Childhood obesity increases duration of therapy during severe asthma exacerbations*

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Objectives: **Childhood obesity contributes to a wide array of medical conditions, including asthma. There is also increasing evidence in adult patients admitted to the intensive care unit (ICU) that obesity contributes to increased morbidity and to a prolonged length of stay. We hypothesized that obesity is associated with the need for increased duration of therapy in children admitted to the ICU with status asthmaticus.**

Design: **Retrospective cohort study.**

Setting: **A tertiary pediatric ICU in a university-affiliated children's hospital.**

Patients: **We retrospectively examined data from all children older than 2 yrs admitted to the ICU with status asthmaticus between April 1997 and June 2004. Children were classified as normal weight (<95% weight-for-age percentile) or obese (>95% weight-for-age).**

Interventions: **None.**

Measurements and Main Results: **Of the 209 children admitted to the ICU with asthma, 45 (22%) were obese. Compared with children of normal weight, the obese children were older (9.7 ± 4.4 vs. 8.0 ± 4.3 yrs, $p = .02$), more likely to be female (60% vs. 37%, $p < .01$), and more likely to have been admitted to the ICU previously (40% vs. 20%, $p = .01$). The obese children also had a statistically significant difference in race (more likely to be Hispanic) and in baseline asthma classification (more likely to have persistent asthma). Despite similar severity of illness at ICU admission, obese children had a significantly longer ICU length of stay (116 ± 125 hrs vs. 69 ± 57 hrs, $p = .02$) and hospital length of stay (9.8 ± 7.0 vs. 6.5 ± 3.4 days, $p < .01$). Obese children also received longer courses of supplemental oxygen, continuous albuterol, and intravenous steroids.**

Conclusions: **Childhood obesity significantly affects the health of children with asthma. Obese children with status asthmaticus recovered more slowly from an acute exacerbation, even after adjustment for baseline asthma severity and admission severity of illness. (Pediatr Crit Care Med 2006; 7:527–531)**

Key Words: obesity; pediatrics; status asthmaticus; critical care

The prevalence of childhood obesity has increased rapidly over the last 2 decades (1–4). According to data from the National Health and Nutrition Examination Survey (1999–2002), 15% of the children in the United States are at risk of being overweight and 16% are overweight (1). Along with obesity, the prevalence of childhood asthma is also increasing (5–7). The annual prevalence of self-reported asthma in children in the United States is between 4% and 8% and accounts for 6–10% of all pediatric office visits (7). Because the increases in asthma and obesity are concomitant, it has been suggested that they may be causally related (8). Although several studies have reported a positive association between asthma and obesity in children and adults (8–10), the results of the studies in children have not been consistent (11–13), and the exact nature of the relationship is unclear.

Status asthmaticus, or a severe asthma exacerbation, is one of the most frequent causes of admission to a pediatric intensive care unit (ICU) (5–6). In the ICU, obesity has been found to contribute to an array of medical complications including the development of multiple organ failure, prolonged ICU length of stay, and increased mortality (14–16). Our hypothesis was that obese children admitted to the ICU with status asthmaticus similarly receive more intensive therapy and require a longer duration of hospitalization for asthma exacerbations than nonobese children.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board at Connecticut Children's Medical Center, and the criteria for informed consent were waived due to its retrospective nature.

We retrospectively examined the medical records of all children between the ages of 2 and 18 yrs admitted to the pediatric ICU for treatment of status asthmaticus between April 1997 and June 2004. Children with chronic medical conditions other than asthma were excluded. Patients were identified from a previously existing database of ICU patients that is maintained by the Division of Critical Care for quality improvement purposes.

Children were classified as normal weight (<95% weight-for-age percentile) or obese (>95% weight-for-age percentile) based on reference data collected by the National Center for Health Statistics (17). We had planned to determine the body mass index (BMI) as a measure of obesity, but this was not calculated due to a lack of retrospective data regarding the height of the children involved in this study. Weight-for-age z scores were calculated using the CDC Epi Info software. Data were collected regarding basic demographics, indications for therapy, duration and level of therapy, duration of ICU and total hospitalization, and medications received. Length of stay was calculated from actual admission and discharge times.

