

Contrasting associations of body mass index and measles with asthma and rhinitis in young adults

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ABSTRACT

Asthma and allergic rhinitis often coexist and are increasing worldwide, particularly among the younger generation. Although the prevalences of adult asthma and allergic rhinitis and their risk factors have been reported, there have been few studies focusing on young adults. The aim of this study was to evaluate the prevalences of asthma and allergic rhinitis and their associated factors in Japanese young adults. A questionnaire survey of new students at Hokkaido University about the presence of current wheeze and rhinitis and a history of several viral infections during childhood was conducted in 2008 and 2010. The prevalences of wheeze and rhinitis and their associated factors were evaluated. Of 4076 nonsmoking subjects aged 18–25 years, 261 (6.4%) had current wheeze and 1373 (33.7%) had allergic rhinitis. On multivariate analyses, current wheeze was associated with high body mass index (BMI), atopic dermatitis, allergic rhinitis, food allergy, and a history of measles infection. In contrast, allergic rhinitis was associated with low BMI, current wheeze, atopic dermatitis, food allergy, and no history of measles. When subjects were classified into four groups by the presence or absence of wheeze and rhinitis, both high BMI and a history of measles were positively associated with wheeze without rhinitis but negatively associated with rhinitis without wheeze. High BMI and past measles infection showed contrasting associations with asthma and allergic rhinitis in nonsmoking young adults. It is important to not only recognize the common pathophysiological characteristics of asthma and allergic rhinitis but also to understand their differences.

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Both asthma and allergic rhinitis have been increasing worldwide, particularly among the younger generation.^{1–4} Because both diseases often coexist, they may represent a continuum, sharing common pathologic and/or physiologic characteristics in the upper and lower airways. The terms “one airway one disease” and “united airways disease” have been proposed for this condition.^{5–10} On the other hand, there are some significant histologic differences between the upper and lower airways,^{11,12} including the resident cell type. For instance, the lower airways, such as bronchi, are characterized by the presence of smooth muscle cells that are responsible for bronchial hyperresponsiveness and bronchoconstriction. Thus, identification of any factors that are differentially associated with each disease would help us to better understand the different pathophysiology and/or pathobiology of the two diseases.

We previously reported the prevalences of asthma and rhinitis in a Japanese population with a wide age

range (20–79-years-old) using the Japanese edition of the European Community Respiratory Health Survey (ECRHS) questionnaire.¹³ In that study, we found that the effects of smoking and obesity were opposite for the two diseases; asthma was positively associated with these factors, whereas rhinitis was negatively associated.¹⁴ Although this survey included a population with a wide age range (20–79-years-old), the proportion of young adults was relatively small, and few studies have conducted similar surveys focusing on young adults. Given the recent pronounced increase in the prevalences of several allergic diseases among the younger generation, determination of the prevalence of allergic diseases and their associated factors in young adults is crucial.

Accordingly, in the current study, a similar questionnaire-based survey to that of our previous study¹⁴ was conducted, focusing on the young adult generation. The first goal of this study was to reconfirm the contrasting effect of obesity on asthma and rhinitis in this particular population. The second goal was to explore whether a similar contrasting relationship might also exist for viral infection history with asthma and rhinitis, which have shown conflicting results in a number of previous reports.^{15–20}

METHODS

Study Population

The study included first-year students at Hokkaido University in 2008 and 2010. In March, approximately

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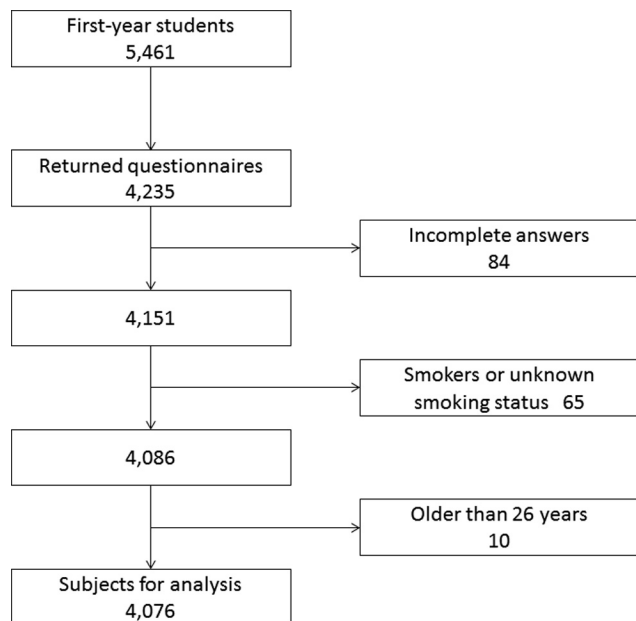


