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Evaluation of the Relationship between Vitamin D Level and Allergic Indicators in Patients with Asthma Referred to Gorgan Asthma and Allergy Clinic

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Abstract

Background: This study was performed to determine the relationship between vitamin D level and allergic factors in patients with asthma referring to asthma and allergy clinic in Gorgan.

Methods: In this observational study that was performed as a cross-sectional survey between April and September 2019, 84 patients with asthma were enrolled. The mean age of the participants was 9.05±2.65, and 46 (54.8%) of them were male. The IgE level of the children was determined using the MicroWell kit (USA) and by ELISA method, from the blood taken from the samples; and the serum concentration of 25-hydroxy vitamin D was measured using the DIA kit made in the United States and Enzyme linked ELISA Immunosorbent assay method. The data were entered into SPSS software version 18 to assess the relationship between the vitamin D level and allergic factors (IgE and eosinophil).

Results: It was found that according to the Spearman test there was a significant reverse correlation (r=-0.77) between serum vitamin D with IgE and serum eosinophil (P=0.001). It was true for medium but not severe asthma patients.

Conclusion: According to the obtained results, it may be concluded that higher serum vitamin D is related to lower asthma severity in patients.

Key Words: Asthma, Allergy, Eosinophils, IgE, Vitamin D.

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1- INTRODUCTION

Asthma is a significant public health issue and has affected more than 300 million people worldwide. It usually begins in early life and is considered to be the most common chronic childhood disease. In 80 to 90% of patients, asthma is diagnosed before the age of 6, and both genetic and environmental factors contribute to the development of asthma. The prevalence of asthma is higher in western and industrialized countries with a desire for countries farther from the equator (1).

The disease is characterized by wheezing, night coughs, and difficulty breathing, and sometimes has a seasonal pattern. In many cases, a family history, early exposure to allergens, infection, diet status, exposure to cigarette smoke, air pollution, and vitamin D status are factors that contribute to the progression and severity of asthma (2).

Recent studies have shown that pharmacotherapy is often ineffective in treating patients with asthma, and only 50% of patients are able to control the disease threshold with the recommended drug therapy (long-acting inhaled corticosteroids). Therefore, understanding the causes of the asthma epidemic and its treatment requires more effort to identify risk factors (3).

Vitamin D deficiency is a risk factor for several chronic diseases and has adverse effects on bones. Recent data have shown that a deficiency of this vitamin can also be effective in the onset of asthma and is also an indicator of the severity of the disease in children with asthma. 25-Hydroxy vitamin D is the best indicator of total vitamin D, because measuring this indicator reflects the total vitamin D in the diet, sun exposure, and also the best fat-soluble vitamin D in the liver (4).

Although the definite role of vitamin D in the pathogenesis of asthma has not been determined yet (5, 6), due to the high prevalence of this disease in children, there seems to be a hundredfold increase in the need for more attention to investigating the factors involved in its incidence, prevention, and treatment, as well as the relationship between the mentioned factors. Therefore, the aim of this study was to investigate the relationship between vitamin D levels and allergic indicators in patients with asthma referred to the Gorgan Asthma and Allergy Clinic.

2- MATERIALS AND METHODS

This cross-sectional study was performed by the census method on all patients referred to Gorgan Asthma and Allergy Clinic between April and September 2019. The inclusion criteria were allergic asthma in accordance with the GINA criteria (7); high immunoglobulin E; children 5-15 years; diagnosis of asthma in children by a subspecialty physician; having no metabolic disease and other allergic disorders; having no liver, kidneys, and endocrine glands diseases that lead to vitamin D abnormalities; taking no vitamin D supplements or medications that modulate serum vitamin D levels (such as antifungal drugs and glucocorticoids), lack of allergic disorders in first-degree relatives of the child. Before the initiation of thre study, informed consents were obtained from the cases to participate in the study, and a checklist was filled by the parents containing the demographic information of the children (age, gender, ethnicity, location) and the variables required in the study including the severity of asthma determined based on the patient's symptoms and spirometry, which was divided into Mild, Moderate and Severe asthma, history of hospitalization during the last year, duration of the illness; number of hospitalizations, and number of asthma attacks during the last year.

