nutrición clínica y Dietética Hospitalaria

Artículo Original

Nutr Clín Diet Hosp. 2024; 44(3):194-203
DOI: 10.12873/443yoon

Gender difference in the relationship between metabolic syndrome and vitamin D in Korean adults with obesity

Hyun HO SUNG[1], Mi YOUNG GI[2], Ju AE CHA[3], So YOUNG PARK[4], Cho HEE PARK[5], Sun GYU KIM[1], Eun SOOK HAN[6], Hyun YOON[7]

1 Department of Clinical Laboratory Science, Dongnam Health University, Cheoncheon-ro 74beon-gil, Jangan-gu, Suwon-si, Gyeonggi-do, South Korea.
2 Department of Nursing, Christian College of Nursing, Gwangju, South Korea.
3 Department of Nursing, Chunnam Technouniversity, Gokseong-gun, Jeollanam-do, South Korea.
4 Department of Dental Hygiene, Wonkwang Health Science University, Iksan-si, Jeollabuk-do, South Korea.
5 Department of Global Medical Beauty, Konyang University, Daehak-ro, Nonsan-si, Chungcheongnam-do, South Korea.
6 Department of Publix Relations, Seoul National University Bundang Hospital, Gumi-ro 173beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do, South Korea.
7 Department of Clinical Laboratory Science, Wonkwang Health Science University, Iksan-daero, Iksan-si, Jeollabuk-do, 54538, South Korea.

Recibido: 19/mayo/2024. Aceptado: 27/junio/2024.

ABSTRACT

Background: The present study was conducted to assess the relationship between metabolic syndrome (MetS) and serum 25-hydroxyvitamin D [25(OH)D] in Korean adults with or without obesity.

Materials and Methods: The study was performed using data from the sixth Korean National Health and Nutrition Examination Survey (KNHANES VI, 2013-2014) and included Korean adults (n = 1,140) with or without obesity (n = 2,359) aged 20 years or older (n = 3,499).

Results: The key results of this study were as follows: first, adjusting related variables in logistic regression analysis, the relationship between MetS and the odds ratio (OR) of vitamin D deficiency [25(OH)D < 10 ng/mL] was not significant in men, premenopausal women, and postmenopausal women without obesity. Second, in a logistic regression analysis of premenopausal women with obesity, the relationship between MetS and vitamin D deficiency was not significant (OR, 1.241; 95% CI, 0.551–2.797; p = 0.603). However, MetS was positively associated with vitamin D deficiency in men (OR, 1.839; 95% CI, 1.038–3.258; p = 0.037) and postmenopausal women (OR, 3.136; 95% CI, 1.316–7.470; p = 0.010) with obesity.

Conclusions: MetS was not associated with vitamin D deficiency in Korean men, and postmenopausal women without obesity. MetS was positively associated with vitamin D deficiency in Korean men and postmenopausal women with obesity but not in premenopausal women with obesity.

KEYWORDS

Vitamin D; metabolic health; insulin resistance; cardiovascular risk; chronic diseases.

INTRODUCTION

The World Health Organization (WHO) estimated that in 2016, over 650 million people worldwide were obese[1]. The prevalence of obesity in Korea showed a steady increase from 35.1% in 2011 to 37.8% in 2013 and 42.3% in 2016[2]. Obesity is a major cause of morbidity and mortality from noncommunicable diseases and their complications, including type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and cancer[3,4]. Metabolic syndrome (MetS) is defined as a disease in which at least three of the five coronary risk factors, including elevated blood pressure (BP), elevated fasting blood glucose (FBG), elevated triglycerides (TGs), reduced high-density lipoprotein cholesterol (HDL-C), and abdominal obesity, occur simultaneously[5]. MetS is a strong risk factor for developing CVD, chronic kidney disease (CKD), and T2DM[6]. In the United States, 44% of those aged 50 or older, and approximately 23.7% of adults aged 20 or older, have MetS, and a leading cause of MetS has been found to be obesity due to lack of external activities and exercise[7]. In the Republic of Korea, the prevalence of MetS showed a steady increase from 22.9% in 2008 to 25.1% in 2013 and 30.3% in 2016[8].

Correspondencia:
Hyun Yoon
yh9074@yahoo.co.kr

Vitamin D, which is a fat-soluble secosteroid, can mostly be synthesized in the body following exposure to UV light or consumption of foods rich in vitamin D, such as milk, eggs, and fatty fish[9,10]. In humans, the most important forms of vitamin D are vitamin D3, which is synthesized from 7-dehydrocholesterol in the skin by UV light, and vitamin D2, which is present in plants, such as mushrooms, and in fatty fish, such as mackerel[10,11]. Vitamin D is transported to the liver, where it is metabolized to 25-hydroxyvitamin D [25(OH)D] (hereafter referred to as 25(OH)D), the major circulating form of vitamin D, which is then metabolized principally to 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], the biologically active form of vitamin D, in the kidneys[12]. Vitamin D status in the human body is generally estimated by measurements of serum 25(OH)D because of its relatively long half-life of 2–3 weeks[13]. In the past, studies of vitamin D have focused on its role in calcium absorption and bone metabolism (e.g., calcium homeostasis maintenance, skeletal growth and maintenance, osteoporosis prevention and treatment)[14]. Currently, many researchers are paying attention to another function of vitamin D: its role in the prevention of chronic diseases such as cancer, CVD, and CKD, and insulin resistance diseases, such as T2DM and MetS[15,16].

There is still much controversy regarding the association between MetS and vitamin D because the findings vary across countries and races and with the health status of the subjects. That is, some studies report that MetS is associated with vitamin D[17,18], but some studies report that MetS is not associated with vitamin D[19,20]. These relationships may vary by gender due to sex hormones, lifestyle, and dietary habits. To the best of our knowledge, there is still no research on the gender-specific association of MetS and vitamin D in populations with obesity. The Republic of Korea is one of the countries with very severe vitamin D deficiency[21], and the prevalence of chronic diseases, such as obesity, MetS, and CVD, is increasing due to the westernization of diet. Therefore, the present study aimed to investigate the association between MetS and vitamin D by gender in adults aged 20 or older using the sixth Korean National Health and Nutrition Examination Survey (KNHANES VI) data.

