
A case-control study of body mass index and asthma in Asian children

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Background: The prevalence of obesity and asthma in the United States has increased in past decades. Numerous studies have focused on the relationship between the 2 factors. However, to our knowledge, this association in Asian Americans has not been extensively studied.

Objective: To assess the association between body mass index (BMI) and asthma in an Asian American pediatric population.

Methods: We conducted a case-control medical record review study of 94 pediatric patients with and without asthma at Tufts–New England Medical Center, Boston, Massachusetts. The BMI of asthmatic children before and after their asthma diagnosis was compared with the BMI of children without asthma.

Results: Multiple analyses showed no significant ($P > .05$) association between various measures of BMI and asthma in this population. After adjustment for atopic dermatitis, allergic rhinitis, and other allergies, the odds ratio in our longitudinal analysis using BMI greater than the 85th percentile for asthmatic children vs nonasthmatic children was 0.92 (95% confidence interval, 0.40–2.20).

Conclusions: Either overweight and obesity do not lead to asthma in Asian immigrant children, consistent with our results, or something about our method limited our ability to observe the association. In either case, more research in the population is needed.

Ann Allergy Asthma Immunol. 2008;100:447–451.

INTRODUCTION

Numerous studies have shown that the prevalence of obesity¹ and asthma^{2,3} in children in the United States has increased in recent decades (1970–2000). In fact, 17.1% of children and adolescents in the United States were overweight in 2003 to 2004, a significant relative increase in the prevalence of overweight from 13.8% in 1999 to 2000.^{4,5} Between 1980 and 1996, asthma increased by almost 74%,⁶ so that in 2003, 12.5% of children and adolescents were reported to have physician-diagnosed asthma.⁷

The National Health and Nutrition Examination Study III, a cross-sectional study that was conducted from 1988 to 1994, was one of the first studies to suggest an association between asthma and overweight or obesity; the researchers showed that children in a representative sample of US children and adolescents, aged 4 to 17 years, with a body mass index (BMI) in the top quartile were at increased risk of being diagnosed as having asthma relative to those with a BMI in the lowest quartile (odds ratio [OR], 1.98).⁸ Prospective studies seem to show a role of sex in the relationship. For example, girls had a strong association between overweight or obesity and asthma.^{9,10} Girls who became obese from the age of 6 to 11 years were 7 times more likely to develop

asthma symptoms by the age of 11 years.¹¹ In contrast, a study¹² of children and adolescents in California reported that being overweight or obese increased the risk of new-onset asthma (relative risk, 2.06) only in boys. A recent prospective study¹³ also found that boys (hazard ratio, 2.4), but not girls (hazard ratio, 0.8), with a higher BMI might be at increased risk of developing asthma. Two other studies^{14,15} of children found an association between obesity and asthma in both sexes, but for girls more so than for boys.

Since 1999, of more than 30 cross-sectional and case-control studies on obesity and asthma, only three¹⁶ (OR, 1.02 for boys and 1.06 for girls¹⁷; and OR, 1.02¹⁸) have reported no association between asthma in the obese or overweight children.¹⁹ Overall, there is growing evidence that obesity increases the risk of asthma, but more studies need to be done to find the molecular basis for this hypothesis.

Several hypotheses have been proposed for a potential causal mechanism connecting obesity and asthma, including common causes (fetal programming and genetic pleiotropy), effects of obesity on lung mechanics (reduced tidal volume and lower than normal functional residual capacity), and adipokines (proteins synthesized and secreted from adipose tissue that may affect airway function).²⁰ For example, a twin cohort study found that obese females have an increased risk of asthma, which may partly be because of common genes.²¹ In addition, studies have shown that gastroesophageal reflux, which is a result of obesity, can exacerbate asthma.²² Furthermore, recent research²³ has hypothesized that immune-related diseases, such as asthma, could, in part, be caused by decreased immunological tolerance because of the secretion of adipokines and cytokines by white adipous tissue. A

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Disclosures: Authors have nothing to disclose.

