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The Effect of Vitamin D Status on Pediatric Asthma at a University Hospital, Thailand

Wijittra Krobtrakulchai,[1] Jittima Praikanahok,[1] Nualanong Visitsunthorn,[1] Pakit Vichyanond,[1] Kotchamol Manonukul,[2] Busadee Pratumvinit,[2] Orathai Jirapongsananuruk[1]*

[1]*Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*
[2]*Department of Clinical Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Purpose: In the USA and Europe, hypovitaminosis D is associated with increased asthma severity, emergency department (ED) visit, and impaired pulmonary function in asthmatic patients. However, in tropical countries, data on the effect of vitamin D status on asthma is limited. This study evaluates the relationship between vitamin D status and the level of asthma control as well as other asthmatic parameters. **Methods:** Asthmatic children were evaluated for serum 25-hydroxyvitamin D, pulmonary function tests, a skin prick test, and the level of asthma control. **Results:** A total of 125 asthmatic children were recruited (boys, 66.4%). Their mean age±SD was 10.8±3.0 years. Vitamin D statuses were: deficiency (<20 ng/mL) in 19.2% of the patients, insufficiency (20-30 ng/mL) in 44.8%, and sufficiency (>30 ng/mL) in 36%. The vitamin D levels were 25.9±9.4 ng/mL in uncontrolled patients, 29.2±8.6 ng/mL in partly controlled patients, and 27.9±8.0 ng/mL in controlled patients ($P>0.05$). There were no significant differences in pulmonary function, asthma exacerbation, inhaled-corticosteroid (ICS) dose, anti-inflammatory drugs, or ED visit or hospitalization between different vitamin D statuses. Vitamin D deficiency patients were older and had a delayed onset of asthma than insufficiency or sufficiency patients. There was no significant correlation between serum vitamin D and pulmonary function/doses of ICS. **Conclusions:** High prevalences of vitamin D deficiency and insufficiency were found in asthmatic children in Thailand; however, there was no significant relationship between vitamin D status and the level of asthma control or other asthma parameters.

Key Words: Asthma; children; corticosteroid; 25-hydroxyvitamin D; vitamin D

INTRODUCTION

Asthma is a significant public health problem throughout the world; however, the prevalence of asthma varies widely between countries. The prevalence of asthma is higher in developed countries than in developing countries.[1] In an International Study of Asthma and Allergies in Childhood (ISAAC), the prevalence of asthma in Thai children increased from 12.2% in 1995 to 14.5% in 2001.[2] The reason for different asthma prevalence in different parts of the world and its upward trend may be partly explained by gene and environment interactions. Vitamin D deficiency has recently been proposed as one of the factors associated with asthma epidemics.[3]

Vitamin D plays an important role in calcium and bone metabolism as well as immunomodulation. Many cells (brain, colon, prostate, breast, immune cells) contain vitamin D receptors and respond to 1,25-dihydroxyvitamin D (the active form of vitamin D).[4] Recent studies in adults and children found a higher prevalence of hypovitaminosis D in asthmatics than in the normal population; in addition, low vitamin D levels are associated with a higher severity of asthma and impaired pulmonary function.[5,6] Patients with vitamin D deficiency have shown to have increased airway hyper-responsiveness and increased corticosteroid requirements. Vitamin D might increase the response to glucocorticoid in asthmatic patients.[7,8] In pregnancy, maternal vitamin D intake has an inverse correlation with risk of recurrent wheezing in childhood.[9]

The problems of vitamin D deficiency/insufficiency are in-

Correspondence to: Orathai Jirapongsananuruk, MD, Division of Allergy and Immunology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Prannok Road, Bangkoknoi, Bangkok 10700, Thailand.
Tel: +66-662-419-7000; Fax: +66-662- 418-4223
E-mail: siojr@mahidol.ac.th
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creasing throughout the world, especially in adolescents, young adults, and elderly populations.[10,11] In Europe, 93%-97% of children in Denmark and Finland have a vitamin D level of less than 20 ng/mL (50 nmol/L).[12] In Southeast Asia, 60%-63% of adults in Malaysia and Indonesia have a vitamin D level of less than 20 ng/mL.[13] It was previously believed that hypovitaminosis D was not a problem in Thailand because Thailand is located near the equator and has abundant sunlight. However, current studies have shown that 77.8% of the premenopausal Thai women had a vitamin D level of less than 35 ng/mL.[14] Vitamin D insufficiency (less than 30 ng/mL) was found in 69% of the Thai elderly population.[15] Life-style modification and foods may be the causes of this problem; however, data on vitamin D levels in Thai children is limited.

