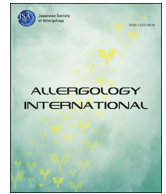




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Original article

Allergies are still on the rise? A 6-year nationwide population-based study in Korea

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NHI	National Health Insurance
HIRA	Health Insurance Review and Assessment Service
KOSIS	Korean Statistical Information Service
ICD	International Classification of Diseases
ISAAC	International Study of Asthma and Allergies in Childhood

ABSTRACT

Background: Some western countries recently have shown a slowdown in the incidence of allergic diseases after worldwide increasing trends, but there are few data from Asian populations concerning changing trend of allergic diseases. We evaluated the recent trends in the prevalence of asthma and other allergic diseases in Korea.

Methods: From the database of Korean National Health Insurance, a nationwide diagnostic data from 2009 to 2014 were extracted and the national prevalence was analyzed.

Results: The prevalence per 1000 people of atopic dermatitis, allergic rhinitis, and asthma in 2014 was 19.0, 133.1, and 36.3, respectively. The prevalence of three diseases was highest in the age group under 10 as, 95.0, 384.1, and 132.1 per 1000 people, while the prevalence in the over-10-year-group was only 11.6, 109.5, and 27.3, respectively. The prevalence of atopic dermatitis and allergic rhinitis gradually decreased with older age, but the prevalence of asthma showed a re-increasing pattern from the age group 30–39 and reached another peak for the age group 70–79. During the study period, the prevalence of asthma and atopic dermatitis showed decreasing tendency. In contrast, the prevalence of allergic rhinitis steadily increased until 2013, especially in the age group under 10.

Conclusions: The national prevalence of atopic dermatitis, and asthma did not show noticeable increase any more in Korea. However, the prevalence of allergic rhinitis still on the rise until recently, especially in the age group under 10. This is the first report in Asia suggesting a slowdown of the incidence of allergic diseases.

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Introduction

The burden of chronic allergic diseases was on the rise worldwide for the past several decades, the so-called ‘allergic epidemic’.^{1,2} However, whether this trend is still ongoing is questionable. Some recent reports in Western developed countries have already shown a stationary or even decreasing prevalence of childhood allergic disease whereas there was still an increase in prevalence in developing countries where the prevalence had been

very low in the past.³ In Asia, there is no data showing changing trend in the prevalence of chronic allergic disease until recently.^{4,5}

Epidemiologic data is important to establish a long-term health care plan for chronic diseases. The heterogeneity and changes of study methods makes it difficult to integrate the epidemiologic results of previous studies to assess changes over time. Therefore, a longitudinal study based on a large standardized population is ideal in order to obtain precise epidemiologic data. However, these studies are costly as well as difficult to perform.

Korea has a nationwide disease database that includes the people of the entire country since a single mandatory government-established nationwide insurance system was established in 1989.⁶ This database is optimized to evaluate serial trend of national prevalence because it contains data of the entire national population with the same method. We evaluated the recent trends of the

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prevalence and the medical cost in atopic dermatitis, allergic rhinitis, and asthma in Korea by analyzing data of nationwide insurance system.

Methods

Subjects

We performed a retrospective, population-based study to assess the prevalence and its changing trend of atopic dermatitis, allergic rhinitis, and asthma in Korea. All patients who ever visited any medical facilities in Korea were included using nationwide claim data from 2009 to 2014.

This study was exempted from full review by the institutional review board of Seoul National University Hospital (number 1506-009-676).

Data source

Korea has adopted the National Health Insurance (NHI) program, which is a nationwide health insurance system providing healthcare coverage to the residents in Korea. Although there are several private medical insurances, the NHI program is the only mandatory health insurance system regulated by the law covering 97.9% of the total population. At the same time, all physicians in the country submit billing claims to the NHI program with diagnostic codes.⁶ Health Insurance Review and Assessment Service (HIRA) reviews and assesses medical fees paid by the NHI program and provides a summary of nationwide annual statistical data on its homepage (www.hira.or.kr) for the recent years. Age data was available as 10-year age groups. Medical cost data from the HIRA included whole expenses paid to clinics and hospitals except expenses paid to pharmacies for medicines prescribed in outpatient clinics. Demographic data including annual total and 10-year age group population numbers registered in the NHI were extracted from the Korean Statistical Information Service (KOSIS) homepage (www.kosis.kr).

