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Overweight children report qualitatively distinct asthma symptoms: Analysis of validated symptom measures

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Abstract

Background—Past studies of asthma in overweight/obese children have been inconsistent. The reason overweight/obese children commonly report worse asthma control remains unclear.

Objective: To determine qualitative differences in symptoms between lean and overweight/obese children with early-onset, atopic asthma.

Methods—We conducted a cross-sectional analytic study of lean (20% to 65% body mass index) and overweight/obese (≥85% body mass index) 10- to 17-year-old children with persistent, early-onset asthma. Participants completed 2 to 3 visits to provide a complete history, qualitative and quantitative asthma symptom characterization, and lung function testing. We determined associations between weight status and symptoms using multivariable linear and logistic regression methods.

Results—Overweight/obese and lean asthmatic children displayed similar lung function. Despite lower fraction of exhaled nitric oxide (30.0 vs 62.6 ppb; $P = .037$) and reduced methacholine responsiveness ($PC_{20}FEV_1$ 1.87 vs 0.45 mg/mL; $P < .012$), overweight/obese children reported more than thrice frequent rescue treatments (3.7 vs 1.1 treatments/wk; $P = .0002$) than did lean children. Weight status affected the child's primary symptom reported with loss of asthma control (Fisher exact test; $P = .003$); overweight/obese children more often reported shortness of breath (odds ratio = 11.8; 95% CI, 1.41–98.7) and less often reported cough (odds ratio = 0.26; 95% CI, 0.08–0.82). Gastroesophageal reflux scores were higher in overweight/obese children (9.6 vs 23.2; $P = .003$) and appear to mediate overweight/obesity-related asthma symptoms.

Conclusions—Overweight/obese children with early-onset asthma display poorer asthma control and a distinct pattern of symptoms. Greater shortness of breath and β -agonist use appears to be partially mediated via esophageal reflux symptoms. Overweight children with asthma may falsely attribute exertional dyspnea and esophageal reflux to asthma, leading to excess rescue medication use. (*J Allergy Clin Immunol* 2015;135:886–93.)

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Keywords

Asthma; overweight; obesity; children; dyspnea; breathlessness; shortness of breath; esophageal reflux

The relationship between overweight/obesity and asthma phenotype in children remains inadequately defined. Several large epidemiologic studies have demonstrated that obesity increases the risk of physician-diagnosed asthma^{1,2} and is associated with greater asthma-related health utilization^{3,4} and asthma that is more problematic and difficult to control.^{3,5–7} The underlying mechanisms for these associations have proven elusive, and to date little evidence supports obesity worsening asthma through the classic mechanisms of enhanced allergic airway inflammation⁸ or airway reactivity.^{8,9} In addition, extensive phenotyping has not confirmed the finding that obesity worsens asthma in all cohorts.^{10–13} This apparent discrepancy regarding the impact of obesity suggests that more in-depth and novel assessments of lean and obese asthmatic children may be required. Specifically, few studies have addressed how obese patients perceive and report asthma symptoms. A greater qualitative understanding of asthma—how it is perceived and reported—may provide an explanation for current discrepancies in the literature on obesity and asthma.

There are several biologically plausible explanations proposed for the link between obesity and greater asthma severity. These include obesity-related comorbidities (eg, depression or gastroesophageal reflux disease [GERD]), restrictive lung physiology, altered airway perception, and exertional dyspnea erroneously attributed to asthma. In addition, asthmatic patients may be at risk for excess weight gain due to concerns about exercise-induced symptoms.^{14,15} Defining asthma severity in a precise manner can be difficult because it relies on patient-reported subjective symptoms and on self-administered short-acting β -agonist (SABA) use. Symptoms common to asthma can also stem from nonasthma causes and can complicate the assessment of severity.¹³ Families often report being confused about self-management and when to administer SABA medications,^{16,17} further challenging the assessment of severity based on SABA use. Therefore, an important public health question for policymakers and clinicians alike is whether obese asthmatic patients are more likely to attribute nonspecific symptoms (eg, breathlessness or digestive symptoms) mistakenly to asthma instead of factors common to obesity, such as increased workload and oxygen demands, GERD, depression/anxiety, and respiratory muscle fatigue. If this attribution error is common, it would explain past findings of excess symptoms and health care utilization among the obese and would suggest that obese asthmatic children are at risk for excessive SABA use, unwarranted controller therapy escalation, and steroid-related side effects.

