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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Rhinitis has an association with asthma in school children

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ABSTRACT

Background: *A relevant relationship exists between the upper and lower airway, indicating the concept of a unified airway. This study aimed to evaluate whether rhinitis has an association with asthma in children.*

Methods: *A cross-sectional nationwide survey was performed among children 6–7, 13–14, and 16–17 years old, using the International Study of Asthma and Allergies in Children (ISAAC) questionnaire in Japan. According to the responses to the ISAAC core questions, a child who had experienced nasal symptoms in the past 12 months in the absence of a cold was defined as having current rhinitis.*

Results: *After excluding 11,475 children because of incomplete data, 136,506 children were analyzed. Even after adjusting for demographics, sex, and obesity, children with current rhinitis were more likely to have asthma (adjusted odds ratio [OR], 3.10 [95% CI, 2.92–3.30] in children aged 6–7 years; OR, 3.76 [95% CI, 3.45–4.10] in children aged 13–14 years; and OR, 3.59 [95% CI, 3.33–3.88] in children aged 16–17 years). Children whose daily activities were more impaired by rhinitis symptoms had a significantly higher prevalence of severe asthma. The adjusted ORs for severe asthma among asthmatic children whose daily activities were severely impaired by rhinitis symptoms were 3.66 (95% CI, 2.29–5.85) in children aged 6–7 years, 2.55 (95% CI, 1.64–3.96) in children aged 13–14 years, and 1.87 (95% CI, 1.24–2.82) in children aged 16–17 years compared with asthmatic children whose daily activities were not impaired at all.*

Conclusion: *There was a close association between rhinitis and asthma in young children to adolescents. Asthma should be examined in children with rhinitis symptoms.*

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A close association between allergic rhinitis and asthma has been established.[1,2] There are many similarities in the pathogenesis of both disorders.[3–5] For example, Th2 cells and allergic inflammatory cells, such as eosinophils and mast cells, infiltrate the nasal mucosa of subjects with allergic rhinitis and the bronchial mucosa of subjects with asthma. A nasal allergen challenge leads to the increased responsiveness of the lower airways in asthmatic subjects comorbid with allergic rhinitis.[6] Similarly, bronchial allergen challenge leads to the nasal inflammation in nonasthmatic allergic rhinitis patients.[7]

In adults, it has been shown that allergic rhinitis has a major impact on asthma morbidity and that treatment of rhinitis helps to improve asthma control. A *post hoc* analysis of data from a clinical trial showed that the presence of comorbid allergic rhinitis in adult patients with asthma resulted in a higher rate of asthma attacks and more emergency department visits compared with patients with asthma alone.[8] A nationwide study of Japanese adults patients with asthma showed that >60% of patients had rhinitis and that asthma control was significantly impaired in patients with rhinitis compared with patients without rhinitis.[9] It has also been reported that treating allergic rhinitis in patients with comorbid asthma significantly lowered the risk of asthma-related emergency department visits and hospitalizations.[10] In children, a recent cross-sectional survey in 203 children with asthma showed that the presence of rhinitis was associated with poor asthma control.[11] However, there have been no large population-based surveys regarding association between rhinitis and asthma in children.

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To evaluate whether rhinitis has an association with asthma in children, we analyzed the data of a cross-sectional population-based nationwide survey that was performed using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. The effect of the severity of rhinitis on the prevalence of asthma was also evaluated.

METHODS

Study Population

This study was a cross-sectional and questionnaire-based survey performed in 6- to 7-, 13- to 14-, and 16- to 17-year-old school children in Japan from April through July 2008. To perform a nationwide survey, schools were randomly selected from all of the prefectures. The total number of children recruited was 179,218, corresponding to ~2% of the pediatric population, according to the data of the National Institute of Population and Social Security Research. This study protocol was approved by the Institutional Review Board of the National Center for Child Health and Development.

Questionnaire

The survey used a Japanese version of the ISAAC questionnaire,[12] which was distributed among teachers of the participating schools. The questionnaires for children 6–7 years old were completed by their parents, and those for older children were answered by the children. The questionnaire also included questions regarding the living area, gender, height, and weight of the participants.

