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폐경 전과 후 여성에서 비타민 D 농도와 우울증상 연관성의 차이: 국민건강영양조사 2010–2012년 자료를 이용

이수미[1], 최희원[2], 배우경[1], 신은영[3]

[1]분당서울대학교병원 가정의학과, [2]서울대학교병원 가정의학과, [3]분당서울대학교병원 보건의료서비스과

The Difference between Serum Vitamin D Level and Depressive Symptoms in Korean Adult Women before and after Menopause: The 5th (2010–2012) Korean National Health and Nutrition Examination Survey

Sumi Lee[1], Hi Won Choi[2], Woo Kyung Bae[1], Eun Young Shin[3]

[1]Department of Family Medicine, Seoul National University Bundang Hospital, Seongnam, Korea
[2]Department of Family Medicine, Seoul National University Hospital, Seoul, Korea
[3]Department of Public Health and Medical Service, Seoul National University Bundang Hospital, Seongnam, Korea

Background: The relationship between serum vitamin D levels and depressive symptoms has not been consistent in previous studies in Korean women. Menopause is known to be related to depression and vitamin D.
Methods: This study included 11,573 women from the 5th Korea National Health and Nutrition Examination Survey. Serum vitamin D levels were divided into four groups according to quartiles, and depressive symptoms were collected into two groups. Multiple logistic regression analysis was conducted in each group of women before and after menopause.
Results: Compared with the highest vitamin D group, the lowest vitamin D group did not show significant differences in all females (odds ratio [OR], 0.98; 95% confidence interval [CI], 0.78-1.22). In premenopausal women, compared to the first quartile, ORs were presented in the second quartile (OR, 0.75; 95% CI, 0.53-1.07), third quartile (OR, 0.70; 95% CI, 0.49-1.00) and fourth quartile (OR, 0.62; 95% CI, 0.43-0.92) respectively, and they were statistically significant (*P*=0.016). In postmenopausal women, compared to the first quartile, ORs were presented in the second quartile (OR, 1.06; 95% CI, 0.78-1.44), third quartile (OR, 1.18; 95% CI, 0.87-1.61), and fourth quartile (OR, 1.27; 95% CI, 0.98-1.66) respectively; however, they were not statistically significant (*P*=0.057).
Conclusions: Depression symptoms increased with a decrease in serum vitamin D in premenopausal women, but the opposite trend was observed in postmenopausal women. In future studies, if the relationship between blood vitamin D and depression is studied, the menopausal status of women can be used as an important criterion.
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■ Corresponding author : Woo Kyung Bae, MD, MPH
Department of Family Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173Beon-gil, Bundang-gu, Seongnam 13620, Korea
Tel: +82-31-787-7805, Fax: +82-31-787-4104
E-mail: naslig@gmail.com
ORCID: https://orcid.org/0000-0001-6729-4128

INTRODUCTION

Depression is a mood disorder, which is characterized by symptoms of eating disorders, memory disorders, and suicide attempts with emotions, such as sadness, disinterest, or loss of motivation. In recent years, depression has emerged as a major threat to health and quality of life worldwide, and the World Health Organization has reported that depression to be a major cause of disability.[1] As of 2018, the number of patients with depression in Korea was 750,000, which increased by 27.7% compared to 2014; considering the gender, the number of female patients was 1.8 times higher than that of men.

Vitamin D is a naturally produced vitamin, which is activated on skin exposure to ultraviolet rays; it is an essential substance for the human body that acts as a steroid hormone in the targeted organs to maintain calcium and phosphorus balance and skeletal health.[2-4] In addition, studies have shown that the level of vitamin D is associated with cancer, diabetes, high blood pressure, and cardiovascular disease. Recently, active vitamin D or vitamin D receptors have been reported to function specifically in the brain tissue or the nervous system, suggesting associations with mental illnesses, such as depression.[5,6] Several studies have suggested that metabolites of 25-hydroxyvitamin D (25[OH]D) in the blood can cross the blood-brain barrier and that 25(OH)D receptors are present in the central nervous system, showing the presence of vitamin D receptors (VDR) and related enzymes (CYP 24A1, cytochrome P450 family 24 subfamily A member 1; CYP 27B1, cytochrome P450 family 27 subfamily B member 1; also known as 25-hydroxyvitamin D 1-alpha-hydroxylase) in various areas of the brain; therefore, vitamin D, neuroactivity and neurotransmitters, can affect brain function.[7,8]

