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Pediatrics

A Study on Correlation Between Recurrent Wheezing and Vitamin D Status in Tertiary Care Centre, Bhagalpur.

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ABSTRACT

***Objective*:** To investigate correlation between recurrent wheezing and Vitamin D status in infants.

***Methods*:** Fifteen infants with recurrent wheezing and Twenty Three healthy, similar aged infants without any history of acute or chronic illness were included in the present study. The clinical features of infants were recorded and serum 25-hydroxyvitamin D[25(OH)D] levels were measured. Data analysis was performed using SPSS 13 package program.

Results: The mean value of 25 (OH) D vitamin levels were 22.1 +/_ 8.9 IU/L for the control and recurrent attack group respectively. 73.3% of subjects with recurrent wheezing had vitamin D levels in the deficient range (<20ng/ml) and 47.8% had vitamin D levels under <20 ng/ml in the control group. The percentage of insufficient vitamin D levels (<30 ng/ml) were 93.3 and 78.2 for the patient and control group respectively. Four patients had extremely deficient vitamin D (<10 ng/ml) levels. There was no statistical significance between the groups in terms of the distribution of 25 (OH) D level.

Conclusions: The present study did not demonstrate significant association between vitamin D status and recurrent wheezing in the infants.

KEYWORDS : Recurrent wheezing, Infants, Vitamin D

Introduction

Vitamin D is a fat-soluble vitamin that plays an important role in bone metabolism and seems to have some anti-inflammatory and immune-modulating properties. Vitamin D is an essential nutrient mainly acquired through endogenous synthesis in the skin after exposure to sunlight, and in a lesser percentage through the diet and dietary supplement . Within the body Vitamin D acts as a hormone and it is well recognized for its role in calcium and phosphorus homeostasis, bone mineralization and skeletal health. The recent identification of Vitamin D receptors in most tissues and cells in the human body, including cells of the immune system, combined with the demonstration that several cells in the body are capable of converting the primary circulating form of Vitamin D, 25-hydroxyvitamin D (25 (OH)D), to the active form 1,25-dihydroxyvitamin D (1,25 (OH2)D), has exponentially increased interest in the extra-skeletal effects of this hormone.

There is an increasing awareness of the important role of vitamin D in the maintenance of general immune and respiratory health [1,2]. The diseases traditionally associated with vitamin D deficiency are rickets and osteomalacia, but growing data suggests that vitamin D plays an important role in the lung development and it is discussed as a risk factor for respiratory infections, recurrent wheezing and asthma [3-6].

The exact mechanism between the vitamin D level and recurrent wheezing is not obvious. There are a few studies investigating the relationship between recurrent wheezing and vitamin D levels and these studies reported the association between maternal vitamin D intake and early infant wheezing [7,8].

The data from both animal models and human subjects showing that low vitamin D levels as a risk factor for respiratory tract infections, the antimicrobial effects of vitamin D producing antimicrobial proteins such as cathelicidin, its protective role against respiratory tract infections and its importance in regulating chronic inflammation in the lung are potential mechanisms to explain the relationship between vitamin D level and wheezing [9-11]. From this point of view, the authors conducted the study to investigate whether there is a relationship between vitamin D levels and recurrent wheezing during the infancy period.

Materials and Methods

The infants followed by Infancy Service between November 2015 – March 2016 were enrolled in the present study. The study group consisted of 15 infants diagnosed as recurrent wheezing (more than 3 wheezing attacks) aged between 1-24 months without any history of congenital heart disease, chronic lung disease, immunodeficiency, neurologic or metabolic diseases. The control group consisted of 23 healthy infants followed by Well Child Clinic without any history of acute lower respiratory infections (ALRI) and chronic diseases. 25-(OH)D levels were measured and clinical features were analyzed in all the 38 infants. The blood samples were collected between November 20115 to March 2016. Serum 25(OH)D levels were measured using RIA (specific radioimmunoassay kit) method. Two different cutoff levels were used in the study to categorize 25(OH)D concenterations. The levels above 30 ng/ml (75 mmol/L) were accepted as sufficient, the levels under <20 ng/ml (50 nmol/L) as vitamin D deficiency and under <10 ng/ml as extreme deficient (25nmol/L) [12-14].

The study was approved by the Local Ethics Committee and informed consent was obtained from the parents of infants. Data analysis was performed by using SPSS Software Version 13 for Windows (SPSS Inc., Chicago, IL, United States). The clinical and anthropometric parameters of the study population were expressed by using mean and standard deviation. The mean levels of 25 (OH) D of two groups were compared by independent samples test. Pearson Chi-square test was used to determine the differences between the levels of 25(OH)D of two groups. P value less than 0.05 was considered statistically significant.

Results

There were 38 cases (15 infants with more than 3 attacks and 23 control cases). The mean age of the control group was 12.52+_6.95 mo and recurrent attack group was 1.9+_4.35mo. The mean value of 25 (OH) D vitamin levels were 22.1+_8.9 IU/L and 18.8+_11 IU/L for the control and recurrent attack group, respectively.

73.3% of subjects with recurrent wheezing had vitamin D levels in the deficient range (<20 ng/ml) and 47.8% had vitamin D levels under <20ng/ml in the control group (Table 1). The percentage of insufficient vitamin D levels (<30 ng/ml) were 93.3 and 78.2 for the patient and control group respectively. Four patients in the control and patient group had extremely deficient vitamin D (<10ng/ml) levels.

