Original Article

Association between body fat and vitamin D status in Korean adults

Seung Seok Han MD¹, Myounghee Kim PhD², Su Mi Lee MD¹, Jung Pyo Lee MD, PhD³, Sejoong Kim MD, PhD⁴, Kwon Wook Joo MD, PhD¹, Chun Soo Lim MD, PhD³, Yon Su Kim MD, PhD¹, Dong Ki Kim MD, PhD¹

¹Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea ²Department of Dental Hygiene, College of Health Science, Eulji University, Gyeonggi-do, Korea ³Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul, Korea ⁴Department of Internal Medicine, Seoul National University Bundang Hospital, Gyeonggi-do, Korea

The relationship between body fat mass and vitamin D appears to vary by ethnicity, but our understanding of this predisposition in Asians is limited due to the scarcity of prior investigations. Data on 1,697 Korean adults were obtained from the second and third years (2008-2009) of the fourth Korean National Health and Nutritional Examination Survey. Body fat mass was measured using dual-energy X-ray absorptiometry. Both linear regression analysis for serum 25-hydroxyvitamin D [25(OH)D] and logistic analysis for vitamin D deficiency [25(OH)D <20 ng/mL] were performed to determine significant predictors among BMI, waist circumference (WC), and body fat percentage (BF), after adjustment of multiple covariates. To explore a possible non-linear relationship between them, the fractional polynomials method was used. All analyses were conducted following stratification by sex. In linear regression analysis, BMI and WC were not associated with 25(OH)D. However, BF was inversely related to 25(OH)D, irrespective of the fat location (both appendicular and truncal fat) in both sexes. In logistic regression analysis, the highest quartile group of BF had a greater OR for vitamin D deficiency than the lower quartile groups, irrespective of the fat location and sex. However, the quartiles of BMI and WC were not associated with vitamin D deficiency. The linear relationships between BF and 25(OH)D (or vitamin D deficiency) were confirmed despite use of the fractional polynomials method. Body fat mass is inversely associated with serum 25(OH)D in Korean adults. Monitoring of vitamin D deficiency in Korean adults with high fat mass is needed.

Key Words: adiposity, body composition, body fat distribution, Koreans, vitamin D

INTRODUCTION

Low vitamin D status is an important issue in global health care because it may lead to a wide range of illnesses and chronic conditions, such as osteoporosis, cancer, the metabolic syndrome, and cardiovascular disease.¹ However, despite increased attention on vitamin D, vitamin D status in many individuals remains suboptimal, thereby contributing to the risks of several diseases.² Thus, it is important to know which factors may affect vitamin D status and to find and predict the subjects who need vitamin D supplementation.

Several factors are related to the vitamin D status: age, season, skin color, and kidney function.³⁻⁵ Obesity, defined as excessive fat accumulation, is also associated with low vitamin D status. It has been suggested that the low vitamin D levels in obesity are due to sequestration in fat, increased clearance by a larger body-fat pool, and decreased sun exposure.⁶⁻⁸ Obesity and vitamin D status are typically assessed by BMI and circulating 25-hydroxyvitamin D [25(OH)D], respectively. However, BMI is not a reliable indicator of obesity because it does not differentiate fat tissue from other tissues. Furthermore,

BMI is affected by confounding variables, including age, gender, and ethnicity.⁹⁻¹¹ For example, Asians exhibit a higher proportion of body fat for a given BMI than do Caucasians.¹¹ In this respect, more accurate techniques for determining body fat content is recommended, including dual-energy X-ray absorptiometry (DXA), bioelectrical impedance analysis, or computed tomography.

Previous studies using these methods have observed the inverse relationship between body fat mass and serum 25(OH)D. However, most studies have focused on Caucasians and African-Americans, and studies on Asian populations are scarce. Furthermore, the two studies including Asians are limited because of the modest sample size or the inclusion of only elderly subjects.^{12,13} First of

Corresponding Author: Dr Dong Ki Kim, Department of Internal Medicine, Seoul National University College of Medicine, 101 Daehakro, Jongno-gu, Seoul, 110-744, Korea. Tel: 82-2-2072-2303; Fax: 82-2-762-9662 Email: dkkim73@gmail.com Manuscript received 20 April 2013. Initial review completed 23 May 2013. Revision accepted 14 September 2013. doi: 10.6133/apjcn.2014.23.1.10 all, the relationship appears to vary by ethnicity.^{13,14} Therefore, it is important to investigate the relationship between body fat and vitamin D levels in Asians. In the present study, we aimed at verifying this issue using a large Korean data set from the Korean National Health and Nutritional Examination Survey (KNHANES).

MATERIALS AND METHODS

Study population

Data were obtained from the second and third years (2008-2009) of the KNHANES IV, which was conducted by the Korea Centers for Disease Control and Prevention. KNHANES used a rolling sampling design that involved a complex, stratified, multistage, probability-cluster survey of a representative sample of the non-institutionalized civilian population in South Korea. The survey consisted of health interviews and examinations, including laboratory tests, and a nutritional survey. In the second and third years, 12,528 and 12,722 subjects were sampled, respectively. In total, 9,744 (77.8% in the second year) and 10,533 (82.8% in the third year) subjects participated in the survey. All participants signed informed consent forms. This cross-sectional analysis was restricted to 4,308 subjects ≥ 20 years of age for whom serum 25(OH)D, DXA, and other results of covariates were available. Furthermore, we excluded 2,611 subjects who reported a previous diagnosis of cardiovascular disease, renal disease, liver disease, or cancer or who were taking medications such as antihypertensive, hypoglycemic, or lipid-lowering agents. Finally, a total of 1,697 subjects without medical illness were analyzed in the present study. The institutional review board at the Korea Centers for Disease Control and Prevention approved the survey of the study population (nos 2008-04EXP-01-C, 2009-01CON-03-2C).

