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The Role of Vitamin D Deficiency in Allergic Rhinitis in Children

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Abstract

Vitamin D deficiency remains a global health concern, including in tropical countries such as Indonesia, where many children still experience inadequate levels. Beyond its role in bone health, vitamin D is essential in immune regulation. Allergic rhinitis, a common condition in children, involves inflammation of the nasal mucosa and can negatively impact quality of life, learning, and daily activities. This study aims to review current evidence on the relationship between vitamin D deficiency and the incidence and severity of allergic rhinitis in children.This research used a narrative review approach by systematically searching PubMed and Google Scholar for relevant articles published between 2014 and 2024. The inclusion criteria focused on original studies involving children under 18 years that examined vitamin D levels or supplementation in relation to allergic rhinitis.Findings indicate that vitamin D plays an immunomodulatory role by reducing IgE levels, regulating cytokines, and enhancing T-regulatory cells. Several studies show that low vitamin D levels are associated with increased risk, severity, and poorer treatment outcomes of allergic rhinitis. However, some studies report inconsistent results.In conclusion, vitamin D deficiency may contribute to allergic rhinitis in children, although further research is needed to confirm this relationship.

Keywords Vitamin D Deficiency, Allergic Rhinitis, Children, Immune Response, Supplementation, Pediatric Allergy

INTRODUCTION

Vitamin D deficiency remains a significant global public health issue, with prevalence rates varying widely across different regions, ranging from as low as 1% to as high as 95% (Lips et al., 2021). This variation is influenced by multiple factors, including geographic location, lifestyle, dietary habits, and sun exposure. In Southeast Asia, particularly in countries such as Indonesia, vitamin D deficiency is highly prevalent among children. This condition is paradoxical considering Indonesia's tropical climate, which provides abundant sunlight throughout the year. Nevertheless, limited outdoor activities, increased screen time, cultural clothing

practices, and inadequate dietary intake contribute to insufficient vitamin D levels. A cross-sectional study conducted among school-aged children in Indonesia demonstrated that approximately 39.2% of children experienced vitamin D insufficiency and deficiency, indicating that this issue remains a considerable concern.

Vitamin D plays a crucial role in the growth and development of children. Traditionally, it has been widely recognized for its importance in calcium and phosphorus metabolism, as well as in bone formation and remodeling (Akimbekov et al., 2022; Pons-Belda et al., 2023). Deficiency in vitamin D can lead to skeletal disorders such as rickets, impaired bone mineralization, and abnormalities in growth plate development. However, beyond its skeletal functions, vitamin D has been increasingly acknowledged for its extra-skeletal roles, particularly in immune system regulation. Vitamin D receptors are found in various immune cells, including T cells, B cells, and antigen-presenting cells, indicating its involvement in both innate and adaptive immune responses. It modulates immune function by promoting anti-inflammatory responses and suppressing excessive immune reactions, thereby playing a protective role against immune-mediated diseases.

Despite these important functions, most existing studies on vitamin D deficiency in children have predominantly focused on its impact on bone health, while its role in non-skeletal conditions, especially allergic diseases, has not been extensively explored. Recent evidence suggests that vitamin D deficiency may be associated with an increased susceptibility to allergic conditions, including asthma, eczema, and allergic rhinitis. This association is thought to be related to the immunomodulatory effects of vitamin D, which influence the balance between T-helper 1 (Th1) and T-helper 2 (Th2) immune responses. An imbalance in this system, particularly the dominance of Th2 responses, is known to contribute to the development of allergic diseases.

Allergic rhinitis is one of the most common allergic disorders affecting children worldwide, with a prevalence estimated to range between 25% and 40%. It is characterized by inflammation of the nasal mucosa triggered by exposure to allergens such as dust mites, pollen, animal dander, or mold. The condition manifests through symptoms such as rhinorrhea (anterior or posterior), sneezing, nasal congestion, and nasal itching. Although allergic rhinitis is not a life-threatening condition, its chronic and recurrent nature can significantly affect children's daily functioning. It has been associated with impaired concentration, emotional disturbances, poor sleep quality, and reduced cognitive performance. Consequently,

these effects may lead to decreased academic achievement and a diminished quality of life.

