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PREVALENCE OF ALLERGIC RHINITIS AND RELATED DISEASES

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SUMMARY – The prevalence of allergic rhinitis and related diseases varies from country to country and even within particular countries. The prevalence is difficult to precisely estimate. There is ample evidence showing the rate of allergic rhinitis to be on an increase worldwide over the last decades, especially so in industrialized countries. The increasing prevalence remains largely unexplained merely by lifestyle changes and environmental pollution. Great effort has therefore been invested to identify the possible impacts, which may hopefully help control this 'allergic march'.

Key words: *Rhinitis – allergic, epidemiology; Prevalence; Respiratory hypersensitivity – epidemiology; Asthma – epidemiology*

Introduction

It is quite difficult to reliably estimate the prevalence of allergic rhinitis. The prevalence estimates range from as low as 4% to over 40%. Epidemiology studies suggest the prevalence of allergic rhinitis to be on a significant increase all over the world[1-4]. The cause of this increase remains unknown, however, the contributing factors may include higher concentrations of airborne pollution, rising dust mite populations, impact of living conditions, hygiene, family size, vaccinations, infections and use of antibiotics, dietary factors, and a trend towards sedentary lifestyle. On the other hand, an increase in the physician-diagnosed allergies is quite likely because of changes in diagnostic patterns as well as higher public awareness of allergic diseases.

Allergic rhinitis is the most common allergic disorder of the respiratory tract. Some 20%-25% of the population are affected with allergic rhinitis, which makes it by far the most common allergic disease in the world. The symptoms of allergic rhinitis commonly begin in childhood and/or adolescence, and continue into adulthood. In general, allergic rhinitis symptoms slowly improve, and the skin-test reactivity tends to subside with increasing age. There is a significant trend of symptom improvement with younger age at onset of allergic rhinitis. With better understanding of the complicated etiology of allergic rhinitis it may be possible to reverse the trend of its prevalence increase. However, it is widely accepted that some essential questions concerning allergic rhinitis and other allergic disorders remain unanswered because, essentially, there have not been enough epidemiologic studies, especially in developing countries. Therefore, thorough analyses of epidemiologic data to determine the possible multifactorial interactions are a crucial step to improve the prevention and treatment of allergic rhinitis and other allergic disorders[5,6].

The aim of this review is to summarize the latest literature reports, spanning the last five years, and to dynamically determine the prevalence of allergic rhinitis and related disorders from different aspects.

The Diagnosis of Allergic Rhinitis

The evaluation of rhinitis should include thorough patient history, careful physical examination, and appropriate diagnostic tests including skin prick tests and serum assays for allergen-specific IgE. Seasonal allergic rhin-

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itis or intermittent allergic rhinitis is readily distinguished from perennial or persistent allergic rhinitis by history, and confirmed by positive skin tests to causative aeroallergens. It is important to differentiate seasonal rhinitis from non-allergic disorders including infectious rhinitis, structural or anatomic problems such as nasal polyps or septum deviation, rhinitis medicamentosa (due to overuse of topical vasoconstrictors), hormonal rhinopathy (e.g., pregnancy, hypothyroidism), nonallergic vasomotor rhinopathy, non-allergic inflammatory rhinitis with eosinophils (NARES), or rarely, a neoplasm.

The International Study of Asthma and Allergies in Childhood (ISAAC)

Geographical distribution of allergic rhinitis

The prevalence of allergic rhinitis largely varies from continent to continent, from country to country, and even from region to region. There are many studies today which deal with epidemiologic characteristics of allergic rhinitis and related disorders. The International Study of Asthma and Allergies in Childhood (ISAAC) is regarded as the one of highest reputation. It was designed to maximize the value of epidemiologic research into asthma and allergic diseases in childhood, establishing a standardized methodology and facilitating collaboration and comparison between several countries. Since the 1990s, the ISAAC group have carried out a similar survey in 56 countries including 721,601 adolescents[7]. Important to note, many of these studies dealing with the prevalence of allergic rhinitis were performed using mailed or telephone and video questionnaires, and could therefore provide just a rough estimate of the incidence and prevalence of the disorder. To investigate the 'definite' prevalence of allergic rhinitis, several attempts have been made based on a combination of the symptoms reported (questionnaire) and immunologic assays[8,9].

