# Comorbidities of pediatric asthma: A narrative review

*Review Article*

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## Abstract

***Background:*** Asthma is one of the most common persistent inflammatory respiratory disorders. Comorbidities are relatively common in asthma. The aim of this review study was to find comorbid disorders in children with asthma.

***Methods:*** For the purpose of this review, we searched databases including Scopus, Google scholar, PubMed, SID, Irandoc and up-to-date. Key words for the search included children asthma, comorbidity and pediatric asthma. There were no time limitations for the search. Full text articles in English language were included in this study.

***Results:*** Neuropsychiatric comorbidities were Attention-deficit/hyperactivity disorder (ADHD) (11.5%), oppositional defiant disorder (ODD) (10.7%), separation anxiety disorder (6.1%), social anxiety disorder (3.8%), specific phobias (2.3%), agoraphobia without panic (1.5%), (mild) manic episodes (1.1%), major depressive episodes (MDE) (0.8%), movement (tic) disorder (0.8%) and dysthymia (0.4%). The prevalence of sinusitis was 13% in children with asthma (17). Prevalence of asthma in chronic rhinosinusitis with polyposis (CRSwP) is 26–48%, but the prevalence of CRSwP in asthmatic patients is only 7%. Asthma was prevalent in 25%–35% patients with allergic rhinitis, and rhinitis symptoms were present in 75%–90% of asthmatic patients. Asthma and obstructive sleep apnea (OSA) commonly coexist. Snoring (49.5%), gastro-esophageal reflux disease (GERD) (46.3%), atopic dermatitis (27.3%), allergic sinusitis (20%) and food allergy (10.5%) were common in children with asthma.

***Conclusions:*** Our review has revealed that allergic rhinitis, gastroesophageal reflux, obesity, food allergy, obstructive sleep apnea, allergic conjunctivitis, chronic rhinosinusitis and psychological abnormalities are common comorbidities in children with asthma.

***Keywords:*** Allergic rhinitis, Asthma, Children, Comorbid, Eczema

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## Introduction

Allergic diseases are common worldwide. Asthma is one of the most common non-communicable diseases in children [1]. Asthma is a chronic inflammatory respiratory disease that has significant morbidity and mortality in children. Asthma in children is the most common cause of emergency department visits, absence from school and hospitalization. Most common clinical manifestations of asthma are cough, wheezing and dyspnea, respectively. The prevalence of asthma is varied in different countries [2, 3]. Globally, more than 300 million people are involved. The prevalence of asthma is higher in children [2-4]. Unfortunately, the prevalence of allergic disorders such as asthma is increasing, likely due to the genetic susceptibilities and environmental factors, economic, and



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nutritional factors [5]. The burden of asthma is high on the healthcare systems and families [6].

Etiologies of asthma are not exactly clear as well as the genetic susceptibility and environmental factors contribute in inducing and exacerbating asthma. Various Cytokines and chemokines play a role in the pathophysiology of asthma [7-9]. History and physical examination are the main diagnostic tools of asthma, although the spirometry and peak flow evaluation are useful in diagnosis and follow-up of treatment [2-5]. Managements of asthma include aversion from dangerous factors such as indoor and outdoor allergens, rescue and maintenance treatments with pharmacotherapy and in a few cases, specific allergen immunotherapy [2].

When an asthmatic patient does not respond to treatment, there are multiple questions to be asked; is the drugs' dose or way of consumption correct? Is asthma the correct diagnosis? Are there any risk factors for asthma exacerbation? Finally, are there any comorbid conditions? Sometimes asthma can be seen with other disorders, allergic (allergic rhinitis (AR), eczema, urticaria) and non-allergic (GERD, obesity, anxiety) ones [3, 4]. The comorbidity of asthma and allergic rhinitis is high in Chinese children [10]. Asthma prevalence was 25-35% in patients with AR [11].

The exact mechanism of effect of comorbid disorders on the asthma is not clear for each condition. Awareness of asthma comorbidities and their treatments can help better control asthma. The aim of this study was to review comorbid disorders in childhood asthma.

## Methods

This is a review article. We searched databases including Google scholar, PubMed, SID, Irandoc, Scopus and up-to-date. Key words for the search include: childhood asthma, comorbidity and pediatric asthma. There were no time limitations for the search. Ages up to 19 years were considered "childhood" asthma. Our inclusion criteria were childhood or pediatric asthma, English language, comorbid disorders, original articles and full text articles. All identified abstracts were assessed by two reviewers. Study quality was assessed of randomization, sample size, blinding, control group and statistical analysis.