2 cc of blood was taken from all cases in order to measure the serum concentration of 25-hydroxy vitamin D using the DIA kit

made in the United States and Enzyme linked ELISA Immunosorbent assay method. According to the kit guidelines and new studies, vitamin D concentrations of <10, 10-30, 30-100, and >100 ng/ml are considered severe deficiency, deficient, normal, and toxic, respectively. From the blood taken from the samples, the IgE level was determined using the MicroWell kit (USA) and by ELISA method and was divided into two groups of eosinophilia ≤5% and >5% (5).

After collection, the data were entered into SPSS software version 18. Mean and standard deviation, frequency, and percentage were used to describe the data. According to the results of Kolmogorov-Smirnov test, Yuman-Whitney and Kruskal-Wallis tests were used to compare the means. Spearman correlation test was used to relate quantitative variables. The significance level of the tests was considered as 0.05.

3- RESULTS

This study was performed on 84 children with asthma referred to Deziani Clinic in Gorgan with a mean age of 9.05±2.65. In this study, 46 (54.8%) were male and 38 (45.2%) were female. 52.4% of the subjects were rural residents and the rest were urban residents. Also, 51.2% of the patients lived in houses and 48.8% in apartments.

Asthmatic patients were classified into three qualitative groups: mild, moderate, and severe, among whom 41 (48.8%), 26 (31%), and 17 (20.2%) were in the group with mild, moderate, and severe asthma, respectively (**Table 1**).

Table-1: Mean, standard deviation, minimum, and maximum of study variables

	Mean± Standard deviation	maximum	minimum
Age	9.05±2.65	14	5
Duration of illness	3.21±2.1	10	1
Number of hospitalization	0.69±0.83	3	0
Number of Asthma Attack/ week	0.95±1.19	4	0
Vitamine D (ng/ml)	24.54±11.62	48	5
Eosiniphilia (cell/µl)	372.10±134.86	600	90
Immunoglobulin E (IU/ml)	117.58±84.12	380	35

Due to the abnormal distribution of data, Spearman's rho test was used and showed that the level of vitamin D had a significant (P = .000), weak inverse (r = -382) correlation with age, i.e., as the age increases, the level of vitamin D decreases.

Due to the abnormal distribution of data, Mann-Whitney test was used between the two groups, which showed that the mean level of vitamin D was not significantly different between males and females (P = 0.592). Also, there was no difference in the mean level of vitamin D based on the location and type of the residential building (P = 0.861 and P = 0.911, respectively) (**Table 2**).

Spearman's rho test was used to evaluate the level of vitamin D in patients with asthma according to the number of hospitalizations and showed an inversely (r = -0.702) significant (p = 0.001) relationship, which means that the longer the hospitalization history, the lower the vitamin D level.

Spearman's rho test was used to evaluate the level of vitamin D in patients with asthma according to the duration of the disease, which showed an inverse (r = -0.505) and significant (p = .000)

relationship .This means that the longer the duration of the illness, the lower the vitamin D level.

Spearman's rho test was used to evaluate the level of vitamin D in patients with asthma according to the number of asthma attacks, which showed an inverse (r = -0.755) and significant relationship (p = .000). This means that the higher the number of asthma attacks, the lower the level of vitamin D.

Table-2: Comparison of the means and standard deviations of vitamin D levels by gender, location, and type of building

		mean ± standard deviation of vitamin D	P. value
gender	Male	26.16±13.93	0.592
	Female	26.47±19.07	
location	Rural	26.87±18.00	0.861
	Urben	25.67±14.44	
Type of building	Villa	24.78±11.72	0.911
	Apartment	27.88±20.05	

In this study, asthmatic patients were classified into three qualitative groups: mild, moderate, and severe. To measure the serum level of vitamin D, which is a quantitative variable, the non-parametric Kruskal Wallis Test was used and showed that the serum level of vitamin D was related to the severity of asthma and in each group, the mean serum level of vitamin D was different from the other group (p = 0.001) (**Table 3**).

Table-3: Comparison of the means and standard deviations of vitamin D levels based on asthma severity

Severity of Asthma	Mean± Standard deviation	P. value
Mild	33.18±8.55	0.001
Moderate	24.14±20.36	
Severe	14.42±15.98	

To measure the relationship between Vit D and the other variables, i.e. EOS and IgE, the normality of the variables was first measured. According to the Shapiro-Wilk test, the data tested were not normally distributed (P <0.05).

