

Vitamin D Deficiency and Allergic Rhinitis in Children: A Narrative Review

Javad Ghaffari,¹ Alireza Ranjbar,^{2,3,4,*} and Annegret Quade²

¹Mazandaran Pediatric Infectious Diseases Research Center, Mazandaran University of Medical Sciences, Sari, IR Iran

²Research Institute of Interventional Allergology and Immunology, Bonn, Cologne, Germany

³Allergy Research Center, Mashhad University of Medical Sciences, Mashhad, IR Iran

⁴Immunology, Asthma and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, IR Iran

*Corresponding Author: Alireza Ranjbar, Research Institute of Interventional Allergology and Immunology, Bonn, Cologne, Germany. Tel: +49-228636737, Fax: +49-228651417, E-mail: ranjbar@iiai.de

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Context: Allergic diseases such as allergic rhinitis (AR) and immune-mediated inflammatory diseases are the most common chronic diseases among children. Although the cause of AR has yet to be clearly identified, genetic and environmental factors are known to play an important role in the development of the disease.

Evidence Acquisition: In a more recent classification, AR is categorized as intermittent and permanent. Vitamin D has a known and important role in the absorption of calcium and preservation of bone density. The prevalence of vitamin D deficiency in children is reported to be between 30% and 50% in the world. Vitamin D confers the growth and development of the immune system including the development of regulatory T cells.

Results: Two-thirds of the reviewed articles show a correlation between serum levels of vitamin D and allergic diseases, while the remaining ones demonstrate no correlation between vitamin D and AR and some even report a rise in the incidence of AR following the use of vitamin D supplement.

Conclusions: It seems that further clinical trials and meta-analytic studies are necessary to confirm this correlation. The present study aimed at reviewing vitamin D deficiency in children with AR.

Keywords: Rhinitis; Allergic; Vitamin D; Children

1. Context

1.1. Allergic Rhinitis

Allergic rhinitis (AR) is one of the most common chronic diseases in children characterized by the symptoms of nasal congestion, rhinorrhea, sneezing, and nasal itching (1). Although AR is not a life-threatening disease, it has a significant influence on the quality of life of the patients and imposes a great economic burden on family and society. Several disorders such as hypochondriasis, hysteria, depression, psychasthenia, and social introversion are more frequent among allergic patients than in the general population (1). Because of geographical and aero-allergen differences, the prevalence of AR varies among countries around the world (2-5).

Even though the cause of AR has not been clearly identified, genetic, and environmental factors are known to play an important role in the development of the disease (6). For example, FOXP33279 AA genotype is more common in AR patients. Also, there is a higher association between polymorphism in FOXP3 gene and susceptibility to

AR (7). In a more recent classification, AR is categorized as mild-intermittent, moderate-severe intermittent, mild-persistent, and moderate-severe persistent (Figure 1) (8).

AR is a type-I immunologic reaction characterized by watery rhinorrhea, sneezing, nasal congestion, and itching. The prevalence of the disease has increased during the last decades (Figures 2 A and 2 B) (9, 10).

According to an evaluation by the international study of asthma and allergy in childhood (ISAAC), the prevalence of AR was 11.9% among Iranian children aged 6 - 7 years and 21.2% in children aged 13 - 14 years, with an average of 17.13% (10). The prevalence of AR is relatively high in the rural areas of Iran (18.1%) (6). Late complications of AR include sleep apnea, oral breathing, malocclusion of jaws, and infectious and/or serous otitis media. As is shown in Figure 3, from Bousquet et al. (11) and Table 1 (9), the treatment of AR, in the first step, is to avoid exposure to sensitizing agents. Drug therapies are composed of antihistamine, intranasal corticosteroids, decongestants, and finally immunotherapy (9, 11).

1.2. Vitamin D

Vitamin D plays a known and important role in the absorption of calcium and preservation of bone density. Vitamin D deficiency results in rickets in children. It is estimated that about one billion people suffer from vitamin D deficiency around the world (12). The prevalence of vitamin D deficiency in children is reported to be between 30% and 50% in the world (13, 14). Vitamin D contributes to the growth and development of the immune system, including the development of regulatory T cells. It provides a balance between Th1 and Th2 cells, dendritic cells, and Th17 cells in the embryonic period. It also has an important role in the growth and development of the lungs after birth or in newborns, which is influenced by the proliferation of the respiratory tract smooth muscles and the decrease in the inflammatory process of these muscles. Vitamin D can decrease the incidence of the inflammatory and infectious diseases of the respiratory tract, improve the lung function, lessen the sensitivity of the respiratory tract response, and alleviate hypersensitivity to aeroallergens and diet (15, 16).

