Asian Pacific Journal of
Allergy and Immunology
APJAI

REVIEW ARTICLE

Aeroallergen sensitization and allergic disease phenotypes in Asia

Elizabeth Huiwen Tham,[1,2] Alison Joanne Lee,[1,2] Hugo Van Bever[1,2]

Abstract

Allergic diseases are on the rise in Asia. Aeroallergen exposure is a strong risk factor for sensitization, development and severity of atopic diseases, especially in the Asian paediatric population. Geographical and seasonal variations in aeroallergen sensitization are seen even within Asian countries and changes in aeroallergen sensitization patterns have been observed over time. Some possible reasons include climate change as well as rapid urbanization and improved sanitation which follow socioeconomic development. House dust mite allergy is present in up to 90% of Asian atopic patients, far exceeding that which is seen in Western populations which report prevalences of only 50% to 70%. Pollen and animal dander affect less than 10% of Asian patients as compared to 40-70% of individuals with asthma and allergic rhinitis living in the West, a burden almost equivalent to the dust mite burden in those regions. There is thus a pressing need for preventive measures to reduce dust mite sensitization in Asian children today.

Keywords: Aeroallergen, Asia, allergy, house dust mites, sensitization

From:
[1] Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore
[2] Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore

Corresponding author:
Elizabeth Huiwen Tham
Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore
Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore
Email: elizabeth_tham@nuhs.edu.sg

Introduction

The prevalence of atopic dermatitis, allergic rhinitis and asthma has risen significantly in Asia over the last two decades.[1] These allergic diseases are now major contributors to the healthcare burden and morbidity in many countries. Treatment of established disease is mainly aimed at symptom control and allergen avoidance. Exposure to aeroallergens such as house dust mites, pollens, mould and animal dander is closely linked to sensitization, a significant risk factor for the development, persistence and severity of allergic airway disease in children.[2,3]

House dust mites (HDM) are ubiquitous in human habitats with a predilection for environments with high relative humidity. Human skin scales (keratin), cellulose from textile fibres and chitin, which are abundant in human living spaces, form essential components of the HDM diet, thus creating an inextricable link between human and HDM populations. *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* are the two pyrogliphid HDM species most implicated in allergic diseases. *Blomia tropicalis*, a storage mite, is also found in high concentrations in human homes in Asia and has been strongly linked to wheezing in children.[4,5] *Tyrophagus putrescentiae*, also a storage mite, thrives in hot, humid climates and is found mainly in grasslands, old hay, mushrooms and is a common pest of stored food products. It has also been referred to as the "mould mite".[6]

Differences in geography, climate and urbanization affect the global distribution of aeroallergens and correspondingly their sensitization patterns in humans. Studies indicate that climate change due to global warming, carbon dioxide emissions and rainfall patterns have altered the timing and severity of pollen, tree and grass seasons as well as indoor mould concentrations in various parts of the world over the last few decades.[7,8] Asia is host to diverse flora and fauna species which are unique to the tropical climate.[8] Aeroallergens in this part of the world are thus phylogenetically and ecologically distinct from those in other temperate climates.[7]

The Asian allergome and allergic disease phenotypes are distinct from those in Europe and the United States. Genetic polymorphisms described in Korean house dust mites are not found in those found in Western countries, but it is still not known if corresponding sensitized allergic phenotypes differ.[9] Genome wide association studies have also reported genetic susceptibility loci which are associated with atopic dermatitis and asthma in ethnic Asians.[10,11]

The interplay between the environment, socioeconomic development and allergens are distinctly shown in the Asian context. This review describes the demographics of aeroallergen distribution, sensitization patterns and their atopic phenotypes which are unique to this part of the world.

Aeroallergen sensitization patterns in Asian countries

Aeroallergen sensitization patterns in atopic individuals in various Asian countries, namely China, Hong Kong, India, Japan, Korea, Malaysia, Philippines, Singapore, Taiwan, Thailand and Vietnam are shown in the **Table 1 and Figure 1**.[5,12-30] No published data from Myanmar, Laos and Cambodia were available. Studies involving aeroallergen distribution alone without human sensitization, and those involving sensitization without associated atopy were not included. Most countries' data were published within the last 10 years and some had data from the preceding decade as well, which offered a comparison of aeroallergen sensitization changes over time.

