Original Article

Vajira Med J
Journal of Urban Medicine

Correlation between Serum Vitamin D Levels and Allergic Rhinitis Severity at Vajira Hospital: A Cross-Sectional Study

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ABSTRACT

OBJECTIVE: Vitamin D affects the immune system and inflammatory process, and its deficiency is significantly associated with an increased prevalence of allergic rhinitis (AR). Therefore, the correlation between the serum 25-hydroxyvitamin D levels and the severity of AR symptoms must be investigated.

METHODS: This research utilized a cross-sectional approach, focusing on patients aged 18 years and above diagnosed with AR at the Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand from August 15, 2023, to January 15, 2024. The relationship between AR severity and serum vitamin D levels was analyzed using Pearson correlation coefficient. AR severity on symptoms and quality of life was assessed using the Thai version of Sinonasal Outcome Test-22 (SNOT-22) and Rhinoconjunctivitis Quality of Life questionnaire-36 (RCQ-36) questionnaires. Serum-specific immunoglobulin E (IgE) and total IgE levels were also measured to examine their relationship with the serum vitamin D level.

RESULTS: Among the 58 participants, 34 (58.60%) had vitamin D deficiency. These individuals with vitamin D deficiency exhibited significantly higher AR severity compared with those without vitamin D deficiency. The mean difference between these groups was 21.90 points for SNOT-22 scores (95%CI: 17.71–26.69, p-value < 0.001) and 19.17 points for RCQ-36 scores (95%CI: 12.08–27.34, p-value < 0.001). Further analysis revealed a significant inverse correlation between serum vitamin D level and AR severity, with Pearson correlation coefficients of −0.72 for RCQ-36 (95%CI: −0.82 to −0.56, p-value < 0.001) and 0.80 for SNOT-22 (95%CI: −0.88 to −0.68, p-value < 0.001). No correlation with serum vitamin D level was found for serum-specific IgE and total IgE levels.

CONCLUSION: A significant inverse relationship existed between serum vitamin D levels and AR severity. No correlation with serum vitamin D level was found for serum-specific IgE and total IgE levels.

KEYWORDS: allergic rhinitis, RCQ-36, serum vitamin D, serum-specific IgE, SNOT-22

INTRODUCTION

Allergic rhinitis (AR) is an immunoglobulin E (IgE)-mediated inflammatory disease that causes allergic reactions to an inhaled allergen. Its symptoms include nasal congestion, nasal discharge, sneezing, and itching nose, all of which affect the quality of life and sleep and performance at school and work[1,2]. The pathophysiology of AR is type 1 hypersensitivity to the specific allergen causing increased IgE production and eosinophil recruitment. The inflammatory processes are driven by type 2 immune response, which is related to the production of many inflammatory cytokines e.g., interleukin (IL)-4, IL-5, IL-9, IL-13,

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Received: 8 July 2024
Revised: 8 September 2024
Accepted: 16 September 2024
Vajira Med J 2024;68(4):e269836
http://dx.doi.org/10.62691/vmj.2024.269836

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and granulocyte–macrophage colony[1]. Genetic disposition, lifestyle, and environmental factors influence AR development[3]. The prevalence of AR in many countries is over 40%–50%, affecting over 500 million people worldwide[4]. In Asia, its prevalence varies widely and is rising up to 45% mostly in low- and middle-income countries[5]. In Thailand, its prevalence is 50.60%[6].

The main function of vitamin D is to maintain bone health and calcium balance. It also has roles in the immune system and anti-inflammation[7,8]. Vitamin D modulates multiple mechanisms of the immune system, both adaptive and innate. It has immunomodulatory effects on allergen-induced inflammatory pathways, suppresses T helper 1 (Th1) and T helper 2 (Th2) immune responses, decreases proinflammatory cytokines, and increases regulatory T cells, which are important in maintaining immune homeostasis[9].

