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Increasing prevalence of allergic rhinitis but not asthma among children in Hong Kong from 1995 to 2001 (Phase 3 International Study of Asthma and Allergies in Childhood)

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There is a worldwide belief that the prevalence of asthma and other allergic diseases is increasing but the measures used in many studies are susceptible to systematic errors. We examined the trend of asthma, allergic rhinitis and eczema prevalence in school children aged 6–7 years in Hong Kong from 1995 to 2001 using standardized ISAAC methodology. There were 4448 and 3618 children participating in 2001 and 1995, respectively. The prevalence of life-time rhinitis (42.4% vs. 38.9%, $p < 0.01$), current rhinitis (37.4% vs. 35.1%, $p < 0.03$), current rhinoconjunctivitis (17.2 vs. 13.6%, $p < 0.01$) and life-time eczema (30.7% vs. 28.1%, $p = 0.01$) increased significantly. There was no significant change in prevalence of life-time asthma, life-time wheeze and current wheeze albeit a significant increase in severe asthma symptoms. We investigated a number of potential risk factors including sex, family history of atopy, sibship size, birth weight, respiratory tract infections, pet ownership and exposure to tobacco smoke. However, the increases in prevalence of rhinitis and eczema could not be entirely explained by the change of prevalence of these risk factors. The odds ratio OR for the study period remained significantly associated with current rhinitis (OR 1.31, 95% confidence intervals CI 1.17–1.46), current rhinoconjunctivitis (OR 1.63, 95% CI 1.41–1.87) and life-time eczema (OR 1.30, 95% CI 1.16–1.45) after adjustment for these confounding variables using logistic regression model. Further study is warranted to elucidate the factors contributing to the observable change in the prevalence of rhinitis in our population.

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There is a worldwide belief that the prevalence of asthma and related allergies is increasing. Nevertheless, changes in diagnostic labeling, heightened awareness of the problem and presence of selection or information bias in previous studies can lead to false interpretation of changes rather than a genuine increase in morbidity (1). It is envisaged that studies using standardized questions and objective measurements can reflect more accurately the trend in asthma prevalence. This is important not only for understanding the etiology of the disease but also for good planning of local health resources.

The International Study of Asthma and Allergies in Childhood (ISAAC) program, using standardized international methods, was designed to allow comparisons of the prevalence of these disorders between populations in different countries and form the basis of further studies to investigate factors that potentially lead to these international patterns (2–5). We participated in this international program in 1995 and

showed that the prevalence of allergic disorders in school children 6–7 yr of age in Hong Kong was comparable with that in Singapore and Great Britain (6). Hong Kong has experienced great economic turmoil and political change over the past 5 yr. Hence, we attempted to re-collect data regarding childhood asthma and allergies in children of school age to compare the trend of prevalence over the past 5 yr using this standardized international methodology.

Methods

The methods for the 1995 survey have been described previously (6) and were repeated in the 2001 survey, i.e. with the same sampling frame, same age group, comparable sample sizes, same questionnaire, same translation and similar time frame of the respective years (with >95% of questionnaires distributed to school during March, April and May) for data collection. The two surveys were approved by the ethics committee of The University of Hong Kong.

Subjects

Each primary school in Hong Kong was given a number and a random list was generated. Schools were approached in the order of the random list and were recruited to participate if consent from the school was obtained. The first 25 primary schools that consented provided an adequate number of 6–7-yr-old children to participate in the study. Four schools were from the Hong Kong Island, 11 were from Kowloon and the remaining 10 were from the New Territories. Individually labeled questionnaires were distributed via the schools with instructions for the children to take them home for their parents to complete. A second identical questionnaire was sent again to non-responders, 1 wk later.

Questionnaire

The ISAAC questionnaires for asthma, rhinitis, and eczema were translated into Chinese following the ISAAC protocol. For question 1 on wheezing, several translated terms including a description of breathing sound of 'HeHe' were used to facilitate recognition of the symptom of wheezing. Because of the rarity and unfamiliarity of hay fever in Hong Kong, the Chinese term for 'pollenosis' was used instead. A question using the Chinese term of allergic rhinitis that was commonly used in our locality was added at the end of the core questionnaire. Some questions on potential factors with wheezing were added in the 1995 survey and were repeated in the 2001 survey. All of these questions were added after the core questions.