In tropical countries, data on the effect of vitamin D status on asthma control is limited. Therefore, this study compared the vitamin D status between controlled, partly controlled, and uncontrolled asthmatic patients in the pediatric population and examine the correlation between vitamin D levels and pulmonary function/corticosteroid requirements.

MATERIALS AND METHODS

Patients

This cross-sectional study was conducted at the pediatric allergy clinic, Siriraj Hospital of Mahidol University (a tertiary care hospital). Thailand is located at the average latitude of 13° 45´ N which has a minute seasonal variation in the peak of sunlight. The Ethics Committee of Siriraj Hospital approved this study. Informed consent was given by each patient and parent.

Children who had a diagnosis of asthma confirmed by allergists and were aged between 6-18 years were enrolled between July 2011 and December 2012. We excluded patients who had underlying liver, kidney, or endocrine diseases that might affect vitamin D levels. Demographic data, dietary history, outdoor exercise (hours/week), adequacy of sun exposure (exposure to sun light more than 15 min/day and more than twice a week), clinical variable factors of asthma, and skin prick test (SPT) results were recorded. Dietary vitamin D was assessed by the intake of vitamin D-enriched foods, such as egg yolks, oily fish, and mushrooms (times/week). Patients who took vitamin D supplements were excluded. Participants' history of asthma and the level of asthma control were assessed by Global Initiative for Asthma (GINA) guidelines.[1]

Blood samples were obtained, and the plasma levels of calcium, phosphorus, creatinine, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were measured by using a Modular P800 analyzer (Roche Diagnostics, Mannheim, Germany). The plasma levels of parathyroid hormone (PTH) and serum 25-hydroxy vitamin D were measured by electrochemiluminescence immunoassay on an Elecsys 2010 analyzer (Roche Diagnostics) that measures both D2 and D3 derivatives of the 25-hydroxy vitamin D (25(OH)D) reported in nanograms per milliliter (ng/mL). Vitamin D levels were categorized into 'insufficiency' (levels between 20-30 ng/mL) and 'deficiency' (levels less than 20 ng/mL).[4] Eosinophil counts were measured by using an UniCel DxH 800 analyzer (Beckman Coulter Inc., Brea, CA, USA).

Skin prick test and pulmonary function test

A skin prick test was done using common allergens: house dust mite (*Dermatophagoides pteronyssinus and Dermatophagoides farinae*), cockroach, animal dander (cat and dog), grass (Bermuda, Johnson), tree (Acacia), weed (careless weed), and mold (*Alternaria, Curvularia, Cladosporium, Penicillium* and *Aspergillus*) manufactured by ALK, Port Washington, NY, USA. Histamine dihydrochloride (10 mg/mL) and 0.9% saline solution were used as positive and negative controls, respectively. The test was interpreted as positive if the mean wheal diameter (MWD) at 15 min was $\geq$ 3 mm when compared with the negative control. A pulmonary function test was performed by using a spirometer (nSpire Health, Inc., Longmont, CO, USA) in a KOKO model.

Statistical Analyses

All statistical analyses were performed with the SPSS package version 16 (SPSS Inc., Chicago, IL, USA). The demographic and clinical data of the patients were expressed using descriptive statistics (frequency, mean, median, SD, and range). Different characteristics between the 3 groups of the level of asthma control were assessed by the one-way analysis of variance (ANOVA) test (for parametric data), the Kruskal-Wallis test (for non-parametric data), and the chi-square test (for descriptive analysis). A P value of <0.05 was considered statistically significant.

The degree of associations between vitamin D levels and pulmonary function as well as the doses of inhaled corticosteroids were estimated using partial linear correlations[16] after adjustment for potential confounders (sex and age).

