

■ Original Article

# The Association between Low Vitamin D Status and Autoimmune Thyroid Disease in Korean Premenopausal Women: The 6th Korea National Health and Nutrition Examination Survey, 2013–2014

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**Background:** This study aimed to analyze the association of low vitamin D status with thyroid autoimmunity and dysfunction in the Korean population according to sex and menopausal status in women.

**Methods:** This study was based on the data acquired from the 6th Korea National Health and Nutrition Examination Survey. We enrolled 4,356 subjects who had data of thyroid function, antithyroid peroxidase antibody (TPOAb), and serum 25-hydroxyvitamin D (25[OH]D) levels. We excluded subjects who were pregnant and who had a history of thyroid disease or thyroid cancer, and those with transient thyroid dysfunction who tested negative for TPOAb (TPOAb[-]).

**Results:** TPOAb positivity (TPOAb[+]) with thyroid dysfunction (subclinical and overt hypothyroidism) was more prevalent in the vitamin D deficient group than in the vitamin D insufficient and sufficient groups including premenopausal ( $P=0.046$ ) and postmenopausal women ( $P=0.032$ ), although no significant differences were observed in men. The mean serum 25(OH)D level was significantly lower in the TPOAb(+) with thyroid dysfunction group than in the TPOAb(+) with euthyroidism and TPOAb(-) groups of premenopausal women ( $P=0.001$ ), although no significant differences were observed in men and postmenopausal women. Multivariate binary logistic regression analysis, adjusted for age, body mass index, and current smoking status, showed that vitamin D insufficiency and deficiency were significantly associated with TPOAb(+) with thyroid dysfunction in premenopausal women ( $P<0.001$ ), although no significant associations were observed in men and postmenopausal women.

**Conclusion:** Low vitamin D status was significantly associated with thyroid autoimmunity and dysfunction in the Korean population, especially in premenopausal women.

**Keywords:** Vitamin D Deficiency; Autoimmune Thyroiditis; Thyroid Diseases; Premenopause

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## INTRODUCTION

Vitamin D is a fat-soluble vitamin that can be ingested via food or synthesized using ultraviolet B irradiation (290–320 nm). Vitamin D not only regulates calcium, phosphorous, and bone metabolism but also performs nonskeletal actions, such as potent modulation of the immune system.<sup>1)</sup> Low vitamin D status is very common in Koreans and has become an important health problem. It is more prevalent in women and in the younger generation. According to the results of the 4th Korea National Health and Nutrition Examination Survey (KNHANES) conducted in 2008, 47.3% of men and 64.5% of women had serum 25-hydroxyvitamin D (25[OH]D) levels <20 ng/mL.<sup>2)</sup>

Several studies have shown an association between low vitamin D status and several autoimmune diseases.<sup>3,4)</sup> The most prevalent organ-specific autoimmune disease is autoimmune thyroid disease (AITD), characterized by lymphocytic infiltration of the thyroid parenchyma, that affects approximately 5% of the population across age groups.<sup>5)</sup> It is more common in regions with high iodine dietary intakes, including Korea, and is most often observed in women aged 30–60 years.<sup>6)</sup> Recent studies have revealed that the prevalence of low vitamin D status is higher in patients with AITD, particularly those with Hashimoto's thyroiditis, than in patients without AITD. These studies revealed that low vitamin D status was associated with antithyroid peroxidase antibody (TPOAb) positivity, subclinical hypothyroidism, or overt hypothyroidism; however, other studies have reported conflicting results.<sup>5,7)</sup>

Choi et al.<sup>8)</sup> showed that low vitamin D status was significantly associated with AITD, especially in premenopausal women; however, this study was based on a single-center experience, and therefore, these results could not be generalized in all Korean individuals. Kim et al.<sup>9)</sup> revealed that low vitamin D status was significantly associated with thyroid dysfunction in participants with excessive iodine intake, using data from the KNHANES VI. However, they did not perform detailed analyses on the association between low vitamin D status and thyroid dysfunction according to sex and menopausal status.

