ABSTRACT

Allergic rhinitis (AR) is a critical public health, medical and economic problem in China. AR is also an important risk factor which will cause many diseases or disorders, especially in children. The trend of AR incidence is still on the rise in recent years and has had a significant effect on the general public. This significant increase is alarming, which highlights an urgent need for better understanding of the prevalence status and characteristics, sensitization patterns, and the associated risk factors of AR in order to improve treatment and develop effective prevention strategies.

Keywords: Allergic rhinitis; prevalence; China; asthma; allergen

INTRODUCTION

Allergic rhinitis (AR) is a hypersensitivity reaction caused when inhaled particles contact the nasal mucosa and induce an immunoglobulin E (IgE)-mediated inflammatory response, which is often accompanied by ocular pruritus, redness and/or lacrimation. AR is one of the most common chronic diseases in all age groups. Epidemiological studies have revealed that the prevalence of AR has increased progressively in more developed countries, and currently affects 10%–40% of adults and 2%–25% of children worldwide. Likewise, with rapid economic development and more Westernized lifestyles in terms of urbanization and dietary habits of developing nations, a rising trend of AR has also been observed in recent decades, with a widely varying prevalence particularly in China. Furthermore, the potential effect of the considerable increases in air pollutant levels and climate change can also not be ignored with regard to the increased prevalence of respiratory disorders. We have reviewed the prevalence of AR, the incidence of comorbid allergic diseases, and trends and patterns of sensitizing allergens of AR in adults and children in China in 2014. The aim of this current review was to elaborate changing features of the prevalence of AR in adults as well as children in China and to assess the possible risk factors contributing to such variations according to publications between March 2013 and June 2018 using PubMed. Citations for articles reporting the prevalence of AR in China were identified using allergic rhinitis as the primary search term in association with China, prevalence/incidence, comorbid allergic disease, asthma and sensitizing allergens as the secondary search terms.
CHANGING PREVALENCE OF AR IN ADULTS

It has been widely recognized that the prevalence of AR in many countries has markedly increased over time.\textsuperscript{7,10,12} A nationwide population-based study assessed self-reported AR using validated questionnaire-based telephone interviews in over 38,000 adult subjects from 11 major cities across China between September 2004 and May 2005 demonstrated that the prevalence of AR was 11.1% (8.7%–24.1%).\textsuperscript{13} Recently, a total of 47,216 telephone interviews were conducted and the standardized prevalence of adult AR in 18 major cities was 17.6% in 2011 (9.8%–23%),\textsuperscript{9} suggesting the obviously increasing trend and the instability of the prevalence of AR in China. Comparison of age-adjusted prevalence of self-reported AR between 2005 and 2011 indicated that the standardized prevalence of AR had significantly increased in 8 of 11 cities ($P < 0.01$ for Guangzhou and $P < 0.001$ for Beijing, Changchun, Shenyang, Shanghai, Nanjing, Hangzhou and Xi’an), decreased in 1 city (Urumqi, $P < 0.01$), and not significantly altered in 2 cities (Wuhan and Changsha) as summarized in Fig. 1.\textsuperscript{9}

![Fig. 1. Comparisons of the prevalence of self-reported AR in 11 major cities in China between 2005 and 2011 according to the study by Wang et al.\textsuperscript{14} AR, allergic rhinitis.](https://e-aair.org)
Furthermore, a total of 6,043 subjects from the grasslands of Northern China completed a study recently and demonstrated a proportion of 32.4% epidemiologic AR and 18.5% physician-diagnosed pollen-induced AR (PiAR).\textsuperscript{14}

These nationwide population studies based on telephone interviews revealed the most commonly reported symptoms of AR were sneezing (81.8%), rhinorrhea (60.2%), blocked nose (54.9%), nasal itching (49.6%), ocular itching (42.9%), pharyngolaryngeal symptoms (35.1%), watery eyes (34.5%), ocular swelling (19.1%) and ocular pain (17.6%).\textsuperscript{9} Moreover, another survey performed in Guangzhou via face-to-face interviews demonstrated that the majority (69%) of the patients indicated that the most severe symptom episodes occurred in the early morning and that the symptom severity gradually reduced over time until midnight. Of the total patients, 287 (49%) patients complained that the symptom severity differed according to the season and that the symptom became more severe in most of the patients (75%) in winter (November, December, January and February).\textsuperscript{15}

