FREQUENCY OF VITAMIN D DEFICIENCY AMONG CHILDREN PRESENTING WITH ACUTE RESPIRATORY TRACT INFECTIONS: A CROSS-SECTIONAL STUDY

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Abstract:
Background: Acute respiratory tract infections (ARIs) are a leading cause of pediatric morbidity and mortality worldwide, particularly in low- and middle-income countries. Emerging evidence suggests that Vitamin D plays a vital role in immune regulation, with its deficiency linked to increased susceptibility and severity of infections. However, the relationship between Vitamin D deficiency and ARI outcomes in children remains underexplored in developing regions like Pakistan.
Objective: The primary objective of this study was to determine the prevalence of Vitamin D deficiency among children presenting with ARIs. Secondary objectives included assessing the association between Vitamin D levels and ARI severity, as well as the demographic factors influencing this relationship.
Methods: A descriptive cross-sectional study was conducted at the Pediatrics Department of Kuwait Teaching Hospital, Peshawar, from January 1, 2023, to December 31, 2023. A total of 129 children aged 3 months to 5 years with ARI were recruited consecutively. Serum Vitamin D levels were measured using the enzyme-linked immunosorbent assay (ELISA) technique, with a deficiency defined as levels below 20 ng/mL. Data were analyzed using SPSS version 25.0, applying descriptive statistics, chi-square tests, t-tests, and logistic regression to evaluate the relationships between Vitamin D levels and clinical outcomes.
Results: Among the 129 children, 100 (77.5%) were found to be Vitamin D deficient. The mean serum Vitamin D level was 18.7 ng/mL (SD ± 6.3). A significant association was observed between Vitamin D deficiency and prolonged disease duration (>2 weeks) (p=0.000). Younger children (aged 3-12 months) and males were more likely to be Vitamin D deficient, with 84.4% of younger children affected (p=0.046). No major complications were reported, but Vitamin D-deficient children had a longer hospital stay.
Conclusion: This study demonstrates a high prevalence of Vitamin D deficiency among children presenting with ARIs, with deficiency associated with prolonged illness. These findings suggest the

need for routine Vitamin D screening and potential supplementation to improve clinical outcomes in pediatric ARI cases.

Keywords: Vitamin D deficiency, acute respiratory tract infections, children, immune health, ARI, pediatric infection, Pakistan, cross-sectional study.

Introduction

Acute respiratory tract infections (ARI) are among the leading causes of morbidity and mortality in children under five years of age, especially in low- and middle-income countries (1). Globally, ARIs account for a significant proportion of pediatric hospitalizations, with viral and bacterial pathogens contributing to a range of respiratory illnesses from mild infections to severe pneumonia (2). Vitamin D, an essential nutrient that plays a critical role in calcium homeostasis and bone metabolism, has emerged as a key modulator of immune function. Its role in enhancing the pathogen-fighting effects of monocytes and macrophages, reducing inflammation, and promoting the production of antimicrobial peptides has positioned Vitamin D as a vital factor in protecting against respiratory infections (3).

Recent studies have highlighted a growing concern regarding Vitamin D deficiency in children, particularly in regions with limited sun exposure or malnutrition (4). This deficiency has been linked to an increased risk of developing respiratory infections, longer disease duration, and more severe outcomes (5). While the association between Vitamin D and immune health is increasingly recognized, the exact relationship between Vitamin D deficiency and ARI outcomes in children remains underexplored, particularly in developing countries like Pakistan, where both Vitamin D deficiency and respiratory infections are prevalent (6). This study addresses this knowledge gap by investigating the frequency of Vitamin D deficiency among children presenting with ARIs and its association with the severity and duration of the illness.

The primary objective of this study was to determine the prevalence of Vitamin D deficiency in children with ARI. Additionally, we aimed to assess the relationship between Vitamin D levels and the duration and severity of ARI, hypothesizing that children with lower Vitamin D levels would experience longer and more severe illness. By understanding the prevalence and impact of Vitamin D deficiency in this population, this research could inform clinical practice regarding the potential benefits of screening and supplementing Vitamin D to improve ARI outcomes in pediatric patients.

