Original articles

Relation of body mass index to asthma and atopy in children: the National Health and Nutrition Examination Study III

E von Mutius, J Schwartz, L M Neas, D Dockery, S T Weiss

Abstract

***Background*—An increase in the prevalence of obesity and asthma over recent decades has been reported in affluent societies. Both overweight and obesity have been shown to be inversely related to having been breastfed, which is also a potential protective factor against childhood atopic diseases. The aim of this analysis was to explore the relation of body mass index (BMI) to asthma and atopy in a large representative sample of the United States population.**

***Methods*—Children aged 4–17 years were included in the NHANES III survey. Prevalences of atopic diseases and potential confounding factors such as exposure to environmental tobacco smoke, birth weight, breast feeding, and household size were assessed using structured interviews with parents. Height and weight were measured, and BMI was calculated as kg/m^2 and transformed into Z scores. Children underwent skin prick tests for atopy to a battery of food and inhalant allergens.**

***Results*—The prevalence of asthma (8.7% *v* 9.3% *v* 10.3% *v* 14.9%, p=0.0001) and atopy (48.6% *v* 50.5% *v* 53.0% *v* 53.2%, p=0.05) rose significantly with increasing quartiles of BMI. After adjustment for confounders, a significant positive association between BMI and asthma remained (adjusted OR 1.77, 95% confidence interval 1.44 to 2.19 between the highest and lowest quartiles of BMI), whereas no independent relation between BMI and atopy was evident. No effect modification by sex or ethnic group was seen.**

***Conclusions*—The effects of increased BMI on asthma may be mediated by mechanical properties of the respiratory system associated with obesity or by upregulation of inflammatory mechanisms rather than by allergic eosinophilic inflammation of the airway epithelium.**

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Keywords: body mass index; obesity; atopy; asthma

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An increase in the prevalence of obesity over recent decades has been reported in Britain and the United States.[1] The simultaneous rise in the prevalence of asthma and atopy[2] has prompted investigators to speculate that obesity might be a causal factor in the inception of atopic diseases. In fact, several studies (most of them cross sectional) have shown positive associations of obesity or body mass index (BMI) with respiratory symptoms, asthma, and airway hyperresponsiveness.[3–10] Little is known about the potential effects of BMI on the development of atopy. While some studies have found an effect of BMI on skin test reactivity[6] and the prevalence of allergy,[9] others have failed to find an association between BMI and hay fever[5] or self-reported allergy.[7] In studies stratified according to sex, associations of BMI with respiratory symptoms and lung function have been more pronounced in women and girls than in men and boys.[5 7 10] Inner city populations may be at a higher risk than residents of suburban or rural environments.[3 8]

A strong inverse relation between having been breast fed and BMI has recently been found in children starting school,[11] confirming previous reports based on smaller study samples.[12 13] Since breast feeding is also a protective factor against asthma and atopy,[14] uncontrolled confounding may have biased the results of previous studies.

The Third National Health and Nutrition Examination Survey (NHANES III) explored the nutritional and health status of a stratified random sample of a non-institutionalised US population aged 6 months to 74 years. Information was obtained on BMI, breast feeding status, prevalence of asthma and hay fever, and atopic sensitisation as assessed by skin prick tests.

Methods

The NHANES III survey, which was conducted in two phases (1988–91 and 1991–4), included a total of 39 695 subjects aged 2 months to >80 years. For the purpose of this report, data analysis was restricted to children aged 4–17 years (n=7505). Details of the survey design and the examination procedures have been published previously.[15] Interviewers visited the subjects at home before the medical examination to gather demographic information and elicit a medical history. For the