The results of these studies to determine the relationship between vitamin D and depression experience are inconsistent, and only certain groups, such as the elderly population and teenagers have been studied in Korea. Furthermore, in a subgroup analysis of gender during the study of all Korean adults; in adult men, the associations have identified, but not in women.[9,10] The reasons for no association with female groups were analyzed, and previous studies have shown that menopause, caused by a decrease in estrogen, affects both blood vitamin D and depression in the process.[11,12] In a double-blind randomized controlled clinical trial in 152 healthy premenopausal women in New Zealand, oral vitamin D had no effect on mood disorders.[13] In addition, in a double-blind placebo-controlled prospective clinical trial conducted on 489 postmenopausal depressed women in the United States, hormone therapy and vitamin D co-supplementation were combined, but there was no improvement in depression.[14] However, no study has been found that compared vitamin D and depression status by dividing all women according to menopausal status.

Therefore, using the data from the 5th Korea National Health and Nutrition Examination Survey (KNHANES) (2010-2012), this study aimed to assess the association of serum vitamin D concentrations in Korea with the experience of depressive symptoms based on the menopausal status.

METHODS

1. Participants

This study integrated the 5th KNHANES data and used it for analysis. From the 33,592 participants, our study included adult women aged 19 years and older, without absence of major exposure-result factors, such as menopause, serum vitamin D levels, and depression (n=11,573). This study was approved by the Institutional Review Board (IRB no. X-2108-701-902) of Seoul National University Bundang Hospital.

2. Key variables

The general characteristics of the participants, including their age, occupation, household income level, education level, marital status, and residential area were analyzed. Smoking habits, drinking habits, physical activities, and underlying diseases among the health survey data were used. Data on menstruation, which is a major condition in women, were used; the dietary survey section analyzed whether dietary supplements were taken.

1) Serum vitamin D measurement

The levels of vitamin D in the participants were evaluated using serum 25(OH)D concentrations. This indicator is used to measure serum vitamin D in a number of vitamin D-related epidemiological studies, and the concentration measurements were analyzed using the radioimmunoassay meth-

Table 1. Characteristics of subjects by vitamin D quartiles in pre- and post-menopausal women