The Modified Pulmonary Index Score (MPIS), a validated asthma severity score in

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The authors have not disclosed financial or other potential conflicts of interest in the subject of this manuscript.

DOI: 10.1097/01.PCC.0000243749.14555.E8

this population and in our institution (18), was used to assess illness severity on admission. Asthma scoring systems are often used in pediatric patients as a measure of severity of illness due to the difficulty in obtaining reliable and reproducible measures of air flow obstruction in critically ill children. Baseline asthma severity was determined using the National Institutes of Health asthma guidelines that classify children with mild intermittent, mild persistent, moderate persistent, and severe persistent asthma based on frequency of symptoms (19).

Although the treatment was not formally protocolized, there were no significant changes in practice during the study period, nor were there significant changes in physician, nursing, or respiratory therapist staffing. Four pediatric intensivists directed the ICU care during this study period, three of whom were the same throughout. The criteria for discharge from the ICU did not change during the study period. A patient was transferred from the ICU to the ward when a) that patient required bronchodilator therapy of ≤20 mg/hr of continuous albuterol aerosol; b) supplemental oxygen was ≤40%; and c) the MPIS was ≤10. At the study institution, patients may be treated with continuous albuterol nebulizer treatments on the ward.

Modified Pulmonary Index Score. The MPIS is a pediatric asthma severity of illness score used to quantify illness severity. The MPIS has been shown to be highly reproducible among groups of medical professionals (respiratory therapists, nurses, and physicians) as well as among individuals within each group (18). At our institution, the MPIS is determined hourly by the nurse, respiratory therapist, or physician as part of the basic assessment of a child with status asthmaticus. In the MPIS, six different categories are evaluated: oxygen saturation in room air, accessory muscle use, inspiratory-to-expiratory ratio, degree of wheezing, heart rate, and respiratory rate. For each of these six measurements or observations, a score of 0–3 is assigned, resulting in a possible minimum score of 0 and a maximum score of 18. In general, scores <6 are associated with mild asthma exacerbations, scores of 6–10 with moderate asthma exacerbations, and scores >10 with severe asthma exacerbations.

Statistical Analysis. Relationships between obesity and outcomes were assessed using appropriate parametric tests and statistics, including chi-square and Student's *t*-tests. When variances were significantly unequal, a Welch analysis of variance was used. Multiple regression was used to determine the influence of obesity controlling for other potential risk factors found to be significantly associated with length of ICU stay. A p value of <.05 was considered statistically significant. Data were analyzed using the JMP statistical software (version 5.0; Cary, NC). Before data collection, we calculated that for an obesity prevalence of 20%, a sample size of 250 patients (i.e., 50 obese and 200 nonobese) would provide a power of 88% to detect a 2-day decrease in ICU length of stay with an SD of 5 days (based on our previous studies). Results are reported as mean ± SD.

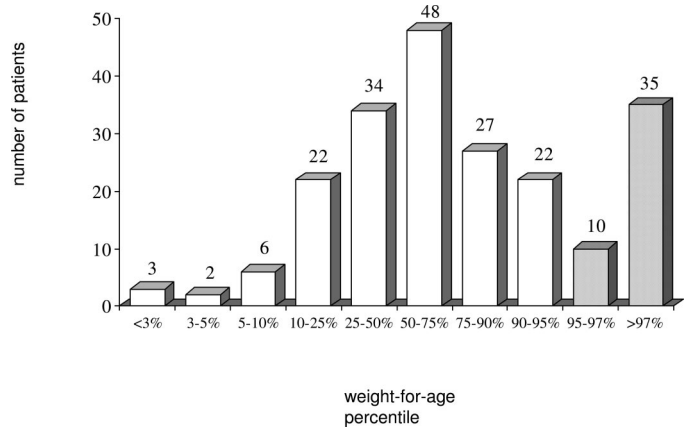

Figure 1. Weight-for-age distributions for the patient population.