Body fat and anthropometric assessment

Total body fat mass (kg) was measured using DXA (Discovery W, Hologic Inc, USA) at the health examination site. All of the subjects were examined in the supine position, and none of the subjects had undergone tests with contrast dye within the past week or tests with radioactive tracers within the past 3 days. Body fat mass, excluding the head, was further separated into appendicular (the sum of arms and legs) and truncal fat mass. Weight (kg), height (cm), and waist circumference (cm) were also measured in subjects wearing only a gown without shoes. Waist circumference was measured at the intersection of mid-axillary line between the lower margin of the last rib and the top of the iliac crest at the expiration state using a flexible plastic tape measure while subjects were standing. All of the assessments were performed by trained examiners. BMI was calculated as [weight (kg)/height (m²)]. Body fat mass was expressed as the body fat percentage (%), which was calculated as [body fat (kg)/total body weight (kg)] × 100. Appendicular and truncal fat percentage (%) were calculated as [appendicular or truncal body fat (kg)/total body weight (kg)] \times 100].

Vitamin D and other study variables

Blood samples were collected during the fasting state of health examination surveys. After collection, the samples were promptly refrigerated and transported to the designated central laboratory (NeoDin Medical Institute, Seoul, Korea). Serum 25(OH)D levels were measured using a radioimmunoassay kit (DiaSorin Inc, Stillwater, MN) with 1470 WIZARD gamma–Counter (PerkinElmer, Finland). Vitamin D deficiency was defined as a 25(OH)D concentration <20 ng/mL.⁸ Other blood tests were also performed to evaluate the levels of glucose, cholesterol, high-density lipoprotein cholesterol, triglyceride, and creatinine [Hitachi 7600 analyzer (Hitachi, Tokyo, Japan)], and parathyroid hormone [LIAISON analyzer (DiaSorin, USA)]. The estimated glomerular filtration rate (mL/min/1.73 m²) was calculated using the Modification of Diet in Renal Disease equation as follows: 186.3 × serum creatinine (mg/dl)^{-1.154} × age (years)^{-0.203} (×0.742, if woman).¹⁵

Demographic variables included age, sex, and residential region. The residential region was categorized as the upper or lower area, according to the latitude. Seasons of blood collection were classified as spring (March to May), summer (June to August), autumn (September to November), or winter (January, February, and December). Smoking status was subdivided into nonsmoker, past smoker, or current smoker. Regular exercise was defined as moderate exercise regularly for ≥ 30 min at a time more than 5 times per week or intense exercise for ≥ 20 min at a time, more than 3 times per week. Moderate exercise was defined as an activity that leaves the subject somewhat breathless, such as badminton, table tennis, slow swimming, or volleyball. Intense exercise was an activity that causes the subject to be out of breath, such as climbing, basketball, football, squash, or running. On the nutritional survey, the subjects were asked about the use of vitamin D supplements. The extent of vitamin D supplementation was categorized into three groups: none, <400 IU/day, or \geq 400 IU/day. Daily energy (kcal), protein (g), and fat (g) intake were assessed using a 24-hour recall method.

Statistical analysis

All of the analyses and calculations were performed using STATA (STATA version 12.0, StataCorp LP, College Station, Texas, USA). In all the analyses, the complex sampling and survey sample weights of the KNHANES were used. Data are presented as the weighted means (SE) for continuous variables and as the weighted proportions (SE) for categorical variables. The demographic variables were compared between male and female subjects using the generalized linear model for continuous variables and the chi-square test for categorical variables, respectively. The association of body fat with serum 25(OH)D was detected using a linear regression model following stratification by sex. In addition to the unadjusted analysis, multivariate linear regression models were performed after adjusting for any covariate with p < 0.1 in a univariate analysis. The variables, which were not normally distributed, were transformed using the natural log prior to linear regression analysis. Univariate and multivariable logistic regression analyses were used to examine the correlation between body fat percentage and vitamin D deficiency. The odds ratios (ORs) and 95% confidence intervals (CIs) for vitamin D deficiency were calculated according to quartiles of body fat percentage after strati-

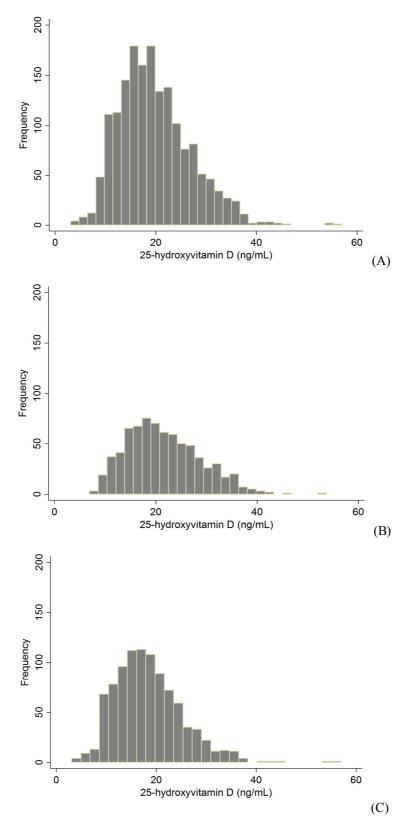


Figure 1. Distribution of 25-hydroxyvitamin D in total (A), male (B), and female (C) subjects.

fication by sex. To account for possible nonlinear relationship with serum 25(OH)D or vitamin D deficiency, we also applied the fractional polynomials method and showed the relationship as a fitted curve.¹⁶ A p value of less than 0.05 was considered significant.

