

## Original Research Article

# A study on association between respiratory tract infection and serum 25 (OH) vitamin D level in children

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### ABSTRACT

**Background:** Acute respiratory tract infection are a major cause of global morbidity and mortality. Observational studies report consistent independent association between low serum concentration of 25-hydroxy-vitamin D and susceptibility to acute respiratory tract infection. This study was done to assess serum vitamin D level in children and correlation with respiratory tract infection.

**Methods:** The present study was undertaken in department of paediatrics medicine, Patna Medical College and Hospital in patients attending out-patients department (OPD) as well as admitted in in-patients department (IPD). Assessment of serum 25(OH) Vitamin D was done by the enzyme immunoassay kit at Patna Medical College and Hospital.

**Results:** The mean serum vitamin D level in cases was (20.52±5.64 ng/ml) where as in control group was (26.46±4.52 ng/ml) with a statically significant p value of <0.0001, hence cases are associated with vitamin D deficiency.

**Conclusions:** The finding in this study showed significantly decreased mean serum vitamin D level in cases than that of control which implies that vitamin D deficiency predisposes to respiratory tract infection in children.

**Keywords:** Respiratory tract infection, Vitamin D deficiency, Global morbidity and mortality

### INTRODUCTION

Acute respiratory tract infection are a major cause of global morbidity and mortality. Observational studies report consistent independent association between low serum concentration of 25-hydroxy-vitamin D and susceptibility to acute respiratory tract infection.

25-hydroxyvitamin D support induction of antimicrobial peptides in response to both viral and bacterial stimuli, suggesting a potential mechanism by which vitamin D inducible protection against respiratory pathogens might be mediated.<sup>1</sup> Vitamin D has an important influence on the host's immune system, modulating both innate and adaptive immunity and regulating the inflammatory cascade. The majority of immune cells express VDRs, mainly after they themselves have been stimulated.

Moreover, treating macrophages with 1,25(OH) D results in the expression of various cytokines and chemokines, including CXCL8, IL-6, and IL-12, and tumor necrosis factor (TNF)- $\alpha$ . Thus, 1,25 (OH)D seems to contribute to the maintenance or enhancing protective innate responses.<sup>2</sup> Vitamin D induces the gene encoding the antimicrobial peptide L3-L7. This peptide has potent bactericidal capacity against a number of important bacteria and viruses, including *M. tuberculosis* and influenza-virus.<sup>3,4</sup>

In humans, the main source of vitamin D is UVB mediated synthesis in the skin. Certain food, such as oily fish and dairy products, contains vitamin D, but it is difficult to achieve sufficient intake by the diet alone. The activation of vitamin D involves two hydroxylation steps, one in the liver and one in the kidney. Vitamin D is

transported bound to vitamin D binding protein to the liver, where 25-hydroxylase converts it into 25-hydroxyvitamin D, the most abundant circulating form of vitamin D.<sup>5</sup> Notably, the final activation of vitamin D, via 1-alpha hydroxylase (CYP27B1), also occurs in extra-renal tissues, including epithelial and immune cells.<sup>6</sup> In the respiratory tract, CYP27B1 is expressed in bronchial epithelial cells and induced by inflammatory stimuli.<sup>7</sup>

López et al did a case-control study on children between 3-60 months from the Guatemala city metropolitan area, hospitalized with community-acquired pneumonia between September and December 2012. The median (IQR) serum 25-hydroxyvitamin D3 concentration for cases was 23.2 ng/ml (14.4-29.9) compared to 27.5 ng/ml (21.4-32.3) in controls ( $p=0.006$ ). Multiple regression analysis using an a priori cut-point for vitamin D of  $<20$  ng/ml showed that children with lower respiratory tract infections were more likely to have low 25-hydroxyvitamin D3 levels than controls (adjusted odds ratio 2.4, 95% confidence interval 1.1-5.2,  $p 0.02$ ). They found children with lower respiratory tract infections in Guatemala had low 25-hydroxyvitamin D3 levels as compared to control.<sup>8</sup>

Larkin et al examined 18 studies and found vitamin D deficiency was associated with increased risk or severity of ALRI in 13 studies; associations were not found in 4 studies. In one study it was found that high maternal vitamin D levels was associated with ALRI in infants.<sup>9</sup>

### **Aims and objectives**

To assess correlation between serum 25(OH) vitamin D level with respiratory tract infection in children.

## **METHODS**

This study is a hospital based case-control study done on children of age group 2 months to 144 months attending out-patients department (OPD) and in in-patients department (IPD) of paediatrics medicine, Patna Medical College and Hospital between December 2017 to December 2019.

