

Vitamin D status of children with lower respiratory tract infections and its correlation with severity of pneumonia: A comparative study



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ABSTRACT

Background: Acute lower respiratory tract infections (LRTI) is responsible for considerable morbidity and mortality among pediatric age group and remains one of the common causes for pediatric intensive care unit admissions. Vitamin D deficiency is one of the important risk factors not only for the occurrence but also for the increased severity of LRTI. We undertook this study to analyze vitamin D status of children admitted for LRTI and to find out its correlation with severity of LRTI. **Aims and Objectives:** The aims of this study were as follows: (1) To find out vitamin D status of children presenting with LRTI and (2) to find out correlation of vitamin D levels with severity of LRTI. **Materials and Methods:** This was a hospital-based comparative study, in which 60 children below age of 5 years and admitted for acute LRTI were included on the basis of a predefined inclusion and exclusion criteria (Group A). Sixty other children admitted for non-respiratory causes were included as control group (Group B). Vitamin D status of children in both the groups was determined. The severity of LRTI and its correlation with vitamin D status was determined. $P < 0.05$ was taken as statistically significant. **Results:** There was a male predominance in both the groups. The mean age of patients in Group A and Group B was found to be 17.70 ± 7.80 months and 18.41 ± 7.11 months, respectively ($P > 0.005$). In Group A, 42 (70%) patients were having bronchiolitis, whereas bronchopneumonia was seen in 16 (26.67%) patients and two patients (3.33%) were found to have lobar pneumonia. Forty-eight (80%) children were having pneumonia and remaining 12 (20%) children were found to have severe pneumonia. Higher number of children were either vitamin D inefficient or deficient in Group A as compared to Group B and the difference was found to be statistically highly significant ($P < 0.0001$). The mean 25 (OH) D levels were found to be low in patients with severe pneumonia as compared to pneumonia and the difference was found to be statistically highly significant ($P < 0.0001$). **Conclusion:** Lower levels of vitamin D were found to be a risk factor not only for the development but also for severity of LRTI. Determination and management of vitamin D deficiency status is one of the important parts of management of children with LRTI.

Key words: Lower respiratory tract infection; Bronchiolitis; Pneumonia; Vitamin D

INTRODUCTION

Acute lower respiratory tract infections (LRTIs) are one of the common causes of pediatric in-patient department admissions and are associated with considerable morbidity and mortality in pediatric age group.¹ The common LRTI in under 5 years of age primarily consist of bronchopneumonia and bronchiolitis. The common causative organisms responsible for LRTI in children below 5 years of age include

viruses such as respiratory syncytial virus, influenza A virus, influenza B virus, adenovirus, rhinovirus, and parainfluenza virus.² The common bacterial agents involved in the lower respiratory infection in children up to 5 years of age include streptococcus pneumoniae, hemophilus influenza B, *Klebsiella pneumoniae*, Beta-hemolytic streptococci, and less commonly mycoplasma. Irrespective of the offending organisms, children with the lower respiratory infection present with similar complaints that include, fever, tachypnea, tachycardia,

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and respiratory distress in the form of subcostal and intercostal retractions and in severe cases even respiratory failure may develop.³ The assessment of child presenting with the lower respiratory infection is usually done by a detailed history, through clinical examination and appropriate investigations such as complete blood count and imaging such as chest X-ray.⁴ Since the most common cause of the lower respiratory infections in children below 5 years of age worldwide is respiratory syncytial virus, the management is usually symptomatic and supportive. In severe cases, oxygen supplementation or even mechanical ventilation may be required. In proven bacterial pneumonias, appropriate parenteral antibiotics are required.⁵

The factors such as small for gestational age babies, bottle feeding, overcrowding, poor nutritional immunodeficiency of any cause, immunosuppressive therapy, or long steroid therapy for various diseases may predispose a child to develop severe LRTI. Recently, there has been an increasing interest in assessing the vitamin D status of pediatric patients presenting with LRTI since many studies have reported that vitamin D deficiency is one of the important predisposing factors for development of LRTI in children particularly in children below 5 years of age.⁶ Vitamin D deficiency is not only reported to be the predisposing factor for development of LRTI but also the severity of LRTI is reported to be more in children having vitamin D deficiency as compared to the children who do not have vitamin D deficiency. Low levels of vitamin D have also been reported in patients having chronic obstructive airway disease. Although the exact mechanism by which vitamin D deficiency predispose children for development of LRTI is not known, there is broad consensus among researchers that vitamin D has an important role in enhance innate immunity and inhibiting inappropriate inflammatory response to offending organism, thereby limiting the severity of inflammation. Vitamin D is known to cause cytokine mediated upregulation of anti-microbial peptides which are also known to have anti-viral activity, thereby reducing incidence as well as severity of LRTI.⁷

We conducted this comparative study to analyze vitamin D status of children admitted in our institute with LRTI.