However, obese children with asthma may sense asthma differently. Heterogeneity in the perception and reporting of asthma exists within the population,^{18,19} as is noted by the example that “poor perceivers” are at an increased risk for near-fatal asthma events. We previously showed that obese children with mild asthma have greater perception of day-to-day variation in lung function.²⁰ This would suggest that obese asthmatic children may have altered sensory perception of airflow limitation and would explain the greater symptoms reported in obese children. Interestingly, Sah et al¹³ reported that among children

with more severe asthma, obesity was associated with an enhanced perception of nonspecific symptoms. Several governing institutes that support asthma research have called for additional studies comparing qualitative symptoms with existing composite scores to better understand asthma control and standardize its measurement.²¹

Objective composite measures of asthma control, quality of life, and symptoms developed by Juniper,²² Juniper et al,^{23,24} and others^{25–27} include both qualitative and quantitative components. These measures have symptom domains that vary in their specificity to asthma. If obesity worsens the underlying mechanisms of asthma, then qualitative analysis of symptom patterns between lean and obese asthmatic subjects would be expected to be similar. Instead, if obesity increases nonspecific respiratory symptoms and health care utilization via altered sensory-perceptual or emotional-affective factors,²⁸ then qualitative symptom patterns would be expected to vary substantially between lean and obese asthmatic children. For example, though obese children report greater worsening of composite symptom scores with changes in peak flows,²⁰ it is not clear specifically what symptoms drive the worsening in asthma control in obese children. If these factors are not better understood, improvements in self-management and health care utilization among the growing number of obese asthmatic subjects may remain difficult. Using directed interviews and validated asthma symptom questionnaires, we sought to define how overweight/obese status affected the pattern and severity of asthma symptoms in children.

METHODS

Participant selection

Children aged between 10 and 17 years with asthma, receiving daily controller therapy, and fitting the age- and sex-adjusted body mass index (BMI) parameters for lean (20–65th percentile) and overweight/obese (BMI ≥ 85th percentile) were enrolled through the Nemours multispecialty pediatric asthma clinic in Jacksonville, Florida. We used common BMI-percentile conventions for overweight/obesity^{29,30} and selected from a narrower BMI-percentile range among normal-weight individuals to avoid misclassification. Asthma was defined by accepted convention: physician-diagnosis of asthma and either a 12% or more improvement in FEV₁ after bronchodilation or a PC₂₀FEV₁ value of 16 mg/mL or less.^{31,32} Participants were excluded if they had any smoking history, been on controller daily oral steroids, had a change in controller therapy in the previous 8 weeks, had any interval illness in the past 4 weeks, or had another significant chronic disease.

Clinical data

Two to 3 clinic visits within 3 weeks were conducted, with no 2 visits occurring on successive days. At visit 1, participants signed an institutional review board–approved parental permission form and minor assent. Participants completed staff-directed, structured interviews and questionnaires providing asthma and medical history, family and environmental history, quality-of-life information, and a comprehensive interview of asthma symptoms, controller treatment, and past health care utilization. Each participant's controller step prescribed by his or her asthma physician was determined.³³ Participants underwent a physical examination, anthropometric measurements, and spirometry (before and after the

administration of a bronchodilator). Highest parental education level, median household incomes, and poverty index (percentage below the poverty level) were determined for each patient's household. Participants completed a methacholine challenge test and exhaled nitric oxide (fraction of exhaled nitric oxide [Feno]) at visits 2 and 3, respectively, adhering to recommended guidelines.^{34,35}

Symptom and quality-of-life analyses

Participants and parents answered structured interview questions regarding symptom patterns, common asthma triggers, and the primary symptom experienced with loss of control. The structured interviews also documented asthma symptom frequency and severity, digestive symptoms, and sleep characteristics. Asthma symptom control was assessed at visit 1 using multiple questionnaires (Asthma Control Questionnaire,²³ Asthma Control Test [ACT],^{26,36} and childhood ACT³⁷) to measure the broad array of symptoms that asthmatic children experience and report (see Table E1 in this article's Online Repository at www.jacionline.org). Symptoms were measured using the Asthma Symptom Utility Index (ASUI).²⁷

Asthma-related quality of life was measured using the Paediatric Asthma Quality of Life Questionnaire (PAQLQ)^{24,38} and the Paediatric Asthma Caregiver Asthma Quality of Life Questionnaire.³⁹ Properties of asthma control scores, symptom scores, and asthma quality-of-life scores can be found in this article's Online Repository at www.jacionline.org.

