

Time trends of co-existing atopic conditions in Singapore school children: prevalence and related factors

Wang XS, Shek LP, Ma S, Soh SE, Lee BW, Goh DYT. Time trends of co-existing atopic conditions in Singapore school children: prevalence and related factors.

Pediatr Allergy Immunol 2009.

© 2009 The Authors

Journal compilation © 2009 Blackwell Munksgaard

Atopic diseases are known to co-exist and are interrelated. Their co-existence in a patient increases disease burden and morbidity. We sought to study the prevalence of co-existing atopic conditions over time and its associated risk factors among Singapore children. Data was collected from two respective The International Study of Asthma and Allergies in Childhood surveys conducted in 1994 and 2001. Data on asthma, rhinitis and eczema were obtained from the responses to questions about wheezing, exercise-induced wheezing, nocturnal cough, rhinitis symptoms, rash, and diagnoses of asthma, rhinitis and eczema in the last 12 months. Data on demographic and known risk factors were also obtained. The prevalence of children who have had more than one atopic disorder increased significantly from 6.0% in 1994 to 10.2% in 2001 ($p < 0.001$). Parental history of atopic disease, maternal educational level, male gender and smoke exposure were significantly associated with co-existent atopic symptoms in the child. Among Singapore schoolchildren, there was a significant prevalence of co-existent atopic disease and this prevalence was rising. The influences of both genetic and environmental factors were likely to have contributed to these observations.

**Xiao Shan Wang¹, Lynette P. Shek^{1,2},
Stefan Ma³, Shu E Soh¹, Bee Wah Lee¹
and Daniel Y. T. Goh^{1,2}**

¹Department of Paediatrics, National University of Singapore, Singapore, ²Department of Paediatrics, National University Hospital, Singapore, ³Ministry of Health, Singapore

Key words: asthma; eczema; allergic rhinitis; prevalence; co-existing; atopy; Singapore

Assoc. Prof. Daniel Goh, Department of Paediatrics, National University Hospital 5, Lower Kent Ridge Road, Singapore 119074

Tel.: +65 67724112

Fax: +65 67797486

E-mail: paegohyt@nus.edu.sg

Accepted 5 February 2009

Atopic diseases, including asthma, allergic rhinitis and eczema are common disorders in children, especially in westernized and industrialized countries (1). The burden of these diseases in terms of quality of life and societal cost are considerable (2, 3). Since atopic diseases are interrelated, their effects on disease morbidity is expected to be accentuated when individuals have co-existent disease. The presence of rhinitis or eczema increases the risk of asthma (4–6). Furthermore, rhinitis has been shown to be an independent risk factor for asthma (5, 7). Treating nasal symptoms have been observed to have protective effects on asthma status (8–10). A common genetic basis has been found for this interrelationship (11, 12).

Although several studies have described co-existence of multiple atopic conditions (13, 14), no study has reported temporal changes in relation to their prevalence and related risk factors. The objective of this study is to describe changes in the prevalence of co-existing (>1) atopic conditions in Singapore schoolchildren based on data obtained from two The International Study of Asthma and Allergies in Childhood (ISAAC) surveys 7 yr apart.

Methods

Sampling methods and data collection procedure for the 1994 and 2001 ISAAC surveys have been described in previous reports (15). In brief,

6–7 yr-old primary school children (total numbers were 2030 in 1994 and 5305 in 2001) and 13–14 yr-old secondary students (4208 in 1994, 4058 in 2001) from randomly selected schools were surveyed in 1994 and 2001, according to ISAAC protocol. The standard ISAAC core questions were used in both surveys. The method of data collection was identical between the two surveys. Questions regarding environmental risk factors related to atopic diseases were included only in the 2001 survey.

The co-existence of more than one atopic condition was deduced from the responses to core questions about wheezing, exercise-induced wheezing, nocturnal cough, rhinitis symptoms, rash, and diagnoses of asthma, rhinitis and eczema in the last 12 months at the time of survey interview. For example, a subject would be classified as having co-existence of asthma and allergic rhinitis when he or she reported asthma symptoms (either wheeze, exercise-induced wheeze or nocturnal cough) and rhinitis symptoms (sneezing or runny or blocked nose with no cold or flu).

Data on monthly household income was collected in 6–7 yr-old schoolchildren and classified into quartiles based on national data on family income as <S\$2000, S\$2000–3999, S\$4000–5999 and ≥S\$6000. Data on mother's highest education level were also obtained (classified as primary, secondary and tertiary levels). Maternal or paternal history of atopic disease was obtained based on reports of any history of doctor-diagnosed atopic disease (asthma, eczema and allergic rhinitis). The number of smokers in a family was classified as: none, 1 and ≥2. The number of siblings within the same household was classified as: none, 1, 2 and ≥3.