RESULTS

Baseline characteristics of the study subjects

The mean age of subjects was 60 years. The proportion of

female subjects was 52.0%. The mean serum 25(OH)D level was 19.6 ng/mL. Approximately 58.5% of subjects exhibited a vitamin D deficiency (<20 ng/mL): men, 49.4%; women, 66.9%. The distribution of serum 25(OH)D was shown in Figure 1. The mean BMI was 23.6 kg/m². The mean waist circumference was 81.8 cm. Other demographic and fat parameters are presented in Table 1.

Table 1. Baseline characteristics of study subjects

	Men	Women	Total
	(n = 743)	(n = 954)	(n = 1,697)
Age (years)	59.4 (0.4)	59.9 (0.4)	59.7 (0.3)
Residential region			
Upper area (%)	56.6 (3.6)	55.7 (3.5)	56.1 (3.3)
Lower area (%)	43.4 (3.6)	44.3 (3.5)	43.9 (3.3)
Smoking ***			
None (%)	17.2 (1.6)	92.1 (1.1)	56.2 (1.4)
Past smoking (%)	39.5 (2.3)	3.3 (1.7)	20.6 (1.2)
Current smoking (%)	43.3 (2.3)	4.6 (0.8)	23.2 (1.4)
Regular exercise (%)	29.1 (2.1)	26.7 (1.9)	27.8 (1.6)
Season of blood collection			
Spring (%)	25.5 (3.8)	26.7 (3.9)	26.1 (3.7)
Summer (%)	29.8 (4.2)	24.8 (3.6)	27.2 (3.8)
Autumn (%)	21.4 (3.6)	22.7 (3.5)	22.1 (3.3)
Winter (%)	23.3 (3.6)	25.8 (4.0)	24.6 (3.6)
Laboratory finding		× ,	
25(OH)D (ng/mL) ***	21.2 (0.4)	18.0 (0.3)	19.6 (0.3)
Glucose (mg/dL) ***	99.1 (0.7)	95.0 (0.5)	97.0 (0.5)
Cholesterol (mg/dL) ***	190 (1.7)	203 (1.3)	197 (1.1)
Triglyceride (mg/dL) ***	161 (5.4)	127 (3.3)	143 (3.3)
HDL cholesterol (mg/dL) ***	45.7 (0.5)	49.1 (0.5)	47.4 (0.3)
eGFR $(mL/min/1.73 \text{ m}^2)^{**}$	91.2 (0.8)	94.1 (0.7)	92.7 (0.5)
PTH (pg/mL)	68.4 (1.2)	66.0(1.1)	67.2 (1.0)
Vitamin D supplement **			
None (%)	94.0 (1.0)	89.1 (1.3)	91.4 (0.9)
<400 IU/day (%)	3.7 (0.8)	8.2 (1.2)	6.0 (0.8)
≥400 IU/day (%)	2.3 (0.7)	2.7 (0.7)	2.6 (0.5)
Daily intake from food			
Energy (kcal/kg/day) ***	32.2 (0.6)	28.2 (0.4)	30.1 (0.4)
Protein (g/kg/day) ***	1.1 (0.1)	1.0 (0.1)	1.0 (0.1)
Fat (g/kg/day) **	0.5 (0.1)	0.4 (0.1)	0.5 (0.1)
Body weight (kg) ***	64.9 (0.4)	55.8 (0.3)	60.2 (0.3)
BMI $(kg/m^2)^*$	23.4 (0.1)	23.7 (0.1)	23.6 (0.1)
Waist circumference (cm) ***	83.6 (0.4)	80.2 (0.4)	81.8 (0.3)
Body fat percentage			- ()
Total (%) ***	20.8 (0.2)	33.1 (0.3)	27.2 (0.3)
Appendicular (%) ***	7.8 (0.1)	14.4 (0.1)	11.2 (0.1)
Truncal (%) ***	11.4 (0.2)	17.2 (0.2)	14.4 (0.2)

Statistical significance of difference is calculated between male and female subjects.

p < 0.05; p < 0.01; p < 0.001; p < 0.001.

25(OH)D, 25-hydroxyvitamin D; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone.

Linear regression analysis between body fat and vitamin D status

In the univariate analysis, both body fat and anthropometric parameters were significantly and negatively associated with serum 25(OH)D levels (Table 2). However, in men, the correlations between serum 25(OH)D and BMI or waist circumference were not significant. Several covariates, such as age, sex, residential region, smoking, season of blood collection, laboratory findings (triglyceride, high-density lipoprotein cholesterol), estimated glomerular filtration rate, vitamin D supplements, and daily intake from food (energy, protein, and fat), were associated with vitamin D deficiency (all p_s <0.10) (Table 3), but exercise, glucose, and cholesterol level were not associated with serum 25(OH)D level (p>0.1). Accordingly, we selected these variables (except exercise, glucose, cholesterol) as the adjustment variables in the following multi-

variate analyses. After adjusting for multiple variables, the statistical significances of BMI and waist circumference disappeared. However, body fat percentage remained significant in the multivariate linear regression models. The inverse relationship with serum 25(OH)D was observed in both the appendicular and truncal fat percentages. We explored possible nonlinear relationships with serum 25(OH)D using the fractional polynomials method (Figure 2). BMI and waist circumference did not have a marked relationship with serum 25(OH)D in male subjects. In female subjects, BMI, waist circumference, and body fat percentage all had an inverse relationship with serum 25(OH)D. However, body fat percentage seemed to have a greater trend than BMI or waist circumference. The linear inverse relationship between body fat and serum 25(OH)D was also consistent, irrespectively of the body fat location (Figure 3).

