Obesity and adiposity indicators, asthma, and atopy in Puerto Rican children

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Background: Whether adiposity indicators other than body mass index (BMI) should be used in studies of childhood asthma is largely unknown. The role of atopy in "obese asthma" is also unclear.

Objectives: To examine the relationship among adiposity indicators, asthma, and atopy in Puerto Rican children, and to assess whether atopy mediates the obesity-asthma association.

Methods: In a study of Puerto Rican children with (n = 351) and without (n = 327) asthma, we measured BMI, percent of body fat, waist circumference, and waist-to-hip ratio. The outcomes studied included asthma, lung function, measures of atopy, and, among cases, indicators of asthma severity or control. We performed mediation analysis to assess the contribution of atopy to the relationship between adiposity and asthma.

Results: BMI, percent of body fat, and waist circumference were associated with increased odds of asthma. Among cases, all 3 measures were generally associated with lung function, asthma severity/control, and atopy; however, there were differences depending on the adiposity indicator analyzed. Atopy considerably mediated the adiposity-asthma association in this population: allergic rhinitis accounted for 22% to 53% of the association with asthma, and sensitization to cockroach mediated 13% to 20% of the association with forced vital capacity and 29% to 42% of the association with emergency department visits for asthma.

Conclusions: Adiposity indicators are associated with asthma, asthma severity/control, and atopy in Puerto Rican children. Atopy significantly mediates the effect of adiposity on asthma outcomes. Longitudinal studies are needed to further investigate the causal role, if any, of adiposity distribution and atopy on "obese asthma" in childhood. (J Allergy Clin Immunol 2014;133:1308-14.)

Key words: *Childhood asthma, obesity, adiposity, body mass index, percent of body fat, obesity and asthma, obesity and atopy*

Abbreviations used
BMI: Body mass index
ED/UC: Emergency department or urgent care
FVC: Forced vital capacity
PBF: Percent of body fat
STR: Skin test reactivity
WC: Waist circumference
WHR: Waist-to-hip ratio

Childhood asthma and obesity are both major public health concerns worldwide, and the prevalence of both diseases has risen markedly in the last several decades.[1-3] There is ample and growing evidence of an association between obesity and asthma, both in children and in adults.[4-8] Compared with children of normal weight, those who are overweight or obese have a greater risk of incident asthma, more severe or frequent symptoms, and a decreased response to inhaled corticosteroids.[9] While there is growing evidence for an "obese asthmatic" phenotype,[10,11] little is known about its specific characteristics.

Body mass index (BMI) has been extensively used as a proxy for overweight or obesity in epidemiologic studies of asthma. Whether other adiposity measures (eg, percent of body fat [PBF] or waist-to-hip ratio [WHR]) provide phenotypic information that differs from or adds to that obtained by measuring BMI for studies of asthma is largely unknown. This is important, because BMI alone may not adequately characterize the relationship between overweight or obesity and complex diseases such as asthma. For example, adults with "normal weight central obesity" (normal BMI but high WHR) may have the highest risk for coronary artery disease.[12]

Several plausible mechanisms have been proposed to explain the observed association between obesity and asthma, including enhanced systemic inflammation.[13] Given conflicting findings from studies of overweight or obesity (largely assessed by BMI) and atopy or atopic diseases (eg, allergic rhinitis),[14-17] the role of atopy or allergic airway inflammation in the "obese asthmatic" phenotype is currently unclear.

Puerto Ricans share a disproportionate burden of asthma and overweight/obesity.[18-20] Very few studies have examined overweight or obesity and childhood asthma in Puerto Ricans,[7,21] and none has assessed adiposity indicators other than BMI in relationship to asthma severity or control, lung function, or markers of allergic sensitization (eg, allergy skin testing).

In this report, we examine the relationship between indicators of adiposity/obesity, allergy markers, and measures of asthma severity or control (eg, lung function) in Puerto Rican children with asthma living in San Juan, Puerto Rico. We hypothesized that indicators of adiposity other than BMI would help characterize the "obese asthmatic" phenotype in Puerto Rican children,

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in whom an association between overweight or obesity and asthma severity or control could be mediated by atopy.

METHODS

Subject recruitment

A detailed description of study methods is provided in the Online Repository at www.jacionline.org. From March 2009 to June 2010, children in San Juan were chosen from randomly selected households. In brief, households in the Standard Metropolitan Area of San Juan were selected by using a multistage probability sample design.[22] Primary sampling units were randomly selected neighborhood clusters based on the 2000 US Census, and secondary sampling units were randomly selected households within primary sampling units. A household was eligible if 1 or more resident was a 6- to 14-year-old child. A total of 6401 households selected for inclusion were contacted. Of these, 1111 households had 1 or more child who met inclusion criteria other than age (4 Puerto Rican grandparents and residence in the same household for ≥1 year). Of these 1111 households, 438 (39.4%) had 1 or more eligible child with asthma (a case, defined as having physician-diagnosed asthma and wheeze in the previous year). From these 438 households, 1 child with asthma was selected (at random if there was more than 1 such child). Similarly, only 1 child without asthma (a control subject, defined as having neither physician-diagnosed asthma nor wheeze in the previous year) was randomly selected from the remaining 673 households. To reach our target sample size (~700 children), we attempted to enroll 783 of the 1111 eligible children selected for inclusion. Parents of 105 (13.4%) of these 783 children refused to participate or could not be reached, leaving 678 study participants (351 cases and 327 control subjects). There were no significant differences in age, sex, or area of residence between eligible children who did (n = 678) and did not (n = 105) agree to participate.