RESULTS

Patient Characteristics. Between September 1997 and June 2004, 209 children with no other chronic medical conditions were admitted to the ICU for status asthmaticus. All charts were available for analysis. Forty-five (22%) of these children were obese. The distribution of weight-for-age percentiles is in Figure 1. There was a bell-shaped distribution of the weight-for-age percentiles except at the highest level. Very obese children (weight-for-age percentile >97%) comprised 17% of the population and 80% of these very obese patients were above the >99% weight-for-age cutoff. There was no statistical difference in frequency of obesity over time (Fig. 2).

Demographic data are shown in Table 1. Compared with nonobese children, obese children with status asthmaticus were older (9.7 ± 4.4 vs. 8.0 ± 4.3, $p = .02$), more likely to be female (60% vs. 37%, $p < .01$), and more likely to have been previously admitted to the ICU (40% vs. 20%, $p = .01$). The obese children also had a statistically significant difference in race (more likely to be Hispanic) and in asthma classification (more likely to have persistent asthma). Additional demographic data are in Table 1. There was no difference in the percent of children who reported receiving chronic inhaled corticosteroid therapy before ICU admission.

Outcome Measures. Despite equivalent severity of illness on ICU admission, we found that obese children with status asthmaticus had a significantly longer ICU length of stay (116 ± 125 vs. 69 ± 57 hrs, $p = .02$) and hospital length of stay (9.8 ± 7.0 vs. 6.5 ± 3.4 days, $p < .01$) compared with nonobese children (Table 2 and Fig. 3). Obese children also re-

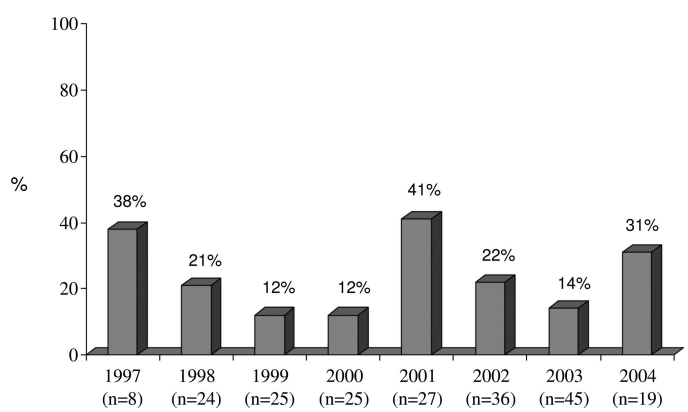

Figure 2. Frequency (%) of obesity in children admitted to the intensive care unit according to year of admission. There was no statistical difference in frequency of obesity over time ($p = .09$).

Table 1. Demographic data

	Normal Weight (n = 164)	Obese (n = 45)	*p* Value
Age	8.0 ± 4.3	9.7 ± 4.4	.02
Female gender, %	37	60	.01
Weight, kg	29 ± 16	57 ± 26	<.0001
Weight-for-age z scores	0.03 ± 1.05	2.26 ± 0.68	<.0001
Previous hospitalization, %	57	69	.17
Previous intensive care unit admission, %	20	40	.01
Previous intubation, %	8	9	.77
Public insurance, %	55	69	.13
Race, %			.01
Hispanic	32	58	
African American	27	16	
Caucasian	39	27	
Asthma class, %			.02
Mild intermittent	35	22	
Mild persistent	23	24	
Moderate persistent	31	22	
Severe persistent	12	31	

Data expressed as mean ± SD unless otherwise indicated.

Table 2. Hospitalization data

	Normal Weight (n = 164)	Obese (n = 45)	*p* Value
Admission Modified Pulmonary Index Score	13.7 ± 2.2	14.2 ± 1.5	.17
Hospital length of stay, days	6.5 ± 3.4	9.8 ± 7.0	.002
Intensive care unit length of stay, hrs	69 ± 57	116 ± 125	.02
Received intravenous terbutaline, %	59	67	.39
Duration intravenous terbutaline, days	4.1 ± 2.4	4.9 ± 3.6	.18
Duration continuous albuterol, days	4.4 ± 2.4	6.5 ± 3.8	.0005
Duration supplemental oxygen, days	4.4 ± 2.6	7.1 ± 4.7	.0003
Duration intravenous steroids, days	4.3 ± 2.6	6.1 ± 4.0	.004
Received magnesium, %	43	69	.002
Received noninvasive positive pressure, %	2	16	.002
Intubation, %	12	20	.22
Duration mechanical ventilation, days	4.5 ± 3.4	7.4 ± 9.2	.38
Discharge Modified Pulmonary Index Score	6.0 ± 2.0	6.3 ± 2.3	.41

Data expressed as mean ± SD unless otherwise indicated.