METHODS

Study Subjects

This study was based on data from the KNHANES VI. The KNHANES is a cross-sectional survey conducted nationwide by the Division of Korean National Health and Welfare. The KNHANES VI (2013–2014) was performed from January 2013 to December 2014. In the KNHANES VI (2013–2014), 11,925 subjects who participated in the KNHANES VI, we limited the analyses to adults aged ≥ 20 years. We excluded participants 2, 516 subjects whose data were missing for important analytic variables, such as blood pressure, body mass index (BMI), waist circumference (WC), various blood chemistry tests, and information about lifestyle. Among them, of the 9,409 subjects who participated in the KNHANES VI, We excluded 5,910 subjects whose data were missing for serum 25(OH)D levels. Finally, 3,499 subjects were included in the statistical analysis. This study has been conducted according the principles expressed in the Declaration of Helsinki (Institutional Review Board No, 2013-07 CON-034C; 2013-12 EXP-03-5C). All participants in the survey signed an informed written consent form. All participants in the survey signed an informed written consent form. Further information can be found in "The KNHANES VI Sample", which is available on the KNHANES website. The data from KNHANES is available on request by email if the applicant logs onto the "Korea National Health and Nutrition Examination Survey" website.

General Characteristics and Blood Chemistry

Research subjects were classified by sex (men, and premenopausal women, and postmenopausal women), alcohol drinking (yes or no), and regular exercise (yes or no). Alcohol drinking was indicated as "yes" for participants who had consumed at least one glass of alcohol every month over the last year. Regular exercise was indicated as "yes" for participants who had exercised on a regular basis regardless of indoor or outdoor exercise. Regular exercise was defined as 30 min at a time and 5 times/wk in the case of moderate exercise, such as swimming slowly, doubles tennis, volleyball, badminton, table tennis, and carrying light objects; and for 20 min at a time and 3 times/wk in the case of vigorous exercise, such as running, climbing, cycling fast, swimming fast, football, basketball, jump rope, squash, singles tennis, and carrying heavy objects. Research subjects were classified by men and women. Anthropometric measurements included measurement of height, weight, BMI, WC, systolic blood pressure (SBP), and diastolic blood pressure (DBP). Blood chemistry included measurement of estimated glomerular filtration rate (eGFR), total cholesterol (TC), HDL-C, TGs, white blood cell (WBC), FBG, and 25(OH)D. Obesity was classified as BMI ≥ 25.0 kg/m^2 [22]. Hypertension was classified as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg or current use of antihypertensive medication[22]. T2DM was classified as FBG ≥ 126 mg/dL or current use of glucose lowering medication[22]. CKD was classified as eGFR < 60 ml/min/1.73 m^2 or CKD medication[22].

Serum 25(OH)D and Metabolic Syndrome

Serum 25(OH)D were measured with a radioimmunoassay (25-hydroxy-vitamin D ^{125}I RIA Kit; DiaSorin, Stillwater, MN, USA) using a 1470 Wizard Gamma Counter (PerkinElmer, Turku, Finland). Serum 25(OH)D was classified as vitamin D deficiency [25(OH)D < 10 ng/mL] or vitamin D normal [25(OH)D ≥ 10 ng/mL] [23]. MetS was defined using the diagnostic criteria of the Revised National Cholesterol Education Program Adult Treatment panel III (Revised NCEP-ATP III) based on common clinical measures, including WC, BP, TGs, HDL-C, and FBG. The criteria for abdominal obesity were WC of over 90 cm and 80 cm for men and women, respectively, according to the Asia-Pacific criteria[24]. SBP over 130 mmHg or DBP over 85 mmHg were set as the criteria for elevated BP. TGs over 150 mg/dL

was set as the criteria for elevated TGs. The criteria for reduced HDL-C were HDL-C of less than 40 mg/dL and 50 mg/dL for men and women, respectively. FBG over 100 mg/dL was set as the criteria for elevated FBG. The presence of defined abnormalities in any three of these five measures constitutes a diagnosis of MetS. The MetS score indicates the presence of abdominal obesity, elevated BP, elevated TGs, reduced HDL-C, and elevated FBG.

Data Analysis

The collected data was statistically analyzed using SPSS WIN version 18.0 (SPSS Inc., Chicago, IL, USA). The distributions of the participant characteristics were converted into percentages, and the resultant data was presented as a series of averages with standard deviations. The distribution and average difference in clinical characteristics according to non-obesity and obesity (Table 1) were calculated using chi-squared