Digestive symptoms

Digestive symptoms were measured using the Pediatric Gastroesophageal Reflux Disease Symptom Assessment Questionnaire, which is a 10-item tool⁴⁰ that has been validated in children in the assessment of GERD and digestive symptoms such as chest/abdominal pain, pain/choking with eating, swallowing dysfunction, regurgitation, and nausea. It assesses symptom severity from the previous 7 days on an 8-point scale, with 0 and 7 indicating the least and greatest severity, respectively.

Lung function testing

Participants completed spirometry (Jaeger MasterScreen, San Diego, Calif) adhering to recommended American Thoracic Society standards.^{41,42} Participants also completed Feno (Sievers 280 NOA analyzer, Boulder, Colo) maneuvers according to recommended standards.⁴³ Participants completed a methacholine challenge by experienced staff using the 10 Provacholine concentrations dosing scheme with a 5-breath dosimeter protocol.³⁴

Statistical analysis

Study variables were summarized by BMI group (lean and overweight/ obese). Quantitative variables were summarized using mean, SD, and number of subjects, while categorical variables were summarized by number of subjects and percentages. The χ^2 test (or the Fisher exact test) was used for comparing categorical variables between groups, while the Student *t* test or the Wilcoxon-Mann-Whitney *U* test (whichever was appropriate) was used to compare quantitative variables between BMI groups. Analyses of covariances were used to detect the effect of BMI status on various asthma symptom control measures. *A priori*

variables used in the model included age, race, ethnicity, sex, and atopy status, along with influential variables found in simple linear regression. Assumptions were checked before using a model, and appropriate steps were taken in case of any violation of assumptions. All tests were 2-tailed at a level of significance of .05. The statistical packages SAS, version 9.1.2 (SAS Institute Inc, Cary, NC), was used.

RESULTS

Characteristics of lean and overweight/obese participants

A total of 74 children and families were screened for eligibility. Fifty-eight children were enrolled, and 96% conducted all 3 clinic visits. Baseline characteristics of lean and overweight/obese participants completing the study ($n = 56$) are given in Table I. Anthropometric measures were significantly greater in the overweight/obese group. Overweight/obesity status was not associated with age, sex, race, ethnicity, parental education received, measures of socioeconomic status, exposure to secondhand tobacco smoke, or *in utero* maternal smoke exposure (data not shown). The overweight/obese group had a lower mean gestational age and higher weight at birth though neither reached statistical significance.

Overweight/obese children with asthma experienced significantly different sleep and digestive symptoms than did lean children (Table I). Among overweight/obese children, 41% reported GERD symptoms at enrollment. Overweight/obese children had significantly higher total GERD scores (9.6 vs 23.2; $P = .003$) and displayed higher frequency and severity in all GERD assessment domains. Nighttime snoring was a common complaint in the overweight/obese group, though there was no significant difference in reported obstructive sleep apnea, sleep disturbances, or duration. The prevalence of sinopulmonary infections, allergic diseases, or psychiatric conditions was not different between BMI groups.

Lung function and airway measures

Baseline spirometry and changes after the administration of a bronchodilator were similar between lean and overweight/obese asthmatic children (Table II). Both BMI groups displayed clinically significant airway hyperresponsiveness measured by methacholine challenge; however, lean children had a significantly lower median $PC_{20}FEV_1$. The overweight/obese group had a significantly lower mean Feno level than did lean children.

Treatment burden and health care utilization

Median controller treatment step was not significantly different between BMI groups (Fig 1), and groups had similar prevalences of inhaled corticosteroid–long-acting β -agonist combination therapy and leukotriene receptor antagonist medication use (data not shown). In addition, health care utilization defined by reported unscheduled clinic visits (including emergency room visits), hospitalizations, and intensive care utilization was similar between groups (data not shown). Despite these similarities, overweight/obese children reported more than 3 times rescue bronchodilator use per week (3.7 vs 1.1, $P = .0002$) (Fig 1).

Primary patient-identified triggers, symptoms, and activity impairment

Roughly two-thirds of all children reported that allergies, viruses, and exercise all were common triggers of asthma symptoms. Just over 50% of all children reported that tobacco smoke was a common trigger. Overweight/obesity status did not affect the prevalence of common triggers (Fisher exact test; $P > .382$ for all). Overweight/obese children also reported similar activities that were most impaired by uncontrolled symptoms (data not shown). However, lean and overweight/obese children reported significantly different patterns of primary symptom seen with loss of asthma control (Table III). Overweight/obese children were more likely to identify shortness of breath (odds ratio = 11.8; 95% CI, 1.41–98.7) and less likely to identify cough (odds ratio = 0.26; 95% CI, 0.08–0.82) than were lean children as the primary symptoms with loss of control.

