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The association between serum vitamin D level and immunoglobulin E in Korean adolescents

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ABSTRACT

Objective: Vitamin D has immune modulatory functions, and thus its relationship with allergic disease has been evaluated in a number of studies. However, no concrete link between serum IgE level and vitamin D has been established. Thus, the purpose of study was to confirm the association of serum vitamin D level with the serum IgE (total and *Dematophagoides farinae* specific IgE) in Korean adolescents.

Methods: A total of 365 subjects between 10 and 18 years of age were enrolled through the Korea National Health and Nutrition Examination Survey (KNHANES). Serum levels of vitamin D, total IgE, and *Dermatophagoides farinae* (Df) specific IgE were measured, and data for potential confounding variables were collected. Multivariate regression analyses were used to determine the independent effects of these variables.

Results: Levels of both total and Df specific IgE were positively correlated with serum concentration of vitamin D (Spearman's rho (R) = 0.126, p = 0.016; R = 0.152, p = 0.004, respectively). These results were confirmed by multivariate linear regression analysis after adjusting for sex, age, and body mass index (coefficient (B): 10.45 95% confidence interval (CI): 0.59–20.31; B: 1.06, 95% CI: 0.31–1.80, respectively). And, the association between serum vitamin D and IgE showed the different results depending on the presence or absence of Df sensitization.

Conclusions: Serum concentration of vitamin D was positively associated with levels of both total IgE and Df-specific IgE in Korean adolescents.

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1. Introduction

The increasing prevalence of allergic disease is a world-wide phenomenon and is more evident in children and adolescents compared to adults [1]. Genetic and environmental factors such as diet and air pollution play a crucial role in increasing the prevalence of allergies [2]. The association between nutritional ingredients and the risk of allergy also has been studied. For example, a high intake of n-3-polyunsaturated fatty acid protects against the development of wheezing and asthma in Greek preschool children [3]. Likewise, serum folate level was inversely correlated with level of total IgE as well as other markers of allergic disease [4].

Vitamin D affects various immune cells such as T cells, B-cells, and dendritic cells [5], and some reports have shown that vitamin D deficiency is positively associated with allergic disease [6,7]. On the contrary, there is conflicting data regarding the use of vitamin D supplements and high serum level of vitamin D increasing the risk of allergic disease [8,9]. Although we do not know the exact cause of conflicting results, racial difference might be a possible cause [7,10].

The majority of previous studies about the association between vitamin D and allergic disease have focused on Western populations. To the best of our knowledge, there was only one published study analyzing the association between vitamin D and allergic disease in Asian adolescents. And, this study was based on data obtained from subjective reporting of allergic disease [11].

In the present study, we investigate the association between serum vitamin D levels and serum IgE level (total and *Dermatophagoides farinae* (Df) specific) in Korean adolescents using data of the Korean National Health and Nutrition Examination Survey (KNHANES).

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2. Materials and methods

2.1. Study population

We used the KNHANES 2010 which was a national survey conducted in 2010 by the Ministry of Health and Welfare of Korea. KNHANES was initiated in 1998 and is conducted periodically to evaluate the status of health and nutrition of the non-institutionalized Korean population. The survey includes a health interview, a nutrition survey, and a health examination. The health interview and nutritional survey were conducted via household interviews and a self-reported survey, respectively. Physical examinations were conducted in mobile examination centers by trained examiners. For our analysis, we limited the study population to 1076 adolescents aged 10–18 years. However, some measurements including serum IgE and vitamin D levels were performed on some participants who were selected randomly before the survey. Therefore, vitamin D levels were missing in 203 participants, and serum IgE levels were missing in 508 participants. After the exclusion, data from a total of 365 subjects (186 male and 179 female) were included in our analysis. Demographic data obtained in the survey included age, gender, and body mass index (BMI) calculated as weight (kg)/height^2 (m^2). Written informed consent was obtained from the legal guardian of all participants. This study was approved by the Institutional Review Board of Yonsei University College of Medicine in Seoul, Korea.

