ISSN (electrónico): 1699-5198 - ISSN (papel): 0212-1611 - CODEN NUHOEQ S.V.R. 318

ARÁN

Nutrición Hospitalaria

Trabajo Original

Pediatría

# Risk of vitamin D deficit in asthmatic children hospitalized in the north area of Santiago

*Riesgo de déficit de vitamina D en niños asmáticos hospitalizados en el área norte de Santiago*

María Elena Herrera[1], Gerardo Weisstaub[2], Ana María Herrera[3], Ricardo Pinto[4]

*[1]Department of Pediatrics and Pediatric Surgery. Hospital Clínico de la Universidad de Chile. Facultad de Medicina. Universidad de Chile. Independencia, Santiago. Chile. [2]Instituto de Nutrición y Tecnología de los Alimentos (INTA). Universidad de Chile. Macul, Santiago. Chile. [3]Clínica Santa María. Facultad de Medicina. Universidad de los Andes. Providencia, Santiago. Chile. [4]Hospital Dr. Roberto del Río. Independencia, Santiago. Chile*

## Abstract

**Introduction:** in recent years asthma hospitalization rate in Chilean children has doubled. Numerous studies have shown an association between hypovitaminosis D and frequent, severe asthmatic exacerbations in children.

**Objective:** to estimate the risk of vitamin D (vitD) deficiency and insufficiency in hospitalized asthmatic children compared with patients who are monitored on an outpatient basis and do not have records of hospitalization in one year.

**Material and methods:** an observational, analytic, and case-control study carried out in one calendar year including asthmatic children between 5 and 15 years of age. This study registered: sociodemographic and clinical data, asthma control test, severity score of hospitalization and measurements of vitD blood levels. Associations between variables were analyzed using the t-test and chi-squared test. The risk for hypovitaminosis D and deficiency was calculated through logistic regression. The data was fed into the Stata 14 software.

**Results:** a total of 117 patients, 9 ± 2.7 years old, were admitted, 64 % were male and 51 % presented with malnutrition by excess. Six out of ten children presented moderate asthma and 55 % had a poor control of their pathology; 73.5 % presented hypovitaminosis D (insufficiency and deficiency), hospitalized patients had 2.8 times more risk of presenting vitD deficiency, adjusted according to seasonality and age (95 %CI, 1.07-7.5, $p < 0.05$) without being associated with a higher severity score of hospitalization.

**Conclusion:** most of the asthmatic children in the sample presented with hypovitaminosis D, with a higher percentage of deficiency in hospitalized patients, which is not associated with greater severity of hospitalization.

**Keywords:**

Asthma. Vitamin D. Vitamin D deficiency. Children.

## Resumen

**Introducción:** la tasa de hospitalización por asma se ha duplicado en los últimos años en Chile. Numerosos estudios demuestran una asociación entre la hipovitaminosis D y la presencia de exacerbaciones frecuentes y severas.

**Objetivo:** comparar el riesgo de déficit e insuficiencia de vitamina D (vitD) en niños asmáticos que se hospitalizan en relación con los que se tratan ambulatoriamente.

**Material y métodos:** estudio observacional, analítico, de casos y controles realizado durante 1 año calendario. Se incluyó a pacientes asmáticos de 5 a 15 años. Se registraron datos sociodemográficos, clínicos, nivel de control de asma, puntaje de severidad de hospitalización y se midió la concentración sanguínea de vitD. Se analizó la asociación entre las variables mediante la prueba de la t y la del chi cuadrado. Mediante regresión logística se calculó el riesgo de hipovitaminosis D y déficit de vitD en los sujetos. Los datos se analizaron con el software Stata 14.

**Resultados:** se enrolaron 117 pacientes de 9 ± 2,7 años, 64 % de varones y 51 % con malnutrición por exceso. Seis de cada diez niños presentaban asma moderada y el 55 % tenían mal control de su enfermedad. El 73,5 % de los sujetos presentaban hipovitaminosis D (déficit o insuficiencia). Los hospitalizados tuvieron 2,8 veces más riesgo de presentar déficit de vitD (IC 95 %: 1,07-7,5), ajustado según estacionalidad y edad, sin asociarse a mayor puntaje de severidad de la hospitalización.