Funding Sources: Mr Henkin was supported by Summer Scholars Funding from Tufts University, and Dr Brugge was supported by the Jonathan M. Tisch College of Citizenship and Public Service at Tufts University.

Received for publication June 25, 2007; Received in revised form September 18, 2007; Accepted for publication October 24, 2007.

study²⁴ that has looked at weight loss and asthma control concluded that consistent weight loss in obese patients improves lung function and other respiratory symptoms.

In most studies concerning overweight or obesity and asthma, the population is primarily composed of white or African American (black) children, whereas Asians are not included or compose a minority of the population. One exception is a study²⁵ of Taiwanese children that found that obesity was a predictor of allergic symptoms. The prevalence of childhood overweight and obesity is highest in the United States (25.4%) and lowest in China (7.0%),²⁶ and asthma symptoms have been reported as 6.0% for 13- to 14-year-old adolescents in China.²⁷ Also relevant to our study is the observation that Chinese persons immigrating to the United States tend to change their dietary patterns toward a more Western eating style²⁸ and tend to have a higher risk of becoming overweight with time spent in the United States.²⁹

We, therefore, conducted a study to examine the association of change in BMI (calculated as weight in kilograms divided by height in meters squared) with the timing of diagnosis of asthma in Asian American children aged 4 to 18 years. We hypothesized that overweight children would have a higher risk for developing asthma.

METHODS

Study Population

The Tufts–New England Medical Center, Boston, Massachusetts, institutional review board approved the medical record review study protocol. Data collected were anonymous and deidentified. An alphabetical list of patients diagnosed as having asthma was obtained from the hospital's data management department. The first 94 Asian patients (48 boys and 46 girls), aged 4 to 18 years, with physician-diagnosed asthma who met the criteria were included. Those patients who transferred to Tufts–New England Medical Center from other medical institutions and were diagnosed as having asthma were excluded. Other exclusion criteria involved incomplete or inadequate medical records (missing weight or height); children with cystic fibrosis, chronic cardiac diseases, and severe mental disorders, such as autism; those with a last physician visit more than 2 years before the asthma diagnosis or no physician visits after the asthma diagnosis; and active smokers (cigarettes or marijuana).

To select control subjects, we obtained an alphabetical list of patients without asthma from the hospital's data management department. The first 94 patients who met the criteria were matched by age (age at asthma diagnosis within 1 year) and sex using the same exclusion criteria as for cases. Height and weight for at least 1 visit before and 2 visits after the age of diagnosis in cases and the corresponding age of the matched cases were recorded.

Additional recorded information included sex, date of birth, place of birth (United States or foreign, if available), atopic dermatitis, allergic rhinitis, food allergy, and other allergies, all of which were obtained from patients' medical records.

Data Entry

Data were entered into a database (Microsoft Access Database; Microsoft Corporation, Redmond, Washington). To eliminate as much height-measurement inaccuracy as possible, age vs height of each patient was graphed using computer software (Microsoft Excel; Microsoft Corporation) and the resulting linear R^2 was generated. We corrected data for those children who showed implausible biological growth in heights, such as having a lower height at the age of 8 years than at the age of 7 years. We set the critical value of R^2 at 0.9; thus, the heights of the individuals with R^2 of less than 0.9 were adjusted by taking out the height point(s) furthest away from the linear trend line, generating a new line, and extrapolating the new heights using the formula created by the computer software. This method was used for 7 cases and 0 controls.

Body mass index percentiles were generated using the Centers for Disease Control and Prevention (CDC) Child and Teen Calculator (available at: <http://apps.nccd.cdc.gov/dnpabmi/Calculator.aspx>). Each child was assigned to 1 of the following categories, consistent with CDC growth charts for boys and girls aged 2 to 20 years: less than 20% (underweight or at risk for being underweight), 20% to 85% (normal weight), 85% to 95% (risk for overweight), and more than 95% (overweight).

Cross-sectional Analyses

Data were transferred into a commercially available software program (SPSS for Windows, version 12.0; SPSS Inc, Chicago, Illinois) and cross-checked by reference to the hard copy for errors. Paired-sample t tests for the variables of age, height, weight, BMI, and BMI percentile at diagnosis were conducted for boys and girls separately and combined.

