

An Overview about Vitamin-D in Children with Bronchial Asthma and its Relation to Severity of the Disease: Review Article

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ABSTRACT

Background: Bronchial asthma is a prevalent health problem. Asthma is characterized by chronic airway inflammation that is thought to have both genetic and environmental roots. Low vitamin D levels have been suspected for a long time as a possible cause of asthma. Lack of vitamin D has been connected to the rising incidence of asthma seen in recent decades.

Objective: Assessment of vitamin D in children with bronchial asthma and its relation to severity of the disease.

Methods: Vitamin D and bronchial asthma were searched for on Science Direct, Google Scholar, and PubMed. The authors also reviewed the relevant literature, however only the most recent or comprehensive study from April 2004 to August 2021 was included. There are no translation resources available, thus non-English documents are out. Unpublished articles, oral presentations, conference abstracts, and dissertations were not included because they were not considered to be part of major scientific projects.

Conclusion: Whether or not vitamin D is associated with asthma and allergies is still up for debate. A higher risk of vitamin D deficiency has been associated with asthma, according to certain studies, Vitamin D supplements may increase allergy risk, according to several studies.

Keywords: Vitamin-D, Bronchial Asthma, Disease severity.

INTRODUCTION

Variable reversible and recurrent symptoms due to airflow restriction, bronchial hyper reactivity, and underlying inflammation characterize asthma, a common chronic condition of the airways. Patients, their families, and the community as a whole feel its effects through things like missed days of work or school, lower quality of life, increased likelihood of hospitalization or even death. As a result, the best available information has been used to produce international guidelines to aid clinicians in their management of asthma ⁽¹⁾.

Asthma is a worldwide epidemic that affects people of all ages. The number of countries where it is a problem is growing. Although asthma-related deaths and hospitalizations have decreased in certain nations, the disease continues to cost economies and families dearly due to missed work and school days (particularly in the case of children) and asthma-related disruptions in the home ⁽²⁾.

One of the most prevalent lifelong diseases in kids is asthma. The effects of asthma on a child and his family, as well as the cost of medical treatment, make asthma a major public health issue that places a heavy financial burden on society ⁽³⁾.

Asthma affects over 6 million American children, or 8.3% of the total, disease rates in 2018 were quite low, per CDC statistics. Males exhibited a slightly higher frequency than females did among both children and adults. The rate was higher in low-income communities and among black children ⁽⁴⁾.

A thorough research found that about 7.5% of Middle Eastern youngsters suffer from asthma. Prevalence ranged greatly, from 1% to 22%, among nations. The

effects of asthma on children and their caretakers are significant. Physical, emotional, and academic outcomes for asthmatic children have all been proven to be lower than for children without the condition. Direct costs to the health care system, such as those associated with hospitalizations, doctor visits, and medication, and indirect costs to society, such as lost productivity, make asthma a major economic burden. About \$56 billion is anticipated to be spent in the United States, with the majority of that going toward health care expenses. Factors that increase the risk of death from asthma include having a history of severe asthma requiring intubation and mechanical ventilation, being recently hospitalized or visiting an emergency room for asthma, using or discontinuing oral corticosteroids (a marker of event severity), not using inhaled corticosteroids, having a history of psychiatric disease or psychosocial problems, and not taking asthma medications as prescribed. Asthma is diagnosed by looking for a specific set of symptoms in addition to the known limitation in expiratory airflow. Asthma diagnosis is best recorded at the time of initial presentation, since confirmation can be challenging after controller medication has begun ⁽⁵⁾.

Children's health and development rely heavily on vitamin D because it is necessary for strong bones and may also contribute to other aspects of overall health ⁽⁶⁾. Vitamin D ensured adequate intestinal calcium absorption from food sources. Consequently, it plays a pivotal role in the maturation and upkeep of a calcified mammalian skeleton. Vitamin D, which can be gotten from diet or the sun, is still necessary for most people to have strong bones ⁽⁷⁾.