RESULTS

A total of 125 asthmatic patients with a mean $\pm$ SD age of 10.8 $\pm$ 3.0 years were enrolled in this study. There were 83 males (66.4%). The proportion of patients with different levels of asthma control according to the GINA classifications were 25.6% for uncontrolled patients, 36.8% for partly controlled patients, and 37.6% for controlled patients. Table 1 shows their major clinical and demographic characteristics.

We found fewer males in the uncontrolled and partly controlled groups than in the controlled group. Vitamin D deficiency occurred in 31.2% of uncontrolled asthmatic patients, which was a higher proportion than in partly controlled and controlled patients (17.4% and 12.8%, respectively); however, the difference was not statistically significant. The proportions of vitamin D

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Table 1. Characteristics of uncontrolled, partly controlled, and controlled asthma

Level of asthma control	Uncontrolled asthma (n=32)	Partly controlled asthma (n=46)	Controlled asthma (n=47)	*P* value
Age (months)	123.3±35.0	129.0±34.5	135.2±36.6	0.339
Sex (male)	18 (56.2%)	26 (56.5%)	39 (83%)	0.010
Vitamin D status				
Deficiency	10 (31.2%)	8 (17.4%)	6 (12.8%)	0.114
Insufficiency	12 (37%)	19 (40.9%)	24 (53.3%)	
Obesity	7 (21.9%)	16 (34.8%)	17 (36.2%)	0.359
Onset of asthma (months)	24 (6-132)	24 (4-148)	24 (8-110)	0.922
Comorbidities				
Allergic conjunctivitis	29 (90.6%)	45 (97.8%)	45 (95.7%)	0.119
Atopic dermatitis	4 (12.5%)	4 (8.7%)	2 (4.3%)	0.405
Food allergy	6 (18.8%)	11 (23.9%)	3 (6.4%)	0.062
Other comobidity*	4 (12.5%)	6 (13%)	2 (4.3%)	0.300
Skin prick test Mites	27 (90%)	39 (84.8%)	33 (70.2%)	0.066
Cockroaches	17 (56.7%)	24 (52.2%)	16 (34%)	0.092
Cat	8 (26.7%)	13 (28.3%)	6 (12.8%)	0.152
Dog	5 (12.9%)	7 (15.9%)	7 (15.9%)	0.088
Grasses	11 (36.7%)	12 (26.1%)	8 (17%)	0.151
Tree	3 (10%)	9 (19.6%)	1 (2.1%)	0.024
Molds	7 (23.3%)	5 (10.9%)	7 (14.9%)	0.337
Pulmonary function test				
FEV1	87.8±14.8	85.9±13.8	89.1±9.3	0.453
FVC	91.5±15.6	87.2±13.7	88.5±8.9	0.495
% changed FEV1	7.6±6.6	7.0±7.3	3.7±4.0	0.004
FEV1/FVC	87.0±13.7	88.1±7.6	89.3±7.5	0.463
Eosinophil count (cell/mm^3)	355.1 (0-1,615)	419.8 (0-2,690)	322 (115.1-1,035)	0.375
Medications				
ICS	7 (21.9%)	18 (39.1%)	20 (42.6%)	0.146
LABA/ICS	11 (34.4%)	20 (43.5%)	15 (31.9%)	0.485
LTRA	2 (6.2%)	7 (15.2%)	3 (6.4%)	0.266
Immunotherapy	3 (9.4%)	3 (6.5%)	1 (2.1%)	0.366
Total dose of ICS (μg/day)	200 (0-1,000)	320 (0-1,500)	100 (0-500)	0.002
Systemic steroid usage in previous month	8 (25%)	7 (15.2%)	0	0.003
Use SABA in previous month	17 (53.1%)	14 (30.4%)	6 (12.8%)	0.001
Healthcare use				
Hospitalization (≥1/year)	13 (40.6%)	12 (26.1%)	0	<0.001
ER visit 1-3 times/year	23 (71.9%)	32 (69.6%)	0	<0.001
3 times/year	6 (18.8%)	5 (10.9%)	0	<0.001
Family history of asthma	11 (34.4%)	14 (30.4%)	12 (25.5%)	0.691
Environment				
Household pets	12 (37.5%)	24 (52.2%)	14 (29.8%)	0.083
Passive smoking	13 (40.6%)	18 (39.1%)	18 (38.3%)	0.979
Income (Baht/month)	20,000 (6,000-100,000)	20,500 (5,000-100,000)	20,000 (3,500-100,000)	0.650

