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Asthma and Subjective Sleep Disordered Breathing in a Large Cohort of Urban Adolescents

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Abstract

Objective—Sleep disordered breathing (SDB) has not been well studied in urban adolescents with asthma in community settings. Nor has the association of SDB symptoms and asthma severity been studied. We characterized self-reported symptoms suggesting SDB and investigated the association of SDB symptoms, probable asthma, and asthma severity.

Methods—9,565 adolescents from 21 inner-city high schools were screened for an asthma intervention study. Students reported on symptoms suggesting SDB using questions from the 2007 NHANES, if they were ever diagnosed with asthma, and on asthma symptoms. Using generalized linear mixed models with logit link with school as a random intercept and adjusting for age, gender, and race/ethnicity, we examined associations of SDB symptoms, and demographic characteristics, probable asthma, and asthma severity.

Results—12% reported SDB symptoms. Older and biracial participants (compared to Caucasian) had higher odds of symptoms suggesting SDB ($p < .001$). Compared to those without probable asthma, adolescents with probable asthma had 2.63 greater odds of reporting SDB symptoms ($p < .001$). Among those with probable asthma, the odds of reporting SDB symptoms increased with asthma severity. When exploring daytime severity and severity due to night waking separately, results were similar. All results remained significant when controlling for age, gender, and ethnicity.

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Conclusions—In a large urban community cohort of predominately ethnic minority adolescents, self-reported SDB symptoms were associated with probable asthma and increased asthma severity. This study highlights the importance of SDB as a modifiable co-morbidity of asthma.

Keywords

Co-morbidities; inner city; snoring; asthma severity; cross-sectional

Asthma prevalence is elevated in adolescents, with up to 12% of adolescents being diagnosed with asthma [1]. Adolescents have greater asthma-related morbidity than younger children, including more exacerbations and higher mortality rates [2]. Moreover, youth who live in urban settings experience multiple stressors that have the potential to negatively impact their asthma control [3]. Asthma symptoms occur more frequently at night and in the early morning than during the day [4]; this in turn results in nocturnal awakening, which is commonly used as an indicator of asthma morbidity [5].

Sleep disordered breathing (SDB) also has high prevalence and morbidity in youth. The spectrum of SDB ranges from primary snoring (PS) to partial or complete airway obstruction, termed the obstructive sleep apnea syndrome (OSAS) [6]. Primary snoring (PS) has been reported in 3 – 12% of the pediatric population, and OSAS in 1 – 3% [6-11]. SDB is elevated in ethnic minorities, particularly in African-American children [12-18], and in adolescents, with rates being reported between 6 – 20% [13, 18]. SDB is associated with long-term consequences including, chronic systemic inflammation [19], metabolic abnormalities, cardiovascular instability [20], and neurocognitive morbidity [21, 22]. Despite these adverse consequences, it may go unnoticed by parents, and is not often screened for by pediatricians [23].

While studies have documented that SDB is highly prevalent in children with asthma aged 13 and younger [12, 15, 24-28], less is known about this association in adolescents; we are aware of only two studies examining adolescent-only, but non-US, populations [17, 29]. Further, most prior studies had relatively small sample sizes (i.e., fewer than 200 participants) [14, 15, 17, 19, 24-26], and often examined convenience samples of children followed at pulmonary, sleep or ENT clinics [12, 14, 19, 25, 27]. With the exception of one study with 4- to 18-year-olds [26], we are also aware of no studies that have examined the association of SDB and asthma severity in adolescents.

SDB treatments have been found to be effective [6]. Therefore, it is critical to understand factors associated with SDB to ensure such treatments are targeted toward those most at-risk. Further, because SDB is a treatable condition that may impact asthma, understanding the relationship of SDB and asthma among urban adolescents is vital to help this at-risk population achieve asthma control.