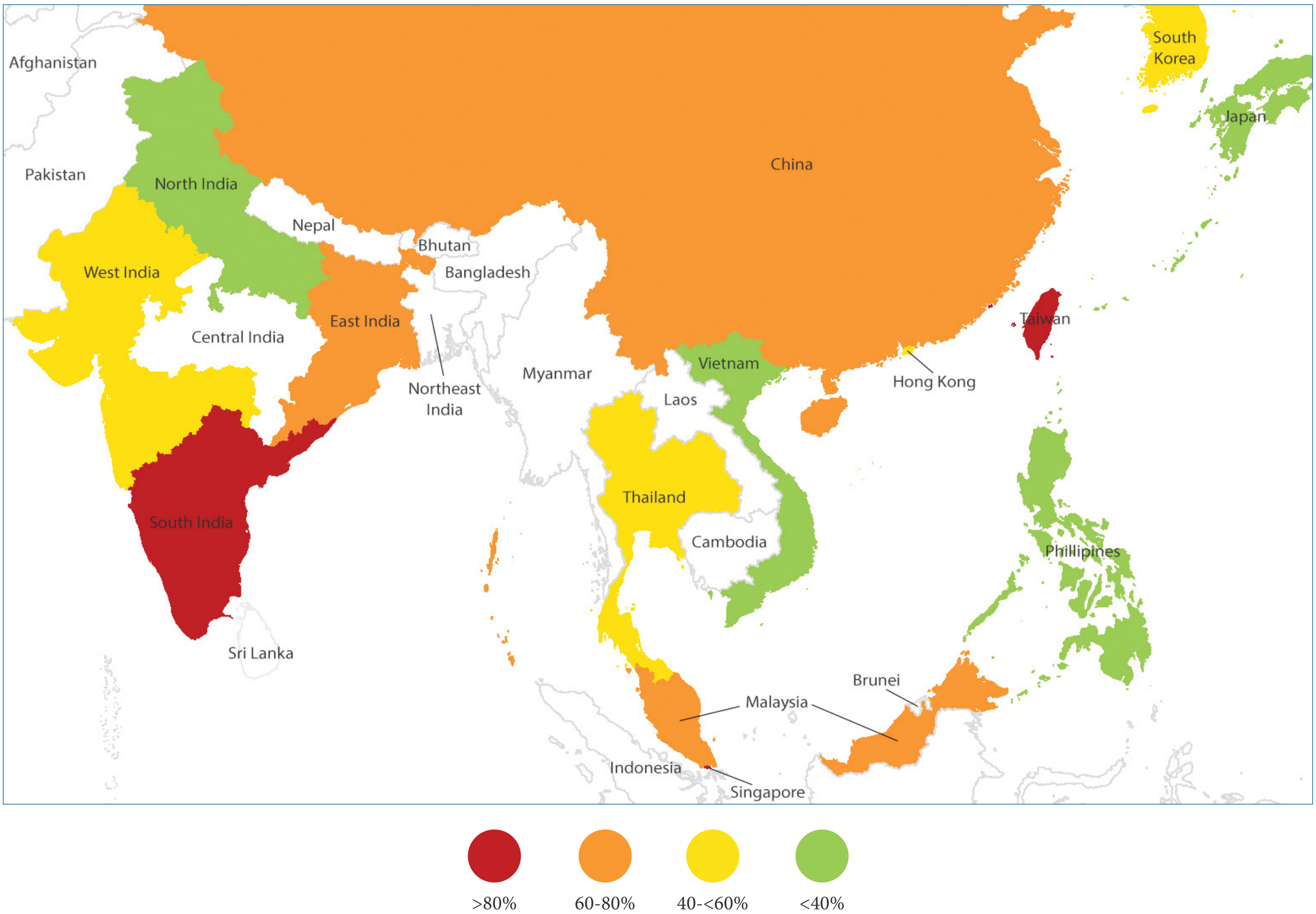
House dust mites (HDM) are by far the most common aeroallergen implicated in allergic individuals in Asian countries. The highest rates of HDM sensitization were reported in Singapore (70 to >90%), followed by Taiwan (85-90%) and South India (89.7%).[5,16,24,25] The lowest sensitization rates were described in North India (7.8%), Vietnam (9-23%) and Philippines (33-47%).[15,22,27]

Atopic Asians were mostly sensitized to the *Dermatophagoides* house dust mite species, with a slightly lower percentage sensitized to *Blomia Tropicalis*. However, exceptions were seen in Vietnam and Singapore (1999 data) where *Blomia Tropicalis* was instead the predominant mite in sensitized atopic individuals.

Sensitization to other aeroallergens was generally lower compared to mites across the Asian population. Cockroach, followed by mould and animal dander, and subsequently grass and tree pollen, in descending order of positivity, formed the remainder of aeroallergens commonly seen in Asia. Rates of sensitization to pollen were almost universally low among all the Asian countries with available data, except for South and East India where subtropical grasses abound and Japan, in which cedar pollinosis is a unique medical entity.[16,17]

Japanese cedar pollen is a major aeroallergen unique to Japan and has been implicated in allergic airway diseases in Japanese children.[31-33] The dispersed cedar pollen load in Japan increased significantly in the last 30 years following maturation of cedar forests planted after the Second World War. Reported sensitization rates in atopic Japanese ranged between 10-30%, second only to house dust mites.[34] Cedar pollen sensitization

Figure 1. House dust mite sensitization rates in atopic individuals in Asia



and allergic airway symptoms (termed cedar pollinosis) appeared to have a "cohort effect" in which the younger generations had a higher prevalence of pollinosis, possibly stemming from high exposures in early life which corresponded well with the environmental load.[35,36]

Aeroallergen sensitization patterns in Africa, Europe and the Americas

Different patterns of aeroallergen sensitization were seen in other parts of the world (**Table 2**).[37-47] In West Africa (Nigeria and Ghana), high prevalences of cockroach sensitization were seen in asthmatic children and adolescents, and cat dander was also a more significant allergen than in Asia. Dust mite sensitization levels were much lower than in Asia at only 50-60%.[37,38] Atopic patients in Europe and the United States were more highly sensitized to animal dander (cat and dog) and pollen than Asians.[39,42-44] Middle Eastern atopic subjects had the highest overall sensitization rates to all aeroallergens – dust mites, cockroach, animal dander, pollen and mould.[45-47]

Aeroallergen sensitization across age groups

Differences in aeroallergen sensitization by age were observed between Asian populations. In atopic Singaporean children, sensitization rates to *D. Pteronyssinus, D. Farinae* and *B. Tropicalis* were around 84.5% in children 3-5 years of age, and this prevalence increased with age to 97.3% in those above 14 years (**Table 1**).[5] A similar pattern of increasing dust mite sensitization with age was observed in Malaysian and Korean children with asthma.[20,48]

The converse was, however, true for atopic children in China, who showed higher mite, cat dander and mould sensitization rates than adults at the same time point.[12] Children aged 7-8 in Taipei also had a higher dust mite sensitization rate than individuals above the age of ten.[25,26]

Cockroach sensitization increased with age from only 28% in children 3-5 years of age to >70% in adults in Singapore.[5] A similar pattern was reported in the multicentre study in China.[12]

In Taiwan, elderly subjects above 50-70 years of age were found to have high sensitization levels to Tyrophagus putrescentiae, the storage mould mite, but this was not seen in adults younger than 40 years of age.[49,50] It was the third most common mite found in Korean homes but its link to allergic disease in the population remains controversial.[51]

