

## Original Research Article

# Vitamin D deficiency among hospitalized infants with acute lower respiratory tract infection

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### ABSTRACT

**Background:** Vitamin D plays important role in immunity and its deficiency might be associated with increased risk of lower respiratory tract infection. This study aimed to determine whether vitamin D deficiency is commoner in infants with acute lower respiratory tract infection as compared to normal infants and to correlate the severity of vitamin D deficiency with severity of ALRTI.

**Methods:** A hospital based prospective case-control study was conducted in a tertiary care hospital. A total of 208 infants (109 cases and 99 controls) older than 7 days to 12 months of age, were enrolled. Cases were selected according to the definition of ALRTI given by WHO (2). Controls were chosen from children attending paediatric outpatients department for immunization or minor short duration ailments. Primary outcome measured as serum 25-hydroxy vitamin D3 (25OHD3) levels and severity of ALRTI was independent variable.

**Results:** Among 109 cases suffering from ALRTI, vitamin D deficiency was present in 65.11%, 92.3%, 88.9% children of 'pneumonia, severe pneumonia and very severe pneumonia group respectively. It was found that vitamin D deficiency was commoner in cases as compared to controls (80.70 % vs 25.50% ) with OR of 12.40 (95 % CI was 6.13 - 25.38). There was inverse relationship between the severity of ALRTI and Vitamin D levels (p value <0.001 and Pearson correlation coefficient -0.32).

**Conclusions:** Vitamin D levels were significantly lower in ALRI cases as compared to controls and had negative correlation between vitamin D levels and severity of pneumonia.

**Keywords:** Infants, Lower respiratory tract infection, Pneumonia, Vitamin D deficiency

### INTRODUCTION

Acute lower respiratory infection (ALRI), or pneumonia, is a common cause of morbidity and mortality in children younger than 5 years of age, particularly in developing countries.<sup>1</sup> Globally Pneumonia accounts for 19% deaths in children among this age group. The role of vitamin D in bone metabolism and calcium homeostasis is well known. More recently, in a WHO bulletin on ALRI it has

been mentioned that nutritional rickets caused by dietary deficiency of vitamin D and calcium have strong association with severe acute lower respiratory tract infection in hospitalized children in some settings.<sup>2-4</sup>

It appears plausible because the pleiotropic effects of vitamin D have been confirmed by various researchers. Vitamin D plays a key role in immune system regulation as it alters cytokine secretion pattern, suppresses effectors

T cell activation, induces regulatory T cells and thus its deficiency can predisposes to infections.<sup>3</sup>

However we despite thorough literature review could not find any Indian study analysing association of vitamin D levels and the severity of respiratory tract infection in infants. Hence this study was undertaken to assess whether the lower levels of vitamin D in hospitalized infants having acute lower respiratory tract infection is associated with more severe illness.

**METHODS**

A hospital based case control study was conducted in a tertiary level hospital of New Delhi, India for a period of one year (January 2010 to December 2010). Cases were infants of more than seven days to 12 months of age, having acute lower respiratory infection diagnosed on the basis of clinical symptoms and signs only. Cases were categorised into pneumonia, severe pneumonia and very severe disease according to WHO classification. Controls were children of same age group, attending pediatrics outpatients department for immunization or minor ailments of short duration other than RTI.

Infants having hepatic and renal insufficiency and history of taking Vitamin supplements in past 3 months were excluded. A total of 220 infants were enrolled (110 cases, 110 controls). The haemolysed blood sample for Vitamin D estimation Were excluded (1case, and 11 controls), so the final number of participants considered for statistical analysis was 109 cases and 99 controls.

**Primary outcome measure**

**Predictor variables**

Severity of respiratory illness as defined by WHO (pneumonia, severe pneumonia and very severe pneumonia).

- Pneumonia = when only respiratory rate was fast (>60/minute in babies below 2 months, >50/mt in infants between 2 months to 12 months).

- Severe pneumonia= if besides fast rate chest wall retractions were also present.
- Very severe pneumonia= presence of any danger sign with respiratory symptoms namely-no oral acceptance, persistent vomiting, seizures or altered sensorium.