*Other comorbidities, such as sinusitis, obstructive sleep apnea and gastroesophageal reflux disease.
ED, emergency department; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; percentage (%) changed FEV1, percent change in FEV1 after received short acting β_2 agonist; FEV1/FVC, ratio between forced expiratory volume in 1 sec and forced vital capacity; ICS, inhaled corticosteroid; LABA, long-acting β_2 agonist; LTRA, leukotriene receptor antagonist; SABA, short-acting β_2 agonist.

insufficiency were not statistically different between the 3 groups.

Short-acting β_2 agonists (SABAs) and systemic corticosteroids were used more often in the uncontrolled group than in the other groups ($P<0.05$). The uncontrolled and partly controlled groups also used higher doses of inhaled corticosteroids (ICSs), with more ED visits and hospitalizations, than the controlled group ($P<0.05$). There was no significant difference between the 3 groups in pulmonary function; however, uncontrolled and partly controlled groups had a higher percent (%) change of forced expiratory volume in 1 second (FEV1) after they received the bronchodilator than the controlled group.

The proportions of obesity (weight for height, higher than 120%), the onset of asthma, eosinophil counts, a family history of asthma, household income, and environmental factors were not significantly different between the 3 groups. Most of the patients had allergic rhinoconjunctivitis (95.2%) as a comorbidity and house dust mite sensitization (80.5%). There were 7 patients (5.6%) who had received subcutaneous immunotherapy.

The mean serum vitamin D levels of the uncontrolled, partly controlled, and controlled groups were 25.9±9.4, 29.2±8.6, and 27.9±8.0 ng/mL, respectively (Fig. 1). There were no significant differences between the 3 groups. Fig. 2 shows the distribution of serum vitamin D levels in asthmatic patients. The plasma levels of calcium, phosphorus, creatinine, AST, and ALT were within the normal range.

There were 24 children (19.2%) with vitamin D deficiency, 56 children (44.8%) with vitamin D insufficiency, and 45 children (36%) with vitamin D sufficiency (Table 2). The vitamin D deficiency patients were older and had a significantly more delayed onset of asthma and higher PTH levels than the vitamin D insufficiency and sufficiency patients. There were no significant differences in sex, obesity, skin test reactivity, eosinophil counts, reliever use, a history of ED visits and hospitalizations for asthma in the previous year between different vitamin D statuses. The medications used, such as ICSs, long-acting β_2 agonists (LABAs)/ICSs, leukotriene receptor antagonists (LTRAs), systemic steroids, and immunotherapy were not significantly different between different vitamin D statuses. There were no significant differences in household income, a history of vitamin D-enriched food (egg yolks, oily fish, and mushrooms) intake, and adequate sun exposure (exposure to sun light more than 15 min/day and more than 2 times a week)[17] between the vitamin D deficiency, insufficiency, and sufficiency patients. The vitamin D deficiency patients spent fewer hours of outdoor exercise than the vitamin D insufficiency and sufficiency patients (but this was not statistically significant). After adjustments for sex and age, there were no significant correlations between serum vitamin D and FEV1 (partial r=0.09, P=0.339), FVC (partial r=-0.007, P=0.944), percent (%) changed FEV1 (partial r=-0.082, P=0.384), FEV1/FVC (partial r=0.124, P=0.190), and the doses of ICSs (partial r=0.126, P=0.165).

DISCUSSION

Our study classified the level of asthma control based on the GINA guideline.[1] The percentage of reliever use, hospitalization, ED visits, systemic corticosteroid usage, and percent (%) change in FEV1 were significantly higher in the uncontrolled group than in the partly controlled and controlled groups. This confirms that our patients were properly classified.

