

Changing Prevalence of Allergic Diseases in the Asia-Pacific Region

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Asia-Pacific is one of the most densely populated regions of the world and is experiencing rapid economic changes and urbanization. Environmental pollution is a significant problem associated with the rapid modernization of many cities in South Asia. It is not surprising that the prevalences of asthma and allergies are increasing rapidly, although the underlying reasons remain largely unknown. Many studies from this region have documented the changing prevalence of allergic diseases in various parts of the world. However, the methodologies used were neither standardized nor validated, making the results difficult to evaluate. The International Study of Asthma and Allergies in Childhood (ISAAC) has provided a global epidemiology map of asthma and allergic diseases, as well as the trend of changes in the prevalence of these diseases. Allergic sensitization is extremely common in many Asian communities. However, the prevalence of allergic diseases remains relatively rare. The rapid urbanization in the region, which increases environmental pollution and can affect the rural environment, will likely increase the prevalence of asthma and allergies in Asia.

Key Words: Asthma; allergies; Asia; pollution; International Study of Asthma and Allergies in Childhood

INTRODUCTION

Recently, many studies have shown that the prevalence of asthma and allergic conditions have increased in various regions of the world.¹⁻³ Comparative studies have demonstrated that asthma and related allergic disorders are more common in westernized or urbanized societies than in rural or developing countries.³⁻⁵ Despite intensive and extensive studies within a number of populations, the etiologies of these “atopic” conditions remain poorly understood. Nevertheless, epidemiological studies have played an important role in generating hypotheses regarding possible causative and protective factors.⁶⁻⁸

Asia is the world’s most populous continent, and the region is undergoing rapid economic development and westernization. Common chronic childhood diseases such as asthma and related allergic diseases have become a major health priority in Asia.⁹ Many studies from this region have reported an increasing prevalence of childhood asthma, but the use of different methodologies and lack of precise definitions of asthma make reliable comparison of the reported prevalence from different regions difficult. Over the past decade, there use of standardized protocols to study asthma prevalence has increased. ISAAC attempted to study global variations of asthma and atopic dis-

orders in children using standardized questionnaires, skin-prick testing and assessment of bronchial hyperresponsiveness.^{3-5,10} ISAAC was a multi-country cross-sectional survey of 2 age-groups of school children (6-7 years and 13-14 years). The study instruments included standardized questionnaires related to symptoms of asthma, allergic rhinoconjunctivitis, and eczema.¹⁰ A number of validation studies have confirmed that the ISAAC written and video questionnaires had excellent sensitivity and specificity for predicting asthma-associated bronchial hyperactivity.¹¹⁻¹³ The questions on eczema and allergic rhinitis have also been validated in a variety of settings with variable sensitivities and specificities depending on their gold standard for diagnosis.¹⁴⁻¹⁶ ISAAC Phase Three was a repetition of ISAAC Phase One that aimed to evaluate the possible trend of disease prevalence after a period of 5-10 years.

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TRENDS IN ASTHMA AND ALLERGIES IN THE ASIA-PACIFIC REGION

ISAAC Phases 1 and 3 have provided a comprehensive world map of asthma prevalence and related atopic conditions using standardized and validated instruments. As shown by Phase 3, within a period of 6-7 years there have been significant changes in the prevalences of asthma and rhinoconjunctivitis across the region. Similar to Phase 1, the highest rates of asthma symptoms were found in English-speaking developed countries such as the United Kingdom, Australia and New Zealand. The regions with the lowest prevalence were areas in Africa and the Indian subcontinent. No further increase was observed among countries with high prevalence when compared to Phase 1 results.¹⁷⁻²¹ For both adolescents (13-14 years) and children (6-7 years), the prevalence of asthma in the Asia-Pacific region ranked in the middle on a global scale, while the prevalence of "current wheeze" and "severe attacks" were relatively low. However, the proportion of subjects with severe asthma was similar to locations with a much higher prevalence.²² Rhinoconjunctivitis was only modestly common in adolescents, but was quite prevalent in the younger children in Asia-Pacific (Tables 1 and 2).

