

Letter to the Editor

Asthma, atopy, and airway inflammation in obese children

To the Editor:

The concurrent increased prevalence of asthma and obesity in adults as well in children has led investigators to consider a possible correlation between the 2 conditions. However, mechanisms underlying this association have not been completely explained.¹

A recent study of a large population-based cohort assessed at age 32 years showed that adiposity is associated with asthma and airflow obstruction in women but not in men.² The authors also demonstrated the absence of a significant association between body fat and airway inflammation in both sexes. Results suggested that being overweight or obese might cause asthma symptoms and airflow limitation in women. Nevertheless, this was not likely originated by an increase in airway inflammation.

These findings encouraged us to develop a pilot study aimed at exploring the association among adiposity and asthma symptoms, lung function, atopy, and airway inflammation, as indicated by exhaled nitric oxide (eNO) levels in a group of obese children.

Patients were recruited from those attending the Obesity Unit, Department of Pediatrics, Federico II University, Naples, Italy. The patients consisted of 50 children with a body mass index (BMI) >95th percentile for age and sex reference values [28 males; median age, 12.2 years (range, 8-16.8); 34 showing signs of initial or advanced pubertal stage]. A questionnaire was administered to patients and their families to obtain information about any physician-diagnosed respiratory disease. Atopy was defined as a positive response to 1 or more aeroallergens during skin prick testing. Median FEV₁ (% predicted), and percent change in FEV₁ after albuterol were obtained. We measured eNO by the single-breath on-line method (NIOX, Aerocrine, Sweden). Patients had not had asthma or rhinitis symptoms or signs, nor did they take inhaled or nasal steroids in the 4 weeks prior to the study. No patient was an active smoker. We also measured eNO levels in 50 age- and sex-matched healthy nonatopic controls. The BMI z score was computed in both obese and healthy children. Because eNO distribution was skewed, analyses were performed with log-transformed data. Comparisons were made using the Student *t* test. A stepwise regression analysis evaluated the contribution to eNO of all subject-specific variables in obese children, including age, sex, BMI, BMI z score, FEV₁, atopy, and asthma. The level of significance was determined as $P < .05$. The Institutional Review Board approved the study, and informed consent was obtained from the parent or legal guardian of each child.

In obese children, median BMI and BMI z scores were 34.5 kg/m² (range, 23-54.7) and 2.51 (range, 1.81-4.08), respectively. Fifty-four percent and 42% of the cases were classified as severely or moderately obese because they had a BMI z score ≥ 2.5 or ≥ 2 , respectively.³

Eighteen (36%) and 11 (22%) children had previously received a diagnosis of asthma or seasonal rhinitis, respectively. Among subjects with asthma, 6 (12% of the whole population) had current asthma defined as physician-diagnosed asthma in the previous year. Skin prick test results were positive in 29 cases (58%). Thirteen atopic children had asthma. In all obese children, median FEV₁ and percent change in FEV₁ after albuterol were 114% predicted (range, 81-168) and 4% (range, -8.8-13.1), respectively.

In healthy controls, median BMI and BMI z scores were 18.9 kg/m² (range, 14.6-24.6) and 0.46 (-1.58-1.61), respectively. In obese children, eNO geometric mean (95% CI) was 12.5 ppb (10.4-15.1) and did not appear significantly different from eNO levels of healthy controls [10.8 ppb (9.6-12.2); $P = .2$; 95% CI of the difference, -0.03-0.2].

No significant difference in eNO was found in obese children with a BMI z score < 2.5 or ≥ 2.5 [12.8 ppb (9.4-17.3) vs 12.3 ppb (9.7-15.8); $P = .8$; 95% CI of the difference, 0.7-1.5]. In obese children, eNO was not significantly different between boys and girls [13 ppb (10.2-16.7) vs 11.9 ppb (8.8-16.2); $P = .6$; 95% CI of the difference, 0.7-1.6], between asthmatics and nonasthmatics [11.6 ppb (7.8-17.2) vs 13.1 ppb (10.7-16.1); $P = .5$; 95% CI of the difference, 0.6-1.3], and between atopic and nonatopic subjects [12.3 ppb (9.6-15.9) vs 12.8 ppb (9.5-17.3); $P = .8$; 95% CI of the difference, 0.7-1.4], respectively (Fig 1). In the 13 children with atopic asthma, eNO was not significantly different from the remaining 37 subjects [14.8 ppb (9.3-23.5) vs 11.8 (9.7-14.5); $P = .3$; 95% CI of the difference, 0.8-1.9]. No differences in BMI were found between asthmatics and nonasthmatics [35.2 kg/m² (range, 24.1-42.1) vs 33.2 kg/m² (range, 23-54.7); $P = .6$; 95% CI of the difference, -4.8-2.6], and between atopic and nonatopic subjects [34.4 kg/m² (range, 23-54.7) vs 34.9 kg/m² (range, 25.5-42.3); $P = .6$; 95% CI of the difference, -2.7-4.8]. The BMI z score was not different between asthmatics and nonasthmatics [2.49 (range, 1.81-2.83) vs 2.52 (range, 2.05-4.08); $P = .1$; 95% CI of the difference, -0.4-0.05] and between atopic and nonatopic patients [2.53 (range, 1.81-4.08) vs 2.5 (range, 2.09-2.95); $P = .7$; 95% CI of the difference, -0.2-0.2]. In the linear regression model, none of the subject-specific variables (age, sex, BMI, BMI z score, FEV₁, atopy, and asthma) showed a significant association with eNO ($P > .05$).

