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Original Article

Serum Vitamin D Status and Risk of Recurrent Acute Respiratory Tract Infections in Libyan Preschool Children

Ali Mohamed Ahmed Ghareba
Department of Paediatrics, Faculty of Medicine, University of Gharyan, Gharyan, Libya
Email. *amaghariba@googlemail.com*

Keywords.
Acute Respiratory Tract Infections; Case-Control Study; Disease Severity; Libyan Children; Recurrent ARTIs; Vitamin D Deficiency.ff

Abstract

Acute respiratory tract infections (ARTIs) remain a primary driver of paediatric hospitalisation and morbidity globally. Beyond its classical role in bone health, vitamin D acts as an immunomodulatory hormone, maintaining respiratory epithelial integrity and enhancing innate immunity. This hospital-based case-control study investigated the association between serum 25-hydroxyvitamin D (25(OH)D) levels, ARTI susceptibility, presentation severity, and history of recurrence. The study was conducted at the Pediatric Department of Gharyan Central Teaching Hospital, Libya, between January and December 2025. It evaluated 79 children aged 1–6 years hospitalised with clinically diagnosed ARTIs (Cases) against an individual frequency-matched comparative baseline of 80 healthy community children (Controls), matched dynamically by age and residency. Total serum 25(OH)D concentrations were quantified using electrochemiluminescence immunoassay (ECLIA). Presentation severity was classified using the Pediatric Respiratory Severity Score (PRESS), and clinical recurrence was defined as experiencing three or more distinct episodes per year. Low vitamin D status (severe deficiency, deficiency, or insufficiency) was detected in 87.3% of ARTI cases, compared with 52.5% of healthy controls. Clinical severity of acute episodes among cases was distributed as mild (34.2%), moderate (49.4%), and severe (16.5%). Chi-square analysis demonstrated no statistically significant association between vitamin D levels and the physiological severity of an isolated acute episode ($p = 0.115$). However, a highly significant correlation was established between low serum vitamin D and a documented history of recurrent ARTIs ($p = 0.019$). Furthermore, a history of recurrence was significantly associated with acute episode severity ($p = 0.021$). Logistic regression models identified hypovitaminosis D as a strong independent risk factor for clinical recurrence, yielding an odds ratio (OR) of 6.24 (95% CI: 2.75–14.15; $p < 0.001$). These findings indicate that while vitamin D status does not dictate the immediate clinical severity of a single infection, it significantly influences recurrence risk. Implementing regional vitamin D screening and standard supplementation strategies could vitalise local paediatric defences, reducing the cumulative burden of recurrent ARTIs and childhood hospitalisations in northwestern Libya.

Introduction

Acute Respiratory Tract Infections (ARTIs) remain one of the leading causes of pediatric morbidity and hospitalisation worldwide [1]. The World Health Organisation (WHO) considers ARTIs a critical public health concern, accounting for nearly 15% of all deaths in children under five years of age [2]. Several pediatric risk factors have been associated with increased susceptibility to ARTIs, including environmental exposures, passive smoking, lack of breastfeeding, low birth weight, and micronutrient deficiencies [3]. Beyond classic bone and calcium homeostasis, vitamin D functions as a potent immunomodulatory hormone [4]. Its active metabolite, 1,25-dihydroxyvitamin D, binds to vitamin D receptors (VDRs) expressed on respiratory epithelial cells and circulating immune cells. In innate defence, vitamin D upregulates the production of antimicrobial peptides such as cathelicidin (LL-37) and beta-defensins, which help eliminate entering respiratory viral and bacterial pathogens [5]. In adaptive immunity, it suppresses excessive pro-inflammatory Th1 and Th17 cytokine pathways, protecting the delicate pulmonary tissue from hyper-inflammatory lung damage [4, 5]. Despite abundant regional solar radiation, hypovitaminosis D has emerged as a substantial community health problem across the Middle East and North Africa (MENA) region. Local cultural clothing styles, limited midday outdoor exposure, and a general lack of routine childhood supplementation contribute to this paradox [6]. While minor pediatric studies in Tripoli and Benghazi have documented high rates of deficiency, local epidemiological data within northwestern Libya—specifically Gharyan city—remains completely absent. This case-control study fills this clinical gap by establishing local serum 25(OH)D baselines in hospitalised paediatric patients and mapping its statistical relationship to acute episode severity and recurrence risks.

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Materials and Methods

Study Design and Setting

A hospital-based, matched case-control study design was utilised to investigate the association between serum vitamin D status and recurrent acute respiratory tract infections (ARTIs). The study was executed at the Pediatric Department of Gharyan Central Teaching Hospital, northwestern Libya, between January and December 2025. To minimise confounding bias from baseline demographic characteristics, individual frequency matching was employed. Healthy controls were closely matched to the recruited ARTI cases based on two primary parameters: age (within a ±6-month window) and geographical residency within the Gharyan region, ensuring a comparable environmental background.

Selection of Participants

Cases (n=79): Included children aged 1–6 years sequentially admitted to the inpatient ward or monitored in the emergency department who met the clinical inclusion criteria. These criteria required a confirmed clinical diagnosis of an acute respiratory presentation, including acute follicular tonsillitis, common cold, bronchiolitis, pneumonia, or acute asthma exacerbation.

The strict exclusion criteria for cases ruled out children presenting with:
* Preexisting chronic systemic diseases (including chronic renal failure, hepatic dysfunction, congenital immunodeficiency, or known malabsorption syndromes).
* Documented usage of regular vitamin D or calcium supplements within the past 3 months.
* Long-term usage of systemic glucocorticoids or anticonvulsant medications known to affect vitamin D metabolism.

Out of 100 initially screened pediatric admissions, 79 patients met all criteria and were included in the final analysis.

Controls (n=80): A comparative group of 80 healthy preschool children within the same age bracket (1–6 years). They were selected using a convenience sampling approach from community pediatric screening registries and routine well-child visits in the Gharyan region. Inclusion criteria for controls required them to be completely free from any active acute respiratory episodes, history of chronic illness, or recent vitamin D supplementation.

Data Collection and Clinical Assessment

,A structured pediatric questionnaire collected baseline demographic features, anthropometrics, nutritional indicators .(birth history, and home environmental parameters (passive smoking, breastfeeding duration

Clinical Severity Assessment

The clinical severity of the current acute respiratory episode among hospitalized cases was graded imm ediately upon admission using two complementary methods. First, patients were categorized according to the standard World Health Organization (WHO) diagnostic criteria for respiratory infections. Second, to ensure objective quantification, the Pediatric Respiratory Severity Score (PRESS) was calculated. The PRESS tool objectively ,($_2$evaluates five clinical parameters: respiratory rate, presence of wheezing, chest retractions, oxygen saturation (SpO and general physical activity. Each parameter is scored from 0 to 2, yielding a total score ranging from 0 to 10. Based on the cumulative score, the clinical presentation was stratified into three distinct severity cohorts: Mild (PRESS score of 1–3), Moderate (PRESS score of 4–6), and Severe (PRESS score of 7–10). All assessments were cross-evaluated .by two independent senior pediatricians to eliminate inter-observer bias

Definition of Recurrent ARTIs

In this study, a history of recurrent ARTIs was strictly defined based on standardized pediatric guidelines as experiencing three or more distinct episodes of acute respiratory tract infections within a single calendar year. Each episode must have been separated by a symptom-free interval of at least 14 days to be considered a distinct new infection rather than the prolongation of a single previous episode.

Laboratory Quantification

Venous blood samples (3–5 mL) were drawn under strict aseptic conditions. Samples were allowed to clot for 30 minutes at room temperature before undergoing centrifugation at 3,000 rpm for 10 minutes (p. 28). Extracted serum was stored at -20°C. Total serum 25-hydroxyvitamin D (25(OH)D) concentrations were quantified using electrochemiluminescence immunoassay (ECLIA) via an automated Roche Cobas platform. Vitamin D status thresholds followed the clinical practice guidelines of the Endocrine Society: Severe Deficiency (<12 ng/mL), Deficiency (12--20 ng/mL), Insufficiency (20--30 ng/mL), and Sufficiency (>30 ng/mL) [9].

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Statistical Analysis

Data management was performed via SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous outcomes were summarised using means ± standard deviations (SD). Categorical metrics were expressed as raw counts and percentages. Chi-square (χ^2) tests analysed categorical associations between vitamin D thresholds, presentation severity, and recurrence rates. Additionally, multivariable binary logistic regression models were executed to compute clinical Odds Ratios (OR) and 95% Confidence Intervals (CI) to identify independent risk factors for clinical recurrence. Two-sided values of $p < 0.05$ indicated statistical significance

Results

Demographic and Clinical Characteristics

The baseline demographic, anthropometric, and clinical parameters of the study participants are detailed in Table 1. The mean age of the studied cohort was 3.86 ± 1.71 years, spanning a range from 1.00 to 5.92 years. In terms of gender distribution, the sample consisted of 50.63% (n=40) females and 49.37% (n=39) males. The anthropometric profiling revealed a mean body weight of 16.93 ± 6.03 kg, with a mean historical birth weight of 2.98 ± 0.60 kg. Regarding the clinical diagnosis distribution, sore throat was identified as the most common acute presentation (27.8%), followed sequentially by acute follicular tonsillitis (17.7%), pneumonia (17.7%), recurrent wheezy chest (13.9%), acute asthma exacerbations (12.7%), and acute bronchiolitis (8.9%). Evaluation of immediate acute presentation severity using the standardized Pediatric Respiratory Severity Score (PRESS) demonstrated that 34.2% of the admitted cases were classified as mild, 49.4% as moderate, and 16.5% as severe (Figure 1).

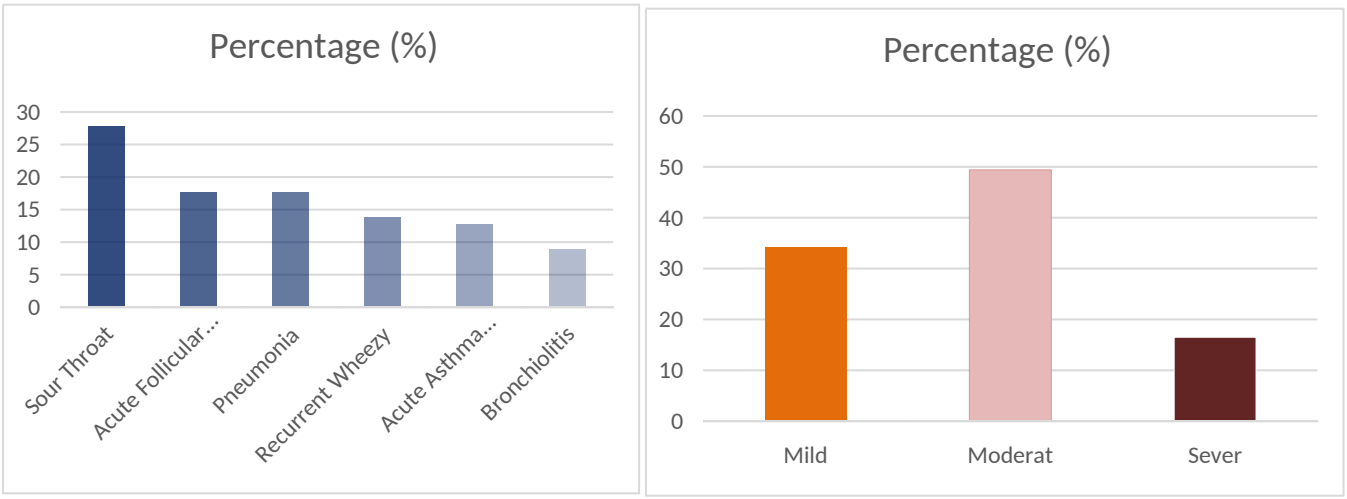


Figure 1: Distribution of Acute Respiratory Tract Infection (ARTI) Subtypes and Clinical Severity Strata Among Hospitalized Pediatric Cases (n = 79)

Furthermore, a substantial majority of the admitted children (78.5%, n=62) had a documented clinical history of recurrent ARTIs.

Vitamin D Status Profiles and Exposure Factors

Environmental and domestic exposure profiles were comprehensively evaluated to trace potential baseline drivers of hypovitaminosis D. The data revealed that restricted solar exposure was highly prevalent among the studied children; 25.3% received under 15 minutes of direct sunlight per day, while 8.9% experienced no direct outdoor solar exposure at all (Figure 3).

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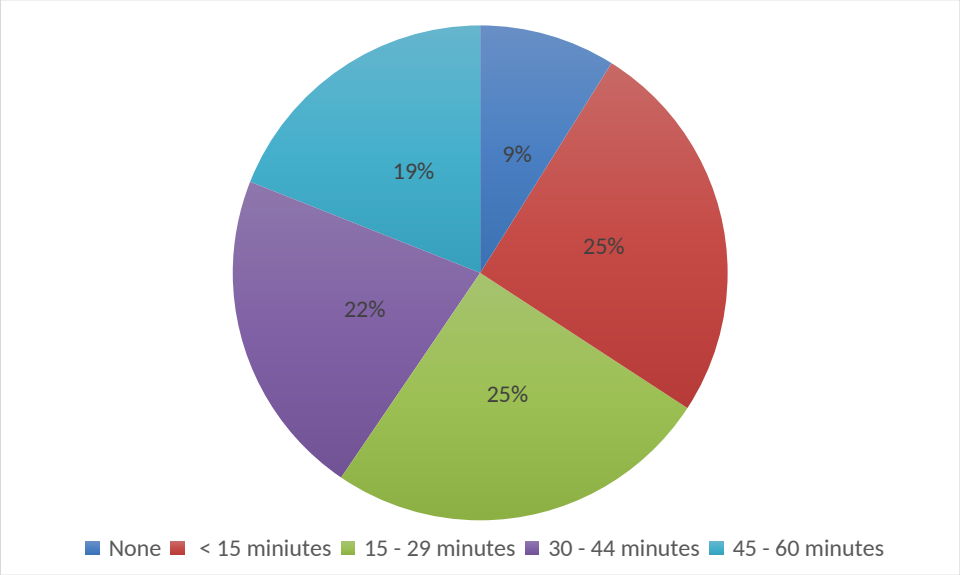


Figure 3: Daily direct Sun exposure duration profile among the studied pediatric cohort (N= 159)

Furthermore, substantial domestic environmental risk factors were prominent, with passive smoking exposure documented in 69.6% of the children's households, alongside a high prevalence of family histories of respiratory disease (Table 2).

Case-Control Comparative Analysis

The prevalence of low vitamin D status (encompassing severe deficiency, deficiency, or insufficiency thresholds) was significantly higher in children admitted with acute respiratory infections (87.3%) than in healthy community-baseline controls (52.5%), establishing a highly significant statistical difference ($p < 0.001$). Furthermore, multivariable binary logistic regression models confirmed that low serum vitamin D levels are strongly and independently associated with higher odds of ARTI hospitalisation, identifying hypovitaminosis D as a profound baseline risk factor (Table 2).

Association with Clinical Severity and Recurrence Vitamin D Level vs. Infection Severity

Inferential Associations and Predictors of Severity and Recurrence

Chi-square (χ^2) cross-tabulation demonstrated no statistically significant association or correlation between baseline serum 25(OH)D concentrations and the immediate clinical severity of an isolated acute ARTI admission episode ($p = 0.115$). Conversely, inferential analysis established highly significant linkages regarding historical paediatric clinical patterns. Low serum vitamin D levels were powerfully correlated with a verified clinical history of recurrent respiratory infections ($p = 0.019$) (Figure 2).

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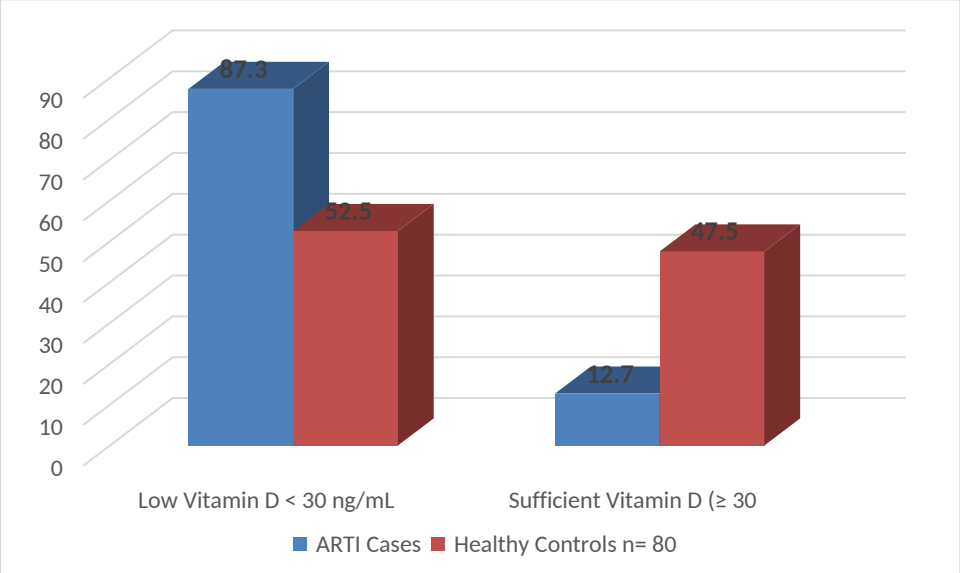


Figure 2: Case- Control comparative analysis of total serum 25-hydroxyvitamin D (25(OH)D) status stratification between hospitalized acute respiratory tract infection (ARTI) cases (n = 79) and matched healthy community controls (n = 80) (p < 0.001)

Furthermore, a documented history of clinical ARTI recurrence was significantly associated with heightened immediate acute severity markers upon hospital admission (p = 0.021). Multivariable regression models isolated compounding confounding variables, confirming that hypovitaminosis D stands as a powerful independent risk factor for infection recurrence, yielding a robust clinical Odds Ratio (OR) of 6.24 (95% CI: 2.75–14.15; p < 0.001), indicating that vitamin-deficient children exhibit over sixfold higher odds of developing recurrent respiratory cycles.

Discussion

This case-control study identified a high prevalence of hypovitaminosis D (87.3%) among preschool children hospitalised with acute respiratory tract infections in Gharyan, Libya. This deficiency rate is consistent with findings from sunnier regions in North Africa, which often trace back to limited sun exposure, poor intake of nutrient-rich foods, and lack of systematic infant supplementation programs [6, 10]. By using a healthy control group, this study demonstrated that low serum vitamin D is not just a general trait of the local community, but a clear clinical factor that increases susceptibility to respiratory diseases (OR: 6.24; p < 0.001). Our findings show no direct link between vitamin D levels and the immediate severity of an acute respiratory admission (p = 0.115). This aligns with a systematic review in India by Raju et al., which concluded that while low vitamin D levels make children more prone to developing respiratory infections, they do not directly dictate the immediate severity of an isolated acute presentation [11]. In contrast, our study established a significant association between low vitamin D status and infection recurrence (p = 0.019) (Figure 2). This link underscores the long-term role of vitamin D in maintaining mucosal immune health [12]. Prolonged deficiency compromises airway epithelial structures and lowers the production of protective antimicrobial peptides, leaving children susceptible to frequent reinfections [5, 12]. Additionally, we observed a significant link between a history of infection recurrence and the clinical severity of acute episodes (p = 0.021). This suggests that recurrent infections may gradually weaken local pulmonary defences, leading to more severe presentations over time [1, 13]. These results are consistent with case-control studies in Egypt and Tunisia, which highlighted hypovitaminosis D as a risk factor for recurrent respiratory illness in early childhood [13, 14]. Our analysis also highlighted several modifiable risk factors within local households, including high rates of passive smoking exposure (69.6%) and low intake of nutrient-rich foods. These elements provide clear targets for local public health campaigns. The findings underscore the need to move from reactive treatment to proactive care, combining lifestyle modifications with targeted vitamin D supplementation to help reduce pediatric hospital admissions in northwestern Libya [15].

Conclusion

In conclusion, this hospital-based matched case-control study demonstrates that while baseline serum vitamin D concentrations do not directly determine the immediate clinical severity of an isolated acute respiratory admission, they are powerfully associated with an increased susceptibility to infection recurrence in preschool children within the Gharyan region. Given the alarmingly high prevalence of hypovitaminosis D (87.3%) detected among hospitalised paediatric cases compared to healthy community controls, immediate public health intervention and structured screening strategies are strongly warranted to vitalise mucosal immunity and protect this vulnerable age cohort.

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Recommendations

Based on the prominent epidemiological and environmental findings of this study, the following clinical and public health measures are recommended:

* **Mandatory Paediatric Supplementation:** Implement standardized, routine vitamin D screening and establish mandated vitamin D supplementation guidelines for infants and preschool children across northwestern Libya to enhance baseline immunity and mitigate the cumulative healthcare burden of recurrent ARTIs.
* **Targeted Public Health Campaigns:** Launch community-driven health education initiatives designed specifically to address modifiable environmental risk factors, focusing on minimizing domestic passive smoking exposure and promoting safe, daily sunlight exposure habits for young children.
* **Clinical Severity Monitoring:** Integrate objective clinical assessment protocols, such as the Pediatric Respiratory Severity Score (PRESS), in routine emergency and inpatient pediatric wards to ensure early identification and optimized management of high-risk cases.
* **Future Longitudinal Research:** Future prospective and longitudinal intervention studies are strongly recommended to systematically monitor the clinical efficacy of therapeutic vitamin D supplementation in directly reducing ARTI recurrence rates and subsequent hospital admission frequencies over extended timelines.

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(79 = Table 1 Baseline Demographic and Clinical Features of the Hospitalized ARTI Cohort (n

Parameter	Mean ± SD	Minimum	Maximum
(Age (Years	1.71 ± 3.86	1.00	5.92
(Current Weight (Kg	6.03 ± 16.93	7.00	30.00
(Birth Weight (Kg	0.60 ± 2.98	1.20	4.09
(Serum 25 (OH) D (ng/mL	10.09 ± 22.90	6.80	74.94

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Table 2: Comparative Analysis of Vitamin D Status and Associated Environmental Exposure factors Between ARTI Cases and Healthy Controls (Total N = 159)

Variable	Cases (ARTI Patients) (n = 79)	Controls(Healthy Children) (n = 80)	Odds Ratio (95% CI)	P - value
Pooled Vitamin D Status:				
- Low Vitamin D (< 30ng/mL)	69 (87.3%)	42 (52.5%)	6.24 (2.75 – 14.15)	> 0.001
- Sufficient Vitamin D (> 30 ng/mL)	10 (12.7%)	38 (47.5%)	Reference	
Passive Smoking at Home:				
Exposed (yes)	55 (69.6%)	31 (38.8%)	3.62 (1.88 – 6.97)	> 0.001
Non Exposed (No)	24 (30.4%)	49 (61.2%)	Reference	
Breastfeeding (First 6 Months) Breastfed (yes)	69 (87.3%)	72 (90.0%)	0.76 (0.28 – 2.07)	0.592
Non -Breastfed	10 (12.7%)	8 (10%)	Reference	

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