We used χ^2 tests to examine differences in risk between cases and controls. First, we compared the rates of atopic dermatitis, allergic rhinitis, food allergy, and other allergies in asthmatic vs nonasthmatic children, for total study population and boys and girls separately. After creating categories for BMI percentile, we tested for significance for this variable for the total population and boys and girls separately. In addition, we tested associations when BMI percentiles were combined from 1% to 85% and greater than 85%.

Longitudinal Analysis

To test for significance between the number of cases and controls that were overweight before or after the diagnosis/matched age, we created 2 new variables: overweight before and overweight after (BMI percentiles $>85\%$). We conducted χ^2 tests on these 2 variables, for the total population and boys and girls separately.

We tested for the difference between cases and controls for the slope of the line of their BMI percentile before and after asthma diagnosis/matched age. We created 2 variables: general slope before asthma diagnosis/matched age and general slope after asthma diagnosis/matched age. For each variable, there were 3 possibilities: flat line ($-0.004 < m < 0.004$),

line going up ($m > 0.004$), and line going down ($m < -0.004$). We conducted χ^2 tests on these variables for the total population and boys and girls separately.

We used the general linear models procedure with computer software (SAS, version 9.1; SAS Institute Inc, Cary, North Carolina) to compare mean differences between cases and controls. To account for the matched design of the study, we used conditional logistic regression to calculate ORs and 95% confidence intervals (CIs) of obesity for asthma risk. Again, risk for overweight was defined as greater than 85%, as classified by the CDC. We adjusted for age of BMI measurement (in months) and presence of atopic dermatitis (yes or no), food and other allergies (yes or no), and allergic rhinitis (yes or no) in the models. We examined potential interaction of overweight with age, atopic dermatitis, food and other allergy, and allergic rhinitis by including multiplicative terms in the regression models. Because the relationship between age and asthma may not be linear, we also included a quadric term for age in the models, with adjustment for other potential confounders. Because the quadric term was not statistically significant ($P > .05$), we used simpler models with the original scale of age in our analyses. All P values were 2 sided. The significance was set at $P < .05$.

RESULTS

Cross-sectional Data

The mean (SD) age for cases at asthma diagnosis was 6.11 (1.83) years, relative to 6.13 (1.89) years for controls (Table 1). t Tests showed no significant difference between asthmatic and nonasthmatic boys at asthma diagnosis in terms of BMI ($P = .27$) and BMI percentile ($P = .86$) (data not shown). There was also no significant difference for asth-

matic and nonasthmatic girls at asthma diagnosis in terms of BMI ($P = .25$) and BMI percentile ($P = .37$) (data not shown). When looking at boys and girls together, no significant difference was found between asthmatic and nonasthmatic patients at asthma diagnosis in terms of BMI ($P = .12$) and BMI percentile ($P = .65$) (data not shown).

At diagnosis, 14% of the cases were underweight or at risk of being underweight (BMI percentile, $<20\%$) and 30% were overweight or at risk of being overweight (BMI percentile, $>85\%$); of the matched controls, 16% were underweight or at risk of being underweight and 26% were overweight or at the risk of being overweight (Table 1). The number of children underweight or at risk of underweight, normal weight, at risk of overweight, and overweight was not significant between cases and controls ($P = .27$). The graph of BMI by deciles for cases and controls showed that they were similar (Fig 1).

Asthmatic patients often had atopic dermatitis (44%) at least once before their asthma diagnosis, compared with 18% of controls (Table 1). There was a sex difference for the difference in the association of atopic dermatitis with asthma ($P < .001$ for girls and $P = .12$ for boys) (data not shown). Allergic rhinitis was also far more common in cases (71%) than in controls (27%) ($P < .001$ combined [Table 1] and for boys and girls separately [data not shown]).

The number of children with food allergies and other allergies was not significantly different between asthmatic and nonasthmatic patients ($P = .62$ and $P > .99$, respectively).