	Menopausal status									
	Pre-menopause (n=5,442)					Post-menopause (n=6,131)				
	Q1 (n=1,365)	Q2 (n=1,359)	Q3 (n=1,359)	Q4 (n=1,359)	P^a	Q1 (n=1,534)	Q2 (n=1,533)	Q3 (n=1,538)	Q4 (n=1,526)	P^a
Mean vitamin D, mg/mL	9.79±0.06	13.15±0.03	16.10±0.04	22.01±0.18	<0.001	10.95±0.08	15.23±0.04	18.97±0.05	26.39±0.20	<0.001
Age, y	35.37±9.29	36.66±8.71	37.06±8.56	38.00±8.43	0.018	61.71±11.23	61.68±10.84	62.35±10.74	63.93±9.97	0.006
BMI					0.038					0.005
≥25 kg/m^2	263 (19.27)	291 (21.41)	301 (22.15)	306 (22.52)		564 (36.77)	624 (40.70)	566 (36.80)	511 (33.49)	
Married (yes)	855 (62.64)	980 (72.11)	1,018 (74.91)	1,057 (77.78)	<0.001	1,101 (71.77)	1,074 (70.06)	1,107 (71.98)	1,013 (66.38)	0.297
Employed (yes)	784 (57.44)	755 (55.56)	749 (55.11)	730 (53.72)	0.376	568 (37.03)	619 (40.38)	680 (44.21)	671 (43.97)	0.057
Area of residence					0.503					0.135
Capital	379 (27.77)	411 (30.24)	398 (29.29)	414 (30.46)		415 (27.05)	374 (24.40)	331 (21.52)	334 (21.89)	
Metropolitan	300 (21.98)	290 (21.34)	266 (19.57)	248 (18.25)		304 (19.82)	292 (19.05)	308 (20.03)	271 (17.76)	
City/town	686 (50.26)	658 (48.42)	695 (51.14)	697 (51.29)		815 (53.13)	867 (56.56)	899 (58.45)	921 (60.35)	
Household income					0.764					0.137
Low	323 (23.66)	313 (23.03)	292 (21.49)	354 (26.05)		369 (24.05)	339 (22.11)	393 (25.55)	419 (27.46)	
Mid-low	352 (25.79)	316 (23.25)	348 (25.61)	338 (24.87)		396 (25.81)	442 (28.83)	369 (23.99)	361 (23.66)	
Mid-high	319 (23.37)	359 (26.42)	364 (26.78)	349 (25.68)		400 (26.08)	396 (25.83)	381 (24.77)	349 (22.87)	
High	371 (27.18)	371 (27.30)	355 (26.12)	318 (23.40)		369 (24.05)	356 (23.22)	395 (25.68)	397 (26.02)	
Education					0.170					<0.001
Elementary	35 (2.56)	18 (1.32)	35 (2.58)	50 (3.68)		812 (52.93)	819 (53.49)	893 (58.06)	934 (61.21)	
Middle/high	700 (5.128)	653 (48.05)	702 (51.66)	704 (51.80)		551 (35.92)	592 (38.67)	496 (32.25)	474 (31.06)	
University	630 (46.15)	688 (50.63)	622 (45.77)	605 (44.52)		171 (11.15)	120 (7.84)	149 (9.69)	118 (7.73)	
METs					0.003					0.003
Low	601 (44.03)	549 (40.40)	506 (37.23)	481 (35.39)		747 (48.70)	663 (43.25)	620 (40.31)	638 (41.81)	
Moderate	594 (43.52)	596 (43.86)	616 (45.33)	616 (45.33)		596 (38.85)	620 (40.44)	652 (42.39)	607 (39.78)	
High	170 (12.45)	214 (15.75)	237 (17.44)	262 (19.28)		191 (12.45)	250 (16.31)	266 (17.30)	281 (18.41)	
Smoking					0.334					0.056
Non-smoker	1,178 (86.30)	1,172 (86.24)	1,185 (87.20)	1,176 (86.53)		1,433 (93.42)	1,387 (90.48)	1,435 (93.30)	1,450 (95.02)	
Past-smoker	81 (5.93)	99 (7.28)	93 (6.84)	100 (7.36)		45 (2.93)	69 (4.50)	60 (3.90)	40 (2.62)	
Current-smoker	106 (7.77)	88 (6.48)	81 (5.96)	83 (6.11)		56 (3.65)	77 (5.02)	43 (2.80)	36 (2.36)	

Table 1. Continued

	Menopausal status									
	Pre-menopause (n=5,442)					Post-menopause (n=6,131)				
	Q1 (n=1,365)	Q2 (n=1,359)	Q3 (n=1,359)	Q4 (n=1,359)	P^a	Q1 (n=1,534)	Q2 (n=1,533)	Q3 (n=1,538)	Q4 (n=1,526)	P^a
Alcohol, n/mon	628 (46.24)	684 (50.44)	684 (50.78)	693 (51.18)	0.488	333 (21.74)	420 (27.54)	411 (26.78)	373 (24.44)	0.229
Comorbidity (yes)	176 (12.89)	170 (12.51)	195 (14.35)	216 (15.89)	0.020	1,012 (65.97)	988 (64.45)	1,020 (66.32)	1,113 (72.94)	0.005
Stress perception					0.222					0.898
Low	904 (66.23)	920 (67.70)	949 (69.83)	966 (71.08)		1,154 (75.23)	1,126 (73.45)	1,142 (74.35)	1,162 (76.30)	
High	461 (33.77)	439 (32.30)	410 (30.17)	393 (28.92)		380 (24.77)	407 (26.55)	394 (25.65)	361 (23.70)	
Dietary supplements (yes)	457 (33.48)	503 (37.07)	571 (42.02)	676 (49.74)	<0.001	644 (41.98)	710 (46.31)	777 (50.52)	889 (58.26)	<0.001

