Original Article

Serum Vitamin D Level And Markers Of Severity Of Children With Asthma In Kosovo

Emir Behluli[1], Lidvana Spahiu[1], Gazmend Temaj[2]

[1] Department of Pediatric, University Clinical Center, Prishtina, Kosovo
[2] College UBT, Faculty of Pharmacy, Prishtina, Kosovo

ORCID ID (recommended)
Emir Behluli 0000-0002-0889-5510
Lidvana Spahiu 0000-0003-0927-3569
Gazmend Temaj 0000-0003-4807-2938

Email addresses of all authors
Emir Behluli- ebehluli_19@hotmail.com
Lidvana Spahiu- lidvanaspahiu@gmail.com
Gazmend Temaj- gazmend.temaj@ubt-uni.net
Corresponding author
Gazmend Temaj- gazmend.temaj@ubt-uni.net
DOI: 10.47750/pnr.2023.14.04.86

Abstract

Asthma is a chronic inflammatory disorder. Observational studies have shown that vitamin D level (low level) is connected with bad lung function and poor asthma control in children with asthma. In this study, vitamin D level in children with asthma from Kosovo concerning anthropometric and biochemical characteristics (IgE, Calcium, Phosphor, ALT, and CPR) was assessed. We have compared it with healthy children.

Material and Methods: The research project started in September 2019 and was completed in May 2020. All patients are diagnosed at the University Clinical Center-Prishtina, Kosovo. Children with asthma (n=51; age 6-16 years) were assessed for serum of vitamin D levels and body anthropometrics (weight, height, and body mass index [BMI]).

Results: Children had vitamin D levels under 30nmol/L (deficiency); eight children had vitamin D levels 30 nmol/L (insufficiency); 2 children had vitamin D levels between 30-100 nmol/L (sufficiency).

Conclusion: In conclusion, we can say that t-tests do not show statistical significance for sufficiency, insufficiency, and deficiency between the children with asthma and healthy children. From biochemical characteristics, the statistical significance for ALP ($P<0.01$) was found. Vitamin D screening and supplementation for children with asthma are recommended.

Keywords: Asthma, Vitamin D, CRP, Ca, P, ALT.

Introduction

Asthma is the most prevalent respiratory disease in the United State. Over 25 million American people suffer from asthma, including 6 million children [1]. Asthma is a heterogeneous disease that affects respiratory airways. It is characterized by airway inflammation and other symptoms such as wheezing, shortness of breath, chest tightness, and/or cough in addition to airflow limitation [1]. These symptoms can vary in frequency and are often triggered by exercises, viral respiratory infections, exposure to different chemicals and environmental allergens, change of weather [2]. Financially, asthma treatment exceeded $ 81 billion in 2013 [3]. The number of new and expensive medications

aimed at treating people with asthma is increasing [4]. Although asthma mortality is declining [5], asthma is still responsible for the deaths of more than 3,000 Americans in 2019 [1].

There has been a global increase in the prevalence of vitamin D deficiency which has been associated with an increasing prevalence of children with asthma [6]. Vitamin D is necessary to regulate the immune system response by stimulating the production of antimicrobial proteins and its effect as a precursor on vitamin D receptors. Deficiency of 25-hydroxyvitamin D3 (25 (OH) D3) is mainly associated with a high incidence of autoimmune diseases as well as upper and lower respiratory tract infections [7,8].

Serum vitamin D levels <50 nmol / L have been observed to be associated with an increase in airway inflammation, poor lung function, and poor prognosis in people suffering from asthma [9]. However, serum vitamin D levels> 50 nmol / L were not observed to be associated with improvement in persons suffering from asthma [10]. Vitamin D intake is associated with an increase in the maximum rate of normalization of respiration, and a reduction in the risk of acute infections of the respiratory tract [11,12]. Therefore, vitamin D level testing and treatment should be performed routinely for all children with asthma, especially those at high risks, such as the overweight and older children [10,13,14,15]. There is currently no agreement on the recommended additional dose of vitamin D that should be appropriate for overweight and obese children [16].

