

Validation of the Pediatric Sleep Questionnaire in Children With Asthma

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Summary. Objective: The prevalence of obstructive sleep apnea (OSA) is higher in children with poorly controlled asthma. We aimed to determine the validity of the Pediatric Sleep Questionnaire (PSQ) to screen for OSA in children with asthma. Methods: This retrospective review encompassed sleep studies and medical records of asthmatic children evaluated in the sleep center at CCHMC over 13 years. Measures of validity were calculated using various cut-off values for obstructive apnea-hypopnea index (OI; >1, >2, >5) and PSQ scores (>0.33, >0.5). Correlation between PSQ and OI, PSQ and spirometry, and OI and spirometry was assessed using Spearman's correlation coefficient. Results: One-hundred and sixty children were included (mean age 11 ± 4 years; 64% males). The mean OI was 4.2 ± 14.3 and the mean PSQ score was 0.57 ± 0.19 . Thirty-eight percent of patients had a diagnosis of allergic rhinitis. A total of 70 children (43%) were obese (BMI ≥ 95 th percentile). The correlation between OI and PSQ was statistically significant ($r = 0.19$, $P = 0.015$). Using a PSQ cutoff of 0.33, and OI cutoffs of 1, 2, and 5, the sensitivities were 81.6%, 81.6%, and 76.2%, and the specificities were 13.1%, 14.4%, and 14.4%, respectively. When the cutoff for PSQ was raised to 0.5 and using an OI of 1, the sensitivity decreased to 71.1%, but the specificity increased to 36.9%. Conclusions: The sensitivity of PSQ in asthmatic children is high and comparable to previous studies, but the specificity is low. The PSQ may be considered a reasonable first-line screening tool for OSA in asthmatic children. **Pediatr Pulmonol.** 2016; 9999:XX–XX. © 2016 Wiley Periodicals, Inc.

Key words: asthma; OSA; children; screening.

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INTRODUCTION

Children with asthma have a higher prevalence of sleep-disordered breathing (SDB) when compared with non-asthmatics.^{1,2} In a prospective study, asthmatic children with SDB were 3.62 times more likely to have severe asthma at 12-month follow-up.³ Furthermore, poorly controlled asthmatic children are at higher risk for severe obstructive sleep apnea (OSA).⁴ Even though both national and international asthma care guidelines recommend assessing for OSA in children with poorly controlled asthma, there is limited evidence regarding appropriate screening tools for SDB in this population.^{5,6} The treatment of OSA with adenotonsillectomy can improve asthma control by decreasing asthma-related exacerbations and the frequency of rescue inhaler use.⁷ Adult studies suggest that treatment of OSA with continuous positive airway pressure also improves asthma-related quality of life, again suggesting a link between the two disease processes.⁸ Therefore, it is important to screen for SDB in children with poorly controlled asthma so that early referral for formal evaluation of OSA can be undertaken. Previous studies have confirmed that history and clinical examination in

the office setting are not sufficient to predict OSA.⁹ Polysomnography is the gold standard for diagnosis of

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Conflict of interest: None.

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OSA; however, factors such as limited availability and expense may hinder its practicality of use considering the high prevalence of primary snoring in children (including those who have asthma). Sleep questionnaires are useful screening tools for both primary pediatricians and consultants caring for children with sleep problems. The pediatric sleep questionnaire (PSQ) is widely used to screen for SDB in both research and clinical settings. It is a 22-item questionnaire comprising three symptom complexes: snoring, excessive daytime sleepiness, and inattentive or hyperactive behavior. Alternatively, the total PSQ score can be divided into four sub-scores: breathing, behavior, sleepiness, and other. A total score of greater than 0.33 (33% of questions answered positively) indicates SDB and has a sensitivity of 81% and specificity of 87% among the general pediatric population.¹⁰ Compared to other sleep questionnaires validated for use in children, the PSQ has a high validity for OSA screening.^{11,12} However, there is limited evidence on the validation of the PSQ in specific subpopulations of patients, especially in those with comorbid pulmonary conditions.^{2,13–15} Given the high prevalence of SDB and OSA in children with asthma, we aimed to determine the validity of the PSQ when compared to standard overnight polysomnography in a cohort of children with asthma. Our hypothesis was that the PSQ is a valid tool to screen for OSA in children with asthma.