Values are presented as mean±standard deviation or number (%).
Vitamin D status was categorized into groups, according to serum 25(OH)D concentrations quartile. Premenopause: (Q1: 2.95-11.75 ng/mL, Q2: 11.76-14.55 ng/mL, Q3: 14.56-17.8 ng/mL, Q4: 17.81-44.59 ng/mL); postmenopause: (Q1: 4.11-13.39 ng/mL, Q2: 13.4-17.02 ng/mL, Q3: 17.02-21.29 ng/mL, Q4: 21.3-53.54 ng/mL).
Chronic diseases included hypertension, diabetes mellitus, dyslipidemia, stroke, cardiovascular disease, degenerative arthritis, rheumatoid arthritis, tuberculosis, asthma, thyroid disease, gastric cancer, liver cancer, colon cancer, breast cancer, cervicovaginal cancer, lung cancer, thyroid cancer, other cancer, chronic kidney disease, liver cirrhosis.
METs, practice vigorous activity of at least 75 min/wk, or moderate-intensity activity and/or walking of at least 150 min/wk, or any combination of walking, moderate-intensity or vigorous-intensity activities achieving at minimum of at least 600 metabolic equivalent-min/wk, according to low (<600), moderate (600-8,000), high (>8,000).
Abbreviations: 25-hydroxyvitamin D; BMI, body mass index; METs, metabolic equivalents; 25(OH)D, Q1, first quartile group; Q2, second quartile group; Q3, third quartile group; Q4, fourth quartile group.
[a]*P*-values were obtained using chi-square test except for age (student *t*-test).

od in specialized clinical institutions, and gamma counters (1470 WIZARD gamma-Counter, PerkinElmer®, Waltham, MA, USA). Serum 25(OH)D levels were categorized into quartiles.

2) Depressive symptoms experience

In the health survey section, the respondents who answered "Yes" to the question "Have you felt sad or hopeless enough to interfere with your daily life for more than 2 weeks in a row?" were designated as "Depressive conditions" and the participants who answered “No” were designated as “Not depressed”.

3. Statistical analysis

This study integrated the 3 years of the KNHANES data, and since there are differences in the number of participants by year, the survey analysis was conducted by generating integrated weights with different proportions. To analyze the general characteristics of the participants, chi-square tests were performed for categorical variables and independent sample *t*-test (independent two-sample *t*-test) for continuous variables, and multivariate logistic regression analysis were conducted to analyze the experience of depression according to serum vitamin D level in each group of women before and after menopause. The contents of each model are as follows. Model 1: uncorrected crude model, model 2: age, obesity, smoking status, frequency of drinking, exercise, comorbidity, and stress recognition rate, model 3: model 2 corrected additionally with marriage, household income, occupation, and education. All statistical processing in this study was conducted using STATA version 16.0 (STATA Corp., College Station, TX, USA). Statistical significance was tested at a significance level of $P<0.05$.

RESULTS

1. Characteristics of the participants

Of the 11,573 women, 5,442 were classified as premenopausal

and 6,131 as postmenopausal women (Table 1). In women before and after menopause, the average serum vitamin D levels were 15.22±4.98 ng/mL and 17.87±6.24 ng/mL, respectively.

There were differences in age, body mass index, metabolic equivalents, comorbidities, and dietary supplements according to serum vitamin D levels in both premenopausal and postmenopausal women. Marriage showed differences only in premenopausal women and education in postmenopausal women.

2. Prevalence of depressive symptoms according to vitamin D quartiles

The prevalence of each group's depression experience on dividing into quartiles based on serum vitamin D concentration in all adult women is shown in Figure 1A. In the group with the lowest serum vitamin D level, the depression experience was 16.2%, 14.6%, 15.3%, and 17.5% in the second quartile (Q2), third quartile (Q3), and fourth quartile (Q4), respectively. In the premenopausal female group, the current prevalence of depression in each group is shown in Figure 1B, 16.3%, 13%, 11.9%, and 12.2% in the first quartile (Q1), Q2, Q3, and Q4, respectively indicating higher rates of depression in the lower serum vitamin D groups (*P*=0.002). In the postmenopausal female population (Figure 1C), the proportion of depression was 16.6%, 17.9%, 18.1%, and 20.1% in Q1, Q2, Q3, and Q4, respectively (*P*=0.083).

3. Multivariate analysis of depressive symptoms associated with vitamin D quartiles in pre- and post-menopausal women

Compared to Q1, the Q2 odds ratio (OR) was 0.85 for experiencing depressive symptoms in female adults. (95% confidence intervals [CI], 0.67-1.08), and in Q3 and Q4, the ORs of the depressive symptoms experience were not statistically significant (Q3: OR, 0.84; 95% CI, 0.65-1.09 and Q4: OR, 0.98; 95% CI, 0.78-1.22; *P*=0.371) (Table 2).