Vitamin D insufficiency and deficiency are defined as a serum 25-hydroxyvitamin D level of 20–30 ng/ml and less than 20 ng/ml, respectively. Vitamin D can be synthesized in the skin following exposure to UVB in the sunlight. Insufficient sun exposure and inadequate vitamin D dietary intake can lead to vitamin D insufficiency and increase the risk of osteoporosis[10].

A meta-analysis suggested that a low serum vitamin D level is associated with a high prevalence of AR[11,12]. In terms of disease severity, a study showed a significant inverse correlation between serum vitamin D level and AR severity[13]. To date, no study has investigated the correlation between serum vitamin D level and AR severity on symptoms and quality of life using disease-specific questionnaires, particularly on Thai populations in Bangkok metropolitan area. These people are expected to have a low serum vitamin D level because of their urban lifestyle of indoor office working, low sunlight exposure, and high pollution, all of which cause inadequate UVB exposure to the skin that reduces its ability to synthesize vitamin D[14,15]. This research aims to examine this correlation and its possible influence on disease knowledge and treatment strategy in the future. The correlation of serum vitamin D level with specific IgE and total IgE levels is also examined as a secondary outcome. The specific IgE level used for calculation is the highest value for the positive allergen of each person measured by ImmunoCAP™ allergy testing.

METHODS

This cross-sectional study was conducted on AR patients selected via consecutive sampling at the Department of Otolaryngology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand between August 15, 2023 and January 15, 2024. The protocol was approved by the ethic committee of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University (certificate of approval 145/2566). All patients gave their signed and informed consent before being recruited to the study.

The participants were 58 patients with AR aged above 18 years with symptoms diagnosed according to Thai clinical practice guidelines for AR 2022[16]. The sample size calculation for the multivariable analysis was conducted using multiple linear regression analysis. The significance level (α) was set at 0.05, and the power of the test was set at 80%. The researcher determined the effect size for the multivariable analysis by using an effect size (f^2) of 0.35 (large effect size), as recommended by Cohen[17]. The number of predictors was 10. The calculated sample size indicated that 57 participants would be required. All the patients were confirmed to exhibit sensitization via serum-specific IgE testing which include *Dermatophagoides pteronyssinus, Dermatophagoides farina*, cockroach, cat, dog, Bermuda grass, Johnson grass, *Aspergillus fumigatus*, *Cladosporium herbarum* and *Alternaria alternata*. The exclusion criteria were as follows: vitamin D supplementation, irrelevant allergen on allergy test, immunotherapy, systemic steroid or immunosuppressive medication, pregnancy, chronic kidney disease, cancer, history of radiotherapy in head and neck area, sinusitis, and sinonasal tumor.

The following demographic data were recorded: sex, age, education level, marital status, underlying diseases, current medication, and smoking status. Furthermore, the patients were asked to complete the Thai version of Rhinoconjunctivitis Quality of Life questionnaire-36 (RCQ-36)[18] and Sinonasal Outcome Test-22 (SNOT-22)[19] which have validated to evaluate their disease severity and impact on quality of life. Serum vitamin D level and total IgE level were evaluated by blood sampling. Descriptive data were presented as frequency or percentage for qualitative data and mean ± standard deviation or median and interquartile range for quantitative data.

The correlation of serum vitamin D level with the disease-specific questionnaire scores, serum-specific IgE level, and serum total IgE level was calculated using Pearson's correlation coefficient. The correlation was presented in a scatter plot. Multivariable analysis was also conducted to calculate the relationship. In particular, the multiple linear regression model was adopted to control the influence of covariates. The factors associated with vitamin D deficiency were also investigated by univariable and multivariable analyses.

RESULTS

Among the 58 patients with AR, 29 were female (50.00%). Their mean age was 37.10 ± 13.64 years. As shown in Table 1, 58.62% completed primary school education level, 48.28% were married, 15.52% had asthma, and 12.07% were current smokers. With regard to serum vitamin D level, 34 patients (58.62%) with mean age of 37.97 ± 14.39 years exhibited vitamin D insufficiency. The mean serum vitamin D level in all patients was 26.80 ng/mL. In particular, the mean serum vitamin D level was 17.15 ng/mL in the group with vitamin D insufficiency and 40.46 ng/mL in the normal group.

