Current asthma was defined as answering positively to the question "Have you (or your child) had wheezing or whistling in the chest during the past 12 months?". Exercise-induced wheezing (EIW) was defined when the question "In the past 12 months, have your (or your child's) chest sounded wheezy during or after exercise?" was answered "yes". Night cough was defined as a positive response to the question "In the past 12 months, have you (or your child) had a dry cough at night, apart from a cough associated with a cold or chest infection?"

Definition of underweight and overweight

The child's weight and height were requested in the questionnaire. BMI was calculated as body weight in kilograms divided by height squared in meters (kg/m^2). The subjects were categorized into three groups based on the 10th and 90th percentiles, according to the reference values of BMI for Japanese children, which were obtained in 1978–1981 period.[8] Children who were at the 10th percentile and less were defined as underweight, those at the greater than 10th to less than the 90th percentile were assigned to normoweight, and those at the 90th percentile and more were defined as overweight.

Statistical analyses

The χ^2 test was used to evaluate differences in BMI distribution for the regions and genders. Multivariate logistic regression analysis was performed to estimate the effects of BMI and other covariates on respiratory symptoms (current asthma, exercise-induced wheezing, and night cough) in subjects with current asthma. Kappa statistics were used to compare the level of inter-individual agreement between current asthma and respiratory symptoms (EIW and nocturnal cough). Kappa scores >0.41 are considered to show moderate agreement: >0.61, good agreement, and >0.81, very good agreement.[9] A value of $P < 0.05$ was considered to be statistically significant. All analysis was performed using the statistical package of SPSS for Windows version 17.0J.

Ethics

This study protocol was approved by the independent review board (IRB) of the National Center for Child Health and Development.

Results

Of the 179 218 children, 149 464 replied to the questionnaire (response rate 83.4%). After omitting incomplete data, 139 117 were analyzed (Fig. 1). Background characteristics of the study population are shown in Table 1. Approximately 14% of the subjects were categorized as overweight and the prevalence of overweight was higher in the northeast region compared with the southwest region in each age group (Table 1). The youngest age group included more children categorized as underweight than the older age groups. There were gender differences in the prevalence of overweight and underweight in each age group. There was a tendency that boys were more slender than girls in the children aged 6–7 years, but this tendency changed with age. In the children aged 16–17 years, the prevalence of overweight in boys was higher than that in girls, and more girls were categorized as underweight. There were age differences in the prevalence of respiratory symptoms (Table 2). The prevalence of current asthma in the youngest age group was higher (13.6%) than that of the older age groups (9.5% in children aged 13–14 years and 8.3% in children 16–17 years old). In contrast, only a very low percentage of children aged 6–7 years old (4.3%) had current episodes of EIW, while approximately 15% of the older age group had such episodes (16.5% in children aged 13–14

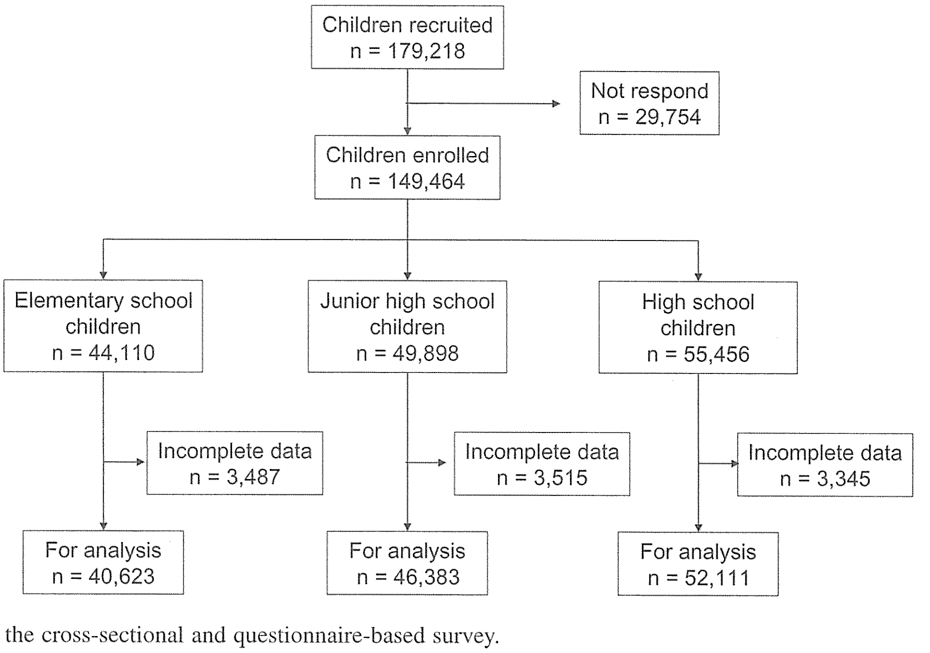

Fig. 1 Participants of the cross-sectional and questionnaire-based survey.

Table 1 Baseline characteristics of the study participants

	Underweight	Normoweight	Overweight	*P*-value
6–7-year-olds				
Total number	6206 (15.3%)	28 374 (69.8%)	6043 (14.9%)	
Region				
Northeast	2745 (15.2%)	12 462 (69.1%)	2824 (15.7%)	<0.001
Southwest	3461 (15.3%)	15 912 (70.4%)	3219 (14.2%)	
Gender				
Boys	3420 (16.6%)	14 210 (68.7%)	3030 (14.7%)	<0.001
Girls	2786 (14.0%)	14 164 (70.9%)	3013 (15.1%)	
13–14-year-olds				
Total number	3722 (8.0%)	36 073 (77.8%)	6588 (14.2%)	
Region				
Northeast	1491 (7.6%)	15 204 (77.0%)	3053 (15.4%)	<0.001
Southwest	2231 (8.4%)	20 869 (78.3%)	3535 (13.3%)	
Gender				
Boys	1920 (8.4%)	17 681 (77.1%)	3333 (14.5%)	0.002
Girls	1802 (7.7%)	18 392 (78.4%)	3255 (13.9%)	
16–17-year-olds				
Total number	4721 (9.1%)	39 729 (76.2%)	7661 (14.7%)	
Region				
Northeast	1929 (8.5%)	17 000 (75.1%)	3725 (16.4%)	<0.001
Southwest	2792 (9.5%)	22 729 (77.1%)	3936 (13.4%)	
Gender				
Boys	2055 (7.5%)	20 759 (76.0%)	4514 (16.5%)	<0.001
Girls	2666 (10.8%)	18 970 (76.5%)	3147 (12.7%)	

years and 14.0% in children 16–17 years old). There were also regional and gender differences in the prevalence of respiratory symptoms. In both the youngest and oldest age groups, the prevalence of current asthma was significantly higher in the northeast region, while it tended to be lower in the 13–14 year-old age group ($P = 0.055$). In the children aged 6–7 years old, significantly more boys had respiratory symptoms compared with girls. These gender differences became unclear with age. In the oldest age group, there were no differences in the prevalence of respiratory symptoms between genders.

Table 2 Prevalence of respiratory symptoms

	CA	*P*-value	EIW	*P*-value	NC	*P*-value
6–7-year-olds						
Total	13.6		4.3		13.4	
Regions						
Northeast	14.1	0.007	4.4	0.375	13.2	0.159
Southwest	13.2		4.2		13.6	
Gender						
Boys	15.8	<0.001	5.0	<0.001	14.5	<0.001
Girls	11.4		3.5		12.3	
13–14-year-olds						
Total	9.5		16.5		11.8	
Regions						
Northeast	9.2	0.055	16.4	0.825	11.1	<0.001
Southwest	9.7		16.5		12.3	
Gender						
Boys	9.7	0.173	15.8	<0.001	11.2	<0.001
Girls	9.3		17.1		12.3	
16–17-year-olds						
Total	8.3		14.0		11.8	
Regions						
Northeast	8.9	<0.001	15.0	<0.001	12.0	0.289
Southwest	7.8		13.3		11.7	
Gender						
Boys	8.4	0.091	14.1	0.421	11.7	0.428
Girls	8.0		13.9		11.9	

CA, current asthma; EIW, exercise-induced wheezing; NC, nocturnal cough.

From these findings, we evaluated the association of under- or overweight with respiratory symptoms, using a multivariate logistic regression analysis, adjusted for geographic region and gender (Table 3). In all the age groups, there was a significant association of overweight with current asthma (adjusted OR: 1.24, 95% CI: 1.15–1.34, $P < 0.001$ in children 6–7 years of age; adjusted OR: 1.31, 95% CI: 1.21–1.42, $P < 0.001$ in those 13–14 years; and adjusted OR: 1.32, 95% CI: 1.22–1.44, $P < 0.001$ in those 16–17 years). With regard to underweight, in the 13–14-year-old group, underweight was significantly associated with current asthma in boys (adjusted OR: 1.17, 95% CI: 1.00–1.36, $P = 0.049$), while underweight tended to negatively associate with current asthma in girls ($P = 0.085$). Furthermore, a significantly negative association was found in the girls aged 16–17 years (adjusted OR: 0.83, 95% CI: 0.70–0.97, $P = 0.020$).

Being overweight also associated with EIW in all the age groups (adjusted OR: 1.32, 95% CI: 1.16–1.50, $P < 0.001$ in children 6–7 years of age; adjusted OR: 1.37, 95% CI: 1.28–1.47, $P < 0.001$ in those 13–14 years; and adjusted OR: 1.36, 95% CI: 1.27–1.46, $P < 0.001$ in those 16–17 years), but being underweight had no effect on EIW (Table 4). There was moderate inter-individual agreement between current asthma and EIW (kappa value = 0.46), while the inter-individual agreement between current asthma and nocturnal asthma was poor (kappa value = 0.28). Therefore, to examine the association of under- or overweight with nocturnal cough, current asthma was added as a covariate (Table 4). In the children aged 13–14 and 16–17 years obesity was significantly associated with nocturnal cough, independent of current asthma (adjusted OR: 1.21, 95% CI: 1.18–1.31, $P < 0.001$ in those 13–14 years; and adjusted OR: 1.17, 95%

Table 3 Association of under- or overweight with current asthma

	Prevalence (%)	*P*-value	Adjusted OR	95% CI
Total[†]				
6–7-year-olds				
Underweight	13.1	0.312	0.96	0.88–1.04
Normoweight	13.2		1	
Overweight	15.9	<0.001	1.24	1.15–1.34
13–14-year-olds				
Underweight	9.3	0.805	1.02	0.90–1.14
Normoweight	9.1		1	
Overweight	11.6	<.0.001	1.31	1.21–1.42
16–17-year-olds				
Underweight	7.5	0.323	0.94	0.84–1.06
Normoweight	7.9		1	
Overweight	10.2	<0.001	1.32	1.22–1.44
Boys[‡]				
6–7-year-olds				
Underweight	14.5	0.138	0.92	0.83–1.03
Normoweight	15.5		1	
Overweight	18.2	<0.001	1.21	1.09–1.34
13–14-year-olds				
Underweight	10.7	0.049	1.17	1.00–1.36
Normoweight	9.3		1	
Overweight	11.2	0.001	1.23	1.09–1.39
16–17-year-olds				
Underweight	8.7	0.269	1.10	0.93–1.29
Normoweight	8.0		1	
Overweight	10.3	<0.001	1.31	1.17–1.46
Girls[‡]				
6–7-year-olds				
Underweight	11.2	0.816	1.02	0.89–1.16
Normoweight	10.6		1	
Overweight	13.5	<0.001	1.26	1.12–1.42
13–14-year-olds				
Underweight	7.8	0.085	0.85	0.71–1.02
Normoweight	9.0		1	
Overweight	12.0	<0.001	1.40	1.24–1.57
16–17-year-olds				
Underweight	6.6	0.020	0.83	0.70–0.97
Normoweight	7.9		1	
Overweight	10.3	<0.001	1.32	1.17–1.50

[†]Adjusted for gender and region.
[‡]Adjusted for region.
CI, confidence interval; OR, odds ratio.