SAS-callable SUDAAN V8.02 (Research Triangle Institute (RTI), North Carolina, USA) was applied for statistical analyses. Weighted multiple logistic regression models were applied for adjusting potential confounding factors, i.e. age, sex,

ethnic group, and socio-economical status (as reflected by type of residential housing and monthly household income), when comparing prevalence between two surveys. Weights were calculated based on the selection probability of schools and the response probabilities (estimated using response rate at school level and at subject level). A sampling design without replacement was chosen in estimation of prevalence.

For studying associated risk factors with co-existing atopic disease, only data from 6–7 yr-old schoolchildren in 2001 survey were included in the data analyses as surveyed covariates were collected only for this particular group. In all weighted multiple logistic regression models, in the outcome variable, subjects without any atopic symptoms were used as comparison group.

Results

Symptoms of multiple atopic conditions

The percentage of children without any of the atopic conditions fell from 68.7 to 46.1% in the 6–7 yr-old and 45.9 to 39.5% in the 13–14 yr-old students from 1994 to 2001. The overall prevalence of children having more than one atopic disorder increased from 6.0% in 1994 to 10.2% in 2001 amongst Singapore school children ($p < 0.001$ after adjustment for gender, age group, ethnic group and housing type). Table 1 shows that subjects who reported having symptoms of both asthma and allergic rhinitis increased from 13.9% in 1994 to 17.7% in 2001 among 13–14 yr-old students, although there was no increase observed in the 6–7 yr age group. For all remaining combinations of allergic disorders and for both age groups, however, it was observed that the prevalence of symptoms of eczema and allergic rhinitis, eczema and asthma, and of all three atopic conditions increased significantly over the period of the two surveys,

Table 1. Crude prevalence, % of co-existent atopic conditions based on current (last 12 months) symptoms

Atopic condition*	6–7 yr-old				13–14 yr-old			
	1994	2001	Crude p	Adjusted p†	1994	2001	Crude p	Adjusted p‡
Asthma and allergic rhinitis	13.8 (269/1954)	11.9 (620/5221)	0.030	0.658	13.9 (579/4169)	17.7 (718/4046)	0.000	0.000
Eczema and allergic rhinitis	0.7 (14/1939)	3.7 (193/5154)	0.000	0.000	3.5 (145/4183)	4.7 (190/4027)	0.004	0.022
Eczema and asthma	1.2 (23/1936)	4.0 (207/5224)	0.000	0.000	3.2 (134/4188)	4.7 (190/4049)	0.000	0.006
All three conditions	0.7 (14/1961)	3.4 (180/5227)	0.000	0.000	3.2 (132/4190)	4.3 (175/4050)	0.005	0.016

*Asthma symptoms – wheeze, exercise-induced wheeze or nocturnal cough; symptoms of allergic rhinitis: rhinitis apart from cold; symptoms of eczema: rash with typical distribution.

†Adjusted for age, sex, ethnic group, housing type and household income.

‡Adjusted for age, sex, ethnic group, and housing type.

Figures in bold denote statistical significance $p < 0.05$.

even after adjustment for age, sex, ethnic group and housing type.

Risk factors for co-existent atopic conditions among 6–7 yr-old school children in 2001 survey

Table 2 shows the results of weighted multiple logistic regression analyses. Paternal and maternal histories of atopic diseases were significantly associated with co-existent atopic conditions. On the combination of asthma and allergic rhinitis, the adjusted odds ratio (OR) was 2.30 [95% confidence interval (95%CI): 1.78–2.99] for the effect of paternal history of any atopic condition and 3.07 (95%CI: 2.40–3.92) for the effect of maternal history of atopy. A higher level of mother's education was also associated with increased risk of multiple atopic conditions. Male school children were more likely to have

the combination of asthma and allergic rhinitis (OR: 1.53, 95% CI: 1.24–1.90). Children whose families had two or more smokers were 1.61 (95% CI: 1.02–2.54) times more likely to have both asthma and allergic rhinitis than those without smokers in families. Compared to Chinese, less Malay students had the combination of both asthma and allergic rhinitis symptoms.

Discussion

This study further supports the common understanding that all three atopic conditions are interrelated, and that the interrelationship would be affected by genetic and environmental factors. Parental histories of atopic disease and mothers' education level positively influenced the co-existence of atopic conditions in their children.