Table 1 Demographic and clinical characteristics of patients by serum 25-hydroxyvitamin D level (25[OH]D) level

Characteristics	All patients (n = 58)	25(OH)D level		P-value
		Low (n = 34)	Normal (n = 24)	
	n (%)	n (%)	n (%)	
Age (years)				
20-39	35 (60.34)	20 (58.82)	15 (62.50)	1.000‡
40-59	17 (29.31)	10 (29.41)	7 (29.16)	
≥ 60	6 (10.34)	4 (11.76)	2 (8.33)	
Male	29 (50.00)	12 (35.29)	17 (70.83)	0.008†
Education				
Primary school	34 (58.62)	21 (61.76)	13 (54.17)	0.446‡
Secondary school	16 (27.59)	10 (29.41)	6 (25.00)	
Bachelor's degree	8 (13.79)	3 (8.82)	5 (20.83)	
Marital status				
Single	26 (44.83)	17 (50.00)	9 (37.50)	0.490‡
Married	28 (48.28)	14 (41.18)	14 (58.33)	
Widowed	4 (6.90)	3 (8.82)	1 (4.17)	
Asthma	9 (15.52)	9 (26.47)	0 (0.00)	0.007‡
Smoking	7 (12.07)	6 (17.65)	1 (4.17)	0.221‡
Medication				
Fluticasone furoate	21 (36.21)	19 (55.88)	12 (50.00)	0.658†
Mometasone furoate	4 (6.90)	3 (8.82)	1 (4.17)	0.635‡
Oral antihistamine	12 (20.69)	7 (20.59)	5 (20.83)	1.000‡

Abbreviation: n, number
†Chi-square test, ‡Fisher's exact test

Total IgE level was 254.03 ± 120.29 and 242.58 ± 119.57 IU/mL in the group with vitamin D insufficiency and the normal group, respectively. No significant difference was observed between these groups (p-value = 0.722). The specific IgE level was 35.91 ± 32.23 and 39.92 ± 46.11 kUA/L in the group with vitamin D insufficiency and the normal group, respectively. No significant difference was found between these groups (p-value = 0.698) (table 2).

For the Thai RCQ-36 questionnaire, the mean score was 68.79 ± 19.00 and 49.08 ± 9.61 points in the group with vitamin D insufficiency and the normal group, respectively. The former had significantly higher mean score (19.17) than the latter (95%CI: 12.08–27.34, p-value < 0.001). For the domains of the questionnaire, the group with vitamin D insufficiency had significantly higher scores in Rhinitis Symptoms, Sleep, Emotion, and Quality of Life domains compared with the normal group as shown in Table 3.

For the Thai SNOT-22 questionnaire, the mean score was 47.76 ± 10.68 and 25.86 ± 5.66 points in the group with vitamin D insufficiency and the normal group, respectively. The former had significantly higher mean score (21.90) than the latter (95%CI: 17.71–26.69, p-value < 0.001). For the domains of the questionnaire, the group with vitamin D insufficiency had significantly higher scores in rhinologic symptoms, psychological dysfunction, and sleep domains compared with the normal group as shown in Table 3.

Table 2 Comparison of total IgE and serum-specific IgE levels between the patients with vitamin D insufficiency and normal patients

Variables	25(OH)D level		P-value
	Low (n = 34)	Normal (n = 24)	
	Median (IQR)	Median (IQR)	
Total IgE (IU/mL)	199 (155-322)	225 (141.5-316)	0.764†
Serum specific IgE (kUA/L)	28.0 (12.1-42.0)	32.1 (13.5-41.0)	0.893†

Abbreviations: IgE, immunoglobulin E; IQR, interquartile range; IU/mL, international unit per milliliter; kUA/L, kilo units of allergen per liter; n, number
†Mann-Whitney U test