The prevalence rate of AR between the urban and rural areas were not always consistent. One cross-sectional investigation performed in 9,899 citizens in Guangzhou from December 2009 to March 2010 using a stratified multistage cluster-sampling method through face-to-face interviews, presented a significantly higher prevalence in the urban area (8.32%) compared with the rural area (3.43%).\textsuperscript{15} Another survey via face-to-face interviews using modified validated questionnaires in a community in Beijing (1,499 participants) and a village in Baoding (803 participants) exhibited that the self-reported AR prevalence was significantly lower in the urban area (13.5%) than in the rural area (19.1%).\textsuperscript{16} It is still worth mentioning that the confirmable AR prevalence in terms of the positive skin prick test (SPT) results was 7.2% and 6.2% among the urban and rural adults, respectively, reflecting the similar prevalence between urban and rural areas in China.\textsuperscript{16} However, a study investigated in the grasslands of Northern China reported that subjects from the urban area showed a higher prevalence of physician-diagnosed PiAR than those from the rural area (23.1% vs. 14.0%, \(P < 0.001\)), making the comparison of AR prevalence between the urban and rural areas more confusing.\textsuperscript{14}

## CHANGING PREVALENCE OF AR IN CHILDREN

The International Study of Asthma and Allergies in Children (ISAAC) has found a slight worldwide increase in the prevalence of AR among children aged 13–14 years (0.18% per year) and 6–7 years (0.17% per year), as well as a > 20-fold variation in the prevalence of self-reported AR among countries in the same region and between centers in the same country.\textsuperscript{5} Over the 12-year period from 2001 to 2012, the prevalence of current rhinitis and lifetime rhinitis prevalence increased by 5.5% (22.6 vs. 28.1, \(P = 0.004\)) and 13% (18.6 vs. 31.7, \(P < 0.001\)) among 2 Isle of Wight birth cohorts.\textsuperscript{6} Comparatively, there was no trend study over time of AR prevalence in children in China; however, the prevalence of asthma in 12,235 children age 0–14 years in Fuzhou, a city in South-east China, was obtained as 1.57% in 1990 and 3.28% in 2000 based on a cross-sectional study with a 2-stage, clustered, stratified random sample design, indicating an increased trend over time.\textsuperscript{17} Very recently, the China, Children, Homes, Health cross-sectional study was conducted in Shanghai. Questionnaires were distributed to 17,898 parents or guardians of pre-school children from 72 kindergartens in 5 districts in Shanghai from April 2011 to April 2012. The prevalence of asthma was detected to increase significantly, almost five-fold, from 2.1% in 1990 to 10.2% in 2011.\textsuperscript{18}
To date, only 1 nationwide survey of the prevalence of AR in children in China has been reported. A total of 23,791 children aged 6–13 years in 8 metropolitan capital cities of provinces in 4 regions were surveyed via standard ISAAC questionnaire between November and December of 2005 using a cluster-stratified sampling method. The study demonstrated that the mean prevalence of childhood AR in the 8 cities was 9.8% (Shanghai 13.1%, Guangzhou 16.8%, Xi’an 3.9%, Wuhan 8.3%, Harbin 4.9%, Chengdu 10.1%, Hohhot 4.5% and Urumqi 10.1%). A smaller cross-sectional survey by Zhao et al. investigated the self-reported prevalence of childhood AR in 3 major cities in China (Beijing, Chongqing and Guangzhou) using the ISAAC questionnaire between October 2008 and May 2009. A total of 24,290 children aged 0–14 years were interviewed using a multi-stage sampling method; the self-reported prevalence of AR was 14.46%, 20.42% and 7.83% in Beijing, Chongqing and Guangzhou, respectively. Actually, besides the questionnaire, the other issues regarding the sampling and investigation were all different between these 2 studies. In this sense, it is hard to attribute the results to 1 reason or clearly explain them. The subjects’ age and area source, the sample size and the sampling methods might be all the possible reasons causing the variation, such as the AR prevalence in Guangzhou (16.8% in 2005 vs. 7.83% in 2008–2009). Stratified sampling and cluster sampling surveys were performed among 10–17-year-old students in Changsha city from June 2011 to April 2012 and the prevalence of AR was 15.8%–19.4%. A current study analyzed the cohort data of 74,688 junior high school students from a national retrospective birth cohort study in Taiwan, and among subjects mainly at 13–15 years of age, the estimated prevalence of AR was 22.4%. In addition, an investigation of clinical features of AR in children in Shanghai demonstrated that 8.6% of AR cases were classified as intermittent mild, 4.2% as persistent mild, 40.5% as intermittent moderate-severe and 46.7% as persistent moderate-severe.