Data analysis

The data did not include any identification information from the individual patients. We used diagnostic codes from the International Classification of Diseases-10 (ICD-10) to extract specific data about atopic dermatitis, allergic rhinitis and asthma. The diagnostic codes are L20 for atopic dermatitis, J301, J302, J303, and J304 for allergic rhinitis, J45 and J46 for asthma.

The prevalence was determined by the number of patients with each diagnostic code divided by the total registered number of patients by the NHI. Means with standard error were used but we did not present standard error because the study subjects accounted for the total population of Korea. With the same reason,

other statistical values such as confidence interval or p-value were not presented either.

Results

Recent changes in the prevalence of three major allergic diseases

Table 1 shows the annual number of patients and costs spent at medical facilities for atopic dermatitis, allergic rhinitis, and asthma in Korea. The prevalence of the three diseases in 2014 was 19.0, 133.1, and 36.3 per 1000 people, respectively. The prevalence was higher in women than in men, especially for allergic rhinitis (Atopic dermatitis: 17.83 vs. 20.10; Allergic rhinitis: 123.15 vs. 143.18; Asthma: 33.17 vs. 39.49 in 2014). For the past six years, the prevalence of allergic rhinitis continuously increased (yearly by 3.2% on average) while that of atopic dermatitis and asthma slightly decreased during the same period (yearly by –2.6% and –5.8% on average) (Fig. 1).

Recent changes in the prevalence of allergic diseases in 10-year age groups

For atopic dermatitis, the age group under 10 years old showed the highest prevalence among the 10-year age groups. In 2014, the prevalence of atopic dermatitis per 1000 people was 95.0 in the age group under 10 years old but decreased to 11.6 in the age group over 10 years old. Especially in people over 30 years old, the prevalence of atopic dermatitis was below 10 per 1000 people. The temporal trend in the prevalence of atopic dermatitis was stationary on average –2.6% yearly change in general (yearly –4.1% for under 10 years old and 0.5% over 10 years old) (Fig. 2a).

The prevalence of allergic rhinitis was also the highest in the age group under 10 years old. In 2014, the prevalence in the under 10 years old was 384.1 per 1000 people and was cut down to 109.0 per 1000 people in over 10 years old. In contrast to atopic dermatitis, the prevalence of allergic rhinitis remained above 100 per 1000 people in people over 30 years old groups (Fig. 2b). For the recent 6 years, prevalence increase was yearly 3.2% on average especially with the yearly 8.2% increase in the age group under 10 years while the age group over 10 years showed relatively modest change (yearly 2.1%).

In 2014, the prevalence of asthma per 1000 people was the highest as 132.1 and 27.3 in the under and over 10 years old group, respectively. Unlike atopic dermatitis and allergic rhinitis, the prevalence of asthma showed two peaks. It reached the lowest in the 20–29 years old group as 13.5 per 1000 people, the 50–59 years old group showed a distinct re-increase in the asthma prevalence, and the 70–79 years old group revealed another epidemiologic peak as 66.3 per 1000 people. Regarding the trend in the past six years, the prevalence of asthma decreased by yearly 5.8% on average. In the under 10 years old group, there was more noticeable

Table 1

Annual number of patients and costs at medical institutions for atopic dermatitis, allergic rhinitis and asthma in Korea from 2009 to 2014.

