

OBESITY

U-Shaped Association between Body Mass Index and the Prevalence of Wheeze and Asthma, but not Eczema or Rhinoconjunctivitis: The Ryukyus Child Health Study

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Background. Studies reporting on the association between obesity and allergies have mostly focused on asthma. Little is known about the relationship of obesity to other allergic diseases, and the information that is available has been inconsistent. We examined the association between body mass index (BMI) and the prevalence of wheeze, asthma, eczema, and rhinoconjunctivitis in Japanese schoolchildren. **Methods.** Study subjects were 24,399 children aged 6–15 years in Okinawa, Japan. Outcomes were based on diagnostic criteria from the International Study of Asthma and Allergies in Childhood. BMI was categorized into five groups; <5th, 5th to 35th, >35th to 65th, >65th to 95th, and >95th percentile groups. Adjustment was made for sex, age, region of residence, number of siblings, smoking in the household, physical activity, paternal and maternal history of allergic disorders, and paternal and maternal educational levels. **Results.** The prevalence values of wheeze, asthma, eczema, and rhinoconjunctivitis in the previous 12 months were 10.8%, 7.6%, 6.9%, and 7.6%, respectively. Compared with the referent category (>35th to 65th percentile group), higher percentile categories were positively associated with the prevalence of wheeze. A U-shaped relationship between BMI and asthma was observed. No material associations between BMI percentile categories and the prevalence of eczema or rhinoconjunctivitis were found. **Conclusion.** These findings suggested that being either underweight or overweight might increase the likelihood of asthma among Japanese schoolchildren.

Keywords asthma, body mass index, cross-sectional study, eczema, rhinitis, wheeze

INTRODUCTION

A number of studies have investigated the association between obesity and asthma in both adults and children. Most studies in adults have shown that obesity and overweight are positively associated with asthma or asthma-like symptoms (1–9); moreover, in some studies, this association was more pronounced in women than in men (1, 7–9). In children, on the other hand, results concerning the association of asthma with obesity have not been consistent (10–24). Data from the National Health and Nutrition Examination Survey showed that a higher body mass index (BMI) was associated with an increased prevalence of asthma among 7505 US children aged 4–17 years (10). A cross-sectional study in Australia demonstrated that a higher BMI was associated with a higher prevalence of wheeze but not asthma in 5993 children aged 7–12 years (11). In a cross-sectional study in the United States involving 853 children aged 2–11 years, the prevalence of asthma in association with the

BMI percentile in boys followed a U-shaped curve, whereas the prevalence of asthma increased linearly with higher BMI percentiles in girls (12).

Research on the association between obesity and allergic diseases has mostly focused on asthma and asthma-like symptoms. Little is known about the relationship of BMI to other allergic disorders in children, such as atopic eczema and allergic rhinoconjunctivitis, and the information that has been available to date is conflicting (13–17). Among 1576 Belgian schoolchildren, higher BMI was associated with higher prevalence of wheezing or dyspnea induced by exercise, but not with higher prevalence of eczema or rhinoconjunctivitis (13). In 45,520 Japanese schoolchildren, on the other hand, in a study treating BMI as a continuous variable, a positive association between BMI and the prevalence of atopic dermatitis and an inverse association between BMI and the prevalence of allergic conjunctivitis were observed (14). Further evidence is needed to clarify the influence of BMI on allergic diseases.

In this cross-sectional study, we investigated the relationship between low or high BMI and allergic diseases including wheeze, asthma, eczema, and rhinoconjunctivitis using data from the Ryukyus Child Health Study (RYUCHS).