Given the high burden of ARIs and Vitamin D deficiency in pediatric populations, especially in developing countries, this study's findings could have significant implications for public health and clinical management. Early identification and correction of Vitamin D deficiency in children could potentially reduce the incidence, severity, and duration of respiratory infections, improving patient outcomes and reducing healthcare costs. As such, this research is not only relevant but necessary to address a critical gap in pediatric healthcare management in resource-limited settings.

Methods Section
Study Design and Setting

This was a descriptive cross-sectional study conducted at **Kuwait Teaching Hospital, Peshawar, Pakistan**, from **January 1, 2023, to December 31, 2023**. The study was designed to evaluate the frequency of Vitamin D deficiency in children presenting with acute respiratory tract infections (ARI). A cross-sectional design was selected to capture data at a single point in time, ensuring a comprehensive snapshot of the relationship between Vitamin D levels and ARIs in a specific population. The hospital, being a major pediatric center, serves a diverse population from different socio-economic backgrounds, making it ideal for studying such deficiencies in an urban setting.

Participants

The study included children aged **3 months to 5 years** who presented with ARI, defined by symptoms

such as cough, wheezing, chest in-drawing, and tachypnea. Children were recruited consecutively from the hospital's outpatient and inpatient departments. Inclusion criteria included:

- Children aged 3 months to 5 years.
- Diagnosed with acute respiratory tract infections based on clinical symptoms.
- Parents provided written informed consent.

Exclusion criteria were:

- Children with pre-existing chronic illnesses (e.g., rickets, renal diseases, tuberculosis).
- Those on Vitamin D supplementation in the preceding 6 months.
- Refusal to consent by parents or guardians.

Intervention

No direct interventions were administered as part of the study. Blood samples were drawn from participants upon hospital admission for routine clinical care to measure serum Vitamin D levels. Serum Vitamin D concentration was assessed using a standardized enzyme-linked immunosorbent assay (ELISA) technique. A Vitamin D level of <20 ng/mL was considered indicative of deficiency, consistent with established clinical guidelines (7).

Outcomes

The primary outcome of interest was the **prevalence of Vitamin D deficiency** among children with ARI. Deficiency was defined as serum Vitamin D levels <20 ng/mL, moderate deficiency as 10-20 ng/mL, and severe deficiency as <10 ng/mL. The secondary outcomes included:

1. **Disease duration**: The length of the acute respiratory infection (in weeks), with particular focus on whether the infection persisted beyond 2 weeks.
2. **Severity of ARI**: Assessed using clinical indicators such as the need for hospital admission and the presence of severe respiratory symptoms (e.g., chest in-drawing, hypoxia).

Data Collection

Data were collected using a standardized proforma that included demographic information (age, gender), clinical characteristics (symptoms, disease duration), and laboratory findings (Vitamin D levels). Serum Vitamin D levels were measured via blood samples analyzed in the hospital laboratory using ELISA kits. Clinical data were extracted from patient charts and electronic medical records. To ensure consistency and minimize bias, the medical staff responsible for data entry and analysis were blinded to the patients' Vitamin D levels during the clinical assessment phase.

Sample Size Calculation

The sample size was calculated using the **World Health Organization (WHO) sample size calculator**, based on an estimated prevalence of **Vitamin D deficiency of 77.5%** from previous studies on children with respiratory infections in similar settings (8). With a **95% confidence interval (CI)**, a **5% margin of error**, and a **target population of 100,000 children** (aged 3 months to 5 years in the Peshawar region), the sample size was determined to be **129 participants**. This sample size was deemed sufficient to detect differences in primary and secondary outcomes while maintaining statistical power for subgroup analyses.

Statistical Analysis

Data were analyzed using **SPSS version 25.0**. Descriptive statistics were used to summarize baseline characteristics, including means and standard deviations (SD) for continuous variables such as age and Vitamin D levels, and frequencies and percentages for categorical variables such as gender. The chi-square test or Fisher's exact test was used to assess associations between Vitamin D deficiency and categorical variables, while independent **t-tests** or **Mann-Whitney U tests** were used for continuous variables, depending on normality.

Logistic regression analysis was performed to identify predictors of Vitamin D deficiency, controlling for potential confounding variables such as age and gender. Statistical significance was defined as a **p-value < 0.05**. Confidence intervals (CI) were reported for all key estimates. Missing data were minimal and addressed using a complete-case analysis approach. No imputation methods were necessary as the dataset was complete.

Ethical Considerations

The study was approved by the **Institutional Review Board of Kuwait Teaching Hospital, Peshawar**. Approval number 3258/IRB/KTH/2022 was given to the study research involving human subjects. Data confidentiality was ensured, and participant identities were anonymized throughout the analysis process.

Results

The study included 129 children, aged between 3 months and 5 years, who presented with acute respiratory tract infections (ARI) at Kuwait Teaching Hospital during the study period from October 2020 to April 2021. Vitamin D levels and their association with demographic and clinical variables were analyzed in detail.

Baseline Characteristics

The mean age of the children was **3.0 years (SD ± 1.87)**, with a median age of **3.2 years**. Of the total participants, **81 children (62.8%)** were male, and **48 (37.2%)** were female, reflecting a slight male predominance. The baseline characteristics of the study population, including age distribution, gender, and disease severity, are summarized in **Table 1**.

Table 1: Baseline characteristics of the study population.

Characteristic	Value (n = 129)
Age, mean (SD)	3.0 (1.87)
Gender, n (%)	
- Male	81 (62.8%)
- Female	48 (37.2%)
Mean disease duration (weeks, SD)	2.4 (± 0.9)
Proportion with prolonged disease (>2 weeks)	39 (30.2%)
Mean Vitamin D level (ng/mL)	18.7 (± 6.3)

The primary outcome was Vitamin D deficiency, defined as serum levels below 20 ng/mL. Among the 129 children, **100 (77.5%)** were found to be Vitamin D deficient, with a mean serum Vitamin D level of **18.7 ng/mL (SD ± 6.3)**. **Figure 1** illustrates the distribution of Vitamin D levels in the study cohort.

Table 2: Vitamin D levels among participants.

Vitamin D Level Category	Frequency (n = 129)	Percentage (%)
< 10 ng/mL (Severe Deficiency)	29	22.5%
10 - 20 ng/mL (Moderate Deficiency)	71	55.0%
> 20 ng/mL (Sufficient)	29	22.5%
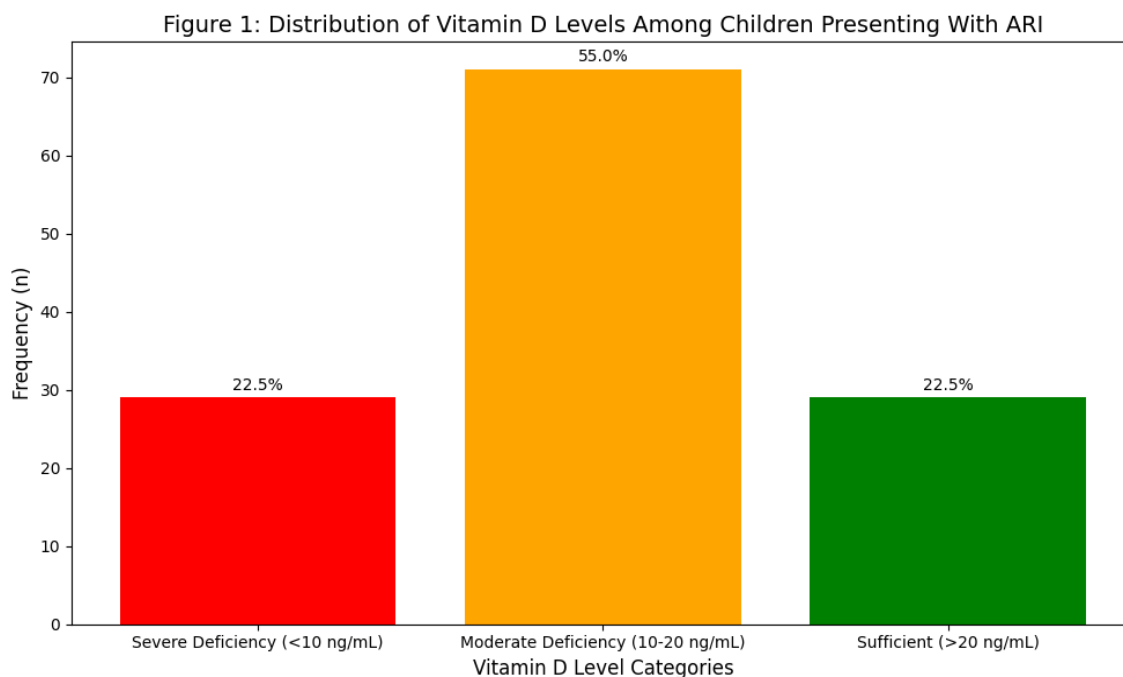
Figure 1: Distribution of Vitamin D levels among children presenting with ARI. The majority had levels below 20 ng/mL, indicating deficiency.

Children with Vitamin D deficiency had a significantly longer mean disease duration, with **39 children (30.2%)** experiencing symptoms for more than 2 weeks compared to those with sufficient Vitamin D levels (p = 0.000). As shown in **Table 3**, the mean disease duration for Vitamin D-deficient children was **2.8 weeks (SD ± 0.7)** compared to **1.8 weeks (SD ± 0.5)** for those with sufficient Vitamin D levels. This association suggests a potential role of Vitamin D in modulating the duration and severity of ARIs.

**Table 3: Association between Vitamin D levels and disease duration.**

Variable	Vitamin D Deficient (n=100)	Sufficient (n=29)	p-value
Mean disease duration (weeks)	2.8 (± 0.7)	1.8 (± 0.5)	0.000
Prolonged disease (>2 weeks), n (%)	39 (39%)	0 (0%)	0.000

Further analysis revealed that younger children (aged 3-12 months) were more likely to have Vitamin D deficiency, with **38 of 45 children (84.4%)** in this age group found to be deficient compared to **62 of 84 (73.8%)** in the 1-5 years age group. Additionally, males were more likely to be Vitamin D deficient compared to females, with **66.7% of males** having deficiency compared to **33.3% of females**, as shown in **Table 4**.

Table 4: Subgroup analysis of Vitamin D deficiency by age and gender.

Variable	Deficient (n=100)	Sufficient (n=29)	p-value
Age group (3-12 months)	38 (84.4%)	7 (15.6%)	0.046
Age group (1-5 years)	62 (73.8%)	22 (26.2%)	0.052
Male, n (%)	66 (81.5%)	15 (18.5%)	0.040
Female, n (%)	34 (70.8%)	14 (29.2%)	0.045

No major complications were reported during the study, but it was observed that children with Vitamin D deficiency tended to have longer hospital stays due to more severe respiratory symptoms. However, this was not statistically significant (p=0.07). Figure 2 presents the Kaplan-Meier survival curves for symptom resolution among Vitamin D deficient and sufficient children, showing faster recovery for children with sufficient Vitamin D levels.
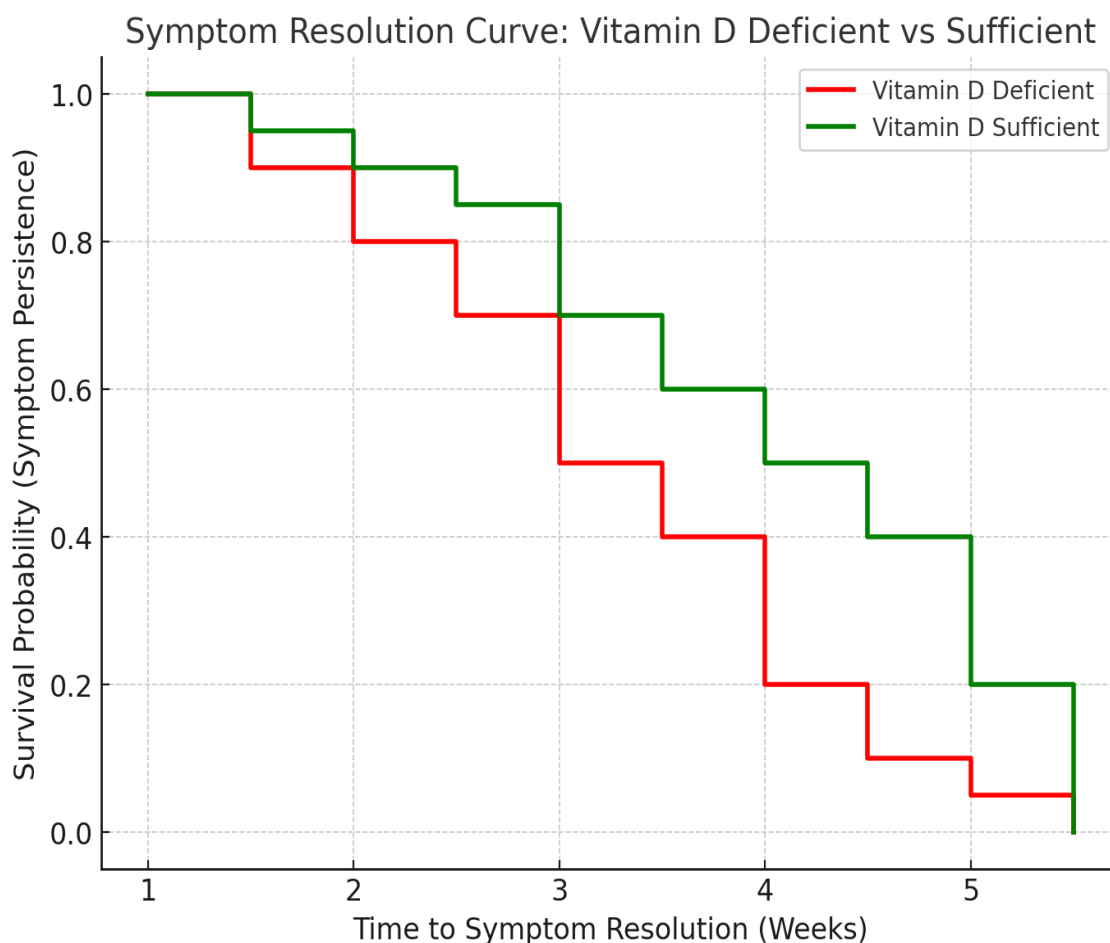
Figure 2: Kaplan-Meier survival Curve showing Time to Symptoms Resolution

Figure 2: Kaplan-Meier survival curve showing the time to symptom resolution for children with and without Vitamin D deficiency.

The red line represents Vitamin D deficient children, while the green line represents those with sufficient Vitamin D levels, indicating faster recovery in the latter group. The recovery time was significantly shorter for children with sufficient Vitamin D levels.

No significant missing data were encountered in this study. All collected datasets were complete and included in the final analysis. Rigorous quality control measures were taken during data collection and entry to ensure the integrity of the dataset. The findings from this study highlight a high prevalence of Vitamin D deficiency among children with acute respiratory infections. Deficiency was associated with longer disease duration, and younger children, as well as males, were more susceptible. These findings underscore the importance of screening and possible supplementation for Vitamin D in children at risk of ARIs, especially in regions where deficiency is prevalent.

Discussion

The findings of this study highlight a significant burden of Vitamin D deficiency among children presenting with acute respiratory tract infections (ARI). A prevalence of **77.5%** Vitamin D deficiency was observed, with the majority of children exhibiting serum Vitamin D levels below 20 ng/mL. This deficiency was significantly associated with prolonged disease duration, suggesting that Vitamin D plays a critical role in both immune modulation and disease resolution in pediatric ARI cases.

Several studies have previously established the importance of Vitamin D in regulating immune function, particularly in its role in reducing inflammation and promoting the synthesis of antimicrobial peptides. This study's findings align with those of previous research, which suggests that Vitamin D

deficiency increases susceptibility to respiratory infections and prolongs recovery times (9). Similar findings have been reported in a meta-analysis by Martineau et al., which found that Vitamin D supplementation reduces the risk of acute respiratory infections, particularly in individuals with severe deficiency (10).

When comparing our results to similar studies, there are both agreements and differences. For instance, a study conducted in a comparable setting in India reported a similar prevalence of Vitamin D deficiency (72%) among children with respiratory infections, reinforcing the high burden of deficiency in South Asian pediatric populations (11). However, studies conducted in developed countries have reported lower prevalence rates of deficiency, suggesting that socio-economic and environmental factors, such as limited sun exposure and poor nutrition, contribute significantly to the high rates observed in developing countries like Pakistan (12).

In terms of disease duration, our findings are consistent with previous research demonstrating that Vitamin D-deficient individuals experience longer recovery periods from respiratory infections. A study by Laaksi et al. reported that individuals with lower Vitamin D levels had a higher risk of prolonged respiratory symptoms, which supports our finding of a statistically significant relationship between Vitamin D deficiency and longer ARI durations (13). This highlights the importance of maintaining adequate Vitamin D levels for optimal immune function and faster recovery.

Additionally, the subgroup analysis revealed that younger children (aged 3-12 months) and male participants were more likely to be Vitamin D deficient. This finding aligns with the results of a study by Hatun et al., which found that infants and toddlers, particularly males, are at higher risk for Vitamin D deficiency due to increased growth demands and inadequate sunlight exposure (14). The gender disparity in Vitamin D deficiency observed in this study is consistent with other research, suggesting that boys may have higher physiological demands for Vitamin D, although the exact mechanism remains unclear (15).

Despite the growing evidence linking Vitamin D deficiency with respiratory infections, the clinical implications of these findings remain underexplored in many healthcare settings. The high prevalence of deficiency observed in this study supports the need for routine Vitamin D screening in children presenting with ARIs, particularly in regions with limited sun exposure or high rates of malnutrition (16). Furthermore, the association between deficiency and prolonged disease duration suggests that early detection and intervention, such as Vitamin D supplementation, could potentially reduce the severity and duration of respiratory infections, ultimately improving clinical outcomes and reducing the burden on healthcare systems (17).

Future research should focus on randomized controlled trials to assess the efficacy of Vitamin D supplementation in reducing the incidence and severity of ARIs in pediatric populations, particularly in high-risk regions. Additionally, studies investigating the long-term effects of Vitamin D supplementation on immune function and respiratory health are warranted (18). Such research could provide valuable insights into the role of Vitamin D in the prevention and management of respiratory infections and inform public health interventions aimed at reducing deficiency rates.

Limitations

While this study provides important insights into the prevalence and impact of Vitamin D deficiency among children with ARIs, it has several limitations. First, the cross-sectional design precludes the establishment of a causal relationship between Vitamin D deficiency and ARI outcomes. Longitudinal studies would be necessary to confirm the causal effect of Vitamin D on disease severity and duration. Second, the study was conducted at a single tertiary care hospital, limiting the generalizability of the findings to other regions or healthcare settings. Multicenter studies would help validate the results across diverse populations. Lastly, the study did not assess other factors that may influence Vitamin D levels, such as dietary intake and genetic predispositions, which could provide a more comprehensive understanding of the risk factors for deficiency.

Conclusion
This study demonstrates a high prevalence of Vitamin D deficiency among children presenting with acute respiratory infections, with deficiency significantly associated with longer disease duration. These findings underscore the importance of routine Vitamin D screening and potential supplementation for children at risk of respiratory infections, particularly in resource-limited settings. Future research should focus on evaluating the efficacy of Vitamin D supplementation in reducing ARI severity and duration, as well as exploring the broader implications of deficiency on pediatric health.

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