The children aged 2 months to 144 months with respiratory tract infection were taken as case. For control age and sex matched children were taken who reported to hospital for non respiratory complain.

In this study total 102 cases of age group 2 months to 12 years from both indoor and OPD patients of Department of Paediatrics Medicine, Patna Medical College and Hospital, were taken as cases who were suffering from respiratory tract infection and 83 disease free, age and sex matched children were taken as control who reported to hospital for non respiratory complain. The selection of case and control was done using inclusion and exclusion criteria.

### **Inclusion criteria**

All children between 2 months to 12 years of age attending the Department of Paediatrics Medicine, Patna Medical College and Hospital between December 2017 to December 2019 in outdoor as well as indoor were examined and those having respiratory tract infection were included for study. For control, age and sex matched children were taken who reported to hospital for non respiratory complain.

### **Exclusion criteria**

Known children having congenital heart disease; known cases of childhood asthma and allergy; known cases of tuberculosis; children known to getting prophylactic vitamin d supplementation; and children known to having immune-deficiency or getting immuno-suppressive therapy.

The purpose of the study and detail of protocol were discussed with the parents and consent from the parents or assent from the children above 7 years of age was taken.

Ethical approval for the study was given by the Chairperson, Ethical Committee, Patna Medical College and Hospital.

Serum vitamin D level of all the included patients and the normal control children age were meticulously assessed. 0.5 ml clotted blood sample was taken for measurement of serum 25(OH) vitamin D level from each of them. Assessment of serum 25(OH) vitamin D was done by the enzyme immunoassay kit at Patna Medical College and Hospital.

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 20.0.1 and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables.

Once a t value is determined, a p-value can be found using a table of values from Student's t-distribution. If the calculated p-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favor of the alternative hypothesis, p value  $\leq 0.05$  was considered as statistically significant.

## **RESULTS**

The present study was done on 185 children of age group 2 months to 144 months, of which 102 were case who were suffering from respiratory tract infection and 83 were age and sex matched healthy control who reported to hospital for non respiratory complain.

**Table 1: Distribution of mean vitamin D level in cases and control.**

	Number	Mean (ng/ml)	SD (ng/ml)	Minimum (ng/ml)	Maximum (ng/ml)	Median (ng/ml)	p-value
<b>Case</b>	102	20.5227	5.6413	5.1000	34.0000	20.2750	<0.0001
<b>Control</b>	83	26.4584	4.5259	17.9000	35.2000	26.7000	

The mean serum vitamin D level in cases was (20.52±5.64 ng/ml) where as in control group was (26.46±4.52 ng/ml) with a statically significant p value of <0.0001, hence cases are associated with vitamin D deficiency.

## DISCUSSION

Total 102 cases having respiratory tract infection were chosen as cases while 83 healthy age and sex matched children were considered as controls. In cases 57 (55.9%) patient belonged to male gender and 45 (44.1%) belonged to female gender, whereas in control group 31 (37.3%) belonged to female and 52 (62.6%) belonged to male. There was no significant difference in base line variables (age, gender) between the groups.

In my study vitamin D deficiency was found in 41.2% of cases while 53.9% of cases had insufficient vitamin D level and only 4.8 % cases had sufficient vitamin D status. In control group 27.7% had sufficient vitamin D status where as insufficient vitamin D level and deficient vitamin D level was found in 67.5% and 4.8 % respectively with a statistical significance (p<0.001). The frequency of vitamin D deficiency is increasing, because of lack of proper sunlight exposure, socio cultural taboos and diet that cannot meet daily vitamin D requirement. Vitamin D plays a contributing role in immunity, it restores immune function and decreases cytokines level, vitamin D deficiency increases release of pro-inflammatory cytokines such as IL-6 and TNF-alpha In my study the mean serum vitamin D level was significantly decreased (p<0.001) in cases (20.52±5.64) than that of control (26.46±4.52), which implies that vitamin D deficiency predisposes to respiratory tract infection in children. This study is almost similar to the findings in other studies by Lopez et al and Larkin et al.<sup>10</sup> In all this studies they compared acute LRTI and mean vitamin D level and found a significant association of vitamin D deficiency with ALRI. However in none of the studies comparison of total RTIs including URTI and LRTI in case and control was done.

## CONCLUSION

The finding in this study showed significantly decreased mean serum vitamin D level in cases than that of control which implies that vitamin D deficiency predisposes to respiratory tract infection in children.

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