**Conclusión:** la mayoría de los niños asmáticos de la muestra presentan hipovitaminosis D, siendo mayor el porcentaje de déficit en los hospitalizados, lo que no se asocia a mayor severidad de la hospitalización.

**Palabras clave**

Asma. Vitamina D. Deficiencia de vitamina D. Niños.

Received: 21/05/2022 • Accepted: 15/11/2022

*Conflicts of interest: the authors declare none.*

Herrera ME, Weisstaub G, Herrera AM, Pinto R. Risk of vitamin D deficit in asthmatic children hospitalized in the north area of Santiago. Nutr Hosp 2023;40(2):273-279

DOI: http://dx.doi.org/10.20960/nh.04249

Correspondence:

María Elena Herrera. Department of Pediatrics and Pediatric Surgery. Hospital Clínico de la Universidad de Chile. Facultad de Medicina. Universidad de Chile. C/ Dr. Carlos Lorca Tobar, 999. Independencia, Región Metropolitana. Chile
e-mail: meherrerag@uchile.cl

## INTRODUCTION

Bronchial asthma is one of the most common chronic diseases in childhood, ranking among the top 20 conditions worldwide for disability-adjusted life years in children (1). In Chile, a significant increase in the rate of hospitalization for asthma in children has been observed, reaching a figure of 7.8 per 10,000 in 2014 (2). On the other hand, hypovitaminosis D is a major health problem that affects more than 2 billion children and adults worldwide (3). Vitamin D (vitD) has multiple functions in the health of children and adolescents. In addition to its importance for the metabolism of calcium and phosphorus, it is an important immunomodulator and has effects on the development of autoimmune diseases, some cancers, insulin resistance, and cardiovascular health, respiratory tract infections and wheezings (4-6).

In recent years, numerous prospective and retrospective studies have been published that demonstrate an increased risk of exacerbations and hospitalizations for asthma in children with hypovitaminosis D (7,8). This is probably due to an immunomodulatory effect of vitD on T helper 1, 2 lymphocyte function and on regulatory T cells (9).

In a pilot study carried out 2 years ago at Hospital Clínico Universidad de Chile (HCUCH), we were able to verify that 62 % of asthmatic children who were hospitalized had hypovitaminosis D (deficit or insufficiency of vitD) and that this deficit was associated with poor control of the disease (10).

The objective of the present study was to evaluate the risk of hypovitaminosis (vitD < 30 ng/ml) and vitD deficiency (< 20 ng/ml) in a group of asthmatic children of similar socioeconomic status who were hospitalized at the HCUCH University Hospital and at the Roberto del Río Public Hospital (HRRIO), in relation to the same number of asthmatic schoolchildren who were controlled at the outpatient level in these hospitals, and who did not underwent hospitalization in the last 12 months prior to the study. Sociodemographic and clinical characteristics were analyzed and the association between hypovitaminosis D and nutritional status and severity of hospitalization was evaluated.

## MATERIAL AND METHODS

A descriptive, analytical, case-control study was carried out between May 2017 and May 2018. The sample size of 54 patients was calculated for each group considering a power of 80 % with a significance level of 0.05, and a difference of 27 percentage points in the frequency of hypovitaminosis D in hospitalized asthmatics (H) versus those treated as outpatients (A). The project was approved by the ethics committee of both hospitals.

Patients between 5 and 15 years of age were recruited, who were treated consecutively either as inpatients or as outpatients at the bronchopulmonary clinic of HCUCH and HRRIO. After signing an assent or informed consent form, a sociodemographic data survey and asthma control questionnaire were applied using the Asthma Control Test (ACT) (11,12). A complete physical examination and calculation of BMI (body mass index) was performed to then make a diagnosis of nutritional status according to the WHO 2007 curve (13). A blood sample was taken from the patients to measure the serum concentrations of vitD. Aliquots were processed in the HCUCH Endocrinology laboratory using the electro-chemiluminescence technique (14). Patients with hypovitaminosis D (vitD < 30 ng/ml) were treated, administering vitamin D3 cholecalciferol 2,000 IU per day for 2 months, as indicated by expert recommendation (15). Calcium intake and supplementation was not evaluated in this study.