The Spearman test, showed a strong inverse linear correlation (r = -0.77) between vitamin D level and serum eosinophil count and immunoglobulin E level (P = 0.0001) in the studied patients.

In the group of patients with non-severe asthma, the relationship between vitamin D and immunoglobulin E (IgE) levels was not significant, based on the results of Spearman's rho test (P = -106), while the association between vitamin D and eosinophilia was significant (P = .038). In patients with a moderate asthma, the relationship between vitamin D, and immunoglobulin E and EOS levels was significant (P = .006 and .035, respectively). In patients with a severe asthma, there was no significant relationship between vitamin D, and immunoglobulin E and eosinophilia levels (P = .238 and .136, respectively) (**Table 4**).

Table-4: Correlation of vitamin D with eosinophil count and immunoglobulin E level by asthma severity

Severity			EOS	IgE
Mild	Vit D	Correlation Coefficient	-.325*	-.256
		P-Value	.038	.106
Moderate	Vit D	Correlation Coefficient	-.416*	-.526**
		P Value	.035	.006
Severe	Vit D	Correlation Coefficient	-.376	-.302
		P Value	.136	.238

Although the definitive role of vitamin D in the pathogenesis of asthma has not been determined yet, due to the high prevalence of this disease in the pediatric age group, the need for more attention in investigating the factors involved in its development, prevention, and treatment and the relationship between these factors increases a hundredfold. Therefore, the aim of this study was to investigate the relationship between vitamin D levels and allergic indicators in patients with asthma who referred to the Asthma and Allergy Clinic. According to the Spearman test, there was a strong inverse linear correlation (r = -0.77) between vitamin D level and serum eosinophil count and immunoglobulin E level (P = 0.0001) in the studied patients.

4- DISCUSSION AND CONCLUSION

This correlation also existed in the subgroup of moderate asthma; however, it did not exist in the severe asthma subgroup, and in the mild asthma group, the correlation existed only with the serum eosinophil count. Golbini et al. evaluated the serum level of 25-hydroxy vitamin D in asthmatic patients and reported a significant relationship between asthma severity and vitamin D level, as well as a significant relationship between the level of this vitamin, and BMI, hospitalization during the last year, and the number of hospitalizations. But it did not have any significant relationship with the number of eosinophils and IgE (8), which, thus, does not agree with the results of our study. The reason for this can be the intervening role of natural and racial factors in two different populations.

Alipour et al. examined vitamin D levels in asthmatic children and found no relationship between gender and vitamin D levels. However, high levels of vitamin D were associated with a decrease in the number of hospitalizations (P = 0.02), an increase in response to bronchodilators (P = 0.01), and a decrease in IgE level (P = 0.02); but no correlation was found between eosinophil count and vitamin D level (P = 0.08) (2). This could be due to differences in the techniques used for cell counting (4).

Sharif et al. conducted a case-control study to investigate the relationship between asthma and serum levels of vitamin D, which did not show an association between vitamin D levels and asthma severity (5) that is contrary to the results of our study, which may be due to the difference in the power of the two studies. Moreover, Rahmati et al. in a study aimed at assessing the serum level of vitamin D in children with asthma hospitalized in Bandar Abbas Children's Hospital and comparing it with healthy children, found that the mean serum level of vitamin D was low in both case and control groups (9).

However, in our study, due to the type and design of the study, there was no control group for comparison, which can be explained as the limitations of this study. In a cross-sectional study in 2011,

Chinellato et al. examined the role of vitamin D levels and markers in the control of asthma in Italian children, which showed a significant association between forced vital capacity (FVC) and 25-hydroxy vitamin D levels ($r = 0.25$; $p = 0.04$). Moreover, individuals with controlled asthma had higher levels of vitamin D than the uncontrolled group ($p = 0.22$). Finally, it was found that there is a relationship between low vitamin D levels and decreased asthma control (10), which is in line with the significant relationship observed in our study regarding the severity of the disease.

In 2011, Alyasin et al. conducted a cross-sectional study to investigate the association between 25-hydroxy vitamin D levels and asthma in children, and the results showed that a decrease in vitamin D levels would lead to a significant prevalence of asthma symptoms; However, there was no association between vitamin D levels and eosinophil counts (11), which is similar to our study in terms of severity; but the number of eosinophils was different from our study.