Figure 1. Flowchart of selection of subjects for analysis. Respondents who provided incomplete answers ($N = 84$), smokers or those with unknown smoking status ($N = 65$), and those older than 26-years-old ($N = 10$) were excluded. Finally, 4076 first-year students were analyzed.

one month before the entrance ceremony, questionnaire sheets were sent by mail to the homes of the parents of all students who had passed the entrance examination ($N = 5461$). These students were requested to bring their completed sheets when a health examination was conducted immediately after the entrance ceremony. In total, 4235 interview sheets were returned, including 84 empty answer sheets (response rate, 82% in 2008 and 68% in 2010); 75 subjects who were more than or equal to 26-years-old ($N = 10$), and smokers ($N = 65$) were excluded due to their small numbers. As a result, data from 4076 nonsmoking subjects (2923 men, 1153 women), aged 18–25 years, were eventually analyzed (Fig. 1). The survey objectives and methods were explained in writing when the questionnaires were distributed. The survey was conducted with the approval of the Research Review Board of Hokkaido University.

Questionnaire

The questionnaire used in this survey included three questions regarding the presence of wheeze and smoking history that were identical to those in the Japanese edition of the ECRHS questionnaire,¹³ as follows: “Have you had wheezing or whistling in your chest at any time in the last 12 months?”, “Have you ever smoked for as long as a year?”, and “Do you now smoke, as of one month ago?”. According to Watanabe *et al.*,¹³ wheezing during the previous 12 months, as specified in the Japanese version of the ECRHS ques-

Table 1. Questionnaire used in this survey (translated into English)

Hometown
1 Hokkaido, 2 Outside of Hokkaido
Infectious diseases during childhood
1 Have you ever had any of the following diseases?
1 measles, 2 rubella, 3 varicella, 4 mumps
2 Have you ever received measles vaccination?
1 yes (1 time), 2 yes (2 times), 3 no
3 Have you ever received rubella vaccination?
1 yes (1 time), 2 yes (2 times), 3 no
Allergic diseases and smoking status
1 Have you had wheezing or whistling in your chest at any time in the last 12 months?
1 yes, 2 no
2 Have you ever had the following allergic diseases?
1 asthma, 2 hay fever (allergic rhinitis), 3 atopic dermatitis, 4 food allergy, 5 drug allergy, 6 other
3 Have you ever smoked for as long as a year?
1 yes, 2 no
4 Do you now smoke, as of 1 month ago?
1 yes, 2 no
5 Have you ever had any pets?
1 dog, 2 cat, 3 guinea pig or hamster, 4 none

tionnaire, is an index used for international comparisons of the prevalence of asthma during a specified period and is considered to have the highest validity for discriminating between those with and without asthma. The questionnaire also included mark-sheet questions regarding the presence of several allergic diseases (asthma, allergic rhinitis, atopic dermatitis, food allergy, and drug allergy), history of viral infections during childhood (measles, rubella, varicella, and mumps), vaccination history (measles, rubella), pet ownership, and the main location where the subject had lived from elementary to high school (ages 6–18 years). The subjects’ height and weight were measured during a medical checkup after the entrance ceremony. The questionnaire used in this study is shown in Table 1.