2.2. Measurement of serum level of vitamin D

After a 12-h overnight fast, blood samples were obtained. Serum concentrations of vitamin D (25(OH)D) were measured by a radioimmunoassay (RIA) method using a 25-Hydroxyvitamin D ^{125}I RIA Kit (DiaSorin, Stillwater, MN, USA). Data from the radioimmunoassay was collected with a 1470 WIZARD gamma-Counter analyzer (PerkinElmer, Turku, Finland). Also, we categorized serum vitamin D levels into three groups according to guideline of Institute of Medicine [12]: deficient ($<$12 ng/ml), insufficient ($\geq$12 and $<$20 ng/ml), and sufficient ($\geq$20 ng/ml).

2.3. Measurement of total and Df-specific IgE

Levels of total IgE and Df-specific IgE were measured using an ImmunoCAP100 kit (Phadia, Uppsala, Sweden) and a 1470 WIZARD gamma-Counter analyzer (PerkinElmer, Turku, Finland). The upper limits of detectable total IgE and Df-specific IgE were 5000.0 kU/L and 100.0 kU/L, respectively. Thus, readings with an IgE level greater than 5000.0 kU/L were set as 5000.0 kU/L. Likewise, readings of Df-specific IgE greater than 100.0 kU/L were set as 100.0 kU/L. Df sensitization was considered Df-specific if the level of IgE was $\geq$0.35 kU/L.

2.4. Statistical analysis

Student's *t*-test and Mann–Whitney test were used to compare differences between the two groups as appropriate. Multivariate linear regression analyses was used to identify independent predictors for total IgE and Df specific IgE levels, respectively. Statistical analysis was conducted with the SPSS statistical software package version 17 (SPSS Inc. Chicago). For all analyses, p values were two-tailed, and $<$0.05 was considered statistically significant.

3. Results

The mean age of the study population was 13.73 $\pm$ 2.47 years old and consisted of 186 boys and 179 girls. The mean serum level of vitamin D in all subjects was 16.8 ng/ml (range: 5.4–34.04 ng/mL). Only 17.5% of subjects showed a sufficient serum level of vitamin D. The majority of children showed insufficient or deficient serum level of vitamin D. The mean concentration of vitamin D in male and female subjects was 17.74 ng/mL and 15.83 ng/mL, respectively, the difference of which was statistically significant according to Student's *t* test ($p < 0.001$). Age and BMI were inversely correlated with serum level of vitamin D (Spearman's rho -0.253, $p < 0.001$; Spearman's rho -0.103, $p = 0.05$, respectively).

Table 1 shows the comparison between the two group categorized by Df sensitization. There were no specific differences between the two groups, except for the median of total IgE. As we expected, the median of total IgE in Df sensitization group was significantly higher than that of the group without Df sensitization. Mean serum vitamin D level was slightly higher in the Df sensitization group than the non-sensitized group, but without statistical significance.

We investigated the correlation between the serum vitamin D level and IgE level (total and Df specific). In addition, we confirmed that serum level of vitamin D was positively correlated with total IgE (Spearman's rho (R) = 0.126, p = 0.016). Df specific IgE was also positively associated with serum vitamin D level (R = 0.152, p = 0.004). And, the same results were observed in linear regression analysis after adjusted with sex, age, and BMI (coefficient (B): 10.45 95% confidence interval (CI): 0.59–20.31; B: 1.06, 95% CI: 0.31–1.80, respectively) (Table 2).

Finally, we divided all participants into two groups, participants with Df sensitization and participants without Df sensitization. In addition, we investigated the association between serum level of vitamin D and IgE level (total and Df specific) in each group using multivariate linear regression analysis. No significant association between both the total and Df specific IgE and serum vitamin D in non-sensitized group (Table 3) were found. For the Df sensitized group, a significant association between vitamin D level and Df specific IgE was shown in participants with Df sensitization (B 1.416, 95% CI 0.186–2.646, Table 4). However, total IgE level was not significantly associated with serum vitamin D level.