In 2014, Yoseph et al. conducted a double-blind clinical trial with a control group to evaluate the effect of vitamin D on systematic markers of allergy and inflammation in patients with asthma and showed no significant difference in the level of immunoglobulin E and eosinophils between the two groups receiving vitamin D supplement and placebo (12), which was inconsistent with the results of our study, probably due to the differences in the laboratory techniques used.

In line with the results of the present study, Ozturk Thomas's study found that serum levels of vitamin D and several allergic markers and asthma severity are correlated with each other (13), while in IQBAL B et al.'s study, which aimed to evaluate serum IgE and bronchial asthma, it was found that serum IgE levels were significantly higher among children with asthma (14). However, in our study, there was no control group for comparison.

5- CONCLUSION

Overall, based on the results of this study and comparing them with other studies in this field, it was concluded that serum vitamin D levels in patients with asthma are inversely related to allergic indicators and higher vitamin D with less severe asthma. It is yet recommended to do more studies in this field to confirm the findings obtained in this study with a larger sample size and in a multicenter manner and for other types of essential vitamins and minerals.

6- REFERENCES

1. Vasiliou J, Lui S, Walker S, Chohan V, Xystrakis E, Bush A, et al. Vitamin D deficiency induces T h2 skewing and eosinophilia in neonatal allergic airways disease. Allergy. 2014; 69(10):1380-9.

2. Aalipour R, Sharqi A, Ahmadabadi F. The relationship between serum vitamin D level and the severity of asthma symptoms in children aged 15-5 years old in Ardabil in the years 2010-2011. Journal of Ardabil University of medical science. 2011.

3. Saintonge S, Bang H, Gerber LM. Implications of a new definition of vitamin D deficiency in a multiracial us adolescent population: the National Health and Nutrition Examination Survey III. Pediatrics. 2009; 123(3):797-803.

4. Devereux G, Litonjua AA, Turner SW, Craig LC, McNeill G, Martindale S, et al. Maternal vitamin D intake during pregnancy and early childhood wheezing. The American journal of clinical nutrition. 2007; 85(3):853-9.

5. Sharif MR, Madani M, Tabatabaei F, Tabatabaee Z. The relationship between serum vitamin D level and attention deficit hyperactivity disorder. Iranian journal of child neurology. 2015; 9(4):48.

6. Tamašauskienė L, Gasiūnienė E, Lavinskienė S, Sakalauskas R, Šitkauskienė B. Evaluation of vitamin D

levels in allergic and non-allergic asthma. Medicina. 2015; 51(6):321-7.
7. Boulet L-P, Reddel HK, Bateman E, Pedersen S, FitzGerald JM, O'Byrne PM. The global initiative for asthma (GINA): 25 years later. European Respiratory Journal. 2019; 54(2).
8. Hatami G, Ghasemi K, Motamed N, Firoozbakht S, Movahed A, Farrokhi S. Relationship between Vitamin D and Childhood Asthma: a case–control study. Iranian journal of pediatrics. 2014; 24(6):710.
9. Rahmati M, Safdarian F. Evaluation of serum vitamin D level in children with asthma attack in Bandar Abbas Children Hospital in 2010 and comparing it with normal children. 2014.
10. Chinellato I, Piazza M, Sandri M, Peroni D, Piacentini G, Boner AL. Vitamin D serum levels and markers of asthma control in Italian children. The Journal of pediatrics. 2011; 158(3):437-41.
11. 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 & immunology research. 2011; 3(4):251-5.
12. Bar Yoseph R, Livnat G, Schnapp Z, Hakim F, Dabbah H, Goldbart A, et al. The effect of vitamin D on airway reactivity and inflammation in asthmatic children: a double-blind placebo-controlled trial. Pediatric pulmonology. 2015; 50(8):747-53.
13. Thomas GO, Tutar E, Tokuc G, Oktem S. 25-hydroxy vitamin D levels in pediatric asthma patients and its link with asthma severity. Cureus. 2019; 11(3.(
14. IQBAL BANO AK, BARI A, Rathore AW, Un Nisa T, Bushra R. Association between Raised Serum IgE Levels and Bronchial Asthma in Children. Pak Pediatr J. 2019; 43(1):10-4.