Obstructive Sleep Apnea in Children With Down Syndrome: Screening and Effect of Guidelines

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Abstract

Previous studies have shown low rates of screening for obstructive sleep apnea in children with Down syndrome (DS), a high-prevalence population. Our study investigated the impact of the 2011 American Academy of Pediatrics guidelines, which recommends screening for obstructive sleep apnea with polysomnogram by age 4 years. We conducted a retrospective chart review of patients 0 to 18 years of age with DS seen at a medical center between 2006 and 2016. Polysomnogram screening frequency was investigated and compared pre- and post-guideline publication. A total of 136 participants were identified. Thirty-two percent (44/136) of children with DS were referred for polysomnogram, all of whom had symptoms. Although overall referral frequency was unaffected, completion frequency by age 18 years improved after publication (30% [21/69] vs 19% [13/67]; $P < .05$). Notably, polysomnogram completion frequency by age 4 years improved after guidelines publication compared with prior (25% [17/69] vs 0% [0/67]; $P < .0001$).

Keywords

obstructive sleep apnea, polysomnography, guidelines, Down syndrome, pediatrics

Down syndrome (DS) is the most common chromosomal disorder affecting live-born children with a prevalence of 12.6 per 10 000 children in the United States.[1,2] It is associated with many medical conditions that affect the quality of life. With the hope of improving care for children with DS, in 2011 the American Academy of Pediatrics (AAP) published clinical practice guidelines for the management of children with DS.[3]

One of the most common conditions affecting children with DS is obstructive sleep apnea (OSA), with an estimated prevalence of 30% to 75%.[1] OSA is characterized by repeated episodes of airflow reduction or cessation during sleep due to pharyngeal airway collapse. Adenotonsillectomy is the primary treatment for children with OSA. If left untreated, OSA can result in cardiovascular complications, impaired growth, learning difficulties, behavioral problems, and increased morbidity.[4] Children with DS are already prone to developing many of these complications, making them especially vulnerable to the effects of OSA.

Parents are often inconsistent in reporting their child's OSA symptoms and the symptoms reported by parents poorly correlate with polysomnogram results.[5] Previous studies have suggested the need for more formal screening for OSA in children with DS.[6] Among 45 children with DS whose parents reported no sleep problems, 54% had abnormal polysomnogram findings.[5] Thus, the new AAP guidelines recommend a baseline polysomnogram in all DS children by age 4 years. To our knowledge, no study has compared OSA screening rates pre- and post-guideline publication. The first aim of this study was to investigate the impact of the AAP guidelines on OSA screening of children with DS at our institution.

Risk factors for developing OSA in the general population are well-documented and include adenotonsillar hypertrophy, obesity, male gender, age, and diseases and substances that affect upper-airway tone.[7,8] Meanwhile, risk factors in children with DS are less well established, and previous studies suggest that this vulnerable population is being underdiagnosed.[6] Therefore, the second aim