In this pilot study, we found that children with moderate to severe obesity have a high prevalence of atopy, a lack of bronchodilator responsiveness, and an absence of airway inflammation. The absence of airway inflammation was confirmed even when asthma or atopy were taken into account.

There is strong evidence that obesity is an inflammatory state because adipose tissue produces proinflammatory molecules that might influence airway smooth muscle.¹ Should airway inflammation be demonstrated in obesity, it might favor asthma development.

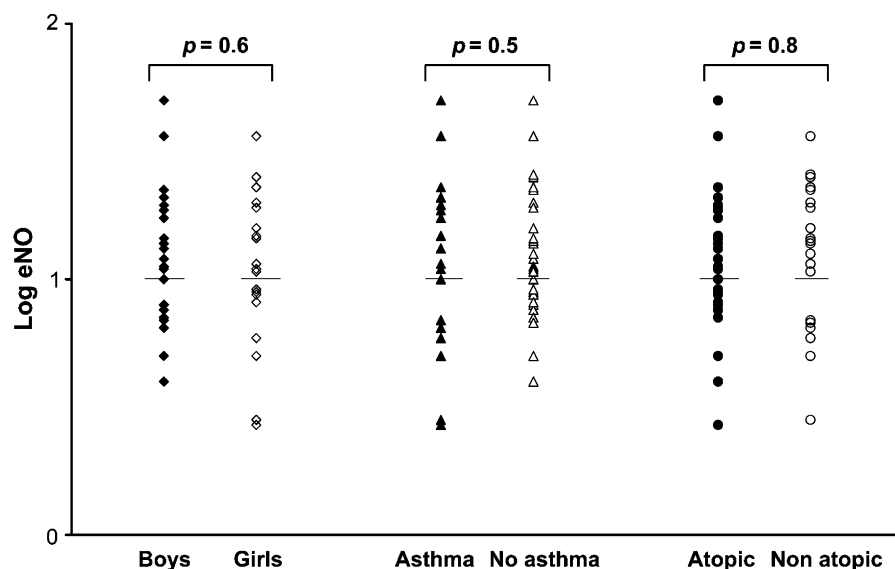


FIG 1. Log eNO in obese children. ♦, Boys. ◇, Girls. ▲, Ever asthma. △, Never asthma. ●, Atopic subjects. ○, Nonatopic subjects.

A potential association between airway inflammation and obesity is being increasingly investigated. Previous studies of obese children with asthma or healthy children have shown the absence of a significant correlation between eNO and adiposity indexes.^{4,5} Two studies of healthy adults found a positive association between eNO and BMI.^{6,7} Patients, however, were not frankly obese⁶ or had a BMI >30 only in a small proportion of cases.⁷ Among adults with asthma, normal weight/underweight subjects showed no relationship between airway inflammation and adiposity, whereas overweight or obese asthmatics had reduced eNO and increasing BMI.⁸ This finding might be explained by a selection bias because subjects were recruited from an asthma rather than an obesity clinic.⁸ Finally, in the large population-based study by McLachlan et al,² eNO did not appear associated with body fat percentage in both men and women at age 32 years.

To our knowledge, this is the first study developed to explore links among adiposity, asthma, and airway inflammation in obese children. The study population was not large. Nevertheless, the sample size required to estimate a 25% difference in eNO between cases and controls with a power of 90% and a type I error (*P*) of .05 is 38.^{9,10} The choice of 50 obese children and 50 controls took into account even missing data and subgrouping.

The major strength of the current study is in the fact that, unlike previous studies, the large majority of patients (96%) had moderate to severe obesity. All cases were recruited from the obesity unit of a large pediatric university hospital and had been not selected on the basis of allergic or respiratory symptoms. Conversely, in previous pediatric and adults studies, the proportion of obese subjects did not exceed 32% of the total.^{2,4,5,7,8}

In at least 3 studies, the population was composed by subjects selected among those with asthma rather than obesity.^{4,7,8}

Some findings from the current study deserve comments. Because atopy and eNO levels have been reported to be positively related, a lack of this association may be surprising.^{11,12} In our study, we had a fairly homogeneous distribution between obese children with positive skin test results and negative skin test results (*n* = 29, age, 12.2 years; and *n* = 21, age, 12.2 years, respectively) and did not find any difference in their eNO levels (12.3 ppb vs 12.8 ppb, respectively). Patients were not selected from an allergy clinic. Although approximately one third of them had asthma, a fairly restricted number (6 of 50) had current asthma, and none of the subjects had symptoms or signs in the 4 weeks prior to the entry into the study. In other words, our patients, who did not show airflow limitation, included only very mild asthmatics. This would further reduce the chance of abnormal eNO levels. Nevertheless, the risk of asthma seems greater in nonatopic than in atopic obese adults or children.^{13,14} This finding, combined with the lack of association between eNO and atopy found in the current study, supports the theory that the association between obesity and asthma might be linked to factors aside from atopy.

The results of this pilot study seem to indicate that eNO levels are not increased in children with moderate to severe obesity. This finding, combined with McLachlan et al's data² in adults, does not suggest a role for airway inflammation in obesity.

Pending further studies on larger groups of obese children, we suggest that factors other than airway inflammation are likely responsible for the development of asthma in obese subjects.

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Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

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doi:10.1016/j.jaci.2007.06.002