There have been numerous reports concerning the prevalence of AR for children compared to adults in the urban versus rural areas. A questionnaire survey was performed on 11,473 children aged 7–12 years in 20 schools from urban Guangzhou and rural Shaoguan, China and showed that the prevalence of self-reported AR (23.2% vs. 5.3%) was significantly higher in Guangzhou compared to Shaoguan. Similarly, from a total of 14,884 questionnaires for 3–7-year-old children in Shanghai, the prevalence of hay fever in urban children was shown to be higher than that in suburban children as well.

**CURRENT STATUS OF COMORBID ALLERGIC DISEASES**

Attaching great importance to concomitant diseases of AR will contribute to the precise management of AR itself. It has been reported that the incidence of AR accompanied by rhinosinusitis, asthma or atopic dermatitis was significantly higher among individuals having self-reported AR compared to the general population, while the occurrence of comorbidities such as allergic conjunctivitis, cough and asthma gradually increased from intermittent mild, persistent mild and intermittent moderate-severe to persistent moderate-severe in terms of an AR children study in Shanghai. To be exact, a cross-sectional, hospital-based survey of 1,931 AR patients in two modernized cities (Guangzhou and Zhuhai) in Southern China and the prevalence of concomitant asthma for AR patients is 5.33% (103 of 1,931). Comparatively, another cross-sectional questionnaire study surveyed the diagnostic methods and treatment patterns for asthma-AR comorbidity by primary respiratory medicine specialty (PRMs) from 98 hospitals across China and the PRMs reported an estimated prevalence of asthma-AR comorbidity of > 30% at their clinics. On the contrary, research conducted...
on 20,051 patients with asthma in an outpatient setting covering all territories of China confirmed that AR presented in 69.9% of patients with asthma, further suggesting the upper and lower airway relationship between AR and asthma.

**PROFILES OF SENSITIZATION TO INHALED ALLERGENS**

The changing prevalence of aeroallergen sensitizations may explain different time trends observed in the cohorts suffering from AR as well as the other allergic diseases. Moreover, a better summary of differences in sensitization patterns within different geographical areas will be beneficial to optimize the optimal panels for allergen tests and efficiently prevent exposure. Due to the effect of geographic, climatic and humanistic factors, the type of allergen inducing AR varies significantly among regions. Zhang et al. summarized the pattern of sensitization to inhalant allergens among AR patients in Mainland China and provided evidence that the prevalence and type of aeroallergens were different in various cities and regions. Dust mites were reported as the most common allergen in many regions for both adults and children. In 2009, Li et al. surveyed 6,304 patients suffering from asthma and/or rhinitis in 17 cities from four regions of China and showed that *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* were the predominant aeroallergens in perennial/persistent AR individuals in China. Similar results were gained by the study in single regions such as Guangzhou, Xiamen, Quanzhou, Zhengzhou, Qingdao, Yichang and Shanghai.