Symptom characterization in lean and overweight/ obese children

Overweight/obese children reported significantly worse asthma symptoms using the composite 6-item Asthma Control Questionnaire without the FEV₁ component (ACQ6), ASUI, ACT, and childhood ACT (Table IV). In all 4 questionnaires, overweight/obesity significantly negatively affected both the shortness-of-breath and short-acting rescue medication frequency subscales. None of the subscales relating to cough or nocturnal symptoms was affected by overweight/obesity. Overweight/obese children experienced lower asthma-related quality of life that was clinically and statistically significant than did lean children (Table V). The subdomains (Symptom, Activity, and Emotional) within the PAQLQ each showed a lower mean value (indicating reduced quality of life) among overweight/obese children. When similar asthma-related quality-of-life symptom questions were asked of caregivers using the Paediatric Asthma Caregiver Quality of Life Questionnaire, no overweight/obesity effect was present (Table V). The only mean difference reported among caregivers of overweight/obese children was a greater worry about medication side effects (Wilcoxon test; $P = .026$).

Impact of covariables

The effect of obesity was analyzed after adjusting for covariables associated with obesity. In each analysis that accounted for the GERD score in the model, we found that the effect of obesity on asthma control (ACQ6) was eliminated (Table VI). These results were further validated when ASUI, ACT, and childhood ACT were used as the dependent variable in the model.

DISCUSSION

This study showed that overweight/obese children with early-onset, persistent asthma reported symptoms that were clinically and statistically worse than those reported by similar lean participants. We found that the worse asthma among overweight/obese children consistently involved the report of shortness of breath and greater SABA use and was not driven by greater cough or nighttime awakenings. Lean and overweight/obese children reported substantively different primary symptoms with the onset of loss of asthma control, with overweight/obese children more often reporting shortness of breath and less often reporting cough. Overweight/obese children had clinically and statistically greater

gastrointestinal symptoms reported by GERD score. Although BMI affected asthma symptoms when reported by children, similar BMI differences in asthma control were not seen when reported by caregivers. When GERD symptoms were assessed in multivariable modeling, we found that asthma symptom differences between lean and overweight/obese children were abolished. These data suggest that overweight/obese children with asthma on average experience and report asthma differently than do lean children and that the greater obesity-related poor asthma control is driven to a large extent by shortness of breath and self-medication with SABAs. These excess symptoms may not stem technically from asthma but rather from obesity-related sequelae such as GERD, chest restriction, or excess demand on the respiratory system. Instead of obesity-related GERD and chest restriction *mediating* worse asthma, these processes may cause dyspnea, which is confused for asthma and leads to worse patient-reported asthma control scores.

Both BMI groups were similar by most important demographic and individual characteristics. Exceptions included significantly greater body circumferences, waist-to-height ratio, and GERD prevalence. Weight status did not affect baseline spirometry or bronchodilator changes, while overweight/obese children displayed reduced eosinophilic airway inflammation measured by Feno and airway responsiveness measured by methacholine PC₂₀FEV₁. Most of the overweight/obese patients reported that environmental allergies triggered their asthma. Despite a similar prevalence of allergy triggering, lean patients had significantly higher (>2×) Feno levels, which likely reflects more allergic airway inflammation. Both BMI groups had low PC₂₀ FEV₁ values, suggesting significant hyperresponsiveness; however, the median methacholine concentration in overweight/obese children was more than 4 times the concentration in lean children, suggesting a substantial difference in airway responsiveness. Excess T_H1 mechanisms that have been associated with obesity^{44,45} may serve to ameliorate allergic airway inflammation, resulting in both lower Feno and reduced airway hyperresponsiveness.