A severity score was recorded for those children who required hospitalization due to an asthmatic crisis. The score included: total number of days of hospitalization, total number of days with oxygen requirement, maximum inspiratory fraction of oxygen ($FiO_2$max) reached, and need to transfer to the critical patient unit (mild score: 0-3, moderate: 4-6, severe: 7-14) (16).

Statistical calculations were performed using the Stata 14 package. The association between quantitative variables was assessed through the t-test and using the chi-squared test for categorical variables. Logistic regression was used to estimate the risk of deficiency and hypovitaminosis D, with a significance of $p < 0.05$.

This protocol was approved by the research ethics committee of HCUCH (Acceptance number, 874/17)

## RESULTS

A total of 117 subjects entered the study, 64 % male and 9 years old on average; 67 % of the patients were hospitalized during the months with the lowest exposure to UVB radiation (May to November). More than half of the patients presented excess malnutrition without significant differences according to group (H/A) or sex. In all, 55 % had poor control of their disease (ACT ≤ 19), with no differences in average score according to group. The majority had a diagnosis of allergic rhinitis, the highest percentage in A patients ($p < 0.05$). The high frequency of underdiagnosis of the disease stands out, which was higher in group H ($p < 0.05$). Most of the patients had moderate asthma at the time of recruitment, this percentage being significantly higher in group H.

We found a high frequency of hypovitaminosis D in the patients studied (vitD < 30 ng/ml). Although we did not find any differences in the frequency of hypovitaminosis D (deficiency and insufficiency) between the groups, the deficit (vitD < 20 ng/ml) in H patients was significantly higher, and the average level of vitD was significantly lower in this group of children (Table I). When performing the analysis separately according to UVB exposure, there were no differences in the mean concentration of vitD, nor in the percentages of hypovitaminosis according to group; however, in months with lower UVB light levels, the deficit of vitD in hospitalized patients triples the deficit in patients A ($p < 0.05$) (Table II). We did not find any significant differences in the percentage of hypovitaminosis D according to sex; however, the mean concentration of vitD was lower and the percentage of deficit was higher in men (Table III).

The characteristics of hospitalization can be seen in table IV. The average severity score achieved during hospitalization was 7 (moderate), with 48 % of the sample scoring severe. There were no differences in the mean concentration of vitD according to the severity score and according to each of its components (Fig. 1).

The risk of hypovitaminosis and vitD deficiency in hospitalized asthmatic children was determined in comparison with those who were controlled and did not undergo hospitalization in the previous year through 2 logistic regression models (Table IV). In the first model, adjusted according to age, sex, presence of obesity and lower UVB; and in the second model, adjusted according to age and UVB (variables that were statistically significant). No risk of hypovitaminosis D was found in hospitalized children in either of the 2 models; however, the deficit of vitD was 2.8 times higher in patients who were hospitalized (OR, 2.8; 95 % CI, 1.08-7.6, $p < 0.05$) adjusted according to sex, obesity, UVB and age. In the second model, the risk of vitD deficiency is also higher in H subjects compared to A subjects (OR, 2.8; 95 % CI, 1.07-7.5, $p < 0.05$). The risk of vitD deficiency increases by 20 % for each year that the age of the subjects increases (OR, 1.2; 95 % CI, 1.02-1.45, $p < 0.05$).

In the second model, the odds of vitD deficiency persists, it being higher in H subjects compared to A subjects (OR, 2.8; 95 % CI, 1.07-7.5, $p < 0.05$). In both models, a lower UVB implies a 3.3 to 3.7 times greater risk of having vitD deficiency.

