Original Research Article

A Study On Association Between Acute Respiratory Distress Syndrome and Serum 25(OH) Vitamin D3 Level In Children In PMCH, Patna, Bihar

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Abstract

Respiratory tract infections (RTIs) are common worldwide and are responsible for significant morbidity and mortality. The most common causal agents are the bacterium Streptococcus pneumonia and influenza-virus. **Aims and Objectives:** To evaluate the level of serum 25(OH) Vitamin D3 in respiratory tract infection (both upper and lower) in children. **Materials and Methods:** A Case control study of total 105 cases of age group 2 months to 12 years from both indoor and OPD patients of Department of Pediatric Medicine, Patna Medical College and Hospital, Patna Bihar, were taken as cases who were suffering from respiratory tract infection and 86 disease free age and sex matched children were taken as control. **Results:** This study included total 196 children of age group 2 months to 12 years. 105 children who were suffering from respiratory tract infection were taken as cases and 86 disease free age and sex matched children were taken as controls.The mean age of cases was 40.88±37.57 months and that of control was 37.66±35.25.Maximum population were in vitamin D insufficient state both in case and control. **Conclusion:** To conclude supplementation of vitamin D may be useful in prevention of RTIs, specially the LRTI group and to decrease the number of PICU admission. However more studies are needed to be performed in this field to assess further correlation with frequency, severity and the types of RTIs.

Keywords: Respiratory tract infection, Vitamin D defficiency

Introduction

Respiratory tract infections (RTIs) are common worldwide and are responsible for significant morbidity and mortality. The most common causal agents are the bacterium Streptococcus pneumonia and influenza-virus. The preventive measure by vaccination may not be completely protective due to non-responders and microbial vaccine escape mechanisms. Treatment options include symptomatic treatment, antibiotics and antiviral. Thus, additional ways to prevent or ameliorate RTIs are needed and modulation of the host immune response could provide such an innovative approach. Recent evidence suggests that vitamin D influences several immune pathways, with the net effect of boosting mucosal defence while simultaneously dampening excessive inflammation [1]. For example, vitamin D induces the gene encoding the antimicrobial peptide L3-L7 [2]. This peptide has potent bactericidal capacity against a number of important bacteria and viruses, including M. tuberculosis and influenza-virus [3,4]. 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 26 hydroxylase converts it into 25-hydroxyvitamin D, the most abundant circulating form of vitamin D [5]. Notably, the final activation of vitamin D, via 1-alpha hydroxylase (CYP27B1), alsooccurs in extra-renal tissues, including epithelial and immune cells [6]. In the respiratory tract, CYP27B1 is expressed in bronchial epithelial cells and induced by inflammatory stimuli [7].Our humble intention in this study is to assess serum 25(OH) vitamin D_3 level in children as compared to age matched disease free control group of children and also to find out any correlation between serum 25-OH vitamin D_3 level with severity and frequency of respiratory tract infection in children.

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Aims And Objectives

1. To assess serum 25(OH) Vitamin D3 level in upper and lower respiratory tract infection in children.
2. To assess serum 25(OH) Vitamin D3 level in age sex matched control group and to compare it with the study group.
3. To assess correlation between serum 25(OH) Vitamin D3 level with severity and frequency of respiratory tract infections in children.

Materials And Methods

A Hospital based Case Control study between age group 2 months to 12 years of both indoor and OPD patients of Department of Paediatric Medicine Patna Medical College and Hospital ,Patna ,Bihar, between February 2019 and July 2020 were taken as cases who were suffering from respiratory tract infection. Age and sex matched healthy children were taken as control.

Inclusion criteria

All children between 2 months to 12 years of age attending the Department of Paediatric Medicine, Patna Medical College and Hospital, Patna, Bihar having respiratory tract infection.

Exclusion criteria

1. Children having congenital heart disease.
2. Cases of childhood asthma and allergy.
3. Cases of tuberculosis
4. Children getting prophylactic vitamin D3 supplementation.
5. Children having immune-deficiency or getting immuno-suppressive therapy.

Parameters studied

a) Clinical:

i. Detailed history

ii. Detailed clinical examination

b) Laboratory Investigations:

i. Complete blood count

ii. Erythrocyte sedimentation rate (1 hour)

iii. Mantoux test

iv. X-ray - chest PA view

v. Serum 25(OH) Vitamin D3 level.