MATERIALS AND METHODS

Patients were identified using an existing clinical database encompassing all children referred to the Cincinnati Children's Hospital Sleep Center for polysomnography between June 1, 2000 and July 1, 2013. Children with a diagnosis of asthma (based on an ICD9 code in the medical chart) who were between 2 and 18 years of age and were referred for polysomnography at CCHMC for symptoms of SDB were included in the study. Furthermore, only patients who had undergone at least one overnight polysomnogram (PSG) and completed at least one PSQ were included in the analysis. Children with significant medical comorbidities such as cystic fibrosis, neuromuscular disorders, or trisomy 21 were excluded. This study was approved by the Institutional Review Board of Cincinnati Children's Hospital Medical Center.

The medical records of the identified study participants were reviewed and information including age; sex; race; body mass index (BMI); BMI percentile; presence of allergic rhinitis; asthma control test (ACT) scores; pulmonary function test (PFT): FEV₁% predicted, FEV₁/FVC%, and FEF_{25–75}%; PSQ scores; and polysomnogram variables were recorded. We only included those children with a PSQ test within 6 months of the PSG.

As part of clinical standard of care at CCHMC, all patients or caregivers are requested to complete an

electronically administered PSQ in the sleep clinic prior to the physician visit. The scales within the questionnaire include a 9-item Breathing subscale, a 2-item Sleepiness subscale, a 6-item Behavior subscale, and a 5-item Other subscale. The Other subscale consists of questions related to weight, rate of growth since birth, nocturnal enuresis, ability to awaken in the morning, and feeling unrefreshed in the morning.

The ACT is a patient or caregiver completed, 5-item questionnaire with a 4-week recall of asthma symptoms (score range from 5 to 25). A score greater than 19 indicates well-controlled asthma. All spirometry data were obtained using American Thoracic Society criteria and age- and race-matched standards.

Polysomnogram studies were performed in the CCHMC sleep laboratory in accordance with the American Academy of Sleep Medicine guidelines.¹⁶ The following variables were recorded simultaneously: body position, left and right electrooculogram (ROC/A1, LOC/A2), 4-channel electroencephalogram (O1A2, O2A1, C4A1, C3A2), chin electromyogram, electrocardiogram, pulse oximetry and pulse waveform, thoracic and abdominal inductance plethysmography, nasal thermistor, end-tidal pCO₂ monitoring (BCI, Capno-checks), and transcutaneous pO₂ and pCO₂ (Tina TCM4/40; Radiometer, Copenhagen, Denmark). Sleep scoring was performed by a registered polysomnographic technologist and validated by board-certified pediatric sleep specialists, using standard pediatric criteria.¹⁶ Studies were analyzed in 30-sec epochs and staged as awake, REM sleep, NREM 1, NREM 2, or NREM3 sleep. Apnea was defined as at least a 90% reduction in airflow from baseline over two or more respiratory cycles. An obstructive apnea (OA) was defined as apnea in the presence of persistent or increased respiratory effort. Hypopnea was defined as a 50% or greater reduction in airflow accompanied by either an oxygen desaturation of at least 3% or arousal. The obstructive index (OI) was defined as the number of obstructive apneas, mixed apneas, and obstructive hypopneas per hour. We defined OSA as an OI > 1 event per hour.

Data Analysis

Unless otherwise noted, descriptive statistics are presented as mean ± standard deviation (SD) for continuous variables; counts and percentages are given for categorical variables. The correlations between PSQ and OI, PSQ and PFT measures (FEV₁% predicted, FEV₁/FVC%, and FEF_{25–75}%), and OI and PFT measures were assessed using Spearman's correlation coefficient. A *P*-value of <0.05 was considered statistically significant. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated based on how a positive PSQ result (defined as

TABLE 1—Sample Measures Table

	OI >1 (>2, >5)	OI ≤1 (≤2, ≤5)	
	OSA+	OSA−	
Positive PSQ	A	B	PPV = A/(A+B)
Negative PSQ	C	D	NPV = D/(C+D)
	Sensitivity = A/(A+C)	Specificity = D/(B+D)	Accuracy = (A+D)/(A+B+C+D)

OI, obstructive apnea hypopnea index; PSQ, pediatric sleep questionnaire, PPV, positive predictive value, NPV, negative predictive value.

a PSQ score >0.33) predicts actual OSA (defined in separate analyses as OI >1, >2, and >5), as illustrated in Table 1. The area under the curve was calculated, and the sensitivity, specificity, NPV, PPV, and accuracy were graphed separately for each OI cutoff to determine the optimal cut point for PSQ based on these characteristics.¹⁷ Because the distribution of OI is skewed, a log-transformation of OI was used in graphs to improve readability. SAS[®] 9.3 software (Cary, NC) was used for all analyses.