Our study aims to assess the condition of vitamin D in children (age range, 6-16 years) with moderate and severe asthma who visited our pediatric clinic in Pristina, Republic of Kosovo. The relationship between the vitamin D level and risk factors including physical characteristics (such as age, sex, and BMI) was examined. Furthermore, we sought to test the hypothesis that vitamin D levels are influenced by risk factors in children with asthma.

Material and Methods

In this prospective research cases-children hospitalized in the Paediatric Clinic in Prishtina-Kosovo are included, i.e. children with bronchial asthma. The study includes 51 patients with asthma. The study was conducted in periods when we expected fewer sunny days, in autumn, winter, spring. The research period includes the period from September 2019 to April 30, 2020. The study was approved by the ethical committee for Clinical Trials (approval reference number 3528 date 16/05/2019) and was performed according to the Helsinki declaration. The research includes children who have been previously diagnosed with mild, moderate, and persistent severe asthma. The criteria for inclusion in the research were diagnosis of asthma with criteria for asthma control according to GINA guidelines (data on the existence of asthma symptoms and previous positive tests on Ventolin). The therapy used was inhaled corticosteroids, and/or leukotriene antagonists, sometimes beta 2 agonists. Only children whose parents signed the consent were included in the research.

Total serum of vitamin D was quantified using COBAS e-411 automated analyzer (Roche Diagnostics, Indianapolis, IN). Vitamin D deficiency was defined at levels <30 nmol/L, Vitamin D insufficiency at a levels 30 and 50 nmol/L, and Vitamin D sufficiency at level >50 nmol/L [17].
Weight (kg) was measured using an electronic scale and height (m) using a stadiometer, and BMI was calculated as a ratio between weight (kg) and height in meter square. BMI at <5th percentile was considered underweight, 5th – 85th percentile was considered normal weight, and >85th was considered overweight [18].

Our data are presented as mean and standard deviation. The sufficiency, insufficiency, and deficiency were compared between both groups by using analysis of variance, followed by a student t-test. A p-value $p<0.05$ was considered significant. Statistical analyses were performed using SPSS 26.0 (SPSS Inc. Chicago, IL). Correlation between asthma and control group for Vitamin D, IgE, Calcium, Phosphor, ALP, and CRP was performed using Spearman correlation. The differences were considered statistically significant when P-value was 0.01.

Results

The total number of children who participated and were included in this study was 119 (51 diagnosed with asthma and 68 from the control group).
Participants were classified into three subgroups according to vitamin D level in their serum (sufficiency >50 nmo/L; insufficiency 30-50nmol/L; and deficiency <30 nmol/L) and the variance among the groups was measured. The t-test for this group was not significant.

Normal, higher and low values for IgE, Calcium, Phosphor, ALT (phosphatase alkaline) and CRP (C-reactive protein) are presented in table 1. The t-test for these parameters shows no statistical significance. The significance is found just for ALP between asthma and the control group ($P<0.01$) (Table 1).

Table 1. Characterization of participants according biochemical analysis. Results are shown as mean and standard deviation for normal value, low value and total absence. The student t-test shown statistical significance for CRP normal value between Asthma and control group.

Variables	Mean	Std. Deviation	Std. Error of Mean	t-test
Calcium /normal value	-1.995	0.982	0.695	-2.871
Calcium/ Low value	-0.253	0.927	0.309	-0.820
Calcium/ Total absence	-0.393	0.788	0.139	-2.82
IGE/ normal value	190.35	290.83	205.65	0.926
IGE/ Low value	524.84	632.65	210.88	2.489
IGE/ Total absence	411.13	996.7	179.02	2.296
Phosphor/ normal value	-1.290	0.820	0.580	-2.224
Phosphor/ Low value	-0.1922	0.448	0.149	-1.285
Phosphor/ Total absence	-0.2437	0.569	0.100	-2.419
ALP/ normal value	-69.15	297.19	210.15	-0.329
ALP/ Low value	9.32	118.57	39.52	0.236
ALP/ Total absence	-47.078	143.53	25.37	-1.85
CRP/ normal value	6.57	0.07	0.05	119.5*
CRP/ Low value	4.40	6.55	2.18	2.017
CRP/ Total absence	4.70	22.51	3.97	1.183

No correlation significance between Vitamin D and biochemical characteristics was observed, but correlation significance between biochemical characteristics was observed (Table 2, 3, 4).