Aims and objectives

To find out vitamin D status of children presenting with LRTI. To find out correlation of vitamin D levels with severity of LRTI.

MATERIALS AND METHODS

This was a comparative study, in which 60 pediatric patients below the age of 5 years and admitted for LRTI were included on the basis of a predefined inclusion and exclusion criteria. The study was conducted in Mahavir institute

of medical sciences Vikarabad, Telangana, and India. An informed written consent was obtained from the parents or guardians of children who have been included in this study. Sample size calculation was done on the basis of pilot studies done for LSCS under spinal anesthesia. Keeping power (1-Beta error) at 80% and confidence interval (1-alpha error) at 95%, the minimum sample size required in each group was 40 patients; therefore, we included 60 patients (more than minimum required number of cases). Two groups of children were compared for vitamin D status.

- Group A: Children below 5 years and admitted for LRTI
- Group B: Children below 5 years of age who were admitted for reasons other than LRTI and in whom blood sample was collected for performing complete blood count, c-reactive protein or any other investigation.

Demographic details, socioeconomic status, as well as nutritional history of the children in case as well control group were analyzed and compared. A detailed history was obtained from parents or guardians regarding previous episodes of respiratory tract infection, duration of symptoms during present episode, any hospital admission required previously, and also history of any other sibling having history of hospitalization due to respiratory tract infection. A thorough general and systemic examination was done. Vitals such as heart rate, respiratory rate, and blood pressure were recorded. The severity of LRTI was assessed by respiratory rate and presence of subcostal and intercostal retractions. SPO₂ levels were monitored. In all children complete blood count, c-reactive protein and 25 (OH) vitamin D levels were done. In selected cases, wrist X-rays were taken. For the purpose of diagnosis of vitamin D status of the patients, 25 (OH) D levels above 30 ng/ml were considered to be normal, whereas vitamin D insufficiency and deficiency were diagnosed if 25 (OH) vitamin D levels were between 20 and 30 ng/ml and below 20 ng/ml, respectively.⁸

The statistical analysis was done using SSPS 21.0 software and for statistical purposes P<0.05 was taken as statistically significant.

Inclusion criteria

The following criteria were included in the study:

1. Parents or guardian gave informed written consent
2. Children below age of 5 years
3. Diagnosed cases of LRTI were included in cases and children admitted for pathologies not involving respiratory tract were included in control group.

Exclusion criteria

The following criteria were excluded from the study:

1. Parents or guardians refused consent
2. Children above 5 years of age

3. Diagnosed cases of rickets already on vitamin D supplementation
4. Children with skeletal dysplasia, congenital heart diseases, on long-term steroid, or immunosuppressive therapy
5. Children with hepatic or renal impairment which may likely to cause altered vitamin D metabolism.

RESULTS

A total of 60 children below 5 years admitted with LRTI (Group A) were included in this study on the basis of a predefined inclusion and exclusion criteria. Sixty children below 5 years of age and admitted for pathologies other than respiratory pathologies were included as control group (Group B). Among study group, there were 33 (55.00%) boys and 27 (45.00%) girls with a M: F ratio of 1:0.8,1 whereas, in control group, there were 41 (68.33%) boys and 19 (31.67%) girls with a M: F ratio of 1:0.46 (Table 1).

The analysis of patients on the basis of age showed that in both the groups, most common affected age group was between 1 and 2 years (26.67% and 40%) followed by below 1 year of age (36.67% and 26.67%). Patients between 2 and 5 years were 10 (16.67%) and 20 (33.33%) in Group A and Group B, respectively. The mean age of patients in Group A and Group B was found to be 17.70±7.80 months and 18.41±7.11 months, respectively. The mean age of children in both the groups was found to be comparable with no statistically significant difference (Table 2).