This study seeks to contribute to the evidence demonstrating the link between pediatric asthma and SDB. We sought (1) to characterize symptoms suggestive of SDB in an urban community sample of predominately low-income, urban Latino/a and African America high school students by examining the association of self-reported SDB symptoms and demographic characteristics, and (2) to test the association of self-reported asthma status and

severity to self-reported SDB symptoms. We hypothesized that symptoms suggestive of SDB will be: (1) relatively common among adolescents; (2) elevated in ethnic minorities relative to White, Non-Hispanics; and (3) associated with an increased risk for probable asthma and with an increase in asthma severity.

Methods

Study Overview

Data are from a cross-sectional survey of 9807 ninth- through twelve-graders from 21 inner city high schools, who completed a case detection survey to determine eligibility for a larger clinical trial examining the efficacy of a school-based intervention for adolescents with undiagnosed asthma [reference removed for blinding]. Students in the larger trial were enrolled over four years; this study makes use of the screening data from Study Year 3 when SDB symptom data was added to the protocol. Schools served predominately low-income, Latino/a or African American students. We excluded 242 students with incomplete asthma or sleep data, for a final sample of 9565 students. The institutional review boards of New York University School of Medicine, Columbia University College of Physicians and Surgeons, and the New York City Department of Education (DOE) approved all study procedures, which were also reviewed by administrators at respective schools.

Measures

All measures were self-reported. A waiver of parental consent was granted for completion of the case detection survey only; informational letters describing the survey were sent home to parents via the students. Students completed the survey as a group in class; trained research assistants proctored the survey twice in each class to ensure absent students had the opportunity to complete the survey. Demographic items included gender, race/ethnicity, and date of birth, which was used to calculate age.

Asthma Status—Students reported if they were ever diagnosed with asthma, reactive airway disease or wheezy bronchitis, and they completed two brief validated measures, which were used to classify students as having probable asthma (yes/no) and determine their asthma severity [30, 31]. First, students reported the frequency of seven signs and symptoms (0 = Never, 1 = Sometimes, 3 = A lot); students who endorsed three or more of these symptoms were considered to have probable asthma. This survey was validated against clinical evaluation and positive endorsement of at least three symptoms provided a sensitivity of 80% and specificity of 70% [30]. Next, students reported the frequency in the past 12 months of six asthma symptoms (0 = Never, 5 = Every day and all the time) to estimate their asthma severity using both daytime and nighttime symptoms [31]. This frequency criterion was found to map onto the on N.H.L.B.I. guidelines in place at the onset of the study [31].

The presence of nighttime asthma symptoms could lead participants to report SDB symptoms, and thus potentially confound the association between asthma severity and SDB. Therefore, we also re-assessed severity of asthma based on only daytime symptoms (i.e.,

night wakening was excluded from severity) and separately from only nighttime symptoms (i.e., daytime symptoms were excluded from severity).

Symptoms of Sleep Disordered Breathing (SDB)—Participants answered two questions from the 2007 National Health and Nutrition Examination Survey (NHANES), a yearly epidemiology survey administered to a nationally representative sample, regarding the frequency in the past 12 months of (1) snoring while sleeping and (2) snorting, gasping, or stop breathing while asleep (0 = Never; 3 = Frequently (5 or more nights per week)).[32] Following criteria established by other investigators [6, 33], adolescents were considered to have self-reported SDB if they endorsed either symptom as “occasionally (3-4 nights per week)” or “frequently (5+ nights per week)”. These sleep questions have been used in other studies as a surrogate for sleep disorders [33-38].

