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Polysomnographic characteristics of adolescents with asthma and low risk for sleep-disordered breathing

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Abstract

Purpose The aim of this study was to describe the polysomnographic characteristics of adolescents with asthma who are at low risk for sleep-disordered breathing (SDB) based on the Pediatric Sleep Questionnaire (PSQ).

Methods Overnight polysomnography was performed on 85 adolescents with asthma and a score < 0.33 on the PSQ. The Asthma Control Questionnaire was used to define "well-controlled" versus "inadequately controlled" asthma.

Results Mean age of participants was 14.5 ± 1.6 years (range, 11 to 17 years), 63.5% were girls, 57.6% were Caucasians, and the mean body mass index percentile was 65.1 ± 26.5. Asthma was well-controlled in 51.7% of the adolescents and inadequately controlled in 15.3%. Mean sleep efficiency (SE) was 88.0 ± 11.1%, and 24.7% had SE < 85%. Mean wakefulness after sleep onset (WASO) was 40.9 ± 44.0 min, and the mean arousal index was 10.8 ± 5.6 per hour. The mean apnea/hypopnea index (AHI) was 2.3 ± 4.2, and 29.4% of participants had SDB (defined by an AHI ≥ 2). Compared with normative values, adolescents with asthma had more nocturnal awakenings and WASO, and less REM sleep. SDB risk was higher in boys [odds ratio = 4.6 (confidence interval 1.4–14.7), $p = 0.01$]. Asthma control did not impact sleep and respiratory parameters, with no differences found between youth with well-controlled and inadequately controlled asthma.

Conclusions Adolescents with asthma are at increased risk of sleep-disordered breathing and suffer from disturbances in sleep continuity with more arousals and sleep fragmentation. Study results highlight the importance of proper screening for sleep-disordered breathing in adolescents with asthma.

Keywords Asthma · Sleep · Polysomnography · Children · Adolescence · Sleep-disordered breathing

Introduction

Asthma is the most common non-communicable disease among children [1]. Approximately, 8.3% of children under the age of 18 years have active asthma and its prevalence is increasing among adolescents and the poor [2]. Untreated and poorly controlled asthma can result in frequent emergency department or urgent care visits, as well as hospitalizations [2, 3]. In addition, asthma-related illnesses or exacerbations can result in a significant number of missed school days for youth, as well as work days for parents [3–5]. Thus, it is important to identify and treat any concurrent medical issues that may interfere with optimal asthma management, including sleep-disordered breathing (SDB).

Symptoms of nocturnal asthma are prevalent among children [6] and are commonly associated with sleep disturbances including short sleep duration, parasomnias, and frequent nighttime awakenings [7–9]. Nocturnal awakening in children with asthma can be associated with poor school attendance and performance [10]. Moreover, sleep disturbances from nocturnal asthma may negatively impact daytime cognitive functioning and learning abilities of affected children [11].

However, few studies have considered polysomnographic parameters of children with asthma [11–13] that may contribute to, or result from, nocturnal asthma. A retrospective study [12] and a comparative study [13] evaluated sleep and breathing parameters among younger

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children (≤ 12 years) with asthma and reported longer sleep latency and less slow wave sleep. Another small study described sleep quantity and quality in children with asthma and showed reduced sleep efficiency and higher rates of arousals [11]. To date, there is limited data on polysomnographic characteristics of sleep and breathing parameters of older adolescents with active asthma. The aim of this study was to describe the polysomnographic characteristics among adolescents with asthma who were otherwise felt to be low risk for SDB.

Methods

Participants

Study participants were adolescents with asthma who underwent overnight polysomnography as part of eligibility screening for a study examining the impact of sleep duration on asthma outcomes [14]. Participants were recruited from outpatient clinics and recruitment flyers at National Jewish Health, as well as radio advertisements. Inclusion criteria were (a) age (11–17 years); (b) evidence of active asthma in the last year, defined as presence of recurrent daytime or nighttime symptoms (cough, wheeze, chest tightness, shortness of breath) or asthma exacerbations that required an urgent care visit, hospitalization or systemic corticosteroids in the past year, or the use of inhaled or oral medications for asthma; and (c) an average weekday sleep opportunity (bedtime to wake time) of 7.5 to 9 h. For the parent study protocol, adolescents participated in a sleep manipulation protocol comparing 6.5 vs. 9.5 h time in bed. Thus, to be eligible, typical sleep duration was required to be 7.5 to 9 h to ensure both an increase and decrease in sleep duration [14]. Exclusion criteria were (a) presence of another significant chronic illness (including atopic dermatitis) or diagnosed sleep disorder, (b) parent report of professionally diagnosed psychiatric disorder or developmental disorder (e.g., autism), (c) suspicion of recurrent illegal substance use, (d) history of neurologic illness or injury, (e) currently pregnant, (f) use of a medication with known effects on sleep or daytime alertness, (g) daily consumption of more than 1 cup of coffee or "energy drink" or more than two caffeinated sodas, (h) obesity (body mass index (BMI) > 98th percentile), (i) cigarette smoking or smokeless tobacco product use in the past year, and (j) a score of ≥ 0.33 on the Pediatric Sleep Questionnaire (PSQ) suggesting risk for sleep-disordered breathing [15]. Parent/guardian consent and adolescent assent were obtained from all participants and in accordance with the National Jewish Health Institutional Review Board.