Given the increasing prevalence of allergic diseases in children and the potential role of vitamin D in immune regulation, numerous studies have attempted to investigate the relationship between vitamin D levels and the occurrence of allergic rhinitis. Some studies have reported that low levels of vitamin D are associated with a higher risk of developing allergic rhinitis, suggesting that vitamin D deficiency may act as a contributing factor. Furthermore, several interventional studies have indicated that vitamin D supplementation may help reduce the incidence or severity of allergic rhinitis by enhancing immune tolerance and reducing inflammatory responses.

However, the evidence regarding this relationship remains inconsistent and controversial. While some studies support the protective role of vitamin D against allergic rhinitis, others have found no significant association between serum vitamin D levels and the occurrence, severity, or duration of the condition. These discrepancies may be attributed to differences in study design, population characteristics, sample size, measurement methods, and environmental factors. Additionally, genetic variations and lifestyle differences may also influence the relationship between vitamin D and allergic diseases.

Considering these conflicting findings, there is a need for a comprehensive review of existing literature to better understand the relationship between vitamin D deficiency and allergic rhinitis in children. A clearer understanding of this association is important not only for advancing scientific knowledge but also for informing clinical practice and public health strategies. Therefore, this study aims to review and synthesize current evidence regarding the role of vitamin D deficiency in the development of allergic rhinitis among children, as well as to identify potential gaps for future research.

METHODS

This study employed a narrative review design aimed at exploring and synthesizing existing evidence regarding the role of vitamin D deficiency in the occurrence of allergic rhinitis among children, including infants, children, and adolescents (Theile & Beall, 2024). A narrative review approach was selected to provide a comprehensive overview of current knowledge, identify research gaps, and integrate findings from various studies with different methodologies. This approach allows for a broader interpretation of evidence compared to systematic reviews, particularly in areas where findings remain inconsistent or heterogeneous.

The literature search was conducted systematically using predefined keywords and Medical Subject Headings (MeSH) terms to ensure the inclusion of relevant studies. The main search terms included combinations of "Vitamin D Deficiency," "Allergic Rhinitis," and "Children." These keywords were carefully selected to capture studies focusing on the relationship between vitamin D status and allergic rhinitis in pediatric populations. Boolean operators such as "AND" and "OR" were used to refine and expand the search strategy, ensuring comprehensive coverage of relevant literature.

The search process was carried out using two major electronic databases, namely PubMed and Google Scholar. PubMed was chosen due to its extensive collection of peer-reviewed biomedical literature, while Google Scholar was included to broaden the search and capture additional relevant studies that may not be indexed in PubMed. The search was limited to articles published between 2014 and 2024 to ensure that the review reflects the most recent evidence and developments in this field. Only articles published in English or Indonesian were considered to ensure accessibility and accurate interpretation of the content.

Inclusion criteria were established to ensure that only relevant and high-quality studies were included in the review. Studies were eligible for inclusion if they were original research articles that aimed to evaluate the relationship between vitamin D levels and the incidence of allergic rhinitis in children, or assessed the effects of vitamin D supplementation on the improvement of symptoms or other clinical parameters related to allergic rhinitis. The population of interest was limited to individuals under 18 years of age, including infants, children, and adolescents. Both observational studies (such as cross-sectional, case-control, and cohort studies) and interventional studies (such as randomized controlled trials) were considered eligible, as long as they directly addressed the research objective.

Exclusion criteria were also clearly defined to maintain the focus and relevance of the review. Studies that examined general allergic conditions without specifically addressing allergic rhinitis were excluded. Additionally, studies involving populations other than children, such as adults or mixed-age groups without separate pediatric analysis, were not included. Articles for which the full text was not accessible were also excluded to ensure that data extraction and critical appraisal could be conducted accurately. Furthermore, non-original research articles, including expert opinions, editorials, narrative reviews, systematic reviews, and meta-analyses, were excluded to avoid duplication of data and ensure that the review was based solely on primary research findings.

The study selection process was conducted in several stages. First, titles and abstracts of all retrieved articles were screened to identify potentially relevant studies. Articles that did not meet the inclusion criteria were excluded at this stage. Next, full-text versions of the remaining articles were obtained and reviewed in detail to confirm their eligibility. During this process, studies were further assessed based on their objectives, study design, population characteristics, and outcomes measured. Data extraction was performed systematically from each included study. The extracted information included the author's name, year of publication, study design, sample size, population characteristics, methods of vitamin D measurement, outcomes related to allergic rhinitis, and key findings. This information was then organized and synthesized to identify patterns, similarities, and differences across studies.