The index results did not show statistical significance between the groups in terms of the distribution of 25 (OH) D level.

Table 1 : Comparison of vitamin D status of patient and control groups (n=38)

Vitamin D level (ng/ml)	Control group (n=23)	>3 attacks (n=5)
<10	2 (8.6%)	2 (13.3%)
11-20	9 (39.1%)	9 (60%)
21-30	7 (30.4%)	3 (20%)
>31	5 (21.7%)	2 (13%)

Discussion

Vitamin D deficiency and insufficiency are widespread and documented from different parts of the world regardless of latitude,

sun exposure or socioeconomic factors. An exact 25(OH)D cutpoint to define suboptimal vitamin D status is controversial. There is increasing agreement that value less than approximately 30 to 32 ng/ml be identified as "low". When this cutpoint is applied, low vitamin D status is extremely common worldwide [15].

Serum 25(OH)D is the most reliable marker of vitamin D status. Adequate levels of serum 25(OH)D are necessary to sustain the claimed pleitropic effects, either skeletal (classical) or extraskeletal (non-classical) [14,16]. As far as bone mineral homeostasis is concerned, the threshold for a sufficient vitamin D status corresponds to the minimum serum 25(OH)D level necessary to normalize 1,25(OH)2D, prevent secondary hyperparathyroidism, optimize intestinal calcium absorption and avoid bone histology abnormalities. Based on these criteria, most leading experts define vitamin D insufficiency as 25(OH)D levels between 50 and 75 nmol/L, vitamin D deficiency as 25(OH)D levels less than 50 nmol/L and extreme deficiency as 25(OH)D less than 25-30 nmol/L and argue that levels of 25(OH)D >_50nmol/L are required for optimal musculoskeletal health, however levels of 25(OH)D above 75 nmol/L may be necessary to maximize musculoskeletal benefits and take advantage of the extraskeletal actions of vitamin D [14, 16-19]. Seventy-two percent of all the infants had subclinical vitamin D deficiency characterized by an inadequate vitamin D status (between 25 and 75 nmol/L) without overt specific signs and symptoms referred to altered mineral homoeostasis, i.e., hypocalcemia, hypophosphatemia, rickets and osteomalacia [16].

In our country, there is insufficient ultraviolet B (UVB) intensity for cutaneous synthesis of 25(OH)D between the months of November and March and the blood smples were collected during this time.

Vitamin D appears to play a role in immune system and lung development in the foetus [3]. Vitamin D receptors (VDR) have been found in foetal Type II alveolar pneumocytes of rats, and may play a role in lung development, pneumocyte differentiation and surfactant secretion [20].

Lung mechanics studied in rats showed decreased compliance in those born to mothers deprived of vitamin D [21]. These studies show that vitamin D deficiency causes a susceptibility to respiratory infections initiating from the foetal period.

Some studies have demonstrated an association between pregnant women with lower vitamin D intake and a higher risk of wheeze in offspring [7, 8]. In a recent study, higher maternal circulating 25(OH)D concentrations in pregnancy were independently associated with lower risk of lower respiratory infections in offspring in the first year of life but no association was found with wheezing at 1 year or 4 year, or asthma at age 4-6 years [22]. The authors have no knowledge about the maternal vitamin D levels but suggest that vitamin D levels of the infants hospitalized for serious infections and recurrent wheezing should be followed carefully.

Recent studies have shown a potential physiologic role of vitamin D in regulating normal innate and adaptive immunity [23]. Vitamin D metabolites contribute to defense at epithelial surfaces by stimulating production of antimicrobial peptides such as defensins and cathelicidin [16, 24]. Janssen et al. recently showed significant associations of a number of innate immunity genes (including the VDR) with thw severity of Respiratory Syncytial Virus (RSV) bronchiolitis [25]. Roth et al. found the association between two VDR gene polymorphisms (FokI ff and TaqI Tt genotypes) and ALRI (predominantly viral bronchiolitis) in young children [26]. Jartti et al. found that serum 25(OH)D levels were inversely associated with RSV, Rhinovirus and multiple viral cause, by contrast no association was found with other viral infections [27]. Taken together, these studies point out the important role of vitamin D in the relation between respiratory viruses and their link to recurring wheezing.

Genetic and epidemiologic studies have shown an association between asthma and vitamin D. Bosse et al. investigated VDR in bronchial smooth muscle cells and showed vitamin D to be a regulator of the expression of over 400 genes, some of which have been implicated in the pathogenesis of asthma. This may be involved in the airway remodeling seen in asthmatics [28]. A study in a large cohort of children with asthma in Costa Rica showed an association between low vitamin D levels (<30ng/ml) and asthma severity in terms of hospitalizations, medication use and airway responsiveness [29]. The rising prevalence of asthma may be linked to vitamin D deficiency but asthma is a multifactorial chronic disease. It may be useful to measure the levels of 25(OH) vitamin D of the infants with recurrent wheezing and give them vitamin D supplementation until the level is increased up to 30 IU/L by controlling the calcium levels in order to prevent asthma. The precise role of Vitamin D in the pathogenesis of asthma is still debated and needs further assessment. Published studies on the topic have had conflicting results and most of them are observational (30).

In the present study, no correlation between vitamin D levels and recurrent wheezing in infants was found but this may be due to the few numbers of patients that we studied with.

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