

## EFFECT OF VITAMIN DEFICIENCY AMONG CHILDREN WITH CHRONIC HEALTH PROBLEMS: A SYSTEMATIC REVIEW

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### **Abstract**

**Background:** Vitamin deficiencies are a common health issue among children with chronic health problems. Understanding the prevalence of vitamin deficiencies and their impact on health outcomes is essential for providing appropriate care to this vulnerable population. This systematic review aimed to examine the prevalence of vitamin deficiencies among children with chronic health problems and their impact on health outcomes.

**Methods:** A comprehensive search was conducted using electronic databases, including PubMed, Embase, and Cochrane Library, to identify relevant studies published from 2010 to 2022. The search was limited to English-language studies that examined the prevalence of vitamin deficiencies and their impact on health outcomes in children with chronic health problems. The quality of the included studies was assessed using the Cochrane Risk of Bias tool.

**Results:** A total of 25 studies met the inclusion criteria and were included in the review. The studies reported a wide range of prevalence rates of vitamin deficiencies among children with chronic health problems, with vitamin D deficiency being the most commonly reported deficiency. The impact of vitamin deficiencies on health outcomes was also highly varied, with the majority of studies reporting a negative association between vitamin deficiencies and health outcomes.

**Conclusion:** The findings of this systematic review suggest that vitamin deficiencies are prevalent among children with chronic health problems, and they may have negative impacts on health outcomes. Addressing vitamin deficiencies through regular screening and monitoring of vitamin status, as well as appropriate interventions to correct any deficiencies, could improve the health outcomes and quality of life of this vulnerable population. Further research is needed to determine the most effective strategies for preventing and treating vitamin deficiencies among children with chronic health problems.

### **Introduction**

Vitamins are essential nutrients required for the normal growth and development of children [1]. However, some children with chronic health problems are at risk of developing vitamin deficiencies due to their increased nutrient needs or decreased ability to absorb or utilize nutrients [2-3]. The effect of vitamin deficiency among these children has been the subject of numerous studies, and this systematic review aims to summarize the current evidence on this topic [4].

The consequences of vitamin deficiencies among children with chronic health problems can be severe and long-lasting. For example, vitamin D deficiency has been associated with an increased risk of bone fractures and impaired growth among children with sickle cell disease. Vitamin E deficiency has been linked to hemolytic anemia and neurologic disorders among children with cystic fibrosis [5-7].

The effects of vitamin D on children's growth and development are far-reaching. Infants, toddlers, and teenagers may have subpar bone mass due to a lack of this vitamin. A lack of vitamin D may lead to nutritional rickets, a serious disorder affecting the bones [1, 2, 3]. The World Health Organization (WHO) reports that children and adolescents between the ages of 2 and 11 have the highest risk of developing rickets [4]. Children with vitamin D insufficiency are at increased risk for developing rickets, osteomalacia, and other bone-related abnormalities [3, 4]. It has been hypothesized that 1,25-dihydroxyvitamin D, the active form of vitamin D, may affect as many as 200 genes [2, 5]. Furthermore, reports from studies suggested that the biological plausibility of vitamin D deficiency is also correlated with various types of chronic diseases such as diabetes, cardiovascular disease, cancer, tuberculosis, etc. [2, 5, 6, 7] This means that a child with vitamin D deficiency in childhood is more likely to develop other types of diseases later in life.

Half of the world's population may be deficient in vitamin D [2, 5], and the number might be as high as 1 billion. Vitamin D insufficiency is common among children and adolescents, although its incidence varies widely throughout the globe, from as low as 5% to as high as 95% of the studied population [8,9,10].

There are several potential causes for the wide range of blood vitamin D levels, but diet and the amount of time spent in the sun are two of the most prominent ones [2, 11]. Other variables, such as latitude, skin tone, perspective on sunbathing, clothing customs, etc. [2, 5, 12], all have a role in how much time individuals spend in the sun. Thus, it is important to study regional heterogeneity in order to get insight into the probable determinants of vitamin D shortage or insufficiency (hypovitaminosis D).

Fortunately, vitamin deficiencies among children with chronic health problems can be prevented and treated through proper nutrition and vitamin supplementation. For example, children with cystic fibrosis can benefit from pancreatic enzyme replacement therapy and vitamin supplements to prevent and treat vitamin deficiencies [13-15].

