	107.5 ± 0.42	117.4 ± 1.18	< 0.001
Inflammatory index						
WBC count, cells/μL	6.5 ± 0.03	7.1 ± 0.05	< 0.001	5.7 ± 0.02	6.5 ± 0.05	< 0.001
Ferritin (ng/mL)	94.6 (62.6-144.2)	122.3 (77.5-188.8)	< 0.001	32.7 (16.5-55.6)	55.3 (29.4-86.0)	< 0.001
25(OH)D (ng/mL)	19.6 ± 0.20	19.2 ± 0.25	0.030	17.6 ± 0.27	12.6 ± 0.22	< 0.001

BMI, Body mass index; WC, Waist circumference; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; HOMA-IR, Homeostasis model assessment of insulin resistance; TC, Total cholesterol; TG, Triglyceride; HDL-C, High density lipoprotein cholesterol; LDL-C, Low density lipoprotein cholesterol; WBC, White blood cell; 25(OH)D, 25-hydroxyvitamin D.
[1)] Values are presented as means ± standard errors, median (inter-quartile range), or number (%).
[2)] Calculated by complex samples general linear model ANOVA or χ^2-test.
[3)] Defined as vigorous intensity exercise ≥ 3/week or moderate intensity exercise ≥ 5/week.

Table 4. Odds ratios and 95% confidence intervals for metabolic syndrome according to vitamin D status

	Vitamin D status in men			Vitamin D status in women		
	Normal	Vitamin D insufficiency	Vitamin D deficiency	Normal	Vitamin D insufficiency	Vitamin D deficiency
Model 1[1)]	1.00	1.16 (0.88-1.53)	1.61 (1.20-2.15)	1.00	1.18 (0.49-2.82)	2.41 (1.78-3.27)
Model 2[2)]	1.00	1.21 (0.90-1.63)	1.42 (1.03-1.95)	1.00	1.34 (0.46-1.32)	1.70 (1.24-2.32)
Model 3[3)]	1.00	1.18 (0.87-1.58)	1.46 (1.06-2.01)	1.00	1.34 (0.45-1.32)	1.62 (1.23-2.13)
Model 4[4)]	1.00	1.16 (0.83-1.56)	1.45 (1.05-2.02)	1.00	1.32 (0.44-1.31)	1.60 (1.21-2.11)

[1)] Unadjusted.
[2)] Adjusted for age.
[3)] Adjusted for age, smoking, alcohol drinking, and regular exercise, occupation.
[4)] Adjusted for age, smoking, alcohol drinking, regular exercise, occupation, BMI, WC, SBP, DBP, fasting glucose, fasting insulin, HOMA-IR, HbA1c, TC, TG, HDL-C, WBC, and ferritin.

according to MS and gender. MS was present in 17.9% of all subjects and in 23.0% of men and 14.1% of men. The mean serum 25(OH)D levels in the MS group were lower than the non-MS group for both genders.

Relationship between vitamin D status and MS

Fig. 1 shows the serum 25(OH)D levels according to the number of MS components. Mean serum 25(OH)D levels decreased continuously with each additional component of MS in both genders.

Fig. 2 shows the prevalence of MS according to the vitamin D status. MS was most prevalent in the vitamin D deficiency group in both genders (12.3%, $P = 0.002$ in men and 9.2%, $P < 0.001$ in women).

Table 4 shows the result of the multiple logistic regression

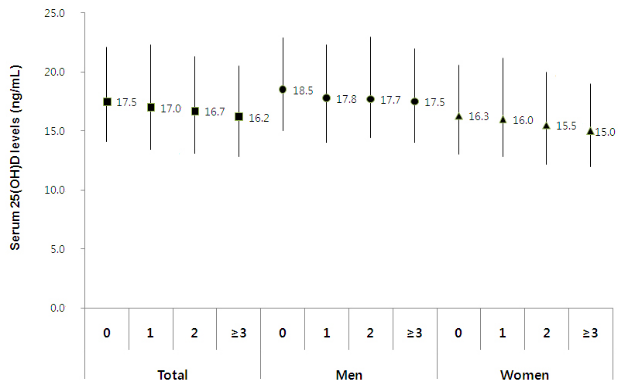

Fig. 1. Serum 25(OH)D levels according to the number of metabolic syndrome components.

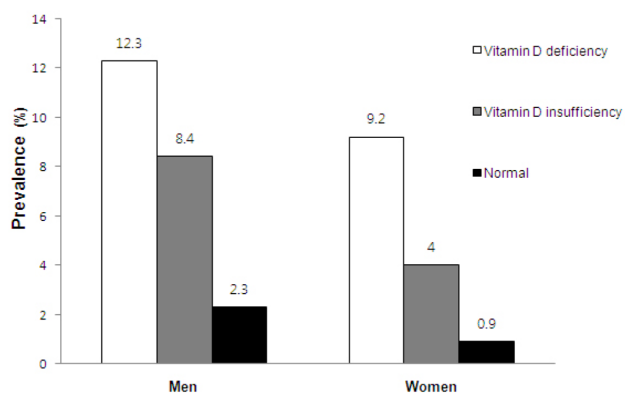

Fig. 2. Prevalence of metabolic syndrome according to the vitamin D status in men and women. The prevalence of metabolic syndrome was significantly higher in vitamin D deficiency group than in any other group in both sexes (12.3%, P= 0.002 in men and 9.2%, P< 0.001 in women).

analyses designed to investigate the relationship between vitamin D status and MS. After adjusting for age, smoking status, alcohol consumption, regular exercise and occupation, the adjusted ORs (95% CIs) for the vitamin D deficiency group vs. normal group were 1.46 (1.05-2.02) in men and 1.60 (1.21-2.11) in women, respectively. Using model 4, these positive associations remained after additional adjustment for BMI, WC, SBP, DBP, fasting glucose, fasting insulin, HOMA-IR, HbA1c, TC, TG, HDL-C, WBC and ferritin in both genders.