Table 4 Association of under- or overweight with exercise-induced wheezing and nocturnal cough

	Prevalence (%)	*P*-value	Adjusted OR	95% CI
Exercise-induced wheeze†				
6–7-year-olds				
Underweight	4.1	0.680	0.97	0.84–1.12
Normoweight	4.1		1	
Overweight	5.3	<0.001	1.32	1.16–1.50
13–14-year-olds				
Underweight	15.3	0.382	0.96	0.87–1.06
Normoweight	15.8		1	
Overweight	20.4	<0.001	1.37	1.28–1.47
16–17-year-olds				
Underweight	12.9	0.308	0.95	0.87–1.05
Normoweight	13.4		1	
Overweight	17.5	<0.001	1.36	1.27–1.46
Nocturnal cough‡				
6–7-year-olds				
Underweight	13.5	0.372	1.04	0.95–1.13
Normoweight	13.2		1	
Overweight	14.8	0.077	1.08	0.99–1.18
13–14-year-olds				
Underweight	11.9	0.306	1.06	0.95–1.18
Normoweight	11.4		1	
Overweight	13.9	<0.001	1.21	1.18–1.31
16–17-year-olds				
Underweight	11.2	0.734	0.93	0.89–1.09
Normoweight	11.5		1	
Overweight	13.7	<0.001	1.17	1.08–1.26

†Adjusted for gender and region.
‡Adjusted for gender, region and current asthma.
CI, confidence interval; OR, odds ratio.

CI: 1.08–1.26, $P < 0.001$ in those 16–17 years), and there was a similar tendency in the children aged 6–7 years ($P = 0.077$).

Discussion

In this study, we found that being overweight was associated with current asthma in children of all the three age groups, and this finding remained even after adjusted for other variables such as gender and geographic region. There are three critical periods in the development and persistence of overweight in childhood: the prenatal period, period of adiposity rebound, and adolescence.[10] The youngest age group of this study corresponds to the period of adiposity rebound, and the children of the older age groups are in the middle of adolescence. As the baseline characteristics of the subjects, prevalence rates of overweight were approximately 14%, and the rates were similar in each age group. Our findings are consistent with the results from a 5-year longitudinal cohort study that followed more than 5000 school children, which found that persistent obesity in adolescence was established before age 11, suggesting the need to target efforts to prevent obesity in the early years.[11] Although the prevalence rates of overweight were similar between the three age groups as mentioned above, there were some gender differences in the prevalence of overweight. Especially in the older age group, the overweight rate between girls was clearly lower than that between boys. Development of obesity is associated with both biological and behavioral factors, and socially constructed attitudes or beliefs may affect this process. Gender differences for body image concerns emerge somewhere between the ages of 8 and 10 years, and body dissatisfaction becomes more pronounced with increasing age, particularly in girls.[12] These factors might explain the lower prevalence of overweight in girls of the older age groups in this study.

There are also conflicting data regarding the impact of gender on the obesity–asthma relationship.[13] Consistent with our results, a cross-sectional study performed in New Zealand showed the associations of BMI with current asthma and inhaled steroid use in children of mean age 11.7 years, and these associations were not significantly different for boys and girls.[14] In contrast, another survey performed in Kyoto, a city in Japan, demonstrated the association of obesity with asthma in girls but not in boys aged 7–15 years.[15] In the Tuscon birth cohort study, girls, but not boys, who became overweight between 6 and 11 years of age were seven times more likely to develop new asthma symptoms at age 11 or 13 years of age.[16] Furthermore, a prospective study in which 4393 US children who were asthma-free during the first 24 months followed up to 14 years showed that boys with high BMI were at increased risk for subsequent asthma.[17] The different outcomes in these studies may be a function of the age at which the children were studied and the duration of follow-up.

In the current study, children who were overweight were more likely to develop wheezing during exercise, as was seen in Belgian children 3–14 years of age.[18] Several studies denied the association between obesity and bronchial hyperresponsiveness.[16] EIW might be caused by reduced lung functions that were found among asthmatic and normal children with high BMI.[19] It was reported that children with asthma combined with excessive body weight had a low quality of life (QOL) compared with children with asthma and normal weight.[20] We previously reported that the presence of EIW among asthmatic children impaired their QOL compared with asthmatics without EIW.[7] Frequent episodes of EIW could be one of the reasons for the low QOL of asthmatic children with asthma. We also found that overweight was a risk factor for nocturnal cough, independent of current asthma in the older age groups. Mechanisms through which obesity related with nocturnal cough might be different from those of obesity-associated wheezing. Several studies showed the relationship between obesity and gastroesophageal reflex (GER),[21] suggesting that nocturnal cough in obese children might be due to GER. However, asthma per se was associated with symptoms of GER,[22] and the higher prevalence of GER in asthmatic children was not attributable to overweight.[23] Further studies are needed to determine the mechanisms of nocturnal cough in obese asthmatic children. Coughing during night may cause sleep disturbance. Interestingly, an inverted relationship between sleep duration and the risk of obesity was reported in children 5–10 years of age,[24] and this phenomenon might be explained by reduced leptin levels due to shorter sleep duration.[25] Clinicians should be aware of these symptoms when they see a child with asthma and overweight.

Most of the studies evaluating a BMI–asthma link have focused mainly on obesity. However, underweight has also been shown to be associated with asthma symptoms[5] and allergen sensitization.[18] In the current study, among children 13–14 years of age, underweight boys had a risk of current asthma, while underweight girls were unlikely to have asthma compared with children with normoweight. These findings are consistent with the previous findings that among children 2–11 years of age in an inner city of the US, a U-shaped association between BMI and the probability of having asthma was observed for boys and a linear trend was observed for girls.[5] Mechanisms for gender differences among underweight children might be different from those among overweight children.

One of the limitations of this study is that body weights and heights were self-reported. A cross-sectional study showed that when self-reported weights and heights were compared with measured values in children 12–16 years of age, influences of gender and racial biases in reporting of weight and height were relatively small, and concluded that self-reported heights and weights were extremely reliable.[26] However, a systematic review showed trends of under-reporting for weight and BMI and over-reporting for height.[27] Recently, a correction method to adjust self-reported measures of BMI to more closely approximate measured values was proposed.[28] Another limitation is that diagnosis of asthma was based on the questionnaire. Although we used the ISAAC questionnaire which has been proven to be valid for epidemiological study of childhood asthma, dyspnea in obese children might be interpreted as a symptom of asthma.[13] Further limitation is that a cross-sectional study cannot address mechanistic questions. Prospective studies that account for variables in the social and physical environment are needed to clarify the pathophysiology linking obesity and asthma.

In conclusion, we have shown that there is a clear association between obesity and current asthma in Japanese school-aged children. Asthma and obesity are multifactorial diseases, and the affecting factors seem independent of each other. Further understanding of the mechanisms that could explain the relationship between both disorders may lead to new preventive strategies.

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References

1 Nishima S, Chisaka H, Fujiwara T *et al*. Surveys on the prevalence of pediatric bronchial asthma in Japan: A comparison between the 1982, 1992, and 2002 surveys conducted in the same region using the same methodology. *Allergol. Int.* 2009; **58**: 37–53.
2 Inokuchi M, Matsuo N, Takayama JI, Hasegawa T. Official Japanese reports significantly underestimate prevalence of overweight in school children: Inappropriate definition of standard weight and calculation of excess weight. *Ann. Hum. Biol.* 2009; **36**: 139–45.
3 Mehta S, Mahajan D, Steinbeck KS, Bermingham MA. Relationship between measures of fatness, lipids and ethnicity in a cohort of adolescent boys. *Ann. Nutr. Metab.* 2002; **46**: 192–9.
4 Sampei MA, Novo NF, Juliano Y, Sigulem DM. Anthropometry and body composition in ethnic Japanese and Caucasian adolescent boys. *Pediatr. Int.* 2008; **50**: 679–86.
5 Kwon HL, Ortiz B, Swaner R *et al*. Childhood asthma and extreme values of body mass index: The Harlem Children's Zone Asthma Initiative. *J. Urban Health* 2006; **83**: 421–33.
6 Asher MI, Montefort S, Bjorksten B *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.
7 Kojima N, Ohya Y, Futamura M *et al*. Exercise-induced asthma is associated with impaired quality of life among children with asthma in Japan. *Allergol. Int.* 2009; **58**: 187–92.
8 Inokuchi M, Matsuo N, Anzo M, Hasegawa T. Body mass index reference values (mean and SD) for Japanese children. *Acta Paediatr.* 2007; **96**: 1674–6.
9 Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; **33**: 159–74.
10 Dietz WH. Overweight in childhood and adolescence. *N. Engl. J. Med.* 2004; **350**: 855–7.
11 Wardle J, Brodersen NH, Cole TJ, Jarvis MJ, Boniface DR. Development of adiposity in adolescence: Five year longitudinal study of an ethnically and socioeconomically diverse sample of young people in Britain. *BMJ* 2006; **332**: 1130–5.
12 Ricciardelli LA, McCabe MP. Children's body image concerns and eating disturbance: A review of the literature. *Clin. Psychol. Rev.* 2001; **21**: 325–44.
13 Schwartzstein RM, Gold DR. Dyspnea in overweight children: Is it asthma? *J. Allergy Clin. Immunol.* 2009; **123**: 1319–20.
14 Wickens K, Barry D, Friezema A *et al*. Obesity and asthma in 11–12 year old New Zealand children in 1989 and 2000. *Thorax* 2005; **60**: 7–12.
15 Kusunoki T, Morimoto T, Nishikomori R *et al*. Obesity and the prevalence of allergic diseases in schoolchildren. *Pediatr. Allergy Immunol.* 2008; **19**: 527–34.
16 Castro-Rodriguez JA, Holberg CJ, Morgan WJ, Wright AL, Martinez FD. Increased incidence of asthmalike symptoms in girls who become overweight or obese during the school years. *Am. J. Respir. Crit. Care Med.* 2001; **163**: 1344–9.