In the United States, Canada and Latin America, for example, the prevalence of allergic rhinitis varies from 6.6% to 24.5%[10-12]. The rate of physician-diagnosed allergic rhinitis (seasonal plus perennial) was 14.2%. In Europe, an increase in the prevalence of allergic rhinitis is frequently reported from most countries. The prevalence of allergic rhinitis is intermediate, ranging from 8.6% to 22.5%[13-19]. Only Malta has reported a rate as high as 32.2%. A large number of studies into the prevalence of allergic rhinitis were conducted in the past ten years in Asian countries[20-25]. Generally speaking, the prevalence is low in Korea, China and Singapore[20,22,25], whereas in Thailand many children suffer from the symptoms of rhinitis. In 1998, Vichyanond *et al.*[24] administered standardized ISAAC Phase One questionnaire in children from Bangkok, Thailand, and the results were compared with the last survey from 1990. It is reported that the prevalence of wheezing has increased fourfold, and of allergic rhinitis nearly threefold. The prevalence of allergic rhinitis is quite high in Africa. Recent studies have reported it to be 32.4% and 52.1% in Kenya and Nigeria, respectively[26,27].

The prevalence of allergic rhinitis in Oceania is intermediate[28]. New Zealand was one of the first to explore the ISAAC program. In ISAAC Phase One, they performed studies of the prevalence of allergic rhinitis in 6-7 and 13-14 year-old groups during the 1991-1992 period, which revealed the prevalence of allergic rhinitis and asthma to be 10.5% and 23.5% in the former, and 10.5% and 22.9% in the latter group of study subjects. The ISAAC Phase Two started in 1998, and was designed to investigate the relative importance of interest that had arisen from Phase One results. The ISAAC Phase Three will examine variations in time trends of asthma, allergic rhinoconjunctivitis and atopic eczema around the world, and assess the relationship between the patterns found and environmental data (see http://isaac.auckland.ac.nz/).

Role of Age and Gender in the Prevalence of Allergic Rhinitis

Allergic rhinitis often occurs in childhood, sometimes even in infants. The incidence of this disorder is decreasing with age, and is significantly lower in people over 65[12]. Kulig *et al.*[29] investigated the longitudinal development of sensitization and symptoms of seasonal allergic rhinitis in 587 children from birth to seventh birthday, and found that up to 7 years of age seasonal allergic rhinitis had developed in 15% of the children. The incidence and prevalence of symptoms and sensitization were low during early childhood (<2%), and increased steadily with age.

As part of ISAAC, prevalence surveys were conducted in representative samples of school children from locations in Europe, Asia, Africa, Australia, and North and South America. The studies included 257,800 children aged 6-7 from 91 centers in 38 countries, and 463,801 children aged 13-14 from 155 centers in 56 countries[7]. The prevalence of rhinitis with itchy-watery eyes (rhinoconjunctivitis) in the past year varied across centers from 0.8% to 14.9% in the 6- to 7-year-old children, and from 1.4% to 39.7% in the 13- to 14-year-old children. The lowest prevalence of

rhinoconjunctivitis was recorded in parts of Eastern Europe, South and Central Asia, and a high prevalence at centers in several regions.

In 1999, Simola *et al.*[30] analyzed 107 rhinitis patients from Finland, who had formerly been investigated. The patients were now reinterviewed and their current allergy was reassessed after a 23-year follow-up to relate the possible changes in reactivity to aging, duration of rhinitis, and changes in severity of rhinitis symptoms. They state that rhinitis symptoms tend to become milder and the allergic skin reactivity usually decreases in the long run, but these changes may occur independently of each other. In this study, the change in the rhinitis symptom severity seems not to be related to the decrease in skin test reactivity.

Despite the evidence supporting the contention that allergic potential declines with aging[31], recent findings indicate that older adults commonly seek care from an allergy/immunology physician. A survey of members and fellows of the American College of Allergy, Asthma and Immunology has revealed that approximately one in every five patients cared for by allergy/immunology practitioners is aged 55 or older (and 6% were aged ≤70). The distribution of diagnoses indicated by survey respondents was remarkably similar across three patient age groups, suggesting that older adult allergy/immunology patients exhibit symptoms that reflect conditions similar to other adults who seek out and/or continue allergy/immunology care. These findings imply that older adults will continue seeking care for conditions within this specialty, allergic rhinitis in particular. This observation is important, as allergic rhinitis in older adults may be trivialized and undertreated, leading to unnecessary impairment of the quality of life, reduced work productivity, predisposing sufferers to secondary complications, including sinusitis and sleep disturbances, and a greater likelihood of poorly controlled symptoms in those with concomitant asthma[32]. Given this, proper recognition and management of allergic rhinitis in older adults have become increasingly important.