Statistical Analysis

We first characterized the sample with respect to demographic and clinical characteristics (i.e., asthma prevalence and severity, and symptom's suggestive of SDB) using descriptive statistics. To explore the relationship between demographic characteristics and symptoms suggestive of SDB, we modeled self-reported SDB (yes/no) as a function of gender, race/ethnicity, and age. To test the association between asthma and symptoms suggestive of SDB we modeled self-reported SDB (yes/no) as a function of probable asthma (yes/no) or asthma severity (intermittent, mild persistent, moderate persistent, and severe persistent) adjusting for age, gender, and race/ethnicity. All multivariable models were fit using a generalized linear mixed models approach with logit link and school as a random intercept with complete cases. We conducted analysis using the R statistical software (version 3.0.3) and a significance level of 0.05, two-sided was used. To explore whether the relationship between asthma severity and symptoms of SDB was due to night wakening, we also conducted analyses where severity was estimated using only daytime symptoms and only nighttime symptoms. Because results from the univariate and multivariate models were consistent, to be parsimonious, we report findings only from the multivariate models.

Results

Demographic and Asthma Characteristics

Table 1 reports the characteristics of the sample. Almost half the sample (46%) was female. The vast majority were Latino/a (44%) and African American (31%), reflecting the demographics of the schools. The mean age of the participants was 15.9 years. More than half of the adolescents reported symptoms of intermittent asthma (62%); 14% reported mild persistent symptoms, 14% moderate persistent, and 10% severe persistent.

Prevalence of Self-reported Sleep Disordered Breathing and Associations to Demographic Characteristics

Nearly 13% of the sample reported symptoms suggestive of SDB (Table 1). Table 2 reports the results of the adjusted models testing the effects of the demographic characteristics. Gender did not significantly predict SDB symptoms. Older adolescents had significantly higher odds of reporting symptoms consistent with SDB (for each 1 year increase in age, the

odds ratio (OR) for reporting SDB symptoms: 1.09; 95% confidence interval (CI): 1.03 to 1.15; $p < .001$. Compared to Caucasian adolescents, bi-racial adolescents had significantly higher odds of reporting symptoms consistent with SDB ($p < .05$).

Asthma Predictors of SDB Symptoms

Compared to those without probable asthma, adolescents with probable asthma had 2.63 higher odds of reporting symptoms suggesting SDB (95% CI, 2.30 to 3.00, $p < .001$), controlling for age, gender, and ethnicity. Table 3 displays the results for all the pair-wise comparisons for asthma severity adjusting for age, gender, and race/ethnicity. When severity was estimated considering N.H.L.B.I. criteria accounting for both day and night symptoms [31] (Row 1 in the Table), those with severe persistent asthma had significantly higher odds of SDB symptoms compared to all other severity groups. Those with moderate persistent asthma had significantly higher odds of symptoms suggesting SDB only when compared to those with intermittent asthma. As detailed in Rows 2 and 3 of Table 3, we found the results were similar when severity assessed using only daytime symptoms and when using only night wakening, respectively.

Discussion

This study is among the largest to assess asthma and self-reported symptoms of SDB in an urban community sample of predominately Latino/a and African American adolescents. We also report results from the first study of which we are aware to examine the association of asthma severity and symptoms suggesting SDB among adolescents. Among 9565 9th through 12th grade public high school students in New York City, symptoms of SDB were common, particularly in older adolescents and those who self-reported being bi-racial. Further, adolescents with self-reported SDB symptoms were more likely to report having probable asthma, and among those with probable asthma, the likelihood of reporting symptoms of SDB increased with increasing asthma severity. Although these relationships have been reported in other pediatric and adult populations, our data extend these findings to the adolescent ethnic minority population, where both conditions are thought to be disproportionately common, and reinforce their generality.

Among demographic correlates, the association of gender and symptoms consistent with SDB is less clear. We did not find an association between SDB symptoms and gender, which contradicts the adult literature [39] and some of the pediatric literature [12, 40], where male gender is an important risk factor. There is a slight predominance of SDB in pre-pubertal boys that increases after puberty [6, 11, 13, 14, 16].