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METHODS

Study Population

The RYUCHS, a cross-sectional school-based study, investigated associations between various selected factors and child health problems. Details of the RYUCHS have been described elsewhere (25, 26). Okinawa Prefecture is an island in the southernmost area of Japan, with a subtropical climate and a total population of almost 1,385,000. During the period from September 2004 to January 2005, all 35 public elementary schools and 17 junior high schools in Naha City, the largest city in Okinawa Prefecture, with a total population of almost 316,000, and 17 public elementary schools and 8 junior high schools in Nago City, which has a total population of almost 60,000, participated in the RYUCHS. Teachers distributed a set of two self-administered questionnaires at school to each of the 38,212 children. These were completed at home by the parents of the elementary schoolchildren and by the junior high school students themselves and/or their parents. When research technicians detected missing answers or illogical data, the teachers returned the questionnaires to the parents for correction or completion. In the end, 28,885 sets of questionnaires were returned (participation rate = 75.6%). Our study was restricted to subjects who provided complete information on the variables under study, leaving data on 24,399 children available for analysis (63.9% of all eligible subjects). Permission to perform the RYUCHS was obtained from the ethics committee of the Faculty of Medicine, Fukuoka University.

Questionnaires

One of the questionnaires included questions regarding wheeze, asthma, eczema, and rhinoconjunctivitis in the previous 12 months which were based on the validated International Study of Asthma and Allergies in Childhood (ISAAC) phase-I questionnaire (27). The definition of wheeze used in this study was a positive response to the question "Have you (Has your child) had wheezing or whistling in the chest in the last 12 months?" A positive response to both the aforementioned question and the question "Have you (Has your child) ever had asthma?" were considered to indicate asthma. For

eczema, affirmative answers to all of the following three questions from the ISAAC questionnaire were required: "Have you (Has your child) ever had an itchy rash which was coming and going for at least 6 months?," "Have you (Has your child) had this itchy rash at any time in the last 12 months?," and "Has this itchy rash at any time affected any of the following places: the folds of the elbow, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes?" Rhinoconjunctivitis was defined as a positive response to the following two questions: "In the last 12 months, have you (Has your child) had a problem with sneezing or running or blocked nose when you (he/she) did not have a cold or flu?" and "In the last 12 months, has this nose problem been accompanied by itchy-watery eyes?" The questionnaire also included questions about sex, age, number of siblings, smoking in the household, physical activity, paternal and maternal history of asthma, atopic eczema and allergic rhinitis, and paternal and maternal educational level. Physical activity was defined as positive if the child had habitually taken exercise other than physical education class at school during the past year. Paternal or maternal history of asthma, atopic eczema, or allergic rhinitis was defined as positive if the respective parent had developed any self-reported symptoms of the allergic disorder in question at any time since birth.

The second questionnaire was a validated self-administered brief diet history questionnaire from which data on the child's weight and height were obtained. BMI was calculated by dividing body weight (kg) by the square of body height (m).

Statistical Analysis

After our population was stratified by age and sex, we classified our subjects according to BMI into five categories using age-specific and sex-specific cutoff points for BMI percentile. The cutoff points were at the 5th, 35th, 65th, and 95th percentile values in each stratum (Table 1). Logistic regression analysis was used to estimate crude odds ratios (ORs) and 95% confidence intervals (CIs) for allergic disorders relative to BMI. Adjusted ORs and 95% CIs were estimated using multiple logistic regression analysis. The following potential confounders were identified *a priori* and were

TABLE 1.—Cutoff points for body mass index (BMI) by sex and age.

Age (years)	Boys				Girls			
	5th percentile	35th percentile	65th percentile	95th percentile	5th percentile	35th percentile	65th percentile	95th percentile
6	13.3	14.9	16.0	19.4	13.1	14.7	15.9	19.0
7	13.4	15.1	16.3	20.2	13.2	14.8	16.1	19.8
8	13.7	15.4	16.8	21.6	13.5	15.3	16.7	20.3
9	13.9	15.8	17.4	22.5	13.7	15.7	17.3	21.9
10	14.3	16.3	18.1	24.0	13.9	16.0	17.7	22.6
11	14.7	16.7	18.7	24.8	14.6	16.7	18.6	23.0
12	15.0	17.2	19.1	25.2	15.2	17.5	19.4	23.9
13	15.5	17.7	19.4	24.7	15.7	18.1	19.8	24.2
14	16.2	18.4	20.1	26.3	16.4	18.9	20.5	25.1
15	16.5	19.0	20.8	27.6	16.7	19.1	20.8	24.6

included in the multivariate model: sex, age, region of residence, number of siblings, smoking in the household, physical activity, paternal and maternal history of allergic disorders, and paternal and maternal educational levels. Age was used as a continuous variable. Region of residence was classified into two categories (Naha City and Nago City), number of siblings into four (0, 1, 2, and 3+), smoking in the household into three (never, former, and current), and paternal and maternal educational levels into four (junior high school, high school, junior college or vocational technical school, and university). All statistical analyses were performed using the SAS software package version 9.2 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