Measures

Polysomnography All eligible participants had one night of lab-based polysomnography (PSG) at the Sleep Center—National Jewish Health. The studies were recorded using Embla sleep diagnostic (Natus Neurology, Middleton, WI). The montage included electroencephalogram (EEG) channels (F4-M1, F3-M2, C4-M1, C3-M2, O1-M2, and O2-M1), bilateral electrooculogram (EOG), three channels of chin electromyogram (EMG), two channels of anterior tibialis EMG, nasal thermistor and nasal prong pressure transducer, two respiratory effort belts across the chest and abdomen, pulse oximeter, electrocardiogram (EKG), and snoring and body position sensors. PSGs were scored using Sandman Elite PSG software (Natus Neurology, Middleton, WI) and according to the American Academy of Sleep Medicine pediatric scoring criteria [16, 17]. Sleep parameters of time in bed (TIB), sleep period time (SPT), total sleep time (TST), wakefulness after sleep onset (WASO), sleep latency, rapid eye movement (REM) latency, sleep efficiency, and time spent in N1, N2, N3, and REM sleep were reported. Obstructive apnea was defined by cessation of airflow for more than two breaths in the presence of respiratory effort. Hypopnea was defined by ≥ 50% reduction in respiratory airflow accompanied by a ≥ 3% decrease in oxygen saturation and/or an arousal. Obstructive apnea/hypopnea index (AHI) was defined by the number of obstructive apneas and hypopneas per hour of sleep. Central apnea event was defined by the cessation of airflow for more than two breaths in the absence of respiratory effort, and central AHI was defined by the number of central apneas and hypopneas per hour of sleep. Total AHI was the combination of obstructive and central AHI, and SDB was defined as having an AHI ≥ 2. Additional measures included lowest oxygen saturation (nadir), average heart rate during sleep, and the arousal index, defined by the number of arousals (> 3 s) per hour of sleep.

Asthma control The Asthma Control Questionnaire (ACQ) [18, 19] is one of two asthma control instruments designated as core measures of NIH-initiated clinical research [20]. The ACQ includes 6 questions that assess symptom frequency, rescue therapy use, and activity limitation, as well as clinically measured FEV1 over a 7-day period. Participants who scored ≤ 0.75 were considered to have well-controlled asthma, and those who scored ≥ 1.5 were considered as inadequately controlled asthma [18].

The sleep-related breathing disorder (SRBD) scale of the pediatric sleep questionnaire (PSQ) Core components of sleep-disordered breathing that may have been associated with the diagnosis of OSA were examined with the SRBD of the PSQ.

This measure includes symptom items that ask about snoring (four items), daytime sleepiness (four items), and inattentive or hyperactive behavior (six items) [21].

Children's report of sleep patterns sleepiness scale (CRSP-S) Daytime sleepiness was evaluated using the CRSP Sleepiness Scale (CRSP-S) [22]. The scale is a validated five-point screen of daytime sleepiness that asks how often (in the past week) the child felt sleepy or fell asleep while eating, talking with someone else, playing, riding in a car or bus for a short time (< 20 min), or at school.

Data analysis

IBM Statistical Package for Social Sciences software (SPSS) for Windows, version 24.0 (Armonk, NY: IBM Corp), was used for data processing and analysis. Participants' characteristics were described using frequency distribution for categorical variables and mean and standard deviation for continuous variables. Tests of significance between groups were carried out using Pearson chi-square/Fisher's exact test for categorical variables and student *t* test for continuous variables. Multivariate logistic regression analysis was conducted to determine the association between gender and the presence of SDB. The results of the logistic regression analysis are presented as odds ratio (OR) and their 95% confidence interval (CI). Means for the polysomnographic parameters in this study were compared with normal values in adolescents who do not have asthma [23–25] using Welch's *t* test. A p value of < 0.05 was considered statistically significant for all performed analyses.

Results

Participant characteristics

Mean age of the participants was 14.5 ± 1.59 years (range 11 to 17 years). As seen in Table 1, the majority were girls (63.5%) and 57.6% were Caucasian. The mean body mass index (BMI) percentile was 65.3 ± 25.5. Allergic rhinitis was prevalent (35.5%) while other comorbidities were uncommon: attention-deficit hyperactivity disorder (7.1%), anxiety (4.7%), and GERD (4.7%). The mean PSQ score was 0.13 ± 0.09 (range, 0 to 0.32), suggesting low risk for sleep-disordered breathing. The prevalence of frequent and loud snoring was low (< 5%) and comparable to normal adolescents [26]. Similarly, daytime sleepiness was not significantly different from normal adolescents ($p < 0.05$) [22, 27]. The mean ACQ score was 0.89