Table 3 Comparison of RCQ-36 and SNOT-22 score between the patients with vitamin D insufficiency and normal patients

Variables	25(OH)D level		Mean difference (95%CI)†	P-value
	Low (n = 34)	Normal (n = 24)		
	Mean ± SD	Mean ± SD		
RCQ-36				
Rhinitis symptoms	22.53 ± 6.12	7.33 ± 3.69	15.20 (12.69, 17.71)	< 0.001
Eye symptoms	4.35 ± 4.70	2.04 ± 1.68	2.31 (0.61, 4.02)	0.008
Other symptoms	5.26 ± 5.75	1.92 ± 1.56	3.35 (1.33, 5.37)	0.001
Physical functioning	3.79 ± 3.60	2.13 ± 2.15	1.67 (0.20, 3.14)	0.026
Role limitations	3.47 ± 3.50	2.29 ± 2.79	1.18 (-0.43, 2.79)	0.150
Sleep	3.00 ± 2.80	1.38 ± 1.74	1.63 (0.47, 2.78)	0.006
Social functioning	3.35 ± 2.70	1.67 ± 0.48	1.69 (0.77, 2.61)	< 0.001
Emotions	12.03 ± 4.15	2.33 ± 1.93	9.70 (8.12, 11.28)	< 0.001
Quality of Life	3.74 ± 1.05	1.79 ± 0.72	1.94 (1.49, 2.40)	< 0.001
RCQ-36 total score	57.79 ± 19.00	21.08 ± 9.61	36.71 (29.31, 44.11)	< 0.001
SNOT-22				
Rhinologic symptoms	15.32 ± 6.80	5.46 ± 4.85	9.87 (6.89, 12.84)	< 0.001
Extra-nasal rhinologic symptoms	6.26 ± 2.87	1.88 ± 1.54	4.39 (3.25, 5.53)	< 0.001

Table 3 Comparison of RCQ-36 and SNOT-22 score between the patients with vitamin D insufficiency and normal patients (continued)

Variables	25(OH)D level		Mean difference (95%CI)†	P-value
	Low (n = 34)	Normal (n = 24)		
	Mean ± SD	Mean ± SD		
Ear/facial symptoms	4.76 ± 2.35	2.92 ± 1.06	1.85 (0.96, 2.74)	< 0.001
Phychological dysfunction	18.41 ± 5.18	5.38 ± 3.27	13.04 (10.88, 15.20)	< 0.001
Sleep dysfunction	3.00 ± 2.80	1.38 ± 1.74	1.63 (0.47, 2.78)	0.006
SNOT-22 total score	47.76 ± 10.68	17.00 ± 5.66	30.77 (26.55, 34.98)	< 0.001

Abbreviations: CI, confidence interval; SD, standard deviation; RCQ, rhinoconjunctivitis quality of life questionnaire; SNOT, sinonasal outcome test
†Mean difference (2-sided 95%CI) estimated by Generalized linear model with Gaussian family.

Pearson's correlation coefficient was used to investigate the correlation of serum vitamin D level with AR severity as assessed by the Thai version of RCQ-36 and SNOT-22, total IgE level, and serum-specific IgE level. The results were as follows: serum vitamin D level and Thai RCQ-36 score had a significantly strong negative correlation (r = −0.72, 95%CI: −0.82 to −0.56, p-value < 0.001). Serum vitamin D level and Thai SNOT-22 score had a significantly strong negative correlation (r = −0.80, 95%CI: −0.88 to −0.68, p-value < 0.001). Serum vitamin D level and total IgE level had no correlation with each other (r = 0.04, 95%CI: −0.22 to −0.30, p-value = 0.755). Serum vitamin D level and serum-specific IgE level had no correlation with each other (r = 0.11, 95%CI: −0.16 to −0.36, p-value = 0.424). These results are shown in the scatter plot in Figure 1.