The analysis of patients in LRTI group showed that out of 60 cases 42 (70%) patients were having bronchiolitis, whereas bronchopneumonia was seen in 16 (26.67%) patients that two patients (3.33%) were found to have lobar pneumonia. The analysis of severity of pneumonia showed that out of 60 cases 48 (80%) children were having

pneumonia and remaining 12 (20%) children were found to have severe pneumonia (Figure 1).

The vitamin D status of children with LRTI as well as those children in control group was assessed and patients were divided to be either vitamin D sufficient, inefficient, or deficient on the basis of serum vitamin D levels. Overall, only 8 (13.33%) patients were vitamin D sufficient and remaining 52 (86.66%) were either inefficient (53.33%) or deficient (33.33%). In control group (Group B), majority of the cases 42 (70%) were vitamin D sufficient. Vitamin D inefficiency and deficiency were seen in 12 (20%) and 6 (10%) patients, respectively. Higher number of children were either vitamin D inefficient or deficient in Group A as compared to Group B and the difference was found to be statistically highly significant (P<0.0001) (Table 3).

The mean 25 (OH) D levels in Group A were found to be 27.23±7.58, whereas mean 25 (OH) vitamin D levels in Group B (control group) were found to be 38.24±9.12. Children in Group A were found to have lower mean plasma 25 (OH) D levels as compared to children in Group B and the difference was found to be statistically highly significant (P<0.0001) (Table 4).

The analysis of patients on the basis of vitamin D levels and severity of pneumonia showed that the mean 25 (OH) D levels in patients with pneumonia was found to be 29.34±5.64 ng/ml whereas, in patients with severe pneumonia, the mean 25 (OH) D levels were found to be 21.12±4.58 ng/ml. The mean 25 (OH) D levels were found to be low in patients with severe pneumonia as compared to pneumonia and the difference was found to be statistically highly significant (P<0.0001) (Table 5).

DISCUSSION

Many studies have reported that vitamin D deficiency in children is one of the important contributing factors for development of lower as well as recurrent respiratory tract infections particularly in children. The mechanism by which vitamin D deficiency may predispose an individual for development of respiratory tract infection is poorly

Table 1: Gender distribution of the studied cases

Gender	Group A (%)	Group B (%)
Male	33 (55.00)	41 (68.33)
Female	27 (45.00)	19 (31.67)

P=0.188 (Not significant)

Table 2: Comparison of age groups of the studied cases

Age	Group A {n (%)}		Group B {n (%)}	
	Number of cases	Percentage	No of cases	Percentage
Below 1 year	22	36.67	16	26.67
13 months–24 Months	28	46.67	24	40
25 months–60 months	10	16.67	20	33.33
Total	60	100	60	100%
Mean±SD	17.70±7.80 months		18.41±7.11 months	

t-test and P-value, T=0.521, d.f=118, P=0.60 (Not significant)

Table 3: Comparison of vitamin D status in both the groups

Vitamin D Status 25 (OH) Vitamin D levels	Group A {n (%)}		Group B {n (%)}	
	No of cases	Percentage	No of cases	Percentage
Sufficient (>30 ng/ml)	8	13.33	42	70.00
Inefficient (20–30 ng/ml)	32	53.33	12	20.00
Deficient (<20 ng/ml)	20	33.33	6	10.00
Total	60	100.00	60	100.00

P<0.0001 (Highly significant)

Table 4: Comparison of mean 25 (OH) D levels in both the groups

Study Group	Mean 25 (OD) levels	SD
Group A	27.23	7.58
Group B	38.24	9.12

P<0.0001 (Highly significant)

Table 5: Comparison of mean 25 (OH) D levels in patients with severity of pneumonia

25 (OH) levels	Pneumonia	Severe pneumonia
Mean 25 (OH) levels	29.34	21.12
SD	5.64	4.58

P<0.0001 (Highly significant)

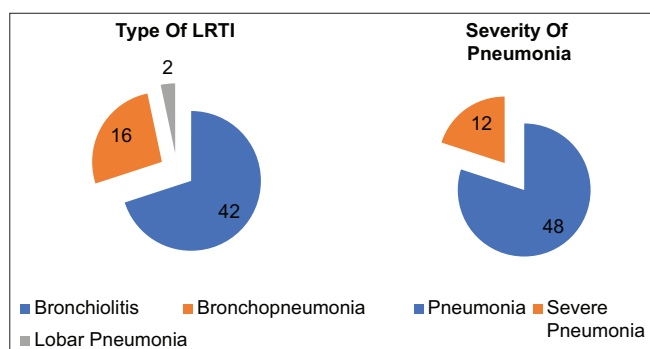


Figure 1: Type of the lower respiratory tract infection and its severity in Group A (cases)

understood; however, the most accepted theory proposes that vitamin D is essential for cytokine mediated upregulation of anti-microbial peptides which also have anti-viral activity that is responsible for reducing incidence as well as severity of LRTI. Therefore, we conducted this study to find out the vitamin D status in children presenting with LRTI.