In this study, 64% of the asthmatic children had vitamin D deficiency/insufficiency. This is almost the same as the prevalences in pre-menopausal and elderly women reported by previous Thai population studies.[14,15] The parathyroid levels were higher in the vitamin D deficiency patients than in the insufficiency and sufficiency patients. This supports the compensatory mechanism of the body for maintaining the normal calcium level. Taken together, it is implied that vitamin D deficiency and insufficiency are serious problems in Thailand as well as in other countries located in abundant sun-exposure areas.[18] This may be due to behavioral factors, such as sunscreen use, de-

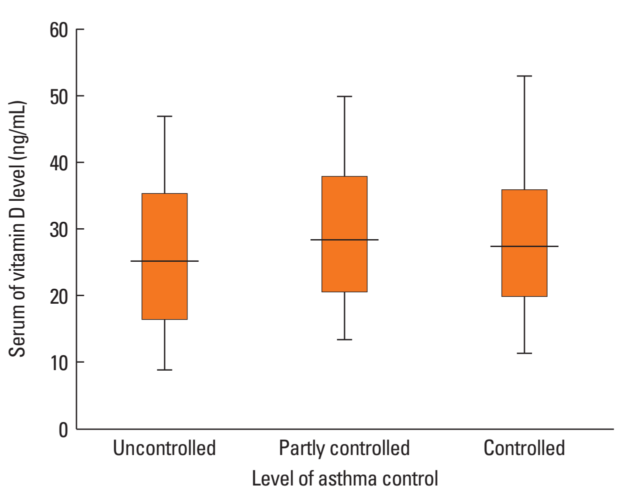

Fig. 1. The box plot of serum vitamin D levels in uncontrolled, partly controlled, and controlled asthmatic patients.

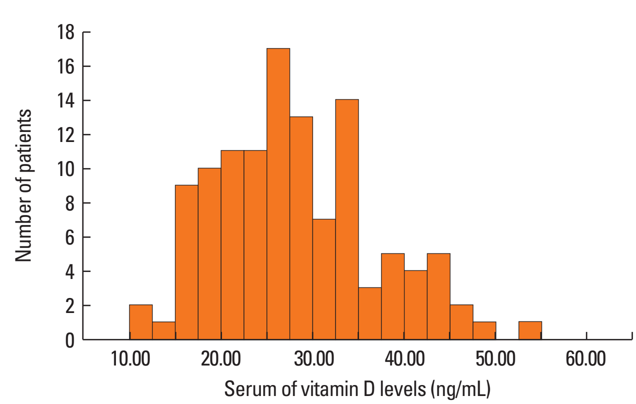

Fig. 2. The distribution of serum vitamin D levels in pediatric asthmatic patients.

Table 2. Investigated parameters according to vitamin D status

Vitamin D status	Deficiency (n=24)	Insufficiency (n=56)	Sufficiency (n=45)	*P* value
Age (months)	145±32.2	133.5±35.8	117.1±32.9	0.003
Sex (male)	13 (54.2%)	40 (71.4%)	30 (66.4%)	0.325
Obesity	7 (29.2%)	23 (41.1%)	10 (22.2%)	0.123
Onset of asthma (months)	48 (7-148)	24 (6-144)	24 (4-110)	0.034
Skin prick test				
Mite	22 (95.7%)	44 (78.6%)	33 (75%)	0.114
Cockroach	10 (43.5%)	26 (46.4%)	21 (47.7%)	0.946
Eosinophil count (median, cell/mm^3)	391.4 (38.6-1,690.9)	400.2 (0-1,671.8)	356.6 (112.7-1,615.3)	0.991
Parathyroid hormone (pg/mL)	55.9 (33.9-92.0)	51 (21.5-170.1)	41.9 (15.3-131.3)	0.002
Medications				
ICS	8 (33.3%)	21 (37.5%)	16 (35.6%)	0.936
LABA/ICS	7 (29.2%)	23 (41.1%)	17 (37.8%)	0.602
LTRA	3 (12.5%)	4 (7.1%)	5 (11.1%)	0.691
Immunotherapy	3 (12.5%)	2 (3.6%)	2 (4.4%)	0.258
Total dose of ICS (μg/day)	180 (0-500)	200 (0-1,500)	200 (0-1,000)	0.481
Receive systemic steroid in previous month	4 (16.7%)	3 (5.4%)	8 (17.8%)	0.141
Use SABA in previous month	8 (33.3%)	17 (30.4%)	12 (29.6%)	0.835
Health care use in previous year				
Hospitalizations	5 (20.8%)	8 (14.3%)	12 (26.6%)	0.494
ER visit	16 (66.7%)	26 (46.4%)	24 (53.3%)	0.250
Outdoor exercise (hours/week)	2 (0-7)	2.3 (0-14)	3.5 (0-7)	0.304
Adequate sun exposure	13 (54.2%)	24 (42.9%)	29 (64.4%)	0.094
Enriched vitamin D containing food* (times/week)	3.8 (0.5-8)	4.8 (0-9)	3.5 (0-10.5)	0.83
Income (Baht/month)	20,000 (5,000-100,000)	21,000 (3,500-100,000)	20,000 (4,000-90,000)	0.303