The prevalence values for symptoms of wheeze, asthma, eczema, and rhinoconjunctivitis in the previous 12 months were 10.8%, 7.6%, 6.9%, and 7.6%, respectively. The mean BMI was 17.8 (SD = 3.1) kg/m². The distribution of selected factors under study is presented in Table 2. Approximately 60% of the subjects had two or more siblings. About one-half were exposed to household smoking at the time of the survey. Physical activity was reported in about 64% of children.

Table 3 shows crude and adjusted ORs and their 95% CIs for allergic disorders in the various BMI percentile categories. Compared with the referent category (>35th to 65th percentile group), being in one of the higher two percentile groups was significantly positively associated with the prevalence of wheeze. Adjustment for sex, age, region of residence, number of siblings, smoking in the household, physical activity, paternal and maternal

TABLE 2.—Distribution of selected characteristics in 24,399 schoolchildren, RYUCHS, Japan.

Variable	n (%)
Male sex	12,013 (49.2)
Age (years)	
6–8	7356 (30.2)
9–11	8858 (36.3)
12–15	8185 (33.6)
Region of residence	
Naha City	20,043 (82.2)
Nago City	4356 (17.9)
Siblings	
0	2240 (9.2)
1	8222 (33.7)
2	9214 (37.8)
≥3	4723 (19.4)
Smoking in household	
Never	10,495 (43.0)
Former	2520 (10.3)
Current	11,384 (46.7)
Physical activity	15,568 (63.8)
Paternal history of allergic disorders ^a	5785 (23.7)
Maternal history of allergic disorders ^a	6934 (28.4)
Paternal educational level	
Junior high school	1889 (7.7)
High school	10,820 (44.4)
Junior college or vocational technical school	3617 (14.8)
University	8073 (33.1)
Maternal educational level	
Junior high school	1231 (5.1)
High school	10,760 (44.1)
Junior college or vocational technical school	10,213 (41.9)
University	2195 (9.0)

Note: RYUCHS, Ryukyus Child Health Study.

^a Asthma, atopic eczema, or allergic rhinitis.

TABLE 3.—Crude and adjusted ORs and 95% CIs for allergic disorders according to BMI percentile among 24,399 schoolchildren, RYUCHS, Japan.

	BMI percentile categories				
	<5th	5 to 35th	>35 to 65th	>65 to 95th	>95th
Wheeze					
Prevalence (%)	11.5	10.9	9.8	11.6	12.0
Crude OR (95% CI)	1.20 (0.98–1.45)	1.12 (1.01–1.25)	1.00	1.20 (1.08–1.34)	1.25 (1.03–1.51)
Adjusted OR (95% CI) ^a	1.22 (1.00–1.48)	1.10 (0.99–1.23)	1.00	1.20 (1.08–1.34)	1.28 (1.05–1.55)
Asthma					
Prevalence (%)	8.6	7.6	6.6	8.2	9.2
Crude OR (95% CI)	1.33 (1.06–1.65)	1.16 (1.03–1.32)	1.00	1.26 (1.12–1.43)	1.42 (1.14–1.76)
Adjusted OR (95% CI) ^a	1.38 (1.09–1.72)	1.15 (1.01–1.30)	1.00	1.26 (1.11–1.43)	1.46 (1.17–1.81)
Eczema					
Prevalence (%)	7.2	6.5	6.8	7.1	7.7
Crude OR (95% CI)	1.07 (0.84–1.35)	0.96 (0.84–1.09)	1.00	1.06 (0.93–1.21)	1.15 (0.91–1.44)
Adjusted OR (95% CI) ^a	1.10 (0.86–1.40)	0.95 (0.83–1.08)	1.00	1.06 (0.94–1.21)	1.23 (0.97–1.55)
Rhinoconjunctivitis					
Prevalence (%)	7.5	7.5	7.7	8.0	6.5
Crude OR (95% CI)	0.98 (0.77–1.23)	0.98 (0.87–1.11)	1.00	1.04 (0.93–1.18)	0.84 (0.66–1.07)
Adjusted OR (95% CI) ^a	1.01 (0.79–1.27)	0.97 (0.85–1.09)	1.00	1.04 (0.92–1.18)	0.88 (0.68–1.11)

Note: CI, confidence interval; OR, odds ratio; RYUCHS, Ryukyus Child Health Study; BMI, body mass index.