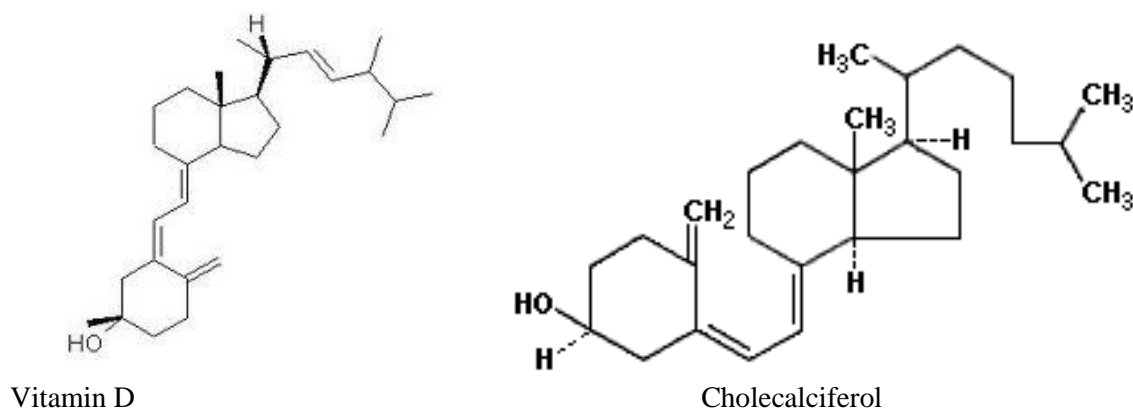


Figure (1): Vitamin D structure ⁽⁷⁾.

Before 1998, a low 25-hydroxyvitamin D [25(OH)D] blood level was thought to indicate vitamin D deficiency ⁽⁸⁾. Inadequate vitamin D levels are a worldwide epidemic. Many kids around the world don't get enough vitamin D. The decline in milk consumption, the rise in the usage of sunscreen when outside, and the epidemic of obesity were blamed ⁽⁹⁾. Where vitamin D is not added to foods, including in Europe, China, India, the Middle East, and South America, vitamin D deficiency and insufficiency are very common. Thirty percent of youngsters around the world are thought to have inadequate vitamin D levels ⁽¹⁰⁾.

The widespread vitamin D deficiency problem can be traced back to the widespread failure to recognise that most children's primary source of vitamin D has been and still is outdoor sun exposure. Vitamin D is a nutrient that is rarely found in diet. Salmon, mackerel, and herring are examples of oily fish, whereas sun-dried mushrooms and cod liver oil are examples of foods that have been exposed to sunshine ⁽⁸⁾.

Vitamin D and asthma:

Vitamin D deficiency may be a result of globalization, urbanisation, and the spread of Western lifestyles. Most people don't get enough vitamin D because they spend too much time indoors, where they aren't subjected to the sun ⁽¹¹⁾.

It is still unclear what impact vitamin D plays in asthma. A correlation between asthma and vitamin D had been hypothesized by a small number of cross-sectional studies. The risk of asthma attacks, hospitalization, and emergency department visits was higher in children with asthma who had low serum 25(OH)D levels, and so was the likelihood that their lung function would deteriorate. Clinical research conducted in recent years have shown that vitamin D supplementation can help people with asthma ⁽¹²⁾.

Evidence from Observational Studies:

Fifty-three percent of the 75 Italian children with asthma in the cross-sectional study had vitamin D deficiencies. Recent research involving 4,999 persons in

Denmark showed conflicting results, despite previous research studying association between low 25(OH)D levels and increased risk of developing asthma and allergy symptoms. The serum 25(OH)D levels of children aged 6 at the beginning of the study were found to be predictive of asthma-related symptoms (uncontrolled asthma and lung function) over a 14-year follow-up period ⁽¹³⁾.

The severity of asthma attacks has been linked to low levels of vitamin D, according to observational studies. The research' limited sample sizes, bias (selection bias), and confounding factors (physical activity, sex, age, etc.) make it difficult to draw conclusions about their association. All of these caveats may have contributed false possible correlation between vitamin D and asthma ⁽¹²⁾.

Asthma was found to be five times more common in children whose mothers' serum 25(OH)D concentrations were above 75 nmol/L by the time the children reached the age of 9. Studies involving more than 750 mother-child couples in Finland and Japan have found that prenatal vitamin D supplementation protects against childhood wheeze. Vitamin D was also assessed late in pregnancy ⁽¹⁴⁾.

It is important to exercise caution when comparing study results because of the studies' many flaws, such as insufficient sample sizes, low retention rates, and unreliable methods for determining vitamin D levels in blood serum. Contradictory evidence links increased 25(OH)D to lower asthma rates, and research showing vitamin D's direct impact in asthma development are needed ⁽¹⁵⁾.

Recent studies have looked into whether vitamin D affects the development of asthma and allergic reactions. Vitamin D has been demonstrated to have both short- and long-term effects on the immune system development and function of pregnant women and their children. Recent research suggests that vitamin D may influence foetal lung development ⁽⁹⁾.