Table 1
Characteristics of study population.

Variables	Df specific IgE $<$ 0.35 kU/L (n = 189)	Df specific IgE $\geq$ 0.35 kU/L (n = 176)	p-Value
Sex[#]			
Man (n = 186)	89	97	0.143
Woman (n = 179)	100	79	
Age (year)[*]	13.78 $\pm$ 0.18	13.68 $\pm$ 0.18	0.697
BMI (kg/m^2)[*]	20.62 $\pm$ 0.26	20.82 $\pm$ 0.27	0.584
Total IgE (kU/L)[*]	96.60 $\pm$ 10.14	423.25 $\pm$ 44.77	$<$0.001
Serum vitamin D level (ng/mL)[*]	16.32 $\pm$ 0.34	17.32 $\pm$ 0.38	0.054

BMI = body mass index, Df = *Dermatophagoides farinae*, IgE = immunoglobulin E.
[*] Values are presented as mean $\pm$ standard deviation and p-value was calculated using student's *t*-test.
[#] p-Values are calculated with $\times$2 test.

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Table 2
Adjusted linear regression analysis with total IgE and Df specific IgE as a dependent variable in all subjects.

	Total IgE			Df specific IgE		
	Adjusted coefficient	95% CI	*p*-Value	Adjusted coefficient*	95% CI	*p*-Value
Sex						
Man		Reference			Reference	
Woman	−28.13	−123.58 to 68.31	0.567	3.41	−3.86 to 10.67	0.357
Age	−13.08	−32.73 to 6.56	0.191	−1.14	−2.62 to 0.34	0.131
BMI	7.03	−6.32 to 20.39	0.301	0.03	−0.98 to 1.04	0.953
Serum vitamin D	***10.45***	***0.59* to *20.31***	***0.038***	***1.06***	***0.31* to *1.80***	***0.005***

Abbreviations: Df = *Dermatophagoides farinae*, IgE = immunoglobulin E, BMI = body mass index.
Bold and italic denote $p < 0.05$.

Table 3
Adjusted linear regression analysis with total IgE and Df specific IgE as a dependent variable in189 subjects without Df sensitization.

	Total IgE			Df specific IgE		
	Adjusted coefficient	95% CI	*p*-Value	Adjusted coefficient	95% CI	*p*-Value
Sex						
Man		Reference			Reference	
Woman	−6.464	−47.451 to 34.522	0.756	−0.011	−0.038 to 0.016	0.422
Age	5.150	−3.294 to 13.594	0.230	0.002	−0.003 to 0.008	0.462
BMI	2.827	−2.934 to 8.588	0.334	0.001	−0.003 to 0.004	0.752
Serum vitamin D	3.074	−1.279 to 7.427	0.165	0.002	−0.001 to 0.005	0.229

Abbreviations: Df = *Dermatophagoides farinae*, IgE = immunoglobulin E, BMI = body mass index.
Bold and italic denote $p < 0.05$.

Table 4
Adjusted linear regression analysis with total IgE and Df specific IgE as a dependent variable in 176 subjects with Df sensitization.

	Total IgE			Df specific IgE		
	Adjusted coefficient	95% CI	*p*-Value	Adjusted coefficient	95% CI	*p*-Value
Sex						
Man		Reference			Reference	
Woman	−15.493	−202.162 to 171.176	0.870	12.186	−0.283 to 23.654	0.055
Age	−32.588	−69.924 to 4.748	0.087	−2.198	−4.691 to 0.296	0.084
BMI	9.491	−15.819 to 34.801	0.740	−0.154	−1.845 to 1.537	0.858
Serum vitamin D	11.468	−6.949 to 29.885	0.221	***1.416***	***0.186* to *2.646***	***0.024***

Abbreviations: Df = *Dermatophagoides farinae*, IgE = immunoglobulin E, BMI = body mass index.
Bold and italic denote $p < 0.05$.