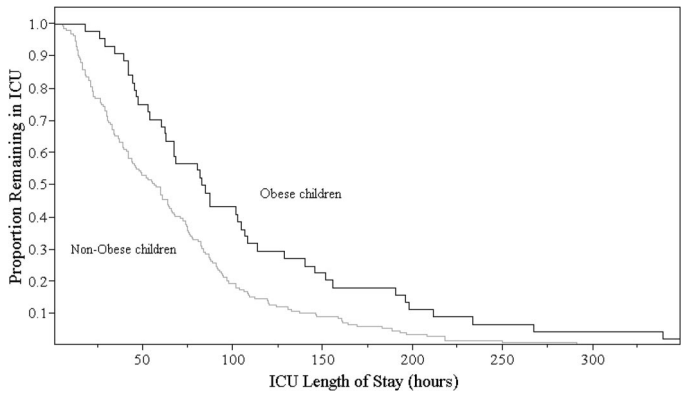

Figure 3. Kaplan-Meier curve of time to discharge from the intensive care unit (*ICU*) for obese and nonobese children ($p = .001$ by log-rank test).

ceived longer courses of supplemental oxygen, continuous albuterol, and intravenous steroids. The rate of clinical improvement was also slower for obese children compared with nonobese children, as quantified by change in clinical asthma score/time (change in MPIS/time in ICU in hours 0.19 ± 0.19 vs. 0.10 ± 0.06, $p = .001$). There was no difference in the percent of children with coexisting pneumonia (22% vs. 22%).

To identify significant predictors of ICU length of stay, a stepwise multiple regression was done in two stages. By univariate analysis, increased length of stay was associated with age ($p = .001$), previous ICU admission ($p = .0005$), severe persistent asthma classification ($p = .0005$), and admission MPIS ($p < .0001$). Although patient race and gender were associated with obesity, these factors were not associated with increased length of stay ($p = .12$ and $p = .27$, respectively). The factors found to be significantly associated with ICU length of stay from the univariate analysis were entered in a stepwise procedure. Three of these (age, admission MPIS, and baseline asthma severity) continued to be statistically significant, all at $p < .01$. Entering obesity into this model resulted in a statistically significant improvement over the prediction achieved by the other factors ($p < .05$). The overall regressions and the increase in R^2 were significant after the addition of each factor (final $R^2 = .22$). The nonstandardized and standardized regression coefficients and their associated *p* values for each of the final regression variables are shown in Table 3.

DISCUSSION

Obese children have increased health-related problems compared with nonobese children. Childhood obesity is associated with the development of obstructive sleep apnea, type 2 diabetes mellitus, early aortic and coronary artery plaques, and significant orthopedic complications, and it is the leading cause of pediatric hypertension (20–22). In addition, childhood obesity is strongly associated with adult obesity (20–22), which also carries a significant risk of serious medical complications that impair quality of life and lead to increased morbidity and mortality (23, 24). In this study, obese children with asthma admitted to the ICU with status asthmaticus required more intensive treatment and longer durations of therapy than children of normal weight, despite adjustment for other predictors including initial severity of illness and baseline level of asthma severity.