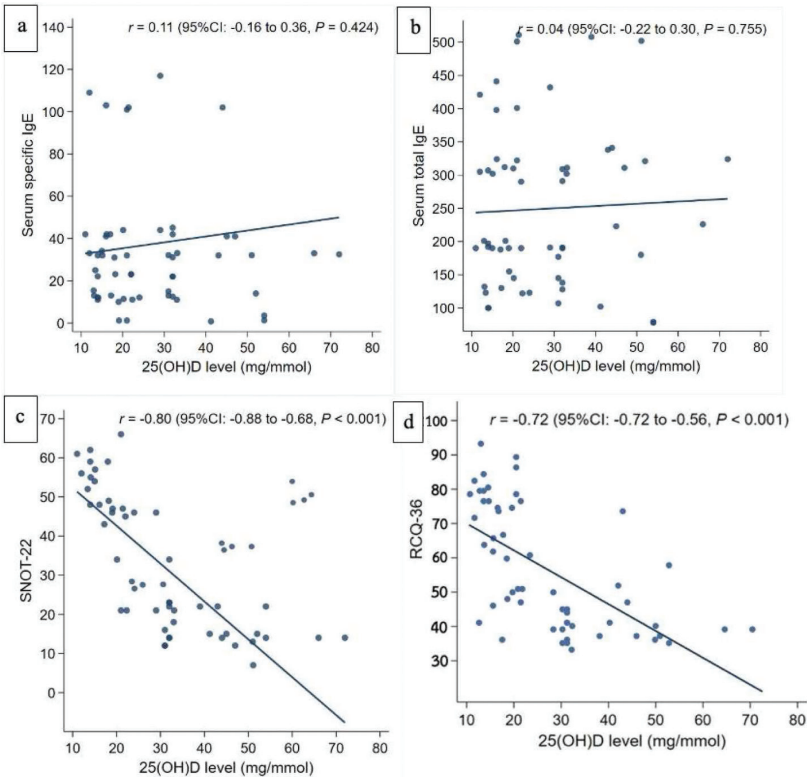

Figure 1 Scatter plot of the relationship between serum vitamin D levels and other variables
Serum vitamin D levels and serum-specific immunoglobulin E (IgE)
Serum vitamin D levels and serum total IgE
Serum vitamin D levels and Sinonasal Outcome Test-22 (SNOT-22) score
Serum vitamin D levels and Rhinoconjunctivitis Quality of Life questionnaire-36 (RCQ-36) score

For the serum-specific IgE results, the allergen that caused the most sensitization was house dust mite (n = 47, 81%), followed by grass pollen. Investigation revealed no significant difference in the number of sensitized allergens between the group with vitamin D insufficiency and the normal group.

For the correlation of serum vitamin D level with AR severity, total IgE level, and serum-specific IgE level, multivariable analysis was conducted using the multiple linear regression method to control the influence of covariates. The results were as follows: Serum vitamin D level and Thai RCQ-36 score had a significant, strong negative linear correlation with a regression coefficient of −0.959 (p-value < 0.001). Serum vitamin D level and Thai SNOT-22 score had a significant, strong negative linear correlation with a regression coefficient of 0.903 (p-value < 0.001). Serum vitamin D level and Total IgE and serum-specific IgE level had no correlation with each other. Details are shown in Table 4.

Univariable and multivariable analyses on the factors associated with vitamin D deficiency showed that only the female sex had a significant association with the high prevalence of vitamin D insufficiency with odds ratio of 4.45 (95%CI: 1.44–13.74, p-value = 0.009) in univariable analysis and 11.97 (95%CI: 2.13–67.22, p-value = 0.005) in multivariable analysis as shown in Table 5.

Table 4 Correlation of serum vitamin D level with allergic rhinitis severity, total IgE level, and serum-specific IgE level

	B	SE(B)	*β*	*t*	P-value†
Total IgE	1.494	1.202	0.184	1.24	0.220
Serum-specific IgE	0.481	0.386	0.184	1.25	0.218
RCQ-36 score	-0.959	0.175	-0.583	-5.49	< 0.001
SNOT-22 score	-0.903	0.108	-0.748	-8.37	< 0.001

Abbreviations: B, regression coefficient; IgE, immunoglobulin E; RCQ, rhinoconjunctivitis quality of life questionnaire; SE(B), standard error of B; SNOT, sinonasal outcome test; β, standardized regression coefficient; *t*, t-value
†Multiple linear regression model adjusted for age, sex, asthma, smoking and medication.