Current rhinitis was defined as a positive answer to the question, "In the past 12 months, have you (or your child) had a problem with sneezing, or a runny, or a blocked nose when you (or he/she) did not have a cold or the flu?" The severity of rhinitis was graded according to the answer to the question, "In the past 12 months, how much did this nose problem interfere with your (or your child's) daily activity"; not at all, a little, a moderate amount, or a lot. Current asthma was defined as answering positively to the question, "In the past 12 months, have you (or your child) had wheezing or whistling in the chest during the past 12 months?" Among children with current asthma, the severity of asthma was estimated with a combination of

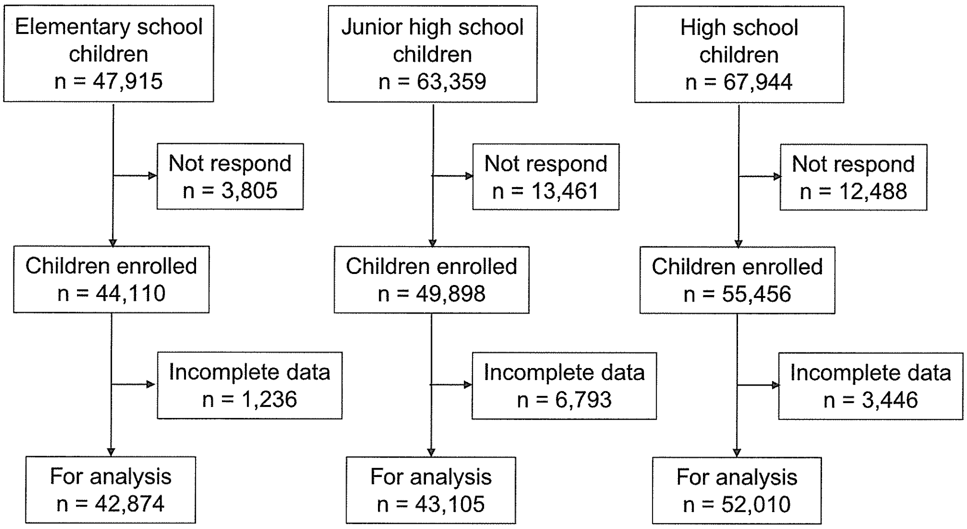

Figure 1. *Participants in the cross-sectional and questionnaire-based survey.*

three questions assessing the severity of asthma: "How many attacks of wheeze have you (or your child) had during the last 12 months? (none, 1 to 3, 4 to 12, or more than 12)"; "In the last 12 months, how often, on average, has your (or your child's) sleep been disturbed due to wheezing? (never, less than one night per week, or one or more nights per week)"; and "In the last 12 months, has wheezing been severe enough to limit your (or your child's) speech to only one or two words at a time between breaths?" Current severe asthma was defined as four or more asthma attacks, when sleep was disturbed for one or more nights per week, or when there had been an episode of speech limitation in the past 12 months.

Statistical Analyses

The χ^2-test was used to compare the differences in the prevalence of current symptoms between groups. A logistic regression analysis was performed to estimate the effects of rhinitis and other confounding factors, such as living area, gender, and obesity, on asthma prevalence. Multivariate analysis was used to evaluate the association of degree of impairment of daily activities caused by nasal symptoms with prevalence of current asthma and current severe asthma. A value of $p < 0.05$ was considered to be statistically significant. All of the analyses were performed using the statistical package SPSS for Windows, Version 17.0J (SPSS, Inc., Chicago, IL) and R Version 2.13.1 (available online).

RESULTS

Of the 179,218 children, 149,464 replied to the questionnaire (response rate, 92.1% in children aged 6–7 years; 78.8% in children aged 13–14 years; 81.6% in children aged 16–17 years). After excluding incomplete data, 139,506 questionnaires were analyzed (Fig. 1). Current rhinitis was found in 44.2–60.1% of the children (Table 1). In children aged 6–7 years, the prevalence of current rhinitis was lower and the prevalence of current asthma was higher than in older children. Significantly more boys had current rhinitis and asthma compared with girls in children aged 6–7 years, whereas these gender differences were not statistically significant in older age groups.

