

Correlation between Level of Vitamin D in Serum and Value of Lung Function in Children Diagnosed with Bronchial Asthma

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Abstract

Introduction: Many authors in their research have suggested an association between vitamin D and asthma, but the results from these publications are sometimes confusing.

Aim: Our aim was to assess the relationship between serum vitamin D and lung function in patients previously diagnosed with asthma.

Materials and methods: The present study started in September 2019 and was completed in May 2020. All patients were diagnosed at the University Clinical Center-Prishtina, Kosovo. Spirometry was performed on children of ages 6-16 years old with a spirometer according to the recommendations of the American Thoracic Society.

Results: Of the 57 children who visited the University Clinical Center of Kosovo-Department of Pediatrics, 29 were diagnosed with asthma. The Spearman coefficient correlation showed statistical significance between vitamin D and body weight, and vitamin D and FEF75% at level 0.05. Other parameters did not show statistical significance with vitamin D, but such statistical significance was found in other parameters between asthma and healthy groups.

Conclusions: Our data suggested that serum vitamin D level was insignificant for FVC%, FEV1%, Tiffeneau Index values, and PEF. Statistical significance was observed between vitamin D and body weight; vitamin D and FEF75% ($p=0.05$).

Keywords

airways, asthma, chronic inflammation, vitamin D

INTRODUCTION

Asthma (according to Global Initiative for Asthma, Global Strategy for Asthma Management and Prevention 2019) is a heterogeneous disease characterized by chronic inflammation of the airways. It is characterized by a history of respiratory symptoms such as wheezing, expiratory dyspnea, chest tightness, and cough that vary in intensity over time along with variable restriction of expiratory air-

flow.^[1] Bronchial hyper-reactivity, broncho-obstruction in chronic inflammation of the airways are present even when symptoms are absent while lung function is normal, but hyper-reactivity and broncho-obstruction can be normalized with therapy. Asthma affects all ages; children and adults. Asthma is a worldwide problem, affecting approximately 300 million individuals.^[2]

Vitamin D is one of the oldest hormones created in the earliest forms of life for more than 750 million years.^[3]

As an immune modulator, vitamin D appeared to have played a pivotal role in the pathogenesis of asthma. Vitamin D in the form of 1,25-dihydroxy, appeared to be involved in suppressing dendritic cell maturation and the Th1 cell development.^[4-7]

Lately, there has been an increased number of studies related to the therapeutic benefits of vitamin D in patients with asthma. There was evidence of the existence of an association between deficiency of vitamin D and asthma patients.^[3] Hall and Agrawal reported an association between vitamin D deficiency and increased inflammation in asthma, asthma exacerbation, and poorly controlled asthma.^[8] Martineau et al.^[9] stated that vitamin D supplementation reduced severe asthma attacks. Jolliffe et al.^[10] reported that asthma attacks requiring systemic steroid treatment reduced with vitamin D supplementation.

Over 900 genes were reported to be regulated by vitamin D.^[11]

The most well-known is CYP24A that belongs to the cytochrome P450 (CYP) family. The members of the P450 (CYP) family appeared to participate in the encoding of multiple enzymes that were used in the oxidative metabolism of many endogenous and exogenous compounds.^[12,13]

AIM

Our purpose was to explore whether there was a correlation between serum vitamin D level and lung function values in patients diagnosed with bronchial asthma in the Department of Pediatrics, University Clinical Center, being the only University center in Kosovo.

MATERIALS AND METHODS

Children with bronchial asthma hospitalized in the Pediatric Clinic in Prishtina-Kosovo were included in this prospective study. It included 28 patients with asthma. The study was conducted in periods when fewer sunny days were expected, in autumn, winter, and spring. The research period included the period from September 2019 to April 30, 2020. Children who had been previously diagnosed with mild, moderate, and persistent severe asthma were included in the research. Only children whose parents signed the informed consent form were included in the study. The inclusion criterion was diagnosis of asthma according to GINA guidelines asthma control criteria (data on the existence of asthma symptoms and previous positive test on Ventolin). The therapy administered was inhaled corticosteroids, and/or leukotriene antagonists, and sometimes beta 2 agonists. Spirometry was performed on children 6–16 years old with a spirometer according to the recommendations of the American Thoracic Society.^[14]