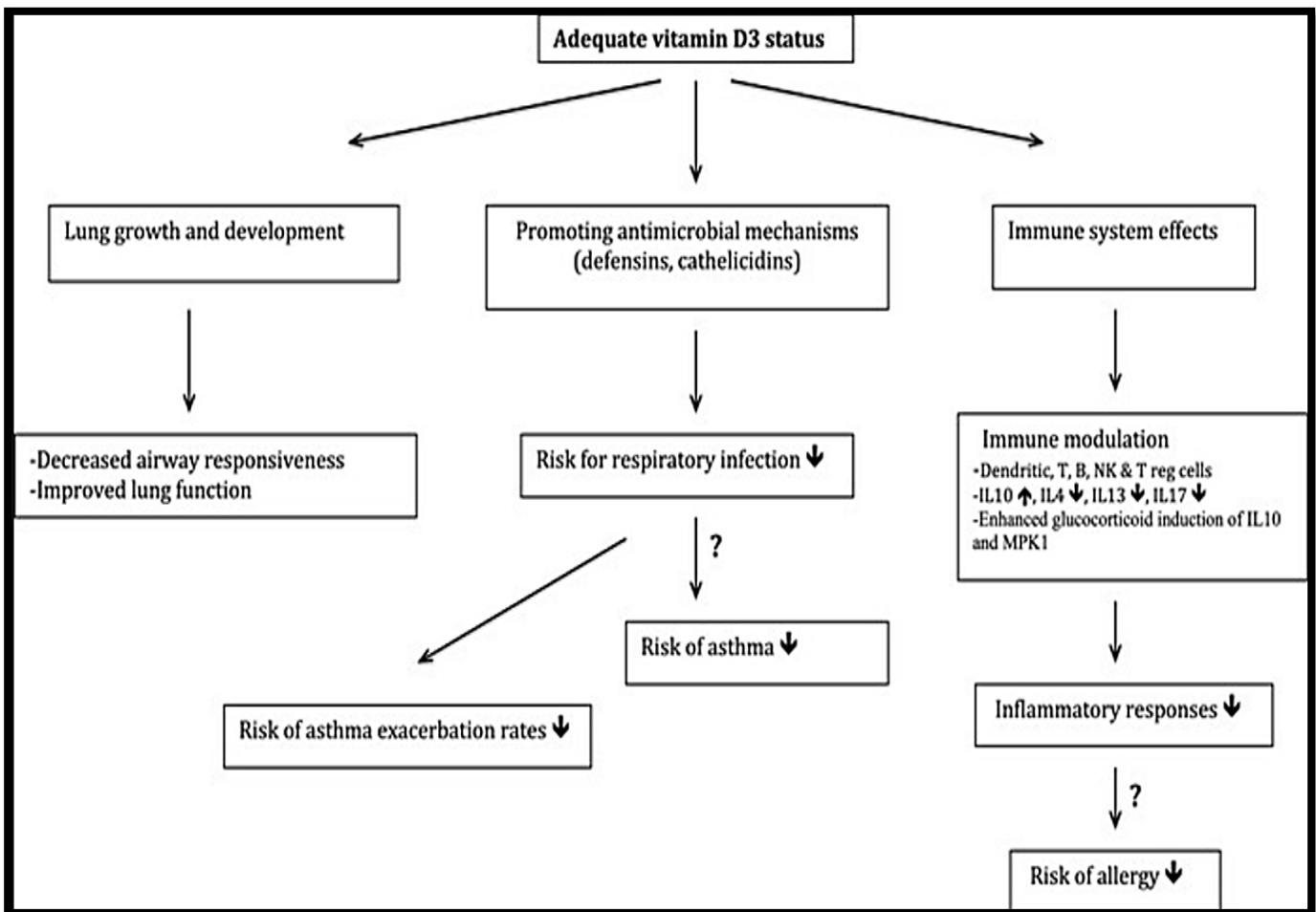


Figure (2): Possible role of vitamin D among the aetiology of asthma and allergic reactions ⁽¹⁴⁾.

Multiple pathways into adult asthma and allergy development may be influenced by vitamin D. Antimicrobial protein production like cathelicidin and beta defensins has been linked to sufficient vitamin D status, which may boost the body's ability to deal with respiratory infections in young children. Because of this, it's possible that respiratory virus infections and the accompanying inflammation they generate will be reduced. A mother's vitamin D status after giving birth may affect her child's respiratory and immune system development and function ⁽¹⁶⁾.