There was a higher incidence of asthma in children with current rhinitis compared with children without rhinitis (20.8% versus 7.7% in children aged 6–7 years, 13.5% versus 4.0% in children aged 13–14 years, 12.4% versus 3.8% in children aged 16–17 years; Table 2). Even after adjusting for living area, gender, and obesity, which are known to have effects on the prevalence of asthma,[13] rhinitis was still associated with asthma (adjusted odds ratio [OR], 3.10 [95% CI, 2.92–3.30] in children aged 6–7 years; OR, 3.76 [95% CI, 3.45–4.10] in children aged 13–14 years; and OR, 3.59 [95% CI, 3.33–3.88] in children aged 16–17 years). Among asthmatic children, severe asthma was also more prevalent in children with current rhinitis than in children with no rhinitis (10.9% versus 6.1% in children aged 6–7 years, 15.6% versus 9.5% in children aged 13–14 years, 15.0% versus 10.1% in children aged 16–17 years; Table 2). Again, even after adjusting for confounding factors, having rhinitis was still a significant risk factor for having severe asthma (adjusted OR, 1.94 [95% CI, 1.55–2.44] in children aged 6–7 years; OR, 1.70 [95% CI, 1.29–2.24] in children aged 13–14 years; and OR, 1.54 [95% CI, 1.22–1.95] in children aged 16–17 years).

More than 80% of the children with current rhinitis answered that their daily activity was impaired by rhinitis symptoms (data not shown). Children whose daily activities were more impaired by rhinitis symptoms had a significantly higher prevalence of current asthma even after adjusting for confounding factors (Table 3). The adjusted ORs for asthma among children whose daily activities were impaired a lot were 1.75 (95% CI, 1.50–2.04) in children aged 6–7 years, 2.54 (95% CI, 2.20–2.94) in children aged 13–14 years, and 2.21 (95% CI, 1.91) in children aged 16–17 years compared with children whose daily activities were not impaired at all. Furthermore, among asthmatic children, a higher degree of impairment of daily activities caused by rhinitis symptoms was associated with increased severity of asthma after adjusting for confounding factors (Table 3). The adjusted ORs for severe asthma among asthmatic children whose daily activities were impaired a lot were 3.66 (95% CI, 2.29–5.85) in children aged 6–7 years, 2.55 (95% CI, 1.64–3.96) in children aged 13–14 years, and 1.87 (95% CI, 1.24–2.82) in children aged 16–17 years compared with children whose daily activities were not impaired at all.

DISCUSSION

Many studies have indicated that allergic rhinitis and asthma are common comorbidities in children.[14–16] However, only a few epidemiological population-based surveys have evaluated this association in young children to adolescents. In this large population-based nationwide survey evaluating >100,000 children aged 6–7, 13–14, and 16–17 years, we reconfirmed a close association between rhinitis and asthma in Japanese school children. Even after adjusting for confounding factors affecting the prevalence of asthma, having rhinitis was a significant risk factor for having current asthma and severe asthma. Furthermore, among asthmatic children, a greater degree of impairment of daily activities caused by rhinitis symptoms was associated with higher prevalence of severe asthma.

Asthma and allergic rhinitis have similar pathophysiological manifestations; therefore, they are considered to be a single syndrome: chronic allergic respiratory syndrome.[3,4] Supporting this concept, the

Table 1 **Baseline characteristics of the study participants**

	Total	Boys	Girls	*p* Value*
Children aged 6–7 yr	42,874	21,861	21,013	
Current rhinitis	18,930 (44.2)	10,592 (48.5)	8338 (39.7)	<0.001
Current asthma	5798 (13.5)	3435 (15.7)	2363 (11.2)	<0.001
Current severe asthma	542 (1.3)	332 (1.5)	210 (1.0)	<0.001
Children aged 13–14 yr	43,105	21,080	22,025	
Current rhinitis	25,891 (60.1)	12,668 (60.1)	13,223 (60.0)	0.906
Current asthma	4195 (9.7)	2098 (10.0)	2097 (9.5)	0.135
Current severe asthma	613 (1.4)	297 (1.4)	316 (1.4)	0.839
Children aged 16–17 yr	52,010	26,815	25,195	
Current rhinitis	27,148 (52.2)	14,222 (53.0)	12,926 (51.3)	<0.001
Current asthma	4311 (8.3)	2264 (8.4)	2047 (8.1)	0.192
Current severe asthma	598 (1.1)	307 (1.1)	291 (1.2)	0.935