We found that the dose of daily inhaled steroid, prevalence of inhaled corticosteroid–long-acting β -agonist combination therapy, prevalence of leukotriene modifiers, and final controller step were similar in both groups. Despite similar controller therapy and significantly reduced airway reactivity, the overweight/obese patients reported self-administered SABA at more than 3 times the rate reported by lean children. Even with greater SABA use, overweight/obese patients did not report greater recent hospitalizations or urgent care. When overweight/obese patients lost asthma control, they were significantly more likely to report shortness of breath and less likely to report cough. Sah et al¹³ recently reported greater shortness of breath and nocturnal cough among obese children with severe asthma. The primary symptom tool used was the ACQ6,^{20,46,47} which showed a clinically meaningful difference between lean and overweight/obese children (0.68 vs 1.26; $P = .021$). The minimally important difference (MID) for the ACQ6 is near 0.5.⁴⁸ Differences between the BMI groups also exceeded the MID for the ASUI (MID = 0.15)³¹ and the ACT (MID = 3).³⁷

Across multiple assessments, overweight/obese children had worse asthma control due primarily to dyspnea and need for rescue medication use, while none of the 4 validated questionnaires found overweight/obese children to have greater nocturnal symptoms, in

contrast to Sah et al's¹³ recent findings. This is important because asthma-related sleep disturbance is of major emphasis in current management guidelines.^{49,50} Cough, which is a well-understood and recognizable symptom for families (as opposed to the concept of "wheeze"), was not reported differently between lean and overweight/obese children. We noted that overweight/obese status was significantly associated with worse asthma-related quality of life when symptoms were reported directly by the child (PAQLQ), while a BMI-related difference was not seen when symptoms for the same children were reported by the caregiver (Paediatric Asthma Caregiver Quality of Life Questionnaire). We speculate that because overweight/obese effect is driven primarily by dyspnea and not cough, caregivers may not fully appreciate their child's symptoms. Alternatively, caregivers of obese children may not attribute the excess impairment—primarily dyspnea and SABA use—to asthma.

Multivariable models that included *a priori* demographic variables and influential independent variables suggest that the GERD score is an independent predictor of asthma control in overweight/obese children. The GERD score was a significant independent factor in ASUI, ACQ6, and PAQLQ ($P < .001$ for each). When demographic and significant covariables were included in the multivariable model, the effects of overweight/obesity on symptom control and quality of life were eliminated. These findings are consistent with the obesity effect on asthma being mediated through GERD.^{51,52} However, this explanation seems unlikely because GERD-induced asthma would also be expected to induce greater cough and airway reactivity,⁵³ which was not seen. GERD could induce esophageal symptoms interpreted by the patient as shortness of breath and mistakenly attributed to asthma. It has been proposed that dyspnea may stem from repeated respiratory afferent signals to the cerebral cortex, eliciting a repeated sensation/awareness of conscious breathing.⁵⁴ Respiratory sensations are the result of neural gating into the cerebral cortex of respiratory afferent input, eliciting a cognitive awareness of breathing and an affective response.⁵⁵ If true, repeated esophageal stimulation (from obesity-related GERD) and subsequent neurally mediated tachykinin signaling in the airway⁵⁶ could provide this repeated afferent signal and explain the excess dyspnea in our obese patients with GERD. However, because of the cross-sectional nature of this study, we cannot determine whether GERD mediates the association between obesity and dyspnea. Future studies that measure esophageal stimulation and subsequent airway and sensory responses may prove insightful.

The recent American Thoracic Society statement on dyspnea describes its complex nature, which includes various qualitatively distinct sensations and affective distress.²⁸ These distinct sensations likely arise from distinct sensory mechanisms. Dyspnea upon exertion is typically the most prominent symptom reported with obesity^{57,58} and restrictive lung diseases.⁵⁹ Data mainly from adults show that obesity negatively affects respiratory system resistance^{60,61} and compliance,⁶² expiratory flows⁶³ and reserve volume,⁶⁴ static inspiratory strength,⁶⁵ A-a gradient,⁶⁶ and oxygen cost of breathing.^{67,68} Obese adults have greater muscle metabolic requirements,⁶⁹ greater ventilatory chemoreflex responsiveness,⁷⁰ and greater neural respiratory motor drive,⁷¹ which is sure to be relevant in our present approach to assessing asthma severity among obese asthmatic subjects. Dyspnea (which is common in active asthma) can also result from deconditioning and simple obesity. Therefore, a sufferer of both obesity and asthma may not always know the source of breathlessness and may mistake exertional breathlessness for loss of asthma control. We speculate that much of the

problematic nature of asthma among obese children with early-onset, allergic asthma stems in part from heightened airflow perception (ie, sensory-perceptual experience) and altered affective distress with GERD, leading to a sensation of breathlessness.²⁸ A recent trial in children with pH probe–confirmed GERD and poor asthma control did not find improved asthma outcomes with pharmacologic acid–suppression.³¹ Lack of asthma improvement with acid suppression suggests that if GERD is important in creating breathlessness, the refluxate pH is not an important factor. Interestingly, SABA use, which was markedly greater in our overweight/obese group, has been shown to reduce lower esophageal sphincter tone,⁷² which is consistent with the pattern of symptoms seen in our overweight/obese cohort and would be consistent with a cycle of GERD, chest symptoms, and more SABA use.