The link between asthma and obesity is controversial (8, 9, 11, 12, 23, 25–29). Although some clinicians believe that obesity may contribute to the development of asthma, associations with objec-

Table 3. Multiple regression analysis of univariate factors influencing intensive care unit length of stay

Factor	Unstandardized Regression Coefficient	95% Confidence Interval for Regression Coefficient	Standardized Regression Coefficient	*p* Value
Age	2.94	0.51–5.37	0.163	.018
Severe persistent asthma	40.0	11.3–68.7	0.187	.007
Admission Modified Pulmonary Index Score	11.6	6.89–16.26	0.307	<.0001
Obesity	28.6	4.40–52.83	0.149	.021

tive asthma-related indexes are less consistent. The hormone leptin, a protein produced by fat cells, has been linked to hypoventilation associated with obesity (29) and to asthma in children (27). Several large studies have been performed, some independently linking asthma and obesity (8–9) and some finding no association (11–13). However, although obesity has been associated with increased subjective symptoms of asthma and wheezing (26), increased medication use (26), and increased emergency department visits (26), obesity itself has not been linked to airway hyperresponsiveness (25).

In this population, obese children also had more persistent asthma and were more likely to have been previously admitted to the ICU than nonobese children. This difference could have potentially affected primary and secondary outcomes. However, more persistent asthma and previous ICU admission were not associated with increased ICU length of stay. Data from this and a previous study (18) indicate that admission MPIS (i.e., severity of illness on admission) most strongly correlated with ICU length of stay and overall duration of hospitalization. Thus, similar illness severity on admission in obese and nonobese children might be expected to lead to similar durations of hospitalization. However, the differences found between the groups in this study and the results of the multiple regression analysis suggest that childhood obesity significantly affects the course of pediatric status asthmaticus, with slower rates of recovery and prolonged ICU and hospital lengths of stay in obese children.

This study is limited by several factors. Although we had intended to use the BMI (the ratio of the weight in kilograms to the square of the height in meters) to quantify level of obesity, the lack of recorded height data precluded us from doing so. There is a strong positive linear correlation between the BMI and the percentage of body weight that is fat and a growing consensus that a BMI >95th percentile is a valid and clinically useful definition of obesity (30, 31). It is possible that children of above or below average heights could have skewed the results of this study. However, despite the limitation of not accounting for height, weight-for-age percentiles are the most commonly used indicator by pediatricians to assess the size and growth patterns of individual children in the United States (32, 33). In addition, length of stay is an outcome measure that is influenced by a variety of confounding factors, including bed availability, nursing staffing, and time of day. However, the close association in this study between ICU length of stay and other outcome variables not associated with these confounders, such as duration of continuous albuterol and supplemental oxygen, suggests that ICU length of stay is a valid outcome measure in this study.

Despite the increased duration of hospitalization found in this study, the relationship between childhood obesity and increased hospitalization rates for asthma is unclear. There are no published studies looking at the relationship between obesity and risk of hospitalization for an asthma exacerbation in children. In a random sample of 185 children followed in the pulmonary clinic at our institution for asthma, 34 children (21%) were obese. This prevalence does not significantly differ from that of obesity among children admitted to the ICU with status asthmaticus (22%) in our institution. Studies are needed to determine whether childhood obesity increases the risk of hospitalization for children with asthma.

It is not possible to determine the potential mechanisms responsible for the association of obesity and increased duration of therapy for status asthmaticus in this study, given its retrospective nature. However, there are several potential explanations for this link. Obese children may have previously undiagnosed concomitant processes related to their obesity, such as upper airway obstruction or gastroesophageal reflux, that lead to prolonged ICU length of stay and increased durations of therapy. The incidence of these processes is difficult to assess in this retrospective trial, since we cannot determine to what extent specific questions were asked to obtain this relevant history. Another potential mechanism is that obese children may have increased ventilation/perfusion mismatching due to atelectasis, possibly from lack of sufficient respiratory effort given their increased body habitus and resultant decreased chest wall compliance. Prospective trials are needed to elucidate the underlying pathophysiology behind this association.

CONCLUSIONS

In this study, we found that obesity was associated with increased duration of hospitalization in children admitted with status asthmaticus. Obese children admitted to the ICU with status asthmaticus recovered more slowly from the acute exacerbation, even after adjustment for baseline asthma severity and admission severity of illness. This study identifies an important area in which obesity adversely affects the health of children.

ACKNOWLEDGMENTS

We thank Trudy Lerer and the Office of Research at Connecticut Children's Medical Center for the statistical support provided and the staff of the Office of Health Information Management for all their hard work in obtaining the data used for this study.

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