Statistical analysis

The prevalence of symptoms of asthma, rhinitis, and itchy rash were 9.2%, 35.1%, and 4.2%, respectively, with a study population of 3618 in our previous study. A sample size of 3000 is required to detect annual changes in prevalence of symptoms of asthma and other allergic diseases of 0.4–0.6% 5 yr after our last study with a power of 90% at the 5% level of significance. All questionnaires were entered twice onto a personal computer. Missing answers were merged with negative answers in the analysis, according to instructions from ISAAC. Statistical analysis included percentages, odds ratios (OR), 95% confidence intervals and chi-square tests. Multiple logistic regression analysis was used to assess whether the increase in prevalence of allergic rhinitis and eczema over time (1995 vs. 2001) could be explained by several risk factors of these conditions. Variables that were associated with severe asthma symptoms, allergic rhinitis or eczema in univariate analysis ($p < 0.05$) and showed significant changes in prevalence between the study periods ($p < 0.05$) were included in the model as described by von Mutius et al. (7). All data were calculated using SAS/PC. Analyses were conducted using SAS Software, Version 6.12 (Cary, NC, USA). A significance level of $p < 0.05$ was used for all analyses.

Results

The result of the 1995 survey has been reported previously (6). For the 2001 survey, there were 4448 participants in total giving a response rate of over 95%. Among them, 2398 (54.1%) students were male, 2037 (45.9%) were female and 4291 (98.7%) were Chinese while only 58 (1.3%) students were non-Chinese. The prevalence and severity of asthma, rhinitis, and eczema symptoms in the two surveys are compared in Table 1. There was no significant change in the prevalence of life-time asthma (asthma ever), life-time wheeze (wheeze ever) and current wheeze (wheeze in the last 12 months) in 1995 and 2001. Among all the indicators of severity of asthma, significant relative increases were observed for the 12-month prevalence of night awakening with wheeze (OR 1.40, $p = 0.01$) and nocturnal cough (OR 1.24, $p < 0.01$). The prevalence of the number of attacks >3, limitation of speech by wheeze and exercise induced attacks in the previous

Table 1. Self reported prevalence of asthma, rhinitis and eczema symptoms

Question		Prevalence in %		Odds ratio (95% CI)	p-value
		2000–2001 (n = 4448)	1994–1995 (n = 3618)		
1. Wheeze ever	Yes	17.2	16.8	1.03 (0.91–1.15)	0.63
2. Wheeze in last 12 months	Yes	9.4	9.2	1.02 (0.88–1.19)	0.76
3. Wheezing episodes in last 12 months	4	2.3	2.3	0.98 (0.73–1.32)	0.88
4. Night awakenings by wheeze in last 12 months	>0	4.0	2.9	1.40 (1.09–1.78)	<0.01
5. Speech limitation during wheeze in last 12 months	Yes	1.0	0.8	1.29 (0.81–2.06)	0.35
6. Asthma ever	Yes	7.9	7.8	1.02 (0.87–1.20)	0.87
7. Exercise-induced wheeze in last 12 months	Yes	7.7	7.1	1.10 (0.93–1.30)	0.31
8. Nocturnal cough in last 12 months	Yes	26.0	22.1	1.24 (1.12–1.37)	<0.01
9. Rhinitis ever	Yes	42.4	38.9	1.16 (1.06–1.27)	<0.01
10. Rhinitis in last 12 months	Yes	37.4	35.1	1.10 (1.01–1.21)	0.03
11. Rhinitis with itch eyes in last 12 months	Yes	17.2	13.6	1.90 (1.66–2.17)	<0.01
12. Rhinitis interfering with daily activities	M-S	4.8	2.1	2.36 (1.81–3.07)	<0.01
13. Hay fever ever	Yes	1.4	1.2	1.21 (0.82–1.79)	0.43
14. Chronic rash ever	Yes	5.4	5.7	0.95 (0.79–1.15)	0.56
15. Chronic rash in last 12 months	Yes	4.2	4.2	1.00 (0.80–1.25)	1.00
16. Chronic rash at typical areas	Yes	3.6	4.2	0.85 (0.68–1.07)	0.18
17. Age rash first occurred	<2	31.8	29.2	1.13 (1.03–1.24)	0.01
18. Rash all cleared in last 12 months	Yes	19.9	28.1	0.64 (0.57–0.70)	<0.01
19. Kept awake by rash in last 12 months	>0	3.0	1.6	1.91 (1.40–2.60)	<0.01
20. Eczema ever	Yes	30.7	28.1	1.13 (1.03–1.25)	0.01
21. Allergic rhinitis ever	Yes	33.9	31.9	1.10 (1.00–1.20)	0.06

Rhinitis refers to sneezing or a runny or blocked nose when the child did not have a cold or the flu.