Changes in aeroallergen sensitization over time periods

Interval data published at different time points in Asia provide a glimpse of possible shifting aeroallergen sensitization patterns over time. In 1999, Blomia tropicalis was reported to be the predominant mite in sensitized atopic Singaporeans.[5] A lower but still significant minority were also sensitized to cockroach, animal dander and mould (**Table 1**). However in 2005, Kidon et al reported that Dermatophagoides mites induced higher rates of sensitization than Blomia tropicalis in Singaporean children.[23]

Relative differences in sensitization to aeroallergen groups have also changed with time. A more recent study in Singaporean adults reported a sensitization profile that was overwhelmingly tilted towards dust mites with a much lower prevalence of other aeroallergens such as cockroach and animal dander compared to the study in 1999. The prevalence of mite sensitization was also at least equally distributed between *Dermatophagoides* and *Blomia* mites in this adult population, instead of a *Blomia* predominance as was previously seen.[24]

The high prevalence of sensitization to the storage mite *T. putrescentiae* in mainly elderly subjects in Taiwan in earlier studies in the 1990s appears to have waned with time. *T. putrescentiae* was no longer reported to be a major inhalant allergen in most parts of Asia including Taiwan in recent reports.[25]

Geographical variations

Epidemiological studies have shown that the worldwide distribution of aeroallergens such as dust mites and pollens demonstrate geographical and seasonal variations. Because of their natural inclination for hot and humid environments, house dust mite allergen levels vary across regions primarily based on environmental factors such as temperature and humidity.[52] Pollen allergens are also typically found in subtropical or temperate climates rather than in the tropics and their ambient levels vary throughout the year corresponding to their ecological seasons.[7,53]

Recent literature has also suggested that these geographical and seasonal fluctuations of aeroallergen exposure are linked to allergic sensitization, development and severity of allergic airway diseases, particularly in children.[7]

Geographical variations appear to be influenced by both climate and degree of urbanization. Singapore, a small tropical metropolitan city state with no rural provinces, has seen a staggering house dust mite burden in stark contrast to the relatively much lower prevalence of other environmental allergens.[24] Children living in rural Taiwan had lower rates of sensitization to *D. Pteronyssinus* in rural Taiwan compared to inhabitants of urban Taipei city.[54] Another study reported a lower proportion of sensitized individuals (45.9%) living in Chiayi county, a rural state in southwestern Taiwan, compared to those in Taipei (71.9%). Both of these regions share similar climatic conditions and relative humidity. Lee SY et al also described lower aeroallergen sensitization in Korean children living in rural farming communities compared to those in rural towns and urban areas (in increasing order) despite a likely higher allergen exposure in the farming environment.[55] Reports also described correspondingly higher prevalence rates of allergic airway diseases in urban residents.[56,57]

Gangwon province, a mainly mountainous county in northeast Korea with a temperate climate, reported low sensitization of only 15-17% to house dust mites.[58] In contrast, the prevalence of dust mite sensitization in Busan city in warmer southeast Korea was as high as 45-50%.[59] In China, a higher prevalence of HDM and cockroach sensitization was observed in south-western counties compared to the temperate northern regions.[12]

Pollen sensitization studies from various parts of India also demonstrate differences in prevalence. In northern India, only 10-14% of subjects were sensitized compared to 40-70% in South and East India.[15-17] Davies et al suggested that subtropical grass pollens such as those found in these regions may invoke a

Table 1. Aeroallergen sensitization patterns in atopic individuals in Asia

Country	Year	Age (yrs)	Atopic disease	House Dust Mites			Cockroach		Animal Dander		Pollen		Mould	Reference
				D. Pteronyssimus	*D. Farinae*	*Blomia Tropicalis*	*Blatella germanica*	Periplaneta Americana	Cat	Dog	Grass pollen	Tree pollen		
China (Guangzhou)	2012	5-72	AS, AR	80.3%	83.7%	66.3%	-	-	-	-	-	-	-	Zhang et al [13]
China (Multicentre)	2009	5-65	AS, AR	57.6%	59%	40.7%	11.5%	16.1%	10.3%	-	3.5%	2.2%	4.4%	Li J et al [27]
				Overall 87.2%										
Hong Kong	1996	12-18	AD, AR, AS	55.4%	-	-	25.7%		10.4%	2.3%	2.1%	-	23.4%	Leung et al [14]
India (West)	2015	1-3	AD, AR, AS	46.9%	24.5%	4.1%	-		-	-	-	-	-	Doshi et al
India (North)	2013	5-18	AS	7.8%			18.3%		-	7.8%	6.7%	6.7%	10-14%	Raj et al [15]
India (South)	2011	0-80	AS (Sinusitis, nasal polyposis)	89.7%			-	-	34.7%		75.8%		42.3%	Lal et al [16]
India (East)	2010	5-50	AS	75%	63.7%	72%	-	-	5.71%	9.23%	40-70%		10-20%	Podder et al [17]
Japan	2012	22-77	AS	34%			-	-	17%	16%	-		-	Shirai et al [18]
Korea	2014	11-19	AS	49.4%	52.9%	-	5.7%		8%	11.5%	10.3	3.4	-	Kim et al
	2005	7-15	AS	72.7%	70.9%	-	16.4%	-	-	-	-	-	14.5%	Choi et al [19]
Malaysia	2015	0-10	AD, AR, AS Urticaria	<2yr - 23.1% 2-10 yr - 63.3%	-	<2 yr - 16.7% 2-10 yr - 63.2%	-	-	-	-	-	-	-	Yadav et al [20]
	2005	>15	AR	-	-	-	-	-	-	-	5.9-14.1%	-	4.7-23.5%	Wan Ishlah et al [21]
Philippines	2011	16-21	AS	33.3%	47.1%	38.2%	-	-	-	-	-	-	-	Albano et al [22]
Singapore	2014	18-40	AR, AS	68.5%	-	68.9%	14.6%	-	2.9%	3.9%	6.8%	1.5%	1.5-2.4%	Andiappan et al [24]
	2005	2-16	AR +/- AD, AS	85%	62%	-	-	-	-	-	-	-	-	Kidon et al [23]
	1999	2-47	AD, AR, AS	Total 93.4% 3-5 yr - 84.5% 6-14 yr - 94.1% >14 yr - 97.3%	Total 92.3% 84.5% 93.2% 95.6%	Total 96.2% 93.1% 97.5% 96.5%	Total 56.4% 27.6% 52.5% 72.5%	Total 59.5% 29.3% 55.1% 79.6%	29.1% 27.6% 25.4% 33.6%	34.3% 17.2% 33.9% 43.3%	-	-	9.3-20.8% 6.9-12.1% 11.9-22.9% 8-23%	Kidon et al [23]
Taiwan (Taipei city)	2010	7-8	AD, AR, AS	90.8%	88.2%	84.6%	15.5%	16.7%	8.7%	29%	1.6-2%	-	2.3%	Wan et al [25]
	2005	10-85	AS +/- AD, AR	59.8%	56.8%	-	38.3%		10%	26.3%	3.5%	-	13.3%	Chiang et al [26]
Thailand	2009	3-11	AS	48.5%	48.5%	-	-	26.3%	7.1%	0%	1-10%	-	2%	Yuenyongviwat et al
	2004	3-11	AS	50.5%	52.5%	-	-	20.2	10.1%	0%	1-4%	-	3%	
Vietnam	2014	23-72	AR, AS	13.3%	9.7%	22.9%	13.1%		6.4%		2.1%	1.1%	1.5%	Lam et al [28]

