



Review Article

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A Review of the Association of Obesity and Vitamin D Levels with Childhood Asthma

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ABSTRACT

Asthma is a chronic inflammatory disease affecting nearly 300 million people worldwide, and 1,000 people die daily due to asthma. The prevalence of this disease is higher in developed countries. Studies have shown that obesity is an independent risk factor for asthma, and obese children are more at risk of developing asthma. These children experience more severe asthma and have a poorer response to treatment. On the other hand, there is a direct relationship between the reduction of vitamin D levels in early life and the development of asthma in the following years of life. Interestingly, obesity is a common risk factor for both asthma and vitamin D deficiency. Therefore, investigating the interaction between asthma, obesity, and vitamin D deficiency can play an important role in understanding the complex nature of asthma. The results of the study on the level of obesity and vitamin D in children with asthma, in addition to the fact that it can provide excellent information about the effect of obesity and vitamin D deficiency on children's asthma, can provide a basis for ecological studies to measure the correlation between the incidence of asthma in children and The amount of sunlight and food and cultural habits in different regions.

Key words: *Obesity, Vitamin D levels, Childhood, Asthma*

INTRODUCTION

Asthma is an inflammatory disease that affects nearly 300 million people worldwide, and 1,000 people die due to asthma every day [1, 2]. The prevalence of this disease is increasing in developed and developing countries. In children, the prevalence of severe asthma has been reported from 0% in India to 20.3% in Costa Rica. Unfortunately, the prevalence of asthma has been increasing since 30 years ago, and it accounts for a high percentage of sufferers in industrialized countries as well [3].

Direct medical costs for asthma in the United States are estimated to be more than 50 billion dollars. Absence from work and missed school days add another 5.9 billion dollars to the indirect costs of asthma [4-6].

Shortness of breath, chest tightness, frequent coughing, especially at night and early morning, and respiratory wheezing are among the main symptoms of asthma that appear intermittently, so if you witness the occurrence and repetition of these symptoms, you may have asthma, and you should see a doctor. Of course, the type of asthma is different in different people, and the occurrence of this disease can be chronic, gradual, very acute, severe, and even fatal [7-9]. Therefore, the doctor's correct diagnosis is very effective with the help of the patient for treatment. It should be noted that late or wrong diagnosis or incorrect and late treatment of asthma has complications that may lead to the spread of asthma, which has aggravated its losses worldwide. Childhood

asthma often appears in the first five years of life, and experience shows that almost 50% of children show asthma symptoms before age two. Children's asthma, unlike adults, is more common in boys than in girls and usually occurs or worsens in the presence of allergens [10-12].

The presence of eczema and other allergies indicates a worse prognosis. Moreover, asthma is more severe in boys. In those who have severe and frequent attacks or in those who have asthma attacks at close intervals and the lung volume does not return to normal, asthma becomes chronic. Respiratory infections, especially viral and sometimes microbial, cause asthma attacks. Severe complications of childhood asthma and most deaths occur in children under five years of age [12-14].

The basis of treatment is the correct management of this disease. In the case of intermittent asthma, it is recommended to use salbutamol spray during symptoms (shortness of breath and cough). In the case of persistent asthma, the use of long-term inhaled corticosteroids is recommended, and in the case of symptoms, it is necessary to use salbutamol spray. In more severe cases, under the supervision of an allergist, beta-agonists are also used in inhalation and oral corticosteroids [15,16].

Studies have shown that obesity is an independent risk factor for asthma, and obese children are more at risk of developing asthma. These children experience more severe asthma and have a poorer response to treatment. On the other hand, there is a direct relationship between the reduction of vitamin D levels in early life and the development of asthma in the following years of life. Interestingly, obesity is a common risk factor for both asthma and vitamin D deficiency. Therefore, investigating the interaction between asthma, obesity, and vitamin D deficiency can play an important role in understanding the complex nature of asthma.

Etiology of children's asthma

The causes involved in the development of asthma can be genetic, psychological, biological, and environmental. Any of the mentioned factors or a combination of them can lead to asthma in childhood and adulthood [17].

Genetics and epigenetics

In many cases, there is a transparent hereditary sensitivity background in the family of a child with asthma. So far, the genes involved in this disease have been traced in different chromosomes of the body, among which we can mention chromosomes 5 and 11, and recently, a gene called Adams 33 has been identified in chromosome number 20, which researchers have also identified in this gene. Asthma disease is considered effective. Meanwhile, epigenetic markers have a strong relationship with asthma [18].