4. Discussion

The results of the present study indicated that serum level of vitamin D is positively associated with total IgE and Df-specific IgE levels in Korean adolescents. There were many studies about the association between serum vitamin D level and risk of allergic diseases, however they showed conflicting results [6–8,13–15]. Higher level of vitamin D and supplementation of vitamin D were shown to increase the risk of allergic disease in children [8,13–15]. On the contrary, several studies have shown that vitamin D deficiency is associated with increased risk of allergy in children [6,7,16–18].

These conflicting results were also shown in animal studies. Matheu et al. reported that vitamin D supplementation increases levels of allergy-related cytokines such as IL-4, IL-13, and serum IgE, suggesting that excess vitamin D may lead to the development of a Th2 response and increased risk of developing allergies [19]. Consistent with these conclusions, both Long et al. and Overbergh et al. demonstrated that a higher level of vitamin D is associated with a shift toward a Th2-mediated inflammatory response [20,21]. However, Matheus et al. also observed a protective role of vitamin D and allergy in the form of decreasing eosinophilia in mice [19].

To the best of our knowledge, only one study has evaluated the relationship between serum vitamin D level and allergy risk in Asian children and adolescents [11]. This type of investigation is important because differences among ethnicities and subjects of various age groups could possibly affect the results [7,10,22].

Our results showed that serum vitamin D level was associated with total IgE level and Df specific IgE level. The clinical implication of elevated total IgE is not clear. However, Oryszczyn et al. reported that higher total IgE levels were associated with a higher risk of developing allergic disease and positive conversion of skin tests in a longitudinal study [23]. Therefore, serum vitamin D level could be associated with an increased risk of allergic disease development. In addition, we do not know the clinical significance of higher Df specific IgE. However, there is a report that showed higher specific IgE level was correlated with more severe allergic symptoms in patients allergic to eggs [24]. Our results showed that Df specific IgE was significantly associated with serum vitamin D level in Df sensitized subjects. Therefore, further studies investigating how increased Df specific IgE is correlated with the patient's symptoms are needed.

Serum vitamin D level was not significantly associated with Df sensitization in our result (data not shown), even though mean serum vitamin D level was slightly higher in the Df sensitization group than the non-sensitized group without statistical significance. However, the prevalence of Df sensitization was higher in subjects with serum vitamin D 20 ng/mL or greater than subjects with less than 12 ng/mL or subjects with 12.00–19.99 ng/mL without statistical significance (data not shown). This result was in agreement with the results from Ito et al. [11]. They showed that the overall prevalence of allergic disease was highest in subjects whose level of vitamin D was ≥30 ng/mL without statistically significance [11]. Also, the association between serum vitamin D and

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serum IgE was different depending on the presence or absence of Df sensitization in our results. When we analyzed the data after dividing the population as two groups according to Df sensitization, only Df specific IgE showed significant association with serum vitamin D in Df sensitized group. Therefore, we could postulate that other factors like genetic background, which could affect the allergic sensitization, might modulate the influence of vitamin D to immune response.

Additionally, our results shows that only 17.5% of participants showed serum vitamin D of 20 ng/mL or greater. These results were very low, even though we considered the results of previous reports which showed vitamin D deficiency was common in adolescents [25–27]. However, Shin et al. showed similar result with ours, that 89% in 91 boys and 96% in 97 girls showed serum vitamin D of less than 20 ng/ml [27]. Kim et al. reported that higher latitude, dark pigmented skin, reduced outdoor activity, and insufficient intake of food containing vitamin D could be a cause of prevalent vitamin D deficiency in Korean adolescents [26].

However, there are still no standard guidelines for optimal serum vitamin D levels, especially in children and adolescents. Many studies considered 30 ng/ml as sufficient, $\geq$20 and $<$30 ng/ml as insufficient, and $<$20 ng/ml as a deficient level for musculoskeletal health [25,28]. However, there were also reports which showed that serum vitamin D of 20 ng/ml was adequate for a healthy life [12,29]. We need more studies to affirm the conclusion, especially in children.