AD = atopic dermatitis, AR = allergic rhinitis, AS = Asthma (Shaded rows indicate paediatric data)

Table 2. Aeroallergen sensitization patterns in atopic individuals in Africa, Europe, USA and the Middle East

Country	Year	Age (yrs)	Atopic disease	House Dust Mites			Cockroach		Animal Dander		Pollen		Mould	Reference
				D. Pteronyssimus	*D. Farinae*	*Blomia Tropicalis*	*Blatella germanica*	Periplaneta Americana	Cat	Dog	Grass pollen	Tree pollen		
Nigeria, Africa	2013	13-14	AS	48%			55%		42%	39%	41%	-	31%	Oluwole et al [37]
Ghana, Africa	2001	8-17	AS	62%	66%	-	30%		4%	0%	4%	4%	-	Addo-Yobo et al [38]
France	2003	18-50	AR	72%			-	-	25%	-	72%		10%	Bousquet et al [39]
Mexico	2014	2-11	AR	75%		-	-	-	-	-	25%	28%	10%	Larenas-Linneman et al [40]
		12-17	AR	72%		-	-	-	-	-	35%	35%	12%	
		>18	AR	46%		-	-	-	-	-	40%	55%	8%	
Sweden	2008	21-40	AR, AS	12%		-	-	-	52%	52%	52%	48%	8%	Warm et al [41]
Hawaii, USA	2014	>18	AS	68%	74%	-	42%		45%	27%	34%	-	18%	Min et al [42]
USA	2014	5m-15yrs	AS, AD	61%		-	-	-	80%	-	56%	-	-	Wisniewski et al [43]
Spain	2009	18-65	AR	84		-	-	-	-	-	76%	-	-	Sala-Cunill et al [44]
			AS	50%		-	-	-	-	-	47.9%	-	-	
Iran	2012	5-42	AR, AS	88-90%		-	-	-	75-77%		68-70%	73-75%	83%	Farrokhi et al [45]
Riyadh	2003	15-39	AR, AS	78%		-	19.2%		33.6%	-	53.8%	72.1%	18.2%	Almogren et al [46]
Israel	2010	16-44	AD, AR, AS	75%	78%	77%	15%		27%	8%	49%		7%	Sade et al [47]

AD = atopic dermatitis, AR = allergic rhinitis, AS = Asthma (Shaded rows indicate paediatric data)

greater allergic burden than tropical grasses.[53] With increasing global warming and carbon dioxide emissions, subtropical grass populations and pollen production are likely to increase, thus adding to the burden of allergic airway diseases in this part of the world.[60,61]

Seasonal variations

Seasonal fluctuations in environmental aeroallergen concentrations influence sensitization profiles as well as disease burden in Asia. In Korea, dust mite concentrations in bedding increased in spring (May to September) and declined between autumn and winter (October to May).[62] These seasonal changes were also reflected in skin test reactivity and mite-specific IgE antibodies in asthmatic patients.[63] In contrast, higher rates of dust mite sensitization were found in children born in winter months in Japan compared to those born in other seasons.[64]

China however, showed little variation in mite sensitization rates throughout the year across four different regions, but instead peaks in grass pollen sensitization rates were noted in August in the northern regions. These corresponded precisely to spikes in environmental pollen concentrations in the autumn.[12]

A multicentre study in Taiwan found that that visible mould was associated with asthma exacerbations in the winter and spring, while the presence of cockroaches was related to a higher asthma burden in the summer and fall.[65]

The tropical south-east Asian nations such as Malaysia and Thailand, however, reported mostly perennial allergic airway diseases with no seasonal variations.[66,67]

Aeroallergens and disease phenotypes

Dust mite sensitization is very strongly associated with wheezing and asthma in atopic Asians, especially children. HDM sensitization was linked to increased wheeze in Chinese adolescents living in Guangzhou.[3] Sensitization to aeroall ergens in general was positively associated with asthma and an earlier onset of more severe allergic airway diseases in China.[12] In Hong Kong, 85% of asthmatic children were aeroallergen-sensitized, with spirometric evidence of greater disease severity.[14] HDM sensitization in Singaporean pre-schoolers was also predictive of persistent wheeze in later childhood.[68] The early development of HDM-specific IgE in Japanese infants with atopic dermatitis was also a major risk factor for the development of asthma.[69]