	2009	2010	2011	2012	2013	2014
Number of patients						
Atopic dermatitis	1,051,747	1,049,290	1,010,527	981,028	1,015,186	954,000
Allergic rhinitis	5,529,050	5,830,136	5,852,544	6,331,813	6,429,755	6,697,490
Asthma	2,377,683	2,245,778	2,264,275	2,181,144	1,969,078	1,827,068
Costs at medical institution [†]						
Atopic dermatitis	29,692,819	30,813,452	30,508,568	29,760,316	32,231,457	35,033,840
Allergic rhinitis	147,251,127	158,200,596	162,763,497	176,711,206	185,180,071	207,205,833
Asthma	175,184,735	168,862,394	170,053,219	156,244,052	146,268,832	146,939,214

[†] Expressed in U.S. dollar.

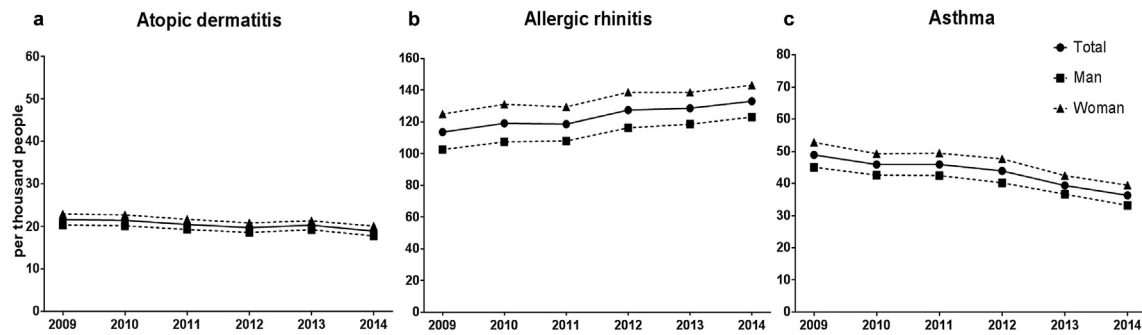


Fig. 1. Prevalence of allergic diseases in Korea.

decrease compared with the age group over 10 years old (yearly -7.1% and -3.7% on average, respectively) (Fig. 2c).

Fig. 3 shows population structures of the total population and the patients of the three allergic diseases in 2014. The patient population was the largest for all three diseases in the age group under 10 years old despite its relatively small proportion in total population. Among over 10 years old, the number of patients for allergic rhinitis and asthma showed another peak in 30–39 and 50–59 years old group, respectively while atopic dermatitis consistently decreased with older age.

Burden of chronic allergic diseases: direct medical cost

Total cost paid to medical institutions by the NHI program in 2014 was 35.0, 207.2 and 146.9 million dollars for atopic dermatitis, allergic rhinitis, and asthma, respectively (Table 1). Costs for atopic dermatitis have changed less for the past six years while those of allergic rhinitis have increased along with the rise of its prevalence (yearly 3.4% and 7.1% change on average, respectively). The costs of asthma have decreased yearly by 4.5% for the past six years (Fig. 4a).

The medical costs per person were 36.7, 30.9, and 80.4 dollars for atopic dermatitis, allergic rhinitis, and asthma, respectively. They have been increased for the past six years (yearly 5.4% , 3.0%

and 1.8% on average for individual disease) (Fig. 4b) and it shows a similar result when divided by the 10-year age groups.

Discussion

The prevalence of chronic allergic diseases has increased for several decades.^{1,2} However, the extent of the increase in allergic diseases shows diversity according to countries. Some reports investigating children in Western developed countries showed a recent decreasing or stationary prevalence of allergic diseases in contrast to the continued increasing prevalence of allergic diseases in developing countries including the Asia–Pacific region where the prevalence had been relatively low in the past.^{3,4} In adults, there are very few reports on the trends in the prevalence of allergic diseases. This study was performed using serial data of the entire nation covering all age groups and observed stationary or decreasing patterns of their prevalence in adult population in Korea.