We hypothesized that low vitamin D status is significantly associated with thyroid autoimmunity and dysfunction, especially in premenopausal women. In this study, we aimed to analyze the association of low vitamin D status with thyroid autoimmunity and dysfunction in the Korean population and to perform subgroup analyses by sex and menopausal status in women using data from the KNHANES VI, a large-scale nationwide survey.

## METHODS

### 1. Study Participants

This study was based on data acquired from the KNHANES VI (2013–2014). The KNHANES is a nationwide representative cross-sectional survey that has been regularly conducted by the Korea Centers for Disease Control and Prevention since 1998. It provides information regarding the health and nutritional status of the Korean population.<sup>2,9,10)</sup> We enrolled 4,356 subjects with results of thyroid function, TPOAb,

and serum 25(OH)D levels. We excluded subjects who were pregnant, who had a previous history of thyroid disease or thyroid cancer, and those with hyperthyroidism, based on the result of the thyroid function test and transient thyroid dysfunction, who tested negative for TPOAb (TPOAb[-]) (subacute thyroiditis or nonthyroidal illness).

### 2. Laboratory Measurements

Serum thyroid-stimulating hormone (TSH; reference range, 0.35–5.50 mIU/L), free thyroxine (free T4; reference range, 0.89–1.76 ng/mL), and TPOAb (reference range, <34.0 IU/mL) levels were measured using an electrochemiluminescence immunoassay (Roche Diagnostics, Mannheim, Germany) with E-TSH kit, E-free T4 kit, and E-anti-thyroid peroxidase kit, respectively. Serum 25(OH)D levels were measured using a gamma counter (1470 Wizard; Perkin-Elmer, Turku, Finland) with radioimmunoassay (DiaSorin, Stillwater, MN, USA).<sup>2,9,10)</sup>

### 3. Definitions of Clinical Characteristics

In the current study, overt hypothyroidism was defined as a serum TSH level >5.50 mIU/L and a serum free T4 level <0.89 ng/mL. Subclinical hypothyroidism was defined as a serum TSH level >5.50 mIU/L with a normal serum free T4 level (0.89–1.76 ng/mL).<sup>11)</sup> TPOAb positivity was defined as a serum TPOAb level  $\geq$ 34.0 IU/mL. We classified the subjects into the positive TPOAb (TPOAb[+]) and TPOAb(-) groups, according to the presence of TPOAb positivity. All subjects in the TPOAb(-) group had normal thyroid function, while those in the TPOAb(+) group were further classified into the euthyroid, subclinical hypothyroid, and overt hypothyroid groups, according to their thyroid function status. The number of subjects with subclinical hypothyroidism and overt hypothyroidism was too small to determine the statistical significance; therefore, we combined these two groups into the thyroid dysfunction group. We used serum 25(OH)D levels to identify subjects with vitamin D deficiency (<10 ng/mL), insufficiency (from 10 to <20 ng/mL), or sufficiency ( $\geq$ 20 ng/mL).<sup>2)</sup> Body mass index (BMI) was calculated by dividing the weight (kg) by the square of the height (m<sup>2</sup>).

### 4. Statistical Analyses

The data were analyzed by complex sample analysis. Survey sample weights of the KNHANES and complex survey design were used. To analyze samples in multiple years, sampling weights were averaged over the sampled years. Generalized linear regression analyses and  $\chi^2$  tests were used to compare continuous and categorical variables, respectively. Continuous variables were expressed as means $\pm$ standard errors, and categorical variables were expressed as unweighted numbers (weighted %). Univariate and multivariate binary logistic regression analyses were used to determine the association of low vitamin D status with thyroid autoimmunity and dysfunction after adjustment for possible confounding factors. The results were expressed as odd ratios (ORs) and 95% confidence intervals (CIs). Data analysis was performed using IBM SPSS for Windows ver. 20.0 software (IBM Corp., Armonk, NY, USA). All the tests were two-sided, and  $P < 0.05$  was con-

sidered statistically significant.

## 5. Ethical Considerations

All the patients enrolled in the KNHANES signed an informed consent form. This was a cross-sectional study based on the KNHANES (<http://knhanes.cdc.go.kr/knhanes/>); therefore, ethical approval was not required.