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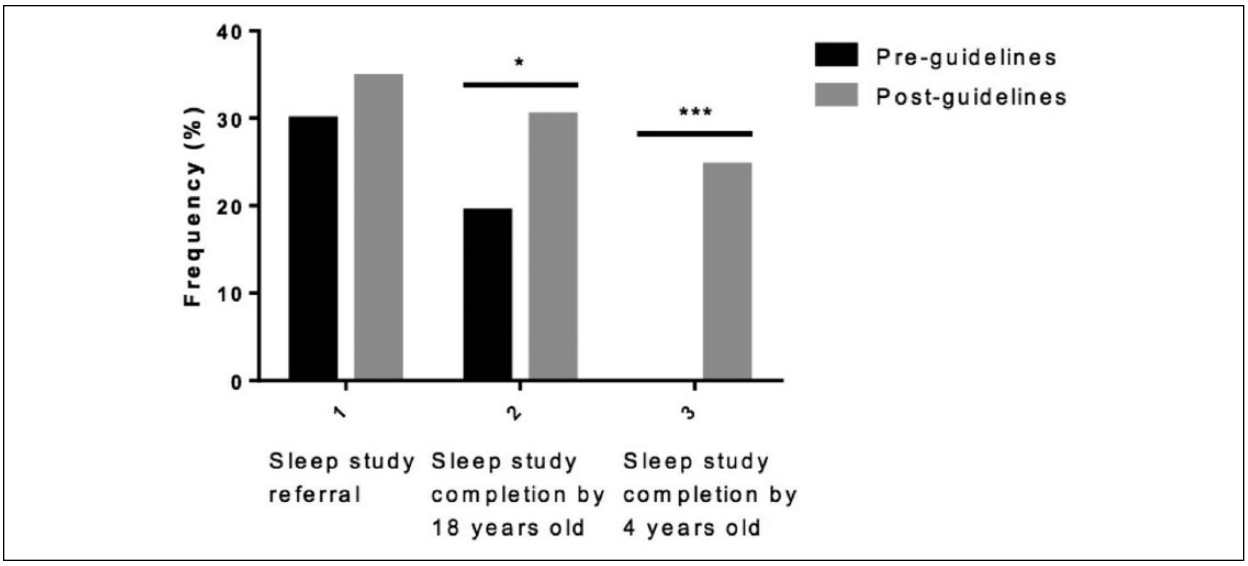

Figure 1. Impact of the 2011 AAP guidelines on obstructive sleep apnea screening in children with Down syndrome. *Indicates $P < .05$. ***Indicates $P < .0001$.

of our study was to investigate the clinical factors, demographics, and sleep architecture of children with DS with and without OSA.

Materials and Methods

Participants

A retrospective chart review at a tertiary hospital, Boston Medical Center (BMC, Boston, MA), was performed after institutional review board approval. A list of patients was compiled by the Clinical Data Warehouse at BMC, consisting of patients who met inclusion criteria of having a diagnosis of DS (*International Classification of Diseases, 10th Revision, ICD-10* code Q90) and being less than or equal to 18 years old when seen at BMC for outpatient care between January 1, 2006, and December 31, 2016. Inclusion criteria were confirmed by manual chart review. A total of 136 eligible participants were identified.

Chart Review

Demographic information including date of birth, language, ethnicity, insurance, gender, and access to an otolaryngologist were recorded. Age and body mass index (BMI) at time of polysomnogram referral and/or completion, and the number of studies completed by age 18 years, were also recorded.

For patients who completed a polysomnogram (defined as generating polysomnogram results and staying the full night of the study), Apnea-Hypopnea Index (AHI) score, total sleep time (TST), time in bed (TIB), time spent in each sleep stage, lowest observed oxygen saturation (SaO_2) and associated time, and peak end-tidal carbon dioxide ($ETCO_2$) were recorded. OSA was defined as either mild (AHI of 2-5 events/hour), moderate (AHI of 6-10 events/hour), or severe (AHI $\geq$10 events/hour), in congruence with the clinical practice guidelines published in 2011.[9]

The presence of other medical conditions was also recorded, including hypertension, diabetes, depression, hypothyroidism, previous adenotonsillectomy surgery, obesity (patient ages 0 to 24 months: weight-for-age $\geq$98th percentile; patients 2 years and older: BMI-for-age $\geq$95th percentile), and gastroesophageal reflux disease. The World Health Organization and Centers for Disease Control and Prevention growth charts were used as reference.

Statistical Analysis

Statistical comparisons of non-OSA and OSA patients were done using unpaired 2-sample Student's *t* test. Pre- and post-AAP guideline publication subgroup analyses were performed using 1-sample test of proportions to assess compliance with guidelines. Logarithmic regression analysis was conducted to determine if any past medical conditions were predictors for OSA. Odds ratios (ORs) were used to measure associations of OSA with other medical conditions. Statistical significance was set at $P < .05$.