Multiple methodologies for assessment of serum 25(OH) Vitamin D3 measurement exist,including RIA, HPLC, and liquid chromatography tandem mass spectroscopy . The total 25(OH) vitamin D3 levels and 1,25(OH) vitamin D3 measured by high performance liquid chromatography (HPLC) or tandem mass spectrometry have been reported as the gold standard for vitamin D metabolite assay[12].

Data interpretation and Analysis

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.

Results

This study included total 196 children of age group 2 months to 12 years.105 children who were suffering from respiratory tract infection were taken as cases and 86 disease free age and sex matched children were taken as controls.The mean age of cases was 40.88±37.57 months and that of control was 37.66±35.25.Maximum population were in vitamin D insufficient state both in case and control.In cases, the number of vitamin D deficient and insufficient children was more as compared to control group.Among all age groups in cases, vitamin D was more deficient in infancy (40.5%) which is a positive finding signifying infants depend more on either sunlight exposure or dietary vitamin D to meet their requirement from birth.Maximum number of LRTI cases was below 60 months whereas URTI cases were above 60 months.Vitamin D deficiency could be an additional contributing factor for recurrent RTI in the age group 12-60 months.Mean serum vitamin D level was significantly decreased in cases than that of control, which implies that vitamin D deficiency predisposes to respiratory tract infection in children. Vitamin D deficiency is more associated with LRTI than URTI (both acute and recurrent). This is one of the unique finding of my study. No relation was found with breast feeding type; in general overall population was in insufficient state.

Comparison of acute and recurrent RTI has no significant relation with serum vitamin D level, however inverse relation is found with recurrent state as compared to control. Recurrent RTI are more common in 12-60 month age group and vitamin D deficiency and insufficiency were more in this age group. So vitamin D deficiency may be an additional contributing factor for recurrent RTI. Among pneumonia cases, there was no significant difference in vitamin D level among the three groups, so vitamin D level may not be related with severity of pneumonia. Mean serum vitamin D level was less in children requiring PICU admission as compared to children discharged from the ward. So vitamin D deficiency may be one of the contributing factors for disease severity.

Table 1: Distribution of cases and control according to Age

	Group		
Age group	**Case**	**Control**	**TOTAL**
2 Months to 12 Months	35	30	65
Row %	53.8	46.2	100.0
Col %	33.3	34.9	34.0
12 Months to 60 Months	39	29	68
Row %	57.4	42.6	100.0
Col %	37.1	33.7	35.6
60 Months to 144 Months	31	27	58
Row %	53.4	46.6	100.0
Col %	29.5	31.4	30.4
TOTAL	105	86	191
Row %	55.0	45.0	100.0
Col %	100.0	100.0	100.0

Table 2: Distribution of cases and control according to gender

	Group		
Gender	**Case**	**Control**	**Total**
F	47	33	80
Row %	58.8	41.3	100.0
Col %	44.8	38.4	41.9
M	58	53	111
Row %	52.3	47.7	100.0
Col %	55.2	61.6	58.1
TOTAL	105	86	191
Row %	55.0	45.0	100.0
Col %	100.0	100.0	100.0

Table 3: Distribution of vitamin D status in cases and control

	Group		
Vitamin D status	**Case(n=105)**	**Control (n=86)l**	**Total**
Deficient(<20ng/ml)	42	4	46
Row %	91.3	8.7	100.0
Col %	40.0	4.7	24.1
Insufficient(21-29ng/ml)	58	58	116
Row %	50.0	50.0	100.0

Col %	55.2	67.4	60.7
Sufficient(>30ng/ml)	5	24	29
Row %	17.2	82.8	100.0
Col %	4.8	27.9	15.2
TOTAL	105	86	191
Row %	55.0	45.0	100.0
Col %	100.0	100.0	100.0

Chi-square value: 42.3688; p-value: <0.0001

Table 4: Distribution of cases according to type of RTI

Type of RTIs	No. of cases(n=105)	Percentage
LRTI	63	60.0%
URTI	42	40.0%
Total	105	100.0%

