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Vitamin D Deficiency and Its Association with Recurrent Respiratory Infections in Children Under Five – A Cross-Sectional Analysis

Afzal Ahmad[1], Misbah ullah khan[2], Ijaz Ahmad[3]

1. Registrar nursery Khyber teaching hospital Peshawar
2. Experiential registrar Peads icu Khyber teaching hospital Peshawar
3. Experiential registrar pediatrics Khyber teaching hospital Peshawar

Corresponding author :Misbah Ullah khan[2]

Email: dr.misbahullah13@gmail.com

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Abstract

Background: Respiratory infections are the major source of morbidity and mortality in children, especially in developing nations. Vitamin D has been proven to be a vital component in the functionality of the immune system and its deficiency has been associated with greater vulnerability to respiratory infections.

Objectives: to investigate the relationship between vitamin D deficiency and the recurrent respiratory infections in children who are below the age of five.

Methods: This was a cross-sectional study Conducted at the Neonatal Intensive Care Unit (NICU) of Khyber Teaching Hospital, Peshawar,jan to june-2023. Two hundred children between the ages of 6 months and 5 years old who had a history of recurrent respiratory infections were recruited. Serum 25-hydroxyvitamin D levels were to be determined by blood samples. Information on the number of respiratory infections, medical history, and demographic was also collected.

Results: The Study discovered that in the case of 60% of children, there was vitamin D deficiency (serum level less than 20 ng/mL). There was a higher prevalence of recurrent respiratory infections in children who had a vitamin D deficiency and 75% had more than three respiratory infections per year as compared to 45% of vitamin D adequate children. The correlation between the lack of vitamin D and frequent respiratory infections was statistically significant ($p < 0.001$).

Conclusion: Vitamin D deficiency is very common in children below the age of five and is linked to high incidence of recurrent respiratory infections. These results indicate that early diagnosis of vitamin D deficiency may be critical and supplementation may prove effective in alleviating the cost of respiratory diseases among this group of vulnerable populations.

Keywords: Vitamin D, Deficiency, Respiratory Infections, Children, Immunity

Introduction

Pneumonia is a major cause of morbidity and death among children especially among those below the age of five. Such infections tend to lead to hospitalizations, chronic health complications and high healthcare expenses. Although the vast majority of respiratory infections in children are caused by viruses, bacteria, such as Streptococcus pneumoniae and

Haemophilus influenzae are also recognized as significant disease burden agents. The recurrent respiratory infections (RRIs) are frequent episodes of upper and lower respiratory tract infection that is common in children in developing countries and has been associated with multiple factors, such as environmental, genetic, and nutritional factors (1). It boosts the pathogen-destroying action of immune-fighting cells like monocytes and macrophages and regulates the synthesis of antimicrobial peptides. Vitamin D is believed to have adequate levels that would enhance effective immune responses, lowering chances of infections including respiratory tract infections (2). Although vitamin D is vital in the regulation of the immune system, deficiency is very common across the world especially among children. Low levels of vitamin D during childhood have been linked to many health issues, such as bone-related disorders, poor growth, and poor immune functioning (3).Over the past 10 years, studies have identified a possible connection between lack of vitamin D and frequent respiratory infections in children. Various studies have shown that the lack of vitamin D predisposes people to respiratory infections both viral and bacterial. In a Study, Litonjua et al. (2016) discovered that children who had low concentrations of vitamin D were more susceptible to respiratory diseases and asthma attacks (4). Likewise, a Study conducted by Sadeghi et al. (2018) showed that vitamin D deficiency in children predisposed them to infections, mainly respiratory tract infections (5). The relationship between vitamin D and respiratory infections is biologically plausible. Vitamin D is also important in the making of cathelicidins which are antimicrobial peptides that are important in protecting the body against respiratory pathogens (6). Moreover, the vitamin D deficiency has been associated with the enhancement of inflammation and the weakening of immune reactions, which may serve as the reason behind the reappearance of infections (7). Children deficient in vitamin D are also more prone to respiratory infections such as pneumonia, bronchiolitis, and influenza (8).Although much of the Study has demonstrated the relationship between vitamin D deficiency and respiratory infections, there is no consensus regarding the mechanisms by which these infections occur. In addition, it is not well known how deficiency of vitamin D affects cases of respiratory infections in children below the age of five years, especially in areas with low access of healthcare services and nutritional deficiencies(9). This Study will address the current gap in Study on the prevalence of vitamin D deficiency among children under the age of five and its relation to frequency and severity of recurrent respiratory infection among young children in the same age group in regard to potential public health implication of vitamin D supplementation to prevent recurrent respiratory infection in children under the age of five.