Table 2. Adjusted OR with 95% CI obtained from four different combination of atopic conditions among 6–7 yr-old school children in 2001 survey

Risk factor	Report symptoms of both asthma and allergic rhinitis	Report symptoms of both eczema and allergic rhinitis	Report symptoms of both eczema and asthma	Report symptoms of all three conditions
	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Sex				
Male	1.53 (1.24–1.90)	1.26 (0.90–1.76)	1.11 (0.80–1.54)	1.23 (0.85–1.76)
Female	1.00	1.00	1.00	1.00
Ethnic group				
Chinese	1.00	1.00	1.00	1.00
Malay	0.60 (0.43–0.82)	1.10 (0.68–1.78)	1.28 (0.80–2.05)	1.12 (0.67–1.85)
Indian	0.82 (0.54–1.24)	0.77 (0.40–1.48)	1.21 (0.67–2.17)	0.78 (0.39–1.55)
Household income (S\$)				
<2000	1.00	1.00	1.00	1.00
2000–3999	0.86 (0.65–1.15)	0.87 (0.53–1.40)	0.89 (0.56–1.44)	1.00 (0.60–1.68)
4000–5999	0.84 (0.59–1.20)	1.03 (0.61–1.74)	1.28 (0.76–2.16)	1.39 (0.80–2.41)
≥6000	1.08 (0.74–1.56)	1.14 (0.65–2.01)	1.39 (0.79–2.44)	1.28 (0.70–2.34)
Mother education				
Primary	1.00	1.00	1.00	1.00
Secondary	1.65 (1.20–2.26)	3.58 (1.78–7.21)	3.06 (1.60–5.87)	4.75 (2.01–11.20)
Tertiary	1.93 (1.27–2.95)	4.58 (2.10–9.99)	2.79 (1.33–5.84)	7.70 (3.08–19.23)
Maternal history*				
Yes	3.07 (2.40–3.92)	4.18 (2.92–5.99)	3.24 (2.25–4.68)	4.83 (3.28–7.11)
No	1.00	1.00	1.00	1.00
Paternal history*				
Yes	2.30 (1.78–2.99)	2.99 (2.07–4.33)	3.10 (2.15–4.47)	3.76 (2.52–5.60)
No	1.00	1.00	1.00	1.00
Number of smokers				
0	1.00	1.00	1.00	1.00
1	0.96 (0.75–1.22)	0.89 (0.60–1.31)	0.97 (0.66–1.41)	0.89 (0.58–1.35)
≥2	1.61 (1.02–2.54)	1.11 (0.53–2.34)	0.92 (0.41–2.05)	0.86 (0.40–1.82)
Number of siblings				
0	1.00	1.00	1.00	1.00
1	1.08 (0.73–1.61)	1.11 (0.63–1.95)	1.03 (0.60–1.78)	1.38 (0.74–2.58)
2	1.16 (0.77–1.76)	0.80 (0.43–1.47)	0.74 (0.41–1.33)	0.92 (0.47–1.80)
≥3	0.87 (0.52–1.46)	0.75 (0.35–1.62)	0.69 (0.32–1.47)	1.04 (0.45–2.42)

OR, odds ratio; 95% CI, 95% confidence interval.

*History of any diagnosed atopic disease.

Comparison group: individuals with no atopic condition.

Figures in bold denote statistical significance $p < 0.05$.

The comparison of the global data obtained from the ISAAC Phase I study found that the prevalence of co-existent atopic conditions was higher in English-speaking western countries compared to other areas, in which the prevalence of multiple conditions was widely different from 0.3% to 18.5%, even between centres with populations of similar ethnic origins (1). Our study shows that prevalence of more than one atopic disorder in Singapore schoolchildren was 10.2% in the 2001 survey, rising significantly from 6.0% in 1994. This increase is caused by the combination of conditions and not by merely one factor as it was observed in the previous report that there was a reduction in asthma symptoms and no significant difference in eczema in the 6–7 yr age group. However, the co-existence of eczema and asthma symptoms increased significantly from 1.2% to 4.0% (Table 1). Our previous report showed that the prevalence of allergic rhinitis remained at the same level from 1994 to 2001, and that only eczema prevalence significantly increased in both age groups (15). In this analysis, prevalence of co-existence of symptoms of asthma or allergic rhinitis with eczema also increased, indicating an increased overlap of eczema with asthma or allergic rhinitis in affected children. Although no other study has previously examined the temporal change in the co-existence of multiple atopic conditions, several other studies have noted the strong association between these diseases. In a ISSAC Phase II study in Turkish children, it was found that asthma and eczema were significantly associated with rhinitis (16).

Mothers' education levels had significant influence on co-existent atopic conditions in these students. A mother's education level may be a surrogate of life style patterns that influence the development of atopic disorders. Passive smoking was significantly associated with an increased risk of co-existent asthma and allergic rhinitis symptoms, indicating that the respiratory system as a whole can be affected by passive smoking (17). An ISAAC Phase III study conducted in the Pacific found that passive smoking is a risk factor for all three forms of atopic conditions – asthma, allergic rhinitis and eczema (18).