A structured questionnaire was used to obtain desired information followed by clinical examination. The evaluation included signs of respiratory distress besides anthropometry. Blood samples were collected from both cases and controls (after informed consent). Vitamin D3 was estimated by ELISA method.

The commercially available kit used was immune diagnostic K 2109 25-OH Vitamin D direct ELISA. The research was reviewed and approved by institutional review board and participation involved informed consent.

Vitamin D levels according to American society of bone and mineral research (2006) was used to classify the deficiency were as follows-

- Severely deficient - <30 nmol/l (< 12 ng/ml)
- Deficient - 30-75nmol/l (12-30ng/ml)
- Adequate - >75nmol/l (>30ng/ml)

**Statistical analysis**

Data were analyzed using SPSS (Version 11.0; SPSS Inc., Chicago, USA). Standard statistical tests were used. Chi square and Fischer exact test was used for categorical variables. Mean and standard Deviation as well as Odds ratio and 95% confidence interval was calculated. P<0.05 was considered as statistically significant. Pearson correlation co-efficient was calculated between levels of vitamin D and severity of ALRTI.

**RESULTS**

A total of 208 infants (109 cases and 99 controls) were enrolled.

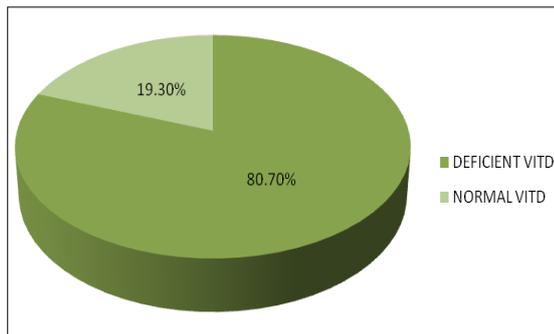
**Table 1: Comparison of anthropological parameters.**

	Cases Mean±SD	Controls Mean±SD	p value
Sample size	109.00	99	-
Age in months	6.98±2.48	6.95±2.77	0.941
Sex	Male	61	0.211
	Female	38	
Weight (kg)	6.49±0.96	6.39±1.08	0.475
Length (cm)	64.62±4.62	64.51±4.54	0.854
Z score	Weight/age	1.028±0.30	0.82
	Length/age	1.082±0.21	

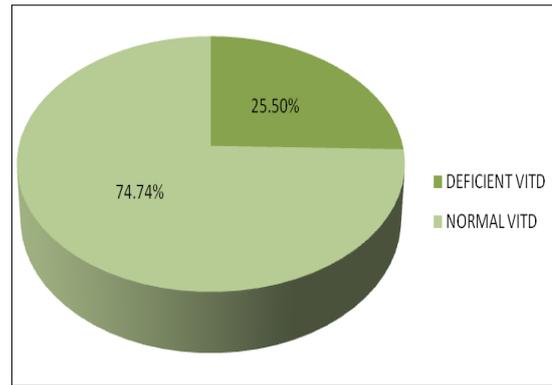
**Population characteristics**

There was male preponderance (67.8% males vs 32.1% females) and majority of the participants (41.2%) were upto or below 6 months of age. The mean age, wt and length of cases were (6.98 months, 6.49 kg and 64.62 cm) not much different from controls (6.95 months, 6.39 kg and 64.51 cm). Table 1 shows comparison of anthropometric parameters between cases and controls.

Vitamin D deficiency was commoner in cases as compared to controls (80.7 % Vs 25.50% ) with OR of 12.40 (95 % CI was 6.13 - 25.38). Figure 1 and 2 shows percentage of Vitamin D level in cases and controls.



**Figure 1: Vitamin D status in cases.**



**Figure 2: Vitamin D status in controls.**

Among 109 cases suffering from ALRTI, vitamin D deficiency was present in 65.11%, 92.3%, 88.9% children of ‘pneumonia’, ‘severe pneumonia’ and ‘very severe pneumonia’ group respectively. The ratio of severe to moderate vitamin D deficiency among these children with ALRTI was 20.9 %:44.1% in ‘pneumonia category’, which increased to 64.1%:28.2% in ‘severe pneumonia’ category. This ratio was highest (74.07%:14.81%) among ‘very severe pneumonia’ subgroup. Table 2 shows distribution of Vitamin D levels in cases according to severity of pneumonia. In cases 43 cases had pneumonia, 39 had severe pneumonia and 27 had very severe disease.