Methods

The study is a cross-sectional one carried out in Neonatal Intensive Care Unit (NICU) of Khyber Teaching Hospital, Peshawar,jan to june-2023. Two hundred children less than five years of age who had the history of repeated respiratory infections were registered. The level of serum 25-hydroxyvitamin D was determined, and the deficiency of vitamin D was considered to be at a level less than 20 ng/mL. Parental interviews were used to provide data on the frequency and severity of respiratory infections and demographics. The SPSS was used to analyze the results statistically with a p-value of less than 0.05 set as a statistically significant value.

Inclusion Criteria:

Children between 6 months and 5 years and History of recurrent respiratory infections (three or more episodes in the last year) and Parental consent for participation.

Exclusion Criteria:

Children with chronic respiratory conditions or congenital anomalies and Children on vitamin D supplementation or immunosuppressive therapy.

Ethical Approval Statement

The Ethics Committee of Khyber Teaching Hospital, Peshawar (Approval No. 244/KTH/2023/06) gave their approval to the study. All the procedures were carried out in connection with the Declaration of Helsinki. Parents or legal guardians of all the participants were informed and their informed consent was sought prior to being enrolled in the study.

Results

Among the 200 children involved, 120 (60 percent) were identified to have vitamin D deficiency (< 20 ng/mL), 50 (25 percent) had insufficient amounts (20-30 ng/mL) and 30 (15 percent) had sufficient amounts (>30 ng /mL). Among the vitamin D deficient children, 75% of them had over three respiratory infections a year, whereas 45% of the adequate group had ($p < 0.001$). The average cases of infection per year were significantly greater in the deficient group (mean = 4.1 episodes/year) than in the sufficient group (mean = 2.3 episodes/year). It was also found that victims of vitamin D deficiency experienced more serious incidences of infection such as pneumonia and bronchitis. The correlation between vitamin D deficit and the rate and intensity of the frequency of recurrent respiratory infections was statistically significant ($p < 0.001$). These results would indicate that low level of vitamin D is strongly related to the predisposition of recurrence respiratory infections in children below the age of five.

Table 1: **Demographic Characteristics of Study Participants**

Characteristic	Vitamin D Deficient Group (n=120)	Vitamin D Insufficient Group (n=50)	Vitamin D Sufficient Group (n=30)
Mean Age (months)	28.5 (SD ± 18.7)	30.2 (SD ± 16.5)	29.8 (SD ± 15.4)
Gender (Male:Female)	60:60	25:25	15:15
Mean Weight (kg)	10.2 (SD ± 2.6)	10.4 (SD ± 2.3)	10.7 (SD ± 2.0)
Socioeconomic Status (Low/High)	80/40	30/20	15/15

Table 2: **Vitamin D Levels and Frequency of Respiratory Infections**

Vitamin D Level	Number of Infections per Year	Frequency of Respiratory Infections (%)	p-value
Vitamin D Deficiency (<20 ng/mL)	4.1 (SD ± 1.2)	75%	< 0.001

Vitamin D Insufficiency (20-30 ng/mL)	3.2 (SD ± 1.0)	55%	
Vitamin D Sufficient (>30 ng/mL)	2.3 (SD ± 0.8)	45%	

Table 3: **Incidence of Severe Respiratory Infections and Vitamin D Levels**

Vitamin D Level	Incidence of Pneumonia (%)	Incidence of Bronchiolitis (%)	Other Respiratory Infections (%)	p-value
Vitamin D Deficiency (<20 ng/mL)	35%	30%	10%	< 0.001
Vitamin D Insufficiency (20-30 ng/mL)	20%	25%	10%	
Vitamin D Sufficient (>30 ng/mL)	10%	15%	5%	

Table 4: **Demographics and Infection Frequency by Age Group**

Age Group (months)	Vitamin D Deficiency (<20 ng/mL) (%)	Vitamin D Insufficient (20-30 ng/mL) (%)	Vitamin D Sufficient (>30 ng/mL) (%)	Mean Infections per Year	p-value
<12 months	40%	25%	10%	4.5 (SD ± 1.3)	< 0.01
12-24 months	35%	20%	15%	3.9 (SD ± 1.1)	< 0.05
25-36 months	25%	20%	25%	3.3 (SD ± 0.9)	< 0.05
>36 months	20%	15%	30%	2.5 (SD ± 0.7)	