Since vitamin D has been demonstrated to affect developing foetuses, it follows that a mother's vitamin D level might determine her child's susceptibility to developing asthma. The Japanese cohort study found that children with higher vitamin D intakes from their mothers during pregnancy had a lower risk of developing wheezing when they were 16 to 24 months old. Previous studies using a meal frequency questionnaire to examine mothers' intake of vitamin D indicate the significance of pregnancy intake of vitamin D. The lack of direct

measurement of vitamin D levels is a weakness shared by this study and others like it ⁽¹⁴⁾.

Morales *et al.* ⁽¹⁷⁾ investigated a population-based sample of 1,724 Spanish kids from four different regions. Infancy respiratory infections were negatively associated with maternal 25OHD levels, while wheezing when aged from 1 to 4 years. Since a newborn's vitamin D level is determined by the level in the mother's bloodstream, studies have been conducted to determine whether or not there is a link between maternal vitamin D levels and the risk of negative childhood outcomes.

Camargo and colleagues ⁽¹⁸⁾ examined 25OHD in 922 infants in a cohort Study, 25OHD levels in cord blood were not associated with acute asthma by age 5 years, but they were inversely related to wheezing infections before that age. Consistent with the results of the study by **Morales *et al.*** ⁽¹⁷⁾ further examination of the available evidence reveals that vitamin D may be linked to reduced asthma symptoms.

Estimates of consumption using FFQs represent greater chronic intakes, which may explain why these studies have shown conflicting results when comparing vitamin D intake estimates to others that have explored vitamin D status. Furthermore, bronchial hyperresponsiveness and a reaction to bronchodilators, two objective markers of asthma, were not obtained. Until the results of planned clinical trials establish or deny the link between high vitamin D levels in cord blood and a higher risk of allergic sensitization, it may be prudent to hold off on taking large doses of vitamin D as a supplement ⁽⁹⁾.

Vitamin D's long-term effects on asthma and allergies have been the subject of numerous studies. Studies comparing children with and without asthma found that children with asthma had a greater rate of vitamin D deficiency compared to controls in several populations (African Americans, Qataris, and Iranians).

The National Health and Nutrition Examination Survey has been used for the second time in this investigation (NHANES). Studying 3,136 children and adolescents, researchers discovered that low vitamin D levels were associated with increased sensitivity to 11 of

17 allergens after controlling for relevant confounders. The patient developed sensitivities to numerous allergens, both indoor and outdoor, as well as peanuts and shrimp ⁽¹⁴⁾.

Vitamin D Deficiency and Disease Severity:

Possible vitamin D-related pathways for ameliorating asthma and allergy symptoms were analysed. Effects on immunological cells, enhanced infection control or prevention, reduced inflammatory responses, and reversal of steroid resistance are just few of these processes.

The amount of smooth muscle in the airways can be affected by vitamin D as well. The average age of the 86 kids **Gupta et al.** ⁽¹⁹⁾ studied was 11.6. This included 36 kids with severe, therapy-resistant asthma, 26 kids with mild asthma, and 24 kids without asthma. In 19 patients with severe, therapy-resistant asthma with usable endobronchial biopsy specimens, Airway smooth muscle mass was inversely associated to vitamin D levels. Consistent with prior research showing that vitamin D can inhibit the production of airway smooth muscles, this has implications for airway remodeling ⁽¹⁹⁾.