Statistical Analysis

Statistical analyses were performed using the statistical software package SYSTAT for Windows, version 13 (SYSTAT, San Jose, CA). For all statistical analyses, $p < 0.05$ was considered significant; and χ^2 tests were used to assess differences in the prevalence of wheeze or rhinitis for several parameters, including sex, hometown, allergic diseases, and pet ownership. The body mass index (BMI) was calculated from the height and weight. BMI analyses were conducted using continu-

Table 2. Subject's characteristics

Number of subjects	4076
Sex	
Male	2923 (71.7%)
Female	1153 (28.3%)
Age (years) median (range)	18 (18–25)
Hometown†	
Hokkaido	2076 (50.9%)
Outside of Hokkaido	2000 (49.1%)
BMI (kg/m ²) mean±SD	21.5 ± 3.1
Current wheeze	261 (6.4%)
Allergic rhinitis	1373 (33.7%)
Food allergy	308 (7.6%)
Atopic dermatitis	768 (18.8%)
Childhood viral infection‡	2753 (67.5%)
Pet ownership§	2025 (49.7%)

BMI = body mass index.

†main location where subjects had lived from elementary to high school.

‡measles, rubella, varicella, or mumps.

§dog, cat, guinea pig, or hamster.

ous variables. Multivariate analyses (logistic regression and multinomial logistic regression) were conducted to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs), using the variables that were significant on univariate analyses, together with age and BMI.

RESULTS

Table 2 shows the characteristics of the subjects evaluated in the final analysis. Of 4076 nonsmoking subjects, 261 (6.4%, 95%CI 5.6%–7.3%) answered “yes” to the question “Have you had wheezing or whistling in your chest at any time in the last 12 months?” (current wheeze). In answer to the question “Have you ever had the next allergic diseases?”, hay fever (allergic rhinitis) was marked by 1373 subjects (33.7%, 95%CI 32.0%–35.4%). Current wheeze and allergic rhinitis were both more frequent among men than among women (wheeze: 7.2%, 95%CI 6.1%–8.3% for men, 4.5%, 95%CI 3.2%–6.1% for women; rhinitis: 35.6%, 95%CI 33.6%–37.6% for men, 28.9%, 95%CI 25.9–32.0% for women).

Table 3 shows the factors associated with current wheeze or allergic rhinitis on univariate analyses. Subjects with allergic rhinitis, atopic dermatitis, or food allergy had a higher prevalence of current wheeze. Similarly, subjects with current wheeze, atopic dermatitis, or food allergy had a higher prevalence of allergic rhinitis (Table 3). A significant relationship between current wheeze and BMI was also observed on univariate analysis but not for allergic rhinitis (Table 4). Anal-

ysis of a history of viral infections during childhood (measles, rubella, varicella, and mumps) showed that subjects with a history of measles had a higher prevalence of current wheeze [10.3% (95%CI 7.3%–13.9%) versus 5.9% (95%CI 5.1%–6.9%); $p = 0.00037$] but a lower prevalence of allergic rhinitis [27.7% (95%CI 23.0%–32.7%) versus 34.4% (95%CI 32.6%–36.2%); $p = 0.0048$]. There was no significant association with any vaccination history (data not shown).

Tables 5 and 6 show the results of the multivariate regression analyses of associated factors. A high prevalence of current wheeze was associated with male sex, residence in Hokkaido, high BMI, history of measles, atopic dermatitis, allergic rhinitis, and food allergy. A high prevalence of allergic rhinitis was associated with male sex, residence in Hokkaido, low BMI, the presence of current wheeze, food allergy, atopic dermatitis, and no history of measles.

Because there was a significant coexistence of current wheeze and allergic rhinitis, all subjects were classified into the next four groups, and the pure association of allergic rhinitis with obesity was evaluated: 1) no rhinitis, no wheeze ($N = 2567$); 2) rhinitis without wheeze ($N = 1248$); 3) wheeze without rhinitis ($N = 136$); and 4) rhinitis with wheeze ($N = 125$). Table 7 shows the results of the multinomial logistic regression analysis using the outcome variables “rhinitis without wheeze,” “wheeze without rhinitis,” and “rhinitis with wheeze.” BMI was positively associated with “wheeze without rhinitis” (OR = 1.05; 95%CI 1.00–1.10; $p = 0.043$) but negatively associated with “rhinitis without wheeze” (OR = 0.97; 95%CI 0.95–0.99; $p = 0.016$). Similarly, a history of measles was positively associated with “wheeze without rhinitis” (OR = 1.96; 95%CI 1.26–3.03; $p = 0.0027$). In contrast, a history of measles was negatively associated with “rhinitis without wheeze” (OR = 0.72; 95%CI 0.57–0.91; $p = 0.0070$).