Table 2. Correlation between children affected with asthma and healthy group for biochemical traits who have normal value

	Vitamin D	IgE	Calcium	Phosphor	ALT	CRP
Vitamin D	1.000	.322*	0.104	0.047	0.034	-0.096
IgE	.322*	1.000	.388*	0.019	0.056	-.362*
Calcium	0.104	.388*	1.000	0.166	.305*	-0.227
Phosphor	0.047	0.019	0.166	1.000	.346*	0.031
ALT	0.034	0.056	.305*	.346*	1.000	-0.274
CRP	-0.096	-.362*	-0.227	0.031	-0.274	1.000

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

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

Table 3. Correlation between children affected with asthma and healthy group for biochemical traits who have Low value

	Vitamin D	IgE	Calcium	Phosphor	ALT	CRP
Vitamin D	1.000	0.351	-0.084	-0.427	-0.234	-0.094
IgE	0.351	1.000	0.300	0.167	-0.083	0.085
Calcium	-0.084	0.300	1.000	.683*	0.233	0.220
Phosphor	-0.427	0.167	.683*	1.000	0.567	-0.136
ALT	-0.234	-0.083	0.233	0.567	1.000	0.305
CPR	-0.094	0.085	0.220	-0.136	0.305	1.000

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

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

Table 4. Correlation between children affected with asthma and healthy group for biochemical traits who have total absence

	Vitamin D	IgE	Calcium	Phosphor	ALT	CPR
Vitamin D	1.000	-1.000	1.000	1.000	1.000	1.000
IgE	-1.000**	1.000	-1.000	-1.000	-1.000	-1.000
Calcium	1.000**	-1.000**	1.000	1.000	1.000	1.000
Phosphor	1.000**	-1.000**	1.000**	1.000	1.000	1.000
ALT	1.000**	-1.000**	1.000**	1.000**	1.000	1.000
CRP	1.000**	-1.000**	1.000**	1.000**	1.000**	1.000

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

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

All asthmatic patients have been on therapy with B 2 agonists, in inhaled form, and corticosteroid therapy in the form of Flixotide spray was included in re-examination. The supplement of vitamin D and dietary intake is recommended also.