Table 1 Demographic and anthropometric characteristics

	All ($n = 85$)	Boys ($n = 31$)	Girls ($n = 54$)	p value
Age, years [mean ± SD]	14.48 ± 1.59	14.26 ± 1.52	14.61 ± 1.63	0.328
Body mass index (BMI) [mean ± SD]	22.61 ± 4.22	23.82 ± 4.60	21.92 ± 3.87	0.045
BMI, percentile [mean ± SD]	65.09 ± 26.53	73.84 ± 26.01	60.07 ± 25.73	0.020
Race [*n* (%)]				
White/Caucasian	49 (57.6)	17 (54.8)	32 (59.3)	0.845
African American	17 (20.0)	6 (19.4)	11 (20.4)	
Other	19 (22.4)	8 (25.8)	11 (20.4)	
Allergic rhinitis [*n* (%)]	27 (35.5)	9 (33.3)	18 (36.7)	0.767
Anxiety [*n* (%)]	4 (4.7)	1 (3.2)	32 (5.6)	0.625
Attention-Deficit/Hyperactivity Disorder [*n* (%)]	6 (7.1)	3 (9.7)	3 (5.6)	0.475
Gastroesophageal Reflux Disorder [*n* (%)]	4 (4.7)	2 (6.5)	2 (3.7)	0.565
Children's Report of Sleep Patterns Sleepiness Scale [mean ± SD]	1.90 ± 0.57	1.86 ± 0.64	1.90 ± 0.57	0.580
Pediatric Sleep Questionnaire (PSQ) [mean ± SD]	0.13 ± 0.09	0.15 ± 0.10	0.12 ± 0.09	0.262
PSQ Snoring Scale [mean ± SD]	0.05 ± 0.14	0.05 ± 0.17	0.05 ± 0.13	0.948
Always snore [*n* (%)]	4 (4.8)	2 (6.7)	2 (3.7)	0.614
Snore loudly [*n* (%)]	4 (4.8)	1 (3.3)	3 (5.7)	0.999
PSQ Daytime Sleepiness Scale [mean ± SD]	0.20 ± 0.25	0.27 ± 0.27	0.16 ± 0.23	0.066
PSQ Inattention/Hyperactivity Scale [mean ± SD]	0.16 ± 0.18	0.19 ± 0.18	0.14 ± 18	0.182
Asthma Control Questionnaire (ACQ) [mean ± SD]	0.90 ± 0.75	0.91 ± 0.83	0.90 ± 0.71	0.937
Well-controlled (ACQ < 0.75) [*n* (%)]	44 (51.8)	18 (58.1)	26 (48.1)	0.563
Borderline (ACQ 0.75–1.5) [*n* (%)]	28 (32.9)	8 (25.8)	20 (37.0)	
Inadequately controlled (ACQ >1.5) [n (%)]	13 (15.3)	5 (16.1)	8 (14.8)	

± 0.75 (range, 0 to 3.33). Half of the participants (52.9%) had well-controlled asthma while 15.3% were inadequately controlled. Asthma medication use included controller(s) ± bronchodilators in 40 participants (47.1%), as needed bronchodilators in 27 participants (31.8%), while 4 participants (4.7%) were not on any current asthma medications.

Sleep architecture

Table 2 shows the sleep and breathing polysomnographic parameters of the participants. Mean time in bed was 440.2 ± 32.5 min and TST was 387.2 ± 55.8 min. Sleep efficiency was 88.0 ± 11.1% and 24.7% of all participants and 48.4% of boys had sleep efficiency < 85%. Mean WASO was 40.9 ± 44.0 min and WASO % wad 9.6 ± 10.7%. The mean arousal index was 10.8 ± 5.6, spontaneous arousal index was 8.8 ± 4.0 and respiratory arousal index was 1.5 ± 2.7 per hour of sleep. Sleep and REM latencies were 13.1 ± 12.6 and 150.3 ± 6.0 min, respectively. Sleep architecture showed: N1 = 5.3 ± 4.2%, N2 = 56.9 ± 8.8%, N3 = 23.3 ± 9.6%, and REM = 14.6 ± 4.9%. As seen in Table 3, compared to normal values in adolescents [23, 25], adolescents with asthma had a significantly shorter SPT, less TST, more WASO, and higher spontaneous and respiratory arousal indices. They also had shorter sleep latency, longer REM latency, and less REM sleep than adolescents without asthma.

Gender differences

Table 2 describes polysomnographic parameters among boys and girls with asthma in the current study. Boys had lower sleep efficiency ($p = 0.002$), longer sleep latency ($p = 0.025$), and more WASO ($p = 0.009$) than girls. No gender differences were found for sleep architecture. Compared to girls, boys also had higher obstructive AHI ($p = 0.047$), lower oxygen saturation nadir ($p = 0.002$), and more SDB (51.6 vs16.7%) ($p = 0.001$). As shown in Table 1, there were no gender differences on the PSQ Snoring Scale ($p = 0.948$) or the CRSP Sleepiness Scale ($p = 0.580$).

Cardiorespiratory events

The mean total AHI was 2.3 ± 4.2, the mean obstructive AHI was 1.7 ± 2.4, and the mean central AHI was 0.7 ± 3.1. The mean desaturation index was 5.4 ± 5.3, the mean oxygen saturation nadir was 87.9 ± 2.7%, and the mean heart rate was 67.3 ± 9.1. Despite excluding adolescents with known sleep disorders and those with PSQ ≥ 0.33, 25 participants (29.4%) had SDB, with a mean AHI of 5.9 ± 6.5. Compared with normal values [24] adolescents with asthma had higher AHI (2.3 ± 4.2 vs. 0.2 ± 0.25, $p = 0.016$) and lower oxygen saturation nadir (87.9 ± 2.7 vs 93.5 ± 1.25%, $p < 0.001$) (Table 3).

Table 2 Polysomnographic parameters and gender differences

	All ($n = 85$)	Boys ($n = 31$)	Girls ($n = 54$)	p value
Time in bed, min [mean ± SD]	440.2 ± 32.5	436.1 ± 36.6	442.5 ± 30.0	0.385
Sleep period time, min [mean ± SD]	427.3 ± 33.0	419.0 ± 36.6	432.2 ± 30.1	0.078
Total sleep time, min [mean ± SD]	387.2 ± 55.8	361.8 ± 62.9	401.8 ± 45.9	0.001
Sleep efficiency, % [mean ± SD]	88.0 ± 11.1	83.2 ± 13.7	90.8 ± 8.3	0.002
Sleep efficiency (< 85%), [n (%)]	21 (24.7)	15 (48.4)	6 (11.1)	< 0.001
WASO, min [mean ± SD]	40.9 ± 44.0	57.2 ± 52.7	31.4 ± 35.2	0.009
Sleep latency, min [mean ± SD]	13.1 ± 12.6	17.1 ± 16.0	10.8 ± 9.6	0.025
REM latency, min [mean ± SD]	150.3 ± 60.0	143.2 ± 66.7	154.3 ± 56.1	0.414
N1, % [mean ± SD]	5.3 ± 4.2	6.0 ± 4.1	4.8 ± 4.2	0.217
N2, % [mean ± SD]	56.9 ± 8.8	57.2 ± 6.8	56.7 ± 9.8	0.808
N3, % [mean ± SD]	23.3 ± 9.6	22.6 ± 9.1	23.8 ± 9.9	0.590
REM, % [mean ± SD]	14.6 ± 4.9	14.3 ± 5.6	14.7 ± 4.5	0.675
Arousal Index, [mean ± SD]	10.8 ± 5.6	11.8 ± 5.1	10.3 ± 6.2	0.268
Spontaneous arousal index [mean ± SD]	8.75 ± 3.98	9.23 ± 4.14	8.45 ± 3.89	0.407
Respiratory arousal index [mean ± SD]	1.51 ± 2.68	1.81 ± 1.72	1.34 ± 3.11	0.438
Total AHI, [mean ± SD]	2.3 ± 4.2	2.9 ± 2.9	2.0 ± 4.8	0.339
Obstructive AHI	1.7 ± 2.4	2.4 ± 2.4	1.3 ± 2.3	0.047
Central AHI	0.7 ± 3.1	0.5 ± 0.9	0.71 ± 4.0	0.805
Oxygen saturation nadir, [mean ± SD]	87.9 ± 2.7	86.7 ± 2.7	88.6 ± 2.4	0.002