In childhood, boys with allergic rhinitis outnumber girls, however, in general equal numbers are affected during adulthood.

Allergic Rhinitis and Atopic Diseases

Numerous studies have provided evidence in support that asthma is an atopic disease. Whether allergic rhinitis is an atopic disease is still unknown. Matsuoka *et al.*[33] investigated the influence of parental allergy on the manifestations and course of allergic disease in school children aged 6 and 9 by use of a questionnaire completed by their parents in a cross-sectional survey conducted in Tokushima, Japan. They found the risk of atopic dermatitis to be particularly high in children whose parents had atopic dermatitis. Children with a parental history of asthma also had a high risk of that disorder. However, the risk of allergic rhinitis did not differ between the children with a parental history of allergic rhinitis and those with a parental history of asthma and atopic dermatitis. Greisner *et al.*[34] investigated the coexistence of asthma and allergic rhinitis by having completed a 23-year follow-up in 738 former Brown University students who were diagnosed with these diseases either before or after their freshman year. This study demonstrated the frequent coexistence of asthma and allergic rhinitis. Among asthmatics, allergic rhinitis occurred in 85.7%, while only 14.3% of asthmatics were free from this comorbidity. Among individuals with allergic rhinitis, asthma occurred in 21.3%. Also, allergic rhinitis often precedes or occurs simultaneously with asthma. A recent study by Leynaert *et al.*[35] examining the results from 34 centers participating in the European Community Respiratory Health Survey has shown asthma to be strongly associated with rhinitis in both atopic and nonatopic subjects. Allergic rhinitis is considered an independent risk factor for asthma.

Risk Factors for Allergic Rhinitis

Generally, there are three groups of risk factors: outdoor factors, indoor factors, and personal factors. Concerning outdoor factors, the environment, ozone and traffic exposure are important factors. Some have also suggested that pollution may have a role, however, there still is much controversy about this issue. Some also suggest that allergic rhinitis was much less prevalent before the industrial revolution because the levels of air pollutants were lower[12]. Following the industrialization, diverse environmental exposure profiles exist in the Americas because of the widely different climates, ambient pollutants, and bioaereosols in these continents. Bascom[36] reviewed selected studies from the Americas and supports the broad hypothesis that environmental factors contribute to respiratory hypersensitivity. However, recent studies suggest that this probably is not the case. In one study comparing the rate of allergic rhinitis in two German cities no significant difference was found despite the significantly higher levels of pollution in the eastern city.

The prevalence of asthma and other allergies in children in Urumqi and Beijing was compared with that in

Hong Kong. A total of 7,754 primary school students were randomly selected to participate in the study. Data were collected in 1995-1996 using the ISAAC protocol for 6- and 7-year-olds. Urumqi, Beijing and Hong Kong represent communities at different stages of westernization and the results from these three cities reflect the worldwide trend of an increasing prevalence of allergies along with westernization. These three cities could assist in identifying the risk factors involved in the increase in asthma, allergic rhinitis and eczema.

Concerning the impact of indoor factors, it is partially attributable to the limited ventilation in most modern housing facilities that are characterized by increased cavity wall insulation to save energy, synthetic furniture, etc. The frequent presence of pets and high levels of domestic pollutants are considered to be the causal factors in the development of respiratory symptoms and sensitization. Tobacco smoke is an important component causing the development of allergic diseases. Three conditions have to be considered: maternal smoking during pregnancy, passive smoke exposure, and active smoking. Annesi-Maesano *et al.*[37] investigated the involvement in allergic as well as in nonallergic upper airway disease of two risk factors, i.e. immediate hypersensitivity and tobacco smoking, in a cohort study of 191 men seen 5 years apart. For seasonal allergic rhinitis, the skin prick test positivity increased significantly over the 5-year period, total IgE level increased but never significantly, and seasonal allergic rhinitis was more associated with previous smoking.

Personal factors such as family size, socioeconomic status, nutrition, and infections can have an effect on allergic sensitization.

Allergic rhinitis and asthma are linked by epidemiologic, histologic, physiologic and immunopathologic characteristics, and by a common therapeutic approach. Epidemiologically, the disorders often coexist. Histologically, the upper and lower airways are lined and linked by respiratory epithelium. Physiologically, the nasobronchial reflex may link them. Pathologically, they are linked by similar early- and late-phase allergic responses throughout the airways, and by the systemic immune response to airborne allergens. Uncontrolled allergic rhinitis may be associated with worsening of the coexisting asthma, and optimal treatment of allergic rhinitis may improve the coexisting asthma. The key to managing both disorders is the prevention and relief of chronic allergic inflammation in both upper and lower airways. The similarities between allergic rhinitis and asthma outweigh the differences. To facilitate appropriate recognition and treatment of the common inflammatory process throughout the airways, consideration should be given to introducing a new term, 'allergic rhinobronchitis'[39].

