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Association of obesity with severity outcomes in hospitalized pediatric asthma exacerbations

Raymond Parlar-Chun, MD^{a,b}, Grace Truong, BS^b, Tasia Isbell, BS MPH^b, Yesenia Delgado, BS^b, and Makenna Arca, BS Med^b

^aChildren's Memorial Hermann, Houston, TX, USA; ^bDepartment of Pediatrics, McGovern Medical School, Houston, TX, USA

ABSTRACT

Introduction: While there seems to be an association between obesity and asthma, the exact nature of the relationship remains unknown. It is unclear if there is increased severity of exacerbation for those that require hospitalization. We examine the association between obesity and severity outcomes such as hospital length of stay, intensive care admissions, and need for continuous albuterol or magnesium administration.

Methods: Patients 4 to 17 years old admitted between 1/1/2012–1/1/2016 with asthma identified by discharge codes were reviewed. Obesity was defined as BMI $\geq 95\%$. Clinical data such as age, gender, family history of asthma, use of controller medication along with outcome data such as length of stay, ICU admission, use of continuous albuterol, and use of magnesium were collected. Binary outcomes were analyzed with multivariate logistic regression while length of stay was analyzed with negative binomial regression.

Results: Overall, 995 patients met inclusion criteria. The median age was 7 years old with 170 (17%) patients categorized as obese. We find no difference in length of stay (IRR 0.99 [0.91, 1.09], $p = 0.9$), PICU admission (OR 0.72 [0.43, 1.21], $p = 0.22$), or magnesium administration (OR 1.34 [0.95, 1.88], $p = 0.09$) between obese and non-obese patients. There were increased odds of continuous albuterol use (OR 1.47 [1.02, 2.11]) for obese patients.

Conclusion: We find no association between obesity and outcomes of length of stay, ICU admission, or magnesium administration. While growing evidence links obesity with asthma, our study suggests it may not be associated with the severity of exacerbation.

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Introduction

Childhood obesity in the United States continues to be a major public health problem with an estimated prevalence of 18.5% in 2016 (1). Obese children are at risk for severe health problems, including development of asthma. One study estimated a quarter of new pediatric asthma diagnoses were directly attributed to obesity (2). While there seems to be a positive association between obesity and asthma, the exact nature of the relationship remains unclear.

There are several biologically plausible mechanisms how obesity might impact asthma. In obese individuals, there is an increase in the pro-inflammatory adipokine leptin, and a decrease in the anti-inflammatory adiponectin (3–6). Obesity can also affect lung function, with studies showing decreased FEV1/FVC, expiratory reserve volume, functional residual capacity, and peak expired flow (7–10).

However, when looking at clinical outcomes, studies have been inconsistent. Some studies have shown that children with obesity are at an increased risk having exacerbations and having worse control (11–13) while others have shown no difference (14–16). Specifically for hospitalizations, in one study, despite similar asthma scores and therapeutic interventions in the emergency room, obese children were 1.76 times more likely to be hospitalized than their non-obese counterparts (17). However in another, admission status did not vary between groups (18). Similar inconsistencies are found in regards to hospital severity outcomes of the exacerbation with some studies showing increased length of hospitalization in obese patients (19,20), while another actually showing an inverse association between BMI and length of hospitalization (21).

If there are differences in severity of exacerbation in obese children compared to non-obese children,

this may have implications for changes in management to optimally treat this population. For example, obesity has been associated with corticosteroid pharmacokinetic abnormalities and resistance (22). Higher dosages of corticosteroids or increased utilization of adjuvant therapies may be needed in this population. In our study, we aim to examine the association between childhood obesity and multiple hospital severity outcomes such as length of stay, intensive care admissions, and need for continuous albuterol or intravenous magnesium administration for children admitted for acute asthma exacerbations.

Methods

A retrospective cohort of patients 4 to 17 years old admitted to an urban tertiary care hospital between January 1, 2012 through January 1, 2016 with asthma exacerbations were reviewed. Cases were identified by ICD 9/10 discharge codes. An age cut off of 4 years was used to exclude potential diagnoses such as bronchiolitis, reactive airway disease, or transient wheezing of infancy. Exclusion criteria included hospitalizations for which asthma was not the primary reason for admission.

Demographic and clinical data such as age, gender, weight, family history of asthma, and use of controller medication were recorded. Positive controller medication use was defined as any use or prescription of inhaled corticosteroids prior to hospitalization regardless of compliance. Obesity was defined as a BMI $\geq$ 95th percentile in accordance with the US Centers for Disease Control definition. BMI percentiles were calculated by the electronic medical record and took into account the admission weight, height, age, and sex of the patient. Outcome data recorded were length of hospitalization in hours (excludes emergency room time and defined as time of admission to the hospital through to the time of discharge), and binary outcomes—need for ICU admission, need for continuous albuterol (nebulized albuterol delivered continuously as opposed to intermittent albuterol usage through metered-dose inhaler), and need for intravenous magnesium sulfate.