The synthesis of findings was conducted qualitatively, given the heterogeneity of study designs, populations, and outcome measures. The results were grouped based on key themes, such as the association between vitamin D deficiency and the incidence of allergic rhinitis, as well as the effects of vitamin D supplementation on symptom improvement. Differences in findings were also analyzed and discussed to provide a balanced interpretation of the evidence. By applying a structured search strategy and clear inclusion and exclusion criteria, this narrative review aims to provide a comprehensive and up-to-date understanding of the relationship between vitamin D deficiency and allergic rhinitis in children, while also highlighting areas that require further research.

FINDINGS AND DISCUSSION

The findings of this narrative review regarding the relationship between vitamin D and allergic rhinitis in children are categorized into three main themes. First, studies that explore the role and mechanisms of vitamin D in the immunological processes underlying allergic rhinitis. Second, studies that support the association between vitamin D deficiency and the incidence or severity of allergic rhinitis in children. Third, studies that report no significant or specific association between vitamin D deficiency and allergic rhinitis. This section begins by discussing the immunological mechanisms linking vitamin D to allergic rhinitis.

The Relationship Between Vitamin D and the Immunological Processes of Allergic Rhinitis

Allergic rhinitis is a complex inflammatory condition characterized by immune system dysregulation in response to environmental allergens. Its pathophysiology involves inflammation of the nasal mucosa, allergen sensitization, and the

production of immunoglobulin E (IgE) mediated by immune cells such as eosinophils. Upon exposure to allergens, sensitized individuals experience an exaggerated immune response, resulting in the release of inflammatory mediators, including histamine, cytokines, and chemokines. These processes lead to the characteristic symptoms of allergic rhinitis, such as rhinorrhea, sneezing, nasal congestion, and itching (Sikorska-szaflik & Soza, 2020).

Vitamin D is increasingly recognized for its immunomodulatory properties, which play a significant role in regulating both innate and adaptive immune responses. One of the key mechanisms by which vitamin D influences allergic rhinitis is through its ability to suppress inflammatory processes. Vitamin D has been shown to reduce the production of pro-inflammatory cytokines by monocytes and other immune cells. Additionally, it decreases serum IgE levels and reduces eosinophilic activity in the respiratory tract during allergen sensitization. These effects suggest that adequate levels of vitamin D may help mitigate the intensity of allergic responses.

Another important immunological mechanism involves the regulation of T-cell differentiation. Vitamin D plays a critical role in modulating the balance between T-helper 1 (Th1) and T-helper 2 (Th2) cells. In allergic conditions, including allergic rhinitis, there is typically a predominance of Th2 cells. This imbalance leads to increased production of cytokines such as interleukin-4 (IL-4), which promotes IgE synthesis and enhances allergic inflammation. Vitamin D contributes to restoring immune balance by promoting the development of regulatory T cells (Treg), which are essential for maintaining immune tolerance and suppressing excessive immune responses. By enhancing Treg activity, vitamin D helps reduce the Th2-mediated allergic response and supports a more balanced immune profile.

The role of regulatory T cells is particularly crucial in preventing hypersensitivity reactions. Treg cells function by inhibiting the activation and proliferation of effector T cells, thereby limiting inflammation and allergic reactions. Vitamin D enhances the differentiation and function of Treg cells, which in turn helps suppress the exaggerated immune responses characteristic of allergic rhinitis. This mechanism provides a plausible explanation for the observed association between vitamin D deficiency and increased susceptibility to allergic diseases.

In addition to its immunomodulatory effects, vitamin D is also believed to play a role in maintaining the structural integrity of the nasal mucosal barrier. The nasal epithelium serves as the first line of defense against environmental allergens and pathogens. A healthy and intact epithelial barrier prevents the penetration of

allergens into deeper tissues, thereby reducing the likelihood of immune activation. Vitamin D contributes to epithelial integrity by regulating the expression of tight junction proteins and promoting cellular repair mechanisms. Deficiency in vitamin D may compromise this barrier function, leading to increased permeability and greater exposure to allergens. As a result, individuals with low vitamin D levels may experience heightened sensitivity to environmental triggers and an increased risk of developing allergic rhinitis.