Infection

The role of infections, especially respiratory viruses, is important in the occurrence of acute asthma attacks in children [15].

Allergies

Patients with allergies and atopy experience asthma attacks after contact with allergens, including pet allergens. In most of these patients, serum IgE will increase [16,19].

Psychological factors

Among the environmental factors of asthma, stress and anxiety are important factors in causing asthma attacks. Anxiety is an unpleasant emotional state that is usually accompanied by a painful and prolonged feeling of fear and worry. Family behavioral disorders and distressing events can play a role in accelerating the onset of asthma symptoms [20].

Taking medicines

The use of some drugs, including aspirin, can have an effect on prostaglandin in the occurrence of an asthma attack, which should not be used in asthmatic patients [21].

Inhaled air

Air changes and inhalation of cold air, pollutants, cigarette smoke, and aeroallergens can be among the causes of asthma [22, 23]. In children who have nasal congestion and inhale cold air through the mouth, the possibility of asthma symptoms is aggravated. Also, asthma attacks intensify in children who have tonsillectomy with adenoid [24].

Sports

Physical activities and exercise can cause bronchospasm and the appearance of asthma symptoms and cause coughing, which is a symptom of asthma. The mechanism of bronchospasm caused by exercise is not completely clear, but exposure to cold air and humidity reduction is considered effective [25].

Other factors

A comprehensive study conducted in 2016 on systematic studies on the factors of asthma showed that the presence of parental asthma, the presence of environmental smoke, smoking during pregnancy, and the prematurity of the child are well-known risk factors for asthma. On the other hand, the existing findings suggest a moderate causal effect for some behaviors and contacts that can be changed during pregnancy (including pregnancy weight gain, maternal use of antibiotics and paracetamol, and maternal stress), birth factors (cesarean delivery), and after birth (severe senile respiratory viral infection, overweight and obesity, household contact with fungi and molds, and city air pollution), which need to be well investigated in future studies [26].

Childhood obesity and asthma

The prevalence of childhood asthma and obesity in developed countries and parts of Asia is increasing, and it has been shown that the prevalence of obesity in children aged 2-15 years from 5% to 13.9%, in children aged 6-11 from 6.5% to 18.8% and for children aged 12-19, it has increased from 5% to 17.4% [27]. Epidemiological data during the last 15 years have shown the existence of a relationship between childhood obesity and asthma [28-31]. Data have shown that obesity is an independent risk factor for asthma, and obese children are more at risk of developing asthma. In a retrospective study for the years 1978-1981, 34,699 children were analyzed. The prevalence of asthma in overweight children was compared with normal and low-weight children (13.2% in overweight children, 10.5% for low-weight, and 11.1% for normal weight) ($0.001 > P$). Even after adjusting for other variables such as gender, other allergic diseases, and the prevalence of asthma in parents, there is still a relationship between weight gain and asthma [32]. Obese children who experience more severe asthma have a weaker response to treatment and show weaker control [33, 34]. These children have more visits to the emergency room and are hospitalized more often [35].

There is a genetic overlap between obesity and asthma genes (q11, q12, P6, and Sq) [36]. In addition to genetic factors, one of the reasons for the increase in obesity in children with asthma is that after the diagnosis of asthma, physical activity and exercise are reduced in these children, which will increase the prevalence of obesity [32]. On the other hand, the reason for the higher prevalence of asthma in them is the decrease in lung function in obese children. Meanwhile, there is evidence of lower airway obstruction with a decreased FEV1/FVC ratio. Decreased ERV and FRC in children with obesity-related asthma may indicate early onset of the effects of obesity on pulmonary function [37]. In any case, Fractional exhaled nitric oxide, one of the measures of allergic inflammation of the airways, was normal or low in these patients, suggesting that a mechanism other than allergic inflammation of the airways could cause obesity-related asthma. With the increasing recognition of obesity as a risk factor for asthma and its effect on lung function, recent studies have identified the pathophysiological mechanisms of the effect of obesity on asthma. These mechanisms include the mechanical load of obesity, especially central obesity, metabolic disorders, and changes in the immune system [38].

