

# Epidemiologic Evidence for Association between Allergic Rhinitis and Bronchial Asthma

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## Abstract

Allergic rhinitis and asthma are often found together, and the characteristics of the two diseases are quite similar. Many epidemiologic studies have provided evidence to support the theory that allergic or perennial rhinitis often precedes the development of asthma in the same patient and that the development of asthma is seen much more frequently in people with both seasonal and perennial rhinitis than in people with either condition alone. Perennial rhinitis has been associated with increase in non-specific bronchial hyper-responsiveness. Rhinitis and asthma were found to be comorbidities regardless of atopic state. Several studies have demonstrated the frequent coexistence of allergic rhinitis and asthma, that allergic rhinitis usually precedes asthma, and that allergic rhinitis is a risk factor for asthma. Further, many studies have suggested that early age of onset of atopy may be an important predictive factor of respiratory symptom. However, not all patients with rhinitis present with asthma and there are some differences between the two conditions.

**Keywords:** Allergic rhinitis, Asthma, Comorbidity

## Introduction

The general pathogenic view of respiratory allergy has deeply changed and evolved during the last two decades. Epidemiologic studies and clinical observation have pointed toward a strong link between allergic rhinitis and asthma. Immunological observation and therapeutic outcomes have further added evidences to the above. Furthermore, an increasing number of evidences have accumulated about (i) the frequent co-existence of rhinitis and asthma; (ii) the possible role of upper respiratory infection in asthma exacerbation; (iii) the presence of rhinitis as a risk factor for developing asthma<sup>1</sup> and the importance of paranasal sinus infection. These observations taken together lead to the definition of allergic rhinobronchitis or united airway disease (UAD). Rhinitis is more common than asthma, especially in adolescents and young adults. Like asthma, its prevalence has increased,<sup>1,2</sup> and it was eventually unknown before the industrial revolution. Pollution and dietary changes have been implicated in this increased incidence.<sup>3</sup>

## Relationship between Rhinitis and Asthma

Epidemiologic studies consistently demonstrate the co-existence of rhinitis and asthma in the same patient. In one study, 98.9% of all allergic asthmatics had rhinosinusitis whereas the prevalence of rhinosinusitis in non-allergic asthmatic subjects was 78.4%.<sup>4</sup> The authors concluded that almost every patient with allergic bronchial asthma had chronic rhinitis. They stated that these findings were consistent with the concept that allergic asthma shall be viewed as a total airway disease and should be treated accordingly.

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In another study, authors found that rhinitis occurs in 78% of patients with allergic asthma and the focus is often on asthma, so that rhinitis may be neglected. In patients with both conditions, onset may be with either.<sup>5</sup> In a study in France, 20,000 households (of which 16,786, i.e., 84% responded) were screened for symptoms of allergic rhinitis (defined as patient having at least two rhinitis symptoms for six months of the year, without any period of remission).<sup>6</sup> The estimated point prevalence of perennial rhinitis was 4.1%. 13.4% patients with perennial rhinitis also had history of asthma in comparison to those without perennial rhinitis (3.8%; odds ratio [OR]=3.26;  $P \leq 0.001$ ).

In epidemiological studies, asthma is present in 20–50% of patients with rhinitis<sup>7-9</sup> and rhinitis was found to occur in up to 80% of patients with asthma.<sup>7</sup> In a group of 1245 subjects with documented history of asthma, 6% had perennial allergic rhinitis, 24% had seasonal allergic rhinitis only and 22% had both seasonal and perennial allergic rhinitis.<sup>7</sup> Leynaert et al.<sup>7</sup> analyzed data from 34 countries which participated in the European Community Respiratory Health Survey (ECRHS) by taking random sample of 20–44 years old subjects. Asthma was seen in 0.8% of participants without rhinitis, in 6% of participants with seasonal rhinitis only, in 9% of participants with perennial rhinitis only, and in 18% of participants with both seasonal and perennial rhinitis. After adjusting for age, sex, family history of asthma, smoking habit, geographical area, and season at the time of examination, asthma was found to be strongly associated with rhinitis, not only among atopic subjects [OR=8.1, 95% confidence interval (CI)=5.4–12.1%] but also among non-atopic subjects [OR, 11.6; 95% CI=6.2–21.9%]. Moreover, the association remained strong when the analysis was confined to non-atopic subjects with IgE level of 80 KU/L or less.

In the Copenhagen Allergy Study,<sup>10</sup> frequency of rhinitis and asthma related to exposure to pollens, animal dander and mites has been seen. 41% of patients with pollen-related rhinitis also had pollen-related asthma whereas it was 0.1% in those without pollen-related rhinitis.