Discussion

The relationship between vitamin D deficiency and frequent respiratory infections (RRIs) among children aged below five, a group that is especially susceptible to respiratory disease. We find a strong association between low levels of vitamin D and a higher rate of recurrent respiratory infections and this is in line with increasing evidence on the same in the world literature in the last ten years. Vitamin D is also involved in the immune modulation process and its deficiency has been reported to contribute to increased vulnerability to infections especially in the respiratory tract (10).In our research, we identified that 60 percent of the children were vitamin D deficient, a statistic that is in accordance with the world statistics that indicate that vitamin D deficiency is very prevalent among children, especially in areas with low sunlight or that those with poor diets are highly affected (11). The great correlation between the lack of vitamin D and frequent respiratory infections confirms the hypothesis that the lack

of vitamin D weakens the immune system and children become more vulnerable to frequent respiratory infections. This result supports the literature, including that of Bunyavanich et al. (2018) who reported that there was a positive association between low vitamin D and a greater chance of catching a respiratory infection in children (12). Moreover, a research study conducted by Patel et al. (2019) has found that cases of respiratory viral infections such as influenza and RSV were more common in children with vitamin D deficiency (13).Vitamin D has been well documented as having a role in immune defense. Vitamin D plays a crucial role in the proper functioning of the innate immune system that involves the activation of the macrophages and dendritic cells that combat infections. It also induces generation of antimicrobial peptides which are very essential in the defense against pathogen (14). Lack of vitamin D has been linked to decreased quantities of such antimicrobial peptides which acts against the respiratory infections in the body. These findings are supported by our research, which revealed that, children with deficiency of vitamin D induced a considerably greater rate of infections, specifically pneumonia and bronchiolitis, which are prevalent severe respiratory diseases of early childhood (15).We find our results consistent with a meta-analysis study by Martineau et al. (2017), who found that vitamin D as supplementation decreases the risk of acute respiratory infections, especially in children with low baseline levels of vitamin D (16). Moreover, a research by Zhang et al. (2018) revealed that vitamin D deficiency was linked to more hospitalizations caused by respiratory infections, which demonstrated the possible advantages of addressing the issue of vitamin D deficiency to decrease health care burdens (17). These results indicate that vitamin D supplementation may be a cost-efficient measure to decrease the rate and severity of respiratory infections in children with a particular focus on children at high risk because of deficiency.Although we have observed in our study that there is strong positive correlation between vitamin D deficiency and frequent respiratory infections, it is necessary to note that our study is cross-sectional, and hence does not indicate causality. Longitudinal research or randomized control trial is required to show whether vitamin D supplementation can directly lower the occurrence of respiratory infections. To illustrate this, vitamin D supplementation, which resulted in a reduction in respiratory infections in children, was demonstrated in the study by Gombart et al. (2019), which supports the notion that vitamin D is protective against respiratory infections (18).The other interesting observation in our study was observed variations of infection frequency in terms of age groups. Children younger than 12 months of age with vitamin D deficiency had the greatest mean number of infections/year. Vitamin D supplementation may benefit this age group most since they are at a greater risk of infections, given that immature immune systems have been shown to be of great significance in immune responses development during early childhood (19). These findings are consistent with a study by Zosky et al. (2020), which determined that early vitamin D supplementation was capable of lowering the rate of respiratory infection in infants (20).Finally, our research confirms the current literature, which is building up that vitamin D deficiency is linked with the high risk of recurring respiratory infections among children below five years old. As there is a great prevalence of vitamin D deficiency among this age group and thus there is a possibility of vitamin D deficiency affecting immune functioning, vitamin D deficiency prevention by the use of supplementation may be an easy and effective way to decrease the burden of respiratory infections. Research on the causal relationship between respiratory infection and deficiency of vitamin D and the effectiveness of the supplementation in high-risk

groups requires further investigation.

Conclusion

Vitamin D deficiency is prevalent among children under five and is significantly associated with an increased frequency of recurrent respiratory infections. These findings highlight the importance of monitoring and addressing vitamin D deficiency in pediatric populations, potentially improving respiratory health outcomes through supplementation.

Limitations

This study's limitations include its cross-sectional design, which does not establish causality, and the potential for recall bias in reporting infection frequencies. Additionally, the sample size from a single center may limit the generalizability of the results to broader populations. Long-term studies with larger sample sizes are needed.

Future Findings

Future Study should focus on longitudinal studies to explore the causal relationship between vitamin D deficiency and recurrent respiratory infections. Randomized controlled trials assessing the effect of vitamin D supplementation on infection rates, particularly in high-risk populations, will be crucial for developing preventive strategies for improving child health outcomes.

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Authors Contributions

Concept & Design of Study: **Ijaz Ahmad**[3]

Drafting: **Misbah ullah khan**[2]

Data Analysis:**Afzal Ahmad**[1]

Critical Review:**Afzal Ahmad**[1]

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