Several clinical studies provide evidence supporting the immunological role of vitamin D in allergic rhinitis. A study conducted by Handoko et al. demonstrated that oral supplementation of vitamin D3 for four weeks in children significantly increased serum levels of 25-hydroxyvitamin D [25(OH)D3] ($p = 0.01$) and the proportion of regulatory T cells ($p = 0.002$) in the treatment group compared to the control group. These findings indicate that vitamin D supplementation can enhance immune regulation and potentially reduce allergic responses in pediatric populations.

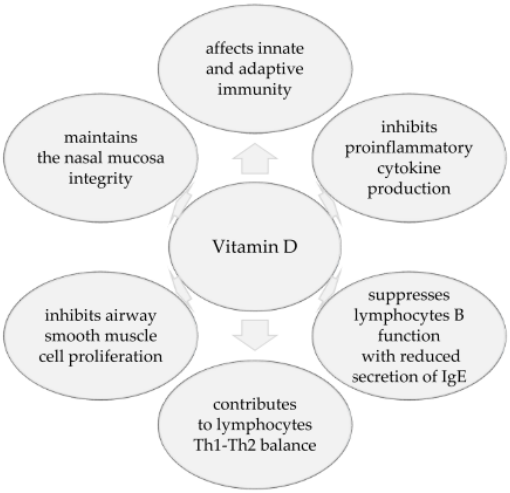
Similarly, another clinical trial involving 38 children aged 5 to 12 years with pollen hypersensitivity showed that daily supplementation with 1000 IU of vitamin D led to a significant increase in serum 25(OH)D3 levels ($p = 0.0001$) and Treg cell percentages ($p = 0.0058$). Importantly, this study also reported significant clinical improvement in symptoms of allergic rhinitis among the participants. These results highlight the potential therapeutic benefits of vitamin D in managing allergic rhinitis through immunological pathways.

Collectively, these findings support the hypothesis that vitamin D plays a multifaceted role in the pathophysiology of allergic rhinitis. Its ability to modulate immune responses, reduce inflammation, enhance regulatory T-cell activity, and maintain epithelial barrier integrity underscores its importance in preventing and alleviating allergic conditions. The immunological mechanisms described above provide a strong biological basis for the observed association between vitamin D deficiency and allergic rhinitis in children.

However, it is important to note that while these mechanisms are well-supported by experimental and clinical evidence, the overall relationship between vitamin D and allergic rhinitis remains complex. Variability in study results may be influenced by differences in population characteristics, environmental exposures, genetic factors, and methodological approaches. Therefore, further research is needed to fully elucidate the role of vitamin D in allergic diseases and to determine optimal strategies for prevention and treatment.

In conclusion, vitamin D exerts significant immunomodulatory effects that are highly relevant to the development and progression of allergic rhinitis. Its influence on cytokine production, T-cell regulation, and mucosal integrity provides a comprehensive explanation for its potential protective role. These findings emphasize the importance of maintaining adequate vitamin D levels in children as part of a broader strategy to reduce the burden of allergic diseases.

Figure 1. Mechanisms Underlying the Relationship of Vitamin D to Allergic Rhinitis in Children (Sikorska-szaflik & Soza, 2020)



Studies Supporting the Association Between Vitamin D and Allergic Rhinitis in Children

A growing body of evidence supports the association between vitamin D deficiency and the incidence, severity, and management outcomes of allergic rhinitis in children. Several observational and interventional studies have demonstrated that children with allergic rhinitis tend to have lower serum vitamin D levels compared to healthy controls, suggesting a potential role of vitamin D in the pathogenesis and clinical progression of this condition.