Our finding that probable asthma and asthma severity are associated with increased risk of symptoms suggesting SDB is concordant with smaller studies that measure SDB objectively, either with PSG evaluation or overnight oximetry monitoring [12-14, 25, 26, 41, 42]. This study makes a novel contribution by examining asthma severity for daytime symptoms and night wakening separately. Our findings indicated that self-reported SDB symptoms were strongly associated with asthma severity, even when the potential confounder of night awakening due to asthma was factored out. While we cannot conclude causation due to the

cross-sectional nature of our data, this finding suggests that nocturnal waking due to asthma is not confabulated with symptoms of SDB, and thus warrants further investigation.

SDB is a modifiable condition, and there are several successful treatment modalities including, weight loss (for the obese child), intramandibular expanders (for those with narrow palates), nasal steroid therapy (for those with only adenoidal hypertrophy), **adenostonsillectomy** (for those with adenoidal and tonsillar hypertrophy) and continuous positive pressure (for those with no surgical correctable condition) [6]. To date, some studies have suggested that pediatric asthma severity improves with OSA treatment [25, 43]. The converse – whether improved pediatric asthma control improves SDB symptoms – has yet to be examined.

The strengths of our study include the large sample size and focus on an understudied, at-risk sample, namely ethnic minority, urban adolescents. Our study has limitations. One is that we used questionnaire data to determine presence of asthma and SDB symptoms, as opposed to pulmonary function tests or attended polysomnography (PSG), respectively. This may have resulted in the over-reporting of asthma prevalence, asthma severity, and symptoms suggestive of SDB in our sample. Although the gold standard for the diagnosis SDB is attended PSG, it is often not feasible to perform this test in a large population due to the time, effort, and expense of laboratory studies. However, questionnaires derived from self-report of snoring and other sleep and wake behaviors have been used as surrogate predictors of SDB [6, 7, 33–38]. Such questionnaires are able to predict those at high risk for having SDB, but are poor at determining SDB severity and may not differentiate primary snoring from OSAS [6–8, 54, 55]. Also, we assessed symptoms of asthma and SDB at a single time point, possibly introducing a recall bias. It also precluded our ability to establish directionality of the relationship between asthma and symptoms consistent with SDB. This brief survey was able to capture limited quality data on a large scale, but in doing was unable to examine other important co-morbidities associated with both asthma and SDB, such as obesity and atopy.

Conclusions

We examined the association of asthma prevalence and severity, and symptoms suggestive of SDB among adolescents in a large urban community setting. Our data adds to the growing literature demonstrating symptoms of SDB as an important co-morbidity of pediatric asthma. Importantly, we report that nighttime awakenings due to asthma did not drive the association between asthma severity and symptoms suggesting SDB, indicating that SDB symptoms are not just misdiagnosed asthma symptoms. These findings should prompt further investigation regarding the potential pathophysiological significance of the relationship of SDB and asthma, as well as the directionality of this relationship. Until then, given the deleterious influence each disorder may have on the other [56], it is important for clinicians to screen for SDB symptoms among patients with asthma, particularly when the asthma is poorly controlled, in order to treat this co-morbid condition. Similarly, investigators enrolling and studying individuals with one of these disorders should consider capturing data on the other entity, as well as generating and testing hypotheses around interactions of the asthma and SDB.

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Abbreviations

aOR	adjusted odds ratio
CI	confidence interval
OSAS	obstructive sleep apnea syndrome
OR	odds ratio
PS	primary snoring
SDB	sleep disordered breathing

Table 1
Demographic and clinical characteristics (N = 9565)