For subjects with animal dander allergy, the values were 52 and 0.2% and for subjects with mite-related allergy, the values were 41 and 1% respectively. Therefore, in all cases >99% of subjects with allergic asthma also had allergic rhinitis. In a study in Delhi, India, the investigator found allergic rhinitis cases to be around 10% and asthma to be around 1% in the population during 1964.<sup>11</sup> Later studies have reported that in India around 20 to 30% of the population has allergic rhinitis and around 15% develop asthma.<sup>12,13</sup>

Aspirin and other non-steroidal anti-inflammatory drugs also induce rhinitis and asthma in certain individuals. In a population-based study using random samples, aspirin intolerance was found to be more frequent among subjects with allergic rhinitis (8.6%) than those without allergic rhinitis (0.3%;  $P < 0.01$ ).<sup>14</sup> Occupational asthma is a well-known entity. But symptoms of rhinitis are also associated with occupational asthma. In one study, 92% of participants with occupational asthma also experienced symptoms of rhinitis.<sup>15</sup> Allergic rhinitis and asthma symptoms can be seen in bakers<sup>16-18</sup> and among people exposed to wood dust.<sup>19-21</sup>

### Rhinitis and Non-specific Bronchial Hyper-responsiveness

Patients with allergic rhinitis, but with no respiratory symptoms, have increased bronchial reactivity to methacholine,<sup>22,23</sup> although usually less so than asthmatics. Patients with seasonal allergic rhinitis show features of seasonal bronchoconstriction that is not associated with clinical bronchospasm.<sup>24</sup> Patients who are allergic to grass or birch pollen, seasonal increase of carbachol, histamine or methacholine showed bronchial hyper-responsiveness and exercise-induced bronchoconstriction.<sup>25,26</sup> In seasonal allergic rhinitis, there is slight increase in functional residual capacity and the volume of trapped gas during the hay fever season,<sup>27</sup> perhaps reflecting sub-clinical bronchospasm. A mild degree of beta adrenergic hyper-responsiveness in patients with allergic rhinitis could cause a readily reversible increase in resting bronchial tone without asthmatic symptoms. It is frequently possible to obtain bronchoconstriction in patients with allergic rhinitis when allergic challenge is given. However, late asthmatic reaction in response to allergic challenge is much more frequent in asthmatics than in rhinitis patients.<sup>28</sup> Asthma is characterized by hyper-reactive airways and epidemiologic studies have established the presence of bronchial hyper-responsiveness in patients with allergic rhinitis but no symptoms of clinical asthma.<sup>29-31</sup> In a more recent study, investigators found that the seasonal rhinitis patients have a reasonably high incidence of non-specific hyper-responsiveness, up to 32% out of season, and up to 48% during the season.<sup>32</sup> Perennial rhinitis patients who are allergic to dust mite or animal dander have the same level of hyper-responsiveness as patients of seasonal allergic rhinitis during the season, i.e., 48%.

### Rhinitis Is a Risk Factor for Asthma

Prospective studies have indicated that rhinitis may be a significant risk factor for subsequent development of

bronchial asthma. One study, done over a stretch of 23 years reported a three-fold increase in the incidence of asthma in patients who previously had allergic rhinitis (without apparent asthma) compared with those who did not had rhinitis (10.5% compared with 3.6%).<sup>33</sup> In another study, the investigators showed that clinical, epidemiological and pathophysiological studies suggest a strong functional and immunological relationship between the nose and the bronchi. Nasal stimulation can induce bronchoconstriction by a proposed rhinobronchial reflex and inflammatory mediators originating from nose can trigger bronchial inflammation. Bronchial provocation in sensitized subjects results in nasal inflammation through systemic circulation.<sup>34</sup> Allergic rhinitis and extrinsic (or allergic) asthma are part of one atopic (i.e., IgE mediated) condition.<sup>35,36</sup> Asthma is seen more commonly in patients with perennial rhinitis. In one study, it was shown that the presence of physician-diagnosed allergic rhinitis in infancy was associated with a doubling of the risk of developing asthma by 11 years of age.<sup>37</sup> In another longitudinal study, the degree to which rhinitis was a risk factor for asthma was studied<sup>38</sup> and even after adjusting for years of follow up, age, sex, atopic status, smoking, presence of COPD, the magnitude of the association was still significantly high (adjusted OR, 3.21%; 95%CI, 2.19–4.71).

The effect of allergic rhinitis was seen in 154 children (aged 3–17) with the help of a detailed questionnaire which was given to them 8–11 years later.<sup>39</sup> Asthma or wheezing had developed in 19% of subjects and was seen more commonly ( $P < 0.01$ ) in those subjects with perennial allergic rhinitis (34%), than among those with seasonal allergic rhinitis (12.7%).

## Conclusion

Epidemiologic studies in general population have provided evidence that allergic rhinitis and asthma are strongly associated with each other. But, whether allergic rhinitis represents an earlier clinical manifestation of asthma in atopic subjects or if allergic rhinitis itself is a causative factor for asthma is still a matter of debate. More longitudinal studies examining the relationship between these conditions will further provide an important insight into these two comorbid conditions.

**Conflict of Interest:** None

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