The spirometer used was Spirolab III S/N 312444; the parameters which we analyzed were: FCV (force vital capacity); FEV1 (forced expiratory volume in one second);

FEV1% /FEV1 -expressed as a percentage; VC (FEV1/VC×100) called the Tiffeneau index; FEF25/75 (volume of air between 25% and 75% FVC); FEF25% (forced volume of expiration during 25% FVC); FEF50% (forced volume of expiration during 50%); FEF75% (forced volume of expiration during 75% FVC); PEF (peak expiratory flow). Spirometry results were presented as a percentage of predicted values. The study did not include the children who had bone fractures during the current year or even during the previous year, as well as children with serious cardiopulmonary diseases, children with immunodeficiency, severe neurological or metabolic disorders. This research was supported and approved by the Ethics Committee of the Faculty of Medicine, University of Prishtina; reference number 3528, date: 16/05/2020.

Statistical analysis

The data were evaluated using SPSS 26 (SPSS, Chicago, Illinois); descriptive statistics and Spearman correlation test were used to compare and find the correlation between children with bronchial asthma and healthy control group. A *p* value less than 0.05 was considered statistically significant.

RESULTS

The study included 28 children with bronchial asthma, 27 with vitamin D deficiency, and one child with a normal value - without deficiency. All spirometry parameters were presented in **Tables 1a, 2b**. The mean age of the patients with asthma was 11.0 and the mean age of the healthy group was 9.82 years. The mean bodyweight of the asthma group was 43.0 kg, and of the control group - 35.56 kg. The mean body height of the asthma group was 146.24 cm and of the control group - 144.04 cm. The values of the *t*-test are presented in **Table 1c**. To verify the correlation for vitamin D and other parameters between the two groups, the correlation coefficient was calculated according to Spearman. Statistical significance was found between parameters that were conveyed and measured, but statistical significance was also found between vitamin D and body weight ($r=-0.329$; $p=0.05$ level); vitamin D and FEF75% ($r=0.375$; $p=0.05$) (**Table 2**). The distribution in percentages between asthma and the healthy group are presented in **Figs 1a, 1b**.

DISCUSSION

The studies that observe the association between vitamin D and lung diseases are limited.

This was the first study in Kosovo performed on asthma patients and healthy persons outside controlled laboratories. These tests were widely used in the study once the pulmonary volumes and flows that were sensitive to identifying possible alternations were assessed.^[15] This study explored spirometry evaluation conducted at different ages.

Table 1a. Anthropometric and spirometry characteristics of patients with asthma

Parameters	Number	Min.	Max.	Mean	Std. Deviation	Std. Error Mean
Age (yrs)	29	7	16	11.0	2.68	0.49
Bodyweight (kg)	29	22	66	43.0	13.34	2.47
Body height (cm)	29	120	175	146.24	15.15	2.81
FVC%	29	70.0	199.0	102.91	23.87	4.43
FEV1%	29	50.0	195.0	99.87	24.09	4.47
FEV1% Tiffeneau index	29	73	115	94.97	10.53	1.95
FEF25/75	29	31	134	87.07	25.55	4.82
FEF25%	29	30	109	75.14	20.50	3.80
FEF50%	29	33.0	133.0	86.46	24.44	4.53
FEF75%	29	23.0	172.0	79.92	33.01	6.13
PEF	29	31.0	118.0	81.54	20.84	3.87
Vitamin D (ng/ml)	29	4.52	33.70	17.003	6.00	1.11

Table 1b. Anthropometric and spirometry characteristics of the control group

Parameters	Number	Min.	Max.	Mean	Std. Deviation	Std. Error Mean
Age (yrs)	28	5	14	9.82	2.82	0.53
Body weight (kg)	28	20	54	35.46	11.39	2.15
Body height (cm)	28	121	173	144.04	14.91	2.81
FVC%	28	34	109	78.50	15.66	2.96
FEV1%	28	39	119	85.68	16.42	3.10
FEV1% Tiffeneau index	28	85.0	94.0	86.67	2.11	0.39
FEF25/75	28	38	160	95.04	29.11	5.50
FEF25%	28	39	115	74.89	21.10	3.98
FEF50%	28	48	143	88.79	23.68	4.47
FEF75%	28	35	205	105.32	37.20	7.03
PEF	28	37	127	77.93	22.62	4.27
Vitamin D (ng/ml)	28	10.2	29.8	17.18	5.29	1.00