One of the key studies in this area was conducted by Saad et al., which aimed to compare vitamin D levels between children diagnosed with allergic rhinitis and healthy children without the condition. The study found that children with allergic rhinitis had significantly lower mean serum levels of 25-hydroxyvitamin D [25(OH)D], 1,25-dihydroxyvitamin D [1,25(OH)2D], and 25(OH)D3 compared to healthy controls ($p < 0.001$). Furthermore, when vitamin D status was categorized, the proportion of vitamin D deficiency was significantly higher among children with allergic rhinitis than in healthy children (30.8% vs. 8%; $p < 0.001$). Importantly, the

study also identified a negative correlation between serum 25(OH)D levels and total nasal symptom scores ($r = -0.62$; $p = 0.002$), indicating that lower vitamin D levels were associated with more severe clinical symptoms. Although the correlation between vitamin D levels and total IgE levels was not statistically significant ($r = -0.27$; $p = 0.13$), the overall findings strongly suggest that vitamin D deficiency is prevalent among children with allergic rhinitis and may contribute to increased disease severity (Lee et al., 2015; Okmen et al., 2021; Saad et al., 2020).

Similar findings were reported in a case-control study conducted by Lee et al., which compared serum 25(OH)D3 levels among children with allergic rhinitis, children with vasomotor rhinitis, and healthy controls. The results demonstrated that children with allergic rhinitis had significantly lower vitamin D levels (19.0 ± 8.5 ng/mL) compared to those with vasomotor rhinitis (25.5 ± 10.9 ng/mL) and healthy children (26.9 ± 10.7 ng/mL) ($p < 0.001$). Additionally, a significant negative correlation was observed between serum vitamin D levels and IgE concentrations ($r = -0.317$; $p < 0.001$), further supporting the hypothesis that vitamin D deficiency is associated with heightened allergic responses (Akram et al., 2020; Bener et al., 2014; Li et al., 2023). Another study by Okmen et al. reinforced these findings by demonstrating that the prevalence of vitamin D deficiency was significantly higher in children with allergic rhinitis compared to healthy controls (67.9% vs. 13.3%; $p = 0.001$). Although this study also reported a negative correlation between vitamin D levels and symptom severity scores, the association did not reach statistical significance ($r = -0.099$; $p = 0.25$). Nevertheless, the markedly higher prevalence of deficiency among affected children highlights the potential importance of vitamin D in the development of allergic rhinitis.

Further evidence was provided by Bener et al., who conducted a large-scale study involving 276 children with allergic rhinitis and 1,082 healthy controls. The study found that vitamin D deficiency (defined as <30 ng/mL) was significantly more common among children with allergic rhinitis ($p < 0.001$). Moreover, the presence of vitamin D deficiency was associated with a 1.63-fold increased risk of developing allergic rhinitis (OR 1.63; 95% CI 1.38–1.95; $p < 0.001$). This finding suggests that vitamin D deficiency may not only be associated with the condition but could also act as a risk factor for its development. In addition to its role in disease occurrence and severity, vitamin D status has also been linked to treatment outcomes in children with allergic rhinitis. A retrospective cohort study involving 153 children with allergic rhinitis reported that the mean serum 25(OH)D3 level was relatively low (20.42 ± 7.48 ng/mL). All participants underwent sublingual immunotherapy as part

of their treatment, and the results indicated that children with serum vitamin D levels ≤22.25 ng/mL were more likely to experience treatment failure. This finding suggests that inadequate vitamin D levels may negatively impact the effectiveness of immunotherapy in managing allergic rhinitis.

Moreover, interventional studies have demonstrated the potential benefits of vitamin D supplementation in improving clinical outcomes. A clinical trial involving children with moderate-to-severe persistent allergic rhinitis found that vitamin D deficiency was more prevalent in affected children compared to healthy controls (42.5% vs. 30.8%; p = 0.009). Participants were divided into two groups: one receiving standard allergic rhinitis treatment combined with vitamin D supplementation (800 IU/day), and the other receiving standard treatment alone. After four weeks of therapy, the group receiving vitamin D supplementation showed a significantly greater reduction in symptom scores compared to the control group. This finding indicates that correcting vitamin D deficiency may enhance treatment efficacy and lead to better symptom control. Overall, these studies consistently demonstrate that vitamin D deficiency is common among children with allergic rhinitis and is associated with increased disease risk, greater symptom severity, and poorer treatment outcomes. The evidence also suggests that vitamin D supplementation may play a beneficial role in improving clinical responses. Collectively, these findings support the hypothesis that maintaining adequate vitamin D levels is important in the prevention and management of allergic rhinitis in children.