Several recent epidemiologic studies in the general population have provided evidence for strong association of asthma development with a previous history of either allergic or perennial rhinitis[40]. Additional links between asthma and rhinitis include a description of increased aspirin intolerance in both disorders and the observation that most subjects with occupational asthma experience rhinitis. Furthermore, the likelihood of the development of asthma is much higher in individuals with both perennial and seasonal rhinitis than in those with either condition alone. Asthma and rhinitis were found to be comorbidities regardless of atopic state, and perennial rhinitis has been associated with an increase in nonspecific bronchial hyperresponsiveness. Several studies have identified rhinitis as a risk factor for asthma, with the prevalence of allergic rhinitis in asthmatic patients being 80% to 90%. These and other studies demonstrate that the coexistence of asthma and allergic rhinitis is frequent, that allergic rhinitis usually precedes asthma, and that allergic rhinitis is a risk factor for asthma[41]. Finally, studies that investigated age at onset of atopy as a confounding factor for the development of asthma and allergic rhinitis have suggested that early age atopy may be an important predictive factor for respiratory symptoms that continue into late childhood. The study by Plavec *et al.*[42], however, has shown that there is not yet sufficient evidence for a straightforward link between nasal and bronchial hyperreactivity in nonasthmatic pollinosis rhinitis subjects, that is no straightforward evidence for the link between allergic rhinitis and asthma.

Comorbidity of Allergy with Other Disorders

Atopic dermatitis is a common disease that appears to be increasing in frequency during recent decades. It is one of the most common atopic disorders related to allergic rhinitis, except for asthma. Tay *et al.*[43] investigated young population, aged 7-21, over a one-year period and found that 69.3% suffered from a 'mixed' type, with 34.3% having allergic rhinitis, 9.5% asthma, and 25.5% both asthma and allergic rhinitis.

Porter *et al.*[44] report that allergic rhinitis (80%) and sinusitis (54%) were the most commonly observed sinonasal symptoms in HIV-infected patients. Moraes *et al.*[45] performed a prospective study in patients with recurrent vaginal candidiasis and found 71% of them to have allergic rhinitis. There was a family history of allergies in 61% of women. These data indicate that recurrent vaginal can-

didiasis is statistically significantly associated with perennial allergic rhinitis and that many women with recurrent vaginal candidiasis tend to be atopic.

Fireman[46] studied epidemiologic data from the literature in the USA and found 40%-50% of children older than 3 years with chronic otitis media to have confirmed allergic rhinitis. He suggests that antiallergic therapies may be used to augment symptom resolution and therapeutic response in such cases.

Conclusion

Allergic rhinitis is the most common allergic disorder of the respiratory tract. Some 20%-25% of the population are affected by allergic rhinitis, making it by far most common allergic disorder in the world. There is ample evidence that the prevalence of allergic rhinitis has been rising worldwide in recent decades. The cause of the disease remains unknown, and changes in the lifestyle and environment appear to provide inadequate explanation. Much effort has been invested to elucidate this phenomenon. Better understanding of the epidemiologic characteristics of allergic rhinitis will help us stop the allergic march.

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Sažetak

UČESTALOST ALERGIJSKOG RINITISA I S NJIM POVEZANIH BOLESTI

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Učestalost alergijskog rinitisa i s njim povezanih bolesti znatno se razlikuje među pojedinim zemljama, pa čak i među pojedinim regijama unutar iste zemlje. Nije jednostavno točno procijeniti rasprostranjenost alergijskog rinitisa. Postoje čvrsti dokazi o porastu učestalosti alergijskog rinitisa u svijetu posljednjih desetljeća, poglavito u razvijenim zemljama. Tendencija rasta ove učestalosti još uvijek nije dovoljno razjašnjena uz dva trenutno najizraženija čimbenika tog porasta, a to su zapadnjački način života i onečišćenje okoliša. Ulažu se znatna sredstva i napori u istraživanje porasta alergija u svijetu, pa postoji nada da će ti napori pomoći u zaustavljanju 'epidemije' alergija.

Ključne riječi: *Rinitis – alergijski, epidemiologija; Učestalost; Respiracijska preosjetljivost – epidemiologija; Astma – epidemiologija*