Table 5 Univariable and multivariable analyses of the factors associated with vitamin D deficiency

Factors	Univariable analysis		Multivariable analysis	
	Crude OR (95%CI)†	P-value	Adjusted OR (95%CI)‡	P-value
Age (years)				
20-39	1.00 Reference			
40-59	1.07 (0.33-3.47)	0.908		
≥ 60	1.50 (0.24-9.30)	0.663		
Sex				
Male	1.00 Reference		1.00 Reference	
Female	4.45 (1.44-13.74)	0.009	6.65 (1.83-24.13)	0.004
Education				
Primary school	1.00 Reference		1.00 Reference	
Secondary school	1.03 (0.30-3.52)	0.960	1.76 (0.41-7.46)	0.445
Bachelor's degree	0.37 (0.08-1.82)	0.222	0.43 (0.07-2.59)	0.360
Marital status				
Single	1.00 Reference			
Married	0.53 (0.18-1.58)	0.255		
Widowed	1.59 (0.14-17.56)	0.706		

Table 5 Univariable and multivariable analyses of the factors associated with vitamin D deficiency (continued)

Factors	Univariable analysis		Multivariable analysis	
	Crude OR (95%CI)†	P-value	Adjusted OR (95%CI)‡	P-value
Smoking	4.93 (0.55-43.94)	0.153	10.79 (0.99-117.65)	0.051
Medication				
Fluticasone furoate	1.27 (0.44-3.61)	0.658		
Mometasone furoate	2.23 (0.22-22.8)	0.500		
Oral antihistamine	0.99 (0.27-3.58)	0.982		

Abbreviations: CI, confidence interval; NA, data not applicable; OR, odds ratio
†Crude odds ratio estimated by logistic regression model.
‡Adjusted odds ratio estimated by multiple logistic regression model adjusting for sex, education and marital status.

DISCUSSION

This study showed that Serum vitamin D level and AR severity have a significant, strong negative linear correlation. Vitamin D contributes to the immune response, both adaptive and innate. It has immunomodulatory effects on allergen-induced inflammatory pathways, suppresses Th1 and Th2 immune responses, decreases proinflammatory cytokines, and increases regulatory T cells[9]. Hence, vitamin D should have a role in the immunologic response to AR severity.

In this study, we found that 34 out of 58 patients with AR had vitamin D insufficiency, and most of them are female. Univariable and multivariable analysis revealed that the female sex had a significant association with the high prevalence of vitamin D insufficiency. Similarly, Nimitphong et al.[20] reported that females have threefold higher prevalence of vitamin D insufficiency than males. This phenomenon may be attributed to the social preference in Thailand where females want to have a light skin color so they tend to avoid outdoor activity, have less sunlight exposure time than males, and routinely apply sunscreen, causing inadequate UVB exposure that results in low vitamin D synthesis in the skin.

Although Thailand is located near the equator with equal hours of sunlight throughout the country[10], the prevalence of vitamin D insufficiency is still high among the Thai population. Siwamogsatham et al.[15] addressed that lifestyle and environmental factors have the major influence on the vitamin D status in the Thai population. For people living in urban areas such as Bangkok, pollution decreases UVB exposure, which is crucial for vitamin D synthesis in the skin. Less sunlight exposure time due to their indoor lifestyle also leads to vitamin D insufficiency. Moreover, Thai dairy products are not fortified with vitamin D, so the vitamin D dietary intake of the Thai population is quite low[15].