Table 1. Clinical characteristics of research subjects

					n (%), M ± SD
Variables	**Category**	**Overall (n = 3,499)**	**Non-obesity (n = 2,359)**	**Obesity (n = 1,140)**	**p-value**
Age (years)		45.52 ± 14.49	44.80 ± 14.83	47.03 ± 14.09	< 0.001
Gender	Men	1,755 (50.2)	1,068 (45.3)	687 (60.3)	< 0.001
	Premenopausal women	1.000 (28.5)	795 (33.7)	205 (18.0)	
	Postmenopausal women	744 (21.3)	496 (33.7)	248 (21.8)	
Alcohol drinking	Current drinker	2,052 (58.6)	1,396 (58.0)	683 (59.9)	0.305
Smoking	Current smoker	841 (24.0)	520 (22.1)	321 (28.2)	< 0.001
Regular exercising	Yes	1,013 (29.0)	688 (29.2)	325 (28.5)	0.720
BMI (kg/m^2)		22.79 ± 3.43	21.93 ± 1.97	27.64 ± 2.44	< 0.001
WC (cm)		80.74 ± 9.86	76.20 ± 7.39	90.14 ± 7.37	< 0.001
SBP (mmHg)		116.48 ± 15.85	113.78 ± 15.40	122.13 ± 15.27	< 0.001
DBP (mmHg)		75.49 ± 10.18	73.62 ± 9.56	79.38 ± 10.33	< 0.001
TC (mg/dL)		188.01 ± 35.16	185.03 ± 33.71	194.18 ± 37.24	< 0.001
TGs (mg/dL)		138.88 ± 115.90	120.10 ± 97.85	177.75 ± 138.52	< 0.001
HDL-C (mg/dL)		52.43 ± 12.10	54.51 ± 12.05	48.14 ± 11.03	< 0.001
WBC (10^3/μL)		6.27 ± 1.71	6.06 ± 1.66	6.70 ± 1.73	< 0.001
FBG (mg/dL)		98.07 ± 19.77	95.07 ± 16.25	104.28 ± 24.42	< 0.001
eGFR (mL/min/1.73 m^2)		95.91 ± 17.66	97.12 ± 17.30	93.40 ± 18.14	< 0.001
25(OH)D (ng/dL)		16.95 ± 6.64	16.97 ± 6.79	16.95 ± 6.31	0.949
	25(OH)D ≥ 10	3,082 (88.1)	2,074 (87.9)	1,008 (88.4)	0.697
	25(OH)D < 10	417 (11.9)	285 (12.1)	132 (11.6)	
Hypertension		803 (22.9)	384 (16.3)	419 (36.8)	< 0.001
T2DM		210 (6.0)	86 (3.6)	124 (10.9)	< 0.001
CKD		51 (1.5)	26 (1.1)	25 (2.2)	0.015
MetS	MSS < 3	2,718 (77.7)	2,078 (88.1)	640 (56.1)	< 0.001
	MSS ≥ 3	781 (22.3)	281 (11.9)	500 (43.9)	

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TGs, triglycerides; HDL-C, high density lipoprotein cholesterol; WBC, white blood cell; FBG, fasting blood glucose; eGFR: estimated glomerular filtration rate; 25(OH)D, 25-hydroxyvitamin D; T2DM; type 2 diabetes mellitus; CKD, chronic kidney disease; metabolic syndrome.

and an independent t test. Mets components of subjects according to vitamin D deficiency without obesity (Table 2) and with obesity (Table 3). In the case of the logistic regression for the incidence odds ratio (OR) for vitamin D deficiency according to MetS in men, premenopausal women, and postmenopausal women without obesity (Table 4), adjusted for age, smoking, drinking, regular exercising, hypertension, CKD, T2DM, and WBC or menstruation (only premenopausal women). The significance level for all statistical data sets was set as $p < 0.05$.

RESULTS

Clinical characteristics according to the non-obesity and obesity groups

Clinical characteristics according to the non-obesity and obesity groups are shown in Table 1. The mean age of the non-obesity and obesity groups were 44.80 ± 14.83 and 47.03 ± 14.09 years. The prevalence rate of MetS and vitamin D deficiency in the non-obesity group were 281 (11.9%) and 285 (12.1%), respectively. The prevalence rate of MetS and vitamin D deficiency in the obesity group were 500 (43.9%) and 132 (11.6%), respectively. The prevalence rate of MetS in the obesity group was higher ($p < 0.001$) than in the non-obesity group. The prevalence rate of vitamin D deficiency in the non-obesity and obesity groups was not significant ($p = 0.697$).

MetS components of subjects according to vitamin D deficiency in subjects without obesity

Clinical characteristics according to vitamin D deficiency in men, premenopausal women, and postmenopausal women without obesity are shown in Table 2. In men, the elevated BP ($p = 0.030$) in the vitamin D deficiency group were higher than those in the vitamin D normal group but other MetS components (the elevated TGs, reduced HDL-C, elevated FBG, and abdominal obesity) and MetS were not significantly associated with vitamin D deficiency. In premenopausal and postmenopausal women, all MetS components and MetS were not significantly associated with vitamin D deficiency.

MetS components of subjects according to vitamin D deficiency in subjects with obesity

Clinical characteristics according to vitamin D deficiency in men, premenopausal women, and postmenopausal women with obesity are shown in Table 3. In men, the elevated TGs ($p = 0.047$), reduced HDL-C ($p = 0.004$), and abdominal obesity ($p = 0.041$) in the vitamin D deficiency group were higher

Table 2. Mets components of subjects according to vitamin D deficiency in subjects without obesity

									(n = 2,359)
Variables	**Men (n = 1,068)**			**Premenopausal women (n = 795)**			**Postmenopausal women (n = 496)**		
	Vitamin D normal (n = 965)	**Vitamin D deficiency (n = 103)**	**p-value**	**Vitamin D normal (n = 662)**	**Vitamin D deficiency (n = 133)**	**p-value**	**Vitamin D normal (n = 447)**	**Vitamin D deficiency (n = 49)**	**p-value**
25(OH)D (ng/dL)	18.93 ± 6.46	8.32 ± 1.33	< 0.001	16.24 ± 4.89	8.13 ± 1.44	< 0.001	19.38 ± 7.28	8.32 ± 1.24	< 0.001
Age (years)	45.69 ± 14.83	42.98 ± 15.83	0.083	35.13 ± 8.93	34.15 ± 9.49	0.255	59.34 ± 6.58	57.88 ± 6.84	0.142
BMI (kg/m^2)	22.28 ± 1.84	22.14 ± 2.09	0.467	21.18 ± 2.04	21.13 ± 2.13	0.255	22.42 ± 1.73	22.33 ± 1.77	0.746
Menstruation	–			21 (3.2)	2 (1.5)	0.402	–		
Elevated BP	229 (23.7)	35 (34.0)	0.030	38 (5.7)	13 (9.9)	0.118	144 (32.2)	22 (44.9)	0.081
Abdominal obesity	44 (4.6)	7 (6.8)	0.328	79 (11.9)	10 (7.5)	0.174	152 (34.0)	12 (24.5)	0.203
Elevated TGs	277 (28.7)	32 (31.1)	0.648	71 (10.7)	16 (12.0)	0.649	119 (26.6)	11 (22.4)	0.610
Reduced HDL-C	134 (13.9)	20 (19.4)	0.140	156 (23.6)	32 (24.1)	0.911	167 (37.4)	23 (46.9)	0.216
Elevated FBG	265 (27.5)	25 (24.3)	0.580	90 (13.6)	11 (8.3)	0.116	136 (30.4)	20 (10.8)	0.146
MetS	102 (10.6)	14 (13.8)	0.322	31 (4.7)	7 (5.3)	0.823	111 (24.8)	16 (32.7)	0.232