Discussion

We examined the prevalence of vitamin D deficiency and the association between vitamin D status and cardiometabolic risk factors, including MS, in the representative sample of Korean adult population aged 20 years or older. In this nationwide cross-sectional study, we found that vitamin D deficiency is a very common health problem among adults in Korea. The vitamin D deficiency group was independently associated with an increased risk of MS in both genders after adjusting for confounding variables.

The level of serum 25(OH)D level is regarded as the best indicator of vitamin D status in healthy individuals. Serum 25(OH)D reflects the total production from exposure to ultraviolet B (UVB) radiation as well as the intake of dietary forms of vitamin D. Skin exposure to sunlight is the prominent source of vitamin D [4,5].

Our findings are consistent with those of previous studies which have suggested that low vitamin D levels in adulthood may influence the risk of developing cardiometabolic outcomes, particularly HTN [15], DM [16] and MS [17]. This finding may be related to the limited food sources of vitamin D. Most Koreans have a low consumption of vitamin D-rich foods [18]. A prospective observational study of middle-aged men and women support an association between low vitamin D levels or dietary intake and incident HTN [15]. In addition, a short-term intervention study, one that assigned patients with mild HTN to receive 800 IU per day of oral vitamin D for 8 weeks, resulted in significant reductions in BP [19]. There is increasing evidence that vitamin D may be a negative endocrine regulator of the renin-angiotensin system. The activated metabolite of 25(OH)D, 1,25-dihydroxyvitamin D (1,25[OH]$_2$D) has been shown to inhibit rennin gene expression [20]. Furthermore, vitamin D receptor null mice exhibit increased renin levels and systemic HTN and ultimately, develop cardiac hypertrophy [21]. In addition, the 1α-hydroxylase enzyme that converts 25(OH)D to 1,25(OH)$_2$D is expressed in a variety of tissues, including human endothelial cells and vascular smooth muscle cells [22], which suggests another mechanism by which vitamin D may influence the systemic control of BP. In this study, we found low vitamin D levels were significantly associated with the glucose tolerance index, such as fasting glucose, fasting insulin, HOMA-IR and HbA1c. Although the exact mechanisms linking vitamin D deficiency with hyperglycemia and subsequent diabetes risk are not completely understood, there is accumulating evidence that vitamin D may directly regulate insulin secretion by binding to pancreatic β-cell vitamin D receptors. Indirect mechanism may include effects on pancreatic β-cell function by regulating extracellular concentrations [23]. The effects of vitamin D on insulin sensitivity may also explain, at least in part, the independent association with MS observed in the current study [24]. Another noteworthy finding in the present study was the significant association between vitamin D status and surrogate CVD risk factors, such as inflammatory markers. A mounting body of evidence suggests that CVD is closely linked to chronic low-grade inflammation, which is known to contribute to the development of atherosclerosis [25]. Higher WBC counts and ferritin levels, even within the normal range, have been associated with CVD and MS [26,27], which are conditions linked to chronic low-grade inflammation and insulin resistance. Thus, vitamin D is drawing the interest of medical researchers with its potential role in a wide variety of health conditions, including CVD [28] and insulin resistance [16].

This study has several limitations. First, this study was cross-sectional, which limits the determination of causality. Therefore, further prospective research to evaluate the potential cause-and-effect relationships between vitamin D status and cardiometabolic risk factors is warranted. Second, unfortunately, because this study used secondary data derived from the KNHANES, we did not inquire into each individual's amount of sunlight exposure. We only assumed that those who work outdoors would have more sunlight exposure, whereas those who work indoors would have less. Thus, we could not estimate how the level of sunlight exposure actually differs among the various occupations. Further, we did not obtain data regarding the behavioral factors which could affect cutaneous synthesis of vitamin D, such as sunscreen use or clothing. We also did not obtain data regarding each individual's vitamin D intake through diet and supplements, which might have affected the subject's vitamin D status to some extent. Additional limitation includes the lack of information regarding the measurement of parathyroid hormone (PTH) level. With the role of serum 25(OH)D levels/PTH axis as maintaining extracellular calcium homeostasis, PTH levels may play a role for the effect of serum 25(OH)D. However, PTH levels were measured only in participants over 50 years of age in the KNHANES; thus, we did not obtain data of PTH levels. Despite these potential limitations, we believe that the present study is the first of its kind to assess the association between vitamin D status and cardiometabolic risk factors in the general population using nationally representative data. Finally, we did not take into consideration of the residual confounding effects of obesity as an intermediate variable. Obesity could play a key role in an intermediate confounder to inversely link between vitamin D and various cardiometabolic risk factors. Thus, the inverse relationship between the vitamin D level and cardiometabolic risk factors might be just an epiphenomenon secondary of the clustering of CVD risk factors due to obesity. These limitations make it difficult to draw firm cause-effect relationships.

In conclusion, we found that vitamin D deficiency was a very common health problem in Korea and was independently associated with an increasing risk of MS in both genders. These findings suggest that more time spent in outdoor activities for sunlight exposure and higher vitamin D intake, such as public health intervention, may be needed to improve the vitamin D status in the prevention and treatment of MS.

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