*Table 1 Characteristics of study population**

Sex (boys)	3630/7370; 49.3%
Ethnicity	
Non-Hispanic white	1938/7370; 26.3%
Non-Hispanic black	2504/7370; 34.0%
Mexican-American	2577/7370; 35.0%
Other	351/7370; 4.8%
Mean (SD), (range) BMI	18.5 (4.2), (7.3–37.2)
Asthma ever	668/7368; 9.1%
Still asthma	463/7345; 6.3%
Treated for asthma	636/7365; 8.6%
Wheeze	1182/7369; 16.0%
Atopy[1]	2480/4742; 52.3%
Passive smoke exposure	2946/7364; 40.0%
Birth weight (g)[2]	
<2500	471/5169; 9.1%
2500–4100	4325/5169; 83.7%
>4100	373/5169; 7.2%
Ever breast fed[3]	944/2137; 44.2%

Data expressed as n/N (%) except for BMI which is expressed as a ratio calculated as kg/m^2.
[1]Information only availabe on subjects aged 6–17 years.
[2]Information only availabe on subjects aged 4–12 years.
[3]Information only availabe on subjects aged 4–6 years,
*A complete data set was not available for every subject.

children, questions were answered by a parent. Interviewers and medical examiners were specifically trained to ensure standardisation of the conduct of the survey at each site.

To assess the prevalence of asthma, subjects were asked whether a physician had ever told them they had asthma, whether they still had asthma, and whether they had ever been treated by a doctor for asthma. The number of episodes of wheeze in the past 12 months, the number of hospital and emergency room visits, the number of hours the subject watched TV on the day before examination, and the frequency of play or exercise resulting in sweating and breathing hard per week were ascertained. Moreover, exposure to environmental tobacco smoke—that is, cigarette smoking by anyone in the household—was determined. For children aged 4–6 years, information on breast feeding status (whether they had ever been breastfed) and the duration of breast feeding was collected.

Height and weight were measured and BMI was calculated as kg/m^2. Z scores of BMI were furthermore computed as suggested for the NHANES III data set (CDC NHANES website: www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm). Skin prick tests were performed in 6–17 year old subjects at the time of the medical examination by teams of technicians trained in standardised procedures. A panel of allergens, including *Alternaria*, bermuda grass, rye grass, ragweed, Russian thistle, white oak, cat, German cockroach, mites, and peanuts was administered. Histamine and phosphate buffered saline controls were also applied. Skin tests were performed on an alcohol prepared arm by applying drops of allergen and then pricking the skin under the drops by lifting it lightly with a 25 gauge BD needle. After 20 minutes the length and width of the flare and weal were measured. A reaction was defined as positive if the mean of the length and the width of the weal was at least 3 mm (with the reaction to the negative control subtracted from that to the respective allergen). Children with a positive reaction to any of the 10 allergens tested were considered atopic.

Data were analysed by multiple linear and logistic regression, using generalised models for intraclass correlation to adjust for random site effects and normalised weighting of data to adjust for the sampling scheme in NHANES III.

Results

The characteristics of the study population are given in table 1. The three ethnic groups that made up most of the study sample (non-Hispanic whites, non-Hispanic blacks, and Mexican Americans) were represented in similar proportions. Approximately half of all subjects were atopic, while 9% had had asthma at some time. Mean BMI was 18.5 kg/m^2 (range 7.3–37.2; 1st quartile 7.3–15.4; 2nd quartile 15.5–17.1; 3rd quartile 17.2–20.4; 4th quartile 20.5–37.2). The prevalence of asthma, wheeze in the past 12 months, hay fever, and atopy rose significantly with increasing BMI (table 2).

Having been breastfed was found to be inversely related to BMI as reported previously.[11] After adjustment for potential confounding factors such as age, sex, ethnicity, household size, and exposure to passive smoke, a significant positive association between BMI and the asthma outcomes remained (table 3). Additional controlling for birth weight (which was assessed only in children <12 years of age) or breast feeding status (which was assessed only in children <6 years of age) did not change the results (data not shown). With stratification for ethnicity and sex, no effect modification for the relation between BMI and asthma was seen (data not shown). When other measures such as waist circumference, arm circumference, and thigh skinfold were used as indicators of obesity, similar results were obtained (data not shown).