Vitamin D normal, 25(OH)D ≥ 10 ng/dL; Vitamin deficiency, 25(OH)D < 10 ng/dL.
Elevated BP is defined as SBP ≥ 130 mmHg or DBP ≥ 85 mmHg; Abdominal obesity is defined as WC ≥ 90 cm in men or WC ≥ 80 cm in women; Elevated TGs is defined as TGs ≥ 150 mg/dL; Reduced HDL-C is defined as HDL-C < 40 mg/dL in men or HDL-C < 50 mg/dL in women; Elevated FBG is defined as FBG ≥ 100 mg/dL.

Table 3. Mets components of subjects according to vitamin D deficiency in subjects with obesity

									(n = 1,140)
Variables	**Men (n = 687)**			**Premenopausal women (n = 205)**			**Postmenopausal women (n = 248)**		
	Vitamin D normal (n = 627)	**Vitamin D deficiency (n = 60)**	**p-value**	**Vitamin D normal (n = 168)**	**Vitamin D deficiency (n = 37)**	**p-value**	**Vitamin D normal (n = 213)**	**Vitamin D deficiency (n = 35)**	**p-value**
25(OH)D (ng/dL)	18.25 ± 5.67	8.13 ± 1.59	< 0.001	16.37 ± 4.59	8.61 ± 1.14	< 0.001	18.98 ± 6.73	8.15 ± 1.14	< 0.001
Age (years)	45.52 ± 13.74	39.13 ± 15.04	0.001	37.76 ± 9.22	36.62 ± 9.01	0.495	60.37 ± 5.89	61.51 ± 6.20	0.290
BMI (kg/m^2)	27.47 ± 2.21	28.14 ± 2.35	0.027	27.96 ± 3.13	27.94 ± 2.50	0.970	27.72 ± 2.51	27.37 ± 1.94	0.442
Menstruation	–			7 (4.2)	0 (0.0)	0.355	–		
Elevated BP	281 (44.8)	22 (36.7)	0.276	40 (23.8)	7 (18.9)	0.522	93 (43.7)	16 (45.7)	0.821
Abdominal obesity	352 (56.1)	42 (70.0)	0.041	136 (81.0)	29 (78.4)	0.721	192 (90.1)	30 (85.7)	0.428
Elevated TGs	334 (53.3)	40 (66.7)	0.047	43 (25.6)	12 (32.4)	0.395	79 (37.1)	18 (51.4)	0.107
Reduced HDL-C	171 (27.3)	27 (45.0)	0.004	68 (40.5)	15 (40.5)	1.000	89 (41.8)	20 (57.1)	0.090
Elevated FBG	304 (48.5)	19 (31.7)	0.013	58 (34.5)	8 (21.6)	0.128	104 (48.8)	19 (54.3)	0.549
MetS	271 (43.2)	30 (50.0)	0.342	55 (32.7)	12 (32.4)	0.971	106 (49.8)	26 (74.3)	0.007

Vitamin D normal, 25(OH)D ≥ 10 ng/dL; Vitamin deficiency, 25(OH)D < 10 ng/dL.
Elevated BP is defined as SBP ≥ 130 mmHg or DBP ≥ 85 mmHg; Abdominal obesity is defined as WC ≥ 90 cm in men or WC ≥ 80 cm in women; Elevated TGs is defined as TGs ≥ 150 mg/dL; Reduced HDL-C is defined as HDL-C < 40 mg/dL in men or HDL-C < 50 mg/dL in women; Elevated FBG is defined as FBG ≥ 100 mg/dL.

than those in the vitamin D normal group but the elevated FBG (p = 0.013) was lower. The elevated BP (p = 0.276) and MetS (p = 0.342) were not significantly associated with vitamin D deficiency. In premenopausal women, all MetS components and MetS were not significantly associated with vitamin D deficiency. In postmenopausal women, MetS (p = 0.007) in the vitamin D deficiency group was higher than those in the vitamin D normal group but all MetS components were not significantly associated with vitamin D deficiency.

Comparisons of MetS and vitamin D deficiency in subjects with and without obesity

Comparisons of MetS and vitamin D deficiency in men, premenopausal women, and postmenopausal women with and without obesity are shown in Table 4. In subjects without obesity, after adjusting for the related variables, MetS was not associated with vitamin D deficiency in men (odds ratio [OR], 1.307; 95% confidence interval [CI], 0.664–2.575; p = 0.439), premenopausal women (OR, 1.166; 95% CI, 0.467–2.907; p = 0.742), and postmenopausal women (OR, 1.596; 95% CI, 0.798–3.191; p = 0.186). In subjects with obesity, MetS was positively associated with vitamin D deficiency in men (OR, 1.839; 95% CI, 1.038–3.258; p = 0.037) and postmenopausal women (OR, 3.136; 95% CI, 1.316–7.470; p = 0.010) but not in premenopausal women (OR, 1.241; 95% CI, 0.551–2.797; p = 0.603).