Our study has several limitations. We only used Df-specific IgE among various allergens. Even though Df is one of the most common allergens known, the study should have included other allergens to obtain a clearer conclusion. Also, various possible confounding variables such as parental allergies and smoking history were not included in this analysis. Our study did not include the individual allergic diseases or symptoms in the analysis. Allergic sensitization did not mean the presence of allergic disease. Therefore, the information on the allergic symptoms should be considered in future studies. Lastly, our cross-sectional analysis could not explain a clear causal relationship between allergic diseases and vitamin D. Thus, a prospective cohort study is needed in order to generate conclusions that are more reliable.

In conclusion, serum level of vitamin D was positively associated with total IgE and Df-specific IgE level in Korean adolescents. These results suggest that a higher serum level of vitamin D might be related to the risk of developing an allergic disease.

Conflict of interest

All the authors declared that they have no conflict of interest.

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References

[1] W. Eder, M.J. Ege, E. von Mutius, The asthma epidemic, N. Engl. J. Med. 355 (2006) 2226–2235.
[2] G.R. Bloomberg, The influence of environment, as represented by diet and air pollution, upon incidence and prevalence of wheezing illnesses in young children, Curr. Opin. Allergy Clin. Immunol. 11 (2011) 144–149.
[3] E. Emmanouil, Y. Manios, E. Grammatikaki, K. Kondaki, E. Oikonomou, N. Papadopoulos, et al., Association of nutrient intake and wheeze or asthma in a Greek pre-school population, Pediatr. Allergy Immunol. 21 (2010) 90–95.
[4] E.C. Matsui, W. Matsui, Higher serum folate levels are associated with a lower risk of atopy and wheeze, J. Allergy Clin. Immunol. 123 (2009) 1253–1259, e1252.
[5] M. Reinholz, T. Ruzicka, J. Schauber, Vitamin D and its role in allergic disease, Clin. Exp. Allergy 42 (2012) 817–826.
[6] J.M. Brehm, J.C. Celedon, M.E. Soto-Quiros, L. Avila, G.M. Hunninghake, E. Forno, et al., Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica, Am. J. Respir. Crit. Care Med. 179 (2009) 765–771.
[7] S. Sharief, S. Jariwala, J. Kumar, P. Muntner, M.L. Melamed, Vitamin D levels and food and environmental allergies in the United States: results from the National Health and Nutrition Examination Survey 2005–2006, J. Allergy Clin. Immunol. 127 (2011) 1195–1202.
[8] A.M. Hughes, R.M. Lucas, A.L. Ponsonby, C. Chapman, A. Coulthard, K. Dear, et al., The role of latitude, ultraviolet radiation exposure and vitamin D in childhood asthma and hayfever: an Australian multicenter study, Pediatr. Allergy Immunol. 22 (2011) 327–333.
[9] M. Wjst, S. Dold, Genes, factor X, and allergens: what causes allergic diseases, Allergy 54 (1999) 757–759.
[10] K.S. Vimaleswaran, A. Cavadino, E. Hypponen, Evidence for a genetic interaction in allergy-related responsiveness to vitamin D deficiency, Allergy 67 (2012) 1033–1040.
[11] Y. Ito, Y. Adachi, K. Yoshida, A. Akasawa, No association between serum vitamin D status and the prevalence of allergic diseases in Japanese children, Int. Arch. Allergy Immunol. 160 (2013) 218–220.
[12] C.J. Rosen, J.C. Gallagher, The 2011 IOM report on vitamin D and calcium requirements for north america: clinical implications for providers treating patients with low bone mineral density, J. Clin. Densitom. 14 (2011) 79–84.