*Table 2 Prevalence of asthma, hay fever and atopy (%) in children aged 4–17 years across quartiles of Z scores of body mass index (BMI)**

	1st quartile (n=1921)	*2nd quartile (n=1948)*	*3rd quartile (n=1778)*	*4th quartile (n=1720)*	*p value†*
Asthma ever (n=668)	8.7	9.3	10.3	14.9	0.0001
Still asthma (n=463)	5.6	6.8	7.3	10.8	0.0001
Treated for asthma (n=636)	8.6	8.7	10.05	14.5	0.0001
Wheeze in past 12 months (n=1182)	14.6	18.3	14.7	20.6	0.0002
Ever hay fever (n=384)	5.6	8.9	8.6	8.0	0.012
Still hay fever (n=360)	5.4	8.5	7.8	7.8	0.011
Treated for hay fever (n=314)	4.5	7.4	7.3	6.7	0.013
Atopy (n=2480)	48.6	50.5	53.0	53.2	0.05

Prevalence (%) in indicated quartile (Z score of BMI range) given as percentages weighted by the normalised weight variable
*A complete data set was not available for every subject.
†Test for trend.

*Table 3 Relation of quartiles of BMI to asthma and atopy in children aged 4–17 years after adjusting for potential confounding factors**

	1st quartile (reference)	2nd quartile	3rd quartile	4th quartile	p value
Asthma ever	1.00	1.03 (0.83 to 1.28)	1.22 (0.98 to 1.51)	1.77 (1.44 to 2.19)	0.0001
Still asthma	1.00	1.19 (0.92 to 1.54)	1.36 (1.05 to 1.76)	1.98 (1.54 to 2.53)	0.0001
Treated for asthma	1.00	0.96 (0.77 to 1.20)	1.19 (0.96 to 1.49)	1.74 (1.41 to 2.15)	0.0001
Wheeze in past 12 months	1.00	1.29 (1.09 to 1.53)	1.02 (0.85 to 1.22)	1.48 (1.24 to 1.76)	0.0004
Ever hay fever	1.00	1.54 (1.19 to 2.01)	1.63 (1.25 to 2.13)	1.42 (1.08 to 1.88)	0.02
Still hay fever	1.00	1.52 (1.17 to 1.99)	1.53 (1.16 to 2.02)	1.44 (1.09 to 1.92)	0.02
Treated for hay fever	1.00	1.59 (1.19 to 2.11)	1.74 (1.30 to 2.32)	1.47 (1.09 to 1.99)	0.02
Atopy	1.00	1.07 (0.91 to 1.27)	1.20 (1.01 to 1.43)	1.14 (0.96 to 1.35)	0.08
Eosinophilia	1.00	1.10 (0.98 to 1.23)	1.00 (0.89 to 1.13)	1.04 (0.93 to 1.17)	0.79
Number of episodes of wheeze	1.00	0.64 (0.45 to 0.93)	0.79 (0.56 to 1.12)	0.92 (0.66 to 1.29)	0.87
Emergency room visits	1.0	1.02 (0.79 to 1.33)	1.05 (0.81 to 1.38)	1.46 (1.13 to 1.87)	0.002

Values are odds ratios with 95% confidence intervals adjusted for sex, ethnicity, age, household size, study area, and passive smoke exposure.
*A complete data set was not available for every subject.

Atopic sensitisation, as assessed by skin prick tests, was only weakly and non-significantly positively related to BMI after adjustment for confounding. With further controlling for birth weight the association disappeared (data not shown). Moreover, in non-asthmatic children, BMI was not related to hay fever and atopy (data not shown). Finally, no significant association of BMI with serum eosinophil counts was seen (table 3). When the association between asthma and BMI was further adjusted for atopy, the effect of BMI remained virtually unchanged (data not shown). No interaction between atopy and BMI was found.

No relation between BMI and the number of episodes of wheeze in the past 12 months was found (table 3). However, the number of emergency room visits because of asthma was positively related to BMI. Among asthmatics only, BMI was inversely associated with the number of episodes of wheeze but not with the number of emergency room visits because of wheeze (data not shown). Time spent watching TV was not related to asthma (β=0.03, p=0.4) or atopy (β=–0.03, p=0.1), and the frequency of exercising per week was also not associated with asthma (data not shown).