## RESULTS

### 1. Clinical Characteristics

The overall clinical characteristics of 4,356 study subjects are presented in Table 1. The overall mean age was 40.2 years; 25.5% subjects were current smokers, and the mean BMI of the subjects was 23.5 kg/m<sup>2</sup>. The overall mean serum TSH, free T4, and TPOAb levels were 2.61 mIU/L, 1.24 ng/mL, and 29.5 IU/mL, respectively. The overall prevalence of TPOAb positivity was 6.8%. We classified the subjects into the TPOAb(-) (n=4,055, 93.2%), TPOAb(+) with euthyroidism (n=238, 5.4%), and TPOAb(+) with thyroid dysfunction (n=63, 1.5%) groups. The overall mean serum 25(OH)D level was 16.7 ng/mL, and we classified the subjects into the vitamin D sufficient (n=1,128, 25.4%), insufficient (n=2,683, 62.0%), and deficient (n=545, 12.6%) groups.

### 2. Clinical Characteristics according to Sex and Menopausal Status

The clinical characteristics of the 4,356 study subjects according to sex and menopausal status are outlined in Table 1. Among the 4,356 subjects, 2,193 (50.3%) were men and 2,163 (49.7%) were women. Among the 2,163 female subjects, 1,329 (61.4%) were premenopausal women

and 655 (30.3%) were postmenopausal women. The mean age was 39.9 years for men, 40.5 years for women (P=0.197), 31.5 years for premenopausal women, and 59.8 years for postmenopausal women (P<0.001). A total of 43.9% of men, 5.8% of women (P<0.001), 7.0% of premenopausal women, and 4.0% of postmenopausal women (P=0.025) were current smokers. The mean BMI was 24.0 kg/m<sup>2</sup> for men, 22.9 kg/m<sup>2</sup> for women (P<0.001), 22.4 kg/m<sup>2</sup> for premenopausal women, and 24.1 kg/m<sup>2</sup> for postmenopausal women (P<0.001).

The differences in mean serum TSH levels were not significant in men, premenopausal women, and postmenopausal women. The mean serum free T4 levels were lower in women than in men (1.19 ng/mL versus 1.28 ng/mL, P<0.001) and were lower in postmenopausal women than in premenopausal women (1.17 ng/mL versus 1.20 ng/mL, P=0.007). The mean serum TPOAb levels (40.8 IU/mL versus 19.3 IU/mL, P<0.001), prevalence of TPOAb positivity (10.1% versus 3.8%, P<0.001), and percentages of TPOAb(+) with euthyroidism (8.2% versus 2.8%) and TPOAb(+) with thyroid dysfunction (1.9% versus 1.0%, P<0.001) were higher in women than in men. Particularly, the mean serum TPOAb levels (53.4 IU/mL versus 36.3 IU/mL, P=0.013), prevalence of TPOAb positivity (14.4% versus 7.9%, P<0.001), and percentages of TPOAb(+) with euthyroidism (12.1% versus 5.9%) and TPOAb(+) with thyroid dysfunction (2.3% versus 1.9%, P<0.001) were higher in postmenopausal women than in premenopausal women.

The mean serum 25(OH)D levels were significantly lower (15.9 ng/mL versus 17.4 ng/mL, P<0.001) and the prevalence of vitamin D deficiency was significantly higher (16.2% versus 9.4%, P<0.001) in women than in men. Contrary to the thyroid function test results, the mean serum 25(OH)D level was lower in premenopausal women (14.8 ng/mL versus 18.2 ng/mL, P<0.001) than in postmenopausal women, and the

