ORIGINAL ARTICLE

Incidence of positive screening for obstructive sleep apnea in patients with isolated cleft lip and/or palate

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OBJECTIVE: To determine the incidence of obstructive sleep apnea (OSA) in children with isolated cleft lip and/or palate (CL/P).
METHODS: The present prospective study was performed at a pediatric tertiary care centre. Consecutive patients evaluated at the cleft clinic from January 2011 to August 2013 were identified. Patients' families prospectively completed the Pediatric Sleep Questionnaire (PSQ), a validated tool used to predict moderate to severe OSA. Patients with CL/P and an underlying syndrome or other craniofacial diagnosis were excluded. A positive OSA screen was recorded if the ratio of positive to total responses was >0.33. Risk factors associated with a positive screen were identified using the Student's *t* or ANOVA test.
RESULTS: A total of 867 patients completed the PSQ, 489 of whom with isolated CL/P met inclusion criteria. The mean age was 8.4 years. The overall incidence of positive screening was 14.7%. The most commonly reported symptoms among positive screeners were 'fidgets with hands or feet' (73.6%), 'interrupts others' (69.4%) and 'mouth breather during the day' (69.4%). The most sensitive items were 'stops breathing during the night' and 'trouble breathing during sleep', with positive predictive values of 0.78 and 0.67, respectively. Sex, body mass index, ancestry and cleft type were not significantly associated with increased risk for positive screening.
CONCLUSION: One in seven children with isolated CL/P screened positively for OSA according to the PSQ. This finding highlights the potential importance of routine screening in this at-risk group.

Key Words: *Cleft lip/palate; Obstructive sleep apnea; Pediatric Sleep Questionnaire*

L'incidence du dépistage positif de l'apnée obstructive du sommeil chez les patients ayant une fente labiale ou palatine isolée

OBJECTIF : Déterminer l'incidence d'apnée obstructive du sommeil (AOS) chez les enfants ayant une fente labiale ou palatine isolée (F/LP).
MÉTHODOLOGIE : La présente étude prospective a été effectuée dans un centre de soins tertiaires. Des patients consécutifs évalués à la clinique de fente labiale ou palatine entre janvier 2011 et août 2013 ont été repérés. Les familles des patients ont rempli prospectivement un questionnaire sur le sommeil pédiatrique (PSQ), un outil validé utilisé pour prédire l'AOS modérée à grave. Les patients ayant une F/LP et un syndrome sous-jacent ou un autre diagnostic crâniofacial étaient exclus. Le dépistage d'AOS était positif si le ratio entre la réponse positive et les réponses totales était supérieur à 0,33. Les facteurs de risque de dépistage positif ont été déterminés à l'aide du test *t* de Student ou du test ANOVA.
RÉSULTATS : Au total, 867 patients ont rempli le PSQ, dont 489 avaient une F/LP qui respectait les critères d'inclusion. Ils avaient un âge moyen de 8,4 ans. L'incidence globale de dépistage positif s'élevait à 14,7 %. Les symptômes les plus déclarés chez les personnes dépistées comme positives étaient « agite les mains ou les pieds » (73,6 %), « interrompt » (69,4 %) et « respire par la bouche pendant la journée » (69,4 %). Les faits les plus inquiétants étaient « arrête de respirer pendant la nuit et « a de la difficulté à respirer pendant qu'il dort », dont les valeurs prédictives positives étaient respectivement de 0,78 et de 0,67. Le sexe, l'indice de masse corporelle, l'ascendance et le type de fente ne s'associaient pas de manière significative à un risque accru de dépistage positif.
CONCLUSION : Un enfant sur sept ayant une F/LP isolée était positif à l'AOS selon le PSQ. Cette observation fait ressortir l'importance potentielle du dépistage systématique dans ce groupe à haut risque.

Recent prospective studies evaluating the prevalence of obstructive sleep apnea (OSA) in the general pediatric population using polysomnography (PSG) have estimated the prevalence to range from 1.2% to 5.8% (1-3). Pediatric OSA is an important cause of morbidity and, if untreated, can lead to adverse effects on growth, behaviour, cognition and cardiopulmonary function (4). Children with craniofacial deformities, including cleft lip and palate (CL/P), are at increased risk for OSA due to abnormalities in the naso- and oropharyngeal anatomy present from birth or acquired as a result of surgical intervention (5,6). Children with CL/P commonly exhibit midface hypoplasia and a retrognathic maxilla, which persist after surgical intervention (7,8). Moreover, surgical treatments for oral rehabilitation include palato- and pharyngoplasty, which have been shown to increase OSA risk (6-8). However, despite its adverse effects, little is known about the incidence of OSA in this high-risk population.

Despite the paucity of literature, the American Academy of Pediatrics acknowledges an increased risk for OSA in children with CL/P (9). Previous studies involving children with CL/P are limited by highly heterogeneous study populations, small patient cohorts and specific surgical interventions. From an epidemiological perspective, children with isolated, nonsyndromic CL/P constitute the majority of patients seen at most cleft clinics (10). Thus, it makes empirical sense to characterize the risk for OSA in this specific population. Furthermore, although PSG remains the gold standard for OSA diagnosis, issues of cost and access to care commonly limit the clinical utility of this tool. Thus, it has been suggested that the majority of children in the United States are treated for OSA based purely on clinical assessment without a PSG diagnosis (11).