Because dyspnea from asthma is a major driver of anxiety, reduced quality of life, health care utilization, and medication use, a greater understanding of the distinct sensory mechanisms of dyspnea is needed. Until systematic weight loss interventions become more feasible, respiratory physicians may serve their patients better by considering and discussing alternative causes of dyspnea in self-management plans and discussing when SABA use is warranted for obese patients with asthma.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations used

ACQ6	6-Item Asthma Control Questionnaire without the FEV ₁ component
ACT	Asthma Control Test
ASUI	Asthma Symptom Utility Index
BMI	Body mass index
Feno	Fraction of exhaled nitric oxide
GERD	Gastroesophageal reflux disease
MID	Minimally important difference
PAQLQ	Pediatric Asthma Quality of Life Questionnaire
SABA	Short-acting β -agonist

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Clinical implications

Overweight/obese asthmatic children with excess dyspnea and rescue medication use, in the absence of specific asthma symptoms, may require weight loss to improve esophageal reflux and asthma-related symptoms and utilization.

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FIG. 1.

Controller and rescue treatment burden in normal and overweight/obese children with asthma. *Black bars* represent the median National Asthma Education and Prevention Program controller step prescribed by the treating asthma physician at the time of study enrollment. The median (interquartile range) for normal weight and overweight/obese children was 3 (2, 4) and 3 (3, 4), respectively (Wilcoxon test; $P = .986$). *Gray bars* represent the number of rescue treatments required (excluding exercise pretreatment) per week over the month before enrollment. The mean (SE) number of rescue treatments needed to manage asthma symptoms for normal weight and overweight/obese children was 1.1 (0.3) and 3.7 (0.6), respectively; # $P = .0002$, Student t test, for normal vs overweight/obese.

TABLE I

Characteristics of normal weight and overweight/obese asthmatic patients

Characteristic	n	BMI 20–65th	BMI > 85th	P value*
n		21	35	
Age (y)	56	12.8 ± 2.5	12.5 ± 2.2	.585
Male	56	14 (67)	20 (57)	.577
Race	56			.367*
White		12 (57)	14 (40)	
Black		8 (38)	20 (40)	
Other		1 (5)	1 (3)	
Hispanic/Latino	56	2 (10)	3 (9)	1.0*
Birth weight (kg)	56	3.17 ± 0.46	3.41 ± 0.60	.114
Age at asthma diagnosis (y)	56	4.0 ± 3.7	5.0 ± 4.1	.376
Gestational age at birth (wk)	56	39.0 ± 1.9	37.6 ± 4.1	.105
Anthropometric measures	56			
BMI-percentile		50.4 ± 12.5	95.6 ± 3.1	<.0001
Waist circumference (cm)		63.8 ± 11.3	87.1 ± 14.2	<.0001
Waist-to-height ratio		0.414 ± 0.07	0.557 ± 0.08	<.0001
Neck circumference (cm)		29.5 ± 4.5	33.6 ± 5.8	.007
Neck-to-height ratio		0.191 ± 0.03	0.215 ± 0.03	.012
Abdominal circumference (cm)		66.2 ± 11.8	90.5 ± 14.8	<.0001
Abdomen-to-height ratio		0.429 ± 0.07	0.577 ± 0.08	<.0001
First-degree relative with				
Atopy [†]	56	v	28 (80)	.727
Asthma	56	13 (62)	21 (60)	1.0
Diabetes	56	2 (10)	9 (26)	.179
Obesity	56	10 (48)	31 (89)	.002
Obese first-degree relatives, median (IQR)	56	0 (0–4)	2(0–4)	.008
Comorbid conditions				
Obstructive sleep apnea	56	3 (14)	7 (20)	.727
Sleep disturbance	56	3 (14)	2 (6)	.352
GERD	56	2 (10)	14 (41)	.015
Taking acid blocker [‡]	56	0 (0)	7 (20)	.038
Allergies make asthma worse	56	14 (67)	23 (66)	.902
Food allergy	56	5 (26)	10 (29)	1.0
Major psychiatric disorder [§]	56	1 (5)	4 (11)	.640
Depression	56	1 (5)	6 (17)	.237
Anxiety	56	4 (19)	10 (29)	.533
Past infections (ever)				