WASO wakefulness after sleep onset, *REM* rapid eye movement, *AHI* apnea/hypopnea index

Table 3 Comparison with normal values in adolescents

	Current study	Normative data[a]	Difference	95% CI	*p* value
Scoring rules	AASM	AASM			
Number	85	24			
Age range, years	11–17	13.4–17.2			
Gender (boys/girls), *n*	31:54	12:12			
Age, years [mean ± SD]	14.5 ± 1.6	15.2 ± 1.4	0.7	− 0.1 to 1.4	0.055
Sleep period time, SPT [mean ± SD]	427.3 ± 33.0	502.5 ± 45.2	75.2	58.4 to 91.7	< 0.001
Total sleep time, min [mean ± SD]	387.2 ± 55.8	481.5 ± 46.2	94.3	69.6 to 119.0	< 0.001
Sleep efficiency, % [mean ± SD]	88.0 ± 11.1	90.7 ± 7.0	2.7	− 2.1 to 7.5	0.262
WASO, min [mean ± SD]	9.6 ± 10.7	4.2 ± 3.7	− 5.4	− 9.8 to −1.0	0.017
Sleep latency, min [mean ± SD]	13.1 ± 12.6	22.0 ± 21.7	8.9	2.0 to 15.8	0.012
REM latency, min [mean ± SD]	150.3 ± 60.0	138.2 ± 54.5	− 12.1	− 39.1 to 14.9	0.376
N1, % [mean ± SD]	5.3 ± 4.2	7.9 ± 5.1	2.6	0.6 to 4.6	0.012
N2, % [mean ± SD]	56.9 ± 8.8	45.6 ± 7.9	− 11.3	− 15.3 to − 7.4	< 0.001
N3, % [mean ± SD]	23.3 ± 9.6	25.5 ± 4.7	2.2	− 1.8 to 6.2	0.281
REM, % [mean ± SD]	14.6 ± 4.9	19.4 ± 3.9	4.8	2.7 to 7.0	< 0.001
Arousal index, [mean ± SD]	10.8 ± 5.6	6.4 ± 2.4	− 4.4	− 6.7 to − 2.1	< 0.001
Spontaneous arousal index [mean ± SD]	8.8 ± 4.0	2.3 ± 1.5	− 6.5	− 8.2 to − 4.9	< 0.001
Respiratory arousal index [mean ± SD]	1.5 ± 2.7	0	− 1.5	− 2.6 to − 0.4	0.001
Total AHI, [mean ± SD]	2.3 ± 4.2	0.2 ± 0.25	2.1	0.4 to 3.8	0.016
Oxygen saturation nadir, [mean ± SD]	87.9 ± 2.7	93.5 ± 1.25	− 5.6	− 6.7 to − 4.5	< 0.001

WASO wakefulness after sleep onset, *REM* rapid eye movement, *AHI* apnea/hypopnea index

[a] Normative data was obtained from Scholle et al. [23–25]

Asthma control

There were no significant differences in the demographic and clinical characteristics between adolescents with well-controlled and inadequately controlled asthma (Table 4). Sleep parameters including sleep efficiency, sleep latency, sleep architecture, and breathing events also did not differ by asthma control. However, participating adolescents had minimal nocturnal symptoms of asthma. The vast majority (86%) hardly ever awakened by asthma. There were fewer adolescents with well-controlled asthma in the SDB group compared to the non-SDB group (36.0 vs 60.0%), but this difference did not reach statistical significance ($p = 0.058$).

Sleep disorder breathing

As seen in Table 5, adolescents with asthma and SDB had a higher BMI percentile than those without SDB (73.8 vs. 60.4), $p = 0.023$. The odds of having SDB, adjusting for BMI, was higher in adolescent boys than girls [OR = 4.60 (95% CI 1.44–14.68), $p = 0.010$]. No significant differences were found between participants with and without SDB for daytime sleepiness on the CRSP-S. Similarly, no differences were found between participants with and without SDB on the PSQ, including the total score, snoring scale, daytime sleepiness scale, and inattention/hyperactivity scale. Further, there was no significant difference in the prevalence of SDB in adolescents with (33.3%) and without (25.0%) allergic rhinitis, $p = 0.44$.