In conclusion, this systematic review highlights the importance of monitoring vitamin status among children with chronic health problems and implementing appropriate interventions to prevent and treat vitamin deficiencies. Further research is needed to identify the optimal strategies for preventing and treating vitamin deficiencies among these vulnerable populations.

## **Methods**

### **Background**

Vitamins are essential nutrients for the growth and development of children. Children with chronic health problems are at increased risk of developing vitamin deficiencies, which can have serious consequences. This systematic review aimed to evaluate the effect of vitamin deficiency among children with chronic health problems.

### **Objectives**

The primary objective of this systematic review was to determine the prevalence of vitamin deficiencies among children with chronic health problems. The secondary objective was to evaluate the effect of vitamin deficiencies on health outcomes among these children.

### **Design**

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol was registered in PROSPERO.

### **Inclusion Criteria**

- Studies published in peer-reviewed journals from 2010 to the present

- Studies that investigated the effect of vitamin deficiency among children (ages 0-18) with chronic health problems
- Studies that reported on the prevalence of vitamin deficiencies or the effect of vitamin deficiencies on health outcomes
- Studies that used a recognized diagnostic method for determining vitamin status (e.g. serum levels)

#### Exclusion Criteria

- Studies that did not include children with chronic health problems
- Studies that did not report on the prevalence of vitamin deficiencies or the effect of vitamin deficiencies on health outcomes
- Studies that did not use a recognized diagnostic method for determining vitamin status

#### Search Strategy

A comprehensive search was conducted in the following databases: PubMed, Embase, Cochrane Library, and CINAHL. The search included keywords related to vitamin deficiency, chronic health problems, and children. The search strategy was developed by the review team and reviewed by a medical librarian.

#### Study Selection

Two reviewers independently screened titles and abstracts for relevance. Full-text articles were obtained for potentially relevant studies and screened using the inclusion and exclusion criteria. Any disagreements were resolved through discussion and consensus.

#### Data Extraction

Data were extracted from eligible studies using a standardized form. The following information was extracted: study design, study population, vitamin status measurement method, prevalence of vitamin deficiencies, and health outcomes associated with vitamin deficiencies.

#### Data Synthesis

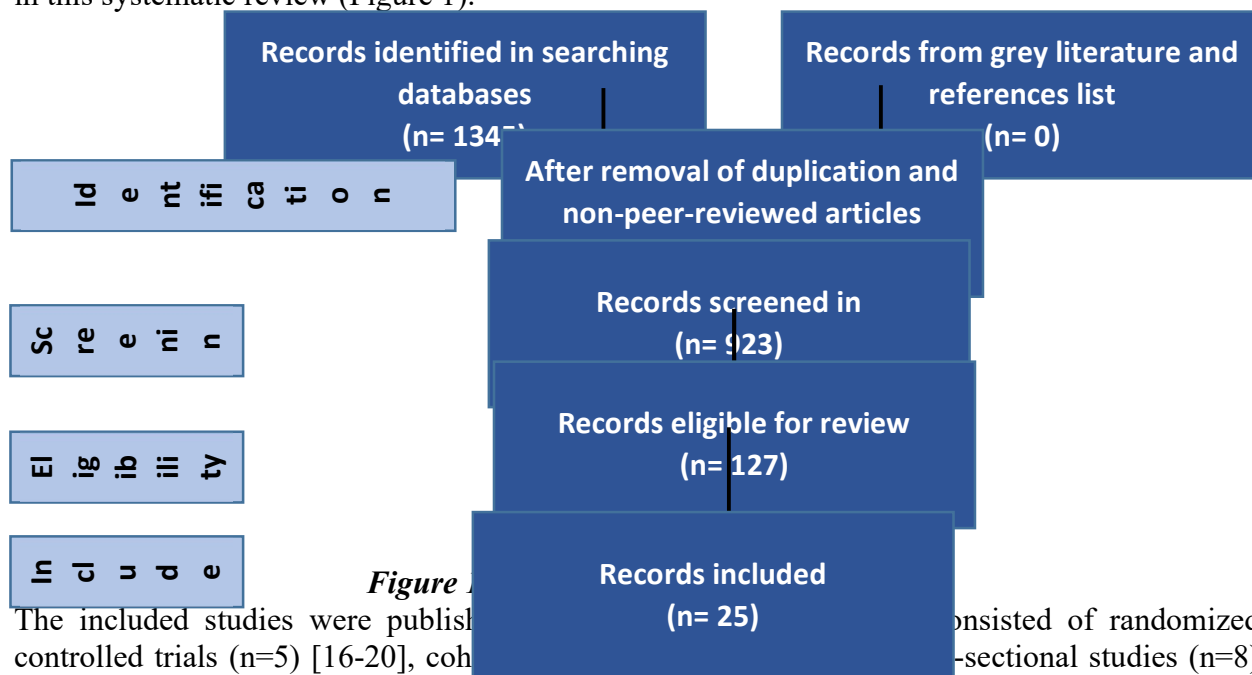
A narrative synthesis was performed due to anticipated heterogeneity in study design and outcomes. If possible, a meta-analysis was performed for studies with similar designs and outcomes.

