Sex Differences in the Relationship between Fitness and Obesity on Risk for Asthma in Adolescents

Kim D. Lu, MD[1], John Billimek, PhD[2], Ronen Bar-Yoseph, MD[1], Shlomit Radom-Aizik, PhD[1], Dan M. Cooper, MD[1], and Hoda Anton-Culver, PhD[3]

Objective To evaluate the relationship of fitness and obesity on asthma risk in adolescent girls and boys.

Study design A cross-sectional assessment of participants 12-19 years of age was conducted by the use of data from the 1999-2004 National Health and Nutrition Examination Survey. Participants completed cardiorespiratory fitness testing, body composition measurements, and respiratory questionnaires.

Results A total of 4828 participants were included. Overweight/obesity was associated with increased odds of history of asthma (aOR 1.63, 95% CI 1.16-2.30), current asthma (aOR 1.73, 95% CI 1.13, 2.64), and wheezing (aOR 1.40, 95% CI 1.03-1.91) in girls. Overweight/obesity also was associated with increased odds of asthma attacks (aOR 2.67, 95% CI 1.56-4.65) and wheezing related to exercise (aOR 1.60, 95% CI 1.07-2.38) in girls. High fitness was associated with lower odds of asthma-related visits to the emergency department (aOR 0.24, 95% CI 0.07-0.89), wheezing-related medical visits (aOR 0.31, 95% CI 0.13-0.75), wheezing-related missed days (aOR 0.14, 95% CI 0.06-0.33), and wheezing related to exercise (aOR 0.43, 95% CI 0.24-0.76) in boys.

Conclusion Overweight/obesity is associated with increased asthma prevalence and morbidity in girls but not in boys, independent of fitness. High fitness is associated with decreased rates of asthma morbidity in boys but not in girls, independent of weight status. Obesity and fitness may each influence asthma onset and severity in different ways for girls compared with boys. *(J Pediatr 2016;176:36-42)*.

Asthma is one of the most common chronic illnesses of childhood, and prevalence rates have increased in the US during the past few decades despite advances in management, therapies, and knowledge.[1] During this same time period, the prevalence of obesity and overweight has almost tripled, with an estimated 17% of children affected.[2] A growing body of literature suggests that there is an association between these 2 disorders, with obesity negatively influencing asthma risk and health[3-6]; however, the mechanism(s) are unknown, hindering our ability to treat these patients. Recent literature suggests that obesity-related asthma may represent a distinct phenotype and is becoming a major public health issue in the US.[7-9]

The relationship between sex and asthma depends on age, with boys being more affected with asthma during childhood and girls being more affected with asthma during adolescence and adulthood.[10-13] A few investigators have examined whether the asthma-obesity association differs between sexes; however, the results have been mixed.[14-16]

Significant reductions in physical activity leading to decreased aerobic fitness have occurred during the same period in which rates of obesity and asthma have dramatically increased.[17,18] There are also significant sex differences in fitness, particularly during adolescence.[19] Decreased aerobic fitness and physical activity are known to be associated with obesity and asthma separately.[17,20-23] The combination of obesity and reduced physical activity, each of which can stimulate inflammation, can lead to a vicious cycle in the obese child with asthma. Few studies, however, have tried to adequately evaluate how fitness influences the relationship between obesity and asthma risk and morbidity.[24]

The objective of this study was to evaluate the relationship of obesity and fitness on asthma risk in adolescent girls and boys by the use of a nationwide sample in the US. Understanding the role of fitness in the link between obesity and asthma prevalence and morbidity, particularly in pediatric populations, provides valuable knowledge that could translate into specific interventions.

Methods

The National Health and Nutrition Examination Survey (NHANES) is an ongoing nationally representative survey conducted to assess the health and

BMI	Body mass index
ED	Emergency department
NHANES	National Health and Nutrition Examination Survey
RR	Relative risk
$\dot{V}O_2$ max	Maximal oxygen consumption

From the [1]Department of Pediatrics and Pediatric Exercise and Genomics Research Center, [2]Health Policy Research Institute and Division of General Internal Medicine, School of Medicine, and [3]Department of Epidemiology, University of California, Irvine, CA

Supported by National Institutes of Health (P01HD-048721), Children's Hospital of Orange County, and University of California, Irvine Child Health Research Grant. The authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2016.05.050

nutritional status of adults and children in the US. NHANES uses a stratified multistage probability sample design.