**Table 1.** Baseline characteristics of the study population according to sex and menopausal status

Characteristic	Total (n=4,356)	Men (n=2,193)	Women (n=2,163)	P-value*	Women		
					Premenopausal (n=1,329)	Postmenopausal (n=655)	P-value*
Age (y)	40.2±0.3	39.9±0.3	40.5±0.4	0.197	31.5±0.3	59.8±0.2	<0.001
Current smoker	862 (25.5)	754 (43.9)	108 (5.8)	<0.001	78 (7.0)	27 (4.0)	0.025
Body mass index (kg/m <sup>2</sup> )	23.5±0.1	24.0±0.1	22.9±0.1	<0.001	22.4±0.1	24.1±0.2	<0.001
Thyroid-stimulating hormone (mIU/L)	2.61±0.12	2.64±0.23	2.59±0.04	0.855	2.59±0.05	2.59±0.06	0.941
Free thyroxine (ng/mL)	1.24±0.01	1.28±0.01	1.19±0.01	<0.001	1.20±0.01	1.17±0.01	0.007
TPOAb (IU/mL)	29.5±2.5	19.3±2.2	40.8±4.7	<0.001	36.3±4.9	53.4±4.8	0.013
TPOAb positivity (≥34.0 IU/mL)	301 (6.8)	85 (3.8)	216 (10.1)	<0.001	105 (7.9)	97 (14.4)	<0.001
Thyroid function status				<0.001			<0.001
TPOAb (-)	4,055 (93.2)	2,108 (96.2)	1,947 (89.9)		1,224 (92.1)	558 (85.6)	
TPOAb (+) with euthyroidism	238 (5.4)	63 (2.8)	175 (8.2)		82 (5.9)	80 (12.1)	
TPOAb (+) with thyroid dysfunction <sup>†</sup>	63 (1.5)	22 (1.0)	41 (1.9)		23 (1.9)	17 (2.3)	
Serum 25(OH)D (ng/mL)	16.7±0.2	17.4±0.2	15.9±0.2	<0.001	14.8±0.2	18.2±0.4	<0.001
Serum 25(OH)D (ng/mL)				<0.001			<0.001
≥20	1,128 (25.4)	668 (29.0)	460 (21.4)		213 (15.9)	213 (32.9)	
10 to <20	2,683 (62.0)	1,322 (61.6)	1,361 (62.4)		869 (65.7)	371 (55.5)	
<10	545 (12.6)	203 (9.4)	342 (16.2)		247 (18.4)	71 (11.6)	

Values are presented as mean±standard error or unweighted numbers (weighted %).

TPOAb, antithyroid peroxidase antibody; 25(OH)D, 25-hydroxy vitamin D.

\*P-values were calculated using generalized linear regression analysis via complex sampling or  $\chi^2$  tests via complex sampling. <sup>†</sup>The subjects with both subclinical hypothyroidism and overt hypothyroidism were included in the thyroid dysfunction group.

proportions of premenopausal women in the vitamin D insufficient (65.7% versus 55.5%) and deficient groups (18.4% versus 11.6%,  $P < 0.001$ ) were significantly higher than those of postmenopausal women.

### 3. Association between Vitamin D Status and Thyroid Function according to Sex and Menopausal Status

The prevalences of TPOAb(+) with euthyroidism and TPOAb(+) with thyroid dysfunction were higher in the vitamin D deficient group than in the other two groups of men, but these differences were not significant ( $P = 0.374$ ). However, the prevalences of TPOAb(+) with euthyroidism (7.4% versus 5.5% versus 6.0%) and TPOAb(+) with thyroid dysfunction (2.7% versus 2.1% versus 0.1%) were higher in the vitamin D deficient group than in the other two groups (insufficient and

sufficient) of premenopausal women ( $P$  for trend=0.046). The prevalence of TPOAb(+) with euthyroidism (22.2% versus 11.1% versus 10.2%) was also higher in the vitamin D deficient group than in the other two groups of postmenopausal women ( $P$  for trend=0.032) (Table 2).

The mean serum 25(OH)D levels were insignificantly different in the TPOAb(+) with thyroid dysfunction, TPOAb(+) with euthyroidism, and TPOAb(-) groups of men and women (Figure 1A). However, the mean serum 25(OH)D level was significantly lower in the TPOAb(+) with thyroid dysfunction group than in the other two groups of premenopausal women (11.7 ng/mL versus 14.4 ng/mL versus 14.9 ng/mL,  $P = 0.001$ ), although no significant differences were observed among the three groups of postmenopausal women (Figure 1B).