Longitudinal Data

No statistical significance was found for the number of cases and controls who were overweight before ($P = .26$) or after ($P = .88$) asthma diagnosis (details not shown). The slopes of BMI linear trends before and after asthma diagnosis were also not different between cases and controls before ($P = .49$) or after ($P = .17$) diagnosis (details not shown). There was also no significant difference between male or female cases and

Table 1. Characteristics of the Study Population for Cases (Asthmatic Patients) and Controls (Nonasthmatic Subjects)^a

Characteristic	Cases (n = 94)	Controls (n = 94)
Sex		
Male	48 (51)	48 (51)
Female	46 (49)	46 (49)
BMI percentile at diagnosis/ matched age, % ^b		
<20	13 (14)	15 (16)
20–85	53 (56)	54 (57)
86–95	15 (16)	19 (20)
>95	13 (14)	6 (6)
Atopic dermatitis	41 (44) ^c	17 (18) ^c
Allergic rhinitis	67 (71) ^d	25 (27) ^d
Food allergy	3 (3)	1 (1)
Other allergies	14 (15)	13 (14)

Abbreviation: BMI, body mass index.

^a Data are given as number (percentage) of each group.

^b Percentages may not total 100 because of rounding.

^c $P < .05$.

^d $P < .001$.

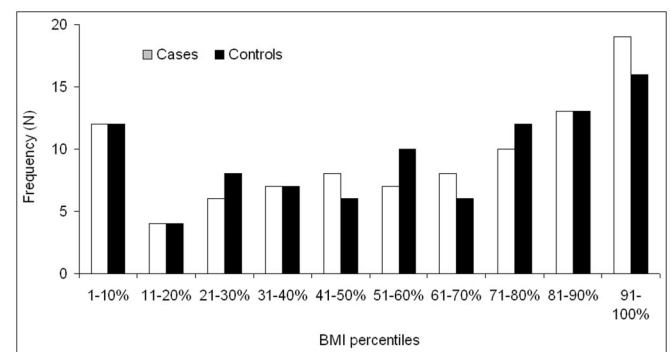


Figure 1. Body mass index (BMI) percentile histograms for cases (asthmatic patients) and controls (nonasthmatic patients) at asthma diagnosis or matched age. The mean (SD) BMI percentile for asthmatic patients is 58.8% (31.8%). The mean BMI percentile for nonasthmatic patients is 57.7% (31.1%).

controls before asthma diagnosis ($P = .75$ and $P = .59$, respectively) or after asthma diagnosis ($P = .13$ and $P = .60$, respectively) (details not shown).

In an age-adjusted longitudinal model, the OR was 1.30 for children with a normal weight vs those at risk for overweight (BMI, $>85\%$) (Table 2). With further adjustment for atopic dermatitis, food and other allergies, and allergic rhinitis, the OR for asthma decreased to 0.92. We obtained a similar nonsignificant association when we used a continuous variable of BMI as a predictor. We also tested potential interaction with sex. The interaction term was not significant. Stratification analyses showed that nonsignificant associations between BMI greater than 85% and asthma persisted among girls and boys (data not shown). When we used 95% as the cutoff for obesity, the association between obesity and asthma remained nonsignificant. The adjusted OR was 1.23 (95% CI, 0.35–4.36; $P = .75$). The patterns for risk of overweight or obese and asthma were not changed over time (Fig 2).

DISCUSSION

We found no association between overweight and onset of asthma in this population of Asian American children as a whole or for boys and girls separately. We used multiple approaches, including cross-sectional statistical analyses and longitudinal analyses. Our study used information found in medical records, which is expected to be reasonably reliable.

Our results differ from those of most other studies, which found significant associations between the 2 factors. However, a few studies have also failed to find an association between BMI and asthma. A large cross-sectional survey study¹⁶ in Canada found an OR of 1.02 for children with a BMI higher than the 85th percentile. Another study (mixed longitudinal)³⁰ of mostly white children from England and Scotland found an OR of 1.04. Finally, a case-control study¹⁸ of primarily African American urban adolescents did not find an association between overweight and asthma. Because these studies used a variety of designs, we doubt that study design explains negative findings.