In particular, *Blomia Tropicalis* (particularly Blo t5) was implicated in children with purely respiratory allergy (asthma and allergic rhinitis) compared to children with atopic dermatitis alone, who were sensitized more often to *D. Pteronyssinus*.[70] This association was also seen in asthmatic patients in Taiwan and India.[4,17]

Aeroallergen sensitization was found to be a risk factor in Chinese patients with concomitant allergic asthma and rhinitis, rather than either disease in isolation, and this risk increased further with polysensitization to multiple aeroallergens.[12] Vietnam, however, found associations between HDM and cockroach sensitization and allergic rhinitis, but not asthma, in their population.[27]

Mould sensitization may in fact play a larger role in allergic rhinitis in Asia than previously thought. This association was seen in 19% of Singaporean children with allergic rhinitis, especially in those living in homes without air-conditioning which predisposes to a warmer, moist environment.[71]

In other parts of the world, the burden of allergic airway diseases appears to be modulated through several other aeroallergens, rather than the HDM predominance observed in Asia. Cockroach and animal dander were shown to be strongly associated with asthma in African, European and American populations.[37,38,41] Studies in the United States have shown that sensitization to mould and animal dander (particularly cat) was significantly associated with increased asthma morbidity and severity in children, to a greater extent than mite allergy.[43,72,73]

Grass and tree pollen, rather than HDM, were strongly associated with allergic rhinitis in Europe.[53] Pollen allergic French and Spanish patients had more severe and persistent rhinitis phenotypes than those who were mite allergic.[39,44] Children living in the West also tended to have seasonal, rather than perennial, allergic disease patterns which correlate closely to the seasonal cycles of the specific pollen triggers.[74]

Discussion

Asia has seen rapid socioeconomic development and urbanization in the last half century, with many countries transitioning from mainly rural, agricultural societies to bustling cities. There has also been a shift towards a more indoor and Westernized lifestyle. These changes have in turn influenced the distribution and diversity of aeroallergens in the Asian environment.

Dust mite sensitization can now be said to be characteristic of the Asian atopic population as a whole. Data from most of the Asian countries have reported rates of greater than 60% and even up to 80% in sensitized atopic individuals. In contrast, the European Community Respiratory Health Survey I observed a much lower mean prevalence of HDM sensitization (21.7%) in their population.[75] A large multicentre study in the United States also described dust mite sensitization rates of only 20% in their population and an only slightly higher prevalence of grass sensitization (27%).[76] Dust mite sensitization in their children was much lower at less than 10%. Data in the warmer southern states showed a slightly higher prevalence of indoor aeroallergen sensitization, but none higher than 50% at most, unlike the staggering burden seen in Asia. Pollen sensitization in Asia, apart from Japan, generally has less medical significance in Asia than in the West.

Data from Singapore clearly demonstrates the shift in aeroallergen sensitization trends over the last 2 decades, from a wide variety of environmental aeroallergens in 1999 to almost universal house dust mite predominance in adults today.[24] Data in children in recent years is still unpublished, but the authors have noticed a clear similar trend in the clinical setting.

The diminishing importance of the storage mites *B. Tropicalis* and *T. putrescentiae* in Asia supports the notion that urbanization has exerted a significant environmental influence on the aeroallergen sensitization patterns over time. The loss of their natural habitat (hay, mould and agricultural land) to the development of modern cities has likely resulted in decliningmite populations and hence its sensitization prevalence in humans, compared to the more highly prevalent *Dermatophagoides* mite species today.

Apart from urbanization, dust mite population abundance and thus sensitization patterns in Asia are also influenced heavily by climatic conditions. Where both factors are favourable, such as in Singapore, significantly high levels of exposure and thus sensitization can be observed. In other regions where either factor may be less favourable for dust mite proliferation, lower and more variable levels are seen. However, the overall burden of dust mite sensitization in Asia is much higher than that seen in the United States and Europe, even in areas of similar climate and/or urbanization, which begs the question as to whether other factors such as genetics may play a role.

Human migration is a good indicator of the geographical determinants of aeroallergen sensitization. In Singapore, atopic migrants from China who initially demonstrated low house dust mite sensitization levels gradually developed increasing sensitization and eventually achieved levels similar to that of Singaporean-born adults after about 8 years of residence in Singapore.[24] This clearly indicates a strong environmental influence in Singapore. The reasons for such changes are likely multi-factorial. Given that this allergen is predominantly an indoor one, evidence suggests that urbanization of society with improved sanitation and a change in lifestyle patterns towards a more indoor, sedentary type has caused this shift in aeroallergen sensitization patterns over time.

Living in rural environments appears to be protective against allergic sensitization in general and the development of allergic disorders. Dust mite sensitization is the exception, with higher prevalence rates in city dwellers, which correlates with a higher mite-induced allergic airway disease burden in the urban community.[57] Postulated reasons for these geographical differences are likely multifactorial, comprising of complex interactions between antenatal exposures (the DoHAD hypothesis), epigenetics and lifestyle factors such as diet, breast feeding, siblings, livestock and microbial exposures which affect the microbiome in rural communities.[77]

Sensitization patterns and allergic airway disease exacerbations in the Western population are closely linked to pollen allergens. In Asia, however, grass and tree pollen play a minor role (except for Japanese cedar pollinosis) and house dust mites are instead the major players in the pathogenesis of allergic rhinitis and asthma. South-east Asian countries with stable year-round tropical climates typically do not experience wide fluctuations in environmental or indoor allergens such as dust mites and thus allergic disease phenotypes tend to be perennial rather than seasonal in these regions.

HDM sensitization is strongly implicated in earlier onset and greater severity of wheezing in Asia and the paediatric atopic population is exceptionally vulnerable. As early life factors set the stage for disease burden in older age, this emerging phenomenon should be taken seriously. Much more needs to be done to ameliorate the modifiable environmental risk factors such as dust mites in the Asian population to reduce the socioeconomic and healthcare burden of allergic diseases in Asia. There is also an urgent need for more studies to look into the primary prevention of house dust mite sensitization in young Asian children.

