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ORIGINAL ARTICLE

Asthma as a Predictor of Obstructive Sleep Apnea in Urban African-American Children

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Background. Asthma is a known co-morbid factor in childhood obstructive sleep apnea (OSA); however, little is known about the effects that asthma might have on the severity of OSA. We hypothesize that children with concomitant asthma and OSA have more severe OSA. **Methods.** We conducted a prospective study of 50 children with OSA diagnosed by polysomnography referred for tonsillectomy and adenoidectomy (T&A). The presence of concomitant asthma was determined by ISAAC questionnaire and spirometry. Atopy to common allergens was determined by skin prick testing. Due to the relatively small sample size, we limited hypothesis testing to cross tabulations with Fisher's Exact Test and *t* testing. We also employed a parsimonious ordinary least squares (OLS) regression assuming a large effect size. **Results.** Subjects (*n* = 50) included 32 males and 41 African-Americans. Age at T&A was 9.3 ± 3.4 years (mean $\pm$ S.D.). Thirty-two subjects reported a history of asthma during their lifetimes, but the ISAAC questionnaire detected only 30 subjects. Twenty-two subjects reported current asthma. Atopy was found in 27 subjects. Apnea-hypopnea index (AHI) was lower in the current asthma group than in the lifetime asthma group but did not reach statistical significance. However, AHI was significantly higher in subjects with poorly controlled asthma. Further, in a parsimonious OLS model controlling for sleep efficiency and age, a history of lifetime asthma increased the AHI by 8.8 (*p* < 0.05). **Discussion.** In urban African-American children referred for T&A to treat OSA, a history of poorly controlled asthma is associated with more severe OSA.

Keywords children; asthma; asthma exacerbations; OSA severity

INTRODUCTION

Asthma and sleep-disordered breathing are two common respiratory disorders that significantly affect the quality of life in children (1). Primary snoring (PS) and obstructive sleep apnea (OSA) are the two most common manifestations of sleep disordered breathing in children (2). The prevalence of PS is 7% to 9% and OSA is 1% to 2% in school-age children. African-American children are disproportionately affected, with prevalence rates for OSA being 2 to 3 times that of Caucasian children (3). The national prevalence of asthma is 12.5% in children 0 to 17 years of age (4). In Maryland, the site of the current study, asthma prevalence is 10.6% (5). The reported prevalence of asthma in some areas of Baltimore is as high as 20% (6).

Asthma and OSA have common risk factors: obesity, atopy, minority ethnicity, and low socioeconomic status (3, 7). Larsson and co-workers identified a link between the two diseases reporting witnessed apnea in 14% of adults diagnosed with asthma (8). This association was further strengthened by the observation that treatment of

OSA by nasal continuous positive airway pressure (CPAP) eliminated symptoms of asthma (9, 10). While the "one-airway" hypothesis suggests that upper airway pathology might influence the course of lower airway disease (11–13), there are no data specifically linking asthma to the severity of OSA.

We previously reported that in a retrospectively studied group of snoring children, self-reported asthma decreased the likelihood of OSA (14). Given the sparse data available on the effect of asthma on OSA, we aimed to determine the relationship between asthma and OSA in a referral population. In the current prospective study, the diagnosis of asthma was made using more objective data. We hypothesized that the presence of asthma would be associated with increased severity of OSA.

METHODS

The University of Maryland Institutional Review Board approved this study. We enrolled a convenience sample of 50 subjects above the age of 6 years, diagnosed with OSA by an overnight polysomnogram (PSG). All subjects were awaiting treatment by tonsillectomy and adenoidectomy for OSA. Subjects were recruited from both pulmonary and ENT clinics. OSA was primarily diagnosed based on the PSG; however, if the patient was symptomatic despite a normal PSG, they were still referred for T&A.

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The presence of asthma was determined in two ways. First, all subjects or their parents (as age appropriate) completed the International Study of Asthma and Allergy in Childhood (ISAAC) questionnaire, as well as answering questions regarding demographics, lifetime and current asthma, medication use, and exacerbations (15). Additionally, 41 subjects underwent spirometry using a portable Micro Loop spirometer (Micro Medical, Kent, England). Of those who underwent spirometry, 32 subjects consented to additional post bronchodilator testing with a standard dose of nebulized pre-mixed albuterol (2.5 mg/3 mL, 0.083% inhalation solution, IVAX Pharmaceuticals, Miami, FL) administered using a pediatric aerosol mask (Salter Labs, Arvin, CA). Follow-up spirometry was performed 15 minutes after dosing. An asthma exacerbation is defined as an increase in symptoms followed by an increase in medication use (16). We defined poorly controlled asthma by the number of exacerbations in the last year, as well as albuterol use in the past month, not strictly in accordance with the NAEPP guidelines (17). History of even a single use of albuterol other than pre-treating for exercise was considered an asthma exacerbation, as it signified an increase in symptoms. This was not confirmed by pulmonary function testing.

The majority of the overnight PSGs ($n = 41$) were performed at the University's pediatric sleep laboratory. Standard overnight monitoring was accomplished with the Alice 4 diagnostic system (Respironics, Murrysville, PA). The patient slept in a quiet darkened room up to 7 hours with a parent or guardian present. The montage included EEG leads O1A2, O2A1, C1A2, C2A1, LOC, ROC, submentalis EMG, EKG, measurements of airflow included oronasal thermistor and end tidal CO_2 (ETCO₂) monitoring; chest and abdominal impedance using strain gauges; and oxyhemoglobin saturation using a pulse oximeter (Nellcor, Boulder, CO). Respiratory events were described as 1) obstructive apneas, with cessations of airflow with continued thoracic and/or abdominal respiratory effort lasting two respiratory cycles in duration, or 2) hypopneas, with reductions of airflow $>50\%$ associated with $\geq 4\%$ decrease in oxygen saturation or post-event arousal (18). The severity of OSA was defined by the apnea-hypopnea index (AHI; number of obstructive apneas and hypopneas per hour of sleep). The arousal index included respiratory and non-respiratory arousals per hour of sleep. Baseline and nadir oxyhemoglobin saturation, baseline, and peak ETCO₂ in addition to sleep stage were recorded. No patient was acutely ill on the night of the study. Polysomnographic scoring was performed in 30-second epochs according to the Rechtschaffen-Kales criteria (19). Reports for the nine subjects who underwent polysomnography at outlying sleep laboratories had fewer channels; however, all reports contained AHI severity. OSA is defined as an obstructive AHI of five or more events per hour and/or an obstructive apnea index of one or more events per hour (2, 3). There is no uniform OSA severity scoring in pediatrics. For this discussion, the levels of OSA severity that were analyzed were absent (AHI <2), mild (AHI $2-5$), moderate (AHI $5-10$), and severe (AHI >10). This was based primarily on overnight polysomnograms, however, for T&A, the history of snoring and witnessed apnea took precedence when the AHI was <2 /hour of sleep.

Atopy to 14 common indoor and outdoor allergens was determined by skin prick testing using the Multi-Test II device (Lincoln Laboratories, Decatur, IL). Skin testing was performed at a clinic visit prior to surgery or the day after T&A, prior to discharge home. Allergens and the positive (histamine) and negative (saline) control were placed on the forearm. Erythema and wheal formation were measured 15 minutes after the skin test. Skin testing was considered valid if the mean wheal diameter of the positive control exceeded 3 mm. Individual skin prick test was considered positive if the mean wheal diameter was at least 3 mm larger than the negative control. Atopy was defined by at least one positive test (20, 21).

STATISTICAL METHODS

Owing to the relatively small sample size, hypothesis testing is limited to cross-tabulations with Fisher's Exact Test and t testing. Before calculating a multivariate regression, we performed a power analysis assuming asthma would have a large effect on AHI giving a statistical power of 0.70 with a sample size ≥ 21 for a parsimonious ordinary least square (OLS) regression model with two controls and one independent variable. Therefore, we calculated a model using AHI as the outcome variable, history of asthma as the independent variable, and sleep efficiency and age as controls. We set beta at 95% for all analyses. We report important and statistically significant findings below.

RESULTS

Clinical Characteristics

The average age of the cohort was 9.3 ± 3.4 years (mean $\pm$ S.D.), with more than half under 10 years ($n = 27$). There were more males ($n = 32$) than females. The majority of subjects were African-American ($n = 41$). The mean BMI was 26.1 ± 11.0 kg/m² and the mean BMI percentile was 78.1 ± 32.0 . Twenty-seven of the subjects were obese with BMI >95 th percentile. Asthma reporting varied by source. ISAAC questionnaires indicated that 32 subjects (64%) experienced asthma in their lifetimes (See table 1). Of those, 30 subjects reported a lifetime history of asthma. We report data on the 30 subjects with lifetime asthma histories. Additionally, the ISAAC questionnaire indicated that 22 subjects had current asthma. Twenty-three subjects reported at least one asthma exacerbation in the past year (frequencies 1–3). Ten subjects were on inhaled steroids at the time of study and 21 had used bronchodilators in the last month. A smaller number were on nasal steroids ($n = 6$) and leukotriene modifiers ($n = 5$) at the time of study.

TABLE 1.—Whole group: clinical characteristics.

Variable	N	%	Mean	SD
Age	50		9.3	3.4
BMI			26.1 Kg/m ²	11.0
BMI percentile			78.1	32.0
Obese (BMI >95 th percentile)	27	54		
Male	32	64		
Female	18	36		
African American	41	82		
Asthma history (ISAAC)	32	64		
Asthma currently (ISAAC)	22	44		
Asthma in lifetime (self-report)	30	60		

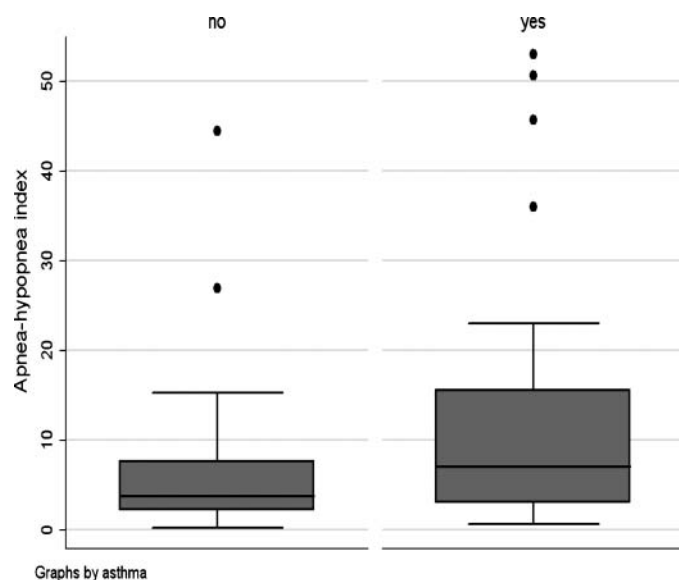


FIGURE 1.—OSA Severity and Lifetime Asthma.

All 50 subjects were skin tested and all demonstrated a positive histamine control. Twenty-seven subjects (54%) were atopic. No subject was on antihistaminics within at least 3 days of testing, as that could have altered the results. Twenty-five/50 (50%) were positive to indoor allergens alone, 14/50 (28%) were positive to both indoor and outdoor allergens. Trees were the most common outdoor allergens and mouse, cockroach, and dust mite were the most common indoor allergens. Spirometry was available on 41 subjects of which 32 also consented to post-albuterol testing. Of the remaining 9, 4 were unable to meet ATS criteria of reproducibility and satisfactory exhalation (22). Five of the subjects had received pre-anesthetic medication and were unable to perform spirometric maneuvers. Although no subject had been on a bronchodilator on the day of testing, only 4 of 32 (8%) showed a positive bronchodilator response demonstrated by at least a 12% increase in FEV₁ (23).

OSA severity was based on AHI, categorized as follows: absent (AHI <2), mild (AHI 2–<5), moderate (AHI 5–10), and severe (AHI >10). The corresponding distribution of the four severity levels were 9 (18%) absent, 11 (22%) mild, 15 (30%) moderate, and 15 (30%) severe. There was no association between current asthma by ISAAC and severity of OSA; however, lifetime history of asthma by ISAAC correlated with significantly higher AHI scores (see Figure 1, Table 2).

There were no significant differences in demographics, pulmonary function test results, or sleep parameters among current asthmatics and non-asthmatics (see Table 3). In the

TABLE 2.—Student's *t* test of AHI means by lifetime asthma history.

Lifetime asthma	Observed	Mean AHI	SE
No	20	5.855	1.407302
Yes	30	14.01	2.884004

AHI = Apnea-hypopnea index.
 $t = -2.19$, $p = 0.033$.

TABLE 3.—Descriptive statistics by current asthma.

	Current Asthma Yes (N = 22) mean ± SD	No (N = 28) mean ± SD
Age (years)	9.7 ± 3.1	8.8 ± 3.6
BMI (kg/m ²)	29.5 ± 13.0	23.3 ± 8.3
BMI (% predicted)	84.0 ± 26.7	73.3 ± 35.3
FEV ₁ (L)	1.7 ± 0.89	1.6 ± 0.72
FEV ₁ (% predicted)	89 ± 22	91 ± 23
FVC (L)	1.8 ± 1.1	1.9 ± 1.1
FVC (% predicted)	87 ± 21	89 ± 21
FEV ₁ /FVC	0.91 ± 0.09	0.94 ± 0.91
FEF _{25–75} (L)	2.1 ± 0.89	1.8 ± 0.77
FEF _{25–75} (% predicted)	88 ± 30	78 ± 19
Peak ETCO ₂ (see Torr)	51 ± 4	52 ± 4
Nadir SaO ₂ (%)	84 ± 11	83 ± 10
AHI	9.6 ± 12	11 ± 14
Arousal Index/hour	13.0 ± 9.0	12.4 ± 6.1
TST (minutes)	348.3 ± 51.4	348.8 ± 82.7
Sleep efficiency (%)	91.6 ± 9.1	90.3 ± 9.0

All comparisons, NS.

regression model, we found that a history of asthma predicts an 8.8 points increase in AHI. As for the patients without asthma, sleep efficiency significantly correlated with a 0.79 point decrease in AHI, while age has no significant correlation (see Table 4).

Assignment into the poorly controlled asthma group was based on whether the subject had had an exacerbation in the last year and/or used a bronchodilator in the prior month. We found that the mean AHI was more than eight points higher in subjects with poorly controlled asthma ($p < 0.05$; see Table 5).

DISCUSSION

The main finding in this study is that a lifetime history of asthma, extracted from the ISAAC questionnaire, was associated with more severe OSA. This is in keeping with our original hypothesis. The following discussion reviews these findings in light of what is known currently in the literature.

Asthma is a known comorbid factor for OSA in both adults and children (1, 24, 25). Both disease entities share risk factors such as allergic rhinitis, gastroesophageal reflux, and obesity (26, 27). Additionally, there are similar cytokine, chemokine, and histologic changes in both asthma and OSA (28). Treatment of OSA with CPAP improved asthma symptoms (29) as well as bronchial hyper-reactivity in adults (30). Although much is known about the association of these two conditions, it is not known whether asthma affects the severity of OSA.

The majority ($n = 32$, 64%) of this referral population reported a lifetime history of asthma by the ISAAC

TABLE 4.—Regression results for apnea-hypopnea index.

AHI	Adjusted R ² = 0.329			P = 0.001		
	Coeff.	SE	T	p > t	95% CI	
Asthma history	8.79575	3.85013	2.28	0.029	0.96261	16.62889
Age	−0.04186	0.59580	−0.07	0.944	−1.25403	1.17032
Sleep efficiency	−0.78798	0.20226	−3.90	0.000	−1.19948	−0.37648
Constant	76.56289	20.05313	3.82	0.001	35.76449	117.36130

TABLE 5.—Poorly controlled asthma and OSA severity.

Group	Obs	Mean AHI	SD
Good control/no asthma	18	5.56111	6.26410
Poor	32	13.66562	15.41168
		$t = -2.13$	$p = 0.039$

OSA = obstructive sleep apnea.

questionnaire. This is five times the national prevalence rate of 10% (4) as well as the statewide rate of 10.6% (6). This rate is also significantly higher than the rate previously reported from urban schools in Baltimore City (6), which constitutes the same catchment area as this referral population. This is not a surprising finding given that the majority of the subjects were African-American and obese (1). The majority ($n = 27$, 54%) were also found to be atopic by skin prick testing. Again, this finding is in keeping with the literature regarding the comorbidities associated with childhood asthma (26). However, this is lower than the reported 80% prevalence of atopy in a multi inner-city study of asthmatic children (31).

Asthma is a known comorbid factor in childhood OSA (3). In our study population, the lifetime history of asthma correlated significantly with an increase in the mean AHI (see Table 2). Conversely, when considering current asthma, there was no significant difference in any of the sleep parameters such as AHI, arousal index, TST, sleep efficiency, peak ETCO_2 , or nadir SaO_2 (Table 3). No significant differences in spirometry were noted between these two groups either. This may not be a surprising finding as prior reports have indicated that airway inflammation may be a more sensitive index of assessing asthma control (32).

Yigla et al. (33) reported the high prevalence of OSA in difficult-to-treat asthma, defined by continuous oral steroid use. While we did not specifically record steroid use or recent treatment with steroid bursts, using our definition for poorly controlled asthma, we supported their finding that poorly controlled asthma correlates with OSA severity (see Table 5). This finding suggests that OSA severity affects how well asthma is controlled.

This study has several major limitations. Most prominent among them is the small number of subjects. Further, we did not consistently test reversibility with albuterol in all subjects. Moreover, we did not obtain details of asthma exacerbations and treatment with steroids. Additionally, this is a referral-based convenience sample and not a population-based study, which may explain the high prevalence of reported asthma. Finally, due to the small sample size, we are hesitant to generalize from these results; however, they are promising for future research using a larger sample.

We previously reported that in a group of inner-city children who snored, asymptomatic asthma decreased the likelihood of OSA (14). The present results are in contrast with our earlier findings in a similar cohort but are in keeping with our original hypothesis. We speculated that in our previous group, parents were "over-vigilant" about reporting asthma in snoring children. This alone does not account for the differences between these findings and those of our previous study. Therefore, we looked at measurable differences between the two cohorts and found several that could explain the inconsis-

tency. First, a smaller proportion of subjects in this group had asymptomatic asthma (not significant). Further, the subjects in this group are significantly older (9.26 years vs. 7.2 years, $p < 0.05$). Finally, subjects in this cohort have a higher mean BMI (26.1 vs. 22.4 $p < 0.05$). While these differences might not fully account for the discrepancy, they do provide evidence suggesting that these two cohorts sampled while from the same catchment area, were not identical.

In conclusion, in this pilot study of predominantly inner-city African-American children, we found evidence of a relationship between OSA severity and asthma severity. Further, the differences between the cohorts in our current and previous studies suggest that a much larger sample is necessary to obtain reliable and valid findings. Findings from such a study could improve our understanding of the relationships between OSA and asthma that could improve success in treatment for children who have both diseases.

DECLARATION OF INTEREST

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

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