17 Mannino DM, Mott J, Ferdinands JM *et al.* Boys with high body masses have an increased risk of developing asthma: Findings from the National Longitudinal Survey of Youth (NLSY). *Int. J. Obes. (Lond)* 2006; **30**: 6–13.
18 Van Gysel D, Govaere E, Verhamme K, Doli E, De Baets F. Body mass index in Belgian schoolchildren and its relationship with sensitization and allergic symptoms. *Pediatr. Allergy Immunol.* 2009; **20**: 246–53.
19 Spathopoulos D, Paraskakis E, Trypsianis G *et al.* The effect of obesity on pulmonary lung function of school aged children in Greece. *Pediatr. Pulmonol.* 2009; **44**: 273–80.
20 van Gent R, van der Ent CK, Rovers MM, Kimpen JL, van Essen-Zandvliet LE, de Meer G. Excessive body weight is associated with additional loss of quality of life in children with asthma. *J. Allergy Clin. Immunol.* 2007; **119**: 591–6.
21 Pashankar DS, Corbin Z, Shah SK, Caprio S. Increased prevalence of gastroesophageal reflux symptoms in obese children evaluated in an academic medical center. *J. Clin. Gastroenterol.* 2009; **43**: 410–13.
22 Thakkar K, Boatright RO, Gilger MA, El-Serag HB. Gastroesophageal reflux and asthma in children: A systematic review. *Pediatrics* 2010; **125**: e925–30.
23 Stordal K, Johannesdottir GB, Bentsen BS, Carlsen KC, Sandvik L. Asthma and overweight are associated with symptoms of gastro-oesophageal reflux. *Acta Paediatr.* 2006; **95**: 1197–201.
24 Chaput JP, Brunet M, Tremblay A. Relationship between short sleeping hours and childhood overweight/obesity: Results from the 'Quebec en Forme' Project. *Int. J. Obes. (Lond)* 2006; **30**: 1080–5.
25 Chaput JP, Despres JP, Bouchard C, Tremblay A. Short sleep duration is associated with reduced leptin levels and increased adiposity: Results from the Quebec family study. *Obesity (Silver Spring)* 2007; **15**: 253–61.
26 Strauss RS. Comparison of measured and self-reported weight and height in a cross-sectional sample of young adolescents. *Int. J. Obes. Relat. Metab. Disord.* 1999; **23**: 904–8.
27 Gorber SC, Tremblay M, Moher D, Gorber B. A comparison of direct vs. self-report measures for assessing height, weight and body mass index: A systematic review. *Obes. Rev.* 2007; **8**: 307–26.
28 Connor Gorber S, Shields M, Tremblay MS, McDowell I. The feasibility of establishing correction factors to adjust self-reported estimates of obesity. *Health Rep.* 2008; **19**: 71–82.

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POSITION PAPER

Prevalence and impact of rhinitis in asthma. SACRA, a cross-sectional nation-wide study in Japan

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Abstract

Background: Asthma and rhinitis are common co-morbidities everywhere in the world but nation-wide studies assessing rhinitis in asthmatics using questionnaires based on guidelines are not available.
Objective: To assess the prevalence, classification, and severity of rhinitis using the Allergic Rhinitis and its Impact on Asthma (ARIA) criteria in Japanese patients with diagnosed and treated asthma.
Methods: The study was performed from March to August 2009. Patients in physicians' waiting rooms, or physicians themselves, filled out questionnaires on rhinitis and asthma based on ARIA and Global Initiative for Asthma (GINA) diagnostic guides. The patients answered questions on the severity of the diseases and a Visual Analog Scale. Their physicians made the diagnosis of rhinitis.
Results: In this study, 1910 physicians enrolled 29 518 asthmatics; 15 051 (51.0%) questionnaires were administered by physician, and 26 680 (90.4%) patients were evaluable. Self- and physician-administered questionnaires gave similar results. Rhinitis was diagnosed in 68.5% of patients with self-administered questionnaires and 66.2% with physician-administered questionnaires. In this study, 994 (7.6%) patients with self-administered and 561 (5.2%) patients with physician-administered questionnaires indicated rhinitis symptoms on the questionnaires without a physician's diagnosis of rhinitis. Most patients with the physician's diagnosis of rhinitis had moderate/severe rhinitis. Asthma control was significantly impaired in patients with a physician's diagnosis of rhinitis for all GINA clinical criteria except exacerbations. There were significantly more patients with uncontrolled asthma as defined by GINA in those with a physician's diagnosis of rhinitis (25.4% and 29.7%) by comparison with those without rhinitis (18.0% and 22.8%).
Conclusion: Rhinitis is common in asthma and impairs asthma control.

Abbreviations
ARIA, Allergic Rhinitis and its Impact on Asthma; CI, confidence interval; GINA, Global Initiative for Asthma; OR, odds ratio; SACRA, State of the Impact of Allergic Rhinitis on Asthma Control; VAS, Visual Analog Scale.

Asthma and rhinitis are common co-morbidities (1–3). Self-reported rhinitis is a significant problem for asthmatics (4). The characterization of rhinitis is difficult as allergic and nonallergic rhinitis may share similar symptoms and may coexist in the same patient (5). However, both allergic and nonallergic rhinitis are associated with asthma. In Japan, it is reported that 44–68% of asthmatics suffer from allergic rhinitis (6, 7). The percentage of co-morbidity varies depending on the area of the country. However, no large national study of this co-morbidity has been performed.

Some studies have suggested an association between asthma and rhinitis severity (8, 9). Asthmatics with documented concomitant allergic rhinitis may experience more asthma-related hospitalizations and physician visits, and incur higher costs than those with asthma alone (10–12). However, the studies are small and/or *post hoc* analyses. Thus, relationships between asthma and rhinitis severity are still unclear.

In the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines, patients are categorized as either having intermittent or persistent rhinitis. The severity of allergic rhinitis has been classified as 'mild' or 'moderate/severe' depending on symptom severity and effect on quality of life (13). This classification better reflects the patient's needs (14) and makes it simpler for primary care physicians to diagnose, assess, and manage rhinitis.

The purpose of this cross-sectional study is to assess rhinitis co-morbidity (prevalence and severity) in patients with diagnosed asthma who are receiving medication for their asthma in a large nation-wide survey in Japan and to determine whether rhinitis impairs control.

Methods

Study design

A cross-sectional multicenter study [State of the Impact of Allergic Rhinitis on Asthma Control (SACRA)] was carried out throughout Japan to assess the prevalence, classification, and severity of rhinitis using the ARIA criteria (1) in patients with diagnosed and treated asthma. The impact of rhinitis on asthma control was also assessed.

The study was performed from March to August 2009. Patients in the waiting room of physicians, or physicians, filled a questionnaire on rhinitis and asthma based on ARIA (1) and the Global Initiative for Asthma (GINA) (15). Questions about the severity of the diseases and Visual Analog Scales (VAS) for both diseases were recorded. Rhinitis diagnosis was made by physicians (Fig. 1) based on ARIA guidelines.

The primary outcome was the prevalence of physician-diagnosed rhinitis in asthmatics. Secondary parameters included individual symptoms of rhinitis, rhinitis severity assessed according to ARIA, and the control of asthma assessed according to GINA. The VAS data for both asthma and rhinitis were used to assess the patients' perceptions of the diseases.

Setting

In the study, 1910 physicians in 1805 offices throughout Japan participated (Fig. S1): 1642 primary care physicians, 155 allergists, and 113 chest physicians. Specialists were randomly selected from the list of members of the Japanese Society of Allergology or the Japanese Respiratory Society. The other physicians were primary care physicians who were following a large number of asthmatics in their practices.

Participants

A maximum of 30 consecutive patients over 15 years of age consulting for asthma and receiving a treatment for asthma were included. All patients fulfilled the following inclusion criteria: The diagnosis of asthma was made prior to the consultation using the Asthma Prevention and Management Guidelines of Japan (16) based on the American Thoracic Society recommendations (Table 1). All patients with asthma were enrolled in the study without any consideration of a previous diagnosis of rhinitis. There was no specific training of participating physicians concerning the use of the ARIA and GINA questionnaires.

Subjects were enrolled after informed consent was obtained. The study conformed to the Ethical Guideline for Epidemiology Research and was approved by the Central Institutional Review Board of Kimura Hospital (Tokyo, Japan).

Variables

Questionnaires

The same questionnaires on asthma and rhinitis were filled in by patients in the physician's waiting room (self-administered) or by the physician during consultation (physician-administered). The questionnaire for rhinitis was approved by ARIA (1), and the questionnaire for asthma by GINA

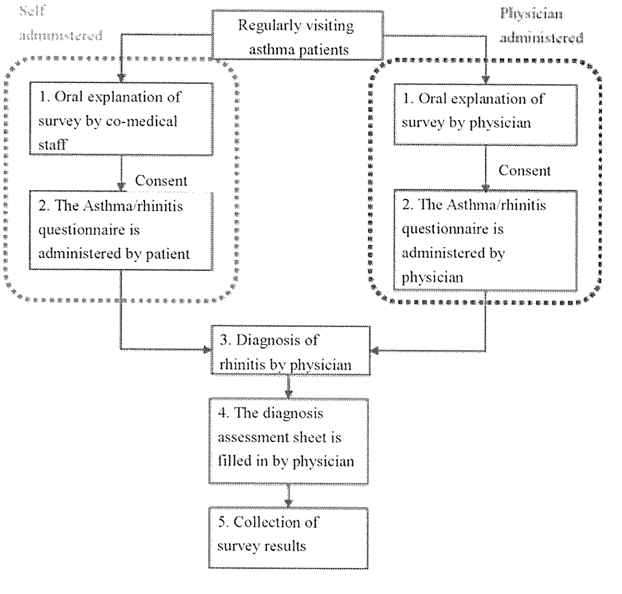

Figure 1 Design of the study.