In premenopausal women, compared to Q1, the OR of depressive symptom experiences were in the order Q2: OR, 0.75 (95% CI, 0.53-1.07); Q3: OR, 0.70 (95% CI, 0.49-1.00); and Q4: OR, 0.62 (95% CI, 0.43-0.92) (*P*=0.016) (Table 3).

In postmenopausal women, compared to Q1, which had the lowest experience of depressive symptoms the ORs of the experience of depressive symptoms were in the order Q2: OR, 1.06 (95% CI, 0.78-1.44); Q3: OR, 1.18 (95% CI, 0.87-1.61); and Q4: OR, 1.27 (95% CI, 0.98-1.66) respectively (*P*=0.057) (Table 4).

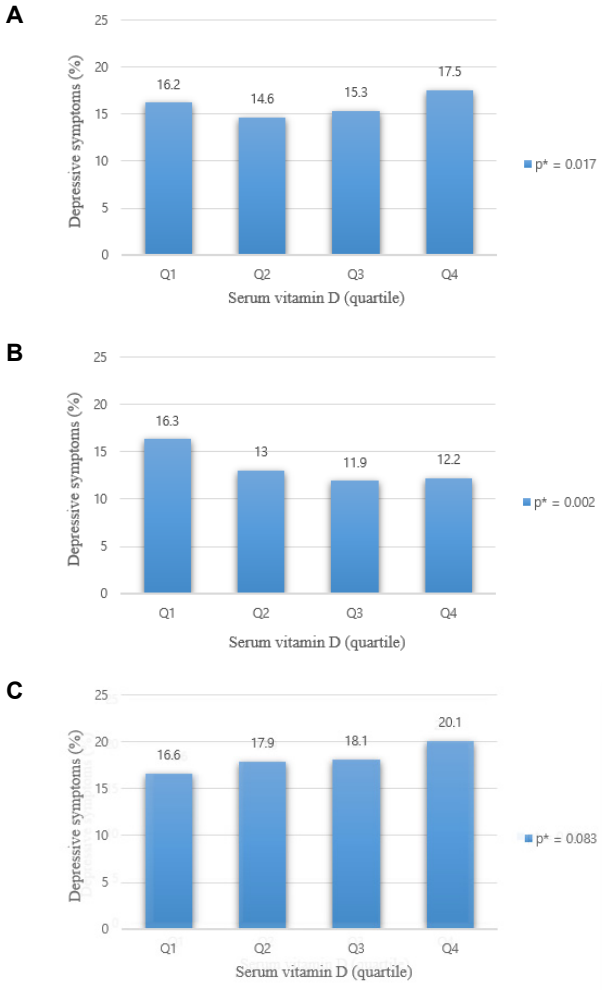

Figure 1. Association between vitamin D status and depression. (A) Total adult women, (B) premenopausal women, (C) postmenopausal women. Serum vitamin D status was categorized into groups, according to serum 25(OH)D concentrations quartile Total adult women: Q1: 2.95-12.48 ng/mL, Q2: 12.49-15.68 ng/mL, Q3: 15.69-19.7 ng/mL, Q4: 19.71-53.54 ng/mL. Premenopausal status: Q1: 2.95-11.75 ng/mL, Q2: 11.76-14.55 ng/mL, Q3: 14.56-17.8 ng/mL, Q4: 17.81-44.59 ng/mL. Postmenopausal status: Q1: 4.11-13.39 ng/mL, Q2: 13.4-17.02 ng/mL, Q3: 17.02-21.29 ng/mL, Q4: 21.3-53.54 ng/mL. **P*-values were obtained using chi-square test. 25(OH)D, Q1, first quartile group; Q2, second quartile group; Q3, third quartile group; Q4, fourth quartile group; 25-hydroxyvitamin D.