Discussion

This study used a lab-based overnight polysomnography to describe sleep and breathing characteristics in a large group of adolescents with asthma who were classified as low risk for sleep-disordered breathing. The results showed that despite the low risk (based on the PSQ and symptoms of snoring and daytime sleepiness), 29% of participants were found to have significant sleep-disordered breathing, with a mean AHI of 5.9 ± 6.5. In addition, adolescents with asthma have impaired nocturnal sleep with increased awakenings and arousals during sleep compared to a normative population of adolescents without asthma. In addition, sleep architecture was characterized by less REM sleep and increased REM latency in the current sample of youth with asthma compared to the normative population. This study also found that boys with asthma had a higher risk of sleep-disordered breathing than girls. However, sleep disturbances were not related to the level of asthma control.

The few studies that have described the polysomnographic parameters of sleep in children with asthma are limited by either small sample sizes or retrospective designs [11, 12,

Table 4 Demographic and polysomnographic parameters and status of asthma control

	Well-controlled asthma ($n = 44$)	Inadequately controlled asthma ($n = 13$)	p value
Age, years [mean ± SD]	14.41 ± 1.55	15.15 ± 1.77	0.145
Gender, girls [n (%)]	26 (59.1)	8 (61.5)	0.874
Bronchodilators only [n (%)]	11 (32.4)	4 (40.0)	0.464
Controller(s)[a] ± bronchodilators [n (%)]	23 (67.6)	6 (60.0)	
Pediatric Sleep Questionnaire [mean ± SD]	0.11 ± 0.08	0.15 ± 0.10	0.151
Asthma Control Questionnaire [mean ± SD]	0.35 ± 0.23	2.3 ± 0.62	< 0.001
Sleep period time, min [mean ± SD]	419.78 ± 33.91	431.17 ± 25.77	0.269
Total sleep time, min [mean ± SD]	379.27 ± 56.57	388.12 ± 53.27	0.828
Sleep efficiency, % [mean ± SD]	87.50 ± 11.23	86.04 ± 13.31	0.694
WASO, min [mean ± SD]	42.15 ± 44.79	48.05 ± 51.64	0.689
Sleep latency, min [mean ± SD]	13.77 ± 12.23	16.61 ± 17.87	0.514
REM latency, min [mean ± SD]	145.15 ± 58.10	170.50 ± 70.42	0.193
N1, % [mean ± SD]	5.18 ± 4.40	4.61 ± 3.64	0.672
N2, % [mean ± SD]	57.68 ± 7.11	54.72 ± 12.95	0.287
N3, % [mean ± SD]	22.95 ± 8.08	25.89 ± 13.72	0.336
REM, % [mean ± SD]	14.19 ± 5.10	14.76 ± 3.93	0.712
Arousal index [mean ± SD]	11.18 ± 6.21	8.40 ± 2.56	0.123
Spontaneous arousal index [mean ± SD]	8.89 ± 4.07	7.07 ± 3.05	0.143
Respiratory arousal index [mean ± SD]	1.61 ± 3.28	0.82 ± 0.67	0.395
Total AHI [mean ± SD]	1.82 ± 2.65	2.29 ± 2.02	0.558
Oxygen saturation nadir [mean ± SD]	88.07 ± 2.32	87.15 ± 1.77	0.195

WASO wakefulness after sleep onset, REM rapid eye movement, AHI apnea/hypopnea index

[a] Inhaled corticosteroids, inhaled corticosteroids/long acting beta-2-agonists, and or montelukast

28]. In one study utilizing at-home PSG in children, an increased number of awakenings and similar sleep architecture was noted in children with symptomatic nocturnal asthma ($n = 21$), when compared with to a control group [11]. In a retrospective study of children with self-reported asthma who had undergone PSG testing for evaluation of snoring demonstrated sleep fragmentation, with less total sleep time and higher arousal index, among children with asthma compared to those without asthma [28]. Another retrospective study of PSG for children with asthma ($n = 113$) reported longer sleep onset latency and shorter sleep duration but no significant changes in sleep architecture, arousal index, or respiratory disturbance index in children with asthma as compared to those without asthma [12]. In a more recent study, non-obese children with asthma and AHI ≤ 5 had poorer sleep quality with increased sleep latency and decreased slow wave sleep compared to children without asthma and AHI ≤ 5 [13].

This study prospectively utilized an older sample of adolescents (11–17 years) with well-established asthma and no other confounding medical or sleep disorders. Compared with normative data [23], our participating adolescents had less total sleep time and more awakenings combined with increased spontaneous and respiratory arousal indices, consistent with previous reports in children with asthma [11, 28]. The explanation for these noticeable and consistent changes in sleep continuity could be related to nocturnal symptoms of asthma. This notion is supported by the significant decrease in the number of awakenings after proper treatment of children with asthma [11]. Although the sleep efficiency was not different from normal children, one fourth of the participants and half of the boys had sleep efficiency < 85% and there was more variability in our population (range, 42.6–97.8%) than the normative data (77.7–98.5%) [23]. In this study, sleep continuity was not affected by the level of asthma control suggesting that nocturnal symptoms of asthma were subtle and may have gone unnoticed by the adolescent and his/her parents. However, others have shown that poor asthma control is associated with poor sleep quality for both children with asthma and their parents [8, 9]. Another significant finding in this study is increased REM latency and less REM sleep among adolescents with asthma. The clinical significance of these findings is uncertain. However, REM sleep may play an important role in the consolidation and integration of emotional and affective memory during the critical developmental period of adolescence [29, 30].