Results

Frequencies of polysomnogram studies pre- and post-AAP guidelines are displayed in Figure 1. In total, 32%

(44/136) of children with DS were referred for polysomnogram, and 25% (34/136) completed the study. Six of the 34 patients who underwent polysomnogram did not complete the entire duration of the study; however, they were included in the completed group as the results of their studies are still clinically relevant, and they were referred for study, which is the primary objective of this study.

All children referred for polysomnogram had a documented history of sleep symptoms, such as snoring, apneas, or restlessness. Publication of the AAP guidelines did not change frequency of polysomnogram referrals; however, the frequency of polysomnogram completion by age 18 years improved after publication (19% [13/67] vs 30% [21/69]; $P < .05$). Notably, frequency of polysomnogram completion by age 4 years improved after guidelines publication as well (0% [0/67] vs 25% [17/69]; $P < .0001$).

The mean age at time of polysomnogram for children with DS was 5.8 ± 5.2 years old, ranging from 3 weeks old to 18 years old. The mean number of sleep studies completed was 1.5, with 13 children having more than one polysomnogram. No child with an initial negative study underwent a subsequent polysomnogram. Subsequent studies were obtained for various reasons including OSA monitoring and adenotonsillectomy follow-up. Of the 13 children who had multiple sleep studies, 9 improved, 2 were unchanged, and 1 had worsened. The remaining child had incomplete data for their first polysomnogram and showed severe OSA on their second polysomnogram. The mean age of children who had a negative polysomnogram was 3.2 years old ± 2.6, whereas the mean age of children with OSA was 5.7 years old ± 5.4. Sixty-four percent of sleep studies on patients 4 years old or younger were positive for OSA versus 89% of sleep studies on patients older than 4 ($P < .05$). The average AHI of patients younger than 4 was 11.3 versus 16.7 for patients older than 4, but this did not meet statistical significance.

Using alternative age cutoffs, it was noted that approximately two thirds of children were positive when the age cutoff was 3 and 5, and similar percentages were maintained up to age 11 years (Table 1).

Demographic and Sleep Architecture Data

Demographic data are summarized in Table 2. Out of the 34 children with DS who completed sleep studies, 47% were male and 53% were female. Spanish (35%) was the most common primary language and Hispanic/Latino (35%) was the most common ethnicity. The most common insurance was Medicaid Managed Care (41%). The

Table 1. Distribution of OSA Diagnoses at Age Cutoffs for Children 0 to 18 Years Old.

		# Patients	%
Age ≤1	+OSA	9	90
	−OSA	1	10
Age >1	+OSA	23	70
	−OSA	10	30
Age ≤2	+OSA	14	70
	−OSA	6	30
Age >2	+OSA	18	78
	−OSA	5	22
Age ≤3	+OSA	16	67
	−OSA	8	33
Age >3	+OSA	16	84
	−OSA	3	16
Age ≤4	+OSA	16	64
	−OSA	9	36
Age >4	+OSA	16	89
	−OSA	2	11
Age ≤5	+OSA	18	67
	−OSA	9	33
Age >5	+OSA	14	88
	−OSA	2	13
Age ≤6	+OSA	21	70
	−OSA	9	30
Age >6	+OSA	11	85
	−OSA	2	15
Age ≤7	+OSA	22	71
	−OSA	9	29
Age >7	+OSA	10	83
	−OSA	2	17
Age ≤9	+OSA	22	67
	−OSA	11	33
Age >9	+OSA	10	100
	−OSA	0	0
Age ≤10	+OSA	24	69
	−OSA	11	31
Age >10	+OSA	8	100
	−OSA	0	0
Age ≤11	+OSA	26	70
	−OSA	11	30
Age >11	+OSA	6	100
	−OSA	0	0
Age ≤12	+OSA	27	71
	−OSA	11	29
Age >12	+OSA	5	100
	−OSA	0	0
Age ≤13	+OSA	28	72
	−OSA	11	27
Age >13	+OSA	4	100
	−OSA	0	0
Age ≤14	+OSA	30	73
	−OSA	11	27

(continued)

Table 1. (continued)

		# Patients	%
Age >14	+OSA	2	100
	−OSA	0	0
Age ≤17	+OSA	31	74
	−OSA	11	26
Age >17	+OSA	1	100
	−OSA	0	0

Abbreviation: OSA, obstructive sleep apnea.