Acknowledgements

We would like to thank Ms Piraporn June Ohata for her kind assistance in the the graphical construction of the map in **Figure 1**.

Conflict of interest statement

All authors declare that they have no relevant conflicts of interest

References

1. Asher MI, Montefort S, Bjorksten B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet. 2006;368:733-43.
2. Wahn U, Lau S, Bergmann R, Kulig M, Forster J, Bergmann K, et al. Indoor allergen exposure is a risk factor for sensitization during the first three years of life. J Allergy Clin Immunol. 1997;99:763-9.
3. Li J, Wang H, Chen Y, Zheng J, Wong GW, Zhong N. House dust mite sensitization is the main risk factor for the increase in prevalence of wheeze in 13- to 14-year-old schoolchildren in Guangzhou city, China. Clinical and experimental allergy. 2013;43:1171-9.
4. Tsai JJ, Wu HH, Shen HD, Hsu EL, Wang SR. Sensitization to Blomia tropicalis among asthmatic patients in Taiwan. International archives of allergy and immunology. 1998;115:144-9.
5. Chew FT, Zhang L, Ho TM, Lee BW. House dust mite fauna of tropical Singapore. Clinical and experimental allergy. 1999;29:201-6.
6. Mullen GR, Durden LA. Medical and veterinary entomology: Academic Press; 2009.
7. Sheffield PE, Weinberger KR, Kinney PL. Climate change, aeroallergens, and pediatric allergic disease. The Mount Sinai journal of medicine, New York. 2011;78:78-84.
8. Seddon AW, Macias-Fauria M, Long PR, Benz D, Willis KJ. Sensitivity of global terrestrial ecosystems to climate variability. Nature. 2016;
9. Jeong KY, Lee IY, Yong TS, Lee JH, Kim EJ, Lee JS, et al. Sequence polymorphisms of Der f 1, Der p 1, Der f 2 and Der p 2 from Korean house dust mite isolates. Experimental & applied acarology. 2012;58:35-42.
10. Andiappan AK, Foo JN, Choy MW, Chen H, Common JE, Tang MB, et al. Validation of GWAS loci for atopic dermatitis in a Singapore Chinese population. The Journal of investigative dermatology. 2012;132:1505-7.
11. Shek LP, Tay AH, Goh DL, Lee BW. Ethnic differences in genetic susceptibility to atopy and asthma in Singapore. Annals of the Academy of Medicine, Singapore. 2000;29:346-50.
12. Li J, Sun B, Huang Y, Lin X, Zhao D, Tan G, et al. A multicentre study assessing the prevalence of sensitizations in patients with asthma and/or rhinitis in China. Allergy. 2009;64:1083-92.
13. Zhang C, Li J, Lai X, Zheng Y, Gjesing B, Spangfort MD, et al. House dust mite and storage mite IgE reactivity in allergic patients from Guangzhou, China. Asian Pacific journal of allergy and immunology. 2012;30:294-300.
14. Leung TF, Lam CW, Chan IH, Li AM, Ha G, Tang NL, et al. Inhalant allergens as risk factors for the development and severity of mild-to-moderate asthma in Hong Kong Chinese children. The Journal of asthma. 2002;39:323-30.
15. Raj D, Lodha R, Pandey A, Mukherjee A, Agrawal A, Kabra SK. Aeroallergen sensitization in childhood asthmatics in northern India. Indian pediatrics. 2013;50:1113-8.
16. Lal A, Sunaina Waghray S, Nand Kishore NN. Skin prick testing and immunotherapy in nasobronchial allergy: our experience. Indian journal of otolaryngology and head and neck surgery. 2011;63:132-5.
17. Podder S, Gupta SK, Saha GK. Incrimination of Blomia tropicalis as a Potent Allergen in House Dust and Its Role in Allergic Asthma in Kolkata Metropolis, India. The World Allergy Organization journal. 2010;3:182-7.
18. Shirai T, Yasueda H, Saito A, Taniguchi M, Akiyama K, Tsuchiya T, et al. Effect of exposure and sensitization to indoor allergens on asthma control level. Allergology international. 2012;61:51-6.
19. Choi SY, Sohn MH, Yum HY, Kwon BC, Kim KE. Correlation between inhalant allergen-specific IgE and pulmonary function in children with asthma. Pediatric pulmonology. 2005;39:150-5.
20. Yadav A, Naidu R. Clinical manifestation and sensitization of allergic children from Malaysia. Asia Pacific allergy. 2015;5:78-83.
21. Wan Ishlah L, Gendeh BS. Skin prick test reactivity to common airborne pollens and molds in allergic rhinitis patients. The Medical journal of Malaysia. 2005;60:194-200.
22. Albano PM, Ramos JD. Association of house dust mite-specific IgE with asthma control, medications and household pets. Asia Pacific allergy. 2011;1:145-51.
23. Kidon MI, Chiang WC, Liew WK, Lim SH, See Y, Goh A, et al. Sensitization to dust mites in children with allergic rhinitis in Singapore: does it matter if you scratch while you sneeze? Clinical and experimental allergy. 2005;35:434-40.
24. Andiappan AK, Puan KJ, Lee B, Nardin A, Poidinger M, Connolly J, et al. Allergic airway diseases in a tropical urban environment are driven by dominant mono-specific sensitization against house dust mites. Allergy. 2014;69:501-9.
25. Wan KS, Yang W, Wu WF. A survey of serum specific-lgE to common allergens in primary school children of Taipei City. Asian Pacific journal of allergy and immunology. 2010;28:1-6.
26. Chiang CH, Wu KM, Wu CP, Yan HC, Perng WC. Evaluation of risk factors for asthma in Taipei City. Journal of the Chinese Medical Association. 2005;68:204-9.
27. Lam HT, Ekerljung L, Bjerg A, Van TTN, Lundback B, Ronmark E. Sensitization to airborne allergens among adults and its impact on allergic symptoms: a population survey in northern Vietnam. Clinical and translational allergy. 2014;4:6.
28. Yuenyongviwat A, Koonrangsesomboon D, Sangsupawanich P. Recent 5-year trends of asthma severity and allergen sensitization among children in southern Thailand. Asian Pacific journal of allergy and immunology. 2013;31:242-6.
29. Doshi A, Tripathi DM. Early House Dust Mite Sensitivity in Mumbai Children. Indian journal of pediatrics. 2016;83:386-90.
30. Kim BS, Jin HS, Kim HB, Lee SY, Kim JH, Kwon JW, et al. Airway hyperresponsiveness is associated with total serum immunoglobulin E and sensitization to aeroallergens in Korean adolescents. Pediatric pulmonology. 2010;45:1220-7.