RESULTS

A total of 277 patient charts were reviewed, 117 of which were excluded (reasons for exclusion included: PSQ data not within 6 months [in either direction] of sleep study, presence of a comorbid condition as previously described). One-hundred and sixty patients (mean age 11 ± 4 years; 64% males) were ultimately included. Fifty-nine patients were African American (36%), 92 were White (57%), and nine were classified as “other” (inclusive of Hispanic, Asian, and biracial). The mean OI was 4.2 ± 14.3 events per hour and the mean PSQ score was 0.57 ± 0.19 . Eighty-four (52.5%) had an OI <1 events per hour and, therefore, did not meet criteria for

diagnosis of OSA. The mean duration between PSQ and sleep study was 40 ± 31 days. Spirometry was available for 66 patients (41%) with a mean FEV₁% predicted of 97.3 ± 14.3 , FEV₁/FVC% predicted 84 ± 9.4 , FEF_{25–75}% predicted 89.5 ± 29.7 . The mean duration between PSQ and spirometry was 12.5 ± 19.4 months. Sixty-two patients (39%) had a diagnosis of allergic rhinitis. ACT scores were available in 21 patients with a mean score of 17.1 ± 5.8 . The mean duration between PSQ and ACT was 10.3 ± 11.3 months. A total of 70 children (43%) were obese (BMI ≥ 95 th percentile). Demographic details and sleep study results are shown in Tables 2 and 3, respectively.

There was a statistically significant direct correlation between OI and PSQ in the positive direction as demonstrated by the scatter plot in Figure 1a ($r=0.19$, $P=0.015$). Given that the PSQ was validated in a primarily pre-adolescent population, we next determined whether this relationship persisted after stratifying the cohort by age groups. We observed a significant correlation between PSQ and OI among children <13 years of age ($r=0.20$, $P=0.043$). There was no significant correlation between PSQ and OI among children ≥ 13 years of age ($r=0.18$, $P=0.160$). We also assessed the correlation of the breathing subscale (PSQ breathing) with OI and found a strong direct correlation between PSQ breathing and OI (Fig. 1b; $r=0.30$, $P<0.0001$). There was a significant inverse

TABLE 2—Demographics of Cohort

Age (years)	11 ± 4
BMI (kg/m ²)	22.9 ± 8.9
BMI percentile	76.5 ± 28
PSQ score (total)	0.57 ± 0.19
PSQ breathing subscale	0.61 ± 0.29
PSQ sleepiness subscale	0.55 ± 0.43
PSQ behavior subscale	0.63 ± 0.33
PSQ other subscale	0.44 ± 0.23
FEV ₁ % predicted ¹	97.3 ± 14.3
FEV ₁ /FVC%	84 ± 9.4
FEF _{25–75} % predicted	89.5 ± 29.7
ACT score ²	17.1 ± 5.8

BMI, body mass index; PSG, pediatric sleep questionnaire; FEV₁, forced expiratory volume in 1 sec; FVC, forced vital capacity; FEF_{25–75}, forced expiratory flow 25–75%.

Variables are presented as mean $\pm$ SD.

¹Spirometry data are presented for 66 children.

²ACT data are presented for 21 children.

TABLE 3—Sleep Study Parameters for Cohort

Sleep efficiency (% of total sleep time)	79.1 ± 11.7
Arousal index	10.7 ± 11.8
PLMI >5	15 children
AHI	4.7 ± 14.3
OI	4.2 ± 14.3
CI	0.5 ± 0.9
%CO ₂ >50	6.6 ± 16.7
Average O ₂ saturation in REM sleep (%)	97.4 ± 1.3
Average O ₂ saturation in NREM sleep (%)	97.3 ± 1.3

PLMI, periodic limb movement with arousal index; AHI, apnea hypopnea index; OI, obstructive apnea hypopnea index; CI, central apnea index; %CO₂ >50, percent of total sleep time that transcutaneous CO₂ is greater than 50 mmHg; REM, rapid eye movement.