Sex	Independent variable	Unadjusted		Adjusted [†]	
		Correlation coefficient (95% CI)	p value	Correlation coefficient (95% CI)	p value
Men	Ln BMI	-0.058 (-0.322 to 0.206)	0.665	0.163 (-0.102 to 0.428)	0.227
	Waist circumference	-0.002 (-0.005 to 0.002)	0.412	0.002 (-0.002 to 0.007)	0.245
	Body fat percentage				
Total	Total	-0.012 (-0.019 to -0.005)	0.001	-0.008 (-0.015 to -0.001)	0.027
	Appendicular	-0.024 (-0.041 to -0.007)	0.005	-0.021 (-0.037 to -0.004)	0.013
	Truncal	-0.018 (-0.028 to -0.008)	< 0.001	-0.010 (-0.020 to 0.001)	0.062
Women Ln BMI Waist circ	Ln BMI	-0.346 (-0.575 to -0.118)	0.003	-0.180 (-0.429 to 0.068)	0.154
	Waist circumference	-0.003 (-0.006 to -0.001)	0.035	-0.001 (-0.004 to 0.002)	0.399
	Body fat percentage				
	Total	-0.014 (-0.022 to -0.006)	0.001	-0.011 (-0.018 to -0.005)	0.001
	Appendicular	-0.022 (-0.038 to -0.005)	0.009	-0.022 (-0.034 to -0.009)	0.001
	Truncal	-0.017 (-0.028 to -0.006)	0.003	-0.013 (-0.022 to -0.003)	0.010

Table 2. Univariate and multivariate linear regression analyses for serum 25-hydroxyvitamin D

[†]Adjusted for age, sex, residential region, smoking, season of blood collection, laboratory findings (triglyceride, high-density lipoprotein cholesterol, parathyroid hormone), estimated glomerular filtration rate, vitamin D supplements, and daily intake from food (energy, protein, and fat). CI, confidence interval; Ln, natural log transformed.

Table 3. Baseline characteristics in the groups with and without vitamin D deficiency

		Presence of vitamin D deficiency		
	No (n = 729)	Yes (n = 968)	<i>p</i> value	
Age (years)	60.1 (0.5)	59.0 (0.4)	0.043	
Sex			< 0.001	
Men (%)	57.9 (0.2)	39.2 (0.2)		
Women (%)	42.1 (0.2)	60.1 (0.2)		
Residential region			0.024	
Upper area (%)	58.4 (0.4)	67.5 (0.3)		
Lower area (%)	41.6 (0.4)	32.5 (0.3)		
Smoking			< 0.001	
None (%)	49.9 (0.2)	62.0 (0.2)		
Past smoking (%)	26.0 (0.2)	17.6 (0.2)		
Current smoking (%)	24.1 (0.2)	20.4 (0.2)		
Regular exercise (%)	26.9 (0.2)	27.5 (0.2)	0.816	
Season of blood collection			< 0.001	
Spring (%)	19.2 (0.4)	32.5 (0.5)		
Summer (%)	38.4 (0.5)	17.9 (0.3)		
Autumn (%)	26.7 (0.5)	19.7 (0.3)		
Winter (%)	15.8 (0.3)	30.0 (0.4)		
Laboratory finding				
25(OH)D (ng/mL)	26.1 (0.3)	14.9 (0.2)	< 0.001	
Glucose (mg/dL)	96.7 (0.6)	97.2 (0.6)	0.532	
Cholesterol (mg/dL)	196 (1.7)	198 (1.4)	0.322	
Triglyceride (mg/dL)	133 (3.8)	151 (4.2)	< 0.001	
HDL cholesterol (mg/dL)	48.2 (0.6)	46.9 (0.4)	0.051	
eGFR (mL/min/1.73 m2)	93.7 (0.7)	91.4 (0.8)	0.020	
PTH (pg/ml)	64.8 (1.3)	68.8 (1.1)	0.003	
Vitamin D supplement			0.004	
None (%)	88.1 (0.1)	93.7 (0.1)		
<400 IU/day (%)	8.1 (0.1)	4.7 (0.1)		
≥400 IU/day (%)	3.8 (0.1)	1.6 (0.1)		
Daily intake from food				
Energy (kcal/kg/day)	31.4 (0.5)	29.2 (0.5)	0.001	
Protein (g/kg/day)	1.1 (0.1)	1.0 (0.1)	0.021	
Fat (g/kg/day)	0.5 (0.1)	0.4 (0.1)	0.049	

Statistical significance of difference is calculated between subjects with and without vitamin D deficiency. 25(OH)D, 25-hydroxyvitamin D; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration rate; PTH, parathyroid hormone.

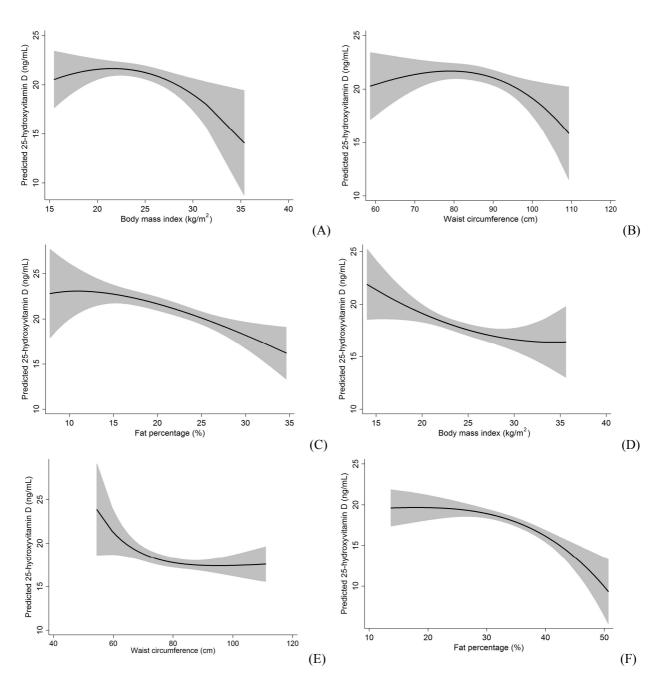


Figure 2. Fitted curve between 25-hydroxyvitamin D and body mass index (A, D), waist circumference (B, E), and total fat percentage (C, F) in male (A, B, C) and female (D, E, F) subjects.