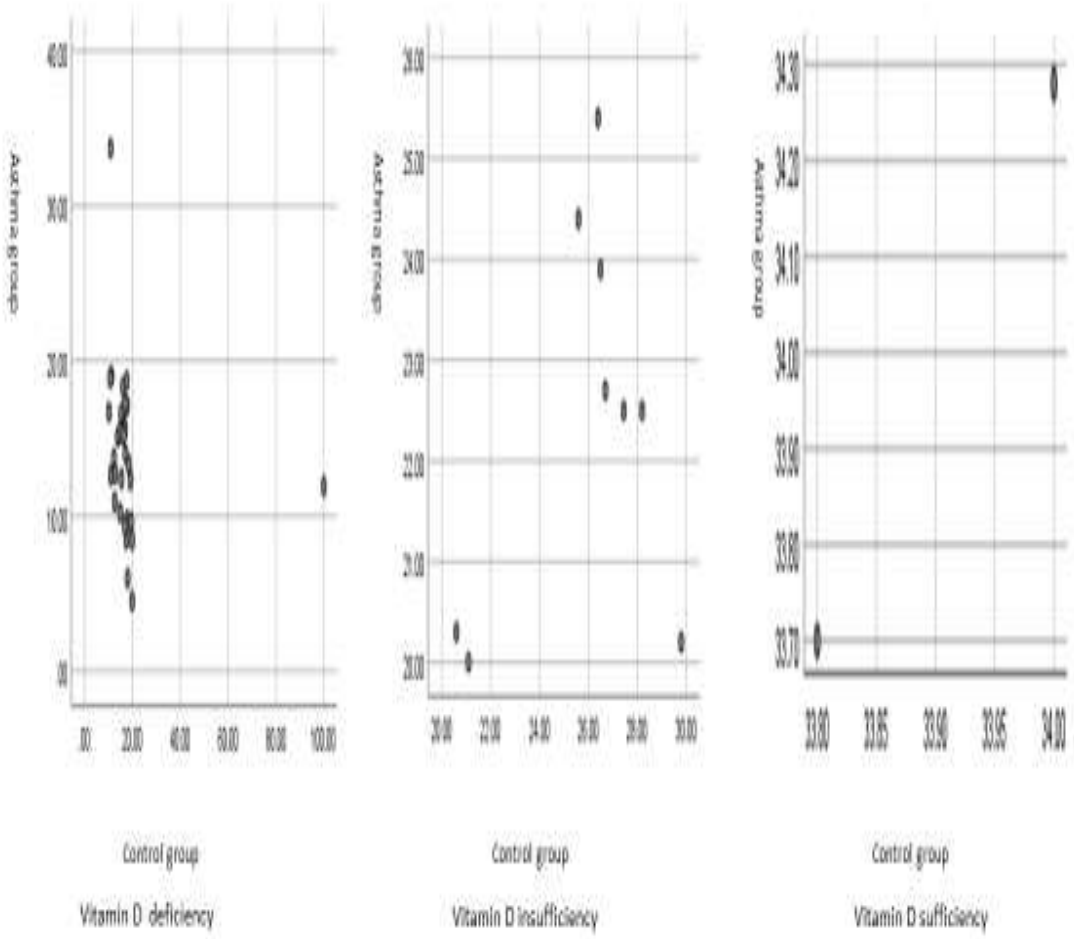

Fig. 1. Scatter plot of serum Vitamin D and biochemical characteristics compared between Asthma and healthy group, for sufficiency, insufficiency, deficiency for vitamin D.

Discussion

The studies that explore the connection between vitamin D and lung diseases are limited. This is the first study in Kosovo performed on asthma patients and healthy persons outside controlled laboratories. There is a growing health concern regarding the low level of vitamin D in children, particularly with permanent illnesses such as pulmonary disease, including asthma [19]. A low level of Vitamin D in serum was observed that has a very important impact on asthma patients and is very severe [20]. The results from our study did not differ from each other for vitamin D and biochemical parameters. Bindayel IA., studied the effect of age and BMI on vitamin D levels in children with asthma and observed that >50% of children with asthma in Saudi Arabia have vitamin D below the level. The same author recommends screening and supplementing older and overweight children with asthma [21]. Some authors report that

the vitamin D level did not correlate with lung function (Laura et al. 2015) [22]. Behluli et al. report for correlation between vitamin D and body weight, and vitamin D and FEF75% [23].

Diet is a very important factor that has been observed to be involved in the regulation of vitamin D levels. Using foods that are rich in Vitamin D (e.g. liver, fish, and eggs) is not considered inadequate. Bindayel IA., reports no correlation between serum vitamin D level and dietary product intake [21].

Conclusion

In conclusion, we can say that we found statistical significance just for CRP parameters between asthma and control groups. We did not find statistical significance between Vitamin D and other parameters. Also, we found a correlation between vitamin D and other biochemical parameters. We suggest additional work is needed to be done for the determination of the role that vitamin D might play in asthma patients. The common receptors for vitamin D and different genes that are involved in the vitamin D pathway should be characterized, especially the connection between vitamin D and asthma diseases.

Funding/support statement to state any funding source/grants: "This research received no specific grants from any funding agency, public, commercial, or not-for-profit sectors."

Conflicts of Interest

The authors declare that there are no conflicts of interest.