^a Adjustment for sex, age, region of residence, number of siblings, smoking in the household, physical activity, paternal and maternal history of allergic disorders, and paternal and maternal educational levels.

history of allergic disorders, and paternal and maternal educational levels did not appreciably change the results; the adjusted ORs for the >65th to 95th and >95th percentile groups were 1.20 (95% CI: 1.08–1.34) and 1.28 (95% CI: 1.05–1.55), respectively. A U-shaped relationship between BMI and asthma was observed. The multivariate ORs for the association between the lowest and highest BMI percentile categories and the prevalence of asthma were 1.38 (95% CI: 1.09–1.72) and 1.46 (95% CI: 1.17–1.81), respectively. No material associations between BMI percentile categories and the prevalence of eczema or rhinoconjunctivitis were found.

For boys, being in the >65 to 95th or >95th BMI percentile category was associated with an increased prevalence of wheeze compared with the reference group (Figure 1). Both the two highest percentile categories and the lowest BMI percentile category were associated

with an increased prevalence of asthma. Among girls, the >65th to 95th percentile category was positively associated with the prevalence of wheeze, although no significant relationship between the highest percentile category and wheeze was shown. The 5 to 35th, >65 to 95th, and >95th percentile categories were significantly associated with an increased prevalence of asthma.

No significant interactions were found in the associations of BMI percentile categories with the prevalence of wheeze, asthma, eczema, or rhinoconjunctivitis between boys and girls (data not shown).

DISCUSSION

Many studies of BMI and allergic diseases among children have tended to focus solely on the higher range of BMI percentiles (14, 17, 21–24). In this