Logistic regression analysis between body fat and vitamin D deficiency

In univariate logistic regression analysis, the quartiles of BMI and waist circumference did not have a relationship with vitamin D deficiency in male subjects (Table 4). In female subjects, the quartiles of BMI had a trend of inverse relationship with vitamin D deficiency, although each quartile group did not have a difference with other quartiles (Table 5). However, this trend was not significant after adjustment of multiple variables. When considering the quartile groups of body fat percentage, the group with the highest quartile had a greater OR for vitamin D deficiency than the lower quartile groups. This correlation remained significant, irrespective of the body fat location (both appendicular and truncal fat) or the adjustment of multiple variables, although the trend was more prominent in male subjects than female subjects.

DISCUSSION

In summary, body fat mass was significantly associated with vitamin D status independent of several other factors in Korean adults. Furthermore, the correlation between fat and vitamin D was consistent irrespective of the body fat location. However, BMI and waist circumference were not independent factors related to the vitamin D status. To examine the correlation with vitamin D status (or vitamin D deficiency), body fat parameters were superior to BMI or waist circumference parameters. This trend was greater in male subjects than female subjects. Although the fractional polynomials method was used, body fat mass was linearly correlated with vitamin D status (or vitamin D deficiency). BMI had a general linear relationship with vitamin D in female but not male subjects, but this trend was weaker than body fat mass. Waist circumference did not have any relationship with vitamin D status, irrespec-

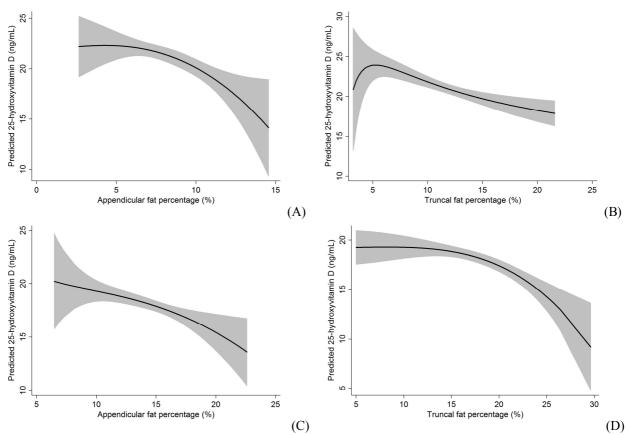


Figure 3. Fitted curve between 25-hydroxyvitamin D and fat percentage according to the location of body fat [appendicular (A, C) and truncal (B, D)] in male (A, B) and female (C, D) subjects.

Table 4. Univariate and multivariate	logistic regression	analyses for vitamin L	deficiency in male subjects

Indonandant variable	Univariate		Multivariable	Ť
Independent variable	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
BMI (kg/m ²)		0.450 ‡	· · ·	0.297 ‡
1^{st} quartile (<21.3)	1 (Reference)		1 (Reference)	
2 nd quartile (21.3–23.3)	0.885 (0.513 to 1.527)	0.658	0.652 (0.339 to 1.252)	0.197
3 rd quartile (23.4–25.2)	0.861 (0.499 to 1.486)	0.589	0.596 (0.294 to 1.207)	0.149
4 th quartile (>25.2)	1.117 (0.646 to 1.932)	0.691	0.648 (0.312 to 1.343)	0.242
Waist circumference (cm)		0.459 [‡]		0.213 ‡
1^{st} quartile (<78.4)	1 (Reference)		1 (Reference)	
2 nd quartile (78.4–83.8)	0.869 (0.489 to 1.544)	0.629	0.591 (0.262 to 1.170)	0.140
3 rd quartile (83.9–89.3)	1.123 (0.658 to 1.919)	0.668	0.729 (0.365 to 1.454)	0.367
4 th quartile (>89.3)	0.996 (0.576 to 1.722)	0.988	0.591 (0.293 to 1.191)	0.121
Total fat percentage (%)		<0.001 ‡		0.004 ‡
1 st quartile (<17.8)	1 (Reference)		1 (Reference)	
2 nd quartile (17.8–20.9)	1.711 (0.967 to 3.028)	0.065	1.442 (0.730 to 2.845)	0.289
3 rd quartile (21.0–24.1)	1.547 (0.864 to 2.772)	0.141	1.442 (0.757 to 2.749)	0.264
4^{th} quartile (>24.1)	3.655 (2.096 to 6.376)	< 0.001	3.029 (1.446 to 6.347)	0.004
Appendicular fat percentage (%)		0.003 ‡		0.007 ‡
1^{st} quartile (<6.7)	1 (Reference)		1 (Reference)	
2^{nd} quartile (6.7–7.9)	1.582 (0.864 to 2.897)	0.136	1.239 (0.622 to 2.470)	0.540
3^{rd} quartile (8.0–9.2)	1.325 (0.737 to 2.382)	0.345	1.034 (0.534 to 2.002)	0.920
4^{th} quartile (>9.2)	3.440 (2.025 to 5.842)	< 0.001	2.903 (1.484 to 5.675)	0.002
Truncal fat percentage (%)		<0.001 ‡		0.017 ‡
1 st quartile (<9.0)	1 (Reference)		1 (Reference)	
2^{nd} quartile (9.0–11.3)	1.029 (0.589 to 1.796)	0.920	0.789 (0.411 to 1.513)	0.473
3 rd quartile (11.4–13.9)	1.775 (1.001 to 3.148)	0.050	1.323 (0.673 to 2.603)	0.415
4 th quartile (>13.9)	2.640 (1.550 to 4.497)	< 0.001	2.028 (0.972 to 4.232)	0.059

[†] Adjusted for age, sex, residential region, smoking, season of blood collection, laboratory findings (triglyceride, high-density lipoprotein cholesterol, parathyroid hormone), estimated glomerular filtration rate, vitamin D supplements, and daily intake from food (energy, protein, and fat).

p for trend. CI, confidence interval.