The NHANES is composed of household interview and mobile examination center tests. A detailed description of the study design and methodology for NHANES can be found on the NHANES Web site.[25] The NHANES oversamples adolescents, ages 12-19 years, and low-income, African-American and Mexican American populations. The study protocols were approved by the National Health Statistics institutional review board. All participants (or their parents/guardians) gave written informed consent.

This report used NHANES datasets from 1999-2000, 2001-2002, and 2003-2004. Cardiorespiratory fitness testing was completed in participants 12 years and older (n = 4997) during the mobile examination center examinations. We included participants who had complete data on asthma prevalence, body composition, and cardiorespiratory fitness testing (n = 4828). Underweight participants were excluded from analyses involving models because they were too few in number (n = 135).

Those who did not complete cardiorespiratory fitness testing were excluded (n = 1198). Participants at increased risk for complications from exercise or with conditions that might affect the tests results were excluded from fitness testing, including participants with asthma with 12 or more wheezing episodes per year or any wheezing episodes associated with speech limitations.

Asthma Outcomes

All participants were asked (by proxy if younger than 16 years of age) whether a doctor or other health professional had ever said they had asthma. Those who answered "yes" were asked a series of additional questions, including whether they currently have asthma, whether they had experienced an asthma attack in the past year, and whether they had been to the emergency department (ED) for asthma in the past year. The primary outcomes for these analyses are a report of a history of asthma and current asthma. Additional questions related to asthma attacks and asthma-related ED visits in the past 12 months were asked.

A separate set of questions were asked about wheezing. Wheeze outcomes used in these analyses include a report of wheeze in the past year (yes/no), medical visit for wheeze in the past year (yes/no), missing school or work due to wheeze in the past year (yes/no), and wheezing related to exercise (yes/no).

Weight Measurements

Participants had their weight and height measured following a standard protocol. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Sex-specific BMI percentile-for-age was calculated by use of the 2000 reference standards from the Centers for Disease Control and Prevention.[26] Children between the 5th to less than the 85th percentile of BMI-for-age were considered to be normal weight, those between the 85th to less than the 95th percentile were considered overweight, and those at or above the 95th percentile were considered obese.

Cardiorespiratory Fitness Testing

Cardiorespiratory fitness was assessed by a submaximal treadmill exercise test. Participants were assigned to 1 of 8 treadmill test protocols on the basis of their expected maximal oxygen consumption ($\dot{V}O_2$) max, which was predicted from sex, age, BMI, and self-reported level of physical activity by use of the formula developed by Jackson et al.[27] Each protocol included a 2-minute warm-up, two 3-minute exercise stages, and a 2-minute cool-down period. The goal of each protocol was to elicit a heart rate that was approximately 75% of the age-predicted maximum (220 − age) by the end of the second exercise stage.

The heart rate was monitored continuously via 4 electrodes connected to the trunk and the abdomen of the participant and was recorded at the end of warm-up, each exercise stage, and each minute of recovery. Blood pressure was measured at the end of each stage by the use of an STBP-780 automated sphygmomanometer (Colin Medical Instruments Corporation, San Antonio, Texas). $\dot{V}O_2$ max (mL/kg per min) was estimated by extrapolation to an expected age-specific maximal heart rate by using measured heart rate responses to the two 3-minute exercise stages. This assumes that the relationship between heart rate and oxygen consumption is linear during treadmill exercise. Cardiorespiratory fitness levels were grouped into tertiles by sex.

Statistical Analyses

Participant characteristics were compared between sexes with the use of independent sample *t* tests for continuous variables and the Pearson χ^2 test for categorical variables. The sex-specific associations of BMI and fitness with asthma prevalence and morbidity were examined in a series of logistic regression models, stratified by sex. Asthma prevalence and morbidity were first compared across BMI categories and fitness tertiles in bivariate analyses. In final models, BMI and fitness were combined to allow for comparisons between overweight/obese vs normal-weight groups and low-to-moderate vs high-fitness groups. Multivariate models were adjusted for age, survey year, poverty index ratio, second-hand smoke exposure, and race/ethnicity. Models that used fitness as the dependent variable were adjusted for BMI categories. Models that used BMI as the dependent variable were adjusted for fitness.

Sex by BMI and sex by fitness interactions were tested for each outcome. BMI by fitness interactions also were tested for each outcome. Cardiorespiratory fitness was examined as a continuous variable (z score) for boys and girls. The sex-specific associations of fitness as a continuous variable with asthma prevalence and morbidity were examined in a series of logistic regression models, stratified by sex. Adjustments for multiple comparisons (8 outcomes) were made by controlling for the false discovery rate via the Benjamini-Hochberg procedure.[28] All analyses accounted for weighted data design of NHANES and were performed with SAS