Table 2. Prevalence of potential risk factors

	Prevalence in %					
	2000–2001 (n = 4448)		1994–1995 (n = 3618)			
	Yes	No	Yes	No	Odds ratio (95% CI)	p-value
Sex (male)	54.1	45.9	50.9	49.1	1.14 (1.04–1.24)	<0.01
Born in Hong Kong (Yes)	87.9	12.1	88.7	11.3	0.92 (0.81–1.06)	0.27
Gestation age (<37 wk)	7.0	93.0	7.0	93.0	1.00 (0.84–1.18)	1.00
Birthweight (>2.5 kg)	81.2	18.8	87.1	12.9	0.64 (0.56–0.72)	<0.01
Number of brothers and sisters (>2)	5.6	94.4	21.6	78.4	0.22 (0.19–0.25)	<0.01
Hospital admission for RTI in first 12 months (≥4)	2.3	97.7	0.4	99.6	6.13 (3.52–10.79)	<0.01
RTI in last 12 months (≥4)	9.7	90.3	34.9	65.1	0.20 (0.18–0.23)	<0.01
Hospital admission for RTI in last 12 months (≥4)	0.4	99.6	0.3	99.7	1.29 (0.63–2.66)	0.61
Parents smoked during pregnancy (Yes)	30.8	69.2	23.4	76.6	1.46 (1.32–1.61)	<0.01
Parents smoked everyday in last 12 months (Yes)	31.7	68.3	22.2	77.8	1.63 (1.48–1.81)	<0.01
Parents atopy* (Yes)	49.7	50.3	45.0	55.0	1.21 (1.10–1.32)	<0.01
Pets ever† (Yes)	8.8	91.2	14.2	85.8	0.58 (0.51–0.67)	<0.01

RTI, respiratory tract infection.
*Asthma, allergic rhinitis or eczema in either parent; †cats or dogs.

12 months remained similar. There was, however, a significant increase in the prevalence of life-time rhinitis (42.4% vs. 38.9%), current rhinitis (37.4% vs. 35.1%), and current rhino-conjunctivitis (17.2 % vs. 13.6%). In addition, there were more respondents with bothersome rhinitis symptoms (rhinitis often interfering with daily activities) in 2001 (4.8% vs. 2.1%). Consistent with the result of the last survey, the reported prevalence of hay fever remained extremely low at 1.4% despite the high prevalence of rhinitis symptoms in both surveys. In contrast, the reported life-time prevalence of allergic rhinitis is very much similar to that of life-time rhinitis. The prevalence of allergic rhinitis also appeared to be increasing (33.9 vs. 31.9, $p = 0.06$).

The prevalence of life-time itchy rash and current itchy rash remained low and there was no significant change over the period. On the contrary, the prevalence of life-time eczema showed significant increase (OR 1.13, $p = 0.01$) and was much higher than the prevalence of life-time

Table 3. Results of multiple logistic regression with prevalence of current rhinitis, current rhino-conjunctivitis and life-time eczema as outcome variables

	Current rhinitis		Current rhino-conjunctivitis		Life-time eczema	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Sex (male)	1.56 (1.41–1.72)	<0.01	1.41 (1.24–1.60)	<0.01	NS	NS
Birth weight (>2.5 kg)	1.17 (1.02–1.35)	0.03	1.26 (1.05–1.51)	0.01	1.23 (1.01–1.41)	<0.01
Siblings (≥2)	0.56 (0.47–0.67)	<0.01	0.81 (0.65–1.00)	0.05	0.67 (0.57–0.80)	<0.01
Hospitalization for RTI in first 12 months (≥4)	1.26 (0.84–1.88)	0.26	0.79 (0.47–1.30)	0.35	NS	NS
RTI in last 12 months (≥4)	2.32 (2.05–2.63)	<0.01	2.34 (2.01–2.71)	<0.01	1.81 (1.60–2.05)	<0.01
Parents smoked during pregnancy	NS	NS	NS	NS	1.08 (0.96–1.20)	0.20
Parents smoked everyday in last 12 months	0.81 (0.72–0.91)	<0.01	NS	NS	NS	NS
Parental history of atopy	3.52 (3.19–3.91)	<0.01	2.72 (2.38–3.11)	<0.01	2.58 (2.33–2.85)	<0.01
Pets ever	NS	NS	NS	NS	1.19 (1.02–1.39)	0.03
Study period 2001	1.31 (1.17–1.46)	<0.01	1.63 (1.41–1.87)	<0.01	1.30 (1.16–1.45)	<0.01

NS, no significant association in univariate analysis.
RTI, respiratory tract infection.