The overall prevalence of specific immunoglobulin E (sIgE)-mediated sensitization to aeroallergens in 5,486 patients with AR who visited the ear, nose, and throat outpatient clinic in Guangzhou, the largest city in Southern China from January 2005 to December 2014 were as follows: 84.4% for house dust mites (HDMs), 23.4% for pet allergens, 21.1% for cockroaches, 9.1% for mold allergens, 7.7% for tree pollen and 6.0% for weed pollen. The prevalence of sensitization to aeroallergens decreased with age. Such results were also reported in a study of Shanghai children suffering from AR, i.e. with age the prevalence of sIgE against inhalant allergens was significantly increased; however, the opposite trend was observed for food allergens. Additionally, the proportion of children with high levels of sIgE against *Der p* increased with age. Furthermore, the prevalence of sensitization to inhaled allergens was significantly higher in children at > 6 years of age compared to that in those at 3–5 years of age. As for PiAR patients in Northern China, most of them were sensitized to 2 or more pollens (79.4%) with *Artemisia*, *Chenopodium* and *Humulus scandens* being the most common pollen types. Interestingly, 7,148 subjects with self-reported AR recently completed a standard questionnaire and were assessed for sensitization to relevant allergens by SPT. Eight allergens (*Der f*, mugwort, *Blatella*, hazel, goosefoot, *Penicillium notatum*, animal dander and *Der p*) allowed identification > 96% of sensitized subjects in Central China. Differences in optimal panels were observed between regions, with 5 to 6 allergens being sufficient for North-east (*Der f*, mugwort, *Blatella*, hazel, goosefoot and dandelion), North-west (mugwort, *Der f*, goosefoot, *Blatella* and hazel) and South (*Der f*, *Blatella*, dandelion, ragweed and birch) China, providing a cost-effective tool to screen sensitized patients in China. Nevertheless, no significant difference in major allergen positivity was observed in developed and developing regions in Guangdong as well as the North-west Hubei Province.

With respect to the changing pattern of inhaled allergens, a study performed in Guangzhou revealed that the prevalence of sensitization to pet allergens in patients with AR increased at an annual rate of 1.3% (95% confidence interval, 0.85% to 1.67 n%, P < 0.01) in the past decade, with a similar trend worldwide.
Last but not least, as regards the fact that correct identification of the culprit allergen is an essential part of diagnosis and treatment in allergic diseases, molecular biology has recently made important advances facilitating such identification and overcoming some of the drawbacks of natural allergen extracts, which consist of a mixture of various proteins that may be allergenic or not, specific for the allergen source or widely distributed. New technologies offer the opportunity for a more accurate component-resolved diagnosis (CRD), especially to polysensitized allergic patients. In China, there is so far a paucity of data about allergen CRD and the prevalence of grass pollen allergen components, in contrast to those from Western countries. As a result, 22.5% of patients with AR and/or asthma were positive for Bermuda-sIgE, 13.6% for Timothy-sIgE and 7.0% for Humulus scandens-sIgE. Of the Bermuda-sIgE-positive patients, 53.4% were Cyn d 1-positive and 60.3% were Timothy-sIgE-positive. Of the Timothy-positive patients, 100% were positive for Phl p 4, 17.1% were positive for Phl p 1, and 8.6% tested positive for Phl p 5/6/7/11/12. Patients with high Bermuda-sIgE levels were more likely to be positive for other grasses. In 41.4% of Bermuda grass-positive patients, cross-reactive carbohydrate determinant (CCD)-sIgE was also positive. Sensitization to Phl p 4 was significantly correlated with CCD. In addition, Chan et al. reported that an HDM genome draft produced from genomic, transcriptomic and proteomic experiments revealed allergen genes and a diverse endosymbiotic microbiome, providing a tool to further identify and characterize HDM allergens and to develop diagnostics and immunotherapeutic vaccines.

**RISK FACTORS ASSOCIATED WITH AR INCIDENCE**

Numerous risk factors have been described for AR in different stages of life, and they can be briefly divided into three aspects: genetic susceptibility, pre- and post-natal events, and environmental exposure as illustrated in Fig. 2.

First, genetically predisposed individuals are under increased risk of developing AR when they are exposed to certain environmental and lifestyle factors. In many studies, the most important risk factor for allergic disease development is reported as genetic susceptibility. If there is a family history of atopy in the first and second degrees, this risk increases further. In China, a genetic epidemiologic study involving 23,825 families from Jiangsu Province reported that the average AR heritability of the first, second and third generations was 81.86%. A family history of allergies and a patient history of allergies within 6 months of birth were significantly associated with the duration and severity of AR symptoms in a Shanghai children survey. A previous study in Shanghai suggested that no siblings, mothers at older ages during pregnancy, shorter breast-feeding period, use of antibiotics in the first year, and home dampness-related exposures, had significant associations
with increased prevalence of rhinitis.⁴⁵ Another 9-year population-based, retrospective cohort study using Taiwan’s National Health Insurance database demonstrated that the overall cumulative incidence and risk of AR in children born to periodontal mothers were significantly higher than those born to non-inflammatory mothers. Gum infection in women during pregnancy is an independent risk factor for allergic diseases in children, and thus its intergenerational consequences should be considered in gestational care.⁴⁶