Indonan dant variable	Univariate		Multivariate	ŕ
Independent variable	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
BMI (kg/m^2)		0.077 ‡		0.961 ‡
1^{st} quartile (<21.7)	1 (Reference)		1 (Reference)	
2^{nd} quartile (21.8–23.5)	1.193 (0.740 to 1.924)	0.467	1.081 (0.656 to 1.782)	0.759
3 rd quartile (23.6–25.5)	1.242 (0.785 to 1.965)	0.352	1.037 (0.641 to 1.678)	0.881
4 th quartile (>25.5)	1.356 (0.842 to 2.184)	0.208	1.001 (0.576 to 1.738)	0.998
Waist circumference (cm)		0.149 [‡]		0.568^{+}
1^{st} quartile (<73.7)	1 (Reference)		1 (Reference)	
2 nd quartile (73.7–80.2)	1.272 (0.766 to 2.113)	0.350	1.200 (0.698 to 2.061)	0.507
3 rd quartile (80.3–85.5)	1.376 (0.902 to 2.097)	0.137	1.443 (0.920 to 2.262)	0.110
4 th quartile (>85.5)	1.219 (0.779 to 1.907)	0.384	1.070 (0.647 to 1.768)	0.791
Total fat percentage (%)		0.001 ‡		0.037 ‡
1^{st} quartile (<29.7)	1 (Reference)		1 (Reference)	
2 nd quartile (29.7–33.3)	0.867 (0.528 to 1.422)	0.569	0.767 (0.449 to 1.313)	0.332
3 rd quartile (33.4–36.2)	1.208 (0.738 to 1.979)	0.450	1.100 (0.655 to 1.847)	0.717
4 th quartile (>36.2)	1.827 (1.075 to 3.103)	0.026	1.603 (0.902 to 2.851)	0.107
Appendicular fat percentage (%)		0.015 ‡		0.073 ‡
1^{st} quartile (<12.6)	1 (Reference)		1 (Reference)	
2 nd quartile (12.6–14.2)	0.768 (0.507 to 1.166)	0.214	0.754 (0.465 to 1.222)	0.249
3^{rd} quartile (14.3–15.8)	0.988 (0.617 to 1.580)	0.958	1.044 (0.618 to 1.765)	0.871
4 th quartile (>15.8)	1.538 (0.940 to 2.517)	0.086	1.487 (0.870 to 2.543)	0.146
Truncal fat percentage (%)		0.002 ‡		0.067 ‡
1^{st} quartile (<14.4)	1 (Reference)		1 (Reference)	
2^{nd} quartile (14.4–17.3)	1.214 (0.784 to 1.881)	0.382	1.119 (0.703 to 1.781)	0.431
3 rd quartile (17.4–19.7)	1.176 (0.690 to 2.004)	0.549	1.236 (0.697 to 2.192)	0.284
4 th quartile (>19.7)	2.021 (1.278 to 3.196)	0.003 ‡	1.855 (1.068 to 3.222)	0.029 ‡

Table 5. Univariate and multivariate logistic regression analyses for vitamin D deficiency in female subjects

[†] Adjusted for age, sex, residential region, smoking, exercise, season of blood collection, laboratory findings (glucose, cholesterol, triglyceride, high-density lipoprotein cholesterol, parathyroid hormone), estimated glomerular filtration rate, vitamin D supplements, and daily

 p^{\ddagger} for trend.

CI, confidence interval.

tive of the body fat location or sex. The results of the present study have important implications on vitamin D research. First, these data firstly confirm the inverse correlation between body fat mass and vitamin D status in a large sample of a Korean population. Because Asians have a relatively lean body shape or low BMI, the associations between BMI and comorbidities may not be clearly exhibited. In light of these results, the risk of vitamin D deficiency should be monitored, especially in the subjects with low BMI but high fat mass, or male subjects.

Caucasian and African-American studies have noted that body fat mass is inversely correlated with vitamin D status. However, the exact mechanism by which higher body fat results in lower vitamin D levels is not known. One suggestion is that obese subjects are less exposed to sunlight due to reduced involvement in outdoor activities.⁸ However, a different lifestyle may not be the only explanation; our data indicate that the correlation between body fat mass and serum 25(OH)D was independent of exercise, although exercise does not represent a degree of full activity. Accordingly, the results suggest that adipose tissue per se contributes to low 25(OH)D status. One of mechanisms is a sequestration of vitamin D, which is fat-soluble, by adipose tissue.⁶ Total-body clearance of vitamin D can be increased during obesityassociated inflammation.⁷ Other possible mechanisms include the increased catabolism of vitamin D with increasing fat mass due to the local action of 24hydroxylase, which is found in human adipose tissue.¹⁷ Taken together, subjects with a high fat mass may have altered vitamin D physiology, but further mechanistic understanding is needed.

The relationship between body fat mass and vitamin D appears to vary by ethnicity. Data from the NHANES III (women, aged ≥ 12 years, n=6,042) indicate that the negative relationship between body fat mass and serum 25(OH)D is stronger in whites than blacks.¹⁴ Other studies with small sample sizes have confirmed the ethnic difference in the correlation between fat mass and serum 25(OH)D status.^{18,19} However, Asians were not a main concern of these studies. Recently, two studies including Asians have been conducted. Elderly Asian men (aged \geq 60 years, n=216) exhibited an inverse correlation between visceral fat mass and 25(OH)D in one study,¹² and the other study [European (n=182) and South Asian adults (n=188)] identified ethnicity as a significant variable in the correlation model between body fat and serum 25(OH)D.¹³ However, these studies are not generalizable to Asians or Koreans because they either were based on limited number of study subjects or included only elderly patients. We evaluated the correlation between body fat mass and serum 25(OH)D status in a large sample of Korean adults. As in other ethnicity studies, the correlation in Koreans was strong irrespective of several other factors. Considering the effect of fat mass per se on the serum 25(OH)D levels, the location of body fat may not be of great significance; both the appendicular and truncal fat masses were important in determining vitamin D status in the present study.