Table 1c. *t*-test values between vitamin D and bodyweight, body height, FVC%, FEV1%, FEF25/75, FEF25%, FEF50%, FEF75%, and PEF

Parameters	t	df	sig. (2-tailed)
Body weight (kg) - Vitamin D (ng/ml)	8.669	28	0.000
Body higher (cm) - Vitamin D (ng/ml)	40.370	28	0.000
FVC% - Vitamin D (ng/ml)	19.372	28	0.000
FEV1% - Vitamin D (ng/ml)	18.870	28	0.000
FEV1% Tiffeneau index - Vitamin D (ng/ml)	39.453	28	0.000
FEF25/75 - Vitamin D (ng/ml)	15.430	27	0.000
FEF25% - Vitamin D (ng/ml)	16.342	28	0.000
FEF50% - Vitamin D (ng/ml)	15.768	28	0.000
FEF75% - Vitamin D (ng/ml)	10.803	28	0.000
PEF	18.029	28	0.000

Table 2. Spearman coefficient correlation between vitamin D and bodyweight, body height, FVC%, FEV1%, FEF25/75, FEF25%, FEF50%, FEF75% and PEF

	Parameters	Vitamin D ng/ml
Spearman's rho	Bodyweight (kg)	-0.329**
	Body higher (cm)	-0.177
	FVC%	0.154
	FEV1%	0.155
	FEV1% Tiffeneau index	0.227
	FEF25/75	0.313
	FEF25%	0.267
	FEF50%	0.197
	FEF75 %	0.375*
	PEF	0.273

** Correlation is significant at the 0.01 level (2-tailed); * Correlation is significant at the 0.05 level (2-tailed)

The results obtained during the research did not differ from each other for vitamin D and most other parameters. The same study was conducted especially with adults. Larsson et al.^[16] studied spirometry in a group of chronic pulmonary diseases and a healthy group in two weeks. In this study, they did not observe interference.

Ozkars et al. showed that low serum vitamin D levels were observed more frequently in children with asthma.^[17]

In the study by Larose et al., it was observed that low serum 25(OH) D level was not in correlation in asthmatics with airway obstruction except in men with asthma but without allergic rhinitis.^[18]

Laura et al. in their study also indicated that vitamin D levels did not correlate with lung function.^[19]

Janeva-Jovanovska et al. found insignificant correlation between serum levels of vitamin D and FEV1.^[20] In our study, there was also no significant correlation between the serum levels of vitamin D and FEV1.

In some studies, significant direct relationship between vitamin D levels and both FEV1 and FEV1/FVC was reported.^[19,21]

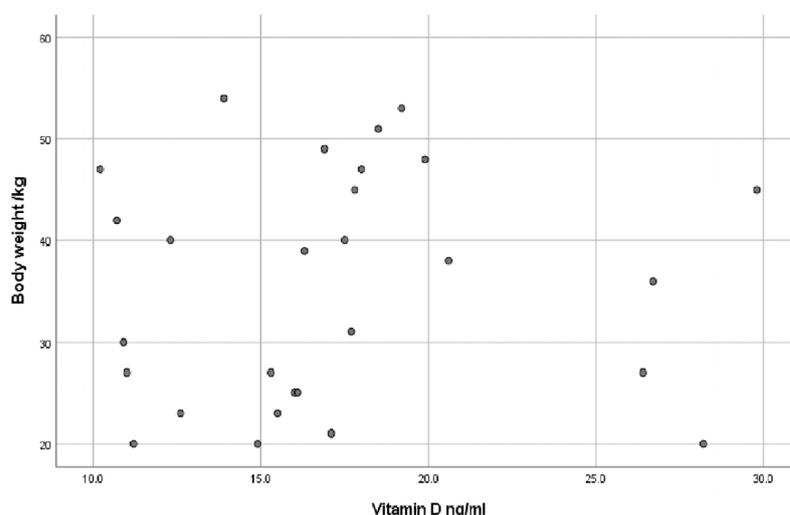


Figure 1a. Correlation between vitamin D and body weight in asthma patients ($r=0.329$; $p=0.05$).