DISCUSSION

In the present study, a questionnaire-based survey focused on young Japanese adults was conducted to identify the prevalences of several allergic diseases, including asthma and allergic rhinitis, and to evaluate their associated factors. Consistent with the results from a number of earlier studies, including ours,^{6,10,14,21–23} a significant association between the presence of current wheeze and allergic rhinitis was observed. This finding suggests that young-onset asthma and allergic rhinitis develop under the predisposition of a common atopic background shared with other allergic diseases.

However, despite the significant overlap, it should be noted that the factors associated with wheeze and allergic rhinitis differed. Obesity was positively associated with the presence of current wheeze, but nega-

Table 3. Factors associated with wheeze and allergic rhinitis (univariate analysis)

	Wheeze	<i>p</i> Value	Rhinitis	<i>p</i> Value
Sex				
Male (<i>n</i> = 2923)	7.2%	0.0019	35.6%	<0.0001
Female (<i>n</i> = 1153)	4.5%		28.9%	
Hometown				
Hokkaido (<i>n</i> = 2076)	7.4%	0.010	25.3%	<0.0001
Outside of Hokkaido (<i>n</i> = 2000)	5.4%		42.4%	
Measles				
Yes (<i>n</i> = 447)	10.3%	0.00037	27.7%	0.0048
No (<i>n</i> = 3629)	5.9%		34.4%	
Rubella				
Yes (<i>n</i> = 394)	8.4%	0.092	31.2%	0.28
No (<i>n</i> = 3682)	6.2%		33.9%	
Varicella				
Yes (<i>n</i> = 2372)	6.5%	0.89	34.1%	0.46
No (<i>n</i> = 1704)	6.3%		33.0%	
Mumps				
Yes (<i>n</i> = 1102)	6.1%	0.61	36.0%	0.064
No (<i>n</i> = 2974)	6.5%		32.9%	
Allergic rhinitis				
Yes (<i>n</i> = 1373)	9.1%	<0.0001	N/A	
No (<i>n</i> = 2703)	5.0%		N/A	
Atopic dermatitis				
Yes (<i>n</i> = 768)	12.2%	<0.0001	38.2%	0.0037
No (<i>n</i> = 3308)	5.0%		32.6%	
Drug allergy				
Yes (<i>n</i> = 71)	9.9%	0.23	35.2%	0.78
No (<i>n</i> = 4005)	6.3%		33.7%	
Food allergy				
Yes (<i>n</i> = 308)	17.9%	<0.0001	48.8%	<0.0001
No (<i>n</i> = 3768)	5.5%		32.5%	
Wheeze				
Yes (<i>n</i> = 261)	N/A		47.9%	<0.0001
No (<i>n</i> = 3815)	N/A		32.7%	
Having cat				
Yes (<i>n</i> = 423)	7.3%	0.41	33.1%	0.79
No (<i>n</i> = 3653)	6.3%		33.8%	
Having dog				
Yes (<i>n</i> = 1176)	7.3%	0.13	37.1%	0.0036
No (<i>n</i> = 2900)	6.0%		32.3%	
Having hamster				
Yes (<i>n</i> = 895)	5.3%	0.11	32.4%	0.36
No (<i>n</i> = 3181)	6.7%		34.0%	

 χ^2 test.

tively associated with the presence of allergic rhinitis. In fact, this result is consistent with that of our previous nationwide survey that included a wide age range (20–79 years) and smokers,¹⁴ suggesting that this interesting association is also present in the younger population. As in our previous study,¹⁴ the contrasting effects of obesity on asthma and allergic rhinitis would

not have been detected using univariate analysis (Table 4). Rather, the association became evident when the coexistence of asthma and allergic rhinitis was considered for statistical analysis by mutually adjusting for multivariate analysis (Tables 5 and 6) and by the classification of all subjects into four groups according to the presence or absence of both diseases (Table 7). We

