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Original Research Article

Vitamin D level as a predictor of pneumonia and asthma in children less than 5 years of age

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ABSTRACT

Background: Childhood pneumonia is a global health problem .It the leading cause of death for children under the age of five years. 95% of all pneumonia cases under the age of five occurs in developing countries. Asthma remains the most common chronic disease of childhood in the world. The observation that vitamin D deficiency and asthma share risk factors such as urban residence, obesity and African American ethnicity has generated interest in exploring a link between these two conditions. This study was taken up to assess the role of vitamin D as a predictor of pneumonia and asthma in children less than 5 years of age.
Methods: A prospective observational case control study was conducted in MLB Medical college, Jhansi from January 2015 to December 2016 (1 year 11 months). A total of 60 children including 30 asthma cases, 20 pneumonia cases and 10 controls, aged, 6-60 months were enrolled. Controls were healthy children attending outpatient services for immunization.
Results: The mean age of the pneumonia patient was 1.5 years, while mean age in asthma patients was 3.1yrs. Ratio of male and female in pneumonia cases was1.5:1, while is asthma ratio was 2:1. In our study 45% pneumonia cases had deficient level of vitamin D (<20ng/ml) and mean level was 11.08±4.68 while 40% of control had deficient level of vitamin D and mean level was 16.04±1.61, p value was 0.0166 and there was significant difference in both the groups. In Asthma cases 53.33% patient had deficient level of vitamin-D and mean level was 10.62±2.908 as compared to 40% control (mean : 16.04±1.62) 'p' value was <0.0001 and was highly significant.
Conclusions: Our study has illustrated that vitamin-D levels were significantly low in pneumonia and asthma patients as compared to control.

Keywords: Asthma, Children, Prevention, Pneumonia, Supplementation, Vitamin D

INTRODUCTION

Pneumonia is an inflammation of the lung parenchyma. Approximately 158 million cases of pneumonia occur worldwide, out of which 154 million are in developing countries.[1] Childhood pneumonia is a global health problem. It is the leading cause of death for children under the age of five, more than AIDS, malaria and measles combined.[2] Ninety five percent of all pneumonia infection in children under the age of 5 years occurs in developing countries. It contributes to 2 million death among children aged less than 5 years each year which accounts for 19% of all mortality in this age group. The estimated proportion of deaths due to ALRI is uptown 52%. Bronchiolitis and pneumonia representing 80-91% of all ALRI are the most common reasons for children hospitalization.[3]

Most cases of pneumonia are caused by microorganisms, but some noninfectious causes including aspiration of food or gastric foreign bodies, hydrocarbons and hypersensitivity reactions to drugs or radiation-induced

pneumonitis are also involved. Streptococcus pneumoniae (*Pneumococcus*) is the most common bacterial pathogen in children aged 3 months to 4 years, while *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* are common pathogens in children older than 5 years. Viruses are the main causes of lower respiratory tract infections in children younger than 5 years.[4] Recent research suggested the role of vitamin D in the prevention of pneumonia and increasing the individual's immunity.[5,6]

Asthma remains the most common chronic disease of childhood in the world.[7] The observation that vitamin D deficiency and asthma share risk factors such as urban residence, obesity and African American ethnicity has generated interest in exploring a link between these two conditions.[8] Recently there is a growing appreciation of the role of vitamin-D deficiency in cases of asthma and pneumonia. But this association is still premature and needs further elaboration to substantiate it.

Vitamin D is important for the normal activity of skeletal and non-skeletal tissues, immune cells and immunity, bone calcification, and brain processes.[9] It is shown that vitamin D deficiency is a prevalent condition and may be a key contributor to both acute and chronic infectious diseases including sepsis, pneumonia, urinary tract infections, and surgical site infections. Most cells, such as B and T lymphocytes, monocytes, and dendritic cells, have specific vitamin D receptors (VDRs). Vitamin D demonstrates its immunomodulatory effects on these cell lines through its effects on the VDRs. Deficiency is associated with reduced innate immunity and an increased risk for infections. Vitamin D deficiency can positively affect a wide variety of microbial infections such as Gram-positive and Gram-negative bacteria, fungi, mycobacteria, and viruses.

An insufficient vitamin D level in the umbilical cord is associated with an increased risk of respiratory infection within the first 3 months of life and wheezing in early childhood.[10] Insufficient serum level of vitamin D increases the risk of allergic and atopic diseases.[11] Vitamin D3 (cholecalciferol) is produced in the body in a two-step process. It is primarily produced by Ultraviolet B radiation of the skin that converts 7-dehydro-cholesterol to pre-vitamin D3, which then undergoes thermal isomerization.

Vitamin D2, as well as vitamin D3, then undergoes hydroxylation reactions in the liver to form 25(OH)D2 or 25(OH)D3 (calcidiol) and then in the kidneys to form the active vitamin D metabolite, 1.25(OH)2D (calcitriol). Several studies in populations from South Asia have reported high prevalence of hypovitaminosis D, despite living in areas with abundant UVB radiation, and in cultures with and without cultural avoidance of the sun.[12-15] This study was therefore taken up to access the role of vitamin-D as a predictor of asthma and pneumonia in children of less than 5 years of age.

METHODS

It is a prospective case control study, conducted in MLB Medical College, Jhansi. Study group was divided into two groups-

- Groups-A: Comprising 30 children (6 months - 5 years) with bronchial asthma and 20 children (6 months - 5 years) with bronchopneumonia.
- Groups-B: Comprising of 10 healthy children serving as control (6 months - 5 years)

A written informed consent of parent/guardian was taken after explaining whole procedure. Detailed history and examination was done. Vitamin-D level was measured by checking 25 hydroxychlocalciferol level in both cases and control by chemiluscent method [Liaison 23OH V-D total]. Vitamin-D levels were categorized as deficient (<20 ng/ml), insufficient (20-30 ng/ml) and sufficient (>30ng/ml).

Inclusion criteria

- Children in age group 6months -5years of either sex.
- Children only with clinical diagnosis of asthma (by Global Initiative of Asthma 2014 guidelines) and pneumonia (IAP textbook of Pediatric, 5th edition).

Exclusion criteria

Children more than 5 yearrs of age.

Statistical analysis

Statistical analysis was performed using Microsoft Excel work sheets. Mid Cal 9, 0.150/tween and Microsoft Word. Chi-square test, t-test, was used to compare between the groups and 'p' value <0.05 was considered to be significant.

RESULTS

Out of 20 cases of pneumonia, 11 cases (55%) were in age groups 6months-1year, 6 cases (30%) were of 1-2 years and 3 cases (15%) were of 2-5 yrs. Mean age in pneumonia patient was 1.5years (Table 1).

Table 1: Age distribution in pneumonia cases.

Age group	Number of patients	Percentage
6 months-1 year	11	55%
1-2 year	6	30%
2-5 year	3	15%
Total	20	100%

Mean age: 1.575 years ±1.5

Out of 20 pneumonia cases, 12 (60%) were males and 8 (40%) were females. Ratio of male and female in pneumonia cases was 1.5:1 (Table 2).

Table 2: Sex distribution in pneumonia cases.

Gender	Number of patients	Percentage
Male	12	60%
Female	8	40%
Total	20	100%

Male:Female-1.5:1

Out of 30 asthma cases,10 (33.33%) were in age group 1-2 years, 20 (66.66%) were in age group 2-5 years and none was in age group 6 months to 1 year (Table 3). Mean age was 3.16 years.

Table 3: Age distribution in asthma cases.

Age group	Number of patients	Percentage
6months - 1 year	-	-
1-2 year	10	33.33
2-5 year	20	66.66
total	30	100

Mean age: 3.16±1.39

Table 4: Sex distribution in asthma cases.

Gender	No. of patients	Percentage
Male	20	66.66%
Female	10	33.33%
Total	30	100%

Male:Female:2:1

Out of 30 asthma cases, 20 (66.66%) were males and 10 (33.33%) were females. Ratio of male and female in asthma cases was 2:1 (Table 4). About 45% patients of pneumonia had deficient level of (<20ng/ml) vitamin D. (Mean-11.08±4.68) while 40% of control had deficient level of vitamin-D (Mean level 16.045±1.618) 'p' value was 0.0166 and there was significant difference in both groups. Similarly 40% of pneumonia cases and 30% of controls had insufficient (20-30ng/ml) level of vitamin D, p value was 0.0056 which is significant, 15 % of pneumonia cases and 30 % controls had sufficient level of V-D, p value is 0.8964 which is not significant (Table 5).

Table 5: Vitamin-D levels in children with pneumonia and normal healthy control.

	Deficient(<20ng/ml) V-D level		Insufficient(20-30ng/ml)V-D level		Sufficient(>30ng/ml)V-D level	
	No. (%)	Mean±(SD)	No. (%)	Mean±(SD)	No. (%)	Mean±(SD)
Control (n=10)	4(40)	16.045±1.618	3(30)	25.667 ± 1.527	3(30)	34.33±1.527
Pneumonia(n=20)	9 (45)	11.08±4.68	8(40)	22.15 ± 1.163	3(15)	34.26±3.5
p value		0.0166 significant		0.0056 significant		0.8964 not significant

Table 6: Vitamin-D levels in children with asthma and normal healthy control.

Group	Deficient(<20ng/ml) V-D level		Insufficient(20-30ng/ml)V-D level		Sufficient(>30ng/ml)V-D level	
	No. (%)	Mean±(SD)	No. (%)	Mean±(SD)	No. (%)	Mean±(SD)
Control (n=10)	4(40)	16.045±1.618	3(30)	25.667±1.527	3(30)	34.33±1.527
Asthma (n=30)	16(53.33)	10.62±2.906	10(34)	23.2784±1.33	4(12)	31.2±0.677
p value		<0.0001 highly significant		0.0326 significant		0.0211 significant

Table 7: Genetic predisposition in asthmatic children.

Groups	Total number	Percentage
First degree relative having history of asthma or other allergic disease		
One parent	11	36.66
Both parents	2	6.66
siblings	7	23.33
Parent and siblings	2	6.66
Second degree relative having asthma or other allergic disease history	-	-

In Asthma cases 53.33% patients had deficient level of vitamin-D (mean: 10.62±2.906) as compared to 40% control. The 'p' value was <0.0001 and was highly significant, 34% asthmatic patients and 30 % controls had

insufficient vitamin D level, p value was 0.0326 which was significant, 12% asthmatic cases and 30% controls had sufficient level of Vitamin D, p value is 0.0211 which was significant (Table 6).

In asthma cases, 11 cases (36.66%) had one parent affected with asthma/allergic disease, 2 cases (6.66%) had both parents affected, 7 cases (23.33%) had siblings affected and 2 cases (6.66%) had both parents and siblings affected. Total 73% asthmatic children had positive family history (Table 7).

Table 8: Asthma triggering factors.

Triggering factors	Total number	Percentage
Viral infection	14	46.66
Cold air/cold drinks	7	23.33
Exercise/crying/laughing	-	-
Seasonal changes	5	16.66
Indoor allergens	4	13.33
Total	30	100

According to detailed history taken following triggering factors were identified in asthmatic cases, 46.66% of asthma attacks were probably provoked by viral infections, 23.33% had triggers like cold dry air /cold drinks. Indoor allergens were found in 13% and seasonal changes in 16.66% (Table 8).

DISCUSSION

This study was under taken with aim to study the association between vitamin D deficiency and asthma and pneumonia in age group 6 months to 5 years. Maximum 55% cases of bronchopneumonia were between 6 months - 1 year and 30% and 15% were between 1-2 years and 2-5 years respectively. According to S. Chatterjee, age specific attack rate of ARI decreased with increasing age and worst sufferers were in age groups 6-11months.[16] In our study, 66.66% asthma patients were of age groups 2-5yrs and 33% were of age groups 1-2yrs and none were of age groups 6months - 1yrs. Male to female ratio in pneumonia cases was 1.5: 1 which means boys were more affected than girls. But Neyestani T R et al noted that girls were more affected than boys in pneumonia.[17] Peskin reported 2:1 ratio of male and female in asthma. In our study also ratio in asthma cases was 2:1. In our study, we found 45% of pneumonia patients had deficient level of vitamin D as compared to 40% controls, 40% pneumonia patients had insufficient level of vitamin-D as compared to 30% control and only 15% patients had sufficient levels of vitamin-D as compared to 30% controls. In a hospital-based case-control study by Wayse et al on 150 Indian children under 5 years of age, one of factors associated with significantly higher OR for having severe acute lower respiratory infection was serum 25(OH)D less than 10 ng/mL (OR =11).[18] It is a well-known fact that children with rickets are predisposed to develop pneumonia.[19] Haider N et al noted that 74% of children's with severe pneumonia had rickets as defined by low or normal calcium, low phosphorous and high serum alkaline phosphatase.[20] Even subclinical vitamin D deficiency was found to be associated with severe acute lower respiratory infection in Indian children less than 5 years of age. The association of vitamin D deficiency and lower respiratory tract infections is not only limited to children but is also found amongst new borns, infants and adults.[21-23] Inamo et al, who found that there was a significant correlation between vitamin D deficiency and the need for supplemental oxygen and ventilator management, also support this conclusion.[24] In contrast to our study, Tuğba Şişmanlar et al found no significant difference in vitamin D levels between the patient and control groups in their study.[25]

In asthmatic patients, 53.33% had deficient levels of vitamin-D as compared to 40% control, 34% had insufficient level of vitamin D as compared to 30% control and only 12% had sufficient level of vitamin D as against 30% control. Similar results were obtained by Banner et al, where 41% patients of asthma had deficient level of vitamin D, 15% had insufficient level and 13% had sufficient level.

It was observed in pneumonia patients as age progresses mean vitamin-D level also increases. V Wayse et al, also found similar observation. There was no positive correlation between sex and vitamin D levels. Similar were the findings in study done by Ways et Al, Belgaum. In present study 73% children had positive history of asthma or other allergic disease in family. Bruce observed that nearby 50% patients of asthma had family history of asthma. 46.6% asthma attack was provoked by viral infections, 23% was provoked by cold air and cold drinks. Vinod H Ratageri, S.K. Kabra et al conducted a study in AIIMS and found that cold air, cold food, upper respiration infection (50%), smoke, dust, pets were involved in provocating episode of asthma.[26]

CONCLUSION

Vitamin-D levels were significantly low in asthma and pneumonia patients as compared to control. Therefore daily supplementation of vitamin-D in children should be given which will help them have immunity and to overcome pneumonia and asthma and complications associated with it.

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