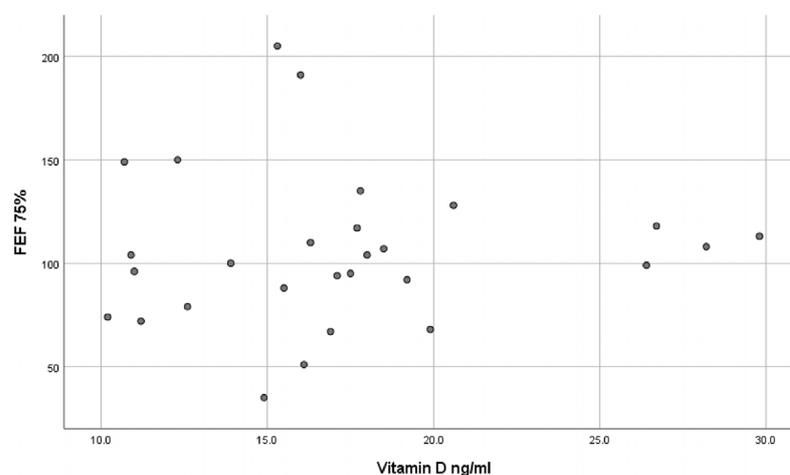


Figure 1b. Correlation between vitamin D and FEF50% in asthma patients ($r=0.375$; $p=0.05$).

Schermer et al. found no statistical or clinical significance^[22] in their study. A lot of studies indicate the involvement of children in this field. It is known that children go through changes as individuals as a result of the influence of the environment. Also, they continue to develop which involves different fields.^[23,24]

CONCLUSIONS

In conclusion, we can say that we observed a statistical significance for the Spearman coefficient between vitamin D and body weight; vitamin D and FEF75%. We did not observe a statistical significance for the Spearman coefficient between vitamin D and other parameters. Our data suggest that further research is needed to determine the role that vitamin D might play, if any, in establishing human asthma and allergy. The common polymorphism in vitamin D receptors and other genes in the vitamin D pathway should be characterized, especially the connection between vitamin D and asthma diseases.

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Competing Interests

The authors have declared that no competing interests exist.