Variables are presented as mean $\pm$ SD.

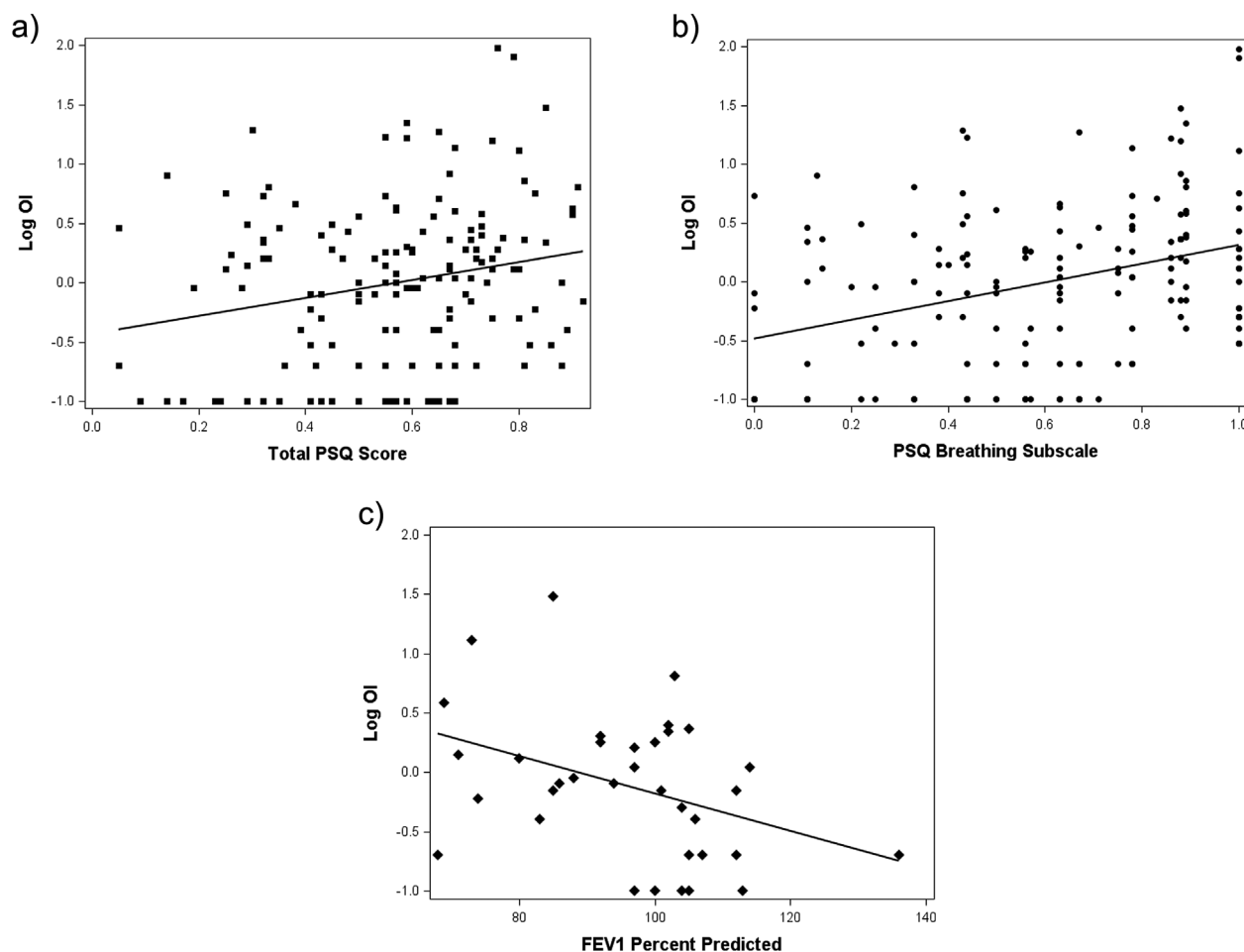


Fig. 1. (a) Scatter plot for PSQ and Log OI for entire cohort; $r = 0.19$, $P = 0.015$. (b) Scatter plot for PSQ breathing subscale and Log OI for entire cohort. $r = 0.30$, $P < 0.0001$. (c) Scatter plot for FEV1 and log OI for entire cohort. OI, obstructive apnea hypopnea index; PSQ score, pediatric sleep questionnaire score; FEV1, forced expiratory volume in 1 sec (% predicted); $r = -0.38$, $P = 0.025$.