Moreover, the most hazardous experiences such as disease and drug use, especially during the neonatal period and in childhood are also unavoidable risk factors for AR development. Children with idiopathic nephrotic syndrome (INS) had adjusted hazard ratio (1.71) for AR. Allergic disorders are common in children with INS, especially within the first year after diagnosis.⁴⁷ Urinary tract infection in newborns is significantly associated with the development of AR (OR, 1.41) in childhood and might be a risk factor for subsequent childhood AR.⁴⁸ Risk of AR was found to be 1.21-fold higher in the febrile convolution group than in the control group, and this risk of AR development is further increased (0.94 vs. 18.9) with frequency of febrile convolution-related medical visits (1 to 3 visits vs more than 3 visits, \( P < 0.0001 \)). Children with more than 3 febrile convolution-related medical visits had a significantly higher cumulative incidence of AR.⁴⁹ Another recent study investigated the correlation between AR and trace elements, and reported that the content of Zn and Se
were lower in AR patients serum than in the control group. In addition, obesity proved to increase the prevalence of AR and excessive weight gain was also confirmed to be an important risk factor developing AR during adolescence, especially among infants born small for their gestational age. Self-medication with antibiotics (OR, 6.35), especially use of at least 1 course of antibiotics in the first year of life (OR, 7.61) was involved.

Thirdly, the current living place, the living place during babyhood, smoking, home renovation and pet ownership were significant risk factors associated with AR prevalence in the population. Change of living environment and lifestyles had strong impacts on the prevalence of AR. Home renovation in the past 2 years was associated with increased likelihood of AR in Chinese women (OR, 1.39). Meanwhile, high vegetable intake, low milk intake and natural ventilation at home might protect against asthma, while supplementary protein feeding before 6 months of age were harmful.

**CLIMATE, ENVIRONMENTAL EXPOSURE AND LIFESTYLE IMPACT ON AR PREVALENCE**

Over recent decades, AR and allergic diseases have become increasingly common, but the reason for this increased prevalence is still unclear. It has been apparent that genetic variation alone is not sufficient to account for the observed changes; rather, changing climate and environment, together with alterations in lifestyle and eating habits, are likely to have driven the increase in prevalence, and in some cases, the severity of disease. For example, no difference in PiAR prevalence between the Han and Mongolian populations was observed in a Chinese study, indicating the more important role of high seasonal pollen exposure, but not ethnic-oriented genetic susceptibility.

It has been confirmed that the potential effect of the considerable increases in climate change should not be ignored with regard to the increased prevalence of respiratory disorders. Actually, climate change is correlated with allergens for several reasons, especially involving the increase in the amount of pollen produced by each plant. Very recently, Wang et al. carried out a sizable population survey in the grasslands of Northern China to study the impact of the intensity and time of pollen exposure on AR prevalence, and they reported that the epidemiologic AR and PiAR was 32.4% and 18.5%, respectively, exhibiting a remarkably higher rate than cities. Furthermore, they found that the PiAR symptoms were positively associated with pollen counts, temperature and precipitation (P < 0.05), but negatively with wind speed and pressure (P < 0.05). In this sense, PiAR prevalence in the grasslands region being extremely high may be due to high seasonal pollen exposure, which was influenced by local environmental and climate conditions.