Characteristic	n	BMI 20–65th	BMI > 85th	P value*
Pneumonias	56	1.9 ± 3.1	0.7 ± 1.0	.126
Ear infections	56	2.2 ± 3.9	3.7 ± 8.6	.387
GERD score ^{//}	56	9.6 ± 9.7	23.2 ± 22.7	.003
Frequency in the past week				
Abdominal pain	56	0.24 ± 0.5	1.1 ± 2.0	.024
Chest pain/heartburn	56	0.24 ± 0.5	1.3 ± 2.2	.012
Difficulty swallowing	56	0.38 ± 0.74	1.4 ± 1.9	.009
Nighttime pain/awakening	56	0 ± 0	0.46 ± 1.1	.021
Nausea	56	0.52 ± 0.87	1.6 ± 1.9	.005
Sleep characteristics				
Sleep per night	56	8.1 ± 1.0	8.0 ± 1.2	.780
Presence of snoring				
> 1 night/wk	56	7 (33)	29 (83)	<.001
Every night	56	1 (5)	16 (46)	<.001

Values are means ± SD or n (%) as noted. Values in boldface depict a significant difference based on BMI group at the level $P < .05$.

ETS, Environmental tobacco smoke; *IQR*, interquartile range; *OSA*, obstructive sleep apnea.

*The Fisher exact test was used to compare ratios.

[†]*Atopy* was defined as allergic rhinitis/hay fever, eczema, food allergy, or anaphylaxis by parent report.

[‡]Proton pump inhibitor or H2 blocker more than twice per week.

[§]Presence of bipolar depression or posttraumatic stress.

^{//}Score range 0 to 441, with higher values suggesting worse symptoms.

TABLE II

Lung function

Variables	n	BMI 20–65th	BMI > 85th	P value
Spirometry		21	35	
FVC percent predicted		101.8 ± 10.9	96.6 ± 21.2	.238
FEV ₁ percent predicted		87.4 ± 15.3	88.6 ± 23.1	.834
FEV ₁ /FVC		0.754 ± 0.10	0.745 ± 0.35	.886
Postbronchodilator change				
FVC	54	3.5 ± 6.0	5.6 ± 6.1	.212
FEV ₁	56	13.4 ± 13.8	11.8 ± 13.4	.668
BDR, n (%) [*]	56	7 (33)	12 (43)	.577
PC ₂₀ (mg/mL), median (IQR)	43	0.45 (0.19, 1.05)	1.87 (0.46, 5.5)	.012[†]
Feno, median (IQR)	30	62.6 (32.0, 91.5)	30.0 (13.8, 42.6)	.037[†]

Values are mean ± SD unless noted. Values in boldface depict a significant difference based on BMI group at the level $P < .05$.

BDR, Bronchodilator reversibility; *FVC*, forced vital capacity; *IQR*, interquartile range.

^{*} Defined as a 12% or greater improvement in FEV₁ or FVC after 4 puffs of albuterol.

[†] Wilcoxon-Mann-Whitney *U* nonparametric test.

TABLE III

Primary symptom reported with loss of asthma control

“What symptom do you first see when your child’s asthma starts acting up?”	BMI 20–65th	BMI > 85th	<i>P</i> value
	n = 21	n = 35	.0027 [*]
Chest pain	1 (4.8)	0 (0)	
Chest tightness	1 (4.8)	3 (8.6)	
Cold symptoms	1 (4.8)	0 (0)	
Cough	12 (57.1)	9 (25.7)	
Shortness of breath	0 (0)	13 (37.1)	
Throat itching	0 (0)	1 (2.9)	
Tiredness/fatigue	2 (9.5)	0 (0)	
Wheeze/wheezing	4 (19.1)	9 (25.7)	

*
Fisher exact test.