Table 1 Diagnosis of asthma

Consideration factors when diagnosing asthma
1. Repeated episode of dyspnea, wheezing, cough (especially at nighttime and in early morning)
2. Reversible airflow limitation : An increase in FEV_1 of ≥12% and ≥200 ml after administration of a bronchodilator or diurnal variation in PEF of more than 20%
3. Airway hyperresponsiveness: indicated by increase in airway responsiveness to acetylcholine, and histamine
4. Atopic predisposition: indicated by presence of specific IgE antibodies to environmental allergens
5. Presence of airway inflammation: sputum (increases in sputum and peripheral blood eosinophils, elevated ECP, creola bodies, elevated levels of exhaled NO)
6. Exclusion of other underlying disorders: Symptoms are not owing to other pulmonary disorders or cardiovascular disease

All subjects had symptoms suggestive of asthma (item 1) excluding other diseases (item 6). Those followed by a specialist had a reversible airflow obstruction (item 2 and eventually 3). Subjects followed in primary care did not always have a pulmonary function test, and items 4–6 were used as minor criteria.

(15) (Tables S1 and S2). The Japanese translation of the questionnaires was made by the Japanese ARIA and GINA Committee, Prof. Ohta, Chair. The rhinitis questionnaire included four symptoms of rhinitis, an evaluation of conjunctivitis, four questions on environmental factors affecting symptoms, and questions on duration and severity of the disease and impact on quality of life. This questionnaire made it possible to classify rhinitis according to ARIA (1). The asthma questionnaire included eight questions on asthma control and eight questions on environmental factors affecting asthma control. This questionnaire made it possible to assess asthma control based on GINA criteria (15) although pulmonary function tests were not performed as previously published (17). The working definition of asthma control is given in Table S3.

- Questionnaire I explains about the pathophysiology of the disease (Rhinitis or asthma) to patients. (Please refer to Table S1 'What is rhinitis?' or Table S2 'What is asthma'.)
- Questionnaire II in the rhinitis questionnaire asks about symptoms highly specific to rhinitis. (Please refer to Table S1 'Could I have rhinitis?'.)
- Questionnaire II in the asthma questionnaire asks specific questions to assess control of asthma (Table S2 'What is asthma'.)
- Questionnaire III asks about the environmental factors affecting rhinitis or asthma symptoms (Please refer to Table S1 'What is rhinitis?' or Table S2 'What is asthma'.)

Diagnosis of rhinitis

The physician made the diagnosis of rhinitis based on symptoms of rhinitis, nasal physical examination, serum allergen-specific IgE, skin prick tests, and/or a nasal provocation test, although not every diagnostic evaluation was carried out during all of these examinations.

Visual Analog Scale

Visual analog scales have been used in rhinitis (18, 19) and asthma (20, 21) to assess the impairment induced by these diseases. Two VAS were recorded by the patient before physician's examination: one for asthma and one for rhinitis. Scores ranged from not at all bothersome (0 cm) to extremely bothersome (10 cm).

Study size

To have the study population be representative of the asthma population in Japan, almost 2000 physicians were selected to enroll up to 30 patients each. According to the report by the Japanese Census and Statistics Department of the Ministry of Internal Affairs and Communications in August 2008, the Japanese population over 15 years of age was about 110 million. With a sample size of 30 000 patients, and an estimated asthma prevalence rate in Japan as 3% (22), the study should include about 1% of the total population of patients with asthma.

Statistical methods

The frequencies and numbers were shown, and chi-square tests were analyzed for subjects with and without rhinitis. An odds ratio and its 95% confidence (OR, 95% CI) interval were calculated for subjects with and without rhinitis.

For continuous data, summary statistics were calculated, and a Mann–Whitney *U*-test was conducted for subjects with and without rhinitis. Bonferroni's correction was applied when multiple data were studied. Age data have been converted to appropriate categories for analysis, the frequencies and proportions for each category were calculated. The correlation between age and the co-morbid rate was analyzed by the Pearson product-moment correlation coefficient method. OR and 95% CI were calculated for subjects with and subjects without rhinitis. Missing data were not replaced.

The study was sufficiently large to analyze two sets of data: self-administered and physician's administered questionnaire with over 13 000 questionnaires in each analysis. Data were analyzed using the software SAS ver. 8.2 (SAS Institute Japan Ltd., Tokyo, Japan).

Results

Participants

Thousand nine hundred and ten physicians enrolled 29 518 asthmatics (15.45 patients per physician); 15 051 (51.0%) questionnaires were physician administered. A complete evaluation (diagnosed subjects with no missing answers on the diagnostic sheet or questionnaires) was available for 19 385 patients (65.67%). However, as the primary outcome is the physician's diagnosis of rhinitis, some questions were not essential for this evaluation (Table S4) and the total number of patients evaluated was 26 680 (90.4%). The disposition of study subjects is shown in Fig. 2.

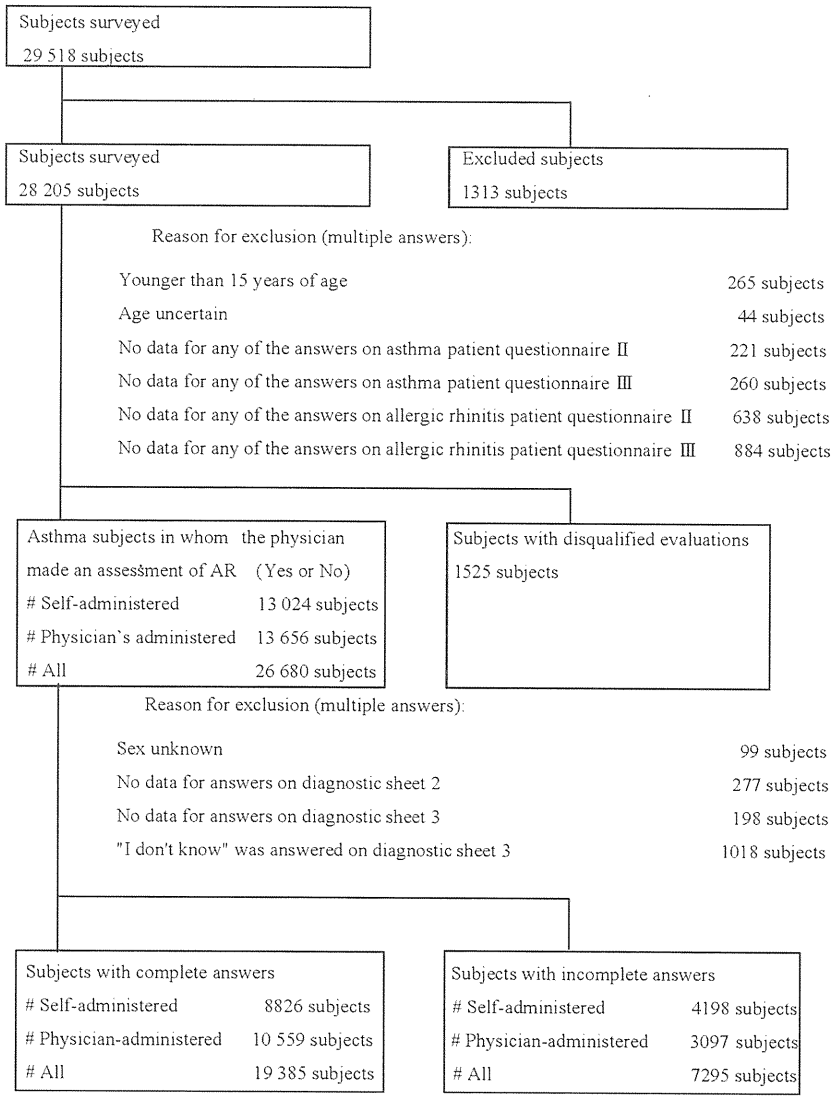

Figure 2 Flow diagram of the study.

Descriptive data

The demographic characteristics of the patients are presented in Table 2. Rhinitis was present in 67.3% of the total evaluable patients. In this study, 68.5% of patients who used the self-administered questionnaire and 66.2% of patients who used the physician-administered had rhinitis. Rhinitis diagnosis was made on symptoms (92.3%), physical examination (39.1%), and more rarely on serum-specific IgE (27.9%) (Table S5). There was no significant difference for patients with self-administered and physician-administered questionnaires.

Main results

Main results are presented in Table 3. For most results, self- and physician-administered questionnaires gave similar results although the magnitude of the differences between self- and physician-administered questionnaires differed. Patients with physician's diagnosed rhinitis were significantly younger than those without rhinitis.

In the 26 680 evaluable patients, rhinitis was present in 68.5% of patients who used the self-administered questionnaire and in 66.2% of those who received the physician-administered questionnaire (Table 3). However, 994 (7.6%) patients with the self-administered questionnaire and 561 (5.2%) patients with physician-administered questionnaire had rhinitis symptoms on questionnaire without a physician's diagnosis of rhinitis.

The majority of patients with a physician's diagnosis of rhinitis had moderate/severe rhinitis; 74.7% and 76.2% (self- and physician-administered questionnaires respectively) of patients had bothersome symptoms. Some patients without a diagnosis of rhinitis had mild rhinitis as determined by

Table 2 Demographic data

		Questionnaire administrator	
	Total population (n = 26 680)	Self-administered (n = 13 024)	Physician's administered (n = 13 656)
Age (years) (OR: per year increase)			
Mean (SD)	52.2 (18.7)	50.6 (17.8)	53.8 (19.4)
Sex, n (%)			
Male	10 976 (41.1)	5271 (40.5)	5705 (41.8)
Female	15 704 (58.9)	7753 (59.5)	7951 (58.2)
VAS for rhinitis (cm)			
Mean (SD)	4.00 (3.41)	4.20 (3.40)	3.82 (3.41)
Data missing, n (%)	766 (2.9)	500 (3.8)	266 (1.9)
ARIA classification, n (%)			
Mild intermittent	10 763 (40.3)	4889 (37.5)	5874 (43.0)
Moderate/severe intermittent	9232 (34.6)	5230 (40.2)	4002 (29.3)
Mild persistent	357 (1.3)	129 (1.0)	228 (1.7)
Moderate/severe persistent	6328 (23.7)	2776 (21.3)	3552 (26.0)
VAS for asthma (cm)			
Mean (SD)	4.27 (3.04)	4.26 (3.05)	4.28 (3.04)
Data missing, n (%)	674 (2.5)	504 (3.9)	170 (1.2)
Control of asthma based on GINA, n (%)			
Controlled	8742 (32.8)	4394 (33.7)	4347 (31.8)
Partly controlled	11 200 (42.0)	5626 (43.2)	5574 (40.8)
Uncontrolled	6739 (25.3)	3004 (23.1)	3735 (27.4)
Existence of rhinitis			
n (%)	17 945 (67.3)	8910 (68.4)	9035 (66.2)
95% CI	66.7–67.8	67.6–69.2	65.4–67.0

ARIA, but only 887 (6.8%) and 342 (2.5%) of these patients had indicated that they had bothersome symptoms of rhinitis on their questionnaires (self- and physician-administered questionnaires respectively). The median VAS value for rhinitis was 5.49 [2.51–7.90 (25–75%)] and 5.6 (2.75–7.85) cm in patients with a physician's diagnosis of rhinitis *vs* 0.38 (0.0–2.32) and 0.07 (0.0–0.42) cm in patients without a physician's diagnosis of rhinitis (self- and physician-administered questionnaires respectively).