The most important factor in analyzing the temporal changes in the prevalence of chronic diseases is that a study must be done with standardized procedures by using the same methods to collect data every year. For the recent decade, there have been sporadic epidemiologic studies on the prevalence of allergic

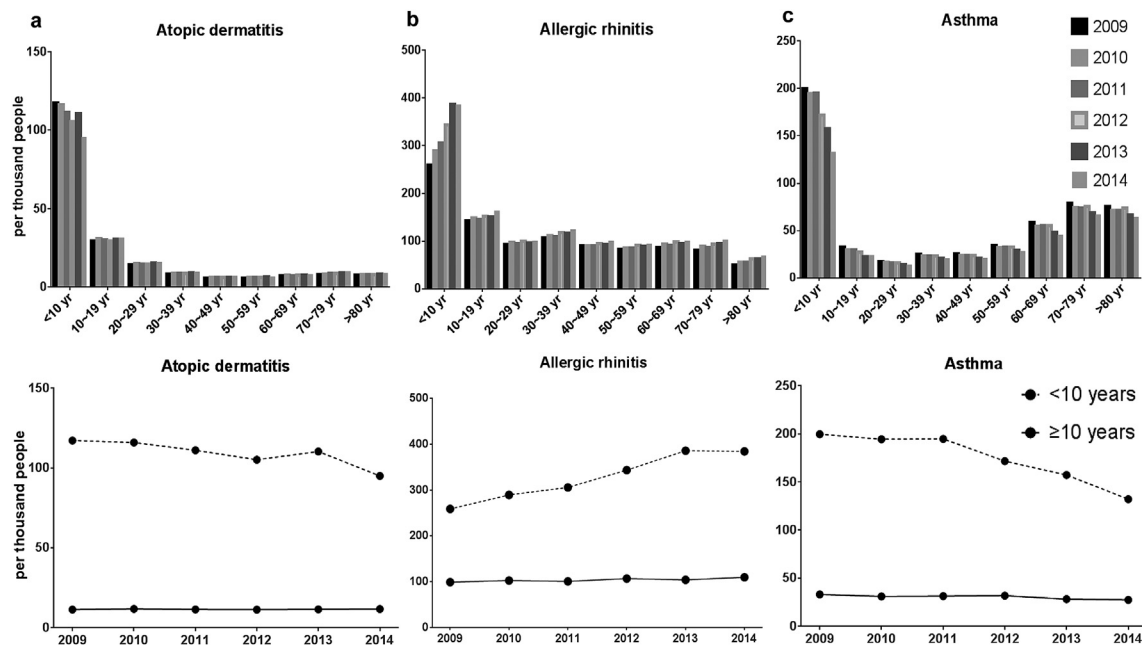


Fig. 2. Prevalence of allergic diseases divided by 10-year age groups.

