# **Original Research Article**

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# Serum vitamin D concentration in acute lower respiratory tract infection in infants: a case control study from Northern India

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## **ABSTRACT**

**Background:** Vitamin D insufficiency is believed to be the most common nutritional deficiency and one of the most undiagnosed medical conditions in this region. People across the world are becoming increasingly aware of the role played by vitamin D in health and disease, especially its role in immunity and its anti-infective role. The present study was conducted to study the relationship between serum vitamin D levels and severity of respiratory tract infections. To study the relation between serum vitamin D levels and severity of acute respiratory tract infections.

**Methods:** 1-year prospective study from September 2014 to August 2015. Children from 1 month to 1 year of age participated in the study. Serum Vitamin D levels were measured in case group suffering from severe acute lower respiratory tract infections (ALRTI) and in a control group. The primary outcome variable was difference in serum vitamin D levels between case group and control group.

**Results:** The median (IQR) age of cases and controls was 5.0 (4.75) months and 4.0 (4.0) months, respectively. There were no significant differences in baseline demographic and anthropometric parameters between the 2 groups. The median vitamin D level in a case group was significantly lower compared with matched controls (p <0.05).

**Conclusions:** Vitamin D deficiency is an important independent risk factor for childhood pneumonia. We found a severe vitamin D deficiency of our infants suffering from severe acute lower respiratory tract infections. The deficiency was more prevalent in exclusive breast feed infants.

Keywords: Vitamin D, Respiratory tract infections

# INTRODUCTION

Vitamin D insufficiency is believed to be the most common nutritional deficiency and one of the most undiagnosed medical conditions in this region of the globe. Till a few decades ago vitamin D was thought of only in relation to calcium homeostasis and bone health. Now people across the globe are finding more and more cognizant of the role played by vitamin D in health and disease beyond bone and calcium, especially its role in immunity, antimicrobial response and pulmonary

function.<sup>2,3</sup> Since vitamin D is produced in the skin due to exposure to sunlight, its deficiency is more commonly seen in temperate regions and in those people whose bodies are covered, resulting in decreased sun exposure.<sup>4</sup> Kashmir is a temperate zone and women being from conservative society dress up orthodoxically resulting in little sun exposure, this may result in lower serum vitamin D levels in this population, which in turn can affect serum vitamin D levels of newborn baby and breast feed infants. In the present study, we intend to study the relation between serum vitamin D levels and severe acute

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lower respiratory tract infections (ALRTI) in the young children of this temperate zone. To study the relation between serum vitamin D levels and severity of acute respiratory tract infections in the children aged 1 month to 1 year by determining serum concentrations of 25-hydroxyvitamin D (25(OH)D).

## **METHODS**

This was a hospital based prospective study from September 2014 to August 2015 in department of pediatrics GMC Srinagar and SKIMS Srinagar, in children between 1 month and 1 year of age with clinical history of severe acute lower respiratory-tract infection. Severe ALRI was defined according to the following case definition: (i) caregiver report of cough and/or difficulty breathing for less than 2 weeks; (ii) rapid respiratory rate for age by WHO criteria (50 breaths per minute for participants <12 months of age) and / or intercostal or lower chest wall indrawing that was persistent throughout the examination. (iii) Central cyanosis and/or inspiratory pulmonary crackles heard on auscultation by the study physician. Children who fulfilled the inclusion criteria were admitted in the study as cases. Children with chronic lung disease and/or congenital heart diseases were excluded from the study.

Control population comprised of children in the age group of 1 month to 1 year attending to well-baby clinic with no active complaint related to respiratory system. Written informed parental consent was taken from all the study participants after explaining the nature of the study in their native language.

### Initial data collection

A detailed history was taken and clinical examination (including signs of rickets, anthropometry was performed for all the participants. Weight and height were measured by standard techniques. Pulse oximeter was used in study group patients to monitor baseline oxygen saturation in room air. Hypoxia was defined as an oxygen saturation <95% on room air. Venous blood sample was obtained for vitamin D levels, calcium, phosphorous, alkaline phosphatase in all study participants (both cases and controls). Hemogram, C-reactive protein, electrolytes, blood culture were taken from case group only.

# Measurement of serum Vitamin-D (250HD)

Two ml of venous blood specimens was collected from a peripheral vein and serum separated by centrifugation and then stored at -20°C and protected from direct exposure to sunlight until the analysis. Samples were assayed at the end of the enrollment period using a commercially available 25-hydroxy vitamin D3 RIA kit (25-Hydroxyvitamin D 125 RIA Kit; DiaSorin Diagnostics) according to the instructions provided by the manufacturer. All the determinations were performed in the Department of Immunology, Sher-I-Kashmir Institute

of Medical Sciences, Soura, Srinagar. Vitamin D deficiency was defined on the basis of American endocrine society criteria i.e. serum 25 (OH)D levels <20 ng/ml.