DISCUSSION

The present study investigated the association between MetS and vitamin D in Korean adults with obesity using data from the sixth KNHANES conducted in 2013-2014. MetS was positively associated with vitamin D deficiency in men and postmenopausal women with obesity but not in premenopausal women with obesity.

The prevalence of MetS in our participants with obesity (43.9%) was higher than in Spanish (13.2%)[18] and New Zealanders (22.4%)[25] but was lower than in Norwegian (68%)[20] and Indian (57.6%)[26]. Obesity has been strongly linked to chronic diseases, such as renal failure, heart failure, hypertension, atherosclerosis, and MetS in humans[27]. The high prevalence of vitamin D deficiency in subjects with obesity is a well-documented finding. Whether vitamin D deficiency is the result or cause of obesity is still unclear. It must also be acknowledged that there could be a mutual causality between vitamin D deficiency and obesity because the greater volumes of

Table 4. Comparisons of vitamin D deficiency according to MetS in subjects with or without obesity

	Gender	Variables	Vitamin D deficiency
Non-obesity (n = 2,359)	Men (n = 1,068)	Non-MetS	1
		MetS	1.307 (0.664–2.575)
		p-value	0.439
	Premenopausal women (n = 795)	Non-MetS	1
		MetS	1.166 (0.467–2.907)
		p-value	0.742
	Postmenopausal women (n = 496)	Non-MetS	1
		MetS	1.596 (0.798–3.191)
		p-value	0.186
Obesity (n = 1,140)	Men (*n* = 687)	Non-MetS	1
		MetS	1.839 (1.038–3.258)
		p-value	0.037
	Premenopausal women (*n* = 205)	Non-MetS	1
		MetS	1.241 (0.551–2.797)
		p-value	0.603
	Postmenopausal women (*n* = 248)	Non-MetS	1
		MetS	3.136 (1.316–7.470)
		p-value	0.010

Vitamin D deficiency, 25(OH)D < 10 ng/dL; MetS, metabolic syndrome.
Adjusted for age, alcohol drinking, smoking, and regular exercising or menstruation (only premenopausal women), hypertension, CKD, T2DM, and WBC.

serum, fat, muscle, and liver allow for greater dilution of 25(OH)D in people with obesity compared to those without obesity[28,29].

The previous studies on the relationship between vitamin D and MetS have yielded varied results by country, ethnicity, and health status. Among previous studies on vitamin D and MetS in populations with obesity, Miñambres et al. reported that the OR for vitamin D deficiency (25(OH)D < 50 nmol/L) was 2.710 (95% CI, 1.147–6.401) for the MetS group versus non-MetS group in Caucasians with overweight or obesity[18]. Mirhoseini et al. revealed that vitamin D levels in the MetS group (18.88 ± 1.24 ng/mL) were lower (p < 0.001) than in the non-MetS group (40.38 ± 2.15 ng/mL) in Iranians with obesity[30]. Some studies have shown that vitamin D and MetS are not related. In a study of Caucasians with obesity, Hjelmesaeth et al. suggested that 25(OH)D level was not a significant independent variable for the prevalence of MetS (OR, 1.06; 95% CI, 0.69–1.63) [20]. Rueda et al. revealed that 25(OH)D levels (men, p_{trend} = 0.1; women, p_{trend} = 0.9) were not independently associated with the pathogenesis of the MetS in Spanish adults with severe obesity[31]. In the presented study, MetS was positively associated with vitamin D deficiency in subjects with obesity (OR, 1.830; 95% CI, 1.230–2.722; P = 0.003) but not in subjects without obesity (OR, 1.321; 95% CI, 0.870–2.006; p = 0.192) (Supplementary table 1).

Research on the gender specific association of MetS and vitamin D is rare, and the results have varied according to the study. Ghadieh et al. reported that MetS was positively associated with vitamin D deficiency in

Supplementary table 1. Comparisons of vitamin D deficiency and MetS in overall population with and without obesity

					(n = 3,499)
Gender	Variables	Vitamin D deficiency			
		Model 1	Model 2	Model 3	Model 4
Non-obesity (n = 2,359)	Non-MetS	1	1	1	1
	MetS	1.123 (0.775–1.626)	1.045 (0.717–1.524)	1.142 (0.761–1.712)	1.321 (0.870–2.006)
	p-value	0.540	0.818	0.522	0.192
Obesity (n = 1,140)	Non-MetS	1	1	1	1
	MetS	1.417 (0.985–2.38)	1.379 (0.955–1.990)	1.685 (1.142–2.488)	1.830 (1.230–2.722)
	p-value	0.060	0.086	0.009	0.003

Vitamin D deficiency, 25(OH)D < 10 ng/dL; MetS, metabolic syndrome.
Model 1(OR, 95% CI), Non-adjusted; Model 2 (OR, 95% CI), adjusted for gender, alcohol drinking, smoking, and regular exercising; Model 3 (OR, 95% CI), Model 2 further adjusted for hypertension, CKD, T2DM, and WBC; Model 4 (OR, 95% CI), Model 3 further adjusted for age.