For the vast majority of analyses comparing the presence or absence of rhinitis, the significance of the results was identical in self-administered and physician-administered questionnaires. However, the magnitude of the differences between patients with and without physician's diagnosed rhinitis differed (Table 3). Patients with physician's diagnosed rhinitis were significantly younger than those without rhinitis.

Asthma control was significantly worse in patients with a physician's diagnosis of rhinitis by comparison with those without rhinitis for all criteria except exacerbations requiring systemic corticosteroid in past year. There were significantly more patients with uncontrolled asthma as defined by GINA in those with a physician's diagnosis of rhinitis (25.4 self-administered and 29.7% physician-administered) by comparison with those without rhinitis (18.0% self-administered and 22.8% physician-administered). The VAS value for asthma was 4.75 (1.85–7.00) and 4.79 (1.90–7.18) cm in patients with a physician's diagnosis of rhinitis *vs* 2.90 (0.83–5.78) and 2.98 (0.81–6.10) cm in patients without rhinitis (self- and physician-administered questionnaires respectively)

Other analyses

The cumulative prevalence of rhinitis in asthmatics differs depending on the age of the patient (Fig. 3A,B). Under the age of 60 years, over 75% of asthmatics have physician's diagnosed rhinitis. Watery rhinorrhea was present in around 60% of the patients with physician's diagnosed rhinitis before the age of 60 years. After the age of 60 years, the prevalence of watery rhinorrhea decreased whereas the prevalence of rhinitis without rhinorrhea was similar in all age groups. Watery rhinorrhea was less reported by patients than by physicians according to the self- and physician-administered questionnaires ($r = -0.238$, $P < 0.0001$). The repartition of VAS for asthma in patients with and without a physician's diagnosis of rhinitis is presented in Fig. S2.

Discussion

Key results

Using the most used guidelines on rhinitis and asthma (ARIA and GINA), in a large nation-wide study of asthmatics in Japan, 67.3% of patients present with physician-diagnosed rhinitis. Some patients without physician's diagnosed rhinitis have nasal symptoms suggestive of rhinitis

Table 3 Main results in the 26 680 selected patients

	Questionnaire administrator					
	Self-administered (n = 13 024)			Physician's administered (n = 13 656)		
	Existence of rhinitis			Existence of rhinitis		
	Yes (n = 8910)	No (n = 4114)	OR (95% CI)	Yes (n = 9035)	No (n = 4621)	OR (95% CI)
Age (years)						
Mean (SD)	47.4 (17.2)	56.8 (17.6)	0.970 (0.968–0.973)	50.5 (18.8)	60.2 (18.8)	0.973 (0.971–0.975)
Sex, n (%)						
Male	3450 (38.7)	1821 (44.3)	0.80 (0.74–0.86)	3649 (40.4)	2056 (44.5)	0.85 (0.79–0.91)
Female	5460 (61.3)	2293 (55.7)		5386 (59.6)	2565 (55.5)	
Rhinitis questionnaire, n (%)						
Watery rhinorrhea						
Yes	5252 (58.9)	475 (11.5)	11.00 (9.91–12.21)	6481 (71.7)	273 (5.9)	40.42 (35.47–46.05)
No	3638 (41.1)	3639 (88.5)		2554 (28.3)	4348 (94.1)	
Any nasal symptom without watery rhinorrhea						
Yes	2157 (24.2)	519 (12.6)	2.21 (1.99–2.46)	1667 (18.5)	288 (6.2)	3.40 (2.99–3.88)
No	6753 (75.8)	3595 (87.4)		7368 (81.5)	4333 (93.8)	
Asthma questionnaire, n (%)						
Wheezing at night						
Yes	4024 (45.2)	1514 (36.8)	1.41 (1.31–1.53)	4848 (53.7)	2041 (44.2)	1.46 (1.36–1.57)
No	4886 (54.8)	2600 (63.2)		4187 (46.3)	2580 (55.8)	
More than twice a week						
Yes	1912 (21.6)	690 (16.8)	1.36 (1.24–1.50)	2263 (25.0)	1006 (21.8)	1.20 (1.10–1.31)
No	6989 (78.4)	3424 (83.2)		6772 (75.0)	3615 (78.2)	
Wheezing during activities or exercise						
Yes	3972 (44.6)	1500 (36.5)	1.40 (1.30–1.51)	4256 (47.1)	1848 (40.0)	1.34 (1.24–1.44)
No	4938 (55.4)	2614 (63.5)		4779 (52.9)	2773 (60.0)	
Cough, dyspnea at night						
Yes	3206 (36.0)	1073 (26.1)	1.59 (1.47–1.73)	3815 (42.2)	1422 (30.8)	1.64 (1.53–1.77)
No	5704 (64.0)	3041 (73.9)		5220 (57.8)	3199 (69.2)	
Dyspnea during daytime of activities						
Yes	2728 (30.6)	978 (23.8)	1.42 (1.30–1.54)	3156 (34.9)	1356 (29.3)	1.29 (1.18–1.40)
No	6182 (69.4)	3136 (76.2)		5879 (65.1)	3265 (70.7)	
Need for rescue inhaler						
Yes	3313 (37.2)	1165 (28.3)	1.50 (1.38–1.62)	3506 (38.8)	1273 (27.5)	1.67 (1.54–1.80)
No	5597 (62.8)	2949 (71.7)		5529 (61.2)	3348 (72.5)	
Need for rescue inhaler over twice a week						
Yes	1701 (19.1)	671 (16.3)	1.21 (1.10–1.34)	1680 (18.6)	698 (15.1)	1.28 (1.17–1.41)
No	7209 (80.9)	3443 (83.7)		7355 (81.4)	3923 (84.9)	

and up to 73.1% of asthmatics may be assumed to suffer from rhinitis. This study is the first to show (i) an age-dependent prevalence of rhinitis, (ii) that most asthmatics have moderate/severe rhinitis as defined by ARIA, and (iii) that patients with physician's diagnosed rhinitis have poorer asthma control, as defined by GINA, than those without rhinitis. The study included two sets of over 13 000 patients each using identical questionnaires for asthma and rhinitis. Similar results have been obtained in both populations showing the validity of results.

Limitations

The subjects included in this study were prediagnosed with asthma. The diagnosis of asthma was made according to the Japanese guidelines (16). These guidelines have been used by the vast majority of physicians in Japan for the past 15 years (23) and have been frequently updated. However, it is possible that, after 60 years of age, some COPD patients may have been diagnosed as asthmatics (24).

The same questionnaire was self-administered and physician-administered. The questions were based on the two most widely used asthma [GINA (15)] and rhinitis [ARIA (1)] guidelines. All questions were filled in, and 26 680 (90.3%) patients had an evaluable questionnaire for the study purpose. Results of both questionnaires were similar. The severity and persistence of rhinitis was based on all ARIA questions (1). The control of asthma was based on GINA questions (15) but did not include pulmonary function (17). It is, therefore, possible that some patients were classified as 'controlled' whereas they were not. However, most asthma control questionnaires do not use pulmonary function tests

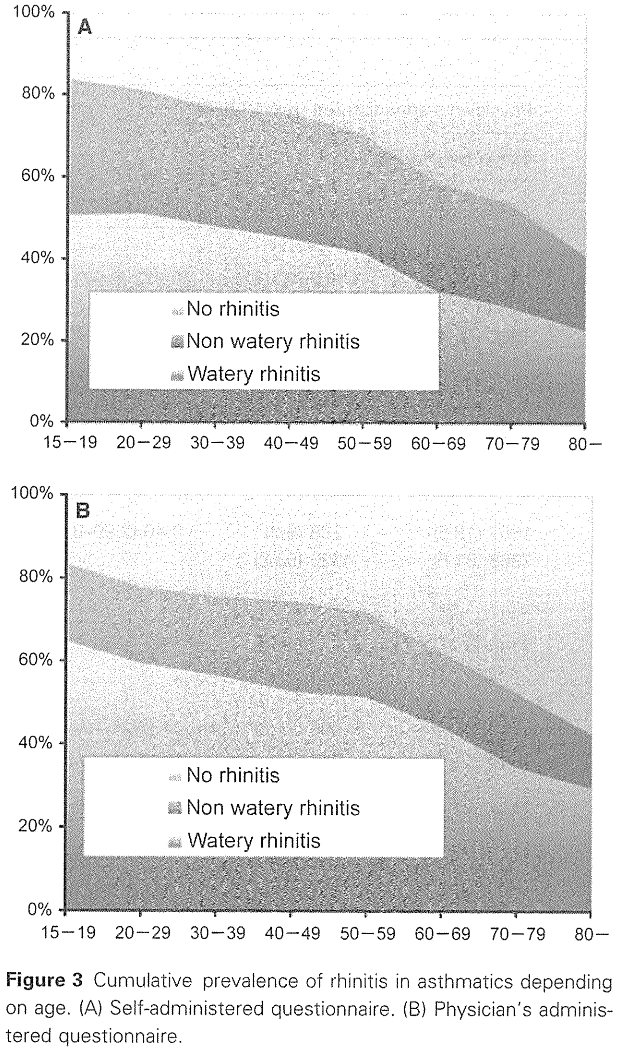

Figure 3 Cumulative prevalence of rhinitis in asthmatics depending on age. (A) Self-administered questionnaire. (B) Physician's administered questionnaire.

(25), and the ACQ (asthma control questionnaire) is more reliable without including data of pulmonary function tests than with them (26). Some questions of GINA control are not fully defined, and we needed to use a specific wording. This is the case for the duration of the survey (4 weeks).

Treatment of patients for asthma or rhinitis was not defined, as, in this sample it appeared very difficult to assess the exact treatment. Moreover, asthma control is independent of treatment (25). On the other hand, some patients receiving treatment for rhinitis may not have had a physician's diagnosis of rhinitis as they may have been asymptomatic.

Visual analog scales are used in many diseases and are of interest in rhinitis (18, 19). The present study confirms the potential importance of VAS in rhinitis as asthmatics without rhinitis have a median level of 0.07–0.38 cm whereas those with physician-diagnosed rhinitis have a median value of 5.49–5.6 cm. These levels are similar to those reported in European populations of rhinitis patients (18, 19). However, for asthma, VAS is not validated yet and it was used as an exploratory outcome.

Allergic and nonallergic rhinitis cannot be differentiated by questionnaire and a structured allergy history may be insufficient for the diagnosis of allergy (27). Around 20% of asthmatics had nasal obstruction without rhinorrhea, and these patients may have nonallergic rhinitis (5). Smoking was not studied and this exposure may have helped to differentiate asthma and COPD in the older population group of the study (24).

The study is a nation-wide survey with an adequate repartition of patients throughout the country. The duration of the study may have been extended to one year to control climatic parameters. However, in autumn and winter, many patients could have viral nasal infections which can mimic rhinitis. We, therefore, reduced the length of the study to around 6 months.

Interpretation

The primary outcome was the rate of rhinitis in asthmatics assessed using physician-diagnosis of rhinitis. As previously reported, rhinitis is common in asthma (1–3). However, this study is unique owing to the diagnosis of rhinitis by physicians in a very large sample, the questionnaire based on GINA and ARIA. No study of this size has ever been published. It appears that physicians may not diagnose rhinitis accurately as a subset of asthmatics without diagnosis of rhinitis had nasal symptoms, and some of them had moderate/severe nasal symptoms. The vast majority of patients without diagnosed rhinitis had intermittent symptoms. Thus, it is likely that the rate of rhinitis was greater than that diagnosed by physicians. In subsequent analyses, it will be important to assess differences between primary care physicians and allergy specialists.

Another novel finding is the age-dependent prevalence of rhinitis. The size of the study allows comparisons between age groups and 1891 patients were over 80 years. Rhinitis prevalence decreases from around 75% below the age of 60 years to 45% after 80 years. Less than 30% of asthmatics over 80 years had rhinorrhea. In older patients, there may be differences in perception of rhinitis or different phenotypes of asthma and/or rhinitis and their interaction (28). These data prompt new studies in elderly to better understand and control rhinitis and asthma and their interaction.

Asthma control is impaired in patients with rhinitis. This is a novel finding as no study included a full questionnaire on GINA in patients with rhinitis and many studies are *post hoc* analyses (29, 30). All GINA clinical criteria (except exacerbations in past year) and VAS levels are consistent. Moreover, the results of self-questionnaire and physician-administered questionnaires show similar results. Patients report fewer criteria of poor control than physicians. It is possible that differences in asthma treatment exist between asthmatics with and without rhinitis.

Generalizability

This study used the same methods in two sets of subjects and experimenters. It may be, therefore, seen as a replication study to determine generalizability to different subjects, age groups, and locations. The results are reliable and valid, and extraneous variables did not modify results. Underreporting of rhinitis symptoms and asthma control was observed when the questionnaires were applied by the patients. This is common in allergy and respiratory fields (31). The sample group is truly representative of the whole Japanese population.

The size of the group allows the statistics to be safely extrapolated to the entire population of Japan and give clues for the expansion outside Japan as many of the outcomes are similar in Japanese and European populations (18, 19).

Conclusions

Asthma is a highly prevalent disease worldwide and although links between asthma and rhinitis have been extensively studied, no large study has been made using the most widely used questionnaires for both asthma and rhinitis. Thus, although the study has been exclusively made in Japan, it can be generalized. This study shows that rhinitis should be examined in all patients with asthma and that rhinitis is a marker of lack of control of the disease.

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Author contributions

Ken Ohta designed the protocol and was involved in the writing and analysis. Jean Bousquet was involved in the design of the protocol, the analysis, and writing. Philippe J. Bousquet was involved on the methodology part and writing of the paper. Lawrence Grouse was involved in the protocol design and the writing of the paper. The other Japanese authors participated in the design of the protocol, recruitment of patients, and drafting of the paper.

Conflict of interest

Ken Ohta has received honorarium for boards, scientific expertize, lectures from AstraZeneca, GSK, Kyorin, Novartis, MSD. Philippe Jean Bousquet has received honorarium for lectures and scientific expertize from Schering Plough and Stallergènes. Jean Bousquet has received honorarium for boards, scientific expertize, lectures from ALK, AstraZeneca, Banyu, Chiesi, GSK, Merck, Novartis, Schering Plough, Stallergènes, UCB. Hisamichi Aizawa has received honorarium for lectures from Boehringer Ingelheim, GSK. Sankei Nishima has received honorarium for scientific expertize from Teijin Pharma. The following authors have no conflict to declare, Kazuo Akiyama, Mitsuru Adachi, Masakazu Ichinose, Motohiro Ebisawa, Gen Tamura, Atsushi Nagai, Takeshi Fukuda, Akihiro Morikawa, Yoshitaka Okamoto, Yoichi Kohno, Hirohisa Saito, Hiroshi Takenaka, Lawrence Grouse.

Supporting Information

Additional Supporting Information may be found in the online version of this article found at: http://www.wileyonlinelibrary.com.

Figure S1. Distribution of Institutions across Japan.

Figure S2. VAS on asthma.

Table S1. Questionnaire on rhinitis in asthmatics.

Table S2. Questionnaire on asthma control with rhinitis.

Table S3. Working definition of GINA classification employed in SACRA to assess asthma control.

Table S4. Number of participants with missing data.

Table S5. Diagnosis of rhinitis.

Table S6. Rhinitis deteriorates asthma control assessed by VAS and GINA criteria.

Table S7. Other results.

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References

1. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 2008;**63**(Suppl. 86):8–160.
2. Shaaban R, Zureik M, Soussan D, Neukirch C, Heinrich J, Sunyer J et al. Rhinitis and onset of asthma: a longitudinal population-based study. *Lancet* 2008;**372**:1012–1014.
3. Ait-Khaled N, Odhiambo J, Pearce N, Adjoh KS, Maesano IA, Benhabyles B et al. Prevalence of symptoms of asthma, rhinitis and eczema in 13- to 14-year-old children in Africa: the International Study of Asthma and Allergies in Childhood Phase III. *Allergy* 2007;**62**:247–258.
4. Walker S, Sheikh A. Self reported rhinitis is a significant problem for patients with asthma. *Prim Care Respir J* 2005;**14**:83–87.
5. Bousquet J, Fokkens W, Burney P, Durham SR, Bachert C, Akdis CA et al. Important research questions in allergy and related diseases: nonallergic rhinitis: a GA2LEN paper. *Allergy* 2008;**63**:842–853.

6. Dobashi K, Nakazawa T, Mori M. [Report on the questionnaire study of actual status of adult bronchial asthma patients in gunma prefecture]. *Nisshoku Kan A J* 2003;**10**:2–26.
7. Okada M, Names PF. [Frequency of seasonal allergic rhinitis, bronchial asthma and atopic dermatitis in adult females in the Area of Osaka, Rinsho to Kenkyu]. *J Clin Pract Res* 2009;**79**:134–137.
8. Bresciani M, Paradis L, Des Roches A, Vernhet H, Vachier I, Godard P et al. Rhinosinusitis in severe asthma. *J Allergy Clin Immunol* 2001;**107**:73–80.
9. ten Brinke A, Grootendorst DC, Schmidt JT, De Bruine FT, van Buchem MA, Sterk PJ et al. Chronic sinusitis in severe asthma is related to sputum eosinophilia. *J Allergy Clin Immunol* 2002;**109**:621–626.
10. Bousquet J, Gaugris S, Kocevar VS, Zhang Q, Yin DD, Polos PG et al. Increased risk of asthma attacks and emergency visits among asthma patients with allergic rhinitis: a subgroup analysis of the improving asthma control trial. *Clin Exp Allergy* 2005;**35**:723–727.
11. Price D, Zhang Q, Kocevar VS, Yin DD, Thomas M. Effect of a concomitant diagnosis of allergic rhinitis on asthma-related health care use by adults. *Clin Exp Allergy* 2005;**35**:282–287.
12. Sole D, Camelo-Nunes IC, Wandalsen GF, Melo KC, Naspitz CK. Is rhinitis alone or associated with atopic eczema a risk factor for severe asthma in children? *Pediatr Allergy Immunol* 2005;**16**:121–125.
13. Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;**108** (5 Suppl.):S147–S334.
14. Ciprandi G, Cirillo I, Vizzaccaro A, Tosca M, Passalacqua G, Pallestrini E et al. Seasonal and perennial allergic rhinitis: is this classification adherent to real life? *Allergy* 2005;**60**:882–887.
15. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, Fitzgerald M et al. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008;**31**:143–178.
16. Nishima S. [New approach and recommendation in JAGL2007 (Japanese guideline for the diagnosis and treatment of allergic diseases 2007)]. *Nippon Rinsho* 2009;**67**:2039–2042.
17. Thomas M, Kay S, Pike J, Williams A, Rosenzweig JR, Hillyer EV et al. The Asthma Control Test (ACT) as a predictor of GINA guideline-defined asthma control: analysis of a multinational cross-sectional survey. *Prim Care Respir J* 2009;**18**:41–49.
18. Bousquet PJ, Combescure C, Neukirch F, Klossek JM, Mechin H, Daures JP et al. Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. *Allergy* 2007;**62**:367–372.
19. Bousquet PJ, Combescure C, Klossek JM, Daures JP, Bousquet J. Change in visual analog scale score in a pragmatic randomized cluster trial of allergic rhinitis. *J Allergy Clin Immunol* 2009;**123**:1349–1354.
20. Flood EM, De Cock E, Mork AC, Revicki DA. Evaluating preference weights for the Asthma Symptom Utility Index (ASUI) across countries. *Health Qual Life Outcomes* 2006;**4**:51.
21. Laforest L, El Hasnaoui A, Pribil C, Ritleng C, Schwalm MS, Van Ganse E. Asthma patients' perception of their ability to influence disease control and management. *Ann Allergy Asthma Immunol* 2009;**102**:378–384.
22. Nakagawa T, Miyamoto T, Ito K, Ohta K. Prevalence of bronchial asthma in adult habitants in Fujieda city. *Nihon Kyobu Shikkan Gakkai Zasshi* 1987;**25**:873–879.
23. Makino S, Furusho K, Ohta K, Mukoyama T. A survey on awareness and utilization of new asthma management guidelines in Japan. *J Asthma* 2003;**40**:701–708.
24. Jenkins CR, Thompson PJ, Gibson PG, Wood-Baker R. Distinguishing asthma and chronic obstructive pulmonary disease: why, why not and how? *Med J Aust* 2005;**183**(1 Suppl.):S35–S37.
25. Humbert M, Holgate S, Boulet LP, Bousquet J. Asthma control or severity: that is the question. *Allergy* 2007;**62**:95–101.
26. Juniper EF, Bousquet J, Abetz L, Bateman ED. Identifying 'well-controlled' and 'not well-controlled' asthma using the Asthma Control Questionnaire. *Respir Med* 2006;**100**:616–621.
27. Smith HE, Hogger C, Lallemant C, Crook D, Frew AJ. Is structured allergy history sufficient when assessing patients with asthma and rhinitis in general practice? *J Allergy Clin Immunol* 2009;**123**:646–650.
28. Busse PJ, Kilaru K. Complexities of diagnosis and treatment of allergic respiratory disease in the elderly. *Drugs Aging* 2009;**26**:1–22.
29. Zhang Q, Thomas M, Wisniewski T, Sazonov Kocevar V, Price D. Treatment and outcomes in patients with asthma and allergic rhinitis in the United Kingdom. *Int Arch Allergy Immunol* 2006;**142**:318–328.
30. Haughney J, Price D, Kaplan A, Chrystyn H, Horne R, May N et al. Achieving asthma control in practice: understanding the reasons for poor control. *Respir Med* 2008;**102**:1681–1693.
31. Holgate S, Bisgaard H, Bjermer L, Haahtela T, Haughney J, Horne R et al. The Brussels Declaration: the need for change in asthma management. *Eur Respir J* 2008;**32**:1433–1442.