REFERENCES

1. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. 2019; Available from: www.ginasthma.org.
2. Masoli M, Fabian D, Holt S, et al. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; 59:469–78.
3. Holick MF. Vitamin D: A millennium perspective. *J Cell Biochem* 2003; 88(2):296–307.
4. Bonanno A, Gangemi S, La Grutta S, et al. 25-Hydroxyvitamin D, IL-31, and IL-33 in children with allergic disease of the airways. *Mediators Inflamm* 2014; 2014:ID 520241.
5. Benson AA, Toh JA, Vernon N, et al. The role of vitamin D in the immunopathogenesis of allergic skin diseases. *Allergy* 2012; 67(3):296–301.
6. Annesi-Maesano I. Perinatal events, vitamin D, and the development of allergy. *Pediatric Research* 2002; 52(1):3–5.
7. Meyts I, Hellings PW, Hens G, et al. IL-12 contributes to allergen-induced airway inflammation in experimental asthma. *J Immunol* 2006; 177(9):6460–70.
8. Hall SC, Agrawal DK. Vitamin D and bronchial asthma: an overview of data from the past 5 years. *Clin Ther* 2017; 3:917–29.
9. Martineau AR, Cates CJ, Urashima M, et al. Vitamin D for the management of asthma. *Cochrane Database Syst Rev* 2016; 9:CD011511.
10. Jolliffe DA, Greenberg L, Hooper RL, et al. Vitamin D supplementation to prevent asthma exacerbations: a systematic review and meta-analysis of individual participant data. *Lancet Respir Med* 2017; 5:881–90.
11. Brehm JM, Schuemann B, Fuhlbrigge AL, et al. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. *J Allergy Clin Immunol* 2010; 126:52–58.
12. Plum LA, DeLuca HF. Vitamin D, disease and therapeutic opportunities. *Nat Rev Drug Discov* 2010; 9:941–55.
13. Goleva E, Searing DA, Jackson LP, et al. Steroid requirements and immune associations with vitamin D are stronger in children than adults with asthma. *J Allergy Clin Immunol* 2012; 129:1243–51.
14. American Thoracic Society. Standardization of spirometry: 1994 update. *Am J Respir Crit Care Med* 1995; 152:1107–36.
15. França DC, Camargos PA, Vieira BS, et al. Cough peak flow in preschoolers: success rate and test-retest reproducibility. *Fisioter Pesq* 2015; 22:275–81.
16. Larsson K, Hedenström H, Malmberg P. Learning effects, variation during office hours and reproducibility of static and dynamic spirometry. *Respiration* 1987; 51:214–22.
17. Ozkars MY, Keskin O, Almacioglu M, et al. The relationship between serum vitamin D level and asthma. *North Clin Istanbul* 2019; 6(4):334–40.
18. Larose TL, Langhammer A, Chen Y, et al. Serum 25-hydroxyvitamin D levels and lung function in adults with asthma: the HUNT Study. *Eur Respir J* 2015; 45(4):1019–26.
19. Tamašauskienė L, Gasiūnienė E, Lavinskienė S, et al. Evaluation of vitamin D levels in allergic and non-allergic asthma. *Medicine* 2015; 51(6):321–7.
20. Janeva-Jovanovska E, Dokic D, Jovkovska-Kaeva B, et al. Relationship between vitamin D, inflammation and lung function in patients with severe uncontrolled asthma. *Open Access Maced J Med Sci* 2017; 5(7):899–903.
21. Lin Z, Li W. The roles of vitamin D and its analogs in inflammatory diseases. *Curr Top Med Chem* 2016; 16(11):1242–61.
22. Schermer TR, Akkermans RP, Crockett AJ, et al. Effect of e-learning and repeated performance feedback on spirometry test quality in family practice: a cluster trial. *Ann Fam Med* 2011; 9:330–6.
23. Biscegli TS, Polis LB, Santos LM, et al. Nutritional status, and neurodevelopment of children enrolled in a daycare center. *Rev Paul Pediatr* 2007; 25:337–42.
24. Vieira ME, Linhares MB. Developmental outcomes and quality of life in children born preterm at preschool- and school-age. *J Pediatr (Rio J)* 2011; 87:281–91.

Корреляция между уровнем витамина D в сыворотке крови и значением функции лёгких у детей с диагнозом бронхиальная астма

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Резюме

Введение: Многие авторы в своих исследованиях предполагают связь между витамином D и астмой, но результаты этих публикаций иногда сбивают с толку.

Цель: Нашей целью было оценить взаимосвязь между сывороточным витамином D и функцией лёгких у пациентов, ранее диагностированных с астмой.

Материалы и методы: Настоящее исследование началось в сентябре 2019 г. и завершилось в мае 2020 г. Диагноз всем пациентам был поставлен в Университетском клиническом центре Приштины, Косово. Детям 6-16 лет спирометрию проводили с помощью спирометра в соответствии с рекомендациями Американского торакального общества.

Результаты: Из 57 детей, посетивших Университетский клинический центр Косово - Кафедра педиатрии, у 29 была диагностирована астма. Корреляция коэффициента Спирмена показала статистическую значимость между витамином D и массой тела, а также витамином D и FEF75% на уровне 0.05. Другие параметры не показали статистической значимости с витамином D, но такая статистическая значимость была обнаружена в других параметрах между астмой и здоровыми группами.

Заключение: Наши данные свидетельствуют о том, что уровень витамина D в сыворотке был незначительным для значений FVC%, FEV1%, значений индекса Тиффно и PEF. Статистическая значимость наблюдалась между витамином D и массой тела; витамина D и FEF75% ($p=0.05$).

Ключевые слова

дыхательные пути, астма, хроническое воспаление, витамин D