Table 2. Demographics of Children With Down Syndrome Who Completed Sleep Studies.

Variable	Patients (n = 34)
Sex (%)	
Male	47
Female	53
Primary language (%)	
Spanish	35
English	29
Haitian Creole	18
Vietnamese	9
Bengali	3
Cape Verdean/Port Creole	3
Somali	3
Ethnicity (%)	
Hispanic/Latino	35
Black/African American	21
Unknown	18
Haitian	15
Asian	12
Insurance (%)	
Medicaid MngCare	41
NHP Medicaid	21
BMC HlthNet Medicaid	15
Netwk Hlth Medicaid	9
Unknown	6
BCBS POS	3
Health Plans Inc	3
Tufts PPO	3
Weight/BMI-for-age percentile (mean)	51.3 ± 40.1
(−) OSA	45.2 ± 36.0
(+) OSA	53.1 ± 41.0
Reported OSA symptoms (%)	100
Seen an otolaryngologist at least once (%)	91

Abbreviations: NHP, Neighborhood Health Plan; BMC, Boston Medical Center; BCBS, Blue Cross Blue Shield; POS, point of service; PPO, Preferred Provider Organization; BMI, body mass index; OSA, obstructive sleep apnea.

mean weight/BMI-for-age percentile was 51.3 ± 40.1. While not statistically significant, there was a trend toward children with OSA having a greater weight/BMI-for-age (53.1 vs 45.2 percentile non-OSA, $P = .08$). All children reported at least 1 OSA symptom (most common were snoring, sleep disturbances, and daytime sleepiness) and 97% had seen an otolaryngologist for various reasons related to sleep or other otolaryngologic complaints.

Sleep architecture data are summarized in Table 3. The mean AHI score was 13.6 ± 23.6. In total, 26% of the sleep studies indicated no OSA, 19% mild OSA, 23% moderate OSA, and 33% severe OSA. The average time spent in sleep stages N1, N2, N3, and rapid eye movement were 1.8%, 48.8%, 31.6%, and 17.8%, respectively. The presence of OSA did not affect time spent in any sleep stage. The average TST/TIB (minutes) ratio for children with OSA was lower than for those without (338/405 vs 402/469; $P < .05$). The average lowest SaO_2 and associated time duration for children with OSA was lower than for those without (80.3%/16.3 seconds vs 91.3%/15.6 seconds; $P < .001$), while the average peak $ETCO_2$ for children with versus without OSA was the same (51.6 torr vs 51.0 torr).

Clinical Factors Predicting OSA

A logistic regression model was performed to ascertain the predictive value of other medical conditions on OSA. No significant predictors were identified by our regression model. While not statistically significant, there was a trend toward children diagnosed with OSA more likely to be obese (38% vs 20% non-OSA; $P = .25$), and have hypertension (50% vs 15% non-OSA; $P = .06$). No child had a diagnosis of depression or diabetes.

Discussion

In 2011, the AAP published guidelines recommending OSA screening by age 4 in children with DS. To date, research regarding the effect of these guidelines on clinical practice has been limited. Our study assesses the effect of these guidelines at one medical institution, and to our knowledge is the first of its kind. As the largest safety net hospital in New England, BMC also has an especially diverse patient population making it well-suited for investigation.