TABLE IV

Symptom characterization

Variable	n	BMI 20–65th	BMI > 85th	P value
		21	35	—
ACQ6 (score range, 0–6) [*]	56	0.68 ± 0.72	1.26 ± 0.97	.021
Nocturnal symptoms	56	0 (0, 0)	0 (0, 2)	.204
Wheeze	56	1 (0, 1)	1 (0, 2)	.030
SOB	56	1 (0, 2)	2 (1, 3)	.019
SOB rescue frequency	56	0 (0, 1)	1 (0, 1)	.011
Limitation	56	0 (0, 1)	1 (0, 2)	.197
Morning symptoms	56	0 (0, 0)	1 (0, 2)	.016
ACT (score range, 5–25) [†]	35	22.2 ± 2.9	19.5 ± 3.2	.019
Getting as much done?	35	5 (5, 5)	4 (4, 5)	.003
SOB frequency	35	4 (4, 5)	4 (3, 4)	.018
Nocturnal symptoms	35	5 (4, 5)	5 (4, 5)	.616
Rescue medication frequency	35	5 (4, 5)	3.5 (3, 4)	.046
Asthma control rating	35	4 (4, 5)	4 (3, 4)	.053
cACT (score range, 0–35) [†]	21	22.5 ± 1.9	19.0 ± 4.8	.032
General	21	3 (2, 3)	2 (2, 3)	.169
Problem with activity	21	2 (2, 2)	2 (1, 2)	.167
Cough frequency	21	2 (1, 2)	1 (1, 2)	.475
Nighttime symptoms (child)	21	2.5 (2, 3)	2 (1, 3)	.489
Awakening frequency (parent)	21	5 (4.5, 5)	4 (4, 5)	.124
Wheeze	21	5 (4, 5)	4 (3, 4)	.095
Daytime symptoms	21	4.5 (4, 5)	4 (3, 5)	.056
ASUI (score range, 0–1) [†]	55	0.86 ± 0.16	0.82 ± 0.15	.426
Frequency of				
Cough	55	2 (1, 2)	2 (1, 3)	.104
Wheeze	55	1 (1, 2)	2 (1, 2)	.092
SOB	55	1 (1, 2)	2 (2, 2)	.006
Nocturnal awakenings	55	1 (1, 1)	1 (1, 2)	.635
Medication side effects	55	1 (1, 1)	1 (1, 1)	.029

Total scores are expressed as mean ± SD, while individual subscores are expressed as median (IQR). Values in boldface depict a significant difference based on BMI group at the level $P < .05$.

ACQ, Asthma Control Questionnaire; cACT, childhood Asthma Control Test; IQR, interquartile range; SOB, shortness of breath.

^{*} Higher score indicates worse asthma.

[†] Lower score indicates worse asthma.

TABLE V

Differences between child- and caregiver-reported asthma-related quality of life

QLQ variable	PAQLQ (child report)			PACQLQ (caregiver report)		
	BMI 20–65th	BMI > 85th	P value	BMI 20–65th	BMI > 85th	P value
Total score* (score range, 1–7)	5.8	5.0	.035	5.5	5.2	.362
Symptoms	5.9	5.1	.024	—	—	—
Activity	5.3	4.3	.01	5.3	4.9	.318
Emotion	6.0	5.3	.07	5.7	5.3	.216

PACQLQ, Paediatric Asthma Caregiver Quality of Life Questionnaire. Values in boldface depict a significant difference based on BMI group.

* Higher value indicates less severe asthma; total and domain scores range from 1 to 7.

TABLE VI

Comparisons of asthma symptom scores and asthma-related quality-of-life scores between overweight/obese and lean children after adjustment for influential covariates

Variable	ACO6	ASUI	PAQLQ	PAQLQ Symptoms*	PAQLQ Activity†	PAQLQ Emotion‡	PAQLQ SOB§
BMI group	.365	.824	.399	.774	.029	.715	.299
Age	—	.033	—	—	—	—	—
Sex	.06	.499	.387	.125	.295	—	.089
Race	—	.243	.330	.158	—	.338	—
Birth weight	.136	.434	.046	—	.011	.067	.217
Gestational age	—	.339	.281	.073	—	.131	—
Age at asthma diagnosis	.032	—	.031	—	.284	.125	—
GERD score	<.001//	<.001//	.005//	.001//	.001//	.106	.028
NAEPP controller level	—	—	—	.126	—	—	—
Anxiety	—	—	—	.072	—	—	—
Depression	.092	.232	.012	.034	.048	.003//	—

Missing values (—) indicate that the covariate was not influential on a given response variable (eg, ACO6) and thus was not used in the adjustment. *P* values of variables in each of the ANCOVA models presented in the table. The models compared the asthma symptom and quality-of-life scores between obese/overweight and lean children with asthma after adjustment for influential covariates. Values in boldface depict a significant difference at the level *P* < .01.

ANCOVA, Analysis of covariance; NAEPP, National Asthma Education and Prevention Program; SOB, shortness of breath.

* PAQLQ Symptom domain score.

† PAQLQ Activity domain.

‡ PAQLQ Emotion domain.

§ PAQLQ SOB score.

// *P* < .01.