# Statistical analysis

Data was entered in Microsoft excel 2007. Continuous variables with normal distribution were analyzed by unpaired students 't' test and expressed as mean ± standard deviation. Non-parametric continuous variables were analyzed by the Mann-Whitney U test and expressed as median (IQR). Normality of data was checked by Shapiro-wilk test and by examining Q-Q plots. Categorical data were analyzed by chi square/fishers exact test.

With 80% power, a type I error risk of 5%, and conservatively assuming a standard deviation (SD) of 25 nmol / L, we had estimated that 34 case control pairs would permit detection of a mean difference in 25(OH)D concentration of 10 nmol /L between matched pairs. However, we have included 40 case-control pairs to cover for some loss during the study period.

### **RESULTS**

This hospital based study comprised of 40 infants between 1 month to 1 year of age with a diagnosis of severe lower respiratory tract infection and 40 age matched controls. 26 patients were between 1 and 6 months of age in case group compared to 24 patients in the control group (P value>0.05). Clinical rickets were seen in 4 patients in case group and 3 patients in matched control. The median (IQR) age of cases and controls was 5.0(4.75) months and 4.0(4.0) months, respectively, and the difference was statistically insignificant (P=0. 335). Table 1 compares demographic and anthropometric parameters in case and control groups.

Table 1: Baseline demographic and anthropometric parameters of 2 groups.

	Case group (40)	Control Group (40)	P value
Sex (%)	62.5% 37.5%	67.5% 32.5%	0.639
Exclusive breast feeding	60%	50%	0.369
Weight (kg), Mean (SD)	5.83 (1.72)	5.89 (1.95)	0.255
Height (cm), Mean (SD)	63.4 (5.9)	62.0 (6.6)	0.30

As seen in above table there were no significant differences in baseline demographic and anthropometric parameters between the 2 groups. However, the median vitamin D level in a case group was significantly lower (9.9 IQR (5.49)) compared with matched controls (13.98 IQR (12)).

### **DISCUSSION**

Vitamin D deficiency is common in infancy due to several factors such as decreased dietary intake, decreased cutaneous synthesis (because of cultural and religious practices, seasonal variation, the practice of not taking the child out, an increase in pigmentation), increasing the rate of exclusive breastfeeding, and low maternal vitamin D.5 Our results indicate that vitamin D deficiency is very common in infants suffering from severe respiratory tract infections in this region and it's an independent risk factor for childhood pneumonia as serum vitamin D levels were significantly lower in case group compared to the control group. Our results confirm anti-infective role of vitamin D like many other previous studies.<sup>6,7</sup> Williams et al in his study on childhood tuberculosis found deficient levels of vitamin D in these patients.6 Similarly, another study evaluated the risk of developing pneumonia in Ethiopian children with nutritional rickets and found a strong positive co-relation between vitamin D deficiency and respiratory compromise.<sup>7</sup>

In our study, 60% of our case group (suffering from severe ALRI) patients were on exclusive breastfeeding, which is in contrast to many studies which have established decreased incidence of ALRI in this group due to its protective role on childhood infections.8 However, this group of patients had lowest mean serum vitamin levels that possibly negated the protective role of breast milk. The reason for low mean serum vitamin D levels in our patients were possibly as a consequence of insufficient sunlight in Kashmir in autumn, winter and spring, also women being from conservative society dress up orthodoxically resulting in little sun exposure, this may result in lower serum vitamin D levels in this population, which in turn could have affected serum vitamin D levels of breast feed infants. However, our results don't endorse any compromise in exclusive breastfeeding policy in our community as it has got enormous health benefits and is a single most important factor to decrease infant mortality rate. Nonetheless, we advocate implementation of the current AAP policy of daily supplementation with 400 units of oral vitamin D in all breast feed babies in our region to prevent its deficiency.

# CONCLUSION

Vitamin D deficiency is an important independent risk factor for childhood pneumonia as established by many other previous studies. We found a severe vitamin D deficiency of our infants suffering from severe acute

lower respiratory tract infections. The deficiency was more prevalent in exclusive breast feed infants. We advocate routine supplementation of our infants with vitamin D especially exclusive breast feed babies who are more prone to develop this deficiency as there is very high prevalence of vitamin D deficiency in our adult population due to geographical and cultural differences that makes our population susceptible to this deficiency.

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