At our institution, the use of continuous albuterol, ICU transfer, and magnesium usage is based on clinician judgment. Once patients are on intermittent albuterol treatments, they are placed on a respiratory therapist driven pathway where the frequency of intermittent treatments is spaced out using a local clinical asthma score. This clinical asthma score includes factors such as respiratory rate, accessory muscle use, air exchange, degree of wheezing, and oxygen saturation. Patients are

considered ready for discharge once their albuterol treatments have been spaced to every four hours.

Descriptive statistics were used to characterize the variables of interest using counts (percentages) for categorical variables and mean (SD) for continuous variables. Continuous data were tested for normality and t-test and Chi-squared tests were used as appropriate to determine differences between obese and non-obese patients. Statistical significance was indicated at $p < 0.05$ level.

Need for ICU admission, use of continuous albuterol, and uses of magnesium were binary outcomes and analyzed using multivariate logistic regression. Length of hospitalization was treated as a count and analyzed using negative binomial regression given the large difference between the mean and variance. Odds ratios (OR) and 95% confidence intervals were reported for logistic regression while incidence rate ratios (IRR) and 95% confidence intervals were reported for the negative binomial model. Local IRB approval was obtained.

Results

Overall, 995 patients were identified. The average age was 7.9 years with 170 (17%) patients categorized as obese. Obese patients were significantly older (9.1 years vs. 7.6 years). There was no difference in sex, family history of asthma, or patient use of controller medication in obese versus non-obese patients. Unadjusted outcomes show obese patients having higher proportions of continuous albuterol and magnesium usage. There were no differences in PICU admission or length of hospitalization between the two groups (Table 1).

There was no difference in adjusted length of stay for obese versus non-obese patients (IRR 0.99, [0.91, 1.09], $p = 0.9$). Older kids, use of magnesium, use of continuous albuterol, and PICU admission were associated with longer length of hospitalization (Table 2). We also find no difference in PICU admission (OR 0.72 [0.43, 1.21], $p = 0.22$) (Table 3), or magnesium administration (OR 1.34 [0.95, 1.88], $p = 0.09$) (Table 4) between obese and non-obese patients. Childhood obesity was significantly associated with an increased odds of continuous albuterol use (OR 1.47 [1.02, 2.11]) (Table 5).

Discussion

In our cohort of children admitted for acute asthma exacerbations, we find no association between

Table 1. Baseline characteristics and unadjusted severity outcomes of obese vs. non-obese patients.

	Obesity		<i>p</i> -value
	Yes <i>n</i> = 170	No <i>n</i> = 825	
Age (years), mean (SD)	9.1 (3.7)	7.6 (3.3)	<0.0001
Male, <i>n</i> (%)	100 (58.8%)	529 (64.2%)	0.19
1° Family history of asthma, <i>n</i> (%)	883 (48.8%)	405 (49.1%)	0.95
Use of controller medication, <i>n</i> (%)	63 (37%)	306 (37.1%)	0.99
PICU Admission, <i>n</i> (%)	20 (11.8%)	117 (14.2%)	0.4
Continuous albuterol, <i>n</i> (%)	120 (70.6%)	502 (60.9%)	0.02
Magnesium Administration, <i>n</i> (%)	86 (50.6%)	339 (41.1%)	0.02
Length of stay (hours), mean (SD)	54.6 (35.6)	51 (39)	0.26

t-test and χ^2 used as appropriate.

Abbreviation: PICU, pediatric intensive care unit.

Table 2. Multiple regression for hospital length of stay adjusted for obesity and other covariates.

IRR	95% CI	<i>p</i> -value
Obesity ^a	0.99	0.91, 1.09
Age (years)	1.02	1.01, 1.03
Used magnesium	1.18	1.08, 1.28
Used continuous albuterol	1.72	1.58, 1.87
PICU Admission	1.55	1.4, 1.7
FH of asthma	1.17	0.9, 1.51
Use of controller medication	1.1	0.83, 1.44

Abbreviations: PICU, pediatric intensive care unit; FH, family history; IRR, incidence rate ratio; CI, confidence interval.

^aAdjusted for all of the covariates listed in rows below.

Table 3. Multiple logistic regression for PICU utilization adjusted for obesity and other covariates.

	OR	95% CI	<i>p</i> -value
Obesity ^a	0.72	0.43, 1.21	0.22
Age (years)	1.07	1.02, 1.13	0.008
FH of asthma	1.14	0.79, 1.64	0.47
Use of controller medication	1.12	0.77, 1.63	0.54

Abbreviations: FH, family history; OR, odds ratio; CI, confidence interval.

^aAdjusted for all of the covariates listed in rows below.

childhood obesity and hospital length of stay, ICU admission, or intravenous magnesium administration. There was a positive association between obesity and use of continuous albuterol.