31. Masuda S, Takeuchi K, Yuta A, Okawa C, Ukai K, Sakakura Y. [Japanese cedar pollinosis in children in our allergy clinic]. Arerugi. 1998;47:1182-9.
32. Yamazaki S, Shima M, Nakadate T, Ohara T, Omori T, Ono M, et al. Patterns of Sensitization to Inhalant Allergens in Japanese Lower-Grade Schoolchildren and Related Factors. International archives of allergy and immunology. 2015;167:253-63.
33. Ozasa K, Hama T, Dejima K, Watanabe Y, Hyo S, Terada T, et al. A 13-year study of Japanese cedar pollinosis in Japanese schoolchildren. Allergology international. 2008;57:175-80.
34. Kaneko Y, Motohashi Y, Nakamura H, Endo T, Eboshida A. Increasing prevalence of Japanese cedar pollinosis: a meta-regression analysis. International archives of allergy and immunology. 2005;136:365-71.
35. Ozasa K, Dejima K, Hama T, Watanabe Y, Takenaka H. Exposure to Japanese cedar pollen in early life and subsequent sensitization to Japanese cedar pollen. Journal of epidemiology. 2000;10:42-7.
36. Okuda M. Epidemiology of Japanese cedar pollinosis throughout Japan. Annals of allergy, asthma & immunology. 2003;91:288-96.
37. Oluwole O, Arinola OG, Falade GA, Ige MO, Falusi GA, Aderemi T, et al. Allergy sensitization and asthma among 13-14 year old school children in Nigeria. African health sciences. 2013;13:144-53.
38. Addo-Yobo EO, Custovic A, Taggart SC, Craven M, Bonnie B, Woodcock A. Risk factors for asthma in urban Ghana. J Allergy Clin Immunol. 2001;108:363-8.
39. Bousquet J, Annesi-Maesano I, Carat F, Leger D, Rugina M, Pribil C, et al. Characteristics of intermittent and persistent allergic rhinitis: DREAMS study group. Clinical and experimental allergy. 2005;35:728-32.
40. Larenas-Linnemann D, Michels A, Dinger H, Shah-Hosseini K, Mosges R, Arias-Cruz A, et al. Allergen sensitization linked to climate and age, not to intermittent-persistent rhinitis in a cross-sectional cohort study in the (sub)tropics. Clinical and translational allergy. 2014;4:20.
41. Warm K, Hedman L, Lindberg A, Lotvall J, Lundback B, Ronmark E. Allergic sensitization is age-dependently associated with rhinitis, but less so with asthma. J Allergy Clin Immunol. 2015;136:1559-65.e1-2.
42. Min K, Yoshida M, Miike R, Tam E. Aeroallergen sensitivity in Hawai'i: association with asthma and increased prevalence of sensitivity to indoor allergens since 1966. Hawai'i journal of medicine & public health. 2014;73:9-12.
43. Wisniewski JA, Agrawal R, Minnicozzi S, Xin W, Patrie J, Heymann PW, et al. Sensitization to food and inhalant allergens in relation to age and wheeze among children with atopic dermatitis. Clinical and experimental allergy. 2013;43:1160-70.
44. Sala-Cunill A, Bartra J, Dalmau G, Tella R, Botey E, Raga E, et al. Prevalence of asthma and severity of allergic rhinitis comparing 2 perennial allergens: house dust mites and Parietaria judaica pollen. Journal of investigational allergology & clinical immunology. 2013;23:145-51.
45. Farrokhi S, Gheybi MK, Movahed A, Tahmasebi R, Iranpour D, Fatemi A, et al. Common aeroallergens in patients with asthma and allergic rhinitis living in southwestern part of Iran: based on skin prick test reactivity. Iranian journal of allergy, asthma, and immunology. 2015;14:133-8.
46. Almogren A. Airway allergy and skin reactivity to aeroallergens in Riyadh. Saudi medical journal. 2009;30:392-6.
47. Sade K, Roitman D, Kivity S. Sensitization to Dermatophagoides, Blomia tropicalis, and other mites in atopic patients. The Journal of asthma. 2010;47:849-52.
48. Shin JW, Sue JH, Song TW, Kim KW, Kim ES, Sohn MH, et al. Atopy and house dust mite sensitization as risk factors for asthma in children. Yonsei medical journal. 2005;46:629-34.
49. Yu SJ, Liao EC, Tsai JJ. House dust mite allergy: environment evaluation and disease prevention. Asia Pacific allergy. 2014;4:241-52.
50. Liao EC, Ho CM, Tsai JJ. Prevalence of Tyrophagus putrescentiae hypersensitivity in subjects over 70 years of age in a veterans' nursing home in Taiwan. International archives of allergy and immunology. 2010;152:368-77.
51. Ree HI, Jeon SH, Lee IY, Hong CS, Lee DK. Fauna and geographical distribution of house dust mites in Korea. The Korean journal of parasitology. 1997;35:9-17.
52. Thomas WR. Geography of house dust mite allergens. Asian Pacific journal of allergy and immunology. 2010;28:211-24.
53. Davies JM. Grass pollen allergens globally: the contribution of subtropical grasses to burden of allergic respiratory diseases. Clinical and experimental allergy. 2014;44:790-801.
54. Chang JW, Lin CY, Chen WL, Chen CT. Higher incidence of Dermatophagoides pteronyssinus allergy in children of Taipei city than in children of rural areas. Journal of microbiology, immunology, and infection. 2006;39:316-20.