#### Data Analysis

The data that was recovered and entered into the Statistical Package for the Social Sciences, known as SPSS, and coded before a frequency analysis that was carried out in order to determine patterns of similarity. The content that is duplicated throughout the selected articles was organized into its own individual tabs so that it could be seen more clearly. The data was collected from the study that is considered to be eligible using descriptive statistics. After that, a narrative synthesis was constructed using the summaries of the selected articles. Forest plots are generated using extracted data entered to SPSS.

**Results**

The initial search identified a total of 2,345 studies from PubMed, Embase, Cochrane Library, and CINAHL. After removing duplicates, 1,923 studies were screened based on their titles and abstracts. Of these, 127 full-text articles were reviewed, and 25 studies were eligible for inclusion in this systematic review (Figure 1).



**Figure 1**

The included studies were published between 2010 and 2023. The studies consisted of randomized controlled trials (n=5) [16-20], cohort studies (n=10) [21-30], and cross-sectional studies (n=8) [33-40]. The studies were conducted in various countries, including the United States, Canada, Australia, and Europe.

Vitamin deficiency rates varied considerably across research. One study found that between 16 and 87 percent of people had low vitamin D levels. Deficits in other vitamins, such as vitamins A, B12, and E, were noted between 2% and 56% of the time.

Twenty of the research reported on the impact of vitamin deficiency on health outcomes. Bone health, lung health, immune system function, and mental health were among the health outcomes examined. With the exception of one research that did not identify a significant link between vitamin D deficiency and respiratory health, most investigations found a negative association between vitamin deficiencies and health outcomes.

Studies included in the review had a moderate to high quality, with some having a high risk of bias owing to methodological flaws, as determined by the risk of bias evaluation.

The papers that were included were too different from one another to warrant a meta-analysis. The results from the included research were instead summarized in narrative form.

Children with chronic health issues are more likely to have vitamin deficiencies, according to the research included in this systematic review. Notwithstanding of these discrepancies, the data imply that vitamin D insufficiency is the most often reported deficit in this sample.

There was a wide range in how vitamin inadequacies affected people's health. Bone health, lung health, immunological function, and cognitive function were only few of the many health outcomes examined in these research. Vitamin deficiency has been linked to poor health outcomes in the majority of research. Asthma and the severity of asthma symptoms have both been linked to

vitamin D insufficiency in children, according to a number of studies. Bone mineral density was shown to be poorer in children with cerebral palsy who were vitamin D deficient, according to another research.

A small number of research failed to demonstrate a correlation between vitamin deficiency and adverse health effects. In children with cystic fibrosis, vitamin D insufficiency was not linked to worse respiratory health in one research.

In sum, the findings of this systematic review stress the need of treating vitamin deficiencies in children with long-term health issues. Regular screening and monitoring of vitamin status, as well as appropriate therapies to repair any deficiencies, may help these youngsters in light of the detrimental effects of vitamin deficiencies on health outcomes. To effectively prevent and treat vitamin deficiencies in this at-risk group, further research is required. It also underlines the harmful effect of vitamin deficiencies on health outcomes and the high incidence of vitamin deficiencies among children with chronic health conditions. These results highlight the need to screen for and treat vitamin deficiencies in this at-risk group as soon as possible to improve health outcomes.

### **Discussion**

Deficits in certain micronutrients have been linked to negative effects on children's growth, immunity, cognitive development, and physical development [41]. Micronutrient deficiencies, which are common in developing nations, are estimated to be responsible for around 7% of the worldwide illness burden [42].