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ORIGINAL ARTICLE

Age-related Prevalence of Allergic Diseases in Tokyo Schoolchildren

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ABSTRACT

Background: The International Study of Asthma and Allergies in Childhood (ISAAC) has reported the prevalence of asthma and allergic diseases in many countries.
Methods: We used the ISAAC core written questionnaire to examine the prevalence of asthma and allergic diseases in 6- to 14-year old schoolchildren in Tokyo. In 2005, we conducted a cross-sectional survey of all schoolchildren in all public schools located in the Setagaya area of Tokyo.
Results: Data were collected from 27,196 children in 95 schools. Prevalence ranged from 10.5% to 18.2% for asthma symptoms and from 10.9% to 19.6% for atopic dermatitis, with both conditions tending to decrease with age. As has been previously reported for all age groups, significantly higher rates of current asthma are observed in boys than in girls. The prevalence of allergic rhinoconjunctivitis exhibited a different pattern from that of asthma and atopic dermatitis, peaking at the age of 10 (34.8%). Prevalence of allergic rhinoconjunctivitis was 1.5 to 2-fold higher than the previous ISAAC studies that were performed in Tochigi and Fukuoka. In all age groups, symptoms of allergic conjunctivitis were more frequent from February to May, which coincides with the Japanese cedar pollen season, and were less frequent between June to September.
Conclusions: The prevalence of asthma and atopic dermatitis was higher in younger schoolchildren. Tokyo schoolchildren appear to have extremely high prevalence rates of seasonal allergic rhinoconjunctivitis.

KEY WORDS

asthma, atopic dermatitis, ISAAC, prevalence, rhinitis

INTRODUCTION

Asthma and allergic diseases are common in children. Urbanization has led to an increase in allergic diseases, and thus, this has become an important health problem in today's society.

Many countries have conducted large prevalence surveys of asthma and allergic diseases. In 1991, the International Study of Asthma and Allergic diseases in Childhood (ISAAC) established a standardized methodology to compare the prevalence and severity of asthma and atopic diseases in children.[1] Since starting the study in 1993, the ISAAC Phase One study group has examined the prevalence rates of asthma in children around the world and found that over a 12-month period, the highest rates were for children living in the UK, Australia, and New Zealand, while the lowest were in children residing in Eastern Europe, the Asia-Pacific, and Africa.[2] In contrast, the highest prevalence rates of symptoms related to allergic rhinoconjunctivitis occurred in countries that were scattered across the world. Moreover, the prevalence of allergic rhinoconjunctivitis in children aged 13-14 years was higher than those aged 6-7 years in all of the countries studied around the world. Interestingly, this pattern was not seen for asthma.

The Japanese Ministry of Education, Culture, Sports, Science and Technology has announced that the prevalence of doctor-diagnosed asthma in children has doubled from 1994 to 2004. They also reported that schoolchildren are more likely than other age groups to develop asthma.[3]

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In Japan, ISAAC surveys have been conducted in Fukuoka, the eighth largest city in Japan, and in Tochigi, which is an average-sized city. In Tochigi in 1995, the prevalence of allergic rhinoconjunctivitis in children aged 13-14 was 21.5%.[4] In Fukuoka, the 12-month prevalence of allergic rhinoconjunctivitis among children aged 6-7 increased from 7.8% in 1994 to 10.6% in 2002, while over the same period of time in children aged 13-14, it increased from 14.9% to 17.6%.[5] Similar trends were also seen in many other Asia-Pacific countries and in India. In contrast, the prevalence of asthma, however, did not notably increase in any of these countries or in Japan.

Children born in urban areas are expected to have higher prevalences of allergic diseases than those born in rural areas.[6] Although Tokyo is the largest city in Japan, and thereby, would be expected to have the highest prevalence of allergic diseases, previous ISAAC surveys have never been done in this city. Thus, there were two aims of the present study. First, the ISAAC protocol was used to determine whether age-related differences are responsible for the prevalence of allergic symptoms observed among Tokyo schoolchildren. Based on these findings, the second part of the study was designed to compare these results with the findings of previous ISAAC studies in Japan and determine if there were differences between large urban areas and other areas that were less populated/more rural in nature.

METHODS

SUBJECTS

The survey was conducted from May to June, 2005, in accordance with the ISAAC protocol.[7] The present survey was part of an investigation by the Japanese Asthma Survey Group (JASG), and was aimed at surveying the prevalence of allergic diseases in all age groups at various places throughout Japan.

Setagaya was chosen as the research zone for this study, as it is located in the center of Tokyo. During the study period, this was the biggest geographical region within the Greater Tokyo Area. Setagaya has a population density that is close to the Tokyo average, with 830,000 inhabitants living in about 58 km^2 (22 square miles).

In Japan, compulsory education consists of nine grades (years). In April of each year, children who have reached the age of 6 enroll in an elementary school that has six grades. After graduating from elementary school, students enter junior high school, which has three grades. The current survey covered all of the schoolchildren in these nine grades. During the study period, Setagaya had 64 public elementary schools and 31 public junior high schools, with approximately 80% of the children attending these public schools. With the help of the Setagaya City Board of Education, we were able to investigate all public elementary and junior high school students.

QUESTIONNAIRE

We used the ISAAC written questionnaire for 6-7 year olds for the elementary school children and the questionnaire for 13-14 year olds for the junior high school children. Our group previously translated the ISAAC written questionnaire from English into Japanese and then back into English to confirm its accuracy. An explanatory note for eczema and rash was added, as the Japanese language does not normally differentiate between the two. The questionnaire was distributed at all of the schools, with the children then taking it home to be filled out. Prior to filling out the questionnaire, all participants in the study provided informed consent. For the younger age group, the children's parents completed the questionnaire, while the children in the older age group completed it on their own. After completing the form, the questionnaires were taken back to the schools for collection.

Based on the questionnaire answers, we evaluated the 12-month point prevalences of asthma, allergic rhinoconjunctivitis, and atopic dermatitis.[7] To define current asthma and examine wheezing during the previous 12 months, we asked the following question, "Have you (has your child) had wheezing or whistling in the chest in the last 12 months?". If current asthma was present, the questionnaire further assessed the frequency and severity of the episodes. Questions pertaining to allergic rhinoconjunctivitis included those regarding sneezing or a running or blocked nose (in the absence of flu) that was associated with itchy-watery eyes over the last 12 months. The monthly frequency among children who had symptoms of allergic rhinoconjunctivitis was evaluated by asking, "In which of the past 12 months did this nose problem occur? (please tick any which apply)." Atopic dermatitis was considered to be present when there was an itchy, relapsing skin rash that affected the flexural areas during the preceding 12 months.

ETHICAL CONSIDERATIONS

The ethics committee of the National Center for Child Health and Development approved the study protocol. The older children directly provided informed consent. However, since parents completed the questionnaire for the younger children, parental informed consent was obtained in this group.

STATISTICAL ANALYSIS

Analyses focused on changes in the 12-month prevalence of the symptoms, which included asthma, rhinitis and dermatitis. Data were analyzed using SPSS 15.0J (SPSS Inc., Chicago, IL, USA), with a p-value of <0.05 defined as being statistically significant. Proportions between the two groups were compared using chi-squared tests. The interrelationship between age and the 12-month point prevalence was evaluated by Pearson's correlation.

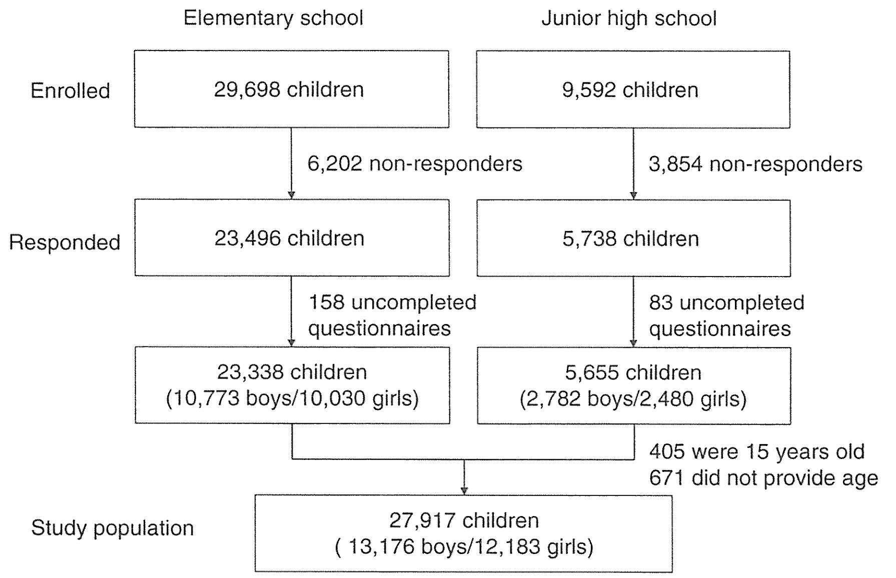


Fig. 1 Study subjects and the study protocol. All students in all public schools in Setagaya from May through June of 2005 were enrolled in the study, with more than 70% of all children aged 6-14 years at these schools included in the analyses.

RESULTS

Of the 95 schools approached, all agreed to participate, which resulted in a target population of 39,290 children (Fig. 1). Out of this population, a total of 23,338 elementary school children (78.6%), aged 6 to 12 years, and 5,655 junior high school children (59.0%), aged 12 to 15 years, completed questionnaires. For the 15-year-old children, numbers were quite small and thus, we excluded this group from the analyses. Of the 27,917 children aged 6 to 14 that we were able to analyze, 13,176 (47.2%) were boys, and 12,183 (43.7%) were girls. In 2,558 children, we were not able to determine the gender.