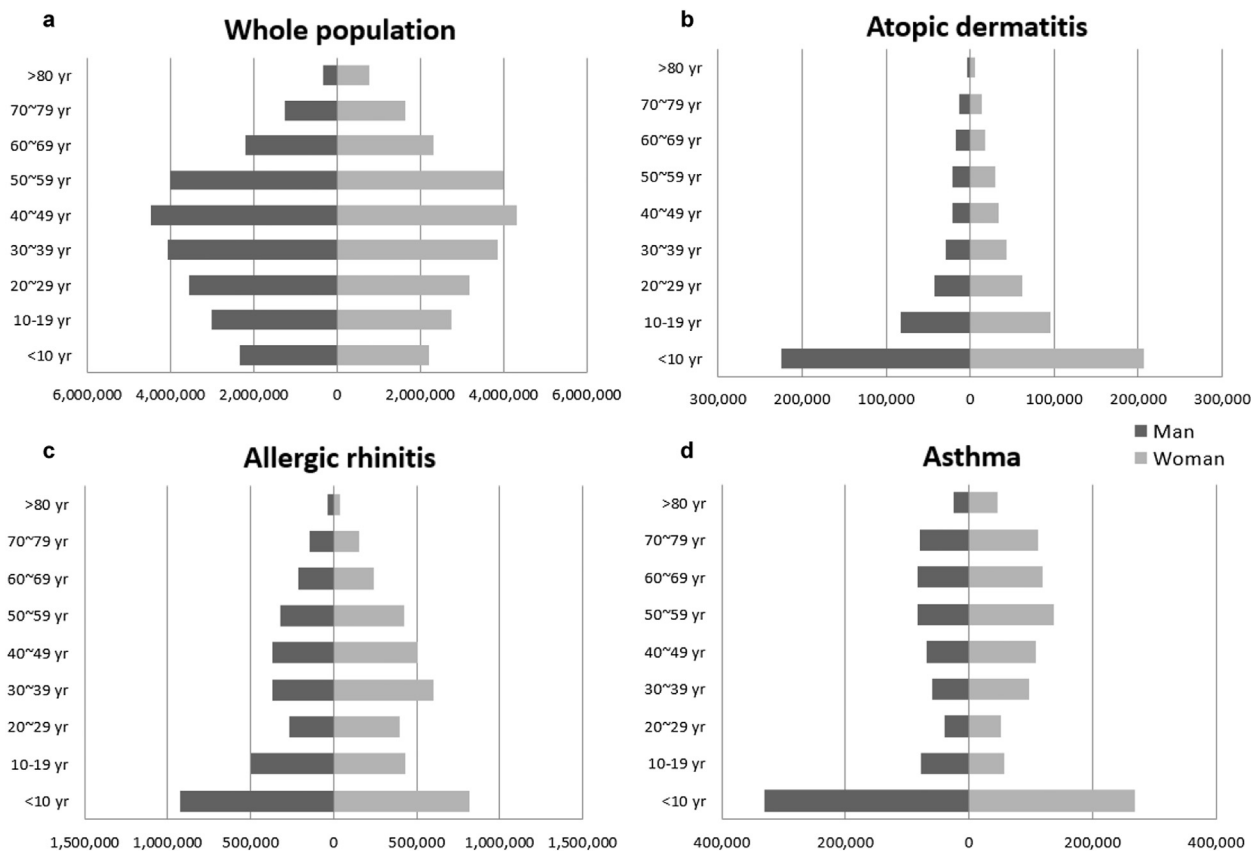


Fig. 3. Population structure of Korea and patients of allergic diseases.

diseases. However, variations in the methodologies used to survey prevalence as well as definitions used to define allergic diseases made it difficult to integrate previous epidemiologic studies to assess time-trends in prevalence. In this regard, NHI database in Korea is the best option for epidemiologic survey because its data are gathered by the same disease definitions based on ICD-10 by physicians covering the whole nation. The strength of this study include extensiveness of the nationwide data collection and the standardized method for evaluating temporal trends of the prevalence of allergic disease, unlike other epidemiologic surveys concerning only a particular region or institutions. This is the first study with nationwide database to suggest that the prevalence of chronic allergic diseases might

have reached a plateau or already have started to decrease in Asian country.

According to previously reported literature, atopic dermatitis generally affects up to approximately 25% of children and 2–3% of adults.⁷ For children, eczema prevalence decreased in the 2000s in developed countries such as New Zealand and the United Kingdom where atopic dermatitis was highly prevalent in contrast to the increasing tendency in developing countries especially in Asia or Eastern Europe.⁸ In adults, the low prevalence of atopic dermatitis, ranging from approximately 2–4%, seems to be stationary worldwide for the recent several decades.⁹ In Korea, the overall prevalence of atopic dermatitis is assumed to be as high as 16.9–17.9% in preschool children and 2.6–7.1% in adults based on the