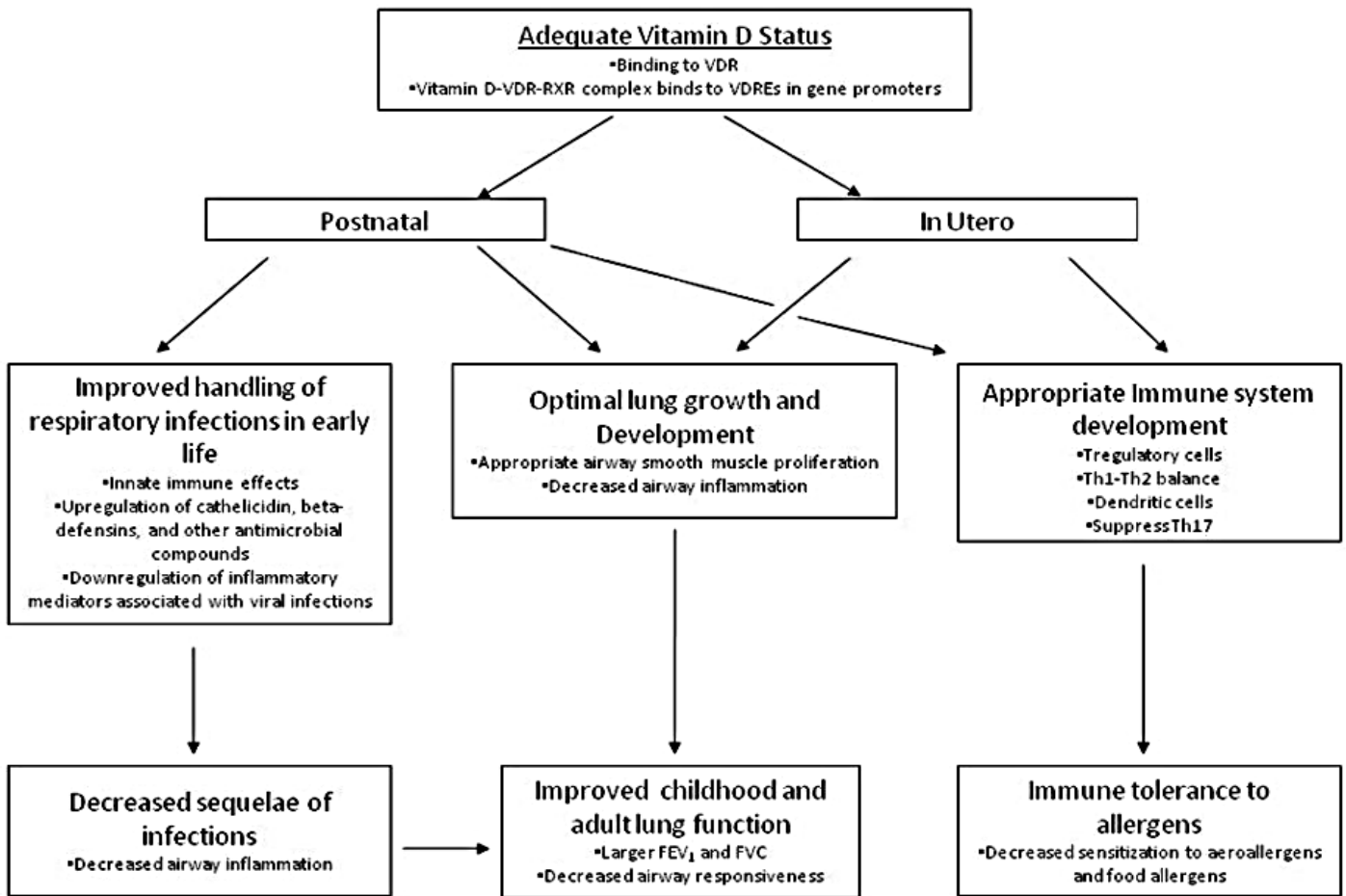


Figure (3): Vitamin D role in reducing asthma exacerbation risk and how it works ⁽¹⁴⁾.

Lack of vitamin D has been linked to an increase in asthma symptoms, according to the research. Data from the Childhood Asthma Management Program (CAMP), a randomised trial of inhaled budesonide, nedocromil, and placebo, showed that children with low vitamin D levels (30 ng/ml) were more likely to experience severe asthma exacerbations requiring visits to the emergency room or hospitalization. Inhaled budesonide medication resulted in a quicker recovery time for the children in the treatment group ⁽²⁰⁾.

The majority of vitamin D metabolite transfer is mediated by vitamin D binding protein [DBP, also known as group-specific component (Gc)] (including 25OHD). Albumin isn't the only protein that can act as a transporter. Although vitamin D binding protein (DBP) has a role in immunological regulation, it has not been linked to asthma and allergies until now ⁽²¹⁾.

Lee and colleagues ⁽²²⁾ found that DBP levels in bronchoalveolar fluid were found to be considerably greater in 67 asthmatics compared to 22 controls. In a mouse model of asthma generated by ovalbumin sensitization and challenge, treatment with an anti-DBP antibody reduced airway hyperreactivity, inflammation, and levels of eotaxin, IL-4, IL-5, IL-13, and interferon- in a dose-dependent manner. Vitamin D insufficiency may be predicted by polymorphisms in the DBP gene (Gc),

however the significance of this finding is still debatable. Finally, it has been established that DBP can control the 25OHD bioavailability in cells. A causal link between vitamin D, DBP, and/or Gc polymorphisms and asthma and allergy symptoms has not yet been established, but this needs to be investigated further ⁽²²⁾.

CONCLUSION

Whether or not vitamin D is associated with asthma and allergies is still up for debate. A higher risk of vitamin D deficiency has been associated with asthma, according to certain studies, Vitamin D supplements may increase allergy risk, according to other studies.

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