In the adolescent group, the Asia-Pacific region was in the mid-range for reported current symptoms of rhinoconjunctivitis at a global scale. However, the prevalences in Hong Kong and Bangkok were among the highest recorded worldwide. In the 6-7-year-old group, Asia-Pacific had a fairly high prevalence of "current rhinoconjunctivitis", ranking as the third highest region globally.⁴ Asthma prevalence appears to have peaked or reached a plateau in countries with a high prevalence, while it is still rising in many Asian cities. Despite their very high degree of urbanization, the prevalence of asthma in cities such as Singapore,

Seoul, and Hong Kong remains lower than those in the UK and Australia. Urbanization and economic development cannot explain such discrepancies. Furthermore, the known risk factors for asthma cannot explain the increased global prevalence, the international variations, or the recent decreases in prevalence in some Western countries.²²⁻²⁴ It is highly likely that these changes are related to the complex interplay between genetic factors and changing environmental exposure.²⁵ A better understanding of these complex interactions could lead to the development of primary preventive strategies that may prevent further increases in the prevalence of allergies among Asian countries.

Similar to the global patterns of allergic diseases, asthma and rhinoconjunctivitis were more prevalent in well-developed areas, such as Korea, Japan, Hong Kong, and Singapore.²⁶⁻²⁸ The lowest prevalences of asthma symptoms were reported in the more underdeveloped countries or regions, such as Indonesia, several centers in Malaysia, and cities in mainland China (Tables 1 and 2).²⁶⁻²⁸ Nearly all the Asia-Pacific centers showed an annual increase in the prevalence of "current rhinoconjunctivitis" for both age groups.

An important aspect for asthma care is the level of control among asthmatic patients, since the most expensive component of asthma care is related to acute care, including emergency visits and hospitalization. The Asthma in Reality in Asia-Pacific (AIRIAP) study has been conducted twice in Asia, and centers from mainland China, Hong Kong, Korea, Malaysia, Philippines, Taiwan, and Vietnam participated.²⁹ In the first survey, more than 3,000 adults and children were studied. More than 40% of the asthmatics had at least one hospitalization or visit to the emergency department for acute exacerbation. Inhaled corticosteroid use was reported by only 13.6% of the respondents. Another study was performed 10 years after the first survey,

Table 1. Trends in self-reported symptoms of asthma and allergic rhinoconjunctivitis in 13-14-year-old Asian children from ISAAC Phases 1 and 3 results: average annual change in prevalence

Cities/Countries	Asthma Ever	Current Wheeze	Rhinoconjunctivitis
Alor Setar	10.8 (+0.09%)	9.3 (+0.05%)	16.3 (-0.06%)
Bangkok	15.9 (+0.30%)	13.9 (+0.06%)	23.9 (+1.41%)
Beijing	6.3 (-0.08%)	7.2 (+0.30%)	10.2 (+0.33%)
Philippines	20.9 (+0.47%)	8.4 (-0.55%)	11.0 (-0.61%)
Chiang Mai	9.9 (+0.10%)	8.7 (-0.65%)	17.2 (+0.26%)
Guangzhou	4.6 (+0.09%)	4.8 (+0.20%)	10.7 (+0.33%)
Hong Kong	10.1 (-0.15%)	8.6 (-0.55%)	22.6 (-0.21%)
Indonesia	12.4 (+1.80%)	5.2 (+0.52%)	4.8 (-0.08%)
Japan	19.9 (+0.12%)	13.0 (-0.05%)	17.6 (+0.34%)
Klang Valley	16.1 (+0.37%)	11.6 (-0.11%)	19.8 (+0.87%)
Kota Bharu	9.0 (+0.04%)	5.8 (-0.20%)	12.5 (+0.46%)
Seoul	5.0 (+0.44%)	9.1 (+0.16%)	11.9 (+0.24%)
Singapore	26.5 (+0.79%)	11.4 (+0.24%)	16.5 (+0.20%)
Taiwan	17.0 (+1.28%)	7.0 (+0.26%)	17.8 (+1.02%)
Mean	12.6 (+0.39%)	8.8 (+0.07%)	15.1 (+0.32%)