In the present study, we used a validated screening tool to assess the incidence of OSA symptoms in children with isolated, nonsyndromic CL/P treated at a large urban cleft centre. We hypothesized that this patient population is at high risk for positive OSA screening. Secondary objectives aimed to characterize clinical and demographic variables that increase risk for positive OSA screening.

METHODS

An Institutional Review Board-approved retrospective chart review was performed on consecutive patients evaluated at the Cleft Clinic at the Children's Hospital of Philadelphia (Pennsylvania, USA) between January 2011 and August 2013. As part of standard clinical care, the Sleep-Related Breathing Disorder subscale of the Pediatric Sleep Questionnaire (PSQ) was prospectively administered to all patients cared for at the Cleft Clinic during the study period. This validated tool is a parent-completed survey that predicts moderate to severe OSA with a sensitivity of 83% and a specificity of 87% in otherwise healthy children (12). The PSQ consists of 22 'yes/no' questions regarding symptoms of sleep-disordered breathing, daytime sleepiness and behavioural issues. Questionnaires were scored by the number of positive responses; a ratio of positive to total responses >0.33 was considered to be a positive OSA screen. Unanswered questions were

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TABLE 1
Patient demographics at time of administration of the Pediatric Sleep Questionnaire (n=489)

Patient characteristic	
Age, years	
2–4	130 (26.6)
5–9	196 (40.1)
10–13	90 (18.4)
14–18	73 (14.9)
Sex, male/female, n/n (%/%)	291/198 (59.5/40.5)
Body mass index, percentile*	
0–20	89 (18.7)
21–40	78 (16.4)
41–60	88 (18.5)
61–80	110 (23.2)
81–100	110 (23.2)
Ancestry	
Caucasian	298 (60.7)
African American	36 (7.5)
Hispanic	29 (5.9)
Asian	126 (25.9)
Cleft type	
Cleft lip	23 (4.7)
Submucous cleft palate	14 (2.9)
†Veau I	33 (6.7)
†Veau II	63 (12.8)
†Veau III	243 (49.7)
†Veau IV	113 (23.2)
Surgical status	
Posterior pharyngoplasty	26 (5.3)
Sphincter pharyngoplasty	9 (1.8)
Tonsillectomy	9 (1.8)
Adenoidectomy	10 (2.0)
Combined tonsillectomy + adenoidectomy	14 (2.9)

*Data presented as n (%) unless otherwise indicated. *14 participants did not have available body mass index data; †Veau classifications: Veau I – cleft of the soft palate only; Veau II – cleft of the soft and hard palate; Veau III – unilateral complete cleft lip and palate; Veau IV – bilateral complete celft lip and palate*

eliminated from the survey so that ratios were generated only from the number of answered questions. In the event that an answer other than 'yes' or 'no' was recorded, the answer was considered to be a positive response unless clear evidence argued to the contrary. For example, a written answer response of 'sometimes' was considered a positive response equivalent to 'yes'.

A chart review was performed on all patients who completed the PSQ to obtain demographic information, clinical diagnoses and surgical history. Demographic variables included age at time of survey, sex, body mass index (BMI) and ancestry. For purposes of comparison, BMI was normalized to age-matched control data from the Centers for Disease Control & Prevention (Georgia, USA) and reported as a percentile. Measured weight was used if it was collected within six months of PSQ administration. Race was reported as Caucasian, African American, Hispanic or Asian. Only nonsyndromic children with isolated CL/P who were otherwise healthy were included in the present study. Patients with underlying chromosomal abnormalities or other craniofacial disorders were excluded. The diagnosis of CL/P was classified as isolated cleft lip (CL), submucosal cleft palate, and CL/P according to the Veau classification: cleft of the soft palate only (Veau I), cleft of the soft and hard palate (Veau II), unilateral complete CL/P (Veau III), and bilateral complete CL/P (Veau IV). Surgical status was documented based on the timing of surgical procedure relative to administration of the PSQ. Surgical procedures for primary cleft

TABLE 2
Prevalence of positive obstructive sleep apnea (OSA+) screening according to sex and age group

Age, years	Male/female, n/n	Patients with OSA+ screen, n (%)	OSA+ screen		P
			Male	Female	
2–4	68/61	13 (10.1)	9	4	0.21
5–9	124/74	25 (12.6)	17	8	0.60
10–13	51/38	13 (14.6)	7	6	0.79
14–18	48/25	3 (4.1)	1	2	0.24
Total	489	54 (11.0)	34	20	0.58