Limitations of this study include the use of screening questionnaires and no clinical examination or allergy skin tests were performed to confirm the symptoms. The risk factors for co-existent atopic conditions were only available for 6–7 yr-old school children in the 2001 survey and no comparisons between age groups or time trends can be examined.

In summary, a considerable proportion of Singapore children and adolescents with atopic symptoms had symptoms for more than one atopic condition and prevalence of multiple conditions increased from 1994 to 2001. Environmental factors are likely to have a role on these trends as the effect of different risk factors in our population is not known.

References

1. WORLDWIDE VARIATION IN PREVALENCE OF SYMPTOMS OF ASTHMA, ALLERGIC RHINOCONJUNCTIVITIS, AND ATOPIC ECZEMA: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998; 351: 1225–32.
2. ACCORDINI S, COSSICO A, CERVERI I, et al. The socio-economic burden of asthma is substantial in Europe. *Allergy* 2008; 63: 116–24.
3. LEWIS-JONES S. Quality of life and childhood atopic dermatitis: the misery of living with childhood eczema. *Int J Clin Pract* 2006; 60: 984–92.
4. GUSTAFSSON D, SJOBERG O, FOUCARD T. Development of allergies and asthma in infants and young children with atopic dermatitis – a prospective follow-up to 7 years of age. *Allergy* 2000; 55: 240–5.
5. LEYNAERT B, BOURQUET J, NEUKIRCH C, et al. Perennial rhinitis: an independent risk factor for asthma in nonatopic subjects: results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1999; 104 (2 Pt 1): 301–4.
6. BERGMANN RL, EDENHORTE G, RERGMANN KE, et al. Atopic dermatitis in early infancy predicts allergic airway disease at 5 years. *Clin Exp Allergy* 1998; 28: 965–70.
7. GUERRA S, SHERRILL DL, MORTINEZ FD, RARBEE RA. Rhinitis as an independent risk factor for adult-onset asthma. *J Allergy Clin Immunol* 2002; 109: 419–25.
8. WILSON AM, ORR LC, SIMS EJ, et al. Antiasthmatic effects of mediator blockade versus topical corticosteroids in allergic rhinitis and asthma. *Am J Respir Crit Care Med* 2000; 162 (4 Pt 1): 1297–301.
9. ADAMS RJ, FUHLBRIGGE AL, FINKELSTEIN JA, WEISS ST. Intranasal steroids and the risk of emergency department visits for asthma. *J Allergy Clin Immunol* 2002; 109: 636–42.
10. CRYSTAL-PETERS J, WESLUSAN C, CROWN WH, TORRES A. Treating allergic rhinitis in patients with comorbid asthma: the risk of asthma-related hospitalizations and emergency department visits. *J Allergy Clin Immunol* 2002; 109: 57–62.
11. COOKSON W. The immunogenetics of asthma and eczema: a new focus on the epithelium. *Nat Rev Immunol* 2004; 4: 978–88.
12. BLUMENTHAL MN. New thoughts regarding the genetics of atopy. *Am J Respir Crit Care Med* 2004; 169: 555–6.
13. MASUDA S, FUJISAWA T, KATSUMATA H, et al. High prevalence and young onset of allergic rhinitis in children with bronchial asthma. *Pediatr Allergy Immunol* 2008; 19: 517–522.
14. PERONI DG, PIACENTINI GL, CERAVOLO R, BONER AL. Difficult asthma: possible association with rhinosinusitis. *Pediatr Allergy Immunol* 2007; 18 (Suppl. 18): 25–7.

The prevalence of co-existent atopic disease in Singapore children is rising

15. WANG XS, TAN TN, SHEK LP, et al. The prevalence of asthma and allergies in Singapore; data from two ISAAC surveys seven years apart. *Arch Dis Child* 2004; 89: 423–6.
16. KUYUCU S, SARAÇLAR Y, TUNCER A, et al. Epidemiologic characteristics of rhinitis in Turkish children: the International Study of Asthma and Allergies in Childhood (ISAAC) phase 2. *Pediatr Allergy Immunol* 2006; 17: 269–77.
17. BOUSQUET J, JACOT W, VIGNOLA AM, et al. Allergic rhinitis: a disease remodeling the upper airways? *J Allergy Clin Immunol* 2004; 113: 43–9.
18. FOLIAKI S, ANNESI-MAESANO I, TUUAU-POLOI N, et al. Risk factors for symptoms of childhood asthma, allergic rhinoconjunctivitis and eczema in the Pacific: an ISAAC Phase III study. *Int J Tuberc Lung Dis* 2008; 12: 799–806.