Table 4. Associations of age and BMI with the presence of wheeze and allergic rhinitis (univariate analysis)

	Wheeze			Allergic rhinitis		
	(+) <i>n</i> = 261	(-) <i>n</i> = 3815	<i>p</i> Value	(+) <i>n</i> = 1373	(-) <i>n</i> = 2703	<i>p</i> Value
Age †	18 (18–25)	18 (18–25)	0.020	18 (18–25)	18 (18–25)	0.14
BMI ‡	22.1 ± 3.2	21.5 ± 3.1	0.0020	21.4 ± 3.1	21.5 ± 3.1	0.34

BMI = body mass index.

†median (range), Mann-Whitney U-test.

‡mean ± SD, *t*-test.

Table 5. Adjusted odds ratios of current wheeze

	OR	95%CI	<i>p</i> Value
Age	1.23	1.07–1.42	0.0040
Sex (male)	1.64	1.19–2.27	0.0027
Home (Hokkaido)	1.54	1.17–2.01	0.0017
BMI	1.05	1.01–1.09	0.0077
Measles	1.80	1.28–2.55	0.00083
Atopic dermatitis	2.30	1.74–3.03	<0.0001
Food allergy	2.86	2.04–4.02	<0.0001
Allergic rhinitis	1.85	1.42–2.42	<0.0001

BMI = body mass index; CI = confidence interval; OR = odds ratio. Logistic regression analysis.

Table 6. Adjusted odds ratios of allergic rhinitis

	OR	95%CI	<i>p</i> Value
Age	1.03	0.94–1.12	0.54
Sex (male)	1.34	1.14–1.57	0.00020
Home (Hokkaido)	0.44	0.39–0.51	<0.0001
BMI	0.97	0.95–0.99	0.013
Measles	0.71	0.56–0.88	0.0024
Current wheeze	1.84	1.41–2.41	<0.0001
Food allergy	1.96	1.53–2.51	<0.0001
Atopic dermatitis	1.24	1.04–1.47	0.014
Having dog	1.10	0.95–1.27	0.21

BMI = body mass index; CI = confidence interval; OR = odds ratio. Logistic regression analysis.

thus emphasize that, although it is important to recognize common pathophysiological characteristics between asthma and allergic rhinitis, it is also necessary to understand the differences between them.

A link between the increase in allergic diseases and the decrease in many types of childhood infections has been proposed, which has been termed the “hygiene hypothesis.”²⁴ Several epidemiologic studies have shown results supporting this hypothesis,^{25–28} whereas others have shown no clear evidence to support this hypothesis.^{29–31} Some studies even indicate that certain types of infections actually increase the risk of

allergic diseases.^{15,18,20} A number of factors could account for these conflicting results in epidemiologic studies, including differences in areas with different ethnicities, genetic backgrounds, and other environmental factors, as well as differences in the timing and intensity of infections.^{32–34} Similar to obesity, measles has been shown to be associated differently with asthma and allergic rhinitis, indicating the importance of identifying risk factors for allergic diseases separately. Conducting statistical analyses without considering the coexistence of several allergic diseases may increase the complexity of the association between childhood infections and allergic diseases, and this factor may be one explanation for the inconclusive results regarding this issue.