*Enriched vitamin D containing food such as egg yolks, oily fish and mushrooms.
ED, emergency department; ICS, inhaled corticosteroid; LABA, long-acting β_2 agonist; LTRA, leukotriene receptor antagonist; SABA, short-acting β_2 agonist.

creased time-spent outdoors, and lower vitamin D input from diets. However, in our study, we could not predict vitamin D statuses using questions about sun exposure or vitamin D-enriched food intake. A well-designed questionnaire with a larger sample size will be needed to find the correlation between vitamin D levels and sun exposure/vitamin D-enriched food intake.

In this study, there were no significant differences in serum vitamin D levels between the levels of asthma control, which is inconsistent with the results of previous studies. Gupta et al. reported that children with severe refractory asthma were found to have lower vitamin D levels than those with moderately controlled or controlled asthma.[19] Chinellato et al. investigated the correlation of serum vitamin D levels and asthma control and found a positive correlation between vitamin D levels and the control of asthma symptoms.[20] However, the asthmatic patients had a high prevalence of vitamin D deficiency/insufficiency and only 9.4% of the patients had sufficient vitamin D levels. In our study, we found a lower prevalence of vitamin D deficiency (19%) and insufficiency (44.8%), which may partly explain the different results.

We also could not find the correlation between serum vitamin D levels and pulmonary function. This is supported by the study of Devereux et al. which showed no association between vitamin D levels and asthma severity/pulmonary function.[21] Chinellato et al. found a weak correlation between serum vitamin D levels and FVC but no cornelations between serum vitamin D levels and other parameters of lung function—total IgE, eosinophil counts, or the size of skin prick test.[20] However, some studies reported that low vitamin D levels are associated with an increased bronchodilator response, pulmonary function, hospitalization, ED visits, the use of anti-inflammatory medications, and ICS doses.[19,20,22,23] Searing et al. demonstrated that serum vitamin D levels inversely correlate with FEV1, FEV1/FVC, the number of positive SPT, the use of ICSs, the use of oral steroids, total steroid dose and the use of LABAs. They also stated that vitamin D enhances glucocorticoid action *in vitro*.[8] In our study, serum vitamin D levels did not correlate with SPT, the use of ICSs, total doses of ICSs, the use of LABAs and eosinophil counts.

The possible explanation for no association of vitamin D statuses with the levels of asthma control or pulmonary function may be that this is a cross-sectional study. Long-term follow-up studies focusing on changes in vitamin D status and asthma parameters will be needed to clarify the effect of vitamin D status on asthma. Furthermore, many confounding factors can affect vitamin D levels or asthma severity. The association between serum vitamin D and asthma severity may depend on the genotype or phenotype of asthmatic patients.

In conclusion, there was no significant correlation between serum vitamin D levels and asthma control statuses in Thai asthmatic children. More studies are required to determine the role of vitamin D in asthma and the promising role of vitamin D supplements in such patients.