Vitamin D and childhood asthma

Calcitriol, with the active form of Vitamin D (1 α , 25-dihydroxy vitamin D₃), is an important regulator for calcium and phosphate absorption in the intestine, calcium reabsorption in the kidney, and calcium absorption in bone. Vitamin D receptor, which belongs to the family of steroid hormone receptors, is expressed in many tissues and cells of the body. Therefore, vitamin D can perform other functions besides its role in calcium-phosphate homeostasis. Of course, despite the identification of the vitamin D receptor in some cells, the function of this vitamin in those cells is still unknown. It has been shown that vitamin D is effective in the differentiation of certain cells and can prevent the proliferation of cancer cells or suppress some cardiovascular and infectious autoimmune diseases [39]. It is estimated that about one billion people worldwide suffer from vitamin D deficiency (less than 75 nmol/L) [40]. Epidemiological data have shown a direct relationship between low levels of vitamin D in early life, and the development of asthma is present later in life. Previous data have shown that vitamin D deficiency increases the risk of lung infections in children with asthma and that vitamin D supplementation reduces lung infections that worsen asthma [41]. Also, studies have shown that vitamin D reduces the consumption of corticosteroids in children with asthma. In vitro studies show that vitamin D directly inhibits airway smooth muscles and increases the bioavailability of corticosteroids in bronchial smooth muscle cells [42]. In a study

conducted by Chinellato *et al.*, children with asthma were evaluated regarding serum vitamin D levels and spirometry findings. The results of their study showed that only 9.4% of children had normal vitamin D levels, and there was a significant positive correlation between vitamin D levels and Forced Vital Capacity percent. Patients with well-controlled asthma had higher vitamin D levels than those without asthma [43]. In a study conducted by Brehm *et al.*, it was seen that serum vitamin D levels are associated with length of hospitalization, anti-inflammatory drugs, and increased airway sensitivity [44].

In a study conducted by Hatami *et al.*, 200 children (3-12 years old) with asthma and 200 healthy children were evaluated. Vitamin D in healthy children was significantly more than in children with asthma [13]. However, their study did not show a significant relationship between vitamin D deficiency and asthma severity. In a systematic review by Riverin *et al.*, eight clinical trials that used vitamin D supplementation in children with asthma were examined. The results of their study showed that vitamin D consumption reduces the risk of asthma exacerbation [45]. In the Bener *et al.* study conducted on children with asthma in Qatar, there was a significant decrease in vitamin D levels in asthmatic children compared to non-asthmatic children. These researchers showed that asthmatic children were significantly less exposed to sunlight and had less physical activity [46]. Alyasin *et al.* showed that the decrease in vitamin D levels substantially increases asthma in children, and even in multivariate analysis after controlling the role of age, gender, and body mass index, the effect of decreasing vitamin D levels on asthma showed a stronger relationship. The level of vitamin D in children with asthma showed a significant relationship with FEV1 and FEV1/FVC indices, but it was not related to the number of eosinophil cells, disease period, days of hospitalization, and unplanned medical visits [47]. A case-control study in Iran showed that the serum concentration of vitamin D in children with asthma was significantly lower than in healthy children. In addition, they showed that total serum IgE concentration was significantly higher in asthmatic children suffering from vitamin D deficiency [48]. Another study in Iran showed that vitamin D deficiency (less than 20 ng/dl) exists in 73.6% of children with asthma. In this study, the risk of developing asthma in children with vitamin D deficiency is estimated to be about 6.3 times that of children with regular vitamin D. However, there was no correlation between the severity of asthma and its control status with vitamin D.

CONCLUSION

Asthma is a chronic inflammatory disease that affects millions of people worldwide. The prevalence of this disease is higher in developed countries. Studies have shown that obesity is an independent risk factor for asthma, and obese children are more at risk of developing asthma. These children experience more severe asthma and have a poorer response to treatment. On the other hand, there is a direct relationship between the reduction of vitamin D levels in early life and the development of asthma in the following years of life. Interestingly, obesity is a common risk factor for both asthma and vitamin D deficiency. Therefore, investigating the interaction between asthma, obesity, and vitamin D deficiency can play an important role in understanding the complex nature of asthma. The results of this study, in addition to providing excellent information about the effect of obesity and vitamin D serum levels on children's asthma, can provide a basis for ecological studies to measure the correlation between children's asthma and the amount of sunlight and dietary and cultural habits in different areas. It is also recommended to understand the issue more deeply, experimental studies to investigate the effect of prescribing vitamin D supplements or using diets rich in vitamin D on the prevention and treatment of asthma in children in different groups, such as infants and school-age children, and to be paid in different ethnicities.

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