BMI is used as an indicator of body fat accumulation, but BMI is not ideal because it does not differentiate fat tissue from other tissues, such as muscle mass. Furthermore, the relationship between BMI and body fat mass is affected by several factors, including ethnicity. For example, Asians exhibit a higher proportion of body fat for a given BMI than do Caucasians.²⁰ Accordingly, the BMI cut-off points for determining overweight and obesity are considered differently according to ethnicity.²¹ Given this low predictive value of BMI for high fat mass, it is reasonable that BMI was not correlated with serum 25(OH)D in the present study subjects with low BMI. Waist circumference also failed to exhibit any correlation with serum 25(OH)D. We attribute this finding to the body shape of Koreans, who are typically lean compared with Caucasians. In contrast to these anthropometric measures, fat mass parameter was correlated with serum 25(OH)D. Taken together, future research on the vitamin D status in Asian subjects with lean body shape (or low fat mass) should utilize fat mass instead of BMI or waist circumference.

The trend of inverse relationship between fat and 25(OH)D was greater in male subjects than female subjects, although the reason for this difference was not completely understood. The sex-difference in correlation with vitamin D was also documented in other studies.^{22,23} The level of sex-hormone such as estrogen may be associated with the sex-difference in the correlation.²⁴ However, the overall trend was similar between male and female subjects.

The present study has some limitations that need to be addressed. First, the study design was cross-sectional, which prevented conclusions regarding the temporal nature of the observed association between fat mass and vitamin D status. Further prospective studies assessing the change in vitamin D status after altering body fat mass are needed. Second, we did not quantify visceral fat mass; we therefore did not conduct a separate analysis for visceral fat mass. Some studies have postulated a distinct role for visceral fat mass on vitamin D status.¹³ However, other studies have presented data to the contrary.²⁵ Most studies have accorded importance to both visceral and subcutaneous fat tissues.^{26, 27} Third, we did not compare the study results with those examining other ethnicities. Therefore, care must be taken when applying our study results to other ethnicities. Fourth, the intake of dairy products containing significant amount of vitamin D was not available in the KNHANES. This factor may lead to differences in vitamin D levels between subjects with low and high fat mass.

In conclusion, we confirmed that body fat mass is inversely associated with vitamin D status in Korean adults. The direct measurement of body fat mass may be needed to explore the correlation with vitamin D status especially in male subjects. Likewise, body fat mass may determine the risk of diseases related to vitamin D deficiency in Koreans. Further body fat–controlled studies are needed to address the temporal relationship with vitamin D status or with diseases related to vitamin D deficiency.

AUTHOR DISCLOSURES

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REFERENCES

- 1. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357: 266-81. doi: 10.1056/NEJMra070553
- Norman AW, Bouillon R, Whiting SJ, Vieth R, Lips P. 13th Workshop consensus for vitamin D nutritional guidelines. J Steroid Biochem Mol Biol. 2007;103:204-5. doi: 10.1016/j. jsbmb.2006.12.071
- Holick MF, Matsuoka LY, Wortsman J. Age, vitamin D, and solar ultraviolet. Lancet. 1989;2:1104-5. doi: 10.1016/ S01 40-6736(89)91124-0
- Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin. J Clin Endocrinol Metab. 1988;67:373-8. doi: 10.1210/jcem-67-2-373
- Oh YJ, Kim M, Lee H, Lee JP, Kim H, Kim S et al. A threshold value of estimated glomerular filtration rate that predicts changes in serum 25-hydroxyvitamin D levels: 4th Korean National Health and Nutritional Examination Survey 2008. Nephrol Dial Transplant. 2012;27:2396-403. doi: 10. 1093/ndt/gfr763
- Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. Am J Clin Nutr. 2000;72:690-3.
- Need AG, Morris HA, Horowitz M, Nordin C. Effects of skin thickness, age, body fat, and sunlight on serum 25hydroxyvitamin D. Am J Clin Nutr. 1993;58:882-5.
- Kull M, Kallikorm R, Lember M. Body mass index determines sunbathing habits: implications on vitamin D levels. Intern Med J. 2009;39:256-8. doi: 10.1111/j.1445-5994.2009.01900.x
- DeNino WF, Tchernof A, Dionne IJ, Toth MJ, Ades PA, Sites CK et al. Contribution of abdominal adiposity to agerelated differences in insulin sensitivity and plasma lipids in healthy nonobese women. Diabetes Care. 2001;24:925-32. doi: 10.2337/diacare.24.5.925
- Zafon C. Oscillations in total body fat content through life: an evolutionary perspective. Obes Rev. 2007;8:525-30. doi: 10.1111/j.1467-789X.2007.00377.x
- VanItallie TB, Yang MU, Heymsfield SB, Funk RC, Boileau RA. Height-normalized indices of the body's fatfree mass and fat mass: potentially useful indicators of nutritional status. Am J Clin Nutr. 1990;52:953-9.
- 12. Seo JA, Cho H, Eun CR, Yoo HJ, Kim SG, Choi KM et al. Association between visceral obesity and sarcopenia and vitamin D deficiency in older Koreans: the Ansan Geriatric Study. J Am Geriatr Soc. 2012;60:700-6. doi: 10.1111/j. 1532-5415.2012.03887.x
- Sulistyoningrum DC, Green TJ, Lear SA, Devlin AM. Ethnic-specific differences in vitamin d status is associated with adiposity. PLoS One. 2012;7:e43159. doi: 10.1371/ journal.pone.0043159
- Looker AC. Body fat and vitamin D status in black versus white women. J Clin Endocrinol Metab. 2005;90:635-40. doi: 10.1210/jc.2004-1765
- 15. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130:461-70. doi: 10.7326/0003-4819-130-6-199903160-00002