The most active metabolite of vitamin D is 1, 25-dihydroxyvitamin D (calcitriol), which has a known effect on the immune system and airway functions. Ninety percent of vitamin D is produced following exposure to sunlight (UVB). The serum level of 25-dihydroxyvitamin D is an established biomarker for determining vitamin D status (17). However, multiple studies have shown a relation between vitamin D levels and atopic disorders (18-21).

1.3. Vitamin D and Immune System

The role of vitamin D in the regulation of the immune system was first recognized through the identification of vitamin D receptors on nearly all cells of the immune system (22, 23). Vitamin D impacts both innate and adaptive immune systems. It blocks the expression of the Toll-like receptor (TLR) on monocytes, inhibits proinflammatory cytokine production, induces antimicrobial peptide synthesis, and affects T-cell activation and function of antigen-presenting cells. It may reduce Th1 cytokine secretion, with there being reports of both increased and decreased expressions of Th-2 cytokines IL-4, IL-5, and IL-10, and modulate the immune system through the induction of Cd4+ CD25+ regulatory T cells (Tregs) (24-28).

It can be concluded that the immunomodulatory effect of vitamin D may influence allergic illnesses positively. The aim of this study was to review vitamin D deficiency in children with AR.

2. Evidence Acquisition

To review vitamin D deficiency and AR, as an immune-mediated inflammatory disease in children, we searched several databases such as PubMed and Google Scholar using the following keywords: vitamin D defi-

ciency, allergic rhinitis, and children. We considered abstract and/or full text papers in the English language without a limited time. Herein, the qualitative results derived from the reviewed articles are presented and discussed.

3. Results

3.1. A Review of Literature Related to Vitamin D Deficiency and Allergic Rhinitis

Vitamin D deficiency may have a role in increasing the prevalence of allergic diseases such as AR. Also, it has been estimated that allergic diseases may be related to lower serum concentrations of 25-hydroxyvitamin D (29-31).

Some studies have revealed a correlation between vitamin D deficiency and allergic diseases (15, 29-32), while some others have found no association between these two variables (33, 34).

In a study by Bener et al. the prevalence of vitamin D deficiency among patients with AR was 18.5% versus 10.5% in healthy people. AR has been reported more frequently in children with higher sunlight exposure despite receiving more vitamin D. Additionally, a higher correlation has been reported between AR and asthma in children receiving cod liver supplement (34, 35). Furthermore, vitamin D deficiency is more common in the mothers of children with AR than in healthy children (35, 36).

It is a fact that vitamin D status is dependent on exposure to the sun and duration of exposure, diet and supplement use, latitude, season, age, skin color, and coverage of the skin. Vitamin D deficiency is also associated with dark-colored skin and low exposure to sun light (37).

A study by Ehlal et al. showed that a reduced vitamin D serum level was more frequent among children with allergic diseases, although they had a higher serum IgE level. The incidence of severe vitamin D deficiency was significantly higher in children with AR than in healthy children (38).

In summary, vitamin D plays an important role in decreasing sensitivity to allergens. Previous studies have revealed that sensitivity to allergens is higher among children with vitamin D deficiency. Vitamin D deficiency is also associated with increased serum IgE levels (30). The results of previous therapeutic studies on allergic diseases such as AR have demonstrated that the use of vitamin D supplement can decrease the severity of allergic diseases. This also indicates a correlation between vitamin D and allergic diseases. Researchers have found significant correlations between the severity of obesity, weight gain, and allergic diseases. Allergic diseases are more common in obese children and children with weight gain because in these subjects, the levels of adiponectin and vitamin D decrease, whereas the level of leptin increases (39).

Recent cohort studies have shown different results

about the association between maternal vitamin D intake during pregnancy and the risk of childhood allergic diseases (40-42). In a study by Erkkola et al. it was concluded that increasing maternal vitamin D intake during pregnancy was inversely associated with allergic diseases in 5-year-old children and with decreasing asthma and AR in the childhood period (43). A primary study in 1966 showed that the use of vitamin D supplement by the first year of life caused increased risk of allergic diseases like AR at the age of 31 years (44). In contrast, Wawro and Hollams found no relation between serum levels of 25-hydroxyvitamin D and AR in children (45, 46). Likewise, Yao et al. found no cor-

relation between allergic diseases and serum levels of 25-hydroxyvitamin D among Asian children (47). Interestingly, Rothers et al. demonstrated that lower serum concentrations of vitamin D in the blood cord of the fetus were associated with the increasing prevalence of AR and aeroallergen sensitization in children (48). Wjst et al. showed that there was a relation between increased AR and low levels of vitamin D (49).

The limitation of the present review is that it is a narrative study. Accordingly, future systematic and/or meta-analytic studies are required to fully investigate the association between AR and vitamin D deficiency in childhood (50).