correlation between OI and FEV₁ (Fig. 1c; $r = -0.38$, $P = 0.025$). However, there were no significant correlations between OI and FEV₁/FVC or OI and FEF₂₅₋₇₅. Subgroup analysis was performed to compare obese and non-obese patients. The correlation between PSQ and OI among those with a BMI <95th percentile was not significant (Fig. 2a; $r = 0.17$, $P = 0.111$). There was a trend toward a significant correlation between PSQ and OI for those with a high BMI (≥ 95 th percentile) (Fig. 2b; $r = 0.22$, $P = 0.066$).

Next, we determined the sensitivity, specificity, NPV, PPV, total accuracy, and area under the receiver operating curve for the PSQ. Using a PSQ cutoff of 0.33, the sensitivity for an OI cutoff of 1, 2, and 5 was 81.6%, 81.6%, and 76.2% and the specificity was 13.1%, 14.4%, and 14.4%, respectively. When the cutoff for PSQ was raised to 0.5 (based on a previous study from our group),¹⁸ and using an OI cutoff of 1, the sensitivity decreased to 71.1%, but the specificity increased to 36.9%.

Additionally, for OI cutoff of 1, the sensitivity was higher for those with a high BMI (≥ 95 th percentile) compared to those with a lower BMI (85.37% vs. 77.14%, respectively). The specificity was very low for both groups: 10.34% in the high BMI group versus 14.55% in the lower BMI group. The PPV was higher, and the NPV was lower in the high BMI group compared to those with a lower BMI (PPV: 57.38% vs. 36.49%; NPV: 33.33% vs. 50%, respectively).

To determine the total PSQ score that best predicts OSA diagnosis in children with asthma using various cutoffs for OI (1, 2, and 5), receiver operating curves were obtained. Using an OI cutoff of 1, the sensitivity and specificity crossed around 0.6 for the entire cohort (Fig. 3). The PPV was maximized at a slightly higher value (0.78 vs. 0.72) for those aged <13 compared with patients ≥ 13 years of age. The accuracy for the entire cohort was maximized around 0.72. The PPV was highest for OI cutoff of 1 (45.93%) and decreased with OI cutoff

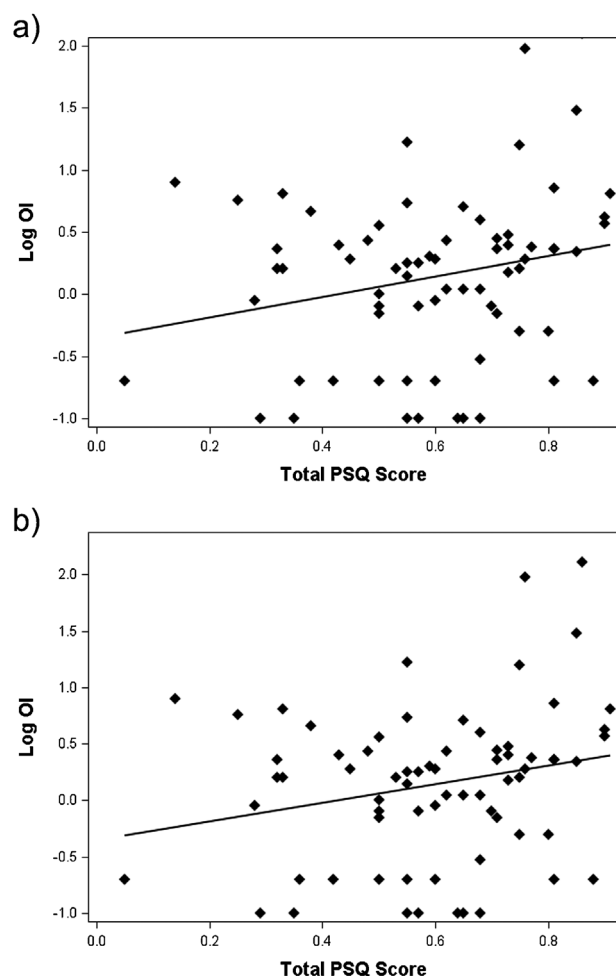


Fig. 2. (a) Scatter plot for PSQ and Log OI for children with a BMI <95th percentile; $r = 0.17$, $P = 0.111$. (b) Scatter plot for PSQ and Log OI for children with a BMI ≥ 95 th percentile. OI, obstructive apnea hypopnea index; PSQ score, pediatric sleep questionnaire score; $r = 0.22$, $P = 0.066$.