**Table 2: Distribution of vitamin D levels in cases according to severity of pneumonia.**

Category of pneumonia (Vitamin D levels)	Pneumonia (n=43)	Severe pneumonia (n=39)	Very severe disease (n=27)
Severely deficient (<30 nmol/l)	9 (20.93%)	25 (64.10%)	20 (74.07%)
Moderately deficient (30-75 nmol/l)	19 (44.18%)	11 (28.20%)	4 (14.81%)
Normal (>75 nmol/l)	15(34.88%)	3 (7.69%)	3 (11.11%)

**Table 3: Comparison of level of vitamin D and severity of acute lower respiratory tract infections.**

Type	No. of cases (n = 109)	Vitamin D levels	Pearson correlation coefficient	p value
Pneumonia	43	173.95±263.88	-0.32	<0.001
Severe pneumonia	39	65.79±148.08		
Very severe pneumonia	27	16.74±10.16		

This inverse relationship between the severity of ALRTI and Vitamin D levels was statistically significant (p value <0.001 and Pearson correlation coefficient (-0.32) Table 3 shows the comparison of Vitamin D levels with severity of pneumonia.

**DISCUSSION**

Vitamin D plays an important role in increasing susceptibility to infections and is associated with poorer outcome. It appears to have systemic antimicrobial

effects by modulating immune system. It exerts this immuno-modulatory effects through VDR (Vitamin D Receptors).<sup>5</sup>

Various studies have found that pneumonia patients have lower levels of vitamin D.<sup>6</sup> Vitamin D deficiency was commoner in cases as compared to controls (80.70% vs 25.50%) with Odds Ratio of 12.40 (95% CI was 6.13 - 25.38). In present research work 80.70% of infants suffering from ALRTI were found to be having vitamin D deficiency, a much higher percentage as compared to

study by Banajeh M et al in which only 47.7% infants under 6 months of age were vitamin D deficient.<sup>7</sup> The plausible explanation for this difference in percentage could partially be because of age difference of participants. In present research around 60% infants were above 6 months of age and only around 40 % were below the age of 6 months

In present research out of, 109 infants with varying severity of pneumonia, 80.7% were vitamin D deficient, of which 61.3% (55) had severe and 38.6% (34) had moderate vitamin D deficiency. It is in concordance with the observations of Wayse V et al who enrolled children below 5 yrs of age and reported that Vitamin D levels of <22.5 nmol/l (severe vitamin d deficiency) was a risk factor for ALRI.<sup>8</sup> In another study by McNally et al it was seen that the mean vitamin D level for the ALRI subjects admitted to the pediatric intensive care unit (49±24 nmol/l) was significantly lower than that observed for both control (83±30 nmol/l) and ALRI subjects admitted to the general pediatrics ward (87±39 nmol/L).<sup>9</sup> In another study by Inamo Y et al on Japanese hospitalized children, mean 25(OH) D concentrations in children with ALRI were significantly lower.<sup>10</sup>

In present study the number of vitamin D deficient infants kept on increasing with increasing severity of pneumonia, 65.11% infants in the pneumonia group were vitamin D deficient. This percentage increased to a staggering 92.3% and 88.9% in infants with severe pneumonia and very severe disease respectively. The ratio of cases having severe to moderate vitamin D deficiency, in pneumonia group was 20.93 to 44.18 whereas in severe pneumonia group it was 64.10 to 28.20. In very severe disease group this ratio was 74.07 to 14.81, pointing to the statistically proven correlation of severity of vitamin d deficiency with severity of pneumonia (Pearson correlation coefficient -0.32; p value <0.001).

## CONCLUSION

Vitamin D levels were significantly lower in ALRI cases as compared to controls. In ALRI cases 80.70% had Vitamin D deficiency. Infants with severe pneumonia were more deficient in vitamin D levels showing a negative correlation between vitamin D levels and severity of Pneumonia. As the vitamin D levels decreased severity of pneumonia increased. This study highlights that vitamin D deficiency is common in Indian children and in children with Pneumonia vitamin D levels were low. What this study adds Vitamin D deficiency is seen even in Indian infants with ALRI.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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