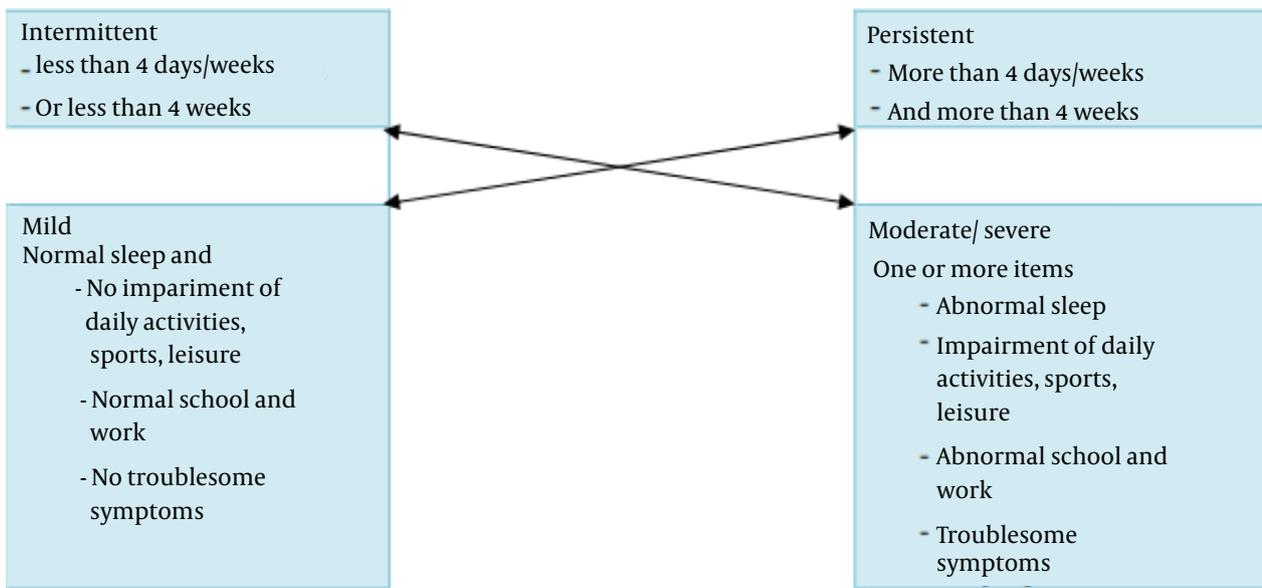


Figure 1. Allergic Rhinitis and Its Impact on Asthma (ARIA) Classification of Allergic Rhinitis