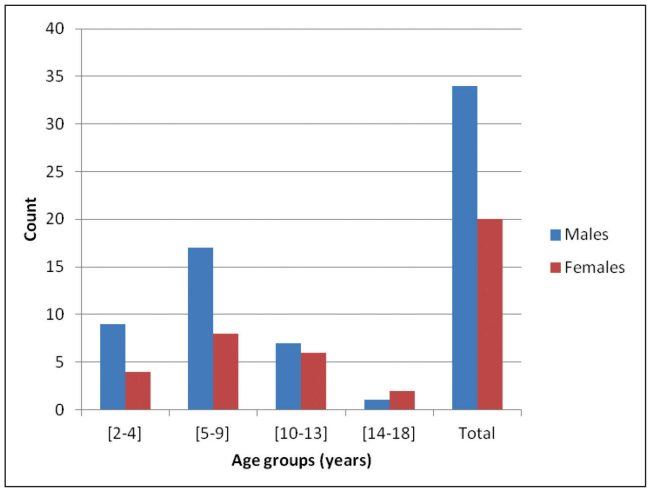

Figure 1) *Distribution of positive obstructive sleep apnea screening according to sex and age group. No significant differences between age, sex and positive obstructive sleep apnea screen (all P>0.21)*

closure included Furlow double-reversing Z-palatoplasty and Veau-Wardill-Kilner V-Y pushback. Revision procedures included posterior pharyngeal flap (PPF) and sphincter pharyngoplasty (SPP). For purposes of comparison according to surgical status or clinical diagnosis, the Student's *t* test or ANOVA test with Tukey's method was used where appropriate. All statistical calculation was performed using STATA version 13 (StataCorp, USA); P<0.05 was considered to be statistically significant.

RESULTS

A total of 867 patients seen in the clinic were administered the PSQ during the study period and 489 with isolated CL/P met inclusion criteria. The mean (± SD) age at time of PSQ administration was 8.4±4.3 years (range two to 18 years). The cohort descriptors are shown in Table 1. The study population was predominately male (59.5%) and Caucasian (60.7%). One-quarter of the cohort was Asian (25.9%). Nearly one-half of the subjects had a Veau class III cleft (49.7%) and nearly one-quarter had a Veau class IV cleft (23.2%).

Of children with nonsyndromic CL/P, 14.7% had a positive screen for OSA. Table 2 summarizes the prevalence of positive OSA screening according to age and sex. There was no conferred risk for positive screening according to either sex or age group in the cohort (Figure 1 and Table 2). Table 3 summarizes the prevalence of positive OSA screening according to BMI percentile while Table 4 summarizes according to ancestry. Neither higher BMI percentile nor ancestry were associated with increased positive OSA screening. Moreover, there were no significant differences between cleft type and positive OSA screening (Table 5).

The frequency of individual OSA symptoms was evaluated (Table 6). The most commonly reported symptoms in the general population were 'mouth breather during the day' (29.5%), 'interrupts others' (27.2%) and 'fidgets with hands or feet' (25.6%). In children

TABLE 3
Prevalence of pediatric positive obstructive sleep apnea (OSA+) screening according to body mass index percentile

Body mass index percentile	n	OSA+ screen, n (%)
0–20	89	8 (9.0)
21–40	78	7 (9.0)
41–60	88	11 (12.5)
61–80	110	13 (11.8)
81–100	110	15 (13.6)

TABLE 4
Prevalence of Pediatric Sleep Questionnaire-diagnosed obstructive sleep apnea (OSA) according to ancestry

Ancestry	n	Patients with OSA+ screen, n (%)
Caucasian	298	31 (10.4)
African American	36	6 (16.7)
Hispanic	29	1 (3.4)
Asian	126	17 (13.5)

+ Positive

with a positive screen, the most common symptoms were 'fidgets with hands or feet' (73.6%), 'interrupts others' (69.4%), 'mouth breather during the day' (69.4%) and 'interrupts others' (69.4%). Questions with the highest positive predictive values were 'stops breathing during the night' and 'trouble breathing during sleep', with values of 0.78 and 0.67, respectively.

In contrast, children with a negative OSA screen most commonly reported 'mouth breather during the day' (21.3%), 'interrupts others' (19.4%), 'fidgets with hands or feet' (17.3%), 'on the go or driven by a motor' (17.3%) and 'occasionally wets the bed' (17.0%). Questions least predictive of a positive PSQ screen were 'fidgets with hands and feet' and 'easily distracted', with negative predictive values of 0.95. Additionally, questions most commonly blank were 'mouth breather during the day' (3.5%), 'wakes in the morning with a dry mouth' (3.7%) and 'occasionally wets the bed' (3.3%).

Thirty-two patients underwent PPF surgery before taking the PSQ (6.5%), and 12 underwent dynamic SPP. The mean time from surgery to completion of the PSQ was 5.83 and 5.56 years, respectively; 1.8% of patients underwent tonsillectomy before OSA screening and 2.0% underwent adenoidectomy. The mean time from surgery to completion of the PSQ was 4.82 and 4.61 years, respectively; 2.9% of patients underwent combined adenotonsillectomy. None of the interventions were associated with increased risk for positive OSA screening (P>0.05) (Table 7).

DISCUