nal o **ORIGINAL RESEARCH PAPER Paediatrics** STUDY OF VITAMIN D DEFICIENCY AMONG **KEY WORDS:** Bronchial asthma ASTHMATIC CHILDREN ATTENDING SMGS , vitamin-D. **HOSPITAL JAMMU** Pooja Bharti Senior resident SMGS hospital Jammu. Ashna kumar* Junior resident SMGS Hospital Jammu. *Corresponding Author Objective: To determine the level of 25-OH-VITAMIN D3 in different groups of asthmatic children (i.e. mild, moderate and severe) Study design: A hospital based observational, descriptive study. Setting: This study was conducted in the Department of Pediatrics, SMGS Hospital an associate hospital of GMC JAMMU, from August 2017 to July 2018.

- Setting: This study was conducted in the Department of Pediatrics, SMGS Hospital an associate hospital of GMC JAMINU, from August 2017 to July 2018. Methods: This cross-sectional study included 107 (29 severe, 37 moderate and 41 mild asthmatic children) aged between 6 and 18 years. Serum 25-hydroxy vitamin-D levels were determined and compared between the three groups. The association between vitamin-D levels and lung function was studied. Percultr: Serum vitamin D level was significantly lower in severe asthmatic children than in mild asthmatic children and vitamin D
 - **Results:** Serum vitamin-D level was significantly lower in severe asthmatic children than in mild asthmatic children and vitamin-D levels had a significant positive correlation with FEV1%.

Conclusion: Vitamin-D deficiency is highly prevalent in asthmatic children and there was a significant inverse relationship between vitamin D levels and severity of asthma symptoms.

INTRODUCTION

Asthma is defined as a common chronic inflammatory disease of the airways characterized by variable and recurrent symptoms, reversible airflow obstruction, and bronchospasm. Children have smaller airways than adults, which makes asthma especially serious for them [1] School absence, emergency department visit and hospitalisation make asthma the leading cause of childhood morbidity from chronic disease.[2] Asthma is classified as intermittent, mild persistent, moderate persistent and severe persistent, according to Global Initiative for asthma.

Vitamin D is both a nutrient and a hormone. Bioactive vitamin D or calcitriol has long been known for its important role in regulating body levels of calcium and phosphorus, and in mineralization of bone. Vitamin D axis has tissue specific autocrine and perhaps paracrine roles distinct from the classical endocrine functions. Although the role of vitamin D in bone health is well known, recent studies have described new non skeletal roles for vitamin D in human health, including a role in preventing chronic diseases such as cardiovascular disease, diabetes and cancer[3]. In addition to these chronic diseases, vitamin D which is a potent modulator of immune system and is involve in regulating cell proliferation and differentiation, may also be linked to bronchial asthma[4]. Vitamin D deficiency has been documented in many populations worldwide, even in areas of the world with abundant sun exposure. Because of its potential role in decreasing the risk for a multitude of chronic diseases associated with westernization, vitamin D deficiency is an important public health problem. The role of vitamin D in inhibiting TH1 immune responses has been well studied, but its effects on TH2 responses are more complex and not fully elucidated.

Effects of vitamin D on the immune system make it a plausible critical regulator of immune system function, whose deficiency can predispose to asthma and allergies in the presence of other environmental Stimuli. Hence, this study was designed to detect the incidence of vitamin D insufficiency and deficiency among asthmatic children and to correlate between vitamin D levels and severity of asthma.

METHODS

This cross-sectional study was carried out on 107 children aged 6 to 18 years, visited Department of Pediatrics, SMGS HOSPITAL, an associated hospital of GMC JAMMU, from august 2017 to july2018. All the families filled out a written consent form. Asthmatic patients were diagnosed according to the Global Initiative for Asthma (GINA) criteria: 1) a physician's diagnosis of asthma, 2) symptoms of recurrent (i.e. more than two) episodes of wheezing, cough, shortness of breath, or a combination of these, 3) documented reversibility with bronchodilators and 4) symptoms

of and/or use of medication for asthma in the previous six months. Out of 107 asthmatic patients included in study , 41 were mild persistent , 37 as moderate persistent and 29 as severe persistent bronchial asthma.

Detailed personal medical histories and physical examination were recorded. Socio-demographic characteristics such as age, sex and place of residence and measurements such as height and weight were recorded.

Appropriate laboratory tests including complete blood cell count, eosinophil count, plasma vitamin D level, plasma calcium (Ca), phosphorus(P) and alkaline phosphatase (ALP) were done. Chest X rays were also carried out to eliminate cases of disease other than asthma. A single measurement of 25-OH-D3 was made in all subjects using a chemiluminescent method.

Ranges for 25 hydroxy vitamin D:

- Normal range for 25 hydroxy vitamin d 30-60 ng/ml. Deficiency was diagnosed at vitamin d level < 30 ng/ml or <75nmol/l Insufficiency was diagnosed at vitamin d level <20 ng/ml or <50nmol/l.

Lung Function Tests

Short-acting bronchodilators were stopped at least 8 hr before the test. Dynamic spirometry was performed with measurement of FEV1% of predicted, The highest value of FEV1 of three forced expiratory manoeuvres was used.

STATISTICAL ANALYSIS

Data were analyzed using standard computer program SPSS Windows version. Continuous data were expressed in the form of mean \pm SD. Categorical data were expressed as numbers and percentage. P value of < 0.05 indicates significant results.

RESULTS

Total of 107 patients were included in the study. 67 (62.6%) were males and 40 (37.4%) were females. Male to female ratio was 1.7:1 (Table 1). 41(38.3%) were mild persistent asthma , 37 (35.5%) patients were moderate persistent and 29(27.1%) as severe persistent disease. Serum alkaline phosphatase levels were highest 251.5 \pm 78.63 IU/L (mean \pm SD) in severe persistent asthma followed by 209 \pm 54.27 IU/L in moderate persistent asthma. The difference in all three categories was statistically significant with P value < 0.001. (Table 2). As far as serum 25(OH)D3 levels were concerned , 85 (79.4%) of patients were having vit D insufficiency, 17 (15.9%) were having deficiency and 5(4.7%) were having vit D sufficiency. (Table 3).

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The mean levels of serum 25(OH) D3 (vitamin D) in asthmatic patients were; mild persistent: 24.52 ± 8.63 ng/dl, moderate persistent: 14.45 ± 5.64 ng/dl and severe persistent: 9.62 ± 7.69 ng/dl; p value of < 0.001 which is significant There was statistically significant negative correlation between vitamin D level and severity of asthma (Table 4). The mean value of vitamin D3 level was 12.7 ± 5.41 ng/ml, 17.8 ± 4.79 ng/ml, and 21.6 ± 7.84 ng/ml for % predicted FEV1 of <60%, 60-79% and >80% of respectively .P value is <0.001 which is statistically significant (Table5).

Table 1: Distribution of subjects according to gender				
Gender	No.	%ge		
Male	67	62.6		
Female	40	37.4		
Total	107	107		
male:female =1.7:1				

Table 2: Serum alkaline phosphatase as per severity of asthma

Severity of asthma		Ν	Mean	SD	P-value
	Mild Persistent	41	176.9	61.82	<0.001*
	Moderate Persistent	37	209.4	54.27	
	Severe Persistent	29	251.5	78.63	

Table 3: Serum 25 (OH) D3 levels with severity of asthma

Sevency of ascilla					
	< 20	20-30	> 30		
Mild Persistent	26 (63.4%)	11 (26.8%)	4 (9.8%)		
Moderate Persistent	31 (83.8%)	5 (13.5%)	1 (2.7%)		
Severe Persistent	28 (96.6%)	1 (3.4%)	0 (0%)		
Total	85 (79.4%)	17 (15.9%)	5 (4.7%)		

Table 4: Mean serum vitamin D3 (ng/ml) with severity of asthma

Severity of asthma	Ν	Mean	SD	Range	P-value
Mild Persistent	41	24.52	8.63	10.3-52.4	<0.001*
Moderate Persistent	37	14.45	5.64	8.7-24.5	
Severe Persistent	29	9.62	7.69	3.9-21.1	
Total	107	16.9	7.84	3.9-52.4	

*Statistically significant difference (P value<0.05)

Table 5: Serum vitamin D3 level (ng/ml) with % of predicted FEV1

% Predicted FEV1	Ν	Mean	SD	P-value
< 60	41	12.7	5.41	<0.001*
60-79	37	17.8	4.79	
> 80	29	21.6	6.32	
Total	107	16.9	7.84	

*Statistically significant difference (P value<0.05)

DISCUSSION

Bronchial asthma is a major health problem especially in children. It has dramatically increased worldwide over the last few decades, in both developed and developing countries. Vitamin D deficiency may predispose to allergic phenotype of asthma and epidemiological evidences suggest that lack of vitamin D has been linked to increased incidence of asthma and increased severity of asthma in children. Vitamin D is a potent modulator of the immune system[5]. Being a tropical country, Vitamin D deficiency is supposed to be uncommon in India [6]. However from the data available in published literature vitamin D deficiency is very common in India in all the age groups and both the sexes across the country. This had been shown by Harinarayan and Marwaha [7,8,9]. Prolonged breastfeeding without vitamin D supplementation, maternal vitamin D deficiency, poor diet and limited exposure to sunshine have been suggested as major contributors to vitamin D deficiency [10,11]

This study was sought to detect the incidence of vitamin D Insufficiency(<20ng/ml), Deficiency(20- <30ng/ml) and normal level(30-60ng/ml) among 107 asthmatic children and to correlate the relation between vitamin D levels and severity of asthma.

A total of 107 asthmatic children aged between 6 and 18 years

were studied. There were 67(62.6%) boys and 40(37.4%) girls in the study. It show that the incidence of asthma is predominant in boy than in girls. The similar finding was also seen in the previous study conducted by Mahmoud T on Egyptian children [3]. It is also in accordance with the study conducted on 3283 Qatari children by Jenahi[12]; a study conducted in Lucknow, India by Awasthi [13] and also in Thailand by Wijittra Krobtrakulchai[14]. In childhood, twice as many males as females are asthmatic, but by adulthood the sex ratio has equalized. Male gender is a risk factors for having childhood asthma in the U.S [15].

The mean value of serum alkaline phosphatase was significantly higher in all patients with asthma. This is shown in a study by Mahmoud T. in Eygyptian children where 100%(n=60 out of 60) of asthmatic children show raised serum alkaline phosphatase (ALP) as compared to 37.5% (n=14 Out of 40) of control have normal ALP; p value is <0.001 which is highly significant[3]. In the our study we also observe the elevated serum levels of alkaline phosphatase being highest in severe asthmatics group $251.5\pm78.631U/L$ and was lowest in mild asthmatics group $176.9\pm61.821U/L$. This difference is statistically significant [p=0.001]. This could be explained by vitamin D deficiency which causes secondary hyperparathyroidism leading to increase turnover of osteoid tissue and elevated serum levels of alkaline phosphatase.

In our study we find that 85(79.4%) of total asthmatic patients were having vitamin D insufficiency, 17(15.9%) were having deficiency and 5(4.7%) were having vitamin D in normal range. The mean serum 25(OH)D3 levels in asthmatic patients in our study was 16.9±7.84 ng/ml. Several studies in the past have concluded that vitamin D deficiency is associated with an increased incidence of asthma and other allergy symptoms. In a cross sectional study carried out in 170 children of age range from 2-14 years by Uysalol et al, it show that 90.6% (n=77 out of 85) of asthmatic patient have vitamin D deficiency as compared to 67.7% (n=55 out of 85) in control group with p value of <0.001.A similar cross sectional study conducted by Somashekar on 44 asthmatic and 44 healthy children in Bangalore, India which show that the mean serum 25 hydroxy cholecalciferol (Vitamin-D) levels in asthmatic children was 12.88±1.79ng/mL, which was significantly lower than the mean serum vitamin D levels in the healthy controls (16.49±1.13ng/mL). 68.18% of the asthmatic children had deficient serum vitamin D levels (≤15ng/mL) and 31.28% of them had insufficient serum vitamin D levels (>15ng/mL to <20ng/mL) that is 100% of asthma children have deficient serum vitamin D level[16].

In our study, the mean levels of serum vitamin D in asthmatic patients were; mild persistent: 24.52±8.63ng/dl, moderate persistent: 14.45 ±5.64ng/dl and severe persistent: 9.62 ± 7.69 mg/dl; p value of < 0.001 which is highly significant. This means that the higher the level of serum vitamin D, the lesser the degree of bronchial asthma severity. Our study demonstrated a highly significant negative correlation between serum vitamin D levels and the severity of asthma. Many studies have shown that low vitamin D levels were associated with increase in severity of bronchial asthma, El-naggar et al observe that serum vitamin D level in intermittent asthma is 41.1±11.8ng/ml, mild persistent asthma is 35.1±6.4ng/ml, moderate persistent asthma is 24.7±3.8ng/ml and severe persistent asthma is 20.7±3.8ng/ml with p value of <0.001 which is statistically significant. It conclude that there is a inverse correlation between vitamin D level and severity of asthma[20]. Avinash Kumar et al observed serum vitamin D level of <10ng/ml in 7.69% of intermittent asthma, 3.5% of mild persistent asthma, 35% of moderate persistent asthma and 100% of severe persistent asthma; p value is < 0.001 which is highly significant and conclude that vitamin D deficiency is associated with severity of childhood asthma..[17].

In our study, we observe that the predicted FEV1 for the mean value of vitamin D level of 12.7 \pm 5.41ng/ml, 17.8 \pm 4.79ng/ml, and 21.6 \pm 6.32ng/ml is <60, 60-79 and >80% respectively; p <0.001, which is significant. This is also supported by study conducted by Brehm which conclude that insufficient vitamin D status predicts a lower FEV1 [18]. Significant positive correlations were found

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between the serum vitamin D level and % of predicted FEV1 (r = 0.871, P < 0.001) in a study conducted by Elnady in Egypt [19].

Our study has some limitations: The sample size was relatively small (n = 107). The healthy controls were not taken. Many confounding factors can affect vitamin-D levels or asthma severity. Long-term follow-up studies focusing on changes in vitamin-D status and asthma parameters will be needed to elucidate the effect of vitamin-D status on asthma.

CONCLUSION

The present study suggests that vitamin D deficiency is relatively frequent in asthmatic patients (95.3%) who were attending to pediatric department of SMGS Hospital Jammu.

There was a significant inverse relationship between vitamin D levels and severity of asthma symptoms. Measuring serum levels of vitamin D may be considered in patients with bronchial asthma . Further studies are needed to determine the role of vitamin D in the treatment of asthma in term of improvement of lung function test and severity of asthma, whether vitamin D supplementation to be given or not.

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