## Results

More than 500 articles were found at the first search. After evaluating article titles, 400 articles were excluded. Then, we evaluated the remaining 100 articles, of which 60 articles were either not accessible to us in full text or were not written in English, were excluded. Finally, 40 articles met the inclusion criteria and were used in this review.

The research's data are mentioned in table 1.

**Table 1: Prevalence of different disorders and clinical manifestations in childhood asthma**

| Reference | Manifestations |
|---|---|
| **12** | Dysthymia (0.4%), separation anxiety disorder (6.1%), Attention-deficit/hyperactivity disorder(*ADHD)* (11.5%), oppositional defiant disorder (ODD) (10.7%), , social anxiety disorder (3.8%), specific phobias (2.3%), agoraphobia without panic (1.5%),(mild) manic episodes (1.1%), movement (tic) disorder (0.8%) and major depressive episodes (MDE) (0.8%). |
| **13** | Sinusitis (13%) |
| **14** | Chronic rhinosinusitis particular without nasal polyps (CRSsNP) 26–48% but prevalence of CRSwP is 7% |
| **15** | AR 15-40% |
| **16** | AR 36.0%–64.3 % |
| **11** | AR 70-90% |
| **17** | Allergic rhinitis (75%), psychological disturbance (71%), snoring (49.5%), gastro-esophageal reflux disease (GERD) (46.3%), atopic dermatitis (27.3%), allergic sinusitis (20%), and food allergy (10.5%) were common in children with asthma |
| **18** | GERD 41% |
| **19** | AD 28% |
| **20** | AR 72.6% |
| **21** | Snoring 34% |
| **22** | Mental health disorders 13.8-62 % |
| **23** | Behavior problems 35% |
| **24** | Anxiety disorder was 43.2% |
| **25** | Anxiety problems (79%), Attention and behavioral problems (48%), |





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## Discussion:

Chronic disorders such as asthma are public health problems. They have negative effects on the mental health, physical condition and quality of life of patients. Asthma may be associated with other acute or chronic diseases that complicate the problem. Prevalence of comorbidities varies from study to study and geographical areas [17]. Comorbid disorders are important in children with asthma. The mechanisms of effect of comorbid diseases on the asthma are not clear for each situation. In some disorders, comorbid disorders induce inflammatory processes occurring in respiratory and non-respiratory system, whereas other comorbidities' mechanisms are not clear exactly. Gastroesophageal reflux disease, depression in adolescents, smoke exposure, African-American race and rhinosinusitis are risk factors and comorbidities that are especially present in severe asthma and are associated with poorly controlled disease [26]. Poor asthma control, severe persistent asthma and duration of disease more than 3 years were identified as independent asthma-related risk factors for mental health conditions in children [12]. Obesity or being overweight is a risk factor for asthma exacerbation, more frequent admission and even increased steroid resistance. Of course, the relation between obesity and asthma is not clear exactly. Obesity is associated with an increase in inflammatory phenotypes. In addition, obstructive sleep apnea (OSA) is more common in obesity, so that it complicates asthma [27-30].

Chronic rhinosinusitis (CRS), particularly CRS without nasal polyps (CRSsNP) was significantly related to childhood asthma [31]. Sinusitis is an important comorbid disorder in children with asthma [13, 14]. Coexistence of AR and CRS with asthma is correlated with poorer asthma control, more exacerbations, emergency visits and decreased quality of life [32].

Gastro-Esophageal Reflux (GER) is more common in severe asthma and induces asthma exacerbation due to Micro-aspirations, acid stimulation of the esophagus and vagus nerve stimulation. However, it is recommended to treat GER in severe asthmatic patients [33]. Sinusitis and GER are associated with children asthma exacerbation [34].

Food allergy might be comorbid with asthma, hospital admission, daytime symptoms, asthma persistent and severe asthma exacerbation are more common in children with food allergy [35]. The prevalence of food allergy in childhood asthma was 20.7% and 32.7% in French and Chinese children, respectively [36].

Asthma and Allergic rhinitis occur concomitantly in most children. The AR is a predicting factor to induce asthma in children. The AR is a risk factor for uncontrolled or poor controlled asthma [15-16, 37-38]. Some studies reported other comorbidities of childhood asthma such as vasomotor rhinitis, allergic rhinitis, sinusitis, conjunctivitis, pneumonia, eosinophilic esophagitis, atopic dermatitis, obesity, gastro-esophageal reflux, vocal cord dysfunction, food allergy, depressive disorders and cardiovascular disease [33, 35, 17, 39-41].