Discussion

A high BMI was associated with an increasing prevalence of asthma in a representative sample of the US population aged 4–17 years after controlling for potential confounding factors such as sex, ethnicity, age, household size, passive smoke exposure, birth weight, and breast feeding status. No effect modification by sex or ethnic group was seen. In contrast, atopy was not related to BMI. The lack of correlation with television viewing hours or frequency of physical exercise suggests that it is obesity per se, and not lack of exercise, that is the issue.

The cross sectional design of this study does not allow an assessment of the timing of exposure in relation to the occurrence of asthma or atopy. Thus, the relation between BMI and asthma may reflect the predisposition of an asthmatic subject to gain weight because of reduced exercise tolerance rather than a causal association between a high BMI and the inception of asthma. However, no association between the number of episodes of wheezing in the past 12 months and BMI was found. In addition, longitudinal data for adults suggest that increases in BMI predict the development of asthma in nurses[16] and in children.[17] It therefore seems highly unlikely that asthma leads to obesity.

Increasing BMI was related to several measures of asthma, but not to atopy assessed as skin test reactivity. A lack of association between eosinophil counts and BMI suggests that the effects of increased BMI may be mediated through factors other than the induction of allergic eosinophilic inflammation of the airway epithelium. An increasing body of literature suggests that obesity is a proinflammatory state.[18] Studies in animal models indicate that increased levels of leptin, IL-6, and IL-1 (all proinflammatory cytokines) may contribute to and upregulate inflammation in the airway, independent of an allergic mechanism.[18] Studies of prior National Health and Nutrition Examination surveys showed that individuals with a high BMI have increased peripheral blood leucocyte counts which also may reflect an upregulation of inflammatory processes.

Mechanical properties of the respiratory system associated with obesity, such as diminished tidal lung expansion in overweight individuals, may partially account for these results. Reduced tidal lung expansion compromises force fluctuations acting on the airways. Impaired force fluctuations result in greater contractile responses of airway smooth muscle,[19] thereby potentially causing increased airway responsiveness, a hallmark of asthma. Although airway responsiveness was not assessed in NHANES III, a previous study of Taiwanese adolescents[6] clearly showed a positive effect of BMI, not only on the prevalence of asthma, but also on the presence of airway responsiveness as assessed by methacholine challenge. In the Normative Aging Study[20] physiological studies suggesting that increases in obesity are associated with increases in methacholine airway responsiveness in adults are consistent with the mechanical impact of obesity on airway smooth muscle.

A strong association between asthma and atopy has been found in clinical studies where over 80% of asthmatic children react to one or more environmental allergens in skin prick tests.[2] On a population level, however, the relation between asthma and atopic sensitisation is much less clear. In some regions of the world, such as rural China and rural Ethiopia, the

prevalence of asthma is low and is unrelated to the prevalence of atopy, whereas in westernised areas the prevalence of asthma is higher and closely linked to a high prevalence of atopy.[21] This discrepancy points to the importance of distinct factors in determining the incidence of asthma and atopy.

We showed in a German survey[11] that prolonged breast feeding is a protective factor against childhood overweight and obesity. These data have been reproduced in this study which shows an increased risk of obesity in children not breastfed for at least 5 months. Recent studies have suggested a protective role of breast feeding against asthma.[14 22] If prolonged breast feeding resulted in less obesity, then increased BMI might be an intermediate step in a causal pathway leading from shortened nursing to the development of asthma. However, the results of multivariate analyses including breast feeding do not support this notion. Breast feeding was no longer a significant predictor of asthma once BMI was introduced into the model. However, this may be because the intermediate variable (BMI) was included in the regression.

BMI may therefore be an independent risk factor for the development of asthma in both sexes and across ethnic groups. Appropriate strategies for the reduction of body weight in children may contribute to a reduced incidence of asthma in childhood.

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