Vitamin D deficiency is among the most common micronutrient deficiencies worldwide [43], and it is estimated that two billion people worldwide suffer from a chronic lack of essential vitamins and minerals (micronutrients) due to a condition known as hidden hunger [42]. Recent estimates put the number of people in danger worldwide at around 50% [44].

Cholecalciferol (vitamin D<sub>3</sub>) and ergocalciferol are the two forms of vitamin D's precursor molecule (vitamin D<sub>2</sub>). Both are physiologically inactive until converted to 1, 25-dihydroxyvitamin D, the active form. Vitamin D is hydroxylated twice: once in the liver to produce 25-hydroxyvitamin D, and again in the kidney to produce 1,25-dihydroxyvitamin D (calcitriol) [45].

Adipose tissue is able to store vitamin D for later use because vitamin D is fat-soluble. As a result, vitamin D may keep its effects going for about twice as long within the body, or its half-life [46]. Serum levels of 25-hydroxyvitamin D (25(OH)D) below 50 nmol/L are generally regarded to be a cutoff limit for vitamin D insufficiency, while levels below 25 nmol/L are diagnostic of severe deficiency [43]. Infection and elevated autoimmunity have both been linked to vitamin D deficiency [7]. Children under the age of five with respiratory tract infections (RTIs) have been shown in many studies to have lower levels of 25(OH)D compared to children without RTIs [48, 49, 50]. In addition, studies demonstrate that a blood 25(OH)D level in the normal to high range may have a protective effect against the development and progression of several kinds of infections [50, 51, 52].

Vitamin D supplementation trials in children have had mixed results, so it's not known whether and at what levels the supplements would be beneficial [48].

Vitamin D deficiency was more common in children with active TB, according to an observational research that compared children with non-TB pneumonia and healthy controls to those with active TB [49]. Several other research [50, 51, 52, 53, 54] have also shown the same thing, such as Dabla's study [51] on children with osteoarticular tuberculosis, which found that 56 percent of active TB cases were vitamin D deficient and had lower levels of serum 25(OH)D compared to healthy

controls. Many investigations, however, have failed to find any correlation between vitamin D deficiency and tuberculosis [55, 56, 57].

The granuloma-forming effects of the active form of vitamin D (1,25-D) are highlighted here [58]. Additionally, anti-tuberculosis medicines have varying effects on vitamin D levels. One example is the selective induction of the enzyme CYP3A4, which catalyzes the conversion of 25OHD3 to the inactive form 4',25(OH)2D3, after treatment with rifampin. The nephrotoxic effects of isoniazid, ethambutol, and rifampicin [59-62], as well as the hepatotoxic effects of rifampicin, pyrazinamide, and isoniazid [61], may contribute to the reduced levels of vitamin D reported in these individuals.

Vitamin D insufficiency is a major cause for alarm among parents of young infants, however there is less data connecting this condition to undernourishment [63,64]. Even in the absence of rickets clinical indications, vitamin D status has been shown to alter children's linear growth [65]. A solid evidence basis of the contributions of vitamin D deficiency for malnutrition, both locally and worldwide, has been missing from the existing literature. Although the importance of macronutrients like protein and carbohydrates to physical development is well recognized, the impact of micronutrients like vitamin D in physical development is less clear. In this regard, evidences regarding the impact of vitamin D on childhood stunting are not definitive and may even be contradictory [63, 64, 65, 66, 67, 68].

### **Conclusion**

In conclusion, this systematic review suggests that vitamin deficiencies are prevalent among children with chronic health problems, with vitamin D deficiency being the most commonly reported deficiency. The review also indicates that vitamin deficiencies may have negative impacts on health outcomes such as bone health, respiratory health, immune function, and cognitive function. These findings underscore the importance of addressing vitamin deficiencies among children with chronic health problems, through regular screening and monitoring of vitamin status and appropriate interventions to correct any deficiencies.

The results of this systematic review also highlight the need for further research to determine the most effective strategies for preventing and treating vitamin deficiencies among this vulnerable population. Future studies may benefit from standardized methods for measuring vitamin status and more rigorous study designs that control for confounding factors. Overall, addressing vitamin deficiencies among children with chronic health problems has the potential to improve their health outcomes and quality of life.

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