Table 2. Association between vitamin D status and depression in female adults

	Vitamin D status				P^a
	Q1 (n=2,896)	Q2 (n=2,894)	Q3 (n=2,892)	Q4 (n=2,891)	
Depressive conditions	468	423	443	507	
Model 1	1	0.89 (0.71-1.12)	0.87 (0.69-1.11)	1.08 (0.88-1.31)	0.112
Model 2	1	0.83 (0.66-1.06)	0.83 (0.64-1.07)	0.99 (0.79-1.23)	0.313
Model 3	1	0.85 (0.67-1.08)	0.84 (0.65-1.09)	0.98 (0.78-1.22)	0.371

Vaules ane presented as odds ratio (95% confidence interrml) or number.
Vitamin D status was categorized into groups, according to serum 25(OH)D concentrations quartile; female adults: Q1: 2.95-12.48 ng/mL, Q2: 12.49-15.68 ng/mL, Q3: 15.69-19.7 ng/mL, Q4: 19.71-53.54 ng/mL.
Model 1: unadjusted; model 2: adjustment for age, BMI, smoking, MET, drinking, comorbidity, stress, dietary supplements; model 3: additional adjustments for marriage, income, employment, education.
Abbreviations: 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index; MET, metabolic equivalent; Q1, first quartile group; Q2, second quartile group; Q3, third quartile group; Q4, fourth quartile group.
[a]By multivariate logistic regression analysis.

Table 3. Association between vitamin D status and depression (premenopause)

	Vitamin D status				P^a
	Q1 (n=1,365)	Q2 (n=1,359)	Q3 (n=1,359)	Q4 (n=1,359)	
Depressive conditions	223	177	162	166	
Model 1	1	0.81 (0.59-1.11)	0.73 (0.53-1.01)	0.67 (0.48-0.94)	0.018
Model 2	1	0.73 (0.52-1.04)	0.69 (0.49-0.98)	0.64 (0.44-0.93)	0.019
Model 3	1	0.75 (0.53-1.07)	0.70 (0.49-1.00)	0.62 (0.43-0.92)	0.016

Vaules ane presented as odds ratio (95% confidence interrml) or number.
Vitamin D status was categorized into groups, according to serum 25(OH)D concentrations quartile; premenopause: Q1: 2.95-11.75 ng/mL, Q2: 11.76-14.55 ng/mL, Q3: 14.56-17.8 ng/mL, Q4: 17.81-44.59 ng/mL.
Model 1: unadjusted; model 2: adjustment for age, BMI, smoking, MET, drinking, comorbidity, stress, dietary supplements; model 3: additional adjustments for marriage, income, employment, education.
Abbreviations: 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index; MET, metabolic equivalent; Q1, first quartile group; Q2, second quartile group; Q3, third quartile group; Q4, fourth quartile group.
[a]By multivariate logistic regression analysis.

Table 4. Association between vitamin D status and depression (postmenopause)

	Vitamin D status				P^a
	Q1 (n=1,534)	Q2 (n=1,533)	Q3 (n=1,538)	Q4 (n=1,526)	
Depressive conditions	254	274	278	307	
Model 1	1	1.08 (0.80-1.44)	1.19 (0.89-1.60)	1.27 (0.99-1.64)	0.047
Model 2	1	1.06 (0.78-1.43)	1.17 (0.86-1.61)	1.29 (0.99-1.67)	0.048
Model 3	1	1.06 (0.78-1.44)	1.18 (0.87-1.61)	1.27 (0.98-1.66)	0.057

Vaules ane presented as odds ratio (95% confidence interrml) or number.
Vitamin D status was categorized into groups, according to serum 25(OH)D concentrations quartile; postmenopause: Q1: 4.11-13.39 ng/mL, Q2: 13.4-17.02 ng/mL, Q3: 17.02-21.29 ng/mL, Q4: 21.3-53.54 ng/mL.
Model 1: unadjusted; model 2: adjustment for age, BMI, smoking, MET, drinking, comorbidity, stress, dietary supplements; model 3: additional adjustments for marriage, income, employment, education.
Abbreviations: 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index; MET, metabolic equivalent; Q1, first quartile group; Q2, second quartile group; Q3, third quartile group; Q4, fourth quartile group.
[a]By multivariate logistic regression analysis.

DISCUSSION

This study examined whether there are differences in the relationship between vitamin D concentrations and depressive symptoms in Korean women based on their menopausal status. Analysis of all adult women showed that the proportion of depressive symptom experience was not related to serum vitamin D levels. Furthermore, this study assumes that the relationship between serum vitamin D concentration and experience of depressive symptoms would be affected by menopause, which was the main classification criterion for the entire adult female population, and further analysis was conducted. When dividing all adult women based on their menopausal status, premenopausal women tended to show decreased rates of depressive symptoms experience as serum vitamin D levels increased; however, it was not the same case in postmenopausal women. After confirming this trend, all female participants were divided into two groups; and the relationship between serum vitamin D concentration and experience of depressive symptoms was analyzed using multivariate logistic regression.