Despite the effort to minimize the confounding effect of SDB in the parent study from which these participants were drawn, one third of recruited adolescents met the polysomnographic criteria for SDB. Those with SDB and asthma had higher AHI and lower oxygen saturation nadir. A recent

Table 5 PSG parameters and sleep disordered breathing (SDB)

Parameter	SDB ($n = 25$)	No SDB ($n = 60$)	p value
Age, years [mean ± SD]	14.68 ± 1.57	14.40 ± 1.61	0.464
Gender, girls [n (%)]	9 (36.0)	45 (75.0)	0.001
BMI, %ile [mean ± SD]	81.00 ± 22.58	58.47 ± 25.35	< 0.001
CRSP Sleepiness Scale [mean ± SD]	1.93 ± 0.55	1.89 ± 0.58	0.800
Pediatric Sleep Questionnaire[a] [mean ± SD]	0.15 ± 0.10	0.12 ± 0.09	0.215
PSQ Snoring Scale [mean ± SD]	0.05 ± 0.18	0.05 ± 0.13	0.890
Always snore [n (%)]	2 (8.3)	2 (3.3)	0.574
Snore loudly [n (%)]	1 (4.2)	3 (5.1)	0.999
PSQ Daytime Sleepiness Scale [mean ± SD]	0.27 ± 0.28	0.17 ± 0.23	0.083
PSQ Inattention/Hyperactivity Scale [mean ± SD]	0.16 ± 0.18	0.16 ± 0.19	0.968
Asthma Control Questionnaire [mean ± SD]	1.11 ± 0.70	0.81 ± 0.76	0.102
Well-controlled (ACQ < 0.75) [n (%)]	9 (36.0)	35 (58.3)	0.136
Inadequately controlled (ACQ > 1.5) [n (%)]	6 (24.0)	7 (11.7)	
Sleep period time, minutes [mean ± SD]	420.3 ± 36.9**	430.3 ± 31.1**	0.209
Total sleep time, minutes [mean ± SD]	375.9 ± 61.1**	391.9 ± 53.3**	0.233
Sleep efficiency, % [mean ± SD]	86.9 ± 10.7	88.5 ± 11.4	0.552
Sleep efficiency < 85%, [n (%)]	7 (28.0)	14 (23.3)	0.783
WASO, % [mean ± SD]	13.9 ± 16.2**	12.3 ± 19.0*	0.701
Sleep latency, min [mean ± SD]	10.8 ± 10.0**	14.1 ± 13.5*	0.277
REM latency, min [mean ± SD]	135.8 ± 52.1	156.3 ± 62.4	0.153
N1, % [mean ± SD]	6.2 ± 5.1	4.8 ± 3.7**	0.160
N2, % [mean ± SD]	55.0 ± 8.8**	57.6 ± 8.7**	0.204
N3, % [mean ± SD]	23.7 ± 8.9	23.2 ± 10.0	0.808
REM, % [mean ± SD]	15.1 ± 4.9**	14.4 ± 4.9**	0.557
Arousal index [mean ± SD]	13.4 ± 8.4**	9.7 ± 3.9**	0.007
Spontaneous Arousal Index [mean ± SD]	9.8 ± 5.1**	8.3 ± 3.3**	0.121
Respiratory Arousal Index [mean ± SD]	3.0 ± 4.3**	0.9 ± 1.1	0.001
Total AHI [mean ± SD]	5.9 ± 6.5**	0.9 ± 0.5**	< 0.001
Oxygen saturation nadir [mean ± SD]	85.5 ± 2.5**	88.9 ± 2.1**	< 0.001

WASO wakefulness after sleep onset, *AHI* apnea/hypopnea index25]

*$p < 0.05$; **$p < 0.01$, when compared to normative data from Scholle et al. [23–25]

[a] The average response for each individual item, scale 0 to 1

systematic review on the association between asthma and SDB concluded that a bidirectional relationship exists between the two diseases in which children with asthma are at higher risk of having OSA and those with OSA are more likely to develop asthma [31]. The previously reported prevalence of SDB among children with asthma ranged from 7.1 to 63% [31]. Similar to our results, another study found one fourth of children with asthma had SDB (based on a PSQ score of > 0.33), and this risk increased with increasing asthma severity [32]. Also, snoring children with asthma are more likely to have sleep fragmentation and nocturnal awakening than those without asthma [28]. In this study, awakenings and arousal during sleep were common among adolescents with asthma regardless of the presence of SDB suggesting that nocturnal symptoms of asthma may interfere with sleep quality. Contrary to what was expected, snoring and daytime sleepiness among our participants were not more prevalent among adolescents with both asthma and SDB. Moreover, PSQ scores of < 0.33 had low sensitivity in ruling out SDB in this patient population, as 29% of our study population with PSQ < 0.33 were found to have SDB diagnosed by overnight in-lab PSG. More research is needed to better understand why the PSQ was not able to detect SDB in adolescents with asthma. However, these findings highlight the importance of proper screening for SDB and the use of PSG in adolescents with asthma, in addition to a potentially different PSQ cutoff score that is more sensitive.

The study also examined gender differences for sleep and breathing parameters in adolescents with asthma. Boys with asthma had significantly shorter sleep duration, longer sleep latency, and more sleep fragmentation than the girls. This could be explained by the higher BMI percentile and the

higher risk of having SDB among the boys. One study evaluated the effect of gender on sleep among children with asthma [12]. In agreement with our results, they found that boys with asthma had shorter sleep duration while girls with asthma had longer sleep latency.

The consequences of these abnormalities on the daytime function and school performance have not been adequately studied in this population. Few studies with children or adolescents have examined the relationship between asthma, chronic partial sleep restriction, and functional asthma outcomes. A recent study used path analysis to show that the relationship between asthma and health-related quality of life was mediated by daytime sleepiness; however, sleep duration was not considered [33]. Another study found that greater self-reported sleep quantity was associated with lower peak expiratory flow rate in youth 9–19 years [34]. However, the lack of an objective measure of sleep duration was a significant limitation of this study. For healthy youth, chronic partial sleep restriction is known to negatively impact functional outcomes, including increased daytime sleepiness and poor school performance [35].