Concerning environmental exposures from outdoor and indoor, most studies provide evidence that both may contribute to AR development. A study conducted on 2,598 children aged 3–6 years in Changsha demonstrated that early life exposure to traffic-related air pollutants including NO₂ and PM₁₀ during pregnancy and first-year of life may contribute to childhood AR. Another survey found that pre-conceptional, prenatal, post-natal exposure to outdoor industrial and traffic air pollutants were significantly associated with increases in the risk of childhood asthma, AR and eczema. New furniture was associated with eczema and AR during post-natal exposure, but redecoration was associated with asthma and eczema during prenatal exposure. A recent study also supported the hypothesis that
childhood allergic diseases originate in fetal life and were triggered by traffic-related air pollution in sensitive trimesters, \textsuperscript{59} i.e., maternal exposure to traffic-related air pollutant NO\textsubscript{2} during pregnancy, especially in specific trimesters, was associated with an increased risk of developing asthma, AR, and eczema in children. There was also evidence proving that the location, type, building area, decoration materials, and construction period of the residence also had significant associations with allergic diseases. \textsuperscript{45} Moreover, a previous study further assessed the impact of residential home characteristics and home environmental risk factors on respiratory diseases in Chinese women, and they reported that living near the main road or near ambient air pollution sources, pet-keeping, humidifier use and home renovation in the past 2 years were all risk factors for asthma, chronic bronchitis and AR. \textsuperscript{53} Comparatively, a parent-completed questionnaire survey administered in Hong Kong in 2003 assessed the influence of indoor and outdoor environmental factors, concluding that the exposure to moisture and mold in the first year of life increased the risk of asthma (OR, 2.56) and rhinoconjunctivitis (OR, 2.09). Current maternal smoking was also associated with a higher prevalence of asthma (OR, 2.00). No association was observed between outdoor traffic-related air pollutants and the prevalence of allergic conditions. Indoor home environments had a stronger influence on allergy development. \textsuperscript{60}

Interestingly, Ouyang \textit{et al.} \textsuperscript{61} recently published an article that illuminated the arguments about why air pollutants might increase the sensitization of pollen. Short-term exposure to oak pollen at high concentrations of SO\textsubscript{2} or NO\textsubscript{2} significantly increased their fragility and disruption, leading to subsequent release of pollen cytoplasmic granules into the atmosphere. These results suggested that heightened air pollution during the oak pollen season may possibly increase the incidence of allergic airway disease in sensitized individuals by facilitating the bioavailability of airborne pollen allergens.

**PROSPECTS**

AR and allergic diseases remain a critical public health, medical and economic problem, and are in fact among the major causes of illness for all ages in China. AR has also proved to be an important risk factor that will cause many diseases or disorders, especially in children. It has been verified that AR exerted significant effects on students’ character, memory and sleep quality, emotion, and memory. \textsuperscript{21} Moreover, AR cases showed a greater risk of otitis media with effusion, \textsuperscript{62} Kawasaki disease, \textsuperscript{63} primary immune thrombocytopenia, \textsuperscript{64} migraine, \textsuperscript{65} attention deficit hyperactivity disorder, and oppositional defiant disorder\textsuperscript{66} in children, sleep disorder-related problems in pregnant women,\textsuperscript{62} and mental disorders in adults.\textsuperscript{68}

Unfortunately, the trend of AR incidence is still on the rise and has become significant economic burden on the general public.\textsuperscript{69} In this regard, China is one of the largest countries in the world with a population of around 1.3 billion citizens and with rapidly expanding industrialization, while the growth rate of national AR prevalence from 2006 to 2011 was 6.5\%.\textsuperscript{9} The significant increase in health cost is alarming, which highlights an urgent need for better understanding of the prevalence status, etiology and its causative mechanisms in order to improve treatment and to develop effective prevention strategies. For example, optimized instruments based on objective tests have been more adequately employed to assess the prevalence of AR in the past 5 years than before. Meanwhile, the definition of PRMs has been given great attention because PRMs with greater work experience and higher professional titles estimated treating a significantly higher proportion of patients with AR as well as asthma-AR comorbidity.\textsuperscript{26} Moreover, allergy specialists in China have confirmed that
the incidence of pollen-, dust mites- and mold-sensitive AR can be predicted by employing models based on prevailing meteorological conditions, providing critical methods for the prevention of environmental exposure. Avoidance behaviors and reverse causation in parental smoking, pet-keeping and dietary habits for childhood rhinitis should be carefully considered. Public health policies should further help patients benefitted by proper diagnosis/treatment as well as help specifically target the local risk factors in order to control AR incidence.

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