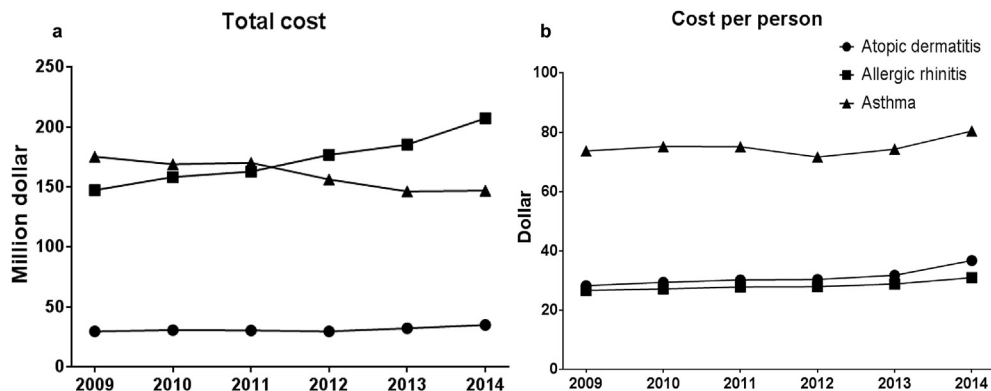


Fig. 4. Total cost and cost per person paid to medical institutions by NHI.

examination of dermatologists in the late 2000s.^{10,11} In under 10 year-old group, the prevalence of atopic dermatitis is highest in one year old and it showed a significant decrease with age.¹² In our data, the prevalence of atopic dermatitis in the under and over 10 year-old group was 9.5% and 1.2%, respectively and it did not show remarkable changes in the past six years in both groups.

The prevalence of allergic rhinitis is also increasing in most countries in the world, but it seems to have hit a plateau or even decreased in previously highly prevalent areas such as Western Europe or North America after the 2000s.¹³ The ISAAC studies provide extensive data on allergic rhinitis in children. Excluding a couple of countries showing extreme deviation, the worldwide prevalence of allergic rhinitis is assumed to be 3–24% in 6–7 year-old children and 4–28% in 13–14 year-old adolescents in the 2000s.³ However, there is no worldwide epidemiologic study in adults and the results of prevalence surveys of some countries tend to be very diverse, ranging from 3% to 34.5%, due to their various definitions.¹³ In Korea, according to the most recent survey after the 2010s, the prevalence of allergic rhinitis was reported to be 34.5% in preschool children and 16.2% in adults.^{10,14} The age showing peak prevalence under 10 years old was 6–8 years.¹⁵ In our study, the prevalence of allergic rhinitis in the age group under 10 showed steep increasing pattern up to 2013 and reached 38.4% in 2014 while the prevalence in the age group over 10 was 11.0% with relatively modest increase.

Asthma is one of the most common diseases in the world. The prevalence of asthma has increased with urbanization, industrialization and lifestyle change.¹⁶ However there are several reports showing that international differences in asthma prevalence have reduced in recent years, mostly in children and adolescents; asthma prevalence is increasing in Asia, Africa, and South America while decreasing in English-speaking countries and Western European countries after the 2000s.^{1,17–20} Between phase I and II of the ISSAC study with an interval of 5–10 years in 2000s, the mean symptom prevalence of wheezing during the last one year increased slightly from 13.2% to 13.7% worldwide but a marked decrease was observed in English-speaking countries in the case of children and adolescents.¹⁸ Although there are only a few studies that show the changing trend of asthma prevalence in adults, some investigators have reported no increase in asthma prevalence after the 2000s based on symptoms in a young adult cohort in Europe.^{21,22} In Korea, the prevalence of asthma was highest in 0–3 year-old group and decreased with age.²³ It seems to be 5–8% in children and reached a plateau in the 13–14 year group during 5-year interval in the 2000s.³ The prevalence of adult asthma in Korea was estimated to be 2% in a survey performed in 2008²⁴ and other report based on drug prescription data estimated it as 5.4% in 2010 and it showed continued increasing pattern until 2010.⁵ In our data, the prevalence of asthma was 13.2% and 2.7% in the under and over 10 year old group in 2014, respectively. Both had a decreasing prevalence during the recent six years and the changing trend in asthma prevalence in Korea seems to have plateaued like in Western developed countries.

Total cost paid to medical institutions by the NHI program was 35.0, 207.2 and 146.9 million dollars for atopic dermatitis, allergic rhinitis and asthma, respectively. Each benefit was ranked 158th, 26th and 34th.²⁵ Medical costs per person for the past six years have slightly increased and it shows a similar result when divided by the 10-year age groups. In other literature about asthma, the proportion of cost reimbursed by the NHI is for about 22.5% of the total expenditure.²⁶ Applying this information to our data, the total cost for asthma management in Korea may be estimated to be 653 million dollars in 2014.