Table 4. Results of multiple logistic regression with prevalence of severe asthma, eczema and rhinitis symptoms as outcome variables

	Woken by wheeze in last 12 months		Nocturnal cough in last 12 months		Kept awake by rash in last 12 months		Rhinitis interfering daily activities	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Sex (male)	1.51 (1.15–1.97)	<0.01	NS	NS	NS	NS	1.37 (1.07–1.75)	0.01
Birth weight (>2.5 kg)	NS	NS	NS	NS	NS	NS	NS	NS
Siblings (≥2)	NS	NS	NS	NS	NS	NS	0.70 (0.43–1.15)	0.16
Hospitalization for RTI in first 12 months (≥4)	1.91 (0.93–3.92)	0.08	1.88 (1.29–2.75)	<0.01	2.80 (1.42–5.52)	<0.01	2.50 (1.39–4.52)	<0.01
RTI in last 12 months (≥4)	3.44 (2.59–4.58)	<0.01	2.07 (1.82–2.35)	<0.01	2.35 (1.37–3.30)	<0.01	2.22 (1.68–2.94)	<0.01
Parents smoked during pregnancy	1.21 (0.91–1.59)	0.19	0.94 (0.78–1.13)	0.50	NS	NS	NS	NS
Parents smoked everyday in last 12 months	NS	NS	1.28 (1.06–1.54)	<0.01	NS	NS	NS	NS
Parental history of atopy	2.52 (1.88–3.38)	<0.01	1.55 (1.39–1.72)	<0.01	1.75 (1.28–2.38)	<0.01	0.42 (0.33–0.55)	<0.01
Pets ever	NS	NS	1.10 (0.94–1.29)	0.25	NS	NS	0.73 (0.48–1.12)	0.15
Study period 2001	1.55 (1.16–2.07)	<0.01	1.50 (1.34–1.68)	<0.01	2.58 (1.82–3.66)	<0.01	2.36 (0.27–0.50)	<0.01

NS, no significant association in univariate analysis.
RTI, respiratory tract infection.

itchy rash or current itchy rash. Moreover, there were more respondents with persistent itchy rash in 2001 and the severity of the itchy rash also increased significantly over this period. We examined potential social and indoor environmental risk factors over time that might account for the change in 12-month prevalence of rhinitis and life-time eczema (Table 2). In the year 2001, there were more male respondents and more respondents with birth weight < 2500 g. Those with more than two sibling, reported respiratory tract infections (RTI) requiring admission in the first 12 months of life and reported RTI in the last 12 months were significantly lower in 2001. Atopic diseases were reported more frequently in the parents in 2001. Parental smoking during pregnancy, past and current exposure to environmental tobacco smoke were significantly increased over the time period. Pets (cats or dogs) ownership became significantly less common during this period. In univariate analysis, a number of factors were found to be associated with current rhinitis, current rhino-conjunctivitis, severe nocturnal asthma symptoms, severe rhinitis symptoms and severe itchy rash and the prevalence of life-time eczema, respectively, in both years. However, the apparent increases in these frequencies could not be simply explained by the change of prevalence of these associated factors. The odds ratios for the study period remained significant even after adjustment for these potential social or indoor environmental factors (Table 3 and 4).

Discussion

Over the past decade, many studies have consistently showed an increased prevalence of asthma particularly in children (8) but there were few studies addressing the trend prevalence of allergic rhinitis and atopic eczema (9–11). Our surveys did not demonstrate a significant rise in the

prevalence of asthma, but did show a significant rise in the prevalence of allergic rhinitis over 5 yr. Information and selection biases because of poor methodology have been incriminated as the cause for the apparent increase in the prevalence of asthma (1). We adhered to the ISAAC protocol to obviate selection bias by using the same methodology. To avoid information bias induced by subjectivity of symptoms and diagnosis of asthma and allergies, people have advocated the use of objective markers in time trend studies (12). However, there is increasing evidence showing that the interrelation between asthma, atopy and bronchial hyper-responsiveness is complex and many factors other than atopy contributes to the development of asthma (13–15). The use of the same and standardized written questionnaire is widely adopted for investigation of time trends in the prevalence of asthma and allergies (16). The consistency of the prevalence of the three disorders and the potential risk factors in the present study and our previous study is strong evidence against random variation. Although the prevalence of asthma remained unchanged, there was an increase in severity of asthma symptoms (Table 1). Night cough might be measuring other respiratory conditions, e.g. postnasal drip because of allergic rhinitis, but sleep disturbance as a result of wheezing should reflect the prevalence of severe asthma.