In our study, we found that serum vitamin D level had significant, strong negative correlations with Thai RCQ-36 and Thai SNOT-22 scores. Awan et al.[21] reported that low serum vitamin D level is associated with the increased severity of AR symptoms. They found that the mean serum vitamin D level was significantly lower in the moderate-to-severe AR symptom group than in the mild symptom group in accordance with ARIA-WHO classification. The patients with vitamin D deficiency were 24 times more likely to have moderate-to-severe AR. Similar results were also reported by Sudiro et al.[13] who found that vitamin D deficiency was significantly correlated with AR severity based on ARIA-WHO classification, with the coefficient of −0.321 ($p = 0.005$) calculated using the Rank–Spearman correlation test.

For the secondary outcome, we found that serum vitamin D level had no correlation with total IgE and serum-specific IgE levels. International consensus statement on allergy and rhinology: AR-2023 and Thai clinical practice guideline for AR 2022 do not support the routine

use of total IgE for AR. The total IgE level can either be elevated or low IgE in allergic diseases[1,16]. It may also be associated with disease severity. Awan et al.[21] found that the mean serum total IgE level in the moderate-to-severe AR group was significantly higher than that in the mild symptom group. By contrast, Alnori et al.[22] found a statistically significant negative correlation between serum total IgE level and serum vitamin D level in patients with AR with coefficient of −0.3643 ($p < 0.05$) calculated with Pearson correlation test. This value is considered as weak negative correlation. Further investigation of this correlation must be conducted.

In our study, the allergen that caused the most sensitization was house dust mite, followed by grass pollens, pet dander, insects, and fungi. This finding was in line with a previous report in Thailand stating that house dust mite was the most sensitized allergen for the Thai population[23].

The strength of this research is that it is the first to investigate the correlation between serum vitamin D levels and AR severity using disease-specific questionnaires, and the results show a significant inverse correlation. The assessment of vitamin D levels in patients with severe AR is especially useful in females to detect and treat vitamin D deficiency. The limitation of this research is that it does not account for all confounding factors, such as participants' dietary habits, sunscreen usage, and sun exposure time, which may affect vitamin D synthesis. Additionally, this research is a cross-sectional study, so it may not show dynamic changes in serum vitamin D levels and AR severity over time. Further research with longitudinal data and larger populations may provide more information about this correlation and the role of vitamin D supplementation in the treatment of AR.

CONCLUSION

Serum vitamin D level and AR severity have a significant, strong negative linear correlation with the Thai version of RCQ-36 and SNOT-22. Most patients with AR and vitamin D insufficiency are female due to their indoor lifestyle. Assessment of vitamin D level in patients with severe AR symptoms is useful especially in female.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

ACKNOWLEDGEMENT

Authors would like to thank the Vajira Scientific Editing Center, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, for their financial support for English language checking service, and Mr. Anucha Kamsom for providing the statistical analysis.

DATA AVAILABILITY STATEMENT

All the data generated and analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

REFERENCES

1. Wise SK, Lin SY, Toskala E, Orlandi RR, Akdis CA, Alt JA, et al. International consensus statement on allergy and rhinology: allergic rhinitis. Int Forum Allergy Rhinol 2018;8(2):108-352.
2. Ciprandi G, Klersy C, Cirillo I, Marseglia GL. Quality of life in allergic rhinitis: relationship with clinical, immunological, and functional aspects. Clin Exp Allergy 2007;37(10):1528-35.
3. Wang DY. Risk factors of allergic rhinitis: genetic or environmental? Ther Clin Risk Manag 2005;1(2):115-23.
4. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy 2008;63 Suppl 86:8-160.
5. Pawankar R, Bunnag C, Khaltaev N, Bousquet J. Allergic rhinitis and its impact on asthma in Asia Pacific and the ARIA update 2008. World Allergy Organ J 2012;5 Suppl 3:S212-7.