Data represent number (percentage).
**χ^2-analysis for evaluating gender differences.*

Table 2 **Association of current rhinitis with asthma**

	All Children			Children with Current Asthma		
	Prevalence of Asthma (%)	AOR*	95% CI	Prevalence of Severe Asthma (%)	AOR*	95% CI
Children aged 6–7 yr						
No rhinitis#	7.7	1		6.1	1	
Current rhinitis	20.8	3.10	2.92–3.30	10.9	1.94	1.55–2.44
Children aged 13–14 yr						
No rhinitis#	4.0	1		9.5	1	
Current rhinitis	13.5	3.76	3.45–4.10	15.6	1.70	1.29–2.24
Children aged 16–17 yr						
No rhinitis#	3.8	1		10.1	1	
Current rhinitis	12.4	3.59	3.33–3.88	15.0	1.54	1.22–1.95

**Adjusted for living area, sex, and obesity.*
#Reference group in regression.
AOR = adjusted odds ratio.

Table 3 **Association of the impairment of daily activities due to rhinitis symptoms with asthma**

	Children with Current Rhinitis			Children with Current Rhinitis and Asthma		
	Prevalence of Asthma (%)	AOR*	95% CI	Prevalence of Severe Asthma (%)	AOR*	95% CI
Children aged 6–7 yr						
Not at all#	17.2	1		5.7	1	
A little	20.2	1.23	1.10–1.37	10.0	1.73	1.13–2.65
Moderate	22.8	1.44	1.27–1.64	12.3	2.31	1.48–3.60
A lot	26.7	1.75	1.50–2.04	18.0	3.66	2.29–5.85
Children aged 13–14 yr						
Not at all#	8.4	1		9.4	1	
A little	12.4	1.57	1.37–1.80	13.2	1.47	0.95–2.27
Moderate	15.0	1.96	1.71–2.26	16.4	1.88	1.21–2.91
A lot	18.5	2.54	2.20–2.94	21.1	2.55	1.64–3.96
Children aged 16–17 yr						
Not at all#	8.4	1		12.8	1	
A little	11.2	1.41	1.23–1.62	12.8	1.10	0.73–1.65
Moderate	13.3	1.70	1.48–1.96	14.4	1.26	0.84–1.91
A lot	16.5	2.21	1.91–2.60	19.8	1.87	1.24–2.82

**Adjusted for living area, sex, and obesity.*
#Reference group in regression.
AOR = adjusted odds ratio.

degree of nasal eosinophil infiltration is inversely correlated with spirometry parameters and bronchial hyperreactivity in allergic rhinitis patients without asthma.[17] In this study, a child who had experienced nasal symptoms in the past 12 months in the absence of a cold was defined as having current rhinitis. It has been reported that rhinitis with itchy–watery eyes (rhinoconjunctivitis) is the symptom combination most closely relating to objective indicators of allergic sensitization in European children.[18,19] Therefore, some children with current rhinitis might be nonallergic, although we did not evaluate allergic sensitization. Recently, it has been shown that asthma is associated with not only allergic rhinitis, but also nonallergic rhinitis.[20] A birth cohort study conducted in Denmark showed that asthma coexisted equally in 7-year-old children with allergic and nonallergic rhinitis.[21] In the same cohort, Chawes *et al.* indicated that in 6-year-old children, there was an association between upper and lower airway patency, which was measured with acoustic rhinometry and spirometry, respectively, and that this association was independent of allergic sensitization.[22] It has been suggested that neuronal mechanisms, T cells, and innate immunity may play a role in nonallergic rhinitis and contribute to asthma symptoms.[20] Additional studies will be needed to understand the mechanisms of a link between the upper and lower airway beyond allergy-driven mechanisms.