Similar arguments hold true for the validity of the core questionnaire for allergic rhino-conjunctivitis. The exceptionally low prevalence of life-time hay fever compared with prevalence of life-time rhinitis or current rhinitis was observed in both surveys, indicating that hay fever is not a widely accepted diagnostic label in our population (Table 1). Instead, the prevalence of life-time rhinitis or current rhinitis matched more closely with the question using the Chinese term of allergic rhinitis which is commonly used in our locality. Perennial rhinitis as well as non-infective rhinitis other than atopic type may partially account for the observable increase. Nevertheless, the combination of rhinitis with itchy eyes in the past year is the best predictor of allergic rhinitis in children in Phase 1 ISSAC study (4) and this has increased in our survey. There were more criticisms concerning the core questionnaire for atopic eczema. The Chinese translated version would underestimate the prevalence of atopic eczema (17). When our Chinese questionnaire was used to collect data from Beijing and Urumqi in Mainland China, the response rate to the questions based on symptoms of atopic eczema were much lower than that of eczema ever (18). The consistency of the response rate across the three centers suggested that the questions based on symptoms were far less sensitive than the use of local term of eczema or that the children were easily labeled as having eczema by the general public in these three cities.

The dissociation of the changes in the prevalence of asthma and allergies has been reported in a trend prevalence study carried out in Leipzig, Germany (7). The authors concluded that even profound changes such as those occurring in the eastern part of Germany do not affect the inception of childhood asthma if they happen after 3 yr of life, while the development of atopic sensitization and allergic rhinitis may be affected by environmental factors occurring beyond this period. In their study, both the prevalence of asthma and related symptoms did not increase between the two surveys, while our study showed that there was an increase in severe asthma symptoms although the prevalence of asthma remained unchanged. Although there were noticeable changes in early-life events in our surveys, such as birth weight, sibship size and exposure to smoke during pregnancy and in infancy, these did not affect the prevalence of asthma in our population supporting the German study that factors other than these were more important in inception of asthma (Table 2). On the contrary, the increasing prevalence of allergic rhinitis and eczema can be partially explained by changes in early-life events, such as decreased sibship size, as the number of siblings is inversely related to the prevalence of allergic rhinitis and other atopies (19). Parental atopy, which is a risk factor for atopy, also increased between the two surveys (Table 2). Birth weight >2.5 kg unadjusted for gestational age appeared to be a risk factor in the development of allergic rhinitis and eczema in our population, yet the prevalence of low birth weight has been increasing over this period (Table 2).

Upper respiratory tract infection (URTI) is an important cause of asthma exacerbations. Nevertheless, there are not many studies showing its effect on allergic rhinitis. Proinflammatory cytokines in nasal lavage are significantly higher in the atopic group than in the non-atopic group during viral URTI indicating a more prolonged up-regulation of cytokine production in the atopic individuals (20). Atopic individuals may be more susceptible to exposure of allergens after an URTI. The positive relationship of frequent RTI (less than four episodes in the last 12 months) with increased prevalence of current rhino-conjunctivitis remained highly significant despite fewer respondents reported frequent RTI in the year 2001 (Table 3).

Interestingly, our surveys also showed a positive relationship of frequent RTI with increased prevalence of severe eczematous symptoms and that of life-time eczema (Tables 3 and 4). Contact with aeroallergens can provoke eczema in a subgroup of patients and the degree of sensitization is directly associated with the severity of atopic eczema (21). This awaits further studies to prove the temporal relationship of respiratory tract infection and exacerbation of eczema.

Although the prevalence of parental smoking during pregnancy has significantly increased over this period, it has no effect on the changing prevalence of rhinitis or eczema. A recent meta-analysis also showed that parental smoking during pregnancy or early childhood is unlikely to increase substantially the risk of allergic sensitization (22). On the contrary, there was a significant negative association of exposure to environmental tobacco smoke in the past 12 months and the prevalence of current rhinitis (Table 3). Phase 1 ISAAC also showed a significant negative correlation between adult male smoking and the prevalence of asthma and rhinitis in the 6–7 yr age group across different countries (23). As individual exposure was not analyzed, this result did not contradict the well-established association of active and passive smoking with asthma. In fact, parental smoking did contribute to the increase in prevalence of nocturnal cough in our surveys (Table 4).

The changes over time in early-life events and indoor environmental factors assessed through our questionnaires did not fully explain the increasing prevalence of current rhinitis, current rhino-conjunctivitis, life-time eczema or severe asthma symptoms. Some studies have shown a significant association of outdoor environmental pollutants and allergic diseases. Noticeable change in outdoor air pollutants was observed during this period in Hong Kong (24). Whether the increasing prevalence of allergic rhinitis, eczema and severe asthma symptoms in our children population is attributed to the change in outdoor environmental pollutants await further study for elucidation.

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