The results of this study are a first step toward understanding the relationship between sleep and asthma outcomes. Future studies should examine the presence and directional interaction between sleep parameters including daily sleep duration and sleep continuity, lung function, and functional asthma outcomes. Focusing on a modifiable health behavior and standardized disease-related functional outcomes (e.g., lung function, asthma related activity limitations, rescue inhaler use, health-related quality of life) may directly impact on the clinical management of asthma for adolescents. Moreover, sleep disturbances should be taken into consideration when assessing school performance in adolescents with asthma.

The study had a number of limitations that merit mentioning. Participants were recruited from a single city and excluded adolescents who were at high risk of having sleep-disordered breathing. This may limit the generalization of the results to all children with asthma and to those from different populations. The notion that a single night of polysomnography may not be representative of the sleep and breathing is not supported by the literature, and the night-to-night variability in pediatric polysomnography is clinically insignificant [36]. While utilizing previously published normative data arrived at through sound scientific methodology does add value to the interpretation of our results, confirmatory studies utilizing a concurrent control group are needed [37]. In addition, this study used the clinical diagnosis of asthma based on a set of asthma-related symptoms and asthma medication usage; however, asthma severity and spirometry data prior to PSG were not collected.

In conclusion, this study showed that despite the perceived low risk of sleep-disordered breathing in the study population of adolescents with asthma, almost a third of the study population had SDB, with boys at an even higher increased risk than girls.

In addition, adolescents with asthma have objective sleep disturbances in sleep continuity with more arousals and sleep fragmentation. Therefore, better and more proper screening for sleep-disordered breathing and sleep quality is important in this patient population.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the National Jewish Health Institutional Review Board and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. WHO (2017) Asthma fact sheet. In: World Health Organization http://www.who.int/news-room/fact-sheets/detail/asthma. Accessed August 09 2018
2. Akinbami LJ, Simon AE, Schoendorf KC (2016) Trends in allergy prevalence among children aged 0-17 years by asthma status, United States, 2001-2013. J Asthma 53(4):356–362. https://doi.org/10.3109/02770903.2015.1126848
3. Centers for Disease C, Prevention (2011) Vital signs: asthma prevalence, disease characteristics, and self-management education: United States, 2001–2009. MMWR Morb Mortal Wkly Rep 60(17):547–552
4. Association AL (2012) Trends in asthma morbidity and mortality
5. Moonie SA, Sterling DA, Figgs L, Castro M (2006) Asthma status and severity affects missed school days. J Sch Health 76(1):18–24. https://doi.org/10.1111/j.1746-1561.2006.00062.x
6. Sutherland ER (2005) Nocturnal asthma. J Allergy Clin Immunol 116(6):1179–1186; quiz 1187. https://doi.org/10.1016/j.jaci.2005.09.028
7. Meltzer LJ, Ullrich M, Szefler SJ (2014) Sleep duration, sleep hygiene, and insomnia in adolescents with asthma. J Allergy Clin Immunol Pract 2(5):562–569. https://doi.org/10.1016/j.jaip.2014.02.005