In >80% of children with rhinitis, their daily activities were impaired. Children whose daily activities were more impaired by nasal symptoms had a significantly higher prevalence of current asthma in children with rhinitis. Furthermore, among asthmatic children, a higher degree of impairment of daily activities because of rhinitis symptoms was associated with increased severity of asthma. Consistent with our data, a cross-sectional study of 3225 patients with allergic rhinitis aged 10–50 years revealed that the severity of allergic rhinitis influenced the development of asthma.[23] The treatment of allergic rhinitis helps to improve the control of asthma. A nested case–control study of patients with both allergic rhinitis and asthma aged ≥6 years old revealed that treatment with either nasal corticosteroids or oral antihistamines was associated with a significant reduction in the risk of asthma-related emergency room visits and hospitalizations.[24] These results suggest that rhinitis should be examined in patients with asthma and that rhinitis could be a marker of the poor control of asthma.

One of the limitations of our study is that the cross-sectional study does not allow for the determination of whether rhinitis precedes the development of asthma or *vice versa*. A prospective cohort study in which 1314 healthy children had been followed from birth to 13 years old showed that allergic rhinitis until the age of 5 years was a predictor for developing wheezing between the ages of 5 and 13 years old, but nonallergic rhinitis was not a risk factor for future wheezing onset.[25] Additional studies will be needed to evaluate the role of atopy in the development of asthma in children with rhinitis. Another limitation of this study was that we failed to account for several important confounding factors, such as parental tobacco smoking, socioeconomic status, medications for rhinitis and asthma, and atopic status. These factors might affect the association between rhinitis and asthma. Additional limitation is that self-reported questionnaires have a tendency toward overdiagnosis, although the ISAAC questionnaire has been widely used in many epidemiological studies. This might explain rather higher prevalence of asthma and rhinitis in our population.

In conclusion, there was a close association between rhinitis and asthma in young children to adolescents. As recommended by the Allergic Rhinitis and its Impact on Asthma,[26] asthma should be examined in children with rhinitis symptoms. Additional studies will be needed to understand the mechanisms underlying the association between the upper and lower airway.

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Letter to the Editor

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No Association between Serum Vitamin D Status and the Prevalence of Allergic Diseases in Japanese Children

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Dear Sir,

There has been accumulating evidence indicating that an adequate concentration of vitamin D is protective against allergic diseases in children [1, 2]. However, most of these findings have been reported from North America and European countries, and there are only a few studies from other regions of the world, including Asia. The article by Bener et al. [3] demonstrated that vitamin D deficiency was the major predictor of asthma in Qatari children. The authors measured serum vitamin D levels in 483 children with asthma and 483 healthy nonasthmatic children and showed that asthmatic children had significantly lower vitamin D levels compared with nonasthmatic children, supporting the hypothesis that there is a strong association between vitamin D deficiency and asthma risk. Although their study was the first epidemiological study on this association in the Middle East, there have been a few studies evaluating this association in East Asia. Recently we conducted a population-based study in Japanese children and found that there was no relationship between serum vitamin D and the prevalence of allergic diseases.

We performed a cross-sectional study in 4th grade elementary students (9–10 years old) in Toyama, Japan, from June through July 2011. To recruit approximately one third of the same-age children in the city, 14 schools were randomly selected out of 65 schools. All of the eligible children (n = 1,193) in these selected schools were asked to participate in this study. The survey used a Japanese version of the ISAAC questionnaire, which was distributed through teachers of the participating schools and completed by the parents. The questionnaire included questions regarding backgrounds, such as gender, parental history of asthma, parental smoking, and early entrance to kindergarten (<1 year old). Blood samples were collected, body size (height and weight) was measured by nurses at the school, and the serum 25 OH vitamin D_3 concentration was quantified using a radioimmunoassay. Vitamin D deficiency was defined as a serum level <20 ng/ml, and insufficiency was defined as a serum level of 20–29 ng/ml [2]. This study protocol was approved by the institutional review board (IRB) of the University of Toyama, and the parents and children gave their written informed consent to be enrolled into the study.

Of the 1,193 children enrolled, 23 parents declined to participate. After omitting 7 children from whom a sufficient blood volume could not be obtained and 48 children whose questionnaire was not adequately completed, 1,115 children were analyzed. Among these children, the prevalence of current asthma, rhinoconjunctivitis, eczema, and any of these diseases was 10.2, 19.4, 14.7, and 36.4%, respectively (table 1). More than 60% of the children had insufficient or deficient vitamin D levels, and the prevalence of normal vitamin D levels was significantly lower in girls compared to boys, suggesting that boys might play outside more often than girls do. Multivariate analysis showed that there was no association between serum vitamin D status and the prevalence of allergic diseases, even after adjusting for confounding factors, such as gender, obesity (BMI ≥95th percentile), parental history of asthma, parental smoking, pet owning, and early entrance to kindergarten (<1 year old) (table 2).