Table 2. Trends in parental-reported symptoms of asthma and allergic rhinoconjunctivitis in 6-7-year-old Asian children from ISAAC Phases 1 and 3 results: average annual change in prevalence

Cities/Countries	Asthma Ever	Current Wheeze	Rhinoconjunctivitis
Alor Setar	9.8 (-0.52%)	5.7 (-0.07%)	4.2 (+0.09%)
Bangkok	10.7 (+0.24%)	15.0 (+0.68%)	13.4 (+0.58%)
Chiang Mai	6.1 (+0.32%)	7.8 (+0.38%)	6.2 (+0.24%)
Hong Kong	7.9 (+0.04%)	9.4 (+0.03%)	17.7 (+0.67%)
Indonesia	4.8 (-0.33%)	2.8 (-0.22%)	3.6 (-0.04%)
Japan	23.0 (+0.59%)	18.2 (+0.10%)	10.6 (+0.35%)
Klang Valley	11.9 (+0.13%)	7.4 (-0.07%)	6.2 (+0.21%)
Kota Bharu	11.2 (+0.14%)	4.3 (-0.21%)	4.2 (+0.06%)
Seoul	9.9 (+0.18%)	6.5 (-1.71%)	9.0 (-0.38%)
Singapore	15.5 (-0.42%)	10.2 (-0.80%)	8.7 (+0.02%)
Taiwan	14.4 (+0.24%)	9.8 (+0.04%)	24.2 (+1.37%)
Mean	11.4 (+0.12%)	8.9 (-0.06%)	10.6 (+0.18%)

which applied the same methodology and recruited 4,805 subjects. Using the latest classification of the level of control derived from GINA, less than 5% of subjects achieved a level of complete control while more than one third of the subjects were in the uncontrolled asthma category. Similar to asthmatics in other parts of the world, patients in Asia tend to overestimate their level of control and tolerate a high degree of impairment of their daily activities.²⁹⁻³²

ASIA-PACIFIC-VARIATIONS AMONG POPULATIONS FROM DIFFERENT COUNTRIES OR CITIES

One of the most interesting findings of the ISAAC was the striking difference in asthma prevalence in populations with similar genetic or ethnic backgrounds from different environments.³³⁻³⁵ There are marked variations of asthma prevalence among different cities within the same countries such as those in Thailand, Malaysia, and China.^{36,37} Among Chinese cities, Hong Kong is the most developed and westernized while Guangzhou is located approximately 200 km north-west of Hong Kong and experiences a similar subtropical climate.³⁸ The prevalence of asthma among children and adolescents was 2 times higher in Hong Kong than in Guangzhou. Furthermore, children recruited from Hong Kong (if they were born and raised in Hong Kong) had an asthma prevalence 2-3 times higher than those born in China who migrated to Hong Kong subsequently.³⁹ These differences illustrated the importance of early or even *in utero* environmental exposure and the subsequent development of asthma. Although various factors such as cooking with gas, foam pillows, and exposure to house dampness were associated with an increased prevalence of asthma in Hong Kong,⁴⁰ mechanistic studies are required to determine if these factors have a true pathogenetic role in causing asthma.

ALLERGIC RHINITIS IN THE ASIA-PACIFIC REGION

In addition to data on asthma, the ISAAC studies (Tables 1 and 2) have provided extensive global data on the prevalence of allergic rhinitis in children.^{4,5,41} Compared with children, adult epidemiology data are more difficult to obtain. For children, random populations can easily be obtained from primary or secondary schools. Therefore, community data of atopic diseases in adults are usually not from random populations. Nevertheless, such data are useful to establish the standard of care, perception, and control of asthma and related atopic diseases in adults. One of the largest studies performed on the impact of allergic rhinitis on adults and children in Asia is the Allergies in Asia-Pacific Survey.⁴² This survey recruited over 1,200 adults and children with physician diagnosis of allergic rhinitis after screening over 33,000 families in Australia, mainland China, Hong Kong, Malaysia, Philippines, Singapore, Taiwan, and Vietnam. Overall, the prevalence of allergic rhinitis was 8.7%. The rates varied from 13.2% in Australia to 4.2% in Hong Kong. Close to half of the subjects reported interference of their work or have missed work in the past year because of their allergic rhinitis. However, only 21% of the subjects were taking nasal inhalation steroids for their disease, despite the recommendation for such treatment based on evidence-based international guidelines.⁴³