As a result, in premenopausal women, the increase in serum vitamin D was associated with the reduced prevalence of depressive symptoms. On the contrary, in postmenopausal women, the increase in serum vitamin D was associated with the increased prevalence of depressive symptoms.

In a study conducted using the data from the National Health and Nutrition Examination Survey in the United States, the likelihood of depression in groups lacking vitamin D increased significantly compared to those with sufficient serum vitamin D.[15] Other studies using the same data, however, showed no meaningful relationship between serum vitamin D concentration and depressive symptoms when classifying the depression groups according to depression levels and comparing their relationship with vitamin D.[16] A study in Korea examined the relationship between the concentration of vitamin D in the blood and depression in adults, but showed conflicting results.[17,18] Furthermore, an analysis of the entire adult population using the KHNAES data in 2014 showed that the lower the serum vitamin D level, the greater the experience of depression in adult men; however a similar association could not be demonstrated in adult women.[19]

Postmenopausal women show a major characteristic of decreased estrogen, which causes 80% of women to undergo physical, hormonal and mental changes.[20] Several studies have shown that estrogen is strongly related to the pathogenesis of mental illness, including emotion and behavior control especially in older women, when they reach menopause.[21-23] Estrogen increases the effects of serotonin and norepinephrine, which are thought to be the neurotransmitters most related to the physiological cause of depression. Estrogen decreases monoamine oxidase (MAO) activity in the central nervous system, hindering the breakdown of serotonin and norepinephrine. In addition, estrogen increases serotonin synthesis, upregulates 5-hydroxytryptamine (5-HT)1 receptors, and downregulates 5-HT2 receptors. Estrogen also increases norepinephrine activity in the brain, perhaps by decreasing reuptake and degradation due to inhibition of MAO and catechol-O-methyltransferase.[23]

Decrease in estrogen is also related to a decrease in serum vitamin D. During menopause, women experience thinner skin and lower ability to produce vitamin D, in addition to reduced intestinal absorption of vitamin D and decreased vitamin D hydroxylation in the liver and kidneys.[24] Vitamin D reportedly reduces depressive symptoms in postmenopausal women by controlling the concentration of the neurotransmitter, serotonin, which increases the production of sex hormones and reduces the frequency of depression-associated receptors, within the pituitary gland in the brain.[25] VDR and 1-alphahydroxylase, which are responsible for active vitamin formation, are widely distributed in the human brain, including the prefrontal cortex, amygdala, hippocampus, hypothalamus, parenchymal nigra, and cerebellum.[26,27] Vitamin D deficiency has received more attention because of its potential effects on neuropsychological functions. In a systematic review and meta-analysis conducted to determine the relationship between vitamin D deficiency and depression, it was found that low vitamin D levels were associated with depression.[28]

Postmenopausal women with low serum vitamin D may have experienced related symptoms, which could have increased the use of dietary supplements, including vitamin D, or treatments for depression.[29] This tendency may have disturbed the association between serum vitamin D concentration and depressive symptoms, and eventually showed a different trend in premenopausal women.

Postmenopausal women had a higher mean age; therefore, they had a high percentage of underlying chronic diseases, and were likely to belong to low-activity groups. Depressive

symptoms are subjective problems affected by various physical and social factors, which can cause emotional instability combined with stress of chronic diseases, lack of confidence due to social and environmental changes, and reduced activity due to physical changes. These conditions in postmenopausal women were found to affect the rate of depression experience and have a greater impact than serum vitamin D concentration, resulting in different results from other groups in postmenopausal women. In this study, we tried to adjust for these factors by using social characteristics, underlying chronic disease and exercise and activity data.