The prevalence of obesity in the United States has doubled in children and tripled in adolescents over the past three decades (23,24). The prevalence of childhood asthma has also increased, with 2018 prevalence reaching 7.5% of children in the United States (25). While there seems to be a link between obesity and asthma, the exact nature of this relationship remains unclear. The evidence is mixed when looking at the association between childhood obesity and the severity of asthma exacerbation. Several studies have linked obesity to more severe asthma exacerbations as indicated by severity scores, longer hospital stays, increased use of mechanical ventilation, and increased ICU level care (19,26,27). In a smaller retrospective cohort of 209 children admitted to the intensive care unit, Carroll et al. found that obese children had longer length of hospitalization by an average 3 days, as

Table 4. Multiple logistic regression for use of magnesium adjusted for obesity and other covariates.

	OR	95% CI	<i>p</i> -value
Obesity ^a	1.34	0.95, 1.88	0.09
Age (years)	1.07	1.03, 1.1	0.001
FH of asthma	1.11	0.86, 1.44	0.4
Use of controller medication	0.99	0.76, 1.3	0.97

Abbreviations: FH, family history; OR, odds ratio; CI, confidence interval.

^aAdjusted for all of the covariates listed in rows below.

Table 5. Multiple logistic regression for use of continuous albuterol adjusted for obesity and other covariates.

	OR	95% CI	<i>p</i> -value
Obesity ^a	1.47	1.02, 2.1	0.04
Age (years)	1.04	0.998, 1.088	0.06
FH of asthma	1.17	0.9, 1.51	0.24
Use of controller medication	1.1	0.83, 1.44	0.5

Abbreviations: FH, family history; OR, odds ratio; CI, confidence interval.

^aAdjusted for all of the covariates listed in rows below.

well as increased duration of supplemental oxygen, continuous albuterol, and intravenous steroids (20). On the other hand, other studies have found no difference in outcomes in obese and non-obese patients (18,28), and others hypothesize that severity of asthma symptoms may be more influenced by atopy, metabolic abnormalities, diet, and epigenetics (2,29,30). In one previous study, Bettenhausen et al. examined a retrospective cohort of 518 children admitted for asthma of which about 20% were obese. They found no differences in length of stay, ICU care, readmissions, or resource utilization outcomes. In multi-variate analysis with BMI subdivided into deciles, they actually showed a small negative association with length of stay with about a 2% decreased length of stay for each decile increase; although they conclude that this effect was likely not clinically meaningful (21). Our study of almost 1000 patients adds to the literature that obesity is not associated with increased severity of the exacerbation as measured by length of stay, need for ICU admission, and use of intravenous magnesium sulfate.

Our baseline characteristics for obese and non-obese patients were similar; with the exception of age where obese patients were older. This is consistent

with the distribution of childhood obesity. According to the CDC, the obesity prevalence among 2 to 5 year olds was 13.9%, among 6 to 11 year olds was 18.4%, and among 12 to 19 year olds 20.6% (1). In our unadjusted outcomes, we find that obese patients were more likely to receive continuous albuterol and magnesium; as well as more likely to receive continuous albuterol in our adjusted outcome. It is important to note that the decision to start continuous albuterol or give magnesium is solely clinician dependent at our institution, without a systematic guideline on when to start these therapies. Anecdotally, those patients that sound “tight” on auscultation with decreased air movement are more likely to be started on continuous albuterol and given magnesium. This may lead to increased utilization in obese patients as the increased tissue mass may make auscultation more difficult and dampen the amplitude of breath sounds.

Our study should be interpreted in the context of some limitations. The retrospective nature of the study limited our ability to extract all relevant confounders. In particular, we were unable to assess for socioeconomic status. Children of families with low resources have less access to care and medications, and the disease burden of obesity is correlated with decreasing economic resources (30). The possibility that obesity is a confounder, and that socioeconomic status and asthma exacerbations are a causal link needs to be explored in future studies. Another relevant piece of information we did not have were baseline severity scores to be able to objectively measure the severity of the exacerbation. Instead we used surrogate outcomes of severity such as use of continuous albuterol, intravenous magnesium, or ICU utilization. Without severity scores, there is the possibility that clinicians made treatment decisions based on BMI itself instead of on severity of the exacerbation (i.e., more likely to place obese patients on continuous albuterol or magnesium because of obesity, regardless of severity). In addition, even though we had a large cohort of almost one thousand patients over a four year period, it was limited to a single tertiary care center that limits the potential generalizability to other locations. In particular, we realize that our outcomes of length of stay, ICU utilization, and usage of continuous albuterol and magnesium are likely institution-dependent.

Conclusions

We find no association between pediatric obesity and many of our severity outcomes we examined including

hospital length of stay, ICU admission, or magnesium administration. There was a positive association between obesity and use of continuous albuterol. The relationship between obesity and asthma remains unclear, and further studies are still needed to clarify this connection.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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