Study procedures

A detailed description of the study procedures is provided in the Online Repository. Study participants completed a protocol that included questionnaires on respiratory health and household characteristics, spirometry, allergy skin testing, and collection of blood and house dust samples. Dust samples were obtained from 3 areas in the home: one in which the child slept (usually his or her bedroom), living room/television room, and kitchen. The dust was sifted through a 50-mesh metal sieve, and the fine dust was reweighed, extracted, and aliquoted for analysis of allergens from dust mite (Der p 1), cockroach (*Blatella germanica* [Bla g 2]), and mouse (mouse urinary protein [Mus m 1]) by using monoclonal-antibody Multiplex array assays using the same reagents used in the established ELISA.[23] Allergen levels were analyzed as continuous (after log10-transformation), with nondetectable levels assigned a constant (half the lowest detectable value).

Measures of obesity and adiposity

BMI was calculated from weight in kilograms and height in meters. PBF was calculated from tricipital and subscapular skin folds,[24] which were obtained by trained study personnel by using calibrated calipers; the average of 3 tricipital and subscapular measurements was used for PBF calculation. All measures were transformed to z scores to obtain standardized/comparable coefficients and odds ratios, as follows: BMI z scores were calculated by using a program based on the 2000 CDC growth charts[25]; PBF z scores were calculated by using a recent study on reference equations for US children and adolescents[26]; and waist circumference (WC) and WHR were standardized by using the distribution of our study sample.

Ethics statement

Written parental consent and written assent were obtained for participating children. The study was approved by the institutional review boards of the University of Puerto Rico (SJ [Protocol no. 0160507]), Brigham and Women's Hospital (Boston, Mass [Protocol no. 2007P-001174]), and the University of Pittsburgh (Pittsburgh, Pa [Protocol no. PRO10030498]).

Statistical analysis

Our outcomes of interest included asthma (defined as above), lung function measures (FEV_1, forced vital capacity [FVC], and FEV_1/FVC), allergic rhinitis (defined as current naso-ocular symptoms apart from colds and at least 1 positive skin test result to allergens), allergy markers (skin test reactivity [STR] to allergens and serum total IgE), and other indicators of asthma severity or control, as follows: (1) number of days on oral or intravenous steroids in the previous year (categorized as 0, 1-8, 9-40, and over 40); (2) missed school days because of asthma in the previous year (categorized as 0, 1-2, 3-5, or at least 6); (3) exercise-induced symptoms in the previous year (categorized as never, occasionally, frequently, or always); and (4) number of visits to the emergency department for asthma, ever.

Bivariate analyses were conducted by using Fisher exact tests for binary variables and 2-tailed t tests for pairs of binary and continuous variables. Linear or logistic regression was used to examine the relationship between each adiposity/obesity indicator and the outcomes of interest, while adjusting for potential confounders. All multivariate models included age, sex, household income (<vs ≥ $15,000/year [the median household income for Puerto Rico in 2008-2009[27]]), parental (maternal or paternal) history of asthma, and percentage of African racial ancestry (determined by using genome-wide genotypic data[28]; see Online Repository at www.jacionline.org). All analyses of FEV_1 and FVC were additionally adjusted for height and height squared, and analyses of STR were additionally adjusted for levels of indoor allergens (see Online Repository for details).

We performed mediation analysis to assess whether part or all of the association between adiposity indicators (eg, BMI) and outcomes of interest (eg, FEV_1) is explained by atopy via a mediated or "indirect effect" (see Online Repository for details). This analysis was performed via structural equation modeling for continuous and ordinal data, and by using the Karlson-Holm-Breen decomposition method[29] for binary outcomes, which adjusts for the rescaling issues that arise from cross-model comparison of nonlinear models.[30,31] Mediation analysis was performed only on measures of atopy (ie, allergic rhinitis, STR to cockroach) that were associated with both the adiposity indicators and the asthma outcomes. Other indicators of atopy (eg, total IgE) did not meet this criterion and were thus not included in the mediation analysis. All statistical analyses were performed by using SAS statistical software, version 9.3 (SAS Institute; Cary, NC), with the exception of the mediation analysis (which was conducted by using Stata 12.1 [StataCorp; College Station, Tex]).

RESULTS

The characteristics of the 678 study participants are shown in Table I. BMI was significantly associated with increased odds of asthma after adjusting for covariates. PBF and WC were also associated with asthma, but these associations only approached significance ($P = .06$ and $P = .08$, respectively) (Table II). As expected, all 4 obesity/adiposity measurements were significantly correlated with each other ($P < .0001$), although the degree of correlation and the slope of the regression coefficient varied (Fig 1).

Table II shows the results of the multivariate analysis of each measure of obesity/adiposity and indicators of asthma severity or control in children with asthma (n = 351). In this analysis, each 1.0 z-score increment in BMI was significantly associated with an approximately 69 mL higher FEV_1. All adiposity measures were positively associated with FVC, ranging from an approximately 50-mL increment per each z score in WHR to an approximately 98-mL increment per z-score increment in BMI, with intermediate results obtained for PBF and WC. Of the 4 adiposity measures, only WC was significantly associated with a decrement in FEV_1/FVC. All adiposity measures except WHR were associated with increased lifetime emergency department or urgent care (ED/UC) visits for asthma, ranging from approximately 3 additional ED/UC visits per each z-score increment in BMI to approximately 4.6 additional ED/UC visits