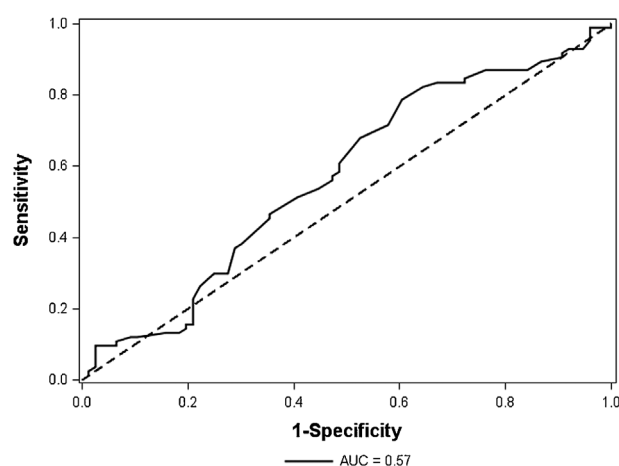


Fig. 3. Receiver operating characteristic curve. AUC, area under the curve.

of 2 (29.63%) and OI cutoff of 5 (11.85%). Similarly, the NPV was lowest for OI cutoff of 1 (44%) and higher with OI cutoff of 2 (64%) and highest for OI cutoff of 5 (80%). Overall, our results show that sensitivity and specificity are maximized when using a PSQ cutoff of 0.6–0.64 for various OI thresholds. The accuracy is maximized around a PSQ cutoff of 0.72–0.76. The PPV is maximized in each case at a higher threshold of PSQ (between 0.70 and 0.80), and the NPV is highest at much lower values (around 0.25). The odds of having an OI >1 were 1.65 times higher for those with PSQ >0.33 compared with PSQ ≤ 0.33 when controlling for BMI percentile.

DISCUSSION

In summary, using the standard cutoff of >0.33 , the PSQ questionnaire is reasonably sensitive for correctly identifying asthma patients who have an OI >1 (OSA patients) with a sensitivity of 81.6%, but a low specificity of 13.1%. Moreover, our data also suggest that raising the PSQ cutoff to 0.50 almost doubles the specificity while keeping the sensitivity reasonable.

Since asthma and OSA are both highly prevalent chronic respiratory conditions, efforts are underway to investigate risk factors leading to comorbidity of disease. Inflammatory mediators have been identified in both asthma and SDB, suggesting a final common pathway linking these diseases of the airway.^{1,19,20} While the influence of asthma on sleep has been summarized in two recent reviews,^{2,21} a few key points warrant mention here. The prevalence of poorly controlled or severe asthma among children with asthma is between 5% and 10%.^{22–24} Children with severe and poorly controlled asthma have poor sleep^{25,26} including decreased sleep efficiency due to frequent awakenings and REM-related breathing abnormalities.^{27,28} Frequent asthma symptoms can lead to daytime sleepiness and tiredness, in turn affecting daytime functioning and cognition.^{29,30} Children with nocturnal asthma symptoms are more likely to have inadequate sleep, impaired asthma-specific health-related quality of life, and poorer parental quality of life, indicating the burden of this dyad on families.^{28,31–33} Furthermore, even when controlling for nocturnal asthma symptoms, poor sleep quality is associated with poor asthma control and asthma-related quality of life.³⁴

The effects of OSA on the clinical severity of asthma are poorly understood and there are limited data regarding the prevalence of OSA (objectively diagnosed by PSG) in this population.² The studies using PSG data to define OSA in children with asthma have shown conflicting results. In one study by Ramagopal et al.,³⁵ asthma was not a significant risk factor for OSA, while in another study by the same author, the obstructive AHI was significantly higher in children with poorly controlled

asthma compared to other asthmatics.^{35,36} Nocturnal symptoms of asthma can be difficult to differentiate from symptoms of SDB, further complicating the use of screening tools in asthmatic children.