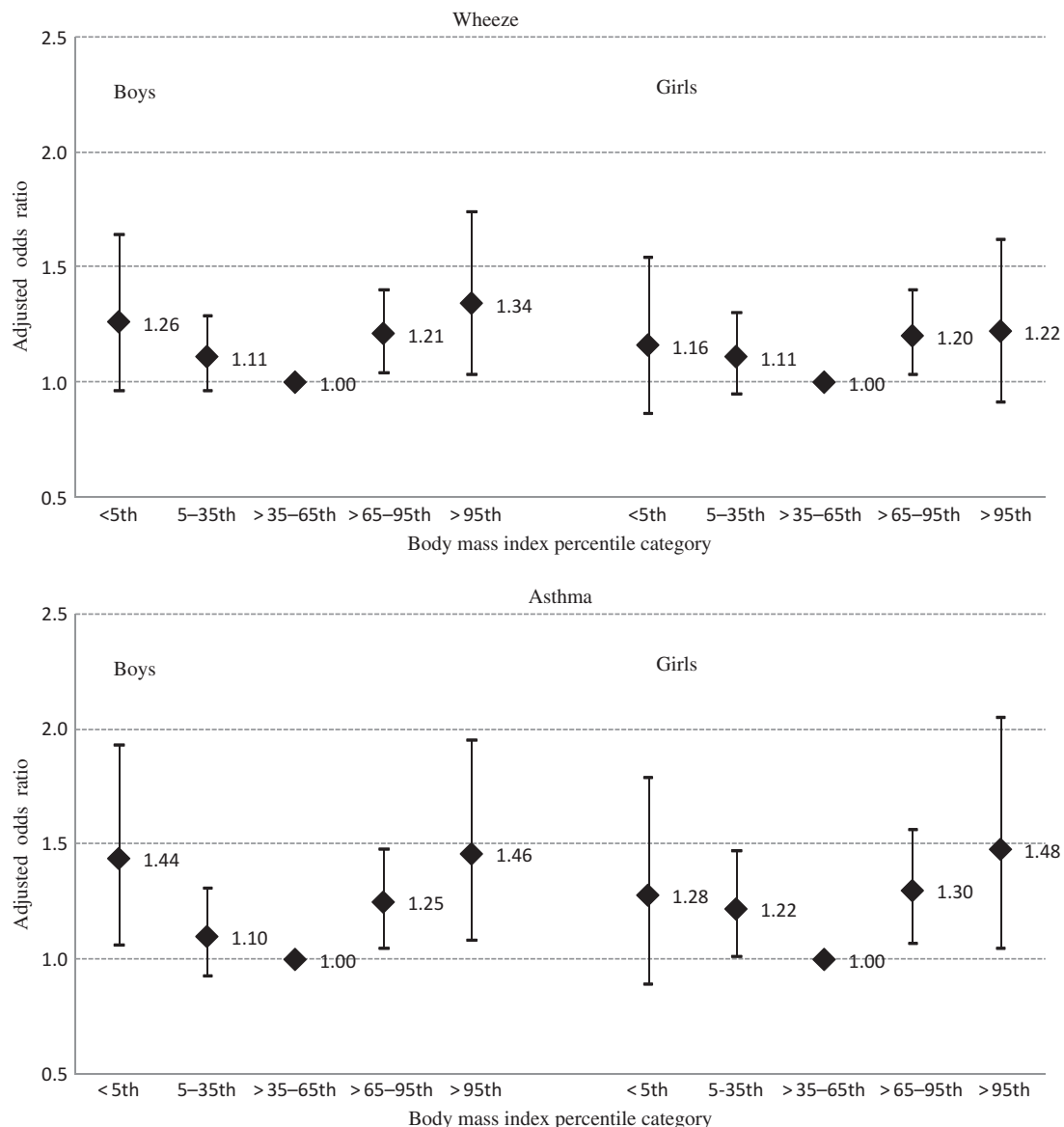


FIGURE 1.—Association of wheeze and asthma with the different body mass index (BMI) categories for boys and girls, respectively, presented as an adjusted odds ratios (ORs) and 95% confidence intervals (CIs). Adjustment for age, region of residence, number of siblings, smoking in the household, physical activity, paternal and maternal history of allergic disorders, and paternal and maternal educational levels.

study, we found that not only high BMI percentile categories but also low BMI percentile categories were significantly positively associated with the prevalence of asthma among Japanese schoolchildren. Our findings are consistent with previous reports of a U-shaped association between BMI and asthma among children and adolescents (12, 28). Similarly, among US boys aged 2–11 years, boys who were classified as either underweight or overweight were more likely to have asthma compared with those who were of normal weight; adjusted ORs for underweight and overweight were 2.9 (95% CI: 1.1–7.7) and 2.4 (95% CI: 1.4–4.3), respectively (12). In a cross-sectional study of Swedish men aged 17–20, both underweight and obesity were associated with an increased prevalence of asthma with and without allergic rhinitis (28). A U-shaped relationship between BMI and asthma has also been observed among adults in the United States (2), China (3), and Australia (4).

The reasons for the positive associations observed in this study between underweight and asthma are not clear. In a cross-sectional study in Taiwan, underweight male students had a significantly lower peak expiratory flow, and a forced expiratory flow of 25–75% of that achieved by students of normal weight (29). Schachter et al. (4) have reported that lung function parameters, such as forced expiratory volume in 1 s, forced vital capacity, peak expiratory flow, forced expiratory flow, and airway responsiveness, are significantly reduced in a low BMI (<18.5) group compared with a normal BMI group (BMI: 18.5–24.9). Impairment of lung function in subjects with a low BMI may contribute to the symptoms of asthma.