Hay fever or respiratory allergies, eczema or skin allergies, sinusitis, food or digestive allergies, difficulty with emotions, concentration, behavior, or getting along and fatigue or lack of energy ≥ 3 days are more common in children asthma. Asthma attacks, emergency department visits and longer periods of medication administration were more common in patients with comorbidities [40]. The GERD, AR, AD and snoring were common in childhood asthma [18-21].

Prevalence of mental health disorders was higher in allergic asthma [22-24, 42]. Comorbidity of diseases is important when the disease itself is persistent. One study showed children with comorbid rhinitis, eczema and asthma at 4 years of age had an increased risk of having sustained comorbidities at 8 years of age [43].

Asthma and obstructive sleep apnea (OSA) commonly coexist; they have significant bidirectional interactions that cause difficulty in controlling both OSA and asthma [30]. The GERD, obesity and chronic sinusitis are an important comorbid disorders in children with asthma. Obesity leads to mechanical disadvantage of the diaphragm, low-grade inflammatory process and increased asthma manifestations [44]. Fungal sensitization (Alternaria, Aspergillus, Penicillium, and Cladosporium) has an impact on asthma severity. They are important comorbidities of asthma [44, 45]. Chronic sinusitis affects asthma by means of infection, allergic inflammation and anatomic processes [44]. Asthma and AR are considered as "one way, one disease", and the inflammatory process is the same in both [44]. Comorbidity of AR, GER, CRS, OSA, food allergy, obesity, being overweight,



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neuropsychiatric issues and eczema should be considered in children with asthma and treated when diagnosed. However, some studies could not confirm these comorbidities [35, 46-47].

Psychological issues including exhaustion, stress, anxiety and depression were higher in allergic asthma and increased atopy and asthma manifestations due to the inflammatory and non-inflammatory mechanisms [42]. In our review, association between GER, CRS, and psychological abnormality has been reported in children with asthma [26-27, 33-35, 18, 22]. Various studies have stated that these disorders affect asthma exacerbations and make it more difficult to control. Most of these research reported improvement of asthma symptoms after treatment of comorbidities [33, 35, 44].

Obesity, overweight and OSA are confirmed comorbidities of childhood asthma. In many instance, treatment of these issues has good effects on asthma manifestation and quality of life [27-30, 35].

Infections of sinus especially chronic rhinosinusitis with (CRSwNP) or without nasal polyposis (CRSsNP) are a significant comorbidity of childhood asthma. We should consider sinus infection in anyone with asthma especially in children with poor or uncontrolled asthma. Improvement in asthma manifestations were seen after treatment of sinus infection [26, 13-14, 31-32, 34].

Food allergy is another common allergic disorder associated with childhood asthma. Children with asthma who have food allergies are at risk for exacerbation of asthma and anaphylaxis. Diagnosis of food allergy is mainly based on patient history. The best treatment of food allergy is to avoid triggering substances [35-36].

The AR is the most common allergic disease in the world. This review revealed that the AR is an important comorbidity in childhood asthma. Treatment of AR leads to improvement of clinical manifestations and quality of life of children with asthma [10-11, 15-16, 20, 37-38]. Early treatment and interventions to decrease AR symptoms can reduce or stop development of asthma. Allergen immunotherapy in refractory symptoms to certain inhalants (dust, grass, tree, and ragweed) may also be beneficial in the management of AR and possibly asthma [44].

The AD is another common allergic disorder especially in early years of life that is a major burden on the quality of life and asthma manifestations. Diagnosis of AD is mainly based on clinical manifestations and AD criteria. Comorbidity of AD and childhood asthma is proven in many studies. Early diagnosis and treatment of AD improve asthma symptoms [33, 35, 39-41, 19]. A few articles have studied snoring in children with asthma and confirmed that the snoring is a comorbidity of childhood asthma. They have observed improved asthma symptoms after treatment of snoring [17, 21].

Treatment of GERD demonstrated improvement in symptoms and quality of life of children with asthma [44]. Weight loss in obese children leads to improvement of clinical symptoms and quality of life of children with asthma [44]. Treatment of OSA may improve asthma symptoms [30, 44]. Finally, more studies are needed to elucidate the mechanisms, pathways, and effective interventions of comorbid disorders. It is suggested that the meta-analysis paper should be written in the future to confirm the relationship between childhood asthma and other comorbid disorders.

In conclusion, our review revealed comorbidity of AR, GER, Obesity, Food allergy, OSA, allergic conjunctivitis, CRS and psychological abnormality in children with asthma. Early detection and intervention of comorbid disorders or condition in children with asthma are necessary. Some of these comorbid conditions subside with well controlled asthma. Good control of comorbid conditions in children with asthma can be effective in treatment of asthma.

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