There is extensive evidence showing that vitamin D has potent immunomodu-

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Table 1. Baseline characteristics of the study participants

	Total (n = 1,115)	Boys (n = 564)	Girls (n = 551)	p value[a]
Current allergic diseases				
Asthma, n (%)	114 (10.2)	55 (9.8)	59 (10.7)	0.334
Rhinoconjunctivitis, n (%)	216 (19.4)	111 (19.7)	105 (19.1)	0.426
Eczema, n (%)	164 (14.7)	81 (14.4)	83 (15.1)	0.403
Any diseases, n (%)	406 (36.4)	210 (37.2)	196 (35.6)	0.303
Obesity				
BMI ≥95th percentile, n (%)	98 (8.8)	48 (8.5)	50 (9.1)	0.752
Serum vitamin D, ng/ml				
Deficiency (<20)	109 (9.8)	47 (8.3)	62 (11.3)	
Insufficiency (20–29)	563 (50.5)	255 (45.2)	308 (59.0)	<0.001
Sufficiency (≥30)	443 (37.7)	262 (46.5)	181 (32.8)	

[a] χ^2 analysis for evaluating gender differences.

Table 2. Association between vitamin D status and the prevalence of allergy diseases

25 OH vitamin D_3 ng/ml	Current asthma			Current rhinoconjunctivitis			Current eczema			Any allergy diseases		
	n (%)	adjusted OR*	95% CI	n (%)	adjusted OR*	95% CI	n (%)	adjusted OR*	95% CI	n (%)	adjusted OR*	95% CI
<20 (n = 109)	10 (9.2)	1.06	0.51–2.21	21 (19.3)	0.85	0.48–1.50	16 (14.8)	0.84	0.46–1.55	35 (32.1)	0.73	0.46–1.18
≥20 to <30 (n = 563)	63 (11.2)	1.22	0.80–1.88	101 (17.9)	0.80	0.58–1.12	78 (13.9)	0.83	0.58–1.20	202 (35.9)	0.93	0.71–1.22
≥30 (n = 443)	41 (9.3)	1		94 (21.2)	1		70 (15.8)	1		169 (38.1)	1	

OR = Odds ratio; CI = confidence interval. ORs were determined for each 25 OH vitamin D_3 category with respect to the reference group (≥30 ng/ml).
* Adjusted for gender, obesity (dichotomous, BMI ≥95th percentile), parental history of asthma, parental smoking, pet owing, and early kindergarten (dichotomous, before age 1 year).

latory properties, and its deficiency is associated with many chronic illnesses, including cancer and autoimmune, infectious, cardiovascular, and allergic diseases [4]. Many epidemiological studies, including the study of Bener et al. [3], support this association. However, we could not find an association between vitamin D insufficiency and allergic diseases, even after adjusting for several confounding factors. Although this study was performed during the summer season in Toyama, located at 36° N, vitamin D insufficiency was found in more than 60% of the children, with similar rates reported in the USA and Europe [5]. Consistent with our results, Deverux et al. [6] showed that there was no difference in serum vitamin D levels between adult asthma patients and age- and gender-matched control subjects in the UK. Hollams et al. [7] showed that there was no significant cross-sectional association between serum vitamin D levels and current asthma in 6- or 14-year-old children in the UK. Our results cannot exclude a role of vitamin D earlier in life. A prospective study showed that higher maternal vitamin D intake during pregnancy decreased the risks for asthma and allergic rhinitis in offspring at the age of 5 years, although maternal serum levels of vitamin D were not measured [8]. Another cohort study revealed that low vitamin D levels at 6 years of age were associated with asthma at 14 years of age in boys [7]. Apart from serum vitamin D levels, vitamin D receptor gene polymorphisms might be associated with allergic diseases [9]. Further studies will be needed to provide a clear answer to the hypothesis that vitamin D could have a role in preventing the development and reducing the morbidity of allergic diseases.

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