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REFERENCES

1. Global Initiative for Asthma. Global strategy for asthma management and prevention [Internet]. NIH publication; c2010 [updated 2010; cited 2010 Aug 12]. Available from: http://www.ginasthma.org.
2. Trakultivakorn M, Sangsupawanich P, Vichyanond P. Time trends of the prevalence of asthma, rhinitis and eczema in Thai children-ISAAC (International Study of Asthma and Allergies in Childhood) Phase Three. J Asthma 2007;44:609-11.
3. Litonjua AA, Weiss ST. Is vitamin D deficiency to blame for the asthma epidemic? J Allergy Clin Immunol 2007;120:1031-5.
4. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266-81.
5. Freishtat RJ, Iqbal SF, Pillai DK, Klein CJ, Ryan LM, Benton AS, Teach SJ. High prevalence of vitamin D deficiency among inner-city African American youth with asthma in Washington, DC. J Pediatr 2010;156:948-52.
6. Brehm JM, Celedon JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, Laskey D, Sylvia JS, Hollis BW, Weiss ST, Litonjua AA. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. Am J Respir Crit Care Med 2009;179:765-71.
7. Sutherland ER, Goleva E, Jackson LP, Stevens AD, Leung DY. Vitamin D levels, lung function, and steroid response in adult asthma. Am J Respir Crit Care Med 2010;181:699-704.
8. Searing DA, Zhang Y, Murphy JR, Hauk PJ, Goleva E, Leung DY. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. J Allergy Clin Immunol 2010;125:995-1000.
9. Devereux G, Litonjua AA, Turner SW, Craig LC, McNeill G, Martindale S, Helms PJ, Seaton A, Weiss ST. Maternal vitamin D intake during pregnancy and early childhood wheezing. Am J Clin Nutr 2007;85:853-9.
10. Peterlik M, Boonen S, Cross HS, Lamberg-Allardt C. Vitamin D and calcium insufficiency-related chronic diseases: an emerging worldwide public health problem. Int J Environ Res Public Health 2009; 6:2585-607.
11. Lips P. Worldwide status of vitamin D nutrition. J Steroid Biochem Mol Biol 2010;121:297-300.
12. Andersen R, Mølgaard C, Skovgaard LT, Brot C, Cashman KD, Chabros E, Charzewska J, Flynn A, Jakobsen J, Kärkkäinen M, Kiely M, Lamberg-Allardt C, Moreiras O, Natri AM, O'Brien M, Rogalska-Niedzwiedz M, Ovesen L. Teenage girls and elderly women living in northern Europe have low winter vitamin D status. Eur J Clin Nutr 2005;59:533-41.
13. Green TJ, Skeaff CM, Rockell JE, Venn BJ, Lambert A, Todd J, Khor GL, Loh SP, Muslimatun S, Agustina R, Whiting SJ. Vitamin D status and its association with parathyroid hormone concentrations in women of child-bearing age living in Jakarta and Kuala Lumpur. Eur J Clin Nutr 2008;62:373-8.
14. Soontrapa S, Soontrapa S, Bunyaratavej N, Rojanasthien S, Kittimanon N, Lektrakul S. Vitamin D status of Thai premenopausal women. J Med Assoc Thai 2009;92 Suppl 5:S17-20.
15. Chailurkit LO, Kruavit A, Rajatanavin R. Vitamin D status and bone health in healthy Thai elderly women. Nutrition 2011;27:160-4.
16. Cohen J. Applied multiple regression correlation analysis for the behavioral sciences. Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.; 2003.
17. Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr 2004;80:1678S-88S.
18. Binkley N, Novotny R, Krueger D, Kawahara T, Daida YG, Lensmeyer G, Hollis BW, Drezner MK. Low vitamin D status despite abundant sun exposure. J Clin Endocrinol Metab 2007;92:2130-5.
19. Gupta A, Sjoukes A, Richards D, Banya W, Hawrylowicz C, Bush A, Saglani S. Relationship between serum vitamin D, disease severity, and airway remodeling in children with asthma. Am J Respir Crit Care Med 2011;184:1342-9.
20. Chinellato I, Piazza M, Sandri M, Peroni D, Piacentini G, Boner AL. Vitamin D serum levels and markers of asthma control in Italian children. J Pediatr 2011;158:437-41.
21. Devereux G, Wilson A, Avenell A, McNeill G, Fraser WD. A case-control study of vitamin D status and asthma in adults. Allergy 2010; 65:666-7.
22. Ciaccio CE, Portnoy JM. Vitamin D insufficiency and risk of severe asthma exacerbations. Curr Allergy Asthma Rep 2010;10:387-8.
23. Alyasin S, Momen T, Kashef S, Alipour A, Amin R. The relationship between serum 25 hydroxy vitamin d levels and asthma in children. Allergy Asthma Immunol Res 2011;3:251-5.