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Original Research Article

Association of Vitamin-D Deficiency with Severity of Pneumonia in Pediatric Patients

Rashmi Kispotta[1], Nikita Patel[2], Ankita Patel[2], B.N. Rao Somanwar[3]

[1]Associate Professor, Department of Paediatrics, Shri Balaji Institute of Medical Sciences, Raipur, Chhattisgarh
[2]Assistant Professor, Department of Paediatrics, Shri Balaji Institute of Medical Sciences, Raipur, Chhattisgarh
[3]Professor & Head, Department of Paediatrics, Shri Balaji Institute of Medical Sciences, Raipur, Chhattisgarh

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Corresponding Author: Dr. B.N. Rao Somanwar
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Abstract:

Background: The association of sub-normal vitamin-D levels with the lower respiratory tract infections (LRTI) in children has been a topic of interest in the recent literature. Vitamin-D insufficiency been explored as modifiable risk-factor in management of the pediatric recurrent respiratory tract infections.

Methods: This cross-sectional study was carried-out on 100 pneumonia cases less than 15 years for the 18 months duration from July 2022 to December 2023. All children from 6 Months to 15 years of age reporting to the Hospital (OPD and IPD) with a clinical diagnosis of LRTI were included.

Results: Based on severity of pneumonia the majority of the cases had mild pneumonia (46.0%) followed by moderate pneumonia (37.0%) and severe pneumonia (17.0%). The association between age and gender with severity of pneumonia was found insignificant ($p>0.05$). The vitamin-D level was significantly lower in severe pneumonia cases than in moderate and mild pneumonia ($p<0.001$). Therefore, the severity of vitamin-D deficiency correlates with the severity of pneumonia.

Conclusion: Subclinical vitamin D deficiency is a significant risk factor for severe LRTI in Indian children of less than 15 years. There was a significant association between Vitamin-D levels and recurrent respiratory tract infections. Education regarding the importance and timing of sun exposure is necessary. Routine Vitamin D supplementation is recommended in children below 15 years.

Keywords: Lower respiratory tract infections, vitamin D, pediatric, pneumonia.

Introduction

Lower respiratory tract infection has long been a leading cause of the morbidity and mortality in infancy. [1,2] It was estimated to be responsible for about 16.4 million episodes of hospital admissions in 2015 and 0.65 million deaths in 2016 among children below 5 years, of which more than half were infant cases. [3,4] Infancy is a key early period in the life course, and poor well-being during such period can not only impact the present health and development but also their later life. [5] Given that, any promising strategies for the prevention of LRTI should be explored as extensively and early as possible.

India, Indonesia, Bangladesh, and Nepal accounted for 40.0% global acute respiratory infection mortality. According to reports, acute respiratory infections affect children under the age of five around five times a year. Furthermore, as a result of acute otitis media, acute respiratory infections are a major cause of deafness. [6] There is a need to identify the modifiable factors that can impact the prevalence and management of respiratory infections among children.

The factors which predispose to lower respiratory tract infections include age (<1 year), low birth weight, premature delivery, malnutrition, underlying morbidity, breast-feeding failure, low socioeconomic level, crowded life conditions (large family, nursery care etc.), poor access to healthcare services, maternal age and education, indoor and outdoor air pollution (including mainly smoking), inadequate immunization and vitamin D deficiency. [7]

Vitamin-D is fat-soluble vitamin that is essential in bone metabolism, immune system regulation, and modulation of inflammatory processes. [8] The synthesis of this essential nutrient occurs in the skin upon exposure to ultraviolet B radiation from sunlight, with dietary intake and supplementation contributing to a lesser extent. [9] Vitamin D

deficiency, which is increasingly recognized as a global public health issue, has been linked to numerous acute and chronic diseases, including autoimmune disorders, cardiovascular diseases, and certain types of cancer. [10,11] In recent years, the potential role of vitamin D in the prevention and treatment of infectious diseases, particularly respiratory infections, has gained growing interest in the scientific community. [12]

The skin's natural production of vitamin D occurs when it is exposed to ultraviolet B (UV-B) radiation, which has a wavelength of between 290 and 320 nm. The widespread perception is that India has an abundance of sunshine, which makes vitamin D deficiency and rickets rare there. That is untrue, though, as evidence indicates that vitamin deficiencies are very common. [13,14] There are several reasons for vitamin D insufficiency and shortage, but one of the most important ones is a lack of understanding of how important it is for both individual and societal health.

Given the significant public health implications of RTI and the potential benefits of vitamin D as an affordable, safe, and accessible intervention, it is important to critically appraise and synthesize the available evidence. [15,16] A comprehensive understanding of the relationship between vitamin-D status and RTI may inform clinical practice and public health policies aimed at reducing the burden of these infections in pediatric populations. Although previous trials and systematic reviews have addressed this topic, with inconclusive results [17], there was no focus on a particular type of infection or age range during childhood, when the immune system is developing and is significantly different from adults' immunity. [18] Moreover, respiratory infections are the most common diseases in children, while the preschool age sets a boundary on community exposure to respiratory infections. Thus, the rapidly evolving evidence necessitates an updated and rigorous evaluation of the literature.

A little amount of research on the relationship between vitamin D level and different paediatric respiratory illnesses has been conducted in India.The main conjecture of this research is that sufficient amounts of vitamin D are linked to a decreased likelihood and intensity of respiratory infections in children. As a result, the aim was to determine the association of vitamin D deficiency with severity of pneumonia in children aged <15 years. The secondary goal is to determine the prevalence of vitamin D deficiency in infant and children aged 6 months to 15 years hospitalised with pneumonia. By synthesizing the available evidence, this study would like to elucidate the role of vitamin-D in childhood respiratory infections, which may ultimately contribute to the development of targeted interventions and strategies to reduce the burden of these common and impactful illnesses.

Material and Methods

Type of study: A cross-sectional study

Place of study: SHRI BALAJI INSTITUTE OF MEDICAL SCIENCE

Study period:18 months duration from July 2022 to December 2023.

Sample size: Considering 9.0% margin of error at 95% confidence interval, sample size was calculated using: Sample size(n)=Z 2 1-a/2p(100-p)/d2 Where, Z 2 1-a/2=1.96 at C.I of 95%, P =expected prevalence =34.5. [19] d=margin of error; $n=(1.96)^2x34.5(65.5)/(9)^2$ n=107 which is our sample size

Study group: All the patients between 6months to 15 years of age with clinical and radiological findings of lower respiratory tract infections were included in the study with consideration of exclusion criteria. [20]

Inclusion Criteria:

- Patient attendant giving informed consent for the study
- All children among 6 Months to 15 years of age reporting to the Hospital (OPD and IPD) with a clinical diagnosis of LRTI.
- Radiologically confirmed cases of LRTI.
- Recurrent chest infections.

Exclusion Criteria:

- Participants whose parents are not willing to give consent for the study
- Recipients of vitamin D supplementation within last 4 Weeks.
- Children with the presence of non-specific symptoms like poor growth, gross motor developmental delay and unusual irritability.
- Children with suspected rickets and osteoporosis
- Chronic kidney disease or congenital cardiac disease.
- Malabsorption syndrome like cystic fibrosis and inflammatory bowel disease.
- On medication like anticonvulsants, glucocorticoids, AIDS medication.

Methodology

This was a hospital based prospective, cross-sectional single-centre study. The study was begun after approval from the ethical committee. Detailed history and clinical examination including anthropometry and radiological findings was evaluated. Eligible study participants were previously healthy children or with recurrent chest infections. Following written informed consent data was obtained from either parents or legal guardians.

Laboratory Methods: A 3 ml blood sample was obtained by venepuncture in the participating subject in trace element-free tubes under all aseptic conditions. Serum heparinized plasma or EDTA plasma sample was acquired for vitamin D measurement by 25(OH) D ELISA.

In this study, a cut-off value of > 30 ng/ml was considered optimal vitamin D status. Patients with 25-OHD conc. between 10-30 ng/ml are insufficient and those with values of 100 ng/ml.

Investigation:

1. Serum Vit D level
2. Chest X-RAY
3. Sputum examination
4. Mantoux test

Statistical Analysis

Microsoft Excel was used in creating the database and producing graphs, while the data were analysed using the Statistical Package for the Social Sciences (SPSS) version 23 for Windows. Mean and standard deviation (±SD) were used to describe quantitative data meeting normal distribution. Continuous two independent groups were compared by parametric independent Student's t test, this was used. Discrete (categorical) groups were compared by chi-square ($\chi 2$) test was used. p values less than 0.05 ($p<0.05$) was considered statistically significant.

Observations and Results

Of 100 cases the majority of the cases had mild pneumonia followed by moderate (37.0%) and severe pneumonia (17.0%). Most of the cases were less than 5 years of age 37 (37.0%) with a mean age of 8.45 years and male predominance (55.0%). The severity of pneumonia was insignificantly associated with age and gender ($p>0.05$). The vitamin D level was significantly lower in severe pneumonia cases than in moderate and mild pneumonia ($p<0.001$). As the severity of pneumonia increases the level of vitamin D significantly decreases.

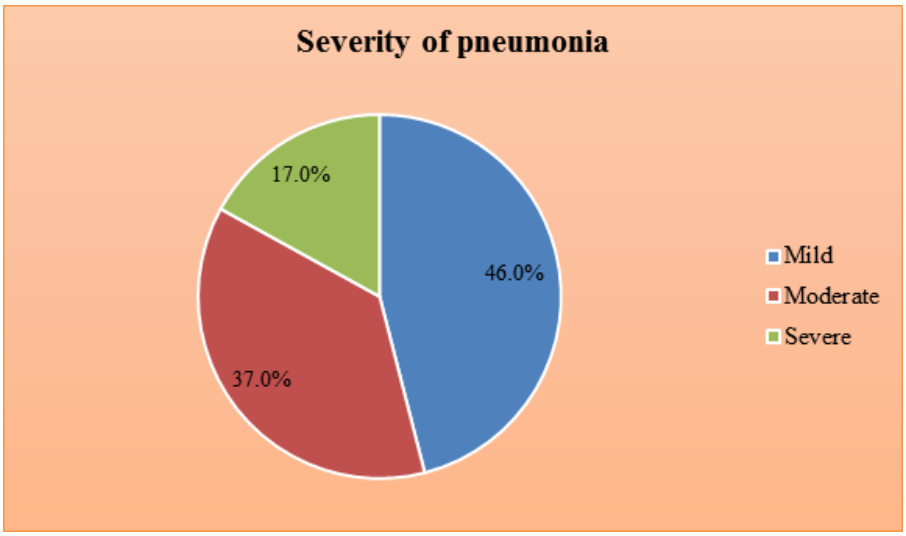

Figure 1: Prevalence of Severity of pneumonia

Table 1: Age group distribution based on severity of pneumonia

Age Group	Severity of pneumonia			χ^2 value/t value	p-value
	Mild (n=46)	Moderate (n=37)	Severe (n=17)		
≤5 years	14 (30.4%)	14 (37.8%)	7 (41.2%)	1.397	0.845
6-10 years	16 (34.8%)	10 (27.0%)	6 (35.3%)		
>10 years	16 (34.8%)	13 (35.1%)	4 (23.5%)		
Mean±SD	8.50±4.19	8.06±4.76	8.80±4.25	0.180	0.836

Table 2: Gender distribution based on severity of pneumonia

Gender	Severity of pneumonia			χ^2 value	p value
	Mild (n=46)	Moderate (n=37)	Severe (n=17)		
Male	28 (60.9%)	17 (45.9%)	10 (58.8%)	2.264	0.322
Female	18 (39.1%)	20 (54.1%)	7 (41.2%)		

Table 3: Vitamin D level distribution based on severity of pneumonia

Grade of Pneumonia	Vit-D Mean	Std. Deviation	F value	P value
Mild	16.28	1.18	241.082	<0.001

Moderate	12.19	1.191		
Severe	9.47	0.92		

*ONE WAY ANOVA

Table 4: Correlation between Vitamin D Level and severity of Pneumonia

Variables	**Vitamin DLevel**	
	r value	**p-value**
Severity of Pneumonia	-0.911**	<0.001
Age	0.079	0.450
Sex	-0.060	0.565
**. Correlation is significant at the 0.01 level (2-tailed).		

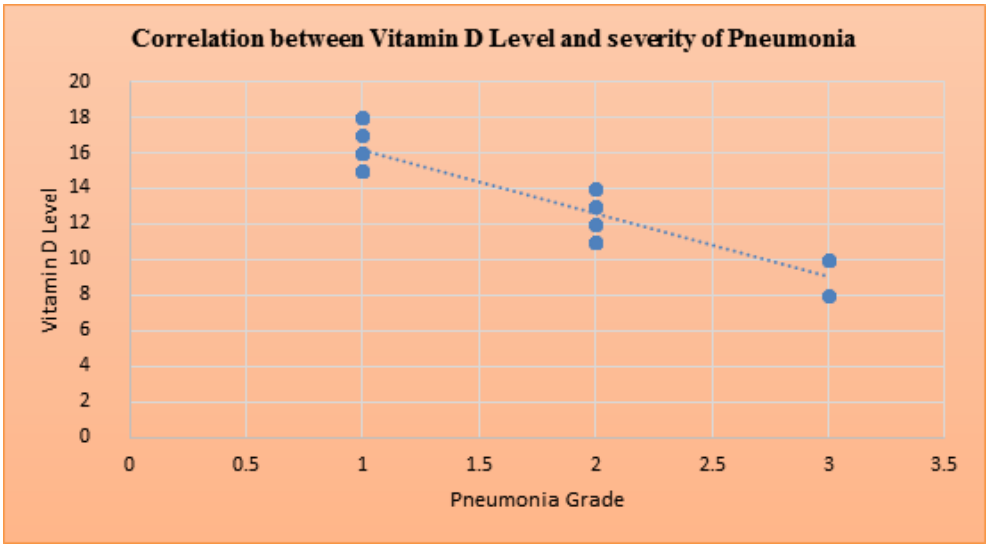

Figure 2: Correlation between Vitamin D Level and Severity of Pneumonia

Pearson's Correlation Coefficient (r value) = -0.911; p value=<0.001.

Discussion

The objective of our study was to find out the association, if any, between respiratory illnesses and serum vitamin-D status in children of 6 months to 15 years of age.

In the present study, most cases were <5 years of age 37 (37.0%) with a mean age of 8.45 years and male predominance (55.0%). The severity of pneumonia was insignificantly associated with age and gender (p>0.05). Our findings were comparable to the findings of Jaybhaye AP et al [21] who reported that mean age of the cases (LRTI) and controls (healthy) was 68.25 ± 40.3 months and 52.6 ± 40.9 months, respectively. In total, 38 children were 6 to 60 months of age, 13 children were 61-120 months of age, and four children were >120 months. The cases and control groups were in significant regarding sex (approximately 57.0% males and 43.0% females in both the groups). In Ruhi A, and Ananth T [22] study, there were no significant differences in Vitamin D deficiency between males and females (P= 0.91). Chandrashekhara, and Pampana S [23] reported that Vitamin-D deficiency was more common in <1 year and also in male children (59.3%). Leis KS et al [24] reported that the ALRI group and control groups were not significantly different with respect to sex (approximately 60% males and 40% females in both groups) and age at enrolment (13.4±13.8 and 13.8±15.2 months respectively). Between the age groups of one month and five years, there were no appreciable variations in the relationship between vitamin D insufficiency and respiratory tract infections in their research. In contrast to our study Wayse V et al [21] showed that serum 25-hydroxy Vitamin-Dlevel increases significantly with age (P-value<0.001). However, Prakash A et al [22] in their study of 137children with LRTI showed highest incidence of Vitamin-D deficiency inage group of 2 to 12 months (79.80%).

Of 100 cases the majority of the cases had mild pneumonia followed by moderate (37.0%) and severe pneumonia (17.0%). The vitamin D level was lower significantly in severe pneumonia cases than in moderate and mild pneumonia (p<0.001). As the severity of pneumonia increases the level of vitamin-D significantly decreases. The mean vitamin-D level in mild pneumonia was 16.28±1.18 and in moderate pneumonia the mean vitamin-D level was 12.19±1.91 and in severe pneumonia it was 9.47±0.92 and the difference was statistically significant (p<0.05). Our findings were consistent

with the findings of Ruhi A, and Ananth T [22]who reported that the serum 25- hydroxy Group I (RRTI) had much lower vitamin D concentrations than Group II (no RRTI). Vitamin D insufficiency was seen in 86% of Group 1 (RRTI) and 35% of Group II (no RRTI), which is close to Wayse V et al [25].'s findings (80% and 31%), Roth DE etal [27] (84.0% and 60.0%), and little higher percentage of the deficiency found in KaratekinG et al [28] i.e. 92.0% in group I and 80.0% in group II.

Özdemir B et al [29] reported that mean vitamin-D levels in the children with recurrent respiratory infections was 11.97 ± 4.04 ng/mL, in children with chronic cough was 13.76 ± 4.81 ng/mL, and in control, group was 31.91 ± 18.79 ng/mL, with a statistically significant difference between study groups. Thus, vitamin-D deficiency in children was associated with an increased frequency of recurrent respiratory infections and chronic cough. A recent study [22] from Telangana state has reported association of vitamin-D levels with the recurrent respiratory infections. Zhang J et al [30] (2015-2018) also reported correlation between vitamin-D deficiency and the recurrent respiratory infections.

Chandrashekhara, and Pampana S [23] reported that out of the 59 patients, 16(27.1%) were diagnosed with bronchiolitis; of these, 10(62.5%), 4(25.0%), and 2(12.5%) patients had normal levels, insufficiency, and shortage of vitamin-D, respectively. Of the 43(72.9%) children who were diagnosed with pneumonia, 40(93.0%), 2(4.6%), and 1(2.3%) had normal levels, deficiencies, and excesses in vitamin-D, respectively.

Vitamin-D deficiency considered to induce weakness of the muscles, especially the diaphragm and intercostals. This likely makes it difficult to clear the secretions of the respiratory tract and facilitate infections. [31] Esposito S and Lelii M [32] reviewed the literature on vitamin-D and respiratory infections and found that vitamin-D deficiency is a risk factor for bronchiolitis, tuberculosis, and the recurrent otitis media. They concluded that maintaining adequate vitamin-D levels could be a low-cost and effective method to prevent some respiratory tract infections. Literature from various parts of the world supports the role of vitamin-D deficiency in respiratory infections. [33,34]

Conclusion

Children with LRTIs exhibited a significantly higher proportion of vitamin Ddeficient subjects. Low vitamin-D level is associated with impaired lung function in cases of pneumonia, thus lower serum vitamin-D levels are a contributory factor in severity of pneumonia. Our study emphasizes the need for serum vitamin-D estimation in various respiratory illnesses so that appropriate and timely therapeutic intervention can be initiated to decrease the morbidity and mortality children< 15 years.

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