Studies Showing Vitamin D Deficiency Is Not Specific to Allergic Rhinitis

Several studies have suggested that the role of vitamin D deficiency in allergic rhinitis among children may not be specific, highlighting inconsistencies in current evidence. One such study by Dogru et al. conducted a case-control analysis involving 48 children with allergic rhinitis, 28 children with non-allergic rhinitis, and 65 healthy controls. The findings revealed that the proportion of vitamin D deficiency was significantly higher in children with allergic rhinitis compared to healthy children (66.7% vs. 38.5%; p = 0.001). However, when comparing children with allergic rhinitis and those with non-allergic rhinitis, no significant difference in vitamin D deficiency was observed (p > 0.05) (Dogru & Suleyman, 2016). Furthermore, the study did not find a significant relationship between serum 25(OH)D3 levels and the severity or duration of allergic rhinitis symptoms. These findings raise an important question: whether vitamin D deficiency is specifically associated with allergic rhinitis, or whether it contributes more broadly to rhinitis symptoms regardless of etiology.

In contrast to studies suggesting a negative association between vitamin D levels and allergic rhinitis, Kutlug et al. reported findings that challenge this assumption. Their study demonstrated that serum 25(OH)D3 levels were actually higher in children with allergic rhinitis compared to healthy controls ($p = 0.002$). Moreover, the proportion of vitamin D deficiency was found to be higher in healthy children than in those with allergic rhinitis (34% vs. 16%; $p = 0.005$) (Kutluğ1 et al., 2017). These results contradict earlier findings and suggest that vitamin D deficiency may not be a consistent risk factor for allergic rhinitis in children. Such contradictory evidence indicates that the relationship between vitamin D and allergic conditions may be more complex than previously assumed.

Additional evidence from a long-term prospective cohort study conducted by Bunyavanich et al. further supports the notion that vitamin D may not have a specific or direct role in the development of allergic rhinitis. This study aimed to evaluate the impact of vitamin D exposure during prenatal, perinatal, and early childhood periods on the development of allergic rhinitis in school-aged children. The results showed no significant association between serum 25(OH)D3 levels and the incidence of allergic rhinitis (Bunyavanich et al., 2016). Moreover, vitamin D levels were not significantly correlated with total serum IgE levels or sensitization to environmental allergens. These findings suggest that vitamin D status alone may not be a reliable predictor of allergic rhinitis or related immunological markers in children.

Taken together, these studies highlight the inconsistency and potential non-specificity of the relationship between vitamin D deficiency and allergic rhinitis in children. While some evidence suggests that vitamin D deficiency is more prevalent in children with allergic rhinitis, other studies demonstrate no significant differences or even contradictory trends. This inconsistency may be attributed to variations in study design, sample size, geographic location, sun exposure, dietary intake, genetic factors, and differences in defining vitamin D deficiency. Furthermore, the relationship between vitamin D and allergic rhinitis may be non-linear and influenced by multiple interacting factors. Vitamin D may act as one of many contributing elements in a broader immunological and environmental context rather than serving as a primary determinant. Factors such as environmental allergens, air pollution, genetic predisposition, and lifestyle behaviors may play a more dominant role in the development and severity of allergic rhinitis in children.

In conclusion, current evidence suggests that the role of vitamin D deficiency in allergic rhinitis is not specific and remains inconclusive. While vitamin D may contribute to immune system regulation, its direct association with allergic rhinitis in

children appears to be complex and multifactorial. Therefore, further large-scale, well-controlled studies are needed to better understand the nature of this relationship and to determine whether vitamin D plays a causal or merely associative role in allergic rhinitis.

CONCLUSION

In addition to its role in children's bone health and development, vitamin D can also induce immunomodulation, which may play a role in the pathophysiology of allergic rhinitis in children. Several studies have demonstrated that vitamin D deficiency can be a factor triggering allergic rhinitis, and several others have shown that correcting vitamin D deficiency can improve symptoms of allergic rhinitis in children, supporting the role of vitamin D supplementation as a preventative measure or adjuvant therapy in the management of allergic rhinitis in children. However, several studies have shown no association between vitamin D levels and clinical and immunological parameters in children with allergic rhinitis. This may be due to heterogeneity in the definition of allergic rhinitis and the vitamin D level threshold considered deficient. Therefore, further clinical and experimental studies are needed to further explore how vitamin D may affect allergic rhinitis in children.

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