Current asthma prevalence ranged from 10.5% to 18.2% among all age groups (Table 1), with the highest found in the younger children. There was a strong inverse correlation between the age and prevalence (r = -0.956, P < .001). When boys were compared to girls in all of the age groups, boys had significantly higher rates of current asthma (P < .001 for ages 6 to 12, P < .05 for ages 13 and 14). While frequent wheezing and sleep disturbance were more common in younger children and in boys, exercise-induced wheezing during the last 12 months was more common in older children of both sexes and in younger boys.

In contrast to the asthma findings, the prevalence of allergic rhinoconjunctivitis tended to be higher in older children (Table 2), increasing rapidly from age 6 to 10. By the age of 10, the prevalence of allergic rhinoconjunctivitis was 34.8%. In all age groups, symptoms of allergic rhinoconjunctivitis were more frequent from February to May, and less frequent from June to September (Fig. 2). On a day-to-day basis, moderate or severe interference due to rhinoconjunctivitis was more common in older children of both sexes and in boys.

Similar to the asthma findings, the prevalence of atopic dermatitis was highest in younger children, with analyses showing a significant inverse correlation with age (r = -0.983, P < .001) (Table 2). However, severe symptoms of atopic dermatitis were more often observed in older children. There were no gender differences noted for the prevalence or severity of atopic dermatitis.

Among the 27,389 children aged 6 to 14 years who completed questionnaires about their current asthma, allergic rhinoconjunctivitis and atopic dermatitis symptoms, 14.0% had current asthma. Of these children, 41.6% and 31.3% had the symptoms of allergic rhinoconjunctivitis and atopic dermatitis, respectively. While 43.1% of the children in this study had ≥1 of the symptoms during the past 12 months, only 2.2% had all three symptoms (Fig. 3). Table 3 shows the overlap of the current symptoms for three diseases based on age among the 27,389 children.

DISCUSSION

In 2005 we examined the prevalence of asthma, allergic rhinoconjunctivitis and atopic dermatitis in a large sample of schoolchildren who resided in the Tokyo metropolitan area of Setagaya. The prevalence of current asthma and atopic dermatitis was inversely correlated with age, whereas that of allergic rhinoconjunctivitis showed an age-dependent increase until

Table 1 Prevalence (%) and severity of asthma symptoms in 6 to 14 year old children

Symptoms	Age (years)								
	6	7	8	9	10	11	12	13	14
Current wheeze									
Total	18.2	15.7	15.6	13.3	14.5	11.9	12.0	10.3	10.5
Boys	***21.4	***17.8	***17.8	***16.0	***17.4	***14.7	***14.9	*12.0	*12.0
Girls	14.5	13.5	12.9	10.9	10.9	9.3	9.3	8.6	8.8
Wheezing attacks ≥ 4 /12 months									
Total	5.1	3.7	4.4	3.7	4.0	3.3	3.1	3.3	3.1
Boys	*6.0	**4.6	**5.5	*4.4	*4.6	*4.2	*4.0	4.1	3.1
Girls	4.3	2.8	3.2	2.9	3.0	2.7	2.3	2.7	3.0
Awakened by wheezing ≥ 1 /wk									
Total	2.4	2.3	2.0	2.0	1.6	1.3	1.2	0.6	1.2
Boys	3.0	2.4	2.2	2.1	1.8	*1.6	1.7	0.6	*2.0
Girls	2.0	2.2	1.7	1.9	1.2	0.8	0.9	0.7	0.5
Speech limitation									
Total	2.4	1.7	1.5	1.8	1.2	1.2	1.4	0.9	1.8
Boys	**3.3	2.0	1.8	2.2	*1.7	***1.8	***2.0	1.2	1.9
Girls	1.6	1.6	1.1	1.5	0.8	0.5	1.0	0.7	2.0
Exercised-induced wheezing									
Total	5.8	6.0	6.2	6.7	7.6	7.1	11.7	13.2	14.4
Boys	***7.6	***7.3	6.6	**7.9	7.8	7.9	12.0	13.6	*14.3
Girls	4.1	4.6	5.7	5.3	6.8	6.4	12.1	13.1	15.0

Comparisons were performed between boys and girls for each symptom and age. *P < .05, **P < .01, ***P < .001.

Table 2 Prevalence (%) and severity of allergic rhinoconjunctivitis and atopic dermatitis symptoms in 6 to 14 year old children

Symptoms	Age (years)								
	6	7	8	9	10	11	12	13	14
Allergic rhinoconjunctivitis									
Total	19.7	22.5	25.1	26.9	34.8	32.5	33.8	27.8	29.1
Boys	*21.2	23.1	26.3	27.1	35.6	33.0	35.2	29.3	27.0
Girls	17.7	22.3	23.9	25.4	34.5	31.9	32.3	27.1	30.1
Moderate to severe interference by rhinitis									
Total	10.2	11.9	14.1	14.6	21.4	19.9	21.5	18.1	20.6
Boys	11.2	*13.1	**16.1	15.1	*23.4	*21.1	*23.8	18.9	20.6
Girls	9.5	10.7	12.3	13.3	20.6	18.1	19.4	15.9	19.8
Atopic dermatitis									
Total	19.6	17.4	16.9	16.6	15.3	15.0	13.6	11.9	10.9
Boys	19.9	17.0	17.3	17.7	15.6	14.8	13.3	10.7	10.3
Girls	19.7	18.5	16.2	15.6	14.8	15.0	14.1	12.8	11.4
Kept awake by rash ≥1/wk									
Total	1.6	1.7	1.7	1.5	1.5	1.3	1.9	2.5	2.5
Boys	1.5	1.8	1.9	1.6	1.2	1.2	2.1	2.0	2.7
Girls	1.8	1.6	1.4	1.5	1.4	1.5	1.6	2.9	2.2

Comparisons were performed between boys and girls for each symptom and age. *P < .05, **P < .01, ***P < .001.

reaching the age of 10. These correlations also showed an overlap of the prevalences for the three diseases in accordance with age. These findings suggest that the peak prevalence of asthma and atopic dermatitis may occur at or before the age of 5, similar to that previously reported. In an Australian study, the frequency of atopic dermatitis increased and reached a maximum prevalence by the age of 1, after which it decreased in an age-dependent manner in a group of preschool-age children.[8] For asthma, the

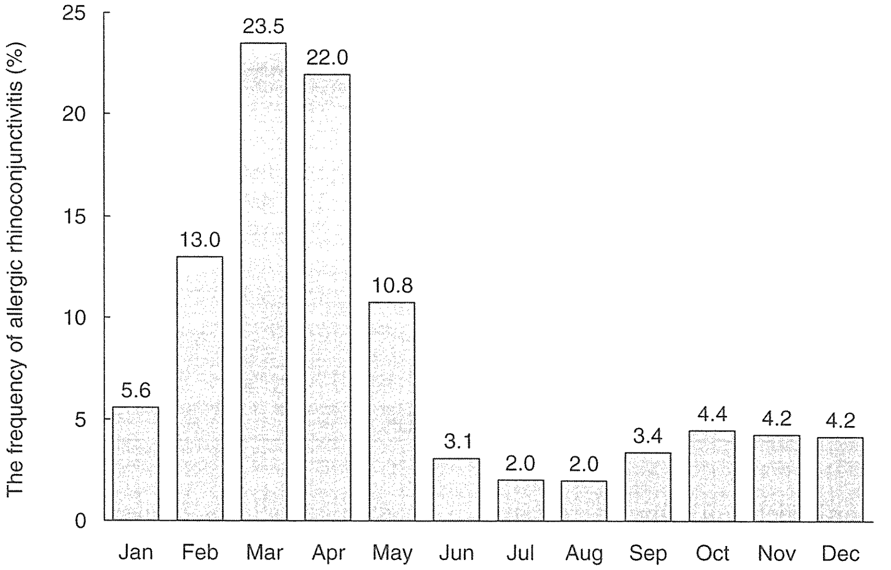
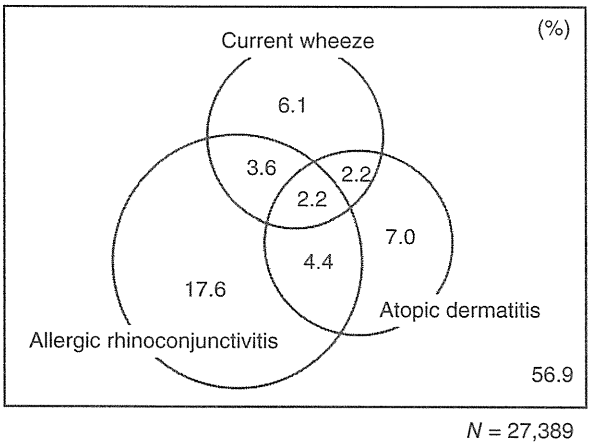


Fig. 2 Monthly frequency of allergic rhinoconjunctivitis in all subject age groups.



N = 27,389

Fig. 3 Venn diagram showing overlap of the current asthma, allergic rhinoconjunctivitis and/or atopic dermatitis symptoms among children aged 6 to 14 who completed questionnaires that gathered symptom prevalence data over a 12-month period.

prevalence in boys was higher than that in girls in each age group of the present study. This supports the findings of previous ISAAC studies, including one that was performed in Fukuoka. This study demonstrated that 6-7 year olds had higher prevalences of asthma and atopic dermatitis and a lower prevalence of allergic rhinoconjunctivitis when compared to 13-14 year olds. The study also showed that the prevalence of asthma was higher in boys.[2]

In the present study, the prevalence of atopic dermatitis also decreased with increasing age. On the other hand, older children were more likely to have severe symptoms. This suggests that even though mild dermatitis appears to have been completely resolved, severe dermatitis actually became exacerbated with increased age. While results of previous ISAAC studies have been mixed with regard to these findings, most Asian studies have shown a similar pattern. Therefore, atopic dermatitis rates in Setagaya, as in other Asian cities, might be influenced by exposure to irritant gases such as car exhaust fumes or by high concentrations of house dust mites.[9]

The prevalence rates of allergic rhinoconjunctivitis in children aged 6-7 and 13-14 in the present study were extremely high as compared to those in the 2002 Fukuoka study, even though the asthma rates were similar. It should also be noted that the prevalence of allergic rhinoconjunctivitis in Tokyo children aged 6-7 was one of the highest that has been documented among all of the ISAAC Phase Three populations.[6] Tokyo has the highest per-capita income in Japan, and thus, our findings are consistent with previous reports that have shown that the prevalence of allergic rhinoconjunctivitis is higher in high-income versus low-income countries.[10]

We compared the present results from Tokyo with those obtained using the same questionnaire several years previously in Fukuoka and Tochigi. These ISAAC Phase Three surveys revealed that the prevalence of allergic diseases in Fukuoka and other Asian areas did not change markedly from Phase One.[11] This suggests that the prevalence of allergic disease in Tokyo is also likely to have remained relatively constant during this period, hence comparisons between the present and previous studies can provide meaningful information.