In our study, in both the groups, there was a male preponderance. The mean age of studied cases in Group A and Group B was found to be 17.70±7.80 months and 18.41±7.11 months, respectively. The mean age of both the groups was found to be comparable. Garg et al., conducted a study of children under 5 years of age to determine the relationship, if any, between respiratory illnesses and serum vitamin D status.⁹ In this study, also there was a male preponderance with a M: F ratio of 1:0.818. This

male preponderance may be multifactorial and may include the discrimination girl child may face by family members. However, the authors such as de Lusignan et al., also reported that boys younger than 15 years have greater odds of presenting with LRTI and atopic conditions, whereas girls may present more with upper respiratory tract infection.¹⁰ Since our study was dealing with LRTI; hence, male preponderance is understandable.

In our study, bronchiolitis was the most common type of LRTI which was seen in 42 (70%) children. Bronchopneumonia and lobar pneumonia were seen in 16 (26.67%) and 2 (3.33%) children, respectively. Joshi et al., conducted a prospective cross-sectional study for 100 children with LRTI.¹¹ The authors found bronchiolitis to be the most common cause of LRTI in children which were seen in 39% patients. The other causes reported in this study were lobar pneumonia and bronchopneumonia. Similarly, van Woensel et al.,¹² and Patria and Esposito¹³ also reported bronchiolitis to be the most common cause of LRTI in children.

In our study, not only children with LRTI were found to have statistically significant lower level of vitamin D but also within the study group (comprising of children with LRTI) children with severe pneumonia were found to have low vitamin D levels as compared to those children who were found to have pneumonia which was not severe, thereby indicating that vitamin D deficiency not only predisposes a child for development of respiratory tract infection but also pneumonia is more likely to be severe in children with vitamin D deficiency as compared to those children who have normal levels of vitamin D. Chandrashekhara and Pampana undertook a hospital based cross-sectional prospective study to study prevalence of vitamin D deficiency in children with LRTI.¹⁴ The authors found that among study group, 16 (27.11%) were diagnosed to have bronchiolitis, out of which 10 (62.5%), 4 (25%), and 2 (12.5%) patients were found to have vitamin D deficiency, insufficiency, and normal values, respectively. Children who diagnosed as pneumonia were 43 (72.88%), out of them 40 (93%), 2 (4.6%), and 1 (2.3%) were having deficiency, insufficiency, and normal values of vitamin D, respectively. On the basis of these findings, the authors concluded that vitamin D deficiency is common in children with LRTI and early recognition and treatment of vitamin D deficiency

can prevent morbidity associated possibly frequent LRTI. In a similar study, Pratima et al., found that there existed an inverse relationship between the severity of ALRTI and vitamin D levels which were statistically significant.¹⁵

Limitations of the study

The limitation of this study was a relatively small number of cases. A study consisting of larger cohort of cases would further substantiate the results of this study. Moreover, this was a tertiary care hospital-based study; a large general population-based study would be more desirable in assessing impact of vitamin D deficiency on incidence and severity of respiratory tract infection.

CONCLUSION

LRTI is a common cause of morbidity as well as mortality in pediatric age group. Children admitted for LRTI were found to have significantly low level of vitamin D as compared to other children. Moreover, pneumonia was found to be severe in children with vitamin D deficiency as compared to those who had pneumonia which was not severe. Therefore, we conclude that vitamin D deficiency must be diagnosed and treated in children presenting with any severity of LRTI.

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MS- Concept and design of the study; interpreted the results, prepared first draft of manuscript, and critical revision of the manuscript; statistically analyzed and interpreted; reviewed the literature and manuscript preparation; **MMQ-** Design of the study, preparation of manuscript, and revision of the manuscript; concept and coordination of the overall study.

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