Lebanese women (p = 0.021) but not in Lebanese men (p = 0.174) [32]. In contrast, Kim et al. reported that the OR of MetS for vitamin D sufficiency was lower than that for vitamin D deficiency in Korean men (OR, 0.824; 95% CI, 0.688–0.988) but was not significant in Korean women (OR, 0.978; 95% CI, 0.823–1.163) [33]. In our results, the outcomes in subjects with obesity differed by gender. In men (OR, 1.839; 95% CI, 1.038–3.258) and postmenopausal women (OR, 3.136; 95% CI, 1.316–7.470), MetS was positively associated with vitamin D deficiency. However, the association between MetS and vitamin D deficiency in premenopausal women was not significant (OR, 1.241; 95% CI, 0.551–2.797) was not significant (Table 4). The mechanism for the gender difference in the association between vitamin D and MetS is not clear. We consider that it may be due

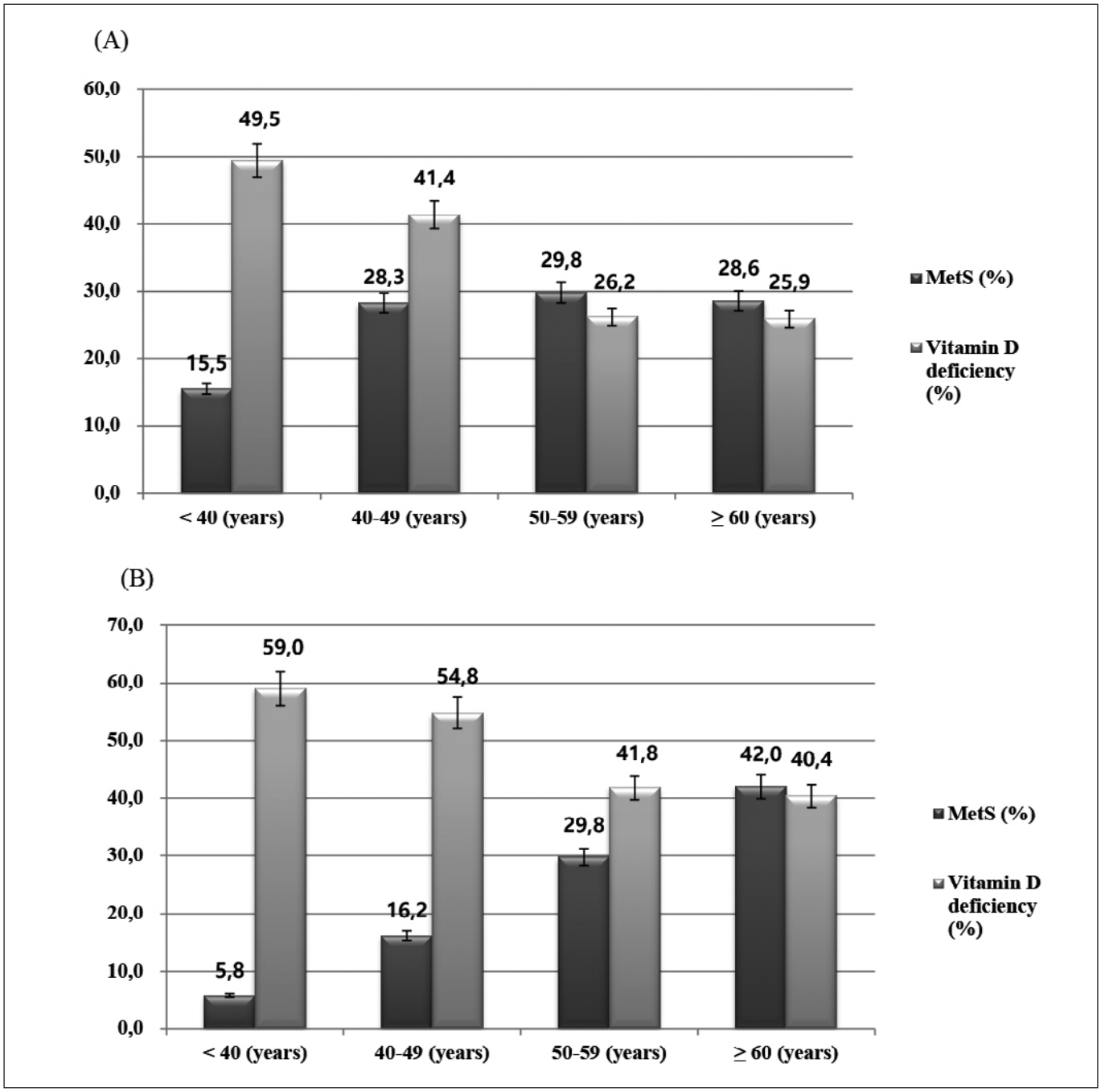

Figure 1. Comparisons of vitamin D deficiency and MetS for age groups in men (A) and women (B). The prevalence of vitamin D deficiency decreased with increasing age in men and women. The prevalence of MetS was continuously increased after 40s age group in women but was not significant after 40s age group in men.

to the physical and body fat composition changes according to an increase in age[34]. In our results, the prevalence of MetS was not significant in the over-40s age group in men but continuously increased in the over-40s age group in women (Figure 1).

We believe that differences in female hormones are the cause of the different results in the relationship between vitamin D deficiency and MetS in premenopausal and postmenopausal women. Women experience a rapid decrease in estrogen levels due to menopause. Hormonal changes that start at the menopausal transition and abrupt cessation of hormone production can cause chronic diseases, such as hypertension, T2DM, and MetS[35]. Huang et al, argued that low estradiol increased MetS risk with Vitamin D deficiency in Chinese women (OR, 3.49; 95% CI, 1.45–8.05 for the lowest vs the highest tertile)[36]. There are gender differences in lifestyle (drinking, smoking, and physical activity) as well as physical changes according to age. Compared to their counterparts without obesity, vitamin D intake has been reported as being lower in men with obesity but not in women with obesity[37,38]. Men with morbid obesity had a significantly higher prevalence of vitamin D deficiency than women[39]. Therefore, some researchers argued that researchers should consider analyzing men and women separately when constructing research hypotheses in medical studies[40,41].