We found that the new guidelines have not changed the overall rate of referrals for sleep studies. The frequency of polysomnograms in children with DS was only 32%, consistent with low rates previously found at other sites.[6] In one retrospective study conducted prior to the 2011 guidelines, only 88/249 (35%) of children with DS had undergone a polysomnogram.[10] In another retrospective study also before guideline publication,

Table 3. Sleep Architecture Characteristics of Children With Down Syndrome Who Completed Sleep Studies.

Variable	All Patients (n = 34)	−OSA (n = 8)	+OSA (n = 26)
AHI score	13.6 ± 23.6	1.1 ± 0.4	17.8 ± 26.0
Sleep stage (%)			
N1	1.8 ± 3.3	0.8 ± 0.6	2.1 ± 3.7
N2	48.8 ± 17.5	49.0 ± 17.7	48.8 ± 17.4
N3	31.6 ± 14.5	32.3 ± 12.8	31.3 ± 15.1
REM	17.8 ± 12.3	17.8 ± 11.8	17.8 ± 12.5
TST/TIB (min)*	355/421 ± 106/106	402/469 ± 59/45	338/405 ± 114/115
MinSaO_2 (%)/time (min)	83.4/16.1 ± 11.0/8.0	91.3/15.6 ± 3.8/4.8	80.3/16.3 ± 11.4/9.0
Max$ETCO_2$ (torr)	51.4 ± 5.4	51.0 ± 3.7	51.6 ± 5.7

Abbreviations: AHI, Apnea Hypopnea Index; REM, rapid eye movement; TST, total sleep time; TIB, time in bed; SaO_2, lowest observed oxygen saturation; $ETCO_2$, peak end-tidal carbon dioxide.
*$P < .05$.

only 55/178 (31%) children with DS had completed a polysomnogram.[11] Recently, a large study examining 24 pediatric sites after guideline publication demonstrated only 17% of children with DS had a polysomnogram performed by age 25.[12]

In contrast to previous studies, our study cohort was not predominantly Caucasian or English speaking. Hispanic/Latino was the most common ethnicity (35%) and Spanish was the most common primary language (35%). Our study therefore provides information on a more diverse and understudied patient population.

Although our study found that overall polysomnogram *referral* frequency has not increased since the 2011 AAP guideline publication, we observed an 11% increase in polysomnogram *completion* post-guidelines. Since the guidelines emphasized that polysomnograms be completed by age 4, we looked specifically at this age and found a 25% increase in children completing a polysomnogram by this age. Without the increase in referral, it is unclear but interesting what is causing the increase in completion of polysomnography post-guidelines. The number of pediatric sleep study beds remained the same from 2006 to 2011 and the otolaryngology/pediatric physicians making the referrals for polysomnography were relatively the same. Thus, some other factors may be contributing to this phenomenon besides guidelines publication, such as better patient education or improved order tracking. Our future studies will identify system changes that may have influenced our outcomes.

In our study, all patients who underwent a polysomnogram had OSA symptoms; however, screening guidelines recommend that all children with DS be referred for polysomnogram regardless of if they are symptomatic. There are many possible reasons why providers delay obtaining polysomnograms, including parent underreporting of OSA symptoms, physician reluctance to elicit symptoms, the need to focus on other competing medical problems, and lack of knowledge of guidelines.

In a healthy population, OSA prevalence increases with age, and peaks around 55 years old.[13] Conversely, children with DS can outgrow OSA.[14] This has implications for polysomnogram timing, because OSA may either develop later or resolve after initial testing, changing the management. Children with OSA were significantly older by approximately 2.5 years compared with children with normal polysomnograms. Furthermore, more tests were positive in children tested after age 4. Thus, a cutoff of 4 may not capture all children with DS and OSA.

Current guidelines do not describe indications for subsequent sleep studies. An average of 1.5 polysomnograms were completed per child with DS. No child who had a negative initial polysomnogram was retested; thus, it is possible that some of these children went on to develop OSA at a later time. This is supported by the finding that the average age of patients with OSA was higher (3.2 vs 5.7 years old; $P = .03$). Future research should re-assess those patients who have negative initial polysomnograms to assess the risk of subsequently developing OSA.