Table 2. Data for Asthma According to BMI Status in a Longitudinal Model

Model	Odds ratio (95% confidence interval) for cases ^a	P value
Age-adjusted model	1.30 (0.64–2.65)	.46
Model further adjusted for atopic dermatitis	1.20 (0.55–2.60)	.65
Model further adjusted for food and other allergies	1.18 (0.54–2.58)	.69
Model further adjusted for allergic rhinitis	0.92 (0.40–2.15)	.86

Abbreviation: BMI, body mass index.

^a The reference group was controls (odd ratio of 1 for all).

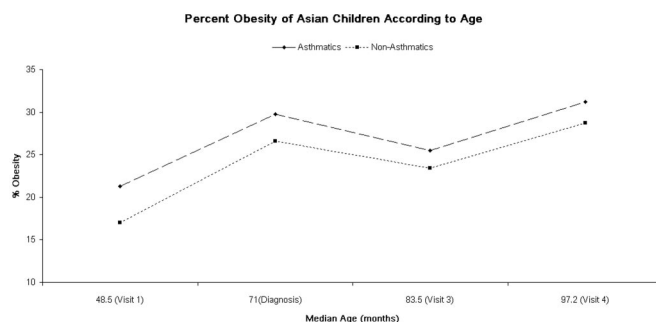


Figure 2. Percentage overweight and risk of overweight of cases and controls according to age and visit number.

There are a couple of reasons why our study might not have shown an expected association between overweight and asthma. First, the low power of our study might have prevented us from seeing a significant association between overweight and asthma. The 95% CI for the OR with adjustments spanned from 0.40 to 2.15; however, the central tendency was close to 1 and the fact that we tried numerous analytical approaches to the data suggests that this is unlikely. Second, there might be something different about our study population compared with non-Asian populations. We hypothesize that a possible explanation for the difference in this population and other populations may have to do with diet.

The traditional Chinese diet is known to be high in fiber and low in saturated fat³¹; however, after emigrating to the United States, the Chinese tend to adopt aspects of the Western diet while maintaining many traditional eating habits,³² resulting in a significant increase in the consumption of fats and sweets.³³ We could not evaluate diet or lifestyle in our study population. Nevertheless, research has shown that the traditional Mediterranean diet may be protective against asthma and rhinitis.³⁴ Future studies might collect data on diet and BMI in Asian children to test this possibility.

There are several strengths to our study. Although this is a case-control study, one of the major problems associated with case-control studies—recall bias—was eliminated because we used information found in medical records created before asthma diagnosis. This should reduce misclassification and bias in the data. Also, this is the first study known to us that has focused specifically on Asian American children. This population is interesting because any generalizable causal association between overweight and asthma should be seen across different populations.

There are some limitations to our research in addition to sample size and lack of dietary information. More important, this is not a prospective cohort study, which would be a stronger design for inferring causation. In addition, because the medical information was recorded from medical records, we cannot ensure that the medical personnel all followed the same standard protocol. Different nurses may have measured weight and height differently (eg, with shoes or clothes), and different physicians may have used different criteria for the

diagnosis of asthma. This would contribute misclassification to the data. There are limitations to the accuracy of BMI measurements derived from heights and weights, but for our purposes, this is a reasonable way to evaluate obesity in children.³⁵ Also, data on whether the children were born in the United States or emigrated from Asia, a factor that has been shown to be strongly associated with asthma in this population,^{36,37} were not consistently available in the medical records we used.

Even though our study does not refute the results and the robustness of other studies that have shown that an association exists between obesity and asthma, future studies should focus on whether our findings show that such an association cannot be extended to Asian American immigrant children. Prospective cohort studies in a population such as ours would clarify the issue.

ACKNOWLEDGMENTS

We thank the Asian clinic at Tufts–New England Medical Center and its staff for their invaluable assistance; David Tybor for comments on the manuscript; and Dora Hui for data entry.

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