The present study has a few limitations. First, parathyroid hormone (PTH) and calcium play an important role in the metabolism of vitamin D. However, KNHANES VI (2013–2014) does not measure the PTH and calcium of these participants. Second, KNHANES VI (2013–2014) does not record the intake of vitamin D and calcium supplements. Third, serum 25(OH)D levels vary across seasons, but KNHANES VI (2013–2014) does not specify the serum 25(OH)D levels for each season. Therefore, we were unable to include these variables as adjustment variables for vitamin D levels. The serum levels for PTH and calcium, seasonal measurements of serum 25(OH)D, and information on vitamin D and calcium supplements should be included as variables of vitamin D status in future studies. Fourth, the two-year continuous data from KNHANES on vitamin D are the most recent data from 2013–2014, but these are old in terms of time point. Therefore, future studies should be utilized the most recent data on vitamin D. Despite these limitations in the present study, it is the first reported study to determine the gender-specific association of MetS and vitamin D in Korean adults with or without obesity. Therefore, more accurate results might be obtained by performing a cohort study that includes these variables.

CONCLUSIONS

The present study investigated the sex-specific association of MetS and serum vitamin D in Korean adults aged 20 and older with or without obesity, using the KNHANES VI (2013–2014) data. In non-obesity group, MetS was not associated with vitamin D deficiency in men, premenopausal women, and postmenopausal women. In obesity group, MetS was positively associated with vitamin D deficiency in men and postmenopausal women but not in premenopausal women.

FUNDING RESOURCES

This paper was financially supported by Dongnam Health University

REFERENCES

1. Obesity and overweight factsheets. World Health Organization. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Published 2021.
2. Ministry of Health Welfare and Family Affairs & Korea Center for Disease Control and Prevention. Korea National Health and Nutrition Examination Survey. 2013.
3. Lin X, Li H. Obesity: Epidemiology, Pathophysiology, and Therapeutics. *Front Endocrinol (Lausanne).* 2021;12:706978. doi:10.3389/fendo.2021.706978.
4. Yang YS, Han BD, Han K, et al. Obesity Fact Sheet in Korea, 2021: Trends in Obesity Prevalence and Obesity-Related Comorbidity Incidence Stratified by Age from 2009 to 2019. *J Obes Metab Syndr.* 2022;31:169–177. doi:10.7570/jomes22024.
5. Reaven GM. Role of insulin resistance in human disease (syndrome X): an expanded definition. *Annu Rev Med.* 1993;44:121–131. doi:10..1146/annurev.me.44.020193.001005.
6. Moukayed M, Grant WB. Linking the metabolic syndrome and obesity with vitamin D status: risks and opportunities for improving cardiometabolic health and well-being. *Diabetes Metab Syndr Obes.* 2019;12:1437–1447. doi:10.2147/DMSO.S176933.
7. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA.* 2002;287:356–359. doi:10.1001/jama.287.3.356.
8. Kim MH, Lee SH, Son DY, Kim SH, Joe H, Yoo BW, Cho CY, Shin HS, Cho YJ, Oh JE. The Change of Metabolic Syndrome Prevalence and Its Risk Factors in Korean Adults for Decade: Korea National Health and Nutrition Examination Survey for 2008–2017. *Korean J Fam Pract.* 2020;10:44–52. doi:10.21215/kjfp.2020.10.1.44.
9. Dominguez LJ, Farruggia M, Veronese N, Barbagallo M. Vitamin D Sources, Metabolism, and Deficiency: Available Compounds and Guidelines for Its Treatment. *Metabolites.* 2021;11:255. doi:10.3390/metabo11040255.
10. Meza-Meza MR, Ruiz-Ballesteros AI, de la Cruz-Mosso U. Functional effects of vitamin D: From nutrient to immunomodulator. *Crit Rev Food Sci Nutr.* 2022;62:3042–3062. doi:10.1080/10408398.2020.1862753.

11. Janoušek J, Pilařová V, Macáková K, Nomura A, Veiga-Matos J, Silva DDD, Remião F, Saso L, Malá-Ládová K, Malý J, Nováková L, Mladěnka P. Vitamin D: sources, physiological role, biokinetics, deficiency, therapeutic use, toxicity, and overview of analytical methods for detection of vitamin D and its metabolites. *Crit Rev Clin Lab Sci.* 2022;59:517–554. doi:10.1080/10408363.2022.2070595.

12. Chen C, White DL, Marshall B, Kim WK. Role of 25-Hydroxyvitamin D3 and 1,25-Dihydroxyvitamin D3 in Chicken Embryo Osteogenesis, Adipogenesis, Myogenesis, and Vitamin D3 Metabolism. *Front Physiol.* 2021;12:637629. doi:10.3389/fphys.2021.637629.

13. Hollis BW. Assessment of vitamin D nutritional and hormonal status: what to measure and how to do it. *Calcif Tissue Int*. 1996; 58:4–5. doi:10./BF02509538.

14. Fleet JC. Vitamin D-Mediated Regulation of Intestinal Calcium Absorption. *Nutrients*. 2022;14:3351. doi:10.3390/nu14163351.

15. Wang H, Chen W, Li D, Yin X, Zhang X, Olsen N, Zheng SG. Vitamin D and Chronic Diseases. *Aging Dis.* 2017;8:346–353. doi:10.14336/AD.2016.1021.

16. Muscogiuri G. Vitamin D: past, present and future perspectives in the prevention of chronic diseases. *Eur J Clin Nutr.* 2018;72: 1221–1225. doi:10.1038/s41430-018-0261-4.

17. Liu L, Cao Z, Lu F, et al. Vitamin D deficiency and metabolic syndrome in elderly Chinese individuals: evidence from CLHLS. Nutr Metab (Lond). 2020;17:58. doi: 10.1186/s12986-020-00479-3.

18. Miñambres I, Sánchez-Hernández J, Sánchez-Quesada JL, Rodríguez J, de Leiva A, Pérez A. The association of hypovitaminosis d with the metabolic syndrome is independent of the degree of obesity. *ISRN Endocrinol.* 2012;2012:691803. doi:10.5402/2012/691803.

19. Abboud M, Rizk R, Haidar S, Mahboub N, Papandreou D. Association between Serum Vitamin D and Metabolic Syndrome in a Sample of Adults in Lebanon. *Nutrients.* 2023;15:1129. doi:10.3390/nu15051129.