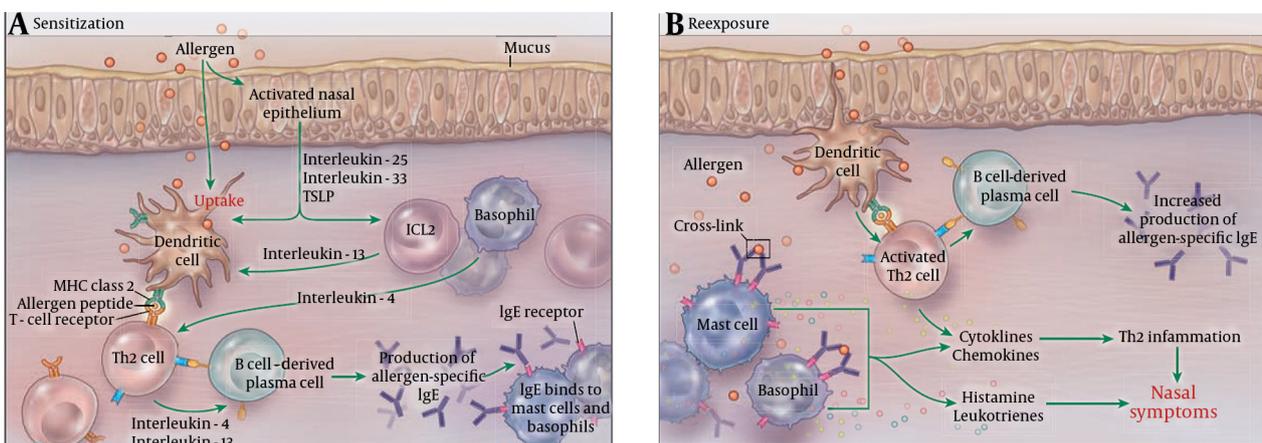
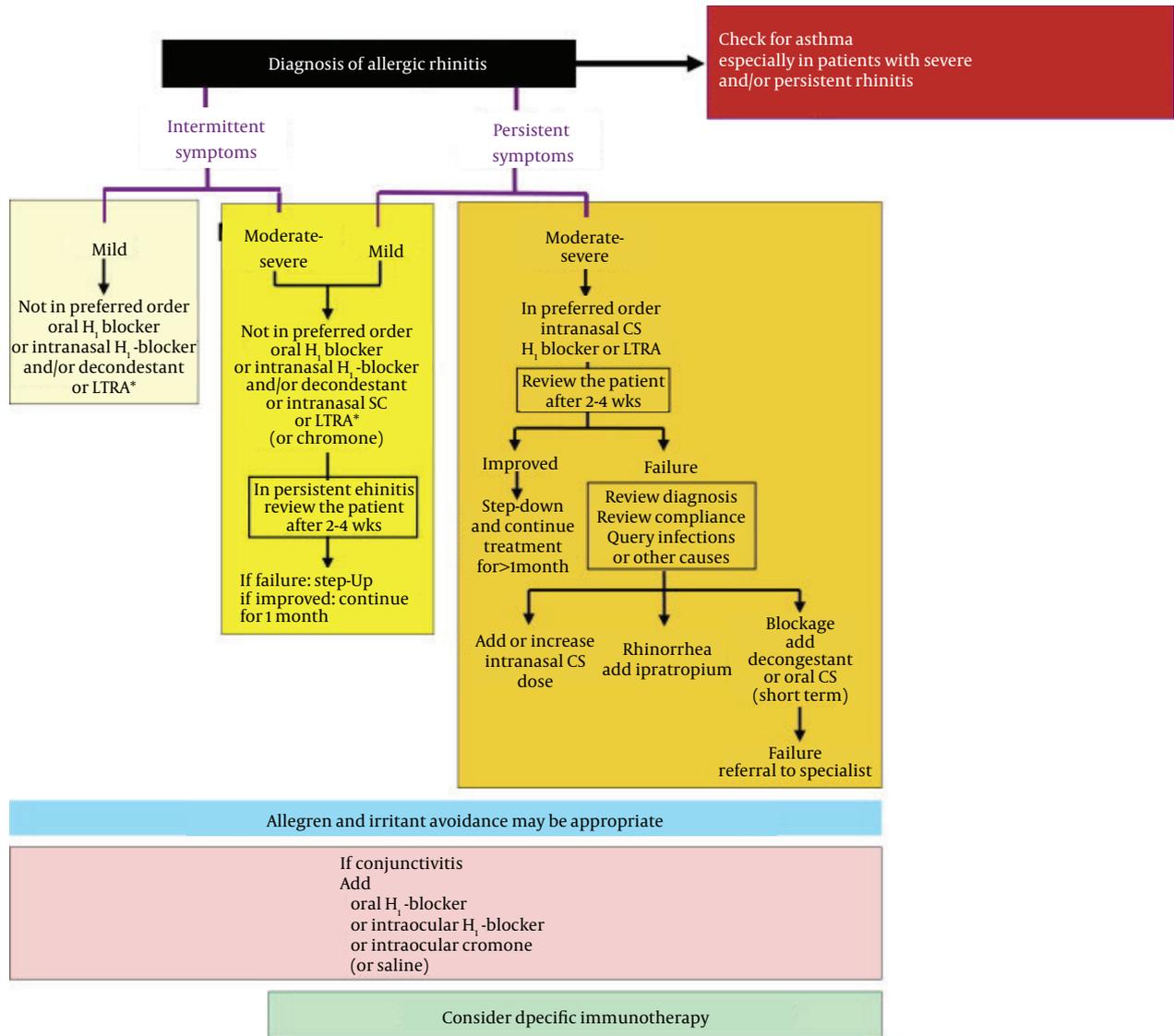


Figure 2. A and B, Immunologic Reaction Pathway in Allergic Rhinitis

Figure 3. Recommendations of the Allergic Rhinitis and Its Impact on Asthma (ARIA) Update



CS, corticosteroid; LTRA, leukotriene receptor antagonist.

Table 1. Pharmacotherapy and Immunotherapy for Allergic Rhinitis

Type of Symptoms	Recommended Treatment Options
Episodic symptoms	Oral or nasal H ₁ -antihistamine, with oral or nasal decongestant if needed
Mild symptoms, seasonal or perennial	Intranasal glucocorticoids, oral or nasal H ₂ -antihistamine, or leukotriene-receptor antagonist (e.g. montelukast)
Moderate-to-severe symptoms	Intranasal glucocorticoids, intranasal glucocorticoids plus nasal H ₁ -antihistamine, or allergen immunotherapy administered subcutaneously or sublingually (the latter for grass or ragweed only)

4. Conclusions

Our findings revealed that two-thirds of the reviewed articles in the existing literature show an association between serum levels of vitamin D and allergic diseases, while the remaining ones have reported no correlation between vita-

min D and AR and some have even demonstrated a rise in the incidence of AR following the use of vitamin D supplement. It seems that further clinical trials and meta-analytic studies are necessary to confirm this correlation.

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