Variable	Available N	N (%) ^a
Age [Mean (SD)]	9374	15.9 (1.2)
Gender (Female)	8812	4090 (46.4)
Ethnicity	9286	
Caucasian		355 (3.8)
African American		2862 (30.8)
Latino		4039 (43.5)
Other		1267 (13.6)
Bi-racial/ethnic		763 (8.3)
Symptoms Suggesting Sleep Disordered Breathing (Yes)	9565	1220 (12.8)
Probable Asthma (Yes)	9556	3033 (31.7)
Asthma Symptom Severity: NHLBI	5617	
Classification ^b		3461 (61.6)
Intermittent		788 (14.1)
Mild Persistent		809 (14.5)
Moderate Persistent		559 (9.9)
Severe Persistent		
Asthma Symptom Severity: Daytime Symptoms ^b	5541	
Intermittent		3574 (64.4)
Mild Persistent		740 (13.4)
Moderate Persistent		831 (15.0)
Severe Persistent		396 (7.2)
Asthma Symptom Severity: Nighttime	1592	
Symptoms ^b		746 (46.8)
Intermittent		337 (21.2)
Mild Persistent		218 (13.7)
Moderate Persistent		291 (18.3)
Severe Persistent		

^aMissing values were excluded from calculation of percentages.

^bAmong those with probable asthma only.

Table 2
Associations of Symptoms Suggesting SDB Among the Full Sample Adjusting for Age, Gender, and Race/Ethnicity

Variable	Self-Reported SDB		Model-based OR ^a (95% CI)
	No (N = 7423)	Yes (N = 1087)	
Age (mean (sd))	15.9 (1.18)	16.01 (1.23)	1.09 *** (1.03, 1.15)
Gender (% Female)	46.65	48.99	1.11 (0.98, 1.27)
Race/Ethnicity (%)			
White, Non-Hispanic	3.8	3.7	(Ref)
African American	29.7	36.7	1.30 (0.91, 1.84)
Latino	44.6	37.6	0.88 (0.62, 1.25)
Other	14.1	10.6	0.82 (0.56, 1.21)
Bi-racial/ethnic	7.8	11.4	1.54 * (1.04, 2.27)

^aResults from a generalized linear mixed model using a logit link with school as a random intercept.

*
 $p < .05$.

 $p < .001$.

Table 3
Effect of Asthma Severity on Symptoms Suggesting SDB Among Those with Probable Asthma Adjusting for Age, Gender, and Race/Ethnicity

Variable/Model	n	Self- Reported SDB (%)	Model-based OR (95% CI) ^a												
			No	Yes	Severe VS Intermittent	Severe VS Mild	Moderate VS Intermittent	Moderate VS Mild	Mild VS Intermittent						
NHLBI Severity (N = 2476)															
Intermittent	1087	46.5	34.2												
Mild Persistent	480	19.6	18.4												
Moderate Persistent	510	20.2	22.5	2.44 ^{***}	(1.86, 3.20)	1.91 ^{***}	(1.40, 2.61)	1.62 ^{**}	(1.20, 2.18)	1.51 ^{**}	(1.16, 1.97)	1.18	(0.87, 1.60)	1.28	(0.97, 1.69)
Severe Persistent	399	13.7	24.9												
Daytime Severity (N = 2450)															
Intermittent	1194	50.8	41.2												
Mild Persistent	458	19.0	17.7												
Moderate Persistent	529	21.1	23.4	2.34 ^{***}	(1.73, 3.15)	2.03 ^{***}	(1.43, 2.86)	1.75 ^{***}	(1.26, 2.42)	1.34 [*]	(1.04, 1.73)	1.16	(0.85, 1.58)	1.15	(0.88, 1.52)
Severe Persistent	269	9.1	17.7												
Nighttime Severity (N = 1124)															
Intermittent	455	43.3	32.9												
Mild Persistent	268	24.3	22.5												
Moderate Persistent	177	15.1	17.6	2.02 ^{***}	(1.41, 2.90)	1.70 ^{**}	(1.15, 2.52)	1.33	(0.86, 2.03)	1.52 [*]	(1.03, 2.26)	1.28	(0.84, 1.96)	1.19	(0.83, 1.70)
Severe Persistent	224	17.3	27.0												

^aResults from generalized linear mixed models using a logit link with school as a random intercept and adjusting for age, gender, and race/ethnicity.

^{*}*p*<.05.

^{**}*p*<.01.

^{***}*p*<.001.