This study had several limitations. First, this was a cross-sectional study; hence, it limits the explanation of the causal relationship between serum vitamin D concentration and the experience of depressive symptoms. If intervention such as vitamin D supplementation or antidepressants is carried out through a prospective future research method rather than a cross-sectional study, it would be possible to monitor the experience of depression following supplementation and reveal the direct causal relationship. Data from the KNHANES revealed only information about whether the participants were currently taking dietary supplements some of which could affect their serum vitamin D levels and depressive symptoms. In addition, depression was assessed using a questionnaire on subjective symptoms, and evaluated whether depression was present with a single question, "Have you felt sad or hopeless enough to interfere with your daily life for more than 2 consecutive weeks in the past year?" The errors could be reduced if information was obtained about depressive mood using structured questionnaires such as Patient Health Questionnaire-9, and about treatments for depression. However, as a screening test for depression, a single question is found to be useful,[30] and simple depression rather than major depressive disorder is frequently observed in primary care. The analysis of postmenopausal women showed statistically insignificant results even though all the variables were calibrated. This could have been derived with the small number of participants, and this limitation could be overcome if further research is conducted on more participants. Finally, this study found that there was a difference in the correlation between serum vitamin D levels and depression in a group of women based on menopause. However, no exact basis for determining the cause of this difference has been provided. Therefore, subsequent research warrants follow-up studies that contain gritty information than those provided in this study to improve the rationale for the results in postmenopausal women.

This study used a representative sample, the KNHANES, and it is the first study to analyze the link between serum vitamin D concentration and experience of depressive symptoms by categorizing Korean adult women on the basis of menopause. The study showed that a stratification analysis based on menopause would show meaningful results and revealed the link between serum vitamin D concentration and depression in adult women. Furthermore, as the interest and the use of dietary supplements such as multivitamin are increasing in Korea, this study is expected to provide useful information in the future studies.

Based on previous studies and this study, it is known that low vitamin D concentrations in premenopausal women increase depressive symptoms; thus vitamin D supplementation could be considered. However, in postmenopausal women, it is need to consider supplementing estrogen along with vitamin D to create synergistic effects against depressive symptoms. In further studies, it will be necessary to study whether it is effective to supplement both vitamin D and estrogen for postmenopausal women, or supplement only estrogen, and or supplement vitamin D alone to depressive symptoms.

This study examined the association between serum vitamin D concentration and depressive symptoms in Korean adult women according to their menopausal status. In premenopausal women, the lower the serum vitamin D concentration, the more the depressive symptoms; however the opposite trend was observed in postmenopausal women.

요 약

연구배경: 혈청 비타민 D와 우울 증상 사이의 관계는 한국 여성에 대한 이전 연구에서 일관되지 않았다. 폐경은 여성에게 중요한 특징적인 시기로 우울증 및 비타민 D와 관련이 있다고 알려져 있다.

방법: 제5차 국민건강영양조사 여성 11,573명을 대상으로 하였다. 혈청 비타민 D 수치는 사분위수에 따라 4개의 그룹으로, 우울 증상은 2개의 그룹으로 나누었다. 폐경 전후 각 그룹에서 다중 로지스틱 회귀분석을 시행하였다.

결과: 모든 여성에서 우울 증상은 가장 낮은 비타민 D 그룹(Q1)과 비교하여 가장 높은 그룹(Q4)에서 유의한 차이를 보이지 않았다(교차비[OR], 0.98; 95% 신뢰구간[CI], 0.78-1.22). 폐경 전 여성에서는 Q1과 비교하여 OR은 각각 Q2 0.75,

Q3 0.70 및 Q4 0.62로 통계적으로 유의하였다(*P*=0.016). 폐경 후 여성에서는 Q1과 비교하여 OR은 Q2 1.06, Q3 1.18 및 Q4 1.27로 각각 나타났다(*P*=0.057).

고찰: 폐경 전 여성에서는 혈청 비타민 D가 감소할수록 우울 증상이 증가하지만, 폐경 후 여성에서는 반대의 경향을 보였다. 향후 연구에서 혈중 비타민 D와 우울증의 연관성을 연구하고자 한다면, 여성의 폐경 상태는 중요한 기준으로 간주될 수 있다.

중심 단어: 비타민 D, 우울 증상, 폐경, 여성

ORCID

Sumi Lee https://orcid.org/0000-0002-6976-0388
Hi Won Choi https://orcid.org/0000-0001-6421-8402
Woo Kyung Bae https://orcid.org/0000-0001-6729-4128
Eun Young Shin https://orcid.org/0000-0001-5402-4292

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