20. Hjelmesaeth J, Hofsø D, Aasheim ET, Jenssen T, Moan J, Hager H, Røislien J, Bollerslev J. Parathyroid hormone, but not vitamin D, is associated with the metabolic syndrome in morbidly obese women and men: a cross-sectional study. *Cardiovasc Diabetol.* 2009;8:7. doi:10.1186/1475-2840-8-7.

21. Palacios C, Gonzalez L. Is vitamin D deficiency a major global public health problem? *J Steroid Biochem Mol Biol.* 2014;144: 138–145. A doi:10.1016/j.jsbmb.2013.11.003.

22. Kim SG, Kim GS, Lee JH, Moon AE, Yoon H. The relationship between vitamin D and estimated glomerular filtration rate and urine microalbumin/creatinine ratio in Korean adults. *J Clin Biochem Nutr.* 2018;62:94–99. doi:10.3164/jcbn.17-69.

23. Cheng Q, Du Y, Hong W, et al. Factors associated to serum 25-hydroxyvitamin D levels among older adult populations in urban and suburban communities in Shanghai, China. *BMC Geriatr*. 2017;17:246. doi:10.1186/s12877-017-0632-z.

24. Yoon H. Relationship between metabolic syndrome and metabolic syndrome score and insulin resistance and beta cell function in Korean adults with obesity. *Korean J Clin Lab Sci.* 2020;52:327–334. doi:10.15324/KJCLS.2020.52.4.327.

25. McGill AT, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. *Nutr J.* 2008;7:4. doi:10.1186/1475-2891-7-4**.**

26. Negi PC, Sondhi S, Merwaha R, Asotra S. Prevalence and risk determinants of metabolic syndrome in obese worksite workers in hill city of Himachal Pradesh, India. *Indian Heart J.* 2019;71:45–51. doi:10.1016/j.ihj.2019.01.001.

27. Canale MP, Manca di Villahermosa S, Martino G, Rovella V, Noce A, De Lorenzo A, Di Daniele N. Obesity-related metabolic syndrome: mechanisms of sympathetic overactivity. *Int J Endocrinol.* 2013;2013:865965. doi:10.1155/2013/865965.

28. Vranić L, Mikolašević I, Milić S. Vitamin D Deficiency: Consequence or Cause of Obesity? *Medicina (Kaunas).* 2019;55:541. doi:10.3390/medicina55090541.

29. Walsh JS, Bowles S, Evans AL. Vitamin D in obesity. *Curr. Opin. Endocrinol. Diabetes Obes.* 2017;24:389–394. doi:10.1097/MED.0000000000000371.

30. Mirhoseini M, Daemi H, Babaiee MM, Asadi-Samani M, Mirhoseini L, Sedehi M. The relationship between vitamin D deficiency and metabolic syndrome in obese individuals. *J Renal Inj Prev.* 2018; 7: 275–279. doi:10.15171/jrip.2018.61.

31. Rueda S, Fernández-Fernández C, Romero F, Martínez de Osaba J, Vidal J. Vitamin D, PTH, and the metabolic syndrome in severely obese subjects. *Obes Surg.* 2008;18:151–154. doi:10.1007/s11695-007-9352-3.

32. Ghadieh R, Mattar Bou Mosleh J, Al Hayek S, Merhi S, El Hayek Fares J. The relationship between hypovitaminosis D and metabolic syndrome: a cross sectional study among employees of a private university in Lebanon. *BMC Nutr.* 2018;4:36. doi:10.1186/s40795-018-0243-x.

33. Kim MH, Lee J, Ha J, et al. Gender specific association of parathyroid hormone and vitamin D with metabolic syndrome in population with preserved renal function. *Sci Rep.* 2018;8:1149. doi:10.1038/s41598-017-17397-9.

34. Ponti F, Santoro A, Mercatelli D, et al. Aging and Imaging Assessment of Body Composition: From Fat to Facts. *Front Endocrinol (Lausanne).* 2020;10:861. doi:10.3389/fendo.2019.00861.

35. Jeong HG, Park H. Metabolic Disorders in Menopause. *Metabolites.* 2022;12:954. doi: 10.3390/metabo12100954.

36. Huang H, Guo J, Chen Q, Chen X, Yang Y, Zhang W, et al. The synergistic effects of vitamin D and estradiol deficiency on metabolic syndrome in Chinese postmenopausal women. *Menopause.* 2019;26:1171–1177. doi:10.1097/GME.0000000000001370.

37. Taslim NA, Bukhari A, As'ad S, et al. The Effects of 10,000 IU Vitamin D Supplementation on Improvement of Clinical Outcomes, Inflammatory and Coagulation Markers in Moderate COVID-19 Patients: A Randomized-Controlled Trial. *Nutr Clín Diet Hosp.* 2023;43:21–33. doi:10.12873/432taslim.

38. Orces C. The Association between Body Mass Index and Vitamin D Supplement Use among Adults in the United States. Cureus. 2019;11:e5721. doi:10.7759/cureus.5721.

39. Almesri N, Das NS, Ali ME, Gumaa K, Giha HA. Gender-Dependent Association of Vitamin D Deficiency with Obesity and Hypercholesterolemia (LDLC) in Adults. *Endocr Metab Immune Disord Drug Targets.* 2020;20:425–436. doi:10.2174/1871530319666191009154528.

40. Kanter R, Caballero B. Global gender disparities in obesity: a review. *Adv Nutr.* 2012;3:491–498. doi:10.3945/an.112.002063.

41. Rich-Edwards JW, Kaiser UB, Chen GL, Manson JE, Goldstein JM. Sex and Gender Differences Research Design for Basic, Clinical, and Population Studies: Essentials for Investigators. *Endocr Rev.* 2018;39:424–439. doi:10.1210/er.2017-00246.