THE FUTURE CHALLENGES OF ALLERGIC DISORDERS IN ASIA

Given the rapid economic development and urbanization in Asia, the prevalence of allergic disorders will continue to rise in the next 2 decades. The loss of protective factors associated with a traditional rural environment and the emergence of risk factors associated with modern urbanized living will increase the total burden of allergic diseases on the health care systems in

Asia. The increasing prevalence and possible increasing severity of asthma and related allergic conditions will become an important issue for physicians. Many of the so-called established risk factors for the development of allergies cannot explain the international and intra-regional variations in asthma prevalence patterns.⁴⁴ The results of the ISAAC study challenge the common belief of a strong deterministic association between atopy and asthma.⁴⁵ Sensitization of the major indoor allergen, house dust mite (HDM), was considered an important risk factor for the development of asthma.⁴⁶ However, HDM exposure was high in many regions in Asia with a relatively low asthma prevalence. Leung and Ho⁴⁷ reported a study of Chinese schoolchildren from Mainland China, Hong Kong and Malaysia Kota Kinabalu, and the overall rate of atopic sensitization (49%-63%) across all 3 regions. The prevalence of asthma in Hong Kong was 2-6 times higher than in the other 2 cities.⁴⁷ Allergic sensitization is a significant factor associated with asthma, and appears to be a marker rather than a causative factor for subsequent asthma development.⁴⁸⁻⁵⁰ Air pollution has been implicated as an important precipitant of asthma exacerbation, but it could not explain the observed patterns of asthma prevalence in Asia.⁵¹⁻⁵³ For example, there was a two-to-three-fold higher prevalence of asthma from Chinese children in Hong Kong than Chinese children living in the far more polluted cities in Mainland China, such as Chongqing.^{38,39}

Recent research has focused on factors that modulate the early immune system towards the development of allergic diseases.⁵⁴⁻⁵⁶ Many studies have documented the protective roles of the rural environment and farming exposure,⁵⁷⁻⁵⁹ daycare attendance,^{60,61} changes in T-helper cell compositions,⁶² endotoxin exposure,⁶³ exposure to farm animals,^{64,65} consumption of unpasteurized farm milk,^{66,67} fruits or vegetables,⁶⁸ and exposure to microbial diversity in the living environment.^{69,70} Many of these factors have not been investigated thoroughly in Asia and likely reduce the prevalence there when compared to the UK or Western Europe. Another emerging challenge is food allergies, which has been described as the second wave of allergies after the rise in the prevalence of asthma in the past few decades.⁷¹ Recent studies from Australia suggested a prevalence as high as 10% in infants.⁷² Little published data are available from Asia regarding the epidemiology of food allergies using standardized and validated tools. The Europrevall study has provided a standardized protocol for the study of food allergies in the community from China. Russia and India have also participated in this study, using the same standardized instrument.⁷³ The prevalence of food allergies will continue to increase in parallel to the improvement of economic levels in Asia. Furthermore, we should not ignore important information regarding the genetic contribution to the development of asthma and allergies. A better understanding of how different genes interact with various environmental factors and the timing of exposure of these factors are all important for the advancement of effective primary preventive strate-

gies against the development of allergies.^{25,74,75}

CONCLUSION

Although the prevalences of asthma and allergies remain relatively low in Asia compared with other regions, they will likely increase. The Asian environment is highly diverse with significant variation in genetic backgrounds. Furthermore, populations with similar genetic backgrounds live in different environments, making Asia ideal for epidemiological and gene-environment interaction studies. Continuing epidemiological studies using standardized and validated tools are important for identification of factors that modulate the immune system towards the development of allergies. Meticulous documentation of environmental changes in Asia may facilitate identification of probable triggers, risk factors and protective factors for allergies. Also, the increasing number of patients with allergic conditions makes necessary changing how we educate our health-care workers and patients regarding achieving better control so as to minimize the morbidity and mortality related to asthma and allergies.

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