Out of 105 cases, 63(60%) were LRTI cases, 42(40%) were URTI

Discussion

Respiratory tract infections (RTIs) are common worldwide and are responsible for significant morbidity and mortality. Recent evidence suggests that vitamin D influences several immune pathways [1]. There are few studies that compared vitamin D with different types of respiratory tract infections from various western countries. Data from Indian studies are limited. We performed a case control study consisting of total 191 children of age group between 2 months to 144 months. Total 105 cases having respiratory tract infection were chosen as cases while 86 healthy age and sex matched children were considered as controls. The mean age of our case group was 40.88±37.57 months in comparison to 37.66±35.25 in control group. In cases 58 (55.2%) patient belonged to male gender and 47 (44.8%) belonged to female gender, whereas in control group 33 (38.4%) belonged to female and 53 (61.6%) belonged to male. There was no significant difference in base line variables (age, gender) between the groups[3].Out of 105 cases, majority belonged to age group 12-60 months (37.1%) followed by age group 2-12 months (33.3%) and rest were from 60 months to 144 months. Among the all age group in cases, vitamin D was more deficient in infant period (40.5%) which is a positive finding signifying infants depend on either sunlight exposure or dietary vitamin D to meet their requirement from birth[10]Vitamin D is naturally deficient in human and cow's milk, thus it may predispose to vitamin D deficiency in younger children who are exclusively breast fed. Wayse V et al in his study, found subclinical vitamin D deficiency and nonexclusive breastfeeding in the first 4 months is a significant risk factor for severe ALRI in Indian children. In our study the mean serum vitamin D level in exclusive breast fed child(19.90±6.33ng/ml) and in non breast fed child (20.90± 5.25ng/ml) were mostly in insufficient and deficient reference range, hence no statistically significant difference of vitamin D level was noted in between these groups.(p=0.4015). Thus my study was in contrary to Wayse V et al study.In children, vitamin D deficiency and insufficiency are important health problems and variable prevalence's have been reported in studies conducted in many countries [11]. In a study conducted in Greece by Lapatsanis D et al, vitamin D deficiency was found with a rate of 14% in children aged between three and 18 years [8]. In USA, in a study conducted byMansbach JM et al on serum 25-hydroxyvitamin D levels among US children aged 1 to 11 years, vitamin D deficiency was found with a rate of 14% and vitamin D insufficiency was found with a rate of 63% in 1799 children aged between one and five years [9]. 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<0.0001) in cases (20.60±5.59) than that of control (26.38±4.58), which implies that vitamin D deficiency predisposes to respiratory tract infection in children.My study is almost similar to the findings in other studies by Velarde Lopez AA et al [5], Roth DE et al [5], Wayse V et al [4], Larkin A et al [1]. 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.Viral pathogen are prominent cause of lower respiratory tract infections in infants and children older than 1 month but younger than 5 year of age. In my study out of 105 cases, 63% cases suffered from LRTI and 40% from URTI. Among them the maximum number of LRTI cases was in age group 2-12 months (54%) followed by age group 12-60 months (38.1%), however the maximum numbers of URTI cases were found in age group 60-144 months (61.9%). It implies that young age group are more prone to LRTI. Pneumonia (65.1%,n=41) was major cause of LRTI, followed by bronchiolitis (27%,n=17) and viral induced wheeze (7.9%, n=5). Ozdemir B et al [9] demonstrated vitamin D deficiency in children was associated with increased frequency of recurrent respiratory infections and chronic cough, with respect to healthy control. In my study the mean serum vitamin D level in acute case was 20.26± 5.45 and in recurrent was 21.41±5.91[5,12]. However, when we tried to compare vitamin D levels between acute and recurrent RTI it did not show any significant difference in serum vitamin D levels (p=0.3393).

Among pneumonia group, the mean serum vitamin D level in pneumonia was 19.78±5.8 ng/ml, in severe pneumonia it was 19.14±5.15 ng/ml and in very severe pneumonia it was 14.96±7.24 ng/ml. Difference of mean vitamin D level in three groups was not statistically significant (p=0.1076). So there was no association of vitamin D with severity of pneumonia. Şişmanlar T, Aslan AT, Gülbahar Ö, Özkan S found no significant correlation between vitamin D levels and lower respiratory tract infection in terms of disease and its severity. However, it was found that vitamin D deficiency/ insufficiency was observed with a high rate in all children included in his study. My study is similar to Şişmanlar T et al study in terms of disease severity.

Conclusion

Deficiency of serum level of 25(OH) Vitamin D3 is significantly associated with RTI, both URTI and LRTI. Deficiency of serum level of 25(OH) Vitamin D3 is more associated with LRTI as compared to URTI; however more studies are warranted to explore the association. No association was found with severity of pneumonia, Though there was significantly low level of serum 25(OH) Vitamin D3 was found in children admitted to PICU that may be due to other co-morbidities. To conclude supplementation of vitamin D may be useful in prevention of RTIs, specially the LRTI group and to decrease the number of PICU admission. However more studies are needed to be performed in this field to assess further correlation with frequency, severity and the types of RTIs.

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