

A CROSS-SECTIONAL STUDY OF SERUM LEVELS OF VITAMIN A AND VITAMIN D IN CHILDREN WITH SEVERE ACUTE RESPIRATORY INFECTIONS (SARI) ATTENDING A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Severe acute respiratory infections (SARI) remain a leading cause of morbidity and mortality in children under five years of age, particularly in developing countries. Micronutrients like Vitamin A and Vitamin D play pivotal roles in immune function and respiratory health. **Objectives:** To estimate the serum levels of Vitamin A and Vitamin D in children with SARI, and to evaluate their association with recurrent lower respiratory tract infections (LRTIs) and COVID-19 positivity. **Materials and Methods:** This hospital-based cross-sectional study was conducted at Niloufer Hospital, Hyderabad, over a two-year period. A total of 100 children aged 1 month to 5 years diagnosed with SARI were enrolled. Serum levels of Vitamin A and D were measured. The presence of recurrent LRTIs and COVID-19 status were recorded. Statistical analysis was done using Student's t-test, and significance was set at $p < 0.05$. **Results:** Vitamin A deficiency was present in 19% and Vitamin D deficiency in 20% of children. Recurrent LRTIs were reported in 22% of the study population, and 17% tested positive for COVID-19. Children with recurrent LRTIs had significantly lower Vitamin A ($p = 0.02$) and Vitamin D ($p < 0.000001$) levels. Similarly, COVID-19 positive children showed significantly reduced levels of Vitamin A ($p = 0.004$) and Vitamin D ($p < 0.000001$). **Conclusion:** Vitamin A and D deficiencies are significantly associated with both recurrent LRTIs and COVID-19 in children with SARI. Early detection and correction of these deficiencies may improve respiratory outcomes.

INTRODUCTION

Acute respiratory infections (ARIs) remain a leading cause of morbidity and mortality in children under five years of age, particularly in low- and middle-income countries. Globally, ARIs account for approximately 3.8 million childhood deaths annually, with pneumonia being the most common and fatal manifestation. Nutritional deficiencies have been increasingly recognized as critical contributors to the susceptibility and severity of these infections.^[1,2]

Among the key micronutrients, Vitamin A plays a vital role in maintaining epithelial integrity, enhancing immune function, and supporting lymphocyte proliferation. Its role in reducing child mortality has been well documented, with studies indicating that Vitamin A supplementation can reduce mortality in children aged 6–59 months by up to 30%.^[2] Despite this, Vitamin A deficiency remains

a significant public health issue in many parts of the world, including India.

Vitamin D, traditionally known for its function in calcium metabolism and bone health, has more recently been identified as a key regulator of the immune system. It influences both innate and adaptive immune responses and has been linked to reduced susceptibility to infections such as bronchiolitis, pneumonia, and even viral illnesses like COVID-19.^[1,3] Subclinical Vitamin D deficiency is common among Indian children despite abundant sunlight, largely due to indoor lifestyles, limited sun exposure, and inadequate dietary intake.^[4,5]

Given the limited data available on the micronutrient status of children presenting with severe acute respiratory infections (SARI) in India, this study aims to evaluate the serum levels of Vitamin A and D in such children and explore their association with recurrent infections and COVID-19 positivity.

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based cross-sectional observational study conducted in the Department of Paediatrics, Niloufer Hospital, a tertiary care referral center affiliated with Osmania Medical College, Hyderabad, Telangana. The study was carried out over a period of two years, from November 2020 to November 2022.

Study Population

The study included children aged 1 month to 5 years who were admitted with a diagnosis of Severe Acute Respiratory Infection (SARI) during the study period.

Inclusion Criteria

Children aged 1 month to 5 years.

Diagnosed with SARI, as per WHO criteria: acute respiratory infection with history of fever (or measured fever $\geq 38^{\circ}\text{C}$), cough, onset within the last 10 days, and requiring hospitalization.

Informed consent obtained from parent or guardian.

Exclusion Criteria

Children older than 5 years.

Known cases of immunodeficiency, congenital heart disease, measles, HIV, or tuberculosis.

Children with xerophthalmia.

Lack of parental consent.

Data Collection

A structured questionnaire was used to record demographic data, clinical features, past history of recurrent respiratory infections, and COVID-19 status. A thorough physical examination and relevant investigations, including chest X-ray and complete blood count, were performed.

Biochemical Analysis

Serum Vitamin A levels were measured using high-performance liquid chromatography (HPLC). A level $<0.7 \mu\text{mol/L}$ was considered deficient.

Serum 25-hydroxyvitamin D [25(OH)D] levels were assessed using chemiluminescence immunoassay.

Levels were categorized as

Deficiency: $<12 \text{ ng/mL}$

Insufficiency: $12\text{--}20 \text{ ng/mL}$

Sufficiency: $>20 \text{ ng/mL}$

Statistical Analysis

Data were entered in Microsoft Excel and analyzed using Epi Info version 7.2.0. Descriptive statistics were expressed as means, standard deviations, and percentages. Student's t-test was used for comparison of continuous variables. A p-value <0.05 was considered statistically significant.

Ethical Considerations

Ethical clearance was obtained from the Institutional Ethics Committee of Osmania Medical College, Hyderabad. Informed written consent was obtained from parents or guardians of all participants prior to enrollment.

RESULTS

A total of 100 children aged between 1 month and 5 years with Severe Acute Respiratory Infections (SARI) were enrolled in the study.

Demographic Characteristics

Among the study participants, the most common age group was 3 months (36%), followed by 4 months (29%) and 2 months (23%). Other age groups each constituted $\leq 8\%$ of the study population. The gender distribution showed a slight male predominance with 56% males and 44% females (Table 1).

Micronutrient Status

Vitamin A assessment revealed that 19% of the children were deficient, 27% had marginal levels, and 54% had normal levels. Similarly, Vitamin D deficiency was present in 20%, insufficiency in 27%, and normal levels in 53% of the study participants (Table 2).

Recurrent Lower Respiratory Tract Infections (LRTI)

Out of the 100 children, 22% had a documented history of recurrent LRTIs (Table 3A). When micronutrient levels were compared based on LRTI history, the mean serum Vitamin A level was significantly lower in those with recurrent LRTI ($0.76 \pm 0.28 \mu\text{mol/L}$) compared to those without ($0.98 \pm 0.42 \mu\text{mol/L}$), with a p-value of 0.02. Similarly, the mean Vitamin D level was significantly lower in the recurrent LRTI group ($19.46 \pm 4.52 \text{ ng/mL}$) versus the non-recurrent group ($28.49 \pm 2.46 \text{ ng/mL}$), with a highly significant p-value <0.000001 (Table 3B).

COVID-19 Status

Seventeen percent of the children tested positive for COVID-19 during admission (Table 4A). When compared with their COVID-negative counterparts, COVID-positive children had significantly lower mean Vitamin A levels ($0.72 \pm 0.32 \mu\text{mol/L}$ vs. $0.92 \pm 0.49 \mu\text{mol/L}$, $p = 0.004$) and Vitamin D levels ($18.42 \pm 6.82 \text{ ng/mL}$ vs. $29.42 \pm 3.42 \text{ ng/mL}$, $p < 0.000001$) (Table 4B).

Clinical Summary of Associations

A consolidated view of clinical associations shows that both Vitamin A and Vitamin D deficiencies were significantly associated with recurrent LRTIs and COVID-19 positivity (Table 5).

Table 1: Age and Gender Distribution of Study Population (N = 100)

Age Group (months)	Frequency	Percentage (%)
2	23	23
3	36	36
4	29	29
5	8	8
6	2	2
7	1	1

10	1	1
Gender	Frequency	Percentage (%)
Male	56	56
Female	44	44

Table 2: Distribution of Vitamin A and Vitamin D Status

Vitamin A Status	Frequency	Percentage (%)
Deficient	19	19
Marginal	27	27
Normal	54	54
Vitamin D Status	Frequency	Percentage (%)
Deficient	20	20
Insufficient	27	27
Normal	53	53

Table 3A: Frequency of Recurrent Lower Respiratory Tract Infections (LRTI) Among Study Participants (N = 100)

Recurrent LRTI	Frequency	Percentage (%)
Yes	22	22%
No	78	78%

Table 3B: Association of Vitamin A and D Levels with Recurrent LRTI

Parameter	Recurrent LRTI Present (Mean ± SD)	Recurrent LRTI Absent (Mean ± SD)	P value
Vitamin A (μmol/L)	0.76 ± 0.28	0.98 ± 0.42	0.02
Vitamin D (ng/mL)	19.46 ± 4.52	28.49 ± 2.46	<0.000001

Table 4A: COVID-19 Status Among Study Participants (N = 100)

COVID Status	Frequency	Percentage (%)
Positive	17	17%
Negative	83	83%

Table 4B: Association of Vitamin A and D Levels with COVID-19 Status

Parameter	COVID Positive (Mean ± SD)	COVID Negative (Mean ± SD)	P value
Vitamin A (μmol/L)	0.72 ± 0.32	0.92 ± 0.49	0.004
Vitamin D (ng/mL)	18.42 ± 6.82	29.42 ± 3.42	<0.000001

Table 5: Summary of Vitamin Deficiencies and Their Clinical Associations

Clinical Association	Lower Vitamin A (P value)	Lower Vitamin D (P value)
Recurrent LRTI	Yes (0.02)	Yes (<0.000001)
COVID-19 Positive Status	Yes (0.004)	Yes (<0.000001)

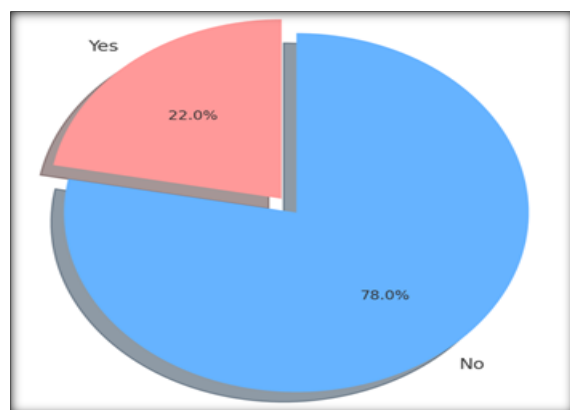


Figure 1: Frequency of Recurrent LRTI among Study Participants

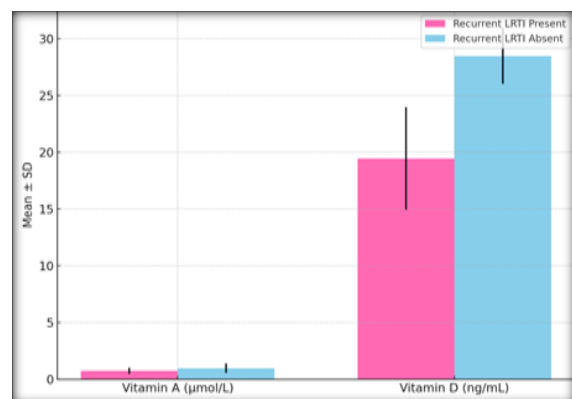


Figure 2: Association of Vitamin A and D Levels with Recurrent LRTI

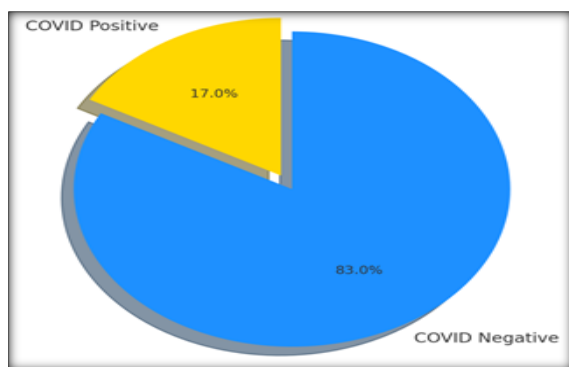


Figure 3: COVID-19 Status among Study Participants

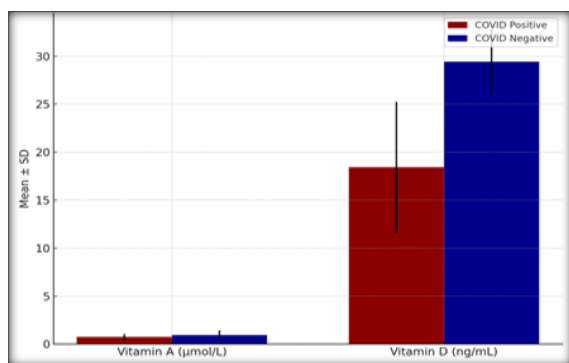


Figure 4: Association of Vitamin A and D Levels with COVID-19 Status

DISCUSSION

This hospital-based cross-sectional study assessed the serum levels of Vitamin A and Vitamin D in children aged 1 month to 5 years admitted with Severe Acute Respiratory Infections (SARI), evaluating their association with recurrent respiratory infections and COVID-19 positivity.

Micronutrient Deficiencies in SARI

In this study, Vitamin A deficiency was found in 19% and Vitamin D deficiency in 20% of participants, indicating a high prevalence of subclinical micronutrient deficiencies even among hospitalized children. Similar findings were observed in earlier research, including a study from Bulgaria that reported widespread Vitamin D deficiency in children hospitalized for acute respiratory infections,^[9] and another study showing a strong link between low Vitamin D levels and acute bronchiolitis.^[10] The coexistence of these deficiencies highlights the need for routine nutritional assessment in pediatric respiratory illnesses.

Association with Recurrent LRTI

Children with a history of recurrent lower respiratory tract infections (LRTI) had significantly lower levels of both Vitamin A (0.76 ± 0.28 µmol/L) and Vitamin D (19.46 ± 4.52 ng/mL), compared to those without recurrence. The association was statistically significant ($p = 0.02$ and $p < 0.000001$, respectively) (Table 3B). These results align with studies by McNally et al., who reported that Vitamin D

deficiency is common in children with severe acute lower respiratory infections,^[6] and by Özdemir et al., who found significantly lower Vitamin D levels in children with recurrent respiratory infections and chronic cough compared to controls.^[11]

Vitamin D's protective role is attributed to its immunomodulatory effects, including stimulation of antimicrobial peptides such as cathelicidin, which help reduce pathogen load in the respiratory tract.^[7,8] Similarly, Vitamin A plays a critical role in maintaining mucosal immunity and epithelial integrity, and its deficiency has been linked to increased infection severity.^[12]

Association with COVID-19 Status

In the present study, 17% of children were COVID-19 positive, and these children had significantly lower levels of Vitamin A (0.72 ± 0.32 µmol/L) and Vitamin D (18.42 ± 6.82 ng/mL), with p-values of 0.004 and <0.000001 , respectively (Table 4B). This supports growing evidence that Vitamin D deficiency may predispose children to viral infections, including SARS-CoV-2. A recent Cochrane review suggested that Vitamin D supplementation may reduce the incidence of acute respiratory infections in children under five years of age.^[8] Furthermore, Petkova et al. emphasized the need to monitor Vitamin D levels in hospitalized children with respiratory illnesses, as a significant proportion had levels below the recommended range.^[9]

These findings are also consistent with results from Zhang et al., who reported that deficiencies in Vitamins A and D were significantly associated with recurrent respiratory infections in children.^[12] The potential synergy between these micronutrients in supporting immune defense warrants further investigation.

Clinical Implications

The findings from this study reinforce the role of micronutrient monitoring and supplementation in the pediatric population, especially among those presenting with or at risk for severe respiratory infections. Identifying and correcting deficiencies in Vitamins A and D may not only help in reducing the frequency and severity of LRTIs but also potentially mitigate the risk of COVID-19 complications.

Limitations

This study was conducted at a single tertiary care hospital, which may limit the generalizability of the findings to the wider population. The cross-sectional design prevents establishing a causal relationship between vitamin deficiencies and respiratory infections. Factors influencing Vitamin D status, such as dietary intake, sunlight exposure, and seasonal variation, were not accounted for. Additionally, serum vitamin levels were measured only once during illness, which may not reflect long-term nutritional status.

CONCLUSION

This study highlights a significant prevalence of Vitamin A and Vitamin D deficiencies among

children with Severe Acute Respiratory Infections (SARI). Both deficiencies were found to be significantly associated with recurrent lower respiratory tract infections and COVID-19 positivity. Children with lower levels of these vitamins had a higher risk of infection and more severe outcomes. These findings underscore the importance of routine screening for micronutrient deficiencies in pediatric patients with respiratory illnesses. Early identification and timely supplementation of Vitamin A and D may help reduce the burden and recurrence of respiratory infections, including those caused by emerging viral pathogens like SARS-CoV-2.

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