The association between high BMI and asthmatic symptoms could be due to various factors, such as a sedentary lifestyle, diet, inflammation, pulmonary dysfunction, and hormonal influence (30). Obesity causes reduced lung function (24); Pelosi et al. (31) have shown an increase in airway resistance in obese subjects. The reduction in deep breathing associated with a sedentary lifestyle may also contribute to airway narrowing by reducing the extent to which bronchial smooth muscle is stretched (20, 32). According to another hypothesis, estrogens are a risk factor for asthma. In a review, Tantisira et al. (30) discussed the possibility that obesity may amplify the inflammatory state through inducing higher level of estrogen in obese women. Although many studies have reported a stronger association between obesity and asthma in female subjects compared with male subjects, few studies have reported a statistically significant interaction between the sexes (9, 33). The current study, likewise, did not reveal a difference according to gender. Finally, dietary factors can also affect asthma. Obese subjects tend to consume food types with poor nutritive value and high total fat (30). Levels of vitamins A, C, E, carotenes, riboflavin, zinc, and magnesium have been noted to correlate inversely with body fat. Deficiency of those nutrients might lead to reduced pulmonary function and increased airway responsiveness (30).

In this study, we observed no association between BMI percentile and the prevalence of eczema or rhinoconjunctivitis. The results of investigations of the association between BMI and eczema and rhinoconjunctivitis have been conflicting (13–17). Among Belgian schoolchildren, there was no association between BMI and the prevalence of eczema or rhinoconjunctivitis (13). In a cross-sectional study of Swedish schoolchildren, no association between high BMI and hay fever was found, although a positive relationship between high BMI and eczema was observed in children with current wheeze, but not in those without current wheeze (17). Obesity has been shown to be associated with a higher prevalence of atopic dermatitis in a cross-sectional study of Japanese schoolchildren (14). In the same study, however, an inverse association between obesity and the prevalence of allergic conjunctivitis was observed (14). These conflicting results among studies might be attributed to differences between the studies in population age range, definitions of overweight/obesity, and adjustment for potential confounders.

This present investigation had several major strengths. Study subjects were homogeneous with respect to age and geographical background. The sample size was large and the participation rate in the study was high (76%). Since information on the personal characteristics of non-participants ($n = 9327$) was not available, however, we could not determine how non-participants affected the strength and direction of our observed results. In the current study, we used an internationally standardized and validated measurement tool (ISAAC), but validation tests for these questions had not been performed in this population. Moreover, no attempt was made to ascertain outcome status through reviews of medical records. There are some limitations that might influence the interpretation of the current results, however. Our study design was cross-sectional; therefore, results do not necessarily indicate a causal relationship. As a measure of body fat, we used BMI, which is easily calculated and convenient to use in large-scale epidemiological studies. Although it is an indirect measurement of body fat, it is thought to be a valid proxy for fat mass in children because of its strong association with total body fat (34). In the current study, BMI was calculated based on reported height and weight. We cannot exclude the possibility of measurement error. However, the misclassification of exposure with respect to disease outcome is usually random and tends to attenuate associations. Although we adjusted for extensive variables, we cannot eliminate the possibility that the observed associations between BMI and allergic diseases are a consequence of residual confounding effects.

Okinawa has unique characteristics due to its geographical location at the southern extremity of Japan. It is close to Taiwan, and is the only prefecture in Japan situated in a subtropical climate zone. Moreover, Okinawa is less developed compared with the mainland because it was not until 1972 that Okinawa reverted to Japanese administration. The distribution of a variety of environmental factors including diet and socioeconomic

status, as well as allergy in Okinawa is likely to differ from that in the mainland of Japan. In fact, the prevalence of allergic disorders in the current study was quite different from that in the mainland of Japan. According to another cross-sectional study among Japanese adolescents in Suita City, which is in an urban area of the mainland, the prevalence values for wheeze, atopic eczema, and allergic rhinoconjunctivitis in the past 12 months based on the ISAAC criteria were 6.7%, 14.5%, and 23.9%, respectively (35). The corresponding figures in this study were 10.8%, 6.9%, and 7.6%, respectively.

CONCLUSIONS

We observed an association of both underweight and overweight with an increased prevalence of asthma among Japanese schoolchildren. There was no association between BMI and the prevalence of eczema or rhinoconjunctivitis. Confirming these associations in prospective studies could further our understanding of the pathogenesis, prevention, and management of allergies.

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DECLARATION OF INTEREST

The authors declare no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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