55. Lee S, Kwon J, Seo J, Song Y, Kim B, Yu J, et al. Prevalence of atopy and allergic diseases in Korean children: associations with a farming environment and rural lifestyle. International archives of allergy and immunology. 2012;158:168-74.
56. Myong JP, Kim H, Lee K, Chang S. Time trends of allergic rhinitis and effects of residence on allergic rhinitis in Korea from 1998 through 2007-2009. Asian nursing research. 2012;6:102-6.
57. Song WJ, Sohn KH, Kang MG, Park HK, Kim MY, Kim SH, et al. Urban-rural differences in the prevalence of allergen sensitization and self-reported rhinitis in the elderly population. Annals of allergy, asthma & immunology. 2015;114:455-61.
58. Lee MK, Lee WY, Yong SJ, Shin KC, Lee SN, Lee SJ, et al. Sensitization rates to inhalant allergens in patients visiting a university hospital in Gangwon region. Korean Journal of Asthma, Allergy and Clinical Immunology. 2011;31:27-32.
59. Seo HR, Lee SM, Koo TH, Shin BC, Kim BK, Heo JH, et al. Sensitization rate to Tetranychus urticae and house dust mite in patients who visited the allergy clinic with allergic diseases in Busan area. Korean Journal of Asthma, Allergy and Clinical Immunology. 2007;27:263-7.
60. Morgan JA, LeCain DR, Pendall E, Blumenthal DM, Kimball BA, Carrillo Y, et al. C4 grasses prosper as carbon dioxide eliminates desiccation in warmed semi-arid grassland. Nature. 2011;476:202-5.
61. Beggs PJ, Bennett CM. Climate change, aeroallergens, natural particulates, and human health in Australia: state of the science and policy. Asia-Pacific journal of public health. 2011;23:46s-53.
62. Kim JH, Choi SY, Lee IY, Lee YW, Yong TS, Kim CW, et al. Seasonal variation of house dust mite and its influence on the inhabitant health. Korean Journal of Asthma, Allergy and Clinical Immunology. 2006;26:27-34.
63. Nahm D-H, Park H-S, Kang S-S, Hong C-S. Seasonal variation of skin reactivity and specific IgE antibody to house dust mite. Annals of Allergy, Asthma & Immunology. 1997;78:589-93.
64. Saitoh Y, Dake Y, Shimazu S, Sakoda T, Sogo H, Fujiki Y, et al. Month of birth, atopic disease, and atopic sensitization. Journal of investigational allergology & clinical immunology. 2001;11:183-7.
65. Han YY, Lee YL, Guo YL. Indoor environmental risk factors and seasonal variation of childhood asthma. Pediatr Allergy Immunol. 2009;20:748-56.
66. Asha'ari ZA, Yusof S, Ismail R, Che Hussin CM. Clinical features of allergic rhinitis and skin prick test analysis based on the ARIA classification: a preliminary study in Malaysia. Annals of the Academy of Medicine, Singapore. 2010;39:619-24.
67. Bunnag C, Jareoncharsri P, Tantilipikorn P, Vichyanond P, Pawankar R. Epidemiology and current status of allergic rhinitis and asthma in Thailand -- ARIA Asia-Pacific Workshop report. Asian Pacific journal of allergy and immunology. 2009;27:79-86.
68. Llanora GV, Ming LJ, Wei LM, van Bever HP. House dust mite sensitization in toddlers predict persistent wheeze in children between eight to fourteen years old. Asia Pacific allergy. 2012;2:181-6.
69. Ohshima Y, Yamada A, Hiraoka M, Katamura K, Ito S, Hirao T, et al. Early sensitization to house dust mite is a major risk factor for subsequent development of bronchial asthma in Japanese infants with atopic dermatitis: results of a 4-year followup study. Annals of allergy, asthma & immunology. 2002;89:265-70.
70. Shek LP, Chong AR, Soh SE, Cheong N, Teo AS, Yi FC, et al. Specific profiles of house dust mite sensitization in children with asthma and in children with eczema. Pediatr Allergy Immunol. 2010;21:e718-22.
71. Kidon MI, See Y, Goh A, Chay OM, Balakrishnan A. Aeroallergen sensitization in pediatric allergic rhinitis in Singapore: is air-conditioning a factor in the tropics? Pediatr Allergy Immunol. 2004;15:340-3.
72. Gent JF, Kezik JM, Hill ME, Tsai E, Li DW, Leaderer BP. Household mold and dust allergens: exposure, sensitization and childhood asthma morbidity. Environmental research. 2012;118:86-93.
73. Rosenbaum PF, Crawford JA, Anagnost SE, Wang CJ, Hunt A, Anbar RD, et al. Indoor airborne fungi and wheeze in the first year of life among a cohort of infants at risk for asthma. Journal of exposure science & environmental epidemiology. 2010;20:503-15.
74. Meltzer EO, Blaiss MS, Derebery MJ, Mahr TA, Gordon BR, Sheth KK, et al. Burden of allergic rhinitis: results from the Pediatric Allergies in America survey. J Allergy Clin Immunol. 2009;124:S43-70.

75. Bousquet PJ, Chinn S, Janson C, Kogevinas M, Burney P, Jarvis D. Geographical variation in the prevalence of positive skin tests to environmental aeroallergens in the European Community Respiratory Health Survey I. Allergy. 2007;62:301-9.
76. Salo PM, Arbes SJ, Jr., Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. J Allergy Clin Immunol. 2014;134:350-9.
77. Waterland RA, Michels KB. Epigenetic epidemiology of the developmental origins hypothesis. Annu Rev Nutr. 2007;27:363-88.