According to the univariate binary logistic regression analysis in the

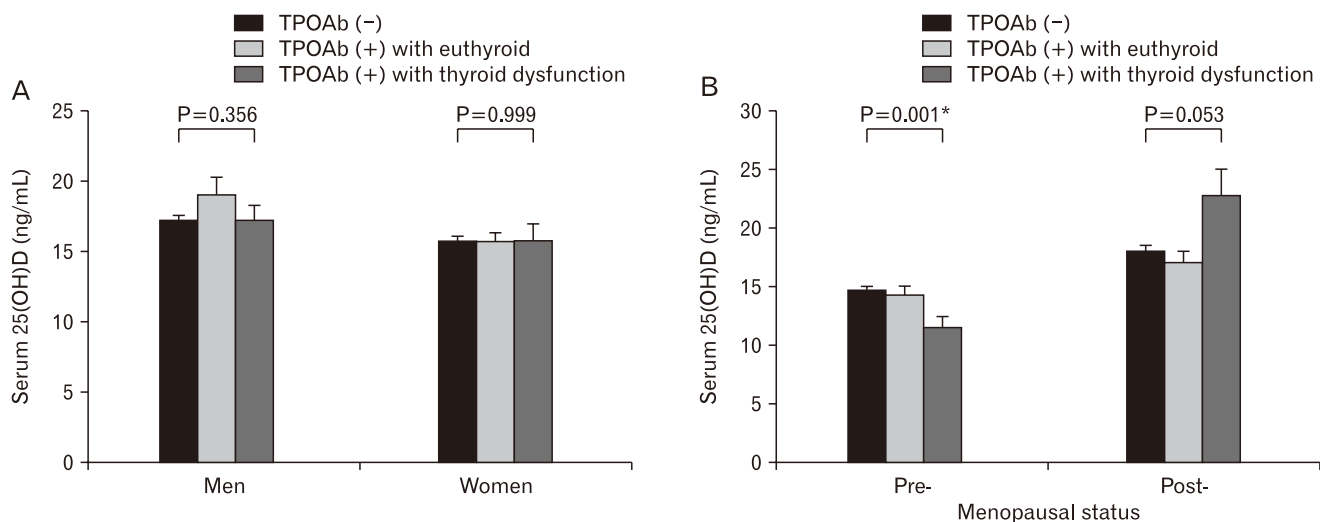
**Table 2.** The association between vitamin D status and thyroid function according to sex and menopausal status

Variable	Serum 25-hydroxy vitamin D (ng/mL)								
	Men			Premenopausal women			Postmenopausal women		
	≥20	10 to <20	<10	≥20	10 to <20	<10	≥20	10 to <20	<10
Thyroid-stimulating hormone (mIU/L)	2.43±0.10*	2.37±0.05*	4.97±0.25*	2.41±0.09	2.60±0.07	2.68±0.13	2.68±0.11	2.49±0.08	2.84±0.18
Free thyroxine (ng/mL)	1.28±0.01	1.28±0.01	1.27±0.01	1.19±0.01	1.20±0.01	1.20±0.01	1.19±0.01	1.16±0.01	1.16±0.02
TPOAb (IU/mL)	18.9±1.2	17.4±2.8	33.1±12.9	55.3±26.4	32.7±3.6	32.8±4.4	66.6±9.2	43.4±7.4	63.6±15.6
TPOAb positivity	32 (4.3)	43 (3.3)	10 (5.5)	16 (6.1)	64 (7.7)	25 (10.1)	34 (14.1)	48 (12.5)	15 (24.8)
Thyroid function status									
TPOAb (-)	636 (95.7)	1,279 (96.7)	193 (94.5)	197 (93.9)*	805 (92.3)*	222 (89.9)*	179 (85.9)*	323 (87.5)*	56 (75.2)*
TPOAb (+) with euthyroidism	26 (3.5)	30 (2.4)	7 (3.6)	15 (6.0)*	47 (5.5)*	20 (7.4)*	26 (10.2)*	41 (11.1)*	13 (22.2)*
TPOAb (+) with thyroid dysfunction†	6 (0.8)	13 (1.0)	3 (1.9)	1 (0.1)*	17 (2.1)*	5 (2.7)*	8 (3.8)*	7 (1.3)*	2 (2.7)*

Values are presented as mean±standard error or unweighted numbers (weighted %).

TPOAb, antithyroid peroxidase antibody.