References

1. CDC. Most Recent National Asthma Data: National Center for Environmental Health; 2020 [cited 2021 February 28]. Available from: https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm
2. Global Initiative for Asthma. 2020 [cited 2021 February 12]. Available from: https://ginasthma.org/
3. Nurmagambetov T, Kuwahara R, Garbe P. The Economic Burden of Asthma in the United States, 2008-2013. Ann Am Thorac Soc. 2018; 15(3):348–56.
4. Inselman JW, Jeffery MM, Maddux JT, Shah ND, Rank MA. Trends and Disparities in Asthma Biologic Use in the United States. J Allergy Clin Immunol Pract. 2020; 8(2):549-54.
5. Pennington E, Yaqoob ZJ, Al-Kindi SG, Zein J. Trends in Asthma Mortality in the United States: 1999 to 2015. Am J Respir Crit Care Med. 2019; 199(12):1575–7. doi: 10.1164/rccm.201810-1844LE.
6. Jat KR, Khairwa A. Vitamin D and asthma in children: a systematic review and meta-analysis of observational studies. Lung India. 2017; 34:355–363.
7. Aranow C. Vitamin D and the immune system. J Investig Med. 2011; 59:881–886.
8. Bozzetto S, Carraro S, Giordano G, Boner A, Baraldi E. Asthma, allergy and respiratory infections: the vitamin D hypothesis. Allergy. 2012; 67:10–17.
9. Hall SC, Agrawal DK. Vitamin D and bronchial asthma: an overview of data from the past 5 years. Clin Ther. 2017; 39 917–929.
10. Bener A, Ehlayel MS, Tulic MK, Hamid Q. Vitamin D deficiency as a strong predictor of asthma in children. Int Arch Allergy Immunol. 2012; 157:168–175.
11. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ. 2017; 356: i6583.
12. Yadav M, Mittal K. Effect of vitamin D supplementation on moderate to severe bronchial asthma. Indian J Pediatr. 2014; 81:650–654.
13. Aldubi HM, Alissa EM, Kamfar HZ, Gaber O, Marzouki ZM. Bronchial asthma and hypovitaminosis D in Saudi children. Asia Pac Allergy. 2015; 5:103–113.
14. Albar R, Banjar N, Bokhari A, Alzahrani F, Fatani A, Althagaf K, et al. Prevalence of vitamin D deficiency in Saudi children and risks of iron deficiency anemia. Curr Pediatr Res. 2017; 21:205–208.
15. Brehm JM, Celedón JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, Laskey D, et al. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. Am J Respir Crit Care Med. 2009; 179:765-771.
16. Zakharova I, Klimov L, Kuryaninova V, Nikitina I, Malyavskaya S, Dolbnya S, et al. Vitamin D insufficiency in overweight and obese children and adolescents. Front Endocrinol. 2019; 10:103.
17. Munns CF, Shaw N, Kiely M, Specker BL, Thacher TD, Ozono K, et al. Global consensus recommendations on prevention and management of nutritional rickets. J Clin Endocrinol Metab. 2016; 101:394–415.
18. WHO. Physical status: the use and interpretation of anthropometry. Geneva (1985).
19. Ali NS, Nanji K. A review on the role of vitamin D in asthma. Cureus. 2017; 9:e1288.

20. Havan M, Razi CH, Bulus AD, Koksal AO, Andıran N. Effects of 25 hydroxy vitamin D levels on the severity and asthma control in school age asthma patients. Arch Argent Pediatr. 2017; 115:336–342.
21. Bindayel IA. Effect of age and body mass index on vitamin D level in children with asthma in Riyadh. Sci Rep. 2021; 11(1):11522.
22. Laura T, Edita G, Simona L, et al. Evaluation of vitamin D levels in allergic and non-allergic asthma. Medicine. 2015; 51(6):321-327.
23. Behluli, E.; et al. Correlation between level of vitamin D in serum and value of lung function in children diagnosed with bronchial asthma. Folia medica. 2021; 64(4):649-654.