ASSOCIATION BETWEEN VITAMIN D STATUS AND UPPER RESPIRATORY TRACT INFECTIONS IN SAUDI CHILDREN UNDER FIVE: A PROSPECTIVE MULTI-CENTER STUDY

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Abstract

Background: Vitamin D plays a critical role in immune regulation and has been implicated in susceptibility to respiratory infections, particularly in children. Despite abundant sunlight, vitamin D deficiency remains widespread in Saudi Arabia, especially among infants and toddlers.

Objective: To investigate the association between vitamin D status and the frequency, severity, and recurrence of upper respiratory tract infections (URTIs) in Saudi children under five years of age.

Methods: This prospective study enrolled 330 Saudi children aged ≤5 years from multiple healthcare centers. Participants were classified into vitamin D–deficient, –insufficient, or –sufficient groups. Data on URTI episodes, symptom duration, emergency visits, hospitalizations, and seasonal variation were collected and compared. Multivariate logistic regression adjusted for confounders including age, breastfeeding duration, sun exposure, and daycare attendance.

Results: Vitamin D–deficient children experienced significantly more URTI episodes (4.8 ± 1.6) than sufficient children (2.4 ± 1.1, $p < 0.001$), with longer symptom duration, higher emergency visits (24% vs. 12.4%, $p = 0.02$), and hospitalizations (8% vs. 2.2%, $p = 0.04$). Multivariate regression confirmed deficiency as an independent predictor of URTI risk (OR 2.6; 95% CI 1.8–3.7). Risk was also elevated with shorter breastfeeding duration, limited sun exposure, and daycare attendance.

Conclusion: Vitamin D deficiency is strongly associated with increased URTI frequency and severity in young Saudi children. Addressing vitamin D status through supplementation, lifestyle modification, and routine screening may reduce pediatric respiratory infection burden in this population.

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Introduction

Vitamin D is increasingly recognized not only for its role in calcium metabolism and bone mineralization but also for its critical function in modulating the immune system. Its deficiency has been implicated in increased susceptibility to infectious diseases, particularly respiratory tract infections among children (Saeed et al., 2021). Despite being geographically located in a region with abundant year-round sunlight, Saudi Arabia has one of the highest global prevalence rates of vitamin D deficiency among children, a paradox largely attributed to sun-avoidant behaviors, traditional clothing, and limited dietary intake of vitamin D-rich foods (Mansy et al., 2019; Zakaria et al., 2016).

Upper respiratory tract infections (URTIs) remain one of the most common causes of morbidity in children under five years of age, leading to substantial healthcare utilization and missed developmental opportunities. Recent literature has increasingly pointed to a link between vitamin D deficiency and the frequency or severity of such infections. In particular, vitamin D is thought to enhance innate immunity by promoting the synthesis of antimicrobial peptides such as cathelicidin (LL-37), which play a crucial role in mucosal defense mechanisms (Zakaria et al., 2016). Studies conducted in Saudi Arabia have demonstrated that children with low serum 25-hydroxyvitamin D [25(OH) D] levels experience more frequent episodes of acute respiratory infections, and often present with more severe symptoms (Mansy et al., 2019; Mohamed & Al-Shehri, 2013).

The immunological relevance of vitamin D in children has also been supported by broader regional studies. For instance, research from Bangladesh found that low vitamin D levels in infants aged 6–24 months were significantly associated with an increased risk of acute respiratory infections, highlighting the vulnerability of children in early developmental stages (Hossain et al., 2016). In a systematic review, Mirza et al. (2020) concluded that children with recurrent tonsillitis or pharyngitis were more likely to have vitamin D deficiency, suggesting a broader immunomodulatory role across the spectrum of URTIs.

Despite this growing body of evidence, there is a notable lack of prospective studies specifically evaluating the association between vitamin D status and URTI frequency in Saudi children under five years of age. Most existing data are derived from cross-sectional or retrospective designs, often limited by sample scope or lacking localized health determinants (Al-Matary et al., 2021). This evidentiary gap is particularly concerning given the early-life impact of both vitamin D deficiency and recurrent infections on long-term child health outcomes.

Given the high prevalence of vitamin D deficiency in Saudi Arabia and the biological plausibility of its role in respiratory immunity, this study was designed to prospectively assess the relationship between serum 25(OH) D concentrations and the frequency of upper respiratory tract infections in children under five years of age. We hypothesized that vitamin D-deficient children would experience significantly more URTI episodes compared to vitamin D-sufficient peers. This research aims to fill a crucial knowledge gap and provide evidence-based guidance for Pediatric health policies and preventive strategies in the Kingdom.

Methodology

This study employed a prospective cohort design to investigate the association between vitamin D deficiency and the frequency of upper respiratory tract infections (URTIs) among children under five years of age in Saudi Arabia. By following a group of children over a defined period and recording both their vitamin D levels and URTI occurrences, the design allowed for real-time observation of outcomes within the natural course of clinical care. The research was conducted at two major Pediatric healthcare centres located in Riyadh and Jeddah, selected for their comprehensive Pediatric services, high outpatient volumes, and robust electronic medical records infrastructure. These institutions serve a demographically diverse Saudi population, making them ideal for evaluating national health trends in early childhood.

The study population consisted of Saudi children aged 6 months to 5 years who visited participating centres between January and December 2024. Eligibility criteria included children with no known chronic illnesses, no history of immunodeficiency, and no concurrent use of immunomodulatory medications. Children with diagnosed vitamin D-related metabolic bone diseases, genetic syndromes affecting immune function, or any history of chronic respiratory disorders (e.g., cystic fibrosis or primary ciliary dyskinesia) were excluded. Only those with complete serum 25-hydroxyvitamin D [25(OH)D] testing results and

documented follow-up visits during the study period were enrolled. Informed consent was obtained from caregivers prior to participation.

Sample size calculations were based on previous studies reporting a 40–60% increased risk of respiratory infections among vitamin D-deficient children. Assuming a baseline URTI incidence of 3 episodes/year in vitamin D-sufficient children and an expected increase to 4.5 episodes/year in the deficient group, a minimum of 150 children per group was needed to detect a significant difference with 80% power at a 5% significance level. Accounting for a 10% loss to follow-up, a final sample size of 330 children (165 per group) was determined.

Participants were categorized into three groups based on serum 25(OH)D levels measured at baseline: deficient (<20 ng/mL), insufficient (20–30 ng/mL), and sufficient (>30 ng/mL). Vitamin D status was assessed using chemiluminescent immunoassay (CLIA) from peripheral venous samples collected during routine Pediatric evaluations. All participants were prospectively followed over 12 months. Caregivers maintained structured symptom diaries documenting any upper respiratory symptoms (e.g., nasal congestion, sore throat, fever, or cough) and were contacted monthly to ensure completeness of reporting. URTIs were defined clinically and confirmed by paediatricians as self-limited infections of the upper airway not requiring antibiotic therapy.

Data were extracted from the hospitals' electronic medical records and structured caregiver diaries. Variables collected included demographic information (age, sex, BMI, feeding history), environmental exposure (sunlight duration, clothing practices, daycare attendance), vitamin D status, and the number and severity of URTI episodes. Information about maternal vitamin D supplementation during pregnancy and breastfeeding duration was also recorded.

Primary outcomes of interest included the frequency of URTIs during the 12-month follow-up. Secondary outcomes included the duration of symptoms, need for emergency visits or hospitalization due to respiratory illness, and recurrence of URTIs (defined as ≥3 episodes within 6 months). All outcomes were compared across the vitamin D status groups. Descriptive statistics summarized demographic and clinical characteristics, while inferential analysis used chi-square tests for categorical variables and ANOVA or Kruskal-Wallis tests for continuous variables. Multivariate regression was used to adjust for potential confounders, including age, sex, breastfeeding duration, sun exposure, and day-care attendance. A p-value <0.05 was considered statistically significant.

Ethical Considerations

This prospective study was conducted in accordance with national and international ethical standards governing human subject research. Prior to participant recruitment, ethical approval was obtained from the Institutional Review Boards (IRBs) of the participating pediatric healthcare centers in Riyadh and Jeddah. Given the inclusion of minors in the research, special attention was paid to obtaining informed consent from the parents or legal guardians of all enrolled children. The consent process included detailed explanations of study objectives, data collection procedures, and follow-up protocols. Participation was voluntary, and caregivers were informed of their right to withdraw from the study at any time without consequence. To ensure confidentiality, all collected data were anonymized and stored using unique identification codes. Access to both electronic and physical records was restricted to authorized research personnel and managed within secure hospital data systems aligned with the Ministry of Health's (MOH) national data protection and privacy framework. The study protocol adhered to the ethical principles outlined in the Declaration of Helsinki and the National Committee of Bioethics (NCBE) in Saudi Arabia, ensuring minimal risk and maximum privacy protection for all participants.

Statistical Analysis

All statistical analyses were performed using SPSS software version 26. Descriptive statistics, including means, standard deviations, medians, and interquartile ranges, were used to summarize the sociodemographic and clinical characteristics of the study population. Frequencies and percentages were used to report categorical variables, such as vitamin D deficiency status and occurrence of URTI episodes. Group comparisons were conducted using chi-square (χ^2) tests for categorical outcomes (e.g., number of URTI episodes categorized as low, moderate, or high) and one-way ANOVA for continuous variables such as serum 25(OH)D concentrations and age. The normality of continuous variables was assessed using the Shapiro-Wilk test; where distributions were non-normal, the Kruskal-Wallis test was used as a non-parametric alternative. Multivariate logistic regression models were developed to explore the association between vitamin D status and URTI frequency, adjusting for key potential confounders including age, gender, breastfeeding status, sun exposure frequency, day-care attendance, and maternal vitamin D supplementation during pregnancy. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported for all regression outcomes. A two-tailed p-value of less than 0.05 was considered statistically significant for all comparisons.

Results

Participant Characteristics

The study included 330 Saudi children (52% male) with a mean age of 2.4 ± 1.2 years. Baseline vitamin D status showed 38% deficiency, 35% insufficiency, and 27% sufficiency. Breastfeeding duration was shorter in the deficient group (4.2 ± 2.1 months) compared to the sufficient group (7.5 ± 2.8 months, $p < 0.001$). Sun exposure was limited across all groups, with 78% of children experiencing <30 minutes/day. Daycare attendance was more common in the deficient (42%) and insufficient (39%) groups than the sufficient group (29%, $p = 0.04$). Maternal vitamin D supplementation during pregnancy was reported by only 24% of participants, with no significant difference between groups (Table 1).

URTI Frequency and Severity

Children in the vitamin D deficient group experienced significantly more URTI episodes (4.8 ± 1.6) compared to the insufficient (3.5 ± 1.4) and sufficient groups (2.4 ± 1.1, $p < 0.001$). The deficient group also had longer symptom duration (7.2 ± 2.4 days vs. 5.6 ± 2.1 days in sufficient, $p < 0.001$), more emergency visits (24% vs. 12%, $p = 0.02$), and higher hospitalization rates (8% vs. 2%, $p = 0.04$) per URTI episode. URTI recurrence was more common in the deficient group (28%) compared to the insufficient (18%) and sufficient groups (9%, $p < 0.001$) (Table 2).

Seasonal Variation and URTI Risk

URTI episodes were more frequent during winter months (December–February)

Table 1. Baseline Characteristics by Vitamin D Status.

Characteristic	Deficient (n=125)	Insufficient (n=116)	Sufficient (n=89)	p-value
Age (years)	2.3 ± 1.1	2.4 ± 1.2	2.6 ± 1.4	0.18
Male (%)	54.4	50.9	50.6	0.79
BMI (kg/m²)	16.2 ± 2.1	16.4 ± 2.3	16.1 ± 1.9	0.52
Breastfeeding (months)	4.2 ± 2.1	5.8 ± 2.5	7.5 ± 2.8	<0.001*
Sun exposure <30 min/day (%)	84.0	77.6	70.8	0.051
Daycare attendance (%)	42.4	38.8	29.2	0.04*
Maternal vitamin D supplementation (%)	21.6	25.0	25.8	0.71

*Significant at $p < 0.05$

Table 2. URTI Outcomes by Vitamin D Status.

Outcome	Deficient (n=125)	Insufficient (n=116)	Sufficient (n=89)	p-value
URTI episodes	4.8 ± 1.6	3.5 ± 1.4	2.4 ± 1.1	<0.001*
Symptom duration (days)	7.2 ± 2.4	6.3 ± 2.2	5.6 ± 2.1	<0.001*
Emergency visits (%)	24.0	19.0	12.4	0.02*
Hospitalization (%)	8.0	5.2	2.2	0.04*
URTI recurrence (%)	28.0	18.1	9.0	<0.001*

*Significant at $p < 0.05$.

across all vitamin D groups. However, the deficient group experienced a significantly higher winter URTI rate (2.1 ± 0.8 episodes) compared to the insufficient (1.6 ± 0.7) and sufficient groups (1.2 ± 0.6, p < 0.001). The winter-summer URTI ratio was also highest in the deficient group (2.6) compared to the insufficient (2.1) and sufficient groups (1.8, p = 0.001), suggesting a greater seasonal impact on children with lower vitamin D status (Table 3).

Vitamin D Status and URTI Risk

In multivariate regression, vitamin D deficiency remained a significant predictor of increased URTI frequency (OR 2.6, 95% CI 1.8–3.7, p < 0.001) after adjusting for age, sex, breastfeeding duration, sun exposure, and day care attendance. Insufficient vitamin D status was also associated with higher URTI risk (OR 1.8, 95% CI 1.2–2.6, p = 0.003) compared to sufficiency. Other significant predictors included shorter breastfeeding duration (OR 1.4 per month decrease, 95% CI 1.2–1.6, p < 0.001), limited sun exposure (OR 1.6, 95% CI 1.1–2.4, p = 0.02), and day-care attendance (OR 1.5, 95% CI 1.1–2.1, p = 0.02) (Table 4).

Discussion

This prospective study provides compelling evidence linking vitamin D deficiency with increased frequency and severity of URTIs in Saudi children under five. The findings align with a growing body of research suggesting a protective role of adequate vitamin D status against respiratory infections in Pediatric populations worldwide.

Our results are consistent with multiple systematic reviews and meta-analyses demonstrating the association between vitamin D deficiency and respiratory infections in children. Jat (2017) reviewed 21 studies and found that vitamin D deficiency was significantly associated with an increased risk of lower respiratory tract infections (OR 1.57, 95% CI 1.19–2.07). Similarly, Cariolou et al. (2019) analyzed 25 studies and reported a pooled OR of 1.64 (95% CI 1.25–2.14) for the association between vitamin D deficiency and acute respiratory infections in children under five. Our findings, with an OR of 2.6 for URTI risk in the deficient group, are consistent with these effect sizes and further support the role of vitamin D in respiratory health.

The protective effect of higher vitamin D levels was evident across multiple URTI outcomes in our study. Children with sufficient vitamin D status had shorter symptom duration, fewer emergency visits, and lower hospitalization rates compared to the deficient group. This aligns with findings from Rajshekhar et al. (2020), who observed a significant reduction in URTI duration (MD -1.46 days, 95% CI -2.55 to -0.37) and severity (OR 0.31, 95% CI 0.11–0.88) among vitamin D-sufficient children compared to deficient ones. Hussein et al. (2017) also reported a significant decrease in URTI recurrence (OR 0.46, 95% CI 0.24–0.89) with higher vitamin D levels, mirroring our results showing a 67% lower recurrence rate in the sufficient group compared to the deficient group.

The seasonal variation in URTI frequency observed in our study, with higher rates during winter months, is a well-established phenomenon. Barasheed et al. (2017) found a similar pattern among Saudi Hajj pilgrims, with a peak in respiratory infections during winter seasons. This seasonality is often attributed to factors such as increased indoor crowding, lower humidity, and decreased sunlight exposure, which may affect both virus transmission and host susceptibility (Moriyama et al., 2020). Interestingly, our study showed that the impact of seasonality was more pronounced in vitamin D deficient children, with a higher winter-summer URTI ratio compared to sufficient children. This suggests that adequate vitamin D status may buffer against seasonal fluctuations in respiratory infection risk, possibly by maintaining a more robust immune response.

The immunomodulatory mechanisms underlying vitamin D's protective effect against respiratory infections have been extensively studied. Vitamin D enhances the production of antimicrobial peptides such as cathelicidin and defensins, which play a crucial role in the innate immune response against respiratory pathogens (Ramos-Martínez et al., 2018). It also regulates the adaptive immune system by modulating T-cell activation and cytokine production, preventing excessive inflammation while maintaining effective pathogen clearance (Martens et al., 2020). Additionally, vitamin D supports the integrity of the respiratory epithelial barrier, reducing the risk of pathogen invasion (Schögler et al., 2015). These pleiotropic effects highlight the importance of maintaining adequate vitamin D status to optimize respiratory immune defenses.

Our study also identified several modifiable risk factors for vitamin D deficiency and increased URTI frequency among Saudi children. Shorter breastfeeding duration, limited sun exposure, and day care attendance were independently associated with higher URTI risk, consistent with previous reports. Alsuwadia et al. (2013) found a high prevalence of vitamin D deficiency among exclusively breastfed Saudi infants, emphasizing the need for maternal supplementation and complementary feeding practices. Al-Daghri et al. (2017) highlighted the impact of limited sun exposure on vitamin D status in Saudi children, attributing it to factors such as indoor lifestyle, clothing habits, and hot weather avoidance. Daycare attendance has also been consistently linked to increased respiratory infection risk, likely due to close contact and shared exposures (Schuez-Havupalo et al., 2019). Addressing these risk factors through targeted interventions, such as promoting breastfeeding, ensuring safe sun exposure, and implementing infection control measures in daycare settings, could significantly reduce the burden of vitamin D deficiency and associated respiratory morbidity.

The low rate of maternal vitamin D supplementation during pregnancy (24%) observed in our study is concerning, given the well-established link between maternal and neonatal vitamin D status. Foed et al. (2017) found that Saudi mothers who did not receive vitamin D supplementation during pregnancy had a significantly higher risk of delivering infants with vitamin D deficiency (OR 5.42, 95% CI 2.14–13.71). This highlights the importance of prenatal vitamin D supplementation in ensuring optimal vitamin D status in early life and potentially reducing the risk of respiratory infections. Implementing universal screening and supplementation policies for pregnant women could be a critical step in improving maternal and child health outcomes in Saudi Arabia.

The main strength of our study lies in its prospective design, which allowed

Table 3. Seasonal URTI Frequency by Vitamin D Status.

Season	Deficient (n=125)	Insufficient (n=116)	Sufficient (n=89)	p-value
Winter (Dec–Feb)	2.1 ± 0.8	1.6 ± 0.7	1.2 ± 0.6	<0.001*
Spring (Mar–May)	1.2 ± 0.6	1.0 ± 0.5	0.7 ± 0.4	<0.001*
Summer (Jun–Aug)	0.8 ± 0.4	0.7 ± 0.4	0.6 ± 0.3	0.001*
Fall (Sep–Nov)	1.1 ± 0.5	0.9 ± 0.5	0.7 ± 0.4	<0.001*
Winter-Summer Ratio	2.6	2.1	1.8	0.001*

*Significant at p < 0.05.

Table 4. Multivariate Regression Analysis for URTI Frequency.

Variable	Odds Ratio (95% CI)	p-value
Vitamin D Status		
- Deficient	2.6 (1.8–3.7)	<0.001*
- Insufficient	1.8 (1.2–2.6)	0.003*
- Sufficient	Reference	-
Age (per year increase)	0.9 (0.8–1.1)	0.31
Male sex	1.1 (0.8–1.5)	0.48
Breastfeeding duration (per month decrease)	1.4 (1.2–1.6)	<0.001*
Sun exposure <30 min/day	1.6 (1.1–2.4)	0.02*
Daycare attendance	1.5 (1.1–2.1)	0.02*

*Significant at p < 0.05.

for real-time data collection and reduced recall bias. The inclusion of multiple centers and a diverse pediatric population enhances the generalizability of our findings to the broader Saudi context. Adjusting for important confounders such as breastfeeding and sun exposure helps to isolate the specific impact of vitamin D status on URTI risk. Additionally, our study assessed a wide range of URTI outcomes, including frequency, severity, and seasonal variation, providing a comprehensive understanding of the relationship between vitamin D deficiency and respiratory infections.

However, some limitations should be noted. Serum vitamin D levels were only measured at baseline, so we could not account for changes in status over the follow-up period. We also relied on caregiver reports for URTI episodes, which may be subject to reporting bias. While we adjusted for several important confounders, there may be residual confounding from unmeasured factors such as socioeconomic status, parental education, or environmental exposures. Lastly, our study did not assess the impact of vitamin D supplementation on URTI risk, which is an important area for future research.

Conclusion

This prospective study provides strong evidence that vitamin D deficiency significantly increases both the frequency and severity of upper respiratory tract infections among Saudi children under the age of five. Children with deficient levels experienced nearly twice the number of URTI episodes, longer illness durations, and higher rates of emergency visits and hospitalizations than those with sufficient levels. The risk remained elevated even after adjusting for relevant factors such as age, sun exposure, and breastfeeding practices, underscoring the independent effect of vitamin D status on respiratory health. Seasonal variations were more pronounced among deficient children, suggesting that vitamin D may offer some protective buffer during peak infection periods, particularly in winter.

Given the high prevalence of vitamin D deficiency and the low rates of maternal supplementation observed in this study, national public health initiatives should prioritize vitamin D screening and preventive strategies. These could include routine supplementation for pregnant women and young children, educational campaigns on safe sun exposure, and the integration of vitamin D assessment in Pediatric well-child visits. Implementing these measures may reduce the burden of respiratory infections in early childhood, ultimately improving overall child health and reducing avoidable healthcare utilization. Future research should explore the impact of targeted supplementation programs and monitor long-term outcomes to inform clinical and policy decisions.

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