Although the reason for the contrasting associations of obesity with asthma and allergic rhinitis is unclear, significant structural differences between the upper and lower airways could be involved. An association between obesity and asthma has been reported by many studies, and several mechanisms have been proposed.^{35–45} Obese subjects have been reported to exhibit significant increases in bronchial hyperresponsiveness in healthy subjects.⁴⁶ In a murine model, obese mice showed enhanced airway responsiveness and attenuation of airway inflammation.⁴⁷ Accordingly, obesity may directly induce hyperresponsiveness in airways without promoting allergic lower airway inflammation, resulting in increased asthmatic symptoms. Conversely, obesity may attenuate upper airway inflammation and result in decreased rhinitis symptoms. An explanation similar to that for the effect of obesity may be plausible with regard to the effect of childhood measles infection. The results of the current study would seem to be in accordance with those from a large longitudinal study that demonstrated that early measles infection is associated with the development of asthma but not rhinitis.¹⁸

This study has several significant limitations. The cross-sectional nature of the study precludes establishing temporal relationships or inferring causality. Thus, another explanation for the negative association of obesity and measles with allergic rhinitis is the possibility that subjects with allergic rhinitis tend not to exercise,

Table 7. Factors associated with the presence of allergic rhinitis and/or current wheeze (multivariate analysis)

	Rhinitis (+) Wheeze (-) <i>n</i> = 1248			Rhinitis (-) Wheeze (+) <i>n</i> = 136			Rhinitis (+) Wheeze (+) <i>n</i> = 125		
	OR	95%CI	<i>p</i> Value	OR	95%CI	<i>p</i> Value	OR	95%CI	<i>p</i> Value
Age	1.06	0.96–1.16	0.26	1.36	1.14–1.62	0.00065	1.11	0.89–1.40	0.34
Sex (male)	1.36	1.16–1.59	0.00017	1.80	1.16–2.80	0.0085	1.94	1.22–3.09	0.0054
Home (Hokkaido)	0.45	0.39–0.52	<0.0001	1.70	1.16–2.49	0.0069	0.65	0.45–0.93	0.021
BMI	0.97	0.95–0.99	0.016	1.05	1.00–1.10	0.043	1.03	0.97–1.08	0.33
Measles	0.72	0.57–0.91	0.0070	1.96	1.26–3.03	0.0027	1.14	0.67–1.95	0.63
Atopic dermatitis	1.27	1.06–1.52	0.0094	2.57	1.76–3.74	<0.0001	2.56	1.72–3.79	<0.0001
Food allergy	2.14	1.64–2.78	<0.0001	3.82	2.39–6.12	<0.0001	4.75	2.96–7.62	<0.0001
Having dog	1.09	0.93–1.26	0.29	1.08	0.73–1.60	0.69	1.40	0.95–2.05	0.088

BMI = body mass index; CI = confidence interval; OR = odds ratio. Subjects were divided into four categories by the presence/absence of wheeze and allergic rhinitis. Adjusted odds ratios are presented in relation to those with neither wheeze nor rhinitis. Multinomial logistic regression analysis.

resulting in obesity, and that subjects with allergic rhinitis tend to have less susceptibility to measles. In the questionnaire, subjects were asked to mark allergic diseases, such as allergic rhinitis, that they have or had. Thus, subjects who had a condition previously but no longer had it at the time of the survey may also have been included. In addition, allergic rhinitis was surveyed based on the item “hay fever (allergic rhinitis).” Thus, it was not possible to determine whether subjects had seasonal or perennial rhinitis. Similarly, subjects were simply asked whether they had a history of viral infections during childhood and any history of vaccination. Assessing a history of infectious diseases during infancy/childhood based on questionnaires is always susceptible to recall bias. Furthermore, no information on ages at the times of infectious diseases was obtained in this survey. Lastly, this study evaluated only first-year students at Hokkaido University, who are considered to be of relatively high intelligence, highly educated, and of a high economic status compared with the general Japanese population. Thus, it is uncertain whether the findings from the current study can be extrapolated to subjects of the same age in the general Japanese population.

In conclusion, the present survey showed the prevalences of several allergic diseases and their associated factors in nonsmoking young adults at a Japanese university. Although asthma and allergic rhinitis coexisted, they were associated with different factors. Obesity and past history of measles had contrasting associations with asthma and allergic rhinitis. This finding suggests that, although it is important to recognize the common pathophysiological characteristics of asthma and allergic rhinitis, it is also necessary to understand their differences. Further studies, particu-

larly with a prospective design, are needed to clarify the differential effects of these factors on the development of asthma and allergic rhinitis.

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