P-values were calculated using generalized linear regression analysis via complex sampling or  $\chi^2$  test for trend via complex sampling (\* $P$  for trend <0.05). †The subjects with both subclinical hypothyroidism and overt hypothyroidism were included in the thyroid dysfunction group.



**Figure 1.** Mean serum levels of 25(OH)D in the negative TPOAb (TPOAb[-]) group, positive TPOAb (TPOAb[+]) with euthyroidism group, and TPOAb(+) with thyroid dysfunction group, according to sex and menopausal status. (A) Mean serum levels of 25(OH)D among the three groups in men and women. (B) Mean serum levels of 25(OH)D among the three groups in premenopausal and postmenopausal women. Error bars represent standard error values. P-values were calculated using generalized linear regression analyses via complex sampling. 25(OH)D, 25-hydroxy vitamin D; TPOAb, antithyroid peroxidase antibody.

premenopausal women, age (OR, 1.07; 95% CI, 1.03–1.11;  $P < 0.001$ ), vitamin D insufficiency (OR, 16.68; 95% CI, 11.19–24.85), and vitamin D deficiency (OR, 21.24; 95% CI, 10.46–43.10;  $P < 0.001$ ) were significantly associated with TPOAb(+) with thyroid dysfunction. Multivariate binary logistic regression analyses, after adjustment for age, BMI, and current smoking status, in premenopausal women showed that age (adjusted OR, 1.06; 95% CI, 1.02–1.10;  $P = 0.004$ ), vitamin D insufficiency (adjusted OR, 17.63; 95% CI, 11.53–26.97), and vitamin D deficiency (adjusted OR, 21.72; 95% CI, 9.44–50.01;  $P < 0.001$ ) were still significantly associated with TPOAb(+) with thyroid dysfunction (Table 3). However, significant associations between vitamin D insufficiency or deficiency and TPOAb(+) with thyroid dysfunction were not observed in men and postmenopausal women.

## DISCUSSION

This study aimed to investigate the association between low vitamin D status and AITD and to perform a more detailed analysis according to sex and menopausal status in the general Korean population based on a nationwide representative cross-sectional survey. Low vitamin D status has become a public health problem in Korea. According to the results of the KNHANES IV (2008), 47.3% of men and 64.5% of women had serum 25(OH)D levels  $< 20$  ng/mL, and low vitamin D status was the most prevalent in the age group of 20–29 years.<sup>2)</sup> Vitamin D synthesis in the skin by sun exposure is the major source of vitamin D in our body. Therefore, the increasing prevalence of low vitamin D status in young adults who live in cities and spend a majority of their time indoors (at work, at school, or at home) without being exposed to sufficient sunlight, which would enable vitamin D synthesis in the skin, raises concerns regarding the resultant health problems.<sup>1)</sup> The main role of vitamin D is in the regulation of calcium and bone homeostasis, and low vitamin D status was originally associated with osteoporosis and fractures. Recently, many nonskeletal actions, such as cellular proliferation and differentiation, muscle function, and immunity, of vitamin D have attracted attention, and low vitamin D status is associated with an increased risk of cardiovascular disease, diabetes mellitus, cancer, infections, and autoimmune diseases.<sup>1)</sup>

AITD is one of the most prevalent organ-specific autoimmune dis-

eases and affects approximately 5% of the population across age groups. It is more common in regions with high dietary iodine intake, including Korea, and is most often observed in women aged 30–60 years.<sup>6)</sup> Low vitamin D status is a primary phenomenon involved in causing AITD or it simply represent the consequence in the pathogenesis of the disease.<sup>12)</sup> One hypothesis is that vitamin D mediates the immunomodulatory effect by binding to the vitamin D3 receptor, the ligand for 1,25-dihydroxyvitamin D3, which is also expressed in the thyroid tissues.<sup>12)</sup>

Recent studies have revealed an association between low vitamin D status and the TPOAb positivity, subclinical hypothyroidism, or overt hypothyroidism.<sup>7)</sup> However, several studies have reported conflicting results about the association between low vitamin D status and AITD. Moreover, few studies have assessed the association between low vitamin D status and AITD in the Korean population. Kim et al.<sup>9)</sup> revealed that low vitamin D status was significantly associated with thyroid dysfunction in participants with excessive iodine intake, based on data from the KNHANES VI. However, even though low vitamin D status and AITD are more common in women and certain age groups, they did not perform detailed analyses regarding the association between low vitamin D status and thyroid dysfunction according to patient characteristics. Choi et al.<sup>8)</sup> showed that low vitamin D status was significantly associated with AITD, especially in premenopausal women; however, this study was based only on a single-center experience. Thus, the results of this study cannot be generalized to all Korean individuals.