A challenge with setting an age cutoff for screening is adequately capturing patients with OSA while not missing out on those that develop OSA later in life. Given that 64% of children screened by age 4 had OSA, we are not recommending delaying screening, merely emphasizing that those children who do not demonstrate OSA on initial polysomnogram may benefit from repeat screening at a later date. Because the supporting data for an age cutoff of 4 is limited, we also looked at how changing the cutoff would change the proportion of patients with OSA. Looking at other cutoffs between 2 and 7, approximately two thirds of patients had OSA. In the future, age cutoffs should be

reassessed by screening all children with DS, not just those who were symptomatic.

In our study, the average AHI was 13.6, which is similar to findings in other studies.[1,6,11] The distribution among mild, moderate, and severe OSA was consistent with several reports in the literature of children of similar ages,[6] while other studies with younger cohorts had either significantly higher or lower AHI severity.[11,15] Moreover, our cohort had a different ethnic profile that may add new information.

We found reduced TST/TIB in DS children when comparing those with OSA against those without OSA, with 64 minutes lost on average for both TST and TIB ($P < .05$). In addition, the average lowest SaO_2 was significantly lower in those with OSA versus those without. Average peak $ETCO_2$ was not different between the groups. In one study, Maris et al, no significant difference was found between DS children with or without OSA in sleep time, sleep efficiency, or oxygen saturation.[1] More research should be done to characterize differences between children with DS and healthy controls, and within the DS population.

Finally, we examined other medical conditions as potential predictors of OSA. From our chart review, hypertension, obesity, gastroesophageal reflux disease, hypothyroidism, and adenotonsillectomy were not associated with the presence of OSA. While not statistically significant, children with obesity (OR = 2.40), hypothyroidism (OR = 2.10), and either past or future adenotonsillectomy surgery were more likely to have OSA. We focused on these medical conditions because of their known associations with OSA in non-DS patients.[13] The relationship of these factors on OSA in children with DS have been mixed. One study found no relationship between obesity or adenotonsillectomy and OSA,[15] whereas other studies have associated higher BMI with increased OSA severity.[11] Further research is warranted to elucidate the relationships between these medical conditions and OSA in this population.

There are several limitations to our study. The main limitation was our modest cohort size. We only scrutinized data from one of several health care institutions in the region that serve pediatric patients with DS. It is also possible that our study did not capture all BMC patients who were screened for OSA as some may have had their polysomnograms at institutions outside of our medical record. As a result, our statistical power was reduced in showing that trends such as obesity may actually be significant in this population. Another limitation is that all patients were symptomatic, so we were unable to assess results in asymptomatic children. Future studies are warranted using larger patient numbers, as well as asymptomatic patients to elicit additional results. We intend to conduct these studies prospectively and in a multi-centered manner.

Conclusion

Children with DS have a significantly higher prevalence of OSA and if untreated are at increased risk for health consequences. Our findings indicate that only a quarter of children under 4 years with DS completed a polysomnogram as recommended in a tertiary hospital. Although polysomnogram completion rate by age 4 has increased, referral for screening has not. Future directions for study would be a prospective, multicenter trial to evaluate compliance with guidelines on a larger scale, and development of quality interventions within our institution, which could be useful to other institutions in ensuring compliance. We also found that more children diagnosed with OSA were older than 4. Therefore, OSA may be underdetected in children with DS if screened younger than 4, suggesting the cutoff may need to be reexamined, and perhaps more so that rescreening should be considered. This study demonstrates the need for ongoing quality improvements to improve compliance at our institution, and may suggest to other institutions that they undertake similar initiatives to evaluate compliance with these and other clinical guidelines

Author Contributions

All authors - AH, AG, KW, MC, and JL - contributed to the research conceptualization and design, data acquisition, results analysis and interpretation, drafting of the article, and critical revisions. All authors had complete access to the study data that support the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

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