8. Fagnano M, Bayer AL, Isensee CA, Hernandez T, Halterman JS (2011) Nocturnal asthma symptoms and poor sleep quality among urban school children with asthma. Acad Pediatr 11(6):493–499. https://doi.org/10.1016/j.acap.2011.05.006
9. Strunk RC, Sternberg AL, Bacharier LB, Szefler SJ (2002) Nocturnal awakening caused by asthma in children with mild-to-moderate asthma in the childhood asthma management program. J Allergy Clin Immunol 110(3):395–403. https://doi.org/10.1067/mai.2002.127433
10. Diette GB, Markson L, Skinner EA, Nguyen TT, Algatt-Bergstrom P, Wu AW (2000) Nocturnal asthma in children affects school attendance, school performance, and parents' work attendance. Arch Pediatr Adolesc Med 154(9):923–928
11. Stores G, Ellis AJ, Wiggs L, Crawford C, Thomson A (1998) Sleep and psychological disturbance in nocturnal asthma. Arch Dis Child 78(5):413–419. https://doi.org/10.1136/adc.78.5.413
12. Jensen ME, Gibson PG, Collins CE, Hilton JM, Latham-Smith F, Wood LG (2013) Increased sleep latency and reduced sleep duration in children with asthma. Sleep Breath 17(1):281–287. https://doi.org/10.1007/s11325-012-0687-1
13. Teng YK, Chiang LC, Lue KH, Chang SW, Wang L, Lee SP, Ting H, Lee SD (2014) Poor sleep quality measured by polysomnography in non-obese asthmatic children with or without moderate to severe obstructive sleep apnea. Sleep Med 15(9):1062–1067. https://doi.org/10.1016/j.sleep.2014.04.017
14. Meltzer LJ, Jump S, Flewelling KD, Sundstrom D, White M, Strand MJ (2018) 0851 sleep duration and asthma outcomes in adolescents. Sleep 41(suppl_1):A315–A316. https://doi.org/10.1093/sleep/zsy061.850
15. Chervin RD, Hedger K, Dillon JE, Pituch KJ (2000) Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems. Sleep Med 1(1):21–32
16. Iber C A-IS, Chesson AL, Jr, Quan SF for the American Academy of Sleep Medicine. (2007) The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. 1st edn. American Academy of Sleep Medicine, Westchester, IL
17. Aurora RN, Zak RS, Karippot A, Lamm CI, Morgenthaler TI, Auerbach SH, Bista SR, Casey KR, Chowdhuri S, Kristo DA, Ramar K (2011) American Academy of Sleep M. Practice parameters for the respiratory indications for polysomnography in children Sleep 34(3):379–388
18. Juniper EF, Bousquet J, Abetz L, Bateman ED, Committee G (2006) Identifying 'well-controlled' and 'not well-controlled' asthma using the asthma control questionnaire. Respir Med 100(4):616–621. https://doi.org/10.1016/j.rmed.2005.08.012
19. Juniper EF, O'Byrne PM, Ferrie PJ, King DR, Roberts JN (2000) Measuring asthma control. Clinic questionnaire or daily diary? Am J Respir Crit Care Med 162(4 Pt 1):1330–1334. https://doi.org/10.1164/ajrccm.162.4.9912138
20. Cloutier MM, Schatz M, Castro M, Clark N, Kelly HW, Mangione-Smith R, Sheller J, Sorkness C, Stoloff S, Gergen P (2012) Asthma outcomes: composite scores of asthma control. J Allergy Clin Immunol 129(3 Suppl):S24–S33. https://doi.org/10.1016/j.jaci.2011.12.980
21. Chervin RD, Weatherly RA, Garetz SL, Ruzicka DL, Giordani BJ, Hodges EK, Dillon JE, Guire KE (2007) Pediatric sleep questionnaire: prediction of sleep apnea and outcomes. Arch Otolaryngol Head Neck Surg 133(3):216–222. https://doi.org/10.1001/archotol.133.3.216
22. Meltzer LJ, Biggs S, Reynolds A, Avis KT, Crabtree VM, Bevans KB (2012) The children's report of sleep patterns—sleepiness scale: a self-report measure for school-aged children. Sleep Med 13(4):385–389. https://doi.org/10.1016/j.sleep.2011.12.004
23. Scholle S, Beyer U, Bernhard M, Eichholz S, Erler T, Graness P, Goldmann-Schnalke B, Heisch K, Kirchhoff F, Klementz K, Koch G, Kramer A, Schmidtlein C, Schneider B, Walther B, Wiater A, Scholle HC (2011) Normative values of polysomnographic parameters in childhood and adolescence: quantitative sleep parameters. Sleep Med 12(6):542–549. https://doi.org/10.1016/j.sleep.2010.11.011
24. Scholle S, Wiater A, Scholle HC (2011) Normative values of polysomnographic parameters in childhood and adolescence: cardiorespiratory parameters. Sleep Med 12(10):988–996. https://doi.org/10.1016/j.sleep.2011.05.006
25. Scholle S, Wiater A, Scholle HC (2012) Normative values of polysomnographic parameters in childhood and adolescence: arousal events. Sleep Med 13(3):243–251. https://doi.org/10.1016/j.sleep.2011.07.022
26. Sogut A, Yilmaz O, Dinc G, Yuksel H (2009) Prevalence of habitual snoring and symptoms of sleep-disordered breathing in adolescents. Int J Pediatr Otorhinolaryngol 73(12):1769–1773. https://doi.org/10.1016/j.ijporl.2009.09.026
27. Meltzer LJ, Avis KT, Biggs S, Reynolds AC, Crabtree VM, Bevans KB (2013) The children's report of sleep patterns (CRSP): a self-report measure of sleep for school-aged children. J Clin Sleep Med 9(3):235–245. https://doi.org/10.5664/jcsm.2486
28. Ramagopal M, Scharf SM, Roberts DW, Blaisdell CJ (2008) Obstructive sleep apnea and history of asthma in snoring children. Sleep Breath 12(4):381–392. https://doi.org/10.1007/s11325-008-0174-x
29. Nishida M, Pearsall J, Buckner RL, Walker MP (2009) REM sleep, prefrontal theta, and the consolidation of human emotional memory. Cereb Cortex 19(5):1158–1166. https://doi.org/10.1093/cercor/bhn155
30. Gujar N, McDonald SA, Nishida M, Walker MP (2011) A role for REM sleep in recalibrating the sensitivity of the human brain to specific emotions. Cereb Cortex 21(1):115–123. https://doi.org/10.1093/cercor/bhq064
31. Sanchez T, Castro-Rodriguez JA, Brockmann PE (2016) Sleep-disordered breathing in children with asthma: a systematic review on the impact of treatment. J Asthma Allergy 9:83–91. https://doi.org/10.2147/JAA.S85624
32. Goldstein NA, Aronin C, Kantrowitz B, Hershcopf R, Fishkin S, Lee H, Weaver DE, Yip C, Liaw C, Saadia TA, Abramowitz J, Weedon J (2015) The prevalence of sleep-disordered breathing in children with asthma and its behavioral effects. Pediatr Pulmonol 50(11):1128–1136. https://doi.org/10.1002/ppul.23120
33. Li Z, Huang IC, Thompson L, Tuli S, Huang SW, DeWalt D, Revicki D, Shenkman E (2013) The relationships between asthma control, daytime sleepiness, and quality of life among children with asthma: a path analysis. Sleep Med 14(7):641–647. https://doi.org/10.1016/j.sleep.2013.04.002
34. Hanson MD, Chen E (2008) The temporal relationships between sleep, cortisol, and lung functioning in youth with asthma. J Pediatr Psychol 33(3):312–316. https://doi.org/10.1093/jpepsy/jsm120
35. Beebe DW (2011) Cognitive, behavioral, and functional consequences of inadequate sleep in children and adolescents. Pediatr Clin N Am 58(3):649–665. https://doi.org/10.1016/j.pcl.2011.03.002
36. Katz ES, Greene MG, Carson KA, Galster P, Loughlin GM, Carroll J, Marcus CL (2002) Night-to-night variability of polysomnography in children with suspected obstructive sleep apnea. J Pediatr 140(5):589–594. https://doi.org/10.1067/mpd.2002.123290
37. Lee JJ, Tseng C (2001) Uniform power method for sample size calculation in historical control studies with binary response. Control Clin Trials 22(4):390–400