6. Bunnag C, Jareoncharsri P, Tantilipikorn P, Vichyanond P, Pawankar R. Epidemiology and current status of allergic rhinitis and asthma in Thailand – ARIA Asia-Pacific workshop report. Asian Pac J Allergy Immunol 2009;27(1):79-86.
7. Jablonski NG, Chaplin G. The roles of vitamin D and cutaneous vitamin D production in human evolution and health. Int J Paleopathol 2018;23:54-9.
8. Kumar R, Rathi H, Haq A, Wimalawansa SJ, Sharma A. Putative roles of vitamin D in modulating immune response and immunopathology associated with COVID-19. Virus Res 2021;292:198235.
9. Mirzakhani H, Al-Garawi A, Weiss ST, Litonjua AA. Vitamin D and the development of allergic disease: how important is it? Clin Exp Allergy 2015;45(1):114-25.
10. The Endocrine Society of Thailand 2017. Recommendations for vitamin D insufficiency in the Thai population [internet]. 2017 [cited 2023 May 20]. Available from:http: // www.thaiendocrine.org/th/wp-content/uploads/2017/10/Vit-D-Booklet-20page_update-9Sep17-2.pdf>
11. Kim YH, Kim KW, Kim MJ, Sol IS, Yoon SH, Ahn HS, et al. Vitamin D levels in allergic rhinitis: a systematic review and meta-analysis. Pediatr Allergy Immunol 2016;27(6):580-90.
12. Aryan Z, Rezaei N, Camargo CA Jr. Vitamin D status, aeroallergen sensitization, and allergic rhinitis: a systematic review and meta-analysis. Int Rev Immunol 2017;36(1): 41-53.
13. Sudiro M, Lestari BW, Madiadipoera T, Setiabudiawan B, Boesoirie TS. Vitamin D deficiency is correlated with severity of allergic rhinitis. OALib 2017;04(08):1-9.
14. Bailey BA, Manning T, Peiris AN. The impact of living in rural and urban areas: vitamin D and medical costs in veterans. J Rural Health 2012;28(4):356-63.
15. Siwamogsatham O, Ongphiphadhanakul B, Tangpricha V. Vitamin D deficiency in Thailand. J Clin Transl Endocrinol 2015;2(1): 48-9.
16. Thai Rhinologic Society. Thai clinical practice guideline for allergic rhinitis (revised 2022) . rcotJ 2022;23(1).
17. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale: Lawrence Erlbaum Associates; 1977.
18. Bunnag C, Leurmarnkul W, Jareoncharsri P, Ungkanont K, Tunsuriyawong P, Kosrirukvongs P, et al. Development of a health-related quality of life questionnaire for Thai patients with rhinoconjunctivitis. Asian Pac J Allergy Immunol 2004;22(2-3):69-79.
19. Lumyongsatien J, Yangsakul W, Bunnag C, Hopkins C, Tantilipikorn P. Reliability and validity study of Sino-nasal outcome test 22 (Thai version) in chronic rhinosinusitis. BMC Ear Nose Throat Disord 2017;17:14.
20. Nimitphong H, Chailurkit LO, Chanprasertyothin S, Sritara P, Ongphiphadhanakul B. The association of vitamin D status and fasting glucose according to body fat mass in young healthy Thais. BMC Endocr Disord 2013;13:60.
21. Awan NU, Sohail SK, Naumeri F, Niazi S, Cheema K, Qamar S, et al. Association of serum vitamin D and immunoglobulin E levels with severity of allergic rhinitis. Cureus 2021;13(1):e12911.
22. Alnori H, Alassaf FA, Alfahad M, Qazzaz ME, Jasim M, Abed MN. Vitamin D and immunoglobulin E status in allergic rhinitis patients compared to healthy people. J Med Life 2020;13(4):463-8.
23. Bunjean K, Sukkasem K, Noppacroh N, Yamkaew N, Janthayanont D, Theerapancharern W, et al. Prevalence of allergic rhinitis and types of sensitized allergen in adult at Wat Intaram community, Hua Raeu, Phra Nakhon Si Ayutthaya District, Phra Nakhon Si Ayutthaya Province, Thailand. J Med Assoc Thai 2012;95 Suppl 5: S63-8.