The current study revealed that low vitamin D status was significantly associated with AITD in the general Korean population. Interestingly, the mean serum 25(OH)D level was significantly lower in the TPOAb(+) with thyroid dysfunction group than in the TPOAb(+) with euthyroidism and TPOAb(-) groups only in premenopausal women. Furthermore, no significant differences were observed among the three groups of men and postmenopausal women. This result supports the reports of Choi et al.<sup>8)</sup> who suggested a possible cross-talk mechanism between vitamin D and estrogen in AITD pathogenesis; however, the underlying mechanism remains unclear. Additionally, multivariate logistic regression analyses after the adjustment for possible confounding factors, such as age, BMI, and current smoking status,

**Table 3.** Univariate and multivariate binary logistic regression models for TPOAb positivity with thyroid dysfunction in premenopausal women

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age (y)	1.07 (1.03–1.11)	$< 0.001$	1.06 (1.02–1.10)	0.004
BMI (kg/m <sup>2</sup> )	1.12 (1.00–1.25)	0.047	1.09 (0.96–1.24)	0.174
Current smoker	0.57 (0.11–2.91)	0.497	0.64 (0.12–3.28)	0.590
Serum 25-hydroxy vitamin D (ng/mL)		$< 0.001$		$< 0.001$
$\geq 20$	1.00		1.00	
10 to $< 20$	16.68 (11.19–24.85)		17.63 (11.53–26.97)	
$< 10$	21.24 (10.46–43.10)		21.72 (9.44–50.01)	

TPOAb, antithyroid peroxidase antibody; OR, odds ratio; CI, confidence interval; BMI, body mass index.

ORs were calculated using univariate or multivariate binary logistic regression analysis, after adjustment for age, BMI, and current smoking status via complex sampling. Reference is negative TPOAb (TPOAb[-]).

showed that vitamin D insufficiency and vitamin D deficiency were still significantly associated with TPOAb(+) with thyroid dysfunction.

We used cutoff values  $\geq 20$  ng/mL and  $< 10$  ng/mL serum 25(OH)D to classify vitamin D sufficiency and deficiency, respectively, although the optimal level to define vitamin D status remains controversial. We chose the cutoff values based on the studies that defined  $\geq 20$  ng/mL serum 25(OH)D levels as being sufficient for sustaining parathyroid hormone levels and bone health.<sup>9)</sup>

This study has certain limitations. First, serum 25(OH)D levels are affected by sunlight exposure, time spent indoors, seasonal variations, and dietary and supplemental vitamin D intake.<sup>2)</sup> However, data regarding the amount of sunlight exposure, timing of blood sample collection, residential area, occupation, sunscreen use, and dietary and supplemental vitamin D intake were not available in the KNHANES VI. Moreover, serum calcium, phosphorous, and parathyroid hormone levels, the most sensitive indicators of calcium homeostasis and vitamin D deficiency, were not measured. However, the strength of this study was that it was based on the data from the KNHANES VI, the first survey that measured serum 25(OH)D, TSH, free T4, and TPOAb levels together in the Korean population. Second, AITD diagnosis was established based only on the laboratory findings, because we were unable to establish the diagnosis using thyroid ultrasonography or pathologic findings. However, several studies have evaluated the association between vitamin D deficiency and AITD using serum TPOAb levels as a marker of thyroid autoimmunity.<sup>8)</sup> These results need to be confirmed in further controlled prospective studies involving large patient cohorts in multi-institutional cooperative groups. Moreover, the effects of vitamin D supplementation on thyroid autoimmunity and dysfunction in patients with AITD need to be established.

In conclusion, low vitamin D status was significantly associated with thyroid autoimmunity and dysfunction in the Korean population, especially in premenopausal women.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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