- 16. Royston P, Ambler G, Sauerbrei W. The use of fractional polynomials to model continuous risk variables in epidemiology. Int J Epidemiol. 1999;28:964-74. doi: 10.10 93/ije/28.5.964
- Li J, Byrne ME, Chang E, Jiang Y, Donkin SS, Buhman KK et al. 1alpha,25-Dihydroxyvitamin D hydroxylase in adipocytes. J Steroid Biochem Mol Biol. 2008;112:122-6. doi: 10.1016/j.jsbmb.2008.09.006
- Parikh SJ, Edelman M, Uwaifo GI, Freedman RJ, Semega-Janneh M, Reynolds J et al. The relationship between obesity and serum 1,25-dihydroxy vitamin D concentrations in healthy adults. J Clin Endocrinol Metab. 2004;89:1196-9. doi: 10.1210/jc.2003-031398
- Rajakumar K, de las Heras J, Chen TC, Lee S, Holick MF, Arslanian SA. Vitamin D status, adiposity, and lipids in black American and Caucasian children. J Clin Endocrinol Metab. 2011;96:1560-7. doi: 10.1210/jc.2010-2388
- Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. Obes Rev. 2002;3: 141-6. doi: 10.1046/j.1467-789X.2002.00065.x
- 21. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004;363:157-63. doi: 10.1016/S0140-6736(03)15268-3
- 22. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K et al. Vitamin D deficiency and risk of cardio-

vascular disease. Circulation. 2008;117:503-11. doi: 10. 1161/CIRCULATIONAHA.107.706127

- 23. Han SS, Kim M, Kim H, Lee SM, Oh YJ, Lee JP et al. Nonlinear relationship between serum 25-hydroxyvitamin D and hemoglobin in Korean females: the Korean National Health and Nutrition Examination Survey 2010-2011. PLoS One. 2013;8:e72605. doi: 10.1371/journal.pone.0072605
- 24. Lim JS, Kim KM, Rhee Y, Lim SK. Gender-dependent skeletal effects of vitamin D deficiency in a younger generation. J Clin Endocrinol Metab. 2012;97:1995-2004. doi: 10.1210/jc.2011-3098
- 25. Lenders CM, Feldman HA, Von Scheven E, Merewood A, Sweeney C, Wilson DM et al. Relation of body fat indexes to vitamin D status and deficiency among obese adolescents. Am J Clin Nutr. 2009;90:459-67. doi: 10.3945/ajcn.2008. 27275
- 26. Freedman BI, Wagenknecht LE, Hairston KG, Bowden DW, Carr JJ, Hightower RC et al. Vitamin D, adiposity, and calcified atherosclerotic plaque in african-americans. J Clin Endocrinol Metab. 2010;95:1076-83. doi: 10.1210/jc.2009-1797
- 27. Cheng S, Massaro JM, Fox CS, Larson MG, Keyes MJ, McCabe EL et al. Adiposity, cardiometabolic risk, and vitamin D status: the Framingham Heart Study. Diabetes. 2010;59:242-8. doi: 10.2337/db09-1011

Original Article

Association between body fat and vitamin D status in Korean adults

Seung Seok Han MD¹, Myounghee Kim PhD², Su Mi Lee MD¹, Jung Pyo Lee MD, PhD³, Sejoong Kim MD, PhD⁴, Kwon Wook Joo MD, PhD¹, Chun Soo Lim MD, PhD³, Yon Su Kim MD, PhD¹, Dong Ki Kim MD, PhD¹

¹Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea ²Department of Dental Hygiene, College of Health Science, Eulji University, Gyeonggi-do, Korea ³Department of Internal Medicine, Seoul National University Boramae Medical Center, Seoul, Korea ⁴Department of Internal Medicine, Seoul National University Bundang Hospital, Gyeonggi-do, Korea

韓國成人體脂肪與維生素D之關聯性

體脂肪與維生素 D 的相關性受到種族的影響,但由於先前研究的缺乏,這個 論點在亞洲人仍未確認。來自於第四次韓國國家健康與營養調查的第二及第三 年(2008-2009)的 1697 名韓國成人資料納入本研究。體脂肪量是以雙能量 X 光 吸收儀測量的。以直線迴歸分析血清 25-羥維生素 D[25(OH)D],及以邏輯斯迴 歸分析維生素 D 缺乏[25(OH)D<20 ng/mL],以評估校正多種共變項後, BMI、腰圍或體脂肪是否為顯著預測因子。以分數多項式法探究它們之間可能 的非線性關係。所有的分析以性別分層。線性迴歸分析結果,BMI 及腰圍與 25(OH)D 沒有相關性。然而,男女性的體脂肪與 25(OH)D 為負相關,並與脂 肪部位(四肢及軀幹脂肪)無關。由邏輯斯迴歸分析結果指出,最高四分位的體 脂肪組比起最低四分位組,有較高的維生素 D 缺乏風險,與脂肪部位及性別 無關。然而,BMI 及腰圍的四分位與維生素 D 缺乏沒有相關性。即使用分數 多項式法分析,體脂肪與 25(OH)D(或是維生素 D 缺乏)間的直線相關仍然存 在。韓國成人的體脂肪量與血清 25(OH)D 呈現負相關。因此有必要監測高體 脂肪量的韓國成人之維生素 D 缺乏。

關鍵字:肥胖、體組成、體脂肪分布、韓國、維生素 D