**Table I.** Characterization of children with asthma treated at the Clinical University of Chile and Roberto del Río hospitals

| | Total | Hospitalized | Outpatients | *p* |
|---|---|---|---|---|
| n | 117 | 58 | 59 | |
| Age (years) X ± sd | 9.0 ± 2.7 | *8.5 ± 2.6* | *9.5 ± 2.7* | < 0.05 |
| Male gender (%) | 64.0 | 69.5 | 62.7 | ns |
| Hospital U. de Chile (%) | 43.5 | *64.7* | *35.2* | < 0.05 |
| Vitamin D (ng/ml) X ± sd | 25.0 ± 9.3 | *22.7 ± 8.6* | *27.2 ± 9.5* | < 0.05 |
| Hypovitaminosis D (%) (< 30 ng/ml) | 73.5 | 79.3 | 67.8 | NS |
| VitD deficiency (%) (< 20 ng/ml) | 27.3 | *27.9* | 16.9 | < 0.05 |
| Samples in months with lower UVB (%) | 53 | *67.3* | *37.3* | < 0.05 |
| Malnutrition due to excess (%) | 51.7 | 48.2 | 55.1 | ns |
| Overweight | 29 | 27.6 | 30.5 | ns |
| Obesity | 22.2 | 20.6 | 23.7 | ns |
| *Asthma severity (%)*<br>Mild<br>Moderate<br>Severe | <br>30.0<br>65.5<br>4.5 | <br>*0*<br>*91.4*<br>*8.6* | <br>*60.0*<br>*39.0*<br>*0* | < 0.05 |
| Asthma score (ACT) | 18.0 ± 3.8 | 18.0 ± 3.6 | 18.0 ± 4.0 | ns |
| Poor asthma control (%) (ACT ≤ 19) | 55.5 | 62.7 | 49.0 | ns |
| Allergic rhnitis (%) | 77.0 | *67.2* | *87.9* | < 0.05 |
| Passive smoking (%) | 51.0 | 48.2 | 53.4 | ns |
| Undiagnosed asthma (%) | 24.7 | *41.0* | *6.0* | 0.01 |

**Table II.** Serum concentration and percentage of deficit and hypovitaminosis D according to seasonality. Hypovitaminosis D < 30 ng/ml; deficiency < 20 ng/mL

| | Greater UVB Exposure (December-April) | | | Lower UVB Exposure (May-November) | | |
|---|---|---|---|---|---|---|
| | **Total** | **H** | **O** | **Total** | **H** | **O** |
| VitD (ng/ml) | *28.5 ± 9.2** | 27.5 ± 6.8 | 28.9 ± 10.3 | *21.8 ± 8.2** | 20.5 ± 8.5 | 24.2 ± 7.3 |
| Hypovitaminosis D (%) | *63.6** | 74.1 | 65.2 | *82.2** | 85.1 | 76.9 |
| Deficiency (%) | *14.5** | 22.5 | 17.3 | *38.7** | *55.5** | *15.3** |

*UVB: ultraviolet B radiation; H: hospitalized patients; O: outpatients. *p < 0.05.*

**Table III.** Distribution of nutritional status and VitD according to sex in schools with asthmatic children

| | **Boys** | **Girls** | ***p*** |
|---|---|---|---|
| n | 75 | 42 | |
| Malnutrition by excess (%) | 50.6 | 53.6 | Ns + jhy'y |
| Obesity (%) | 25.0 | 17.0 | ns |
| VitD (ng/ml) | *23.2* | *28.4* | < 0.01 |
| Hypovitaminosis D (%) | 78.6 | 64.2 | ns |
| VitD deficciency (%) | *33.3* | *16.6* | < 0.05 |

**Table IV.** Risk of hypovitaminosis D (< 30 ng/ml) and VitD deficit (< 20 ng/ml) in hospitalized asthmatic children

| **Risk of hipovitaminosis D** | **Model 1** | | | **Model 2** | | | |
|---|---|---|---|---|---|---|---|
| | **OR** | **95 % CI** | **p** | | **OR** | **95 % CI** | **p** |
| Hospitalized | 1.7 | 0.6-4.5 | ns | Hospitalized | 1.4 | 0.5-3.4 | ns |
| Age | 1.1 | 0.9-1.4 | ns | Lower UVB | 2.3 | 0.9-5.8 | ns |
| Male sex | 2 | 0.8-5.2 | ns | | | | |
| Obesity | 3.6 | 0.9-14 | Ns | | | | |
| UVB | 3.2 | 1.2-8.5 | p < 0.05 | | | | |
| Risk of vitamin D deficiency | OR | 95 % CI | | | OR | 95 % CI | |
| Hospitalized | *2.8** | 1.08-7.6 | < 0.05 | Hospitalized | *2.8** | 1.07-7.5 | < 0.05 |
| Age | *1.2** | 1.02-1.45 | < 0.05 | Age | *1.2** | 1.05-1.4 | < 0.05 |
| Male sex | 2.5 | 0.88-7.1 | ns | Lower UVB | *3.3** | 1.2-9.0 | < 0.05 |
| Obesity | 1.56 | 0.53-4.53 | ns | | | | |
| UVB | 3.7 | 1.38-10.14 | < 0.05 | | | | |

**p < 0.05. Hosmer-Lemeshow > 0.05 (appropriate goodness of fit). OR: odds ratio; CI: confidence interval; UVB: ultraviolet B radiation.*

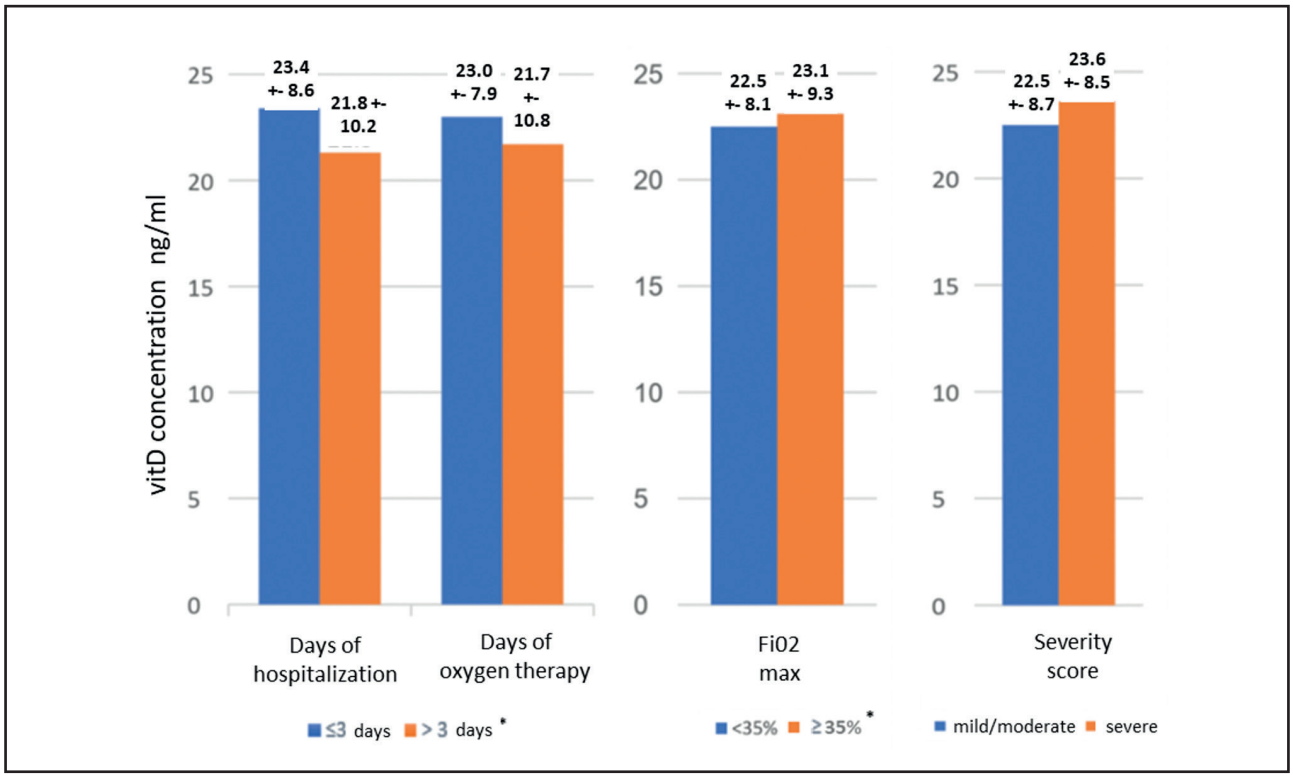


**Figure 1.**

Vitamin D according to hospitalization characteristics ($p > 0.05$).

## DISCUSSION

The main finding of our study was that hospitalized asthmatic subjects have a higher frequency of vitD deficiency, an association that disappears in the months of greater exposure to UVB radiation and increases in the months of less exposure. In inpatients the risk of having vitD deficiency is higher than that of outpatients, even after adjusting for seasonality and age. Few studies evaluate the frequency of deficiency and insufficiency of vitD in asthmatic patients who are hospitalized, and there are numerous studies that evaluate the concentration of vitD according to level of control, severity of asthma, and response to treatment. Bugadze, for example, found in a group of 50 Russian asthmatic schoolchildren a higher frequency of vitD deficiency in those with frequent and severe exacerbations compared to those with good control of the disease ($p < 0.05$) (17).

We found a high frequency of hypovitaminosis D (< 30 ng/ml) in the children studied (73.5 %). This result differs from that described in Costa Rica and Puerto Rico, where there is a much lower frequency than ours (28 % and 44 %, respectively), while the hypovitaminosis D rate found in Italian asthmatic children was 90.6 % (18,19). These differences could be explained by the different UVB exposures in these countries.

The high frequency of hypovitaminosis D found in our patients could be due to a low exposure to UVB light and/or a low intake of milk and fortified cereals, frequent conditions in the age group to which they belong (20,21). Numerous publications describe the relationship between vitD deficiency and increased risk of hospitalization for asthma. Brehm in Costa Rica finds that, as the concentration of vitD increases, a decrease in the risk of hospitalization is observed, after adjusting for age, sex, BMI-z and parental education (OR, 0.05; 95 % CI, 0.004-0.71; $p = 0.03$). This study also detected a decrease in the need for anti-inflammatory medication and bronchial hyperresponsiveness, variables that were not evaluated in our study (4). Other prospective cohort publications carried out in North American asthmatic children show that 35 % of them had hypovitaminosis D. After adjusting for age, sex, BMI, income, treatment received, and seasonality, it was observed that both deficit and insufficiency of vitD were associated with a higher risk of hospitalization or emergency service consultation (OR, 1.5; 95 % CI, 1.2-2.1; $p = 0.004$) (22).

In our study, the high prevalence of allergic rhinitis in H and A subjects stands out, a figure higher than that found in a study carried out in Japan (23) and in a multicenter study recently carried out in our country (24). Proper management of allergic rhinitis is very important, observing that this improves asthma control and exacerbations decrease (25).

Most of the asthmatic children in our study presented excess malnutrition, without differences between the group of hospitalized patients and that of outpatients, and without differences

according to sex. We did not find any association between obesity and a higher frequency of hospitalization; however, it is described that excess malnutrition is a factor that may worsen the clinical management of asthma. Tashiro observed that obesity was associated with an increase in the incidence and prevalence of asthma, and that the more overweight, the more severity increased (26). This association could be due to the fact that asthmatic children with malnutrition due to excess have a lower response to corticosteroids, have a higher degree of airway inflammation, alteration of the intestinal and pulmonary microbiome and often vitD deficiency.

In our work, we did not find any association between nutritional status and vitD concentration. This could be explained by poor asthma control in these patients, which could be associated with a short time spent in outdoor activities, with the consequent low sunlight exposure.

In contrast to these results, in a study carried out in Costa Rica it was verified that as BMI increases, the average concentration of vitD decreases (5).

The average days of hospitalization and the concentration of $O_2$ administered in our patients agrees with that described in the literature (27,8). Lastly, we found that serum VitD concentration was not associated with in-hospital evolution or with severity score in hospitalized subjects. In agreement with our findings, Iqbal found that in pediatric patients hospitalized for respiratory causes (66.7 % asthmatics) the concentration of vitD was not associated with severity of the disease (28). On the contrary, a study carried out in Concepción shows that vitD deficiency is frequent in children hospitalized in the Pediatric Critical Patient Unit (UPCP), and that this is associated with a greater probability of requiring mechanical ventilation, fluids and inotropic drugs (29).

Regarding the limitations of our work, it seems important to highlight that the power (72 %) to detect differences between the subjects with vitD deficiency was lower than expected. Furthermore, most of the hospitalized patients were recruited during the months of lower UVB exposure, which may have influenced the concentration of vitD. On the other hand, one of the centers participating in this study does not have a UPCP, which could have limited the admission of patients with greater severity. An element to be highlighted is that this study is the first in Chile to compare the serum concentration of vitD with associated factors in pediatric, hospitalized and outpatient asthmatic patients. Given the results obtained, it seems important to consider the systematic measurement of vitD in all asthmatic patients, especially in those who are hospitalized. We recommended the systematic supervision of intake and measurements of vitD blood levels before supplementing it. More clinical trials and cohort studies in asthmatic children are still needed to determine the optimal dose to be supplemented, the cut-off point to define the deficiency of vitD, as well as the clinical role it produces in asthmatic patients with hypovitaminosis when supplemented with this vitamin. On the other hand, it seems important to us to insist that asthmatic children perform physical activity outdoors to allow greater exposure to UVB light.

## CONCLUSIONS

In all, 73.5 % of asthmatic children who are controlled in HCUCH and HRRio have vitD deficiency or insufficiency. VitD deficiency is 2.8 times higher in hospitalized patients than in outpatients. This risk increases with age and in the months with less UVB exposure. Clinical trials and cohort studies are needed to evaluate the optimal doses required by asthmatic children to achieve vitD concentrations and determine the clinical changes associated with vitamin supplementation.

## REFERENCES


1. Serebrisky D, Wiznia A. Pediatric Asthma: A Global Epidemic. Ann Glob Health 2019;85(1):6. DOI: 10.5334/aogh.2416
2. Herrera AM, Cavada Ch G, Mañalich MJ. Pediatric asthma hospitalization in Chile: 2001-2014. Rev Chil Pediatr 2017;88(5):602-7. DOI: 10.4067/S0370-41062017000500005
3. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357(3):266-81. DOI: 10.1056/NEJMra070553
4. Hossein-Nezhad A, Holick MF. Vitamin D for health: a global perspective. Mayo Clin Proc 2013;88(7):720-55. DOI: 10.1016/j.mayocp.2013.05.011
5. Wang Q, Ying Q, Zhu W, Chen J. Vitamin D and asthma occurrence in children: A systematic review and meta-analysis. J Pediatr Nurs 2022;62:e60-8. DOI: 10.1016/j.pedn.2021.07.005
6. Cai B, Luo X, Zhang P, Luan Y, Cai X, He X. Effect of vitamin D supplementation on markers of cardiometabolic risk in children and adolescents: A meta-analysis of randomized clinical trials. Nutr Metab Cardiovasc Dis 2021;31(10):2800-14. DOI: 10.1016/j.numecd.2021.06.013
7. Scheffer-Rath ME, Boot AM. The Many Facets of Vitamin D in the Pediatric Population. Pediatr Endocrinol Rev 2020;17(4):293-301. DOI: 10.17458/per.vol17.2020.srb.vitamindpediatricpopulation
8. Pojsupap S, Iliriani K, Sampaio TZ, O'Hearn K, Kovesi T, Menon K, et al. Efficacy of high-dose vitamin D in pediatric asthma: a systematic review and meta-analysis. J Asthma 2015;52(4):382-90. DOI: 10.3109/02770903.2014.980509
9. May E, Asadullah K, Zügel U. Immunoregulation through 1,25-dihydroxyvitamin D3 and its analogs. Curr Drug Targets Inflamm Allergy 2004;3(4):377-93. DOI: 10.2174/1568010042634596
10. Herrera ME, Herrera AM, Rojas A, Muñoz M. Hypovitaminosis D and malnutrition by excess in hospitalized asthmatic children. Neumol Pediatr 2021;16(2):85-9.
11. Vega JM, Badia X, Badiola C, López-Viña A, Olaguíbel JM, Picado C, et al. Validation of the Spanish version of the asthma control test (ACT). J Asthma 2007;44:867-72. DOI: 10.1080/02770900701752615
12. Pérez-Yarza EG, Castro-Rodríguez JA, Villa JR, Garde J, Hidalgo FJ. Validation of a Spansih version of the childhood asthma control test (SC-SCT) for use in Spain. An Pediatr (Barc) 2015;83:94-103. DOI: 10.1016/j.anpedi.2014.10.031
13. Norma técnica de evaluación nutricional del niño de 6 a 18 años. Rev chil nutr 2004;31(2):128-37.
14. Batista MC, Menegat FD, Ferreira CES, Faulhaber ACL, Campos DALS, Mangueira CLP. Analytical and clinical validation of the new Roche Elecsys Vitamin D Total II assay. Clin Chem Lab Med 2018;56(12):e298-e301. DOI: 10.1515/cclm-2018-0406
15. Pludowski P, Holick MF, Grant WB, Konstantynowicz J, Mascarenhas MR, Haq A, et al. Vitamin D supplementation guidelines. J Steroid Biochem Mol Biol 2018;175:125-35. DOI: 10.1016/j.jsbmb.2017.01.021
16. Larrañaga CL, Ampuero SL, Luchsinger VF, Carrión FA, Aguilar NV, Morales PR, et al. Impaired immune response in severe human lower tract respiratory infection by respiratory syncytial virus. Pediatr Infect Dis J 2009;28(10):867-73. DOI: 10.1097/INF.0b013e3181a3ea71
17. Bugadze L, Manjavidze N, Jorjoliani L. Asthma control status and lung function in relation to vitamin D level in children with bronchial asthma. Georgian Med News 2018;(283):115-8.
18. Brehm JM, Acosta-Pérez E, Klei L, Roeder K, Barmada M, Boutaoui N, et al. Vitamin D insufficiency and severe asthma exacerbations in Puerto Rican children. Am J Respir Crit Care Med 2012;186(2):140-6. DOI: 10.1164/rccm.201203-0431OC

19. 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(3):437-41. DOI: 10.1016/j.jpeds.2010.08.043
20. Klinker CD, Schipperijn J, Kerr J, Ersbøll AK, Troelsen J. Context-Specific Outdoor Time and Physical Activity among School-Children Across Gender and Age: Using Accelerometers and GPS to Advance Methods. Front Public Health 2014;11;2:20. DOI: 10.3389/fpubh.2014.00020
21. Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ. Prevalence of vitamin D deficiency among healthy adolescents. Arch Pediatr Adolesc Med 2004;158(6):531-7. DOI: 10.1001/archpedi.158.6.531
22. Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW, Strunk RC, Zeiger RS, et al. Childhood Asthma Management Program Research Group. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. J Allergy Clin Immunol 2010;126(1):52-8. DOI: 10.1016/j.jaci.2010.03.043
23. Yu CL, Huang WT, Wang CM. Treatment of allergic rhinitis reduces acute asthma exacerbation risk among asthmatic children aged 2-18 years. J Microbiol Immunol Infect 2019;52(6):991-9. DOI: 10.1016/j.jmii.2018.10.003
24. Herrera AM, Brand P, Cavada G, Koppmann A, Rivas M, Mackenney J, et al. Hospitalizations for asthma exacerbation in Chilean children: A multicenter observational study. Allergol Immunopathol (Madr) 2018;46(6):533-8. DOI: 10.1016/j.aller.2018.02.006
25. Thomas M. Allergic rhinitis: evidence for impact on asthma. BMC Pulm Med 2006;6(Suppl 1):S4. DOI: 10.1186/1471-2466-6-S1-S4
26. Tashiro H, Shore SA. Obesity and severe asthma. Allergol Int 2019;68(2):135-42. DOI: 10.1016/j.alit.2018.10.004
27. Lee DS, Gross E, Hotz A, Rastogi D. Comparison of severity of asthma hospitalization between African American and Hispanic children in the Bronx. J Asthma 2020;57(7):736-42. DOI: 10.1080/02770903.2019.1609981
28. Iqbal S, Mosenkis EV, Jain P, Wiles A, Lerner J, Benton AS, et al. Vitamin d in pediatric inpatients with respiratory illnesses. Hosp Pediatr 2013;3(4):371-6. DOI: 10.1542/hpeds.2013-0001
29. Bustos BR, Rodríguez-Nuñez I, Peña Zavala R, Soto Germani G. Vitamin D deficiency in children admitted to the pediatric intensive care unit. Rev Chil Pediatr 2016;87(6):480-6. DOI: 10.1016/j.rchipe.2016.05.008