[13] O. Back, H.K. Blomquist, O. Hernell, B. Stenberg, Does vitamin D intake during infancy promote the development of atopic allergy, Acta Derm. Venereol. 89 (2009) 28–32.
[14] E. Hypponen, U. Sovio, M. Wjst, S. Patel, J. Pekkanen, A.L. Hartikainen, et al., Infant vitamin d supplementation and allergic conditions in adulthood: northern Finland birth cohort 1966, Ann. N. Y. Acad. Sci. 1037 (2004) 84–95.
[15] I. Kull, A. Bergstrom, E. Melen, G. Lilja, M. van Hage, G. Pershagen, et al., Early-life supplementation of vitamins A and D, in water-soluble form or in peanut oil, and allergic diseases during childhood, J. Allergy Clin. Immunol. 118 (2006) 1299–1304.
[16] R.J. Mullins, S. Clark, C. Katelaris, V. Smith, G. Solley, C.A. Camargo Jr., Season of birth and childhood food allergy in Australia, Pediatr. Allergy Immunol. 22 (2011) 583–589.
[17] D.G. Peroni, G.L. Piacentini, E. Cametti, I. Chinellato, A.L. Boner, Correlation between serum 25-hydroxyvitamin D levels and severity of atopic dermatitis in children, Br. J. Dermatol. 164 (2011) 1078–1082.
[18] R. Sidbury, A.F. Sullivan, R.I. Thadhani, C.A. Camargo Jr., Randomized controlled trial of vitamin D supplementation for winter-related atopic dermatitis in Boston: a pilot study, Br. J. Dermatol. 159 (2008) 245–247.
[19] V. Matheu, O. Back, E. Mondoc, S. Issazadeh-Navikas, Dual effects of vitamin D-induced alteration of TH1/TH2 cytokine expression: enhancing IgE production and decreasing airway eosinophilia in murine allergic airway disease, J. Allergy Clin. Immunol. 112 (2003) 585–592.
[20] K.Z. Long, J.I. Santos, Vitamins and the regulation of the immune response, Pediatr. Infect. Dis. J. 18 (1999) 283–290.
[21] L. Overbergh, B. Decallonne, M. Waer, O. Rutgeerts, D. Valckx, K.M. Casteels, et al., 1alpha,25-dihydroxyvitamin D3 induces an autoantigen-specific T-helper 1/T-helper 2 immune shift in NOD mice immunized with GAD65 (p524–543), Diabetes 49 (2000) 1301–1307.
[22] C.A. Keet, M.C. McCormack, R.D. Peng, E.C. Matsui, Age- and atopy-dependent effects of vitamin D on wheeze and asthma, J. Allergy Clin. Immunol. 128 (2011) 414–416, e415.
[23] M.P. Oryszczyn, I. Annesi, F. Neukirch, M.F. Dore, F. Kauffmann, Longitudinal observations of serum IgE and skin prick test response, Am. J. Respir. Crit. Care Med. 151 (1995) 663–668.
[24] A.H. Benhamou, S.A. Zamora, P.A. Eigenmann, Correlation between specific immunoglobulin E levels and the severity of reactions in egg allergic patients, Pediatr. Allergy Immunol. 19 (2008) 173–179.
[25] S.Y. Huh, C.M. Gordon, Vitamin D deficiency in children and adolescents: epidemiology, impact and treatment, Rev. Endocr. Metab. Disord. 9 (2008) 161–170.
[26] S.H. Kim, M.K. Oh, R. Namgung, M.J. Park, Prevalence of 25-hydroxyvitamin D deficiency in Korean adolescents: association with age, season and parental vitamin D status, Public Health Nutr. 26 (October) (2012) 1–9 (epub ahead of print).
[27] Y.H. Shin, K.E. Kim, C. Lee, H.J. Shin, M.S. Kang, H.R. Lee, et al., High prevalence of vitamin D insufficiency or deficiency in young adolescents in Korea, Eur. J. Pediatr. 171 (2012) 1475–1480.
[28] M.F. Holick, Resurrection of vitamin D deficiency and rickets, J. Clin. Invest. 116 (2006) 2062–2072.
[29] C.L. Wagner, F.R. Greer, Prevention of rickets and vitamin D deficiency in infants, children, and adolescents, Pediatrics 122 (2008) 1142–1152.

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