As mentioned above, atopic dermatitis, allergic rhinitis and asthma have rapidly increased for the past several decades

worldwide with urbanization and industrialization.^{2,13,27} There are some hypotheses explaining the cause of this phenomenon, including the hygiene hypothesis.²⁸ In addition, there are many possible risk factors to explain 'allergic epidemic' such as allergen levels in the air, diet change, smoking, vaccination level, exposure to pets, socioeconomic status, etc.^{28–32} However, there are several studies suggesting that the prevalence of chronic allergic diseases has plateaued or decreased recently in some countries, especially in children and young adults.^{1,3,8,18,21,22} Risk factors or a hygiene hypothesis cannot fully explain this phenomenon. In the ISSAC trial, discordance in prevalence in the 6–7 and 13–14 year age-groups was explained with the collapse of the communist system of Europe in the 1990s.³ Therefore, the trends in epidemiology would be more explainable by taking into account social and environmental changes.

Our data showing that the recent prevalence of allergic diseases in Korea are not increasing suggests several important points to understand current epidemiology of allergic diseases. First, it might be reflection of changing disease patterns keeping pace with rapid transition to an industrialized society. As Korea went through extremely rapid urbanization and industrialization from the 1960s to the 1990s, residential environment and hygiene dramatically changed: family size diminished, and lifestyle became similar with those of western countries. From the 2000s, the urbanization and industrialization of Korea was almost completed, and Korea reached post-industrialization era.^{33,34} While the prevalence of chronic allergic diseases up until recently in Korea reflects the rapid urbanization and industrialization before the 2000s, it seems to come up to the plateau by the completion of rapid industrialization after the 2000s. Recent changes of trend according to change of society are important to expect the future pattern of allergic diseases in other countries which have been on a similar development process. Second, our data show that there are still age groups of which prevalence is higher than other group even though overall prevalence does not increase. In under 10 year-old group, prevalence of all three diseases is higher than over 10 year-old group and, moreover, that of allergic rhinitis is still increasing. In fact there are many potential factors influencing allergic diseases in children but it is still unknown whether and how they contribute to the development of allergic disease in childhood.³⁵ It emphasizes that the unmet needs for proper management and prevention of allergic disease in children.

Our data has several limitations. First, since we estimated prevalence with medical insurance data, only those who received medical treatment were enrolled. Several surveys report that only 25–74% of patients with asthma symptoms visit clinics or hospitals for treatment.^{36,37} Therefore, the prevalence in our data might be somewhat underestimated and influenced by socioeconomic status and medical environment. Second, we used the open data of HIRA and additional information was not accessible. Therefore we could not analyze the peak age of prevalence.

However, it contains data about entire country of large sample size more than 50 million, which was not attainable with survey. The method for data collection was uniform and standardized during study period. In addition there was no considerable change in medical issues in diseases such as new drug or treatment, new approval of over-the-counter drug. The report of which population of this size showing changing trend of prevalence in chronic allergic disease is the first one in Asia and it might be important because it implies that such a trend is not limited to western countries anymore and possibility of change in future epidemiology of chronic allergic diseases in other Asian countries.

We analyzed recent prevalence changes of atopic dermatitis, allergic rhinitis and asthma using nationwide insurance data collected with a uniform method and condition covering the entire

nation. The recent prevalence of these diseases did not show rapid increase any longer in adult population in Korea similar to Western developed countries while still increasing trend of allergic rhinitis in children under 10 year old.

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Conflict of interest

The authors have no conflict of interest to declare.

Authors' contributions

All the authors contributed to conception and design of the study, and analysis and interpretation of the data. BKK, MKK, MSY and HRK carried out data generation. BKK, JYK, HWP, KUM, SHC and HRK prepared the manuscript.

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