Using the available spirometry and ACT (ACT score) data as a surrogate for asthma severity and control, our cohort likely represents children with poorly controlled asthma (ACT score 17.1 ± 5.8 representing inadequately controlled asthma and low FEF₂₅₋₇₅%, suggesting small airway obstruction). Moreover, the negative correlation between OI and FEV₁% predicted in our study suggests that severity of airway obstruction related to asthma is associated with worsening degree of sleep apnea. There are several postulations regarding the association of severe asthma with OSA. Nocturnal asthma can lead to sleep fragmentation which in turn promotes upper airway collapsibility (a risk factor for OSA).^{28,37} Also, a large proportion of asthmatics and OSA patients have both allergic and non-allergic rhinitis. Rhinitis can contribute to changes in nasal airway resistance (and therefore, airflow velocity), resulting in an increase in upper airway negative pressure, exaggerating collapse of the upper airway, and leading to symptoms of SDB.^{38,39}

The limitations of polysomnography (including time, effort, expertise, and expense) have hindered relevant epidemiological research using this modality as large sample sizes are required. Due to the high prevalence of OSA in asthmatic children and the impact of OSA on asthma control, there is a need to develop accurate screening tools for OSA in this population. As stated earlier, polysomnography is the gold standard for diagnosis of OSA, but more feasible and less labor-intensive methods are required to screen this high-risk population in the outpatient setting. These screening tools can then be useful to channel polysomnography resources to those that would benefit most from diagnosis and treatment. The demographics of our cohort are very similar to the those studied by Chervin et al.¹⁰ in their landmark paper validating the PSQ. The mean age of children with SDB was 9.3 ± 4.1 (SD) years compared to our cohort with a mean age 11 ± 4 (SD) years.

Our results show that the PSQ has an acceptable sensitivity, but the specificity is low in children with asthma. Of note, the specificity of the PSQ in our study is lower than previous studies.^{10,14} This could be because the nocturnal symptoms of asthma may mimic symptoms of SDB, leading to a false positive PSQ questionnaire. In addition, daytime consequences of asthma could result in positive responses in sleepiness and behavior components of PSQ. We found that using a higher cutoff for PSQ increased the specificity. The choice of a particular cut-off value for a test is essentially a decision based on maximizing sensitivity

and specificity. In general, there is a trade-off between sensitivity and specificity, and the decision must be based on their relative importance (an increase in sensitivity is accompanied by a decrease in specificity and vice-versa). Our results support the use of the PSQ as a screening tool in the outpatient clinic setting to prompt referral of asthma patients to a sleep specialist for evaluation for SDB. Interestingly, we found that the breathing subscale had a better correlation with OI when compared to the total PSQ score. This is somewhat intuitive as this subscale pertains to questions related to SDB symptoms that may overlap with asthma such as snoring, heavy or troubled breathing, and respiratory pauses. Future studies delineating the roles of specific PSQ subscales in OSA-related comorbid medical conditions will be insightful.

Our study was limited by a number of factors. First, this was a retrospective review of the PSQ in children with asthma who were referred to sleep clinics for symptoms of SDB. Therefore, this validation is limited to children who are likely to have OSA (a referral population with a high pre-test probability). Prospective validation of the PSQ (on a larger scale) is needed in the asthma population including children who have no symptoms of SDB. Second, the validation was done using OI as the only parameter for OSA, other parameters such as hypoventilation and arousal index were not analyzed. Third, PSQ was collected in the sleep clinics, not on the night of the PSG. Since there is a lag time between PSQ and PSG, there may be seasonal changes in symptoms of SDB, especially in children with atopy. Lastly, about 43% of our cohort was obese. This is not surprising since obesity is a risk factor for both asthma and OSA. Although the data were controlled for BMI, the prevalence of obesity may have an influence on results. A prospective study designed to assess the validity of the PSQ in obese and non-obese asthmatic children compared with non-asthmatic children will certainly be more beneficial in determining this relationship.

CONCLUSIONS

The sensitivity of PSQ in asthmatic children is high and comparable to previous studies, but the specificity is low. These results suggest that the PSQ may be useful as a screening tool for OSA in children with asthma. Given that snoring and asthma are both highly prevalent conditions, this tool may help prioritize patients at higher risk for OSA and expedite overnight polysomnography for those children. However, prospective work is needed in order to determine whether a higher PSQ cutoff is more suited to this subpopulation of children. In addition to this, the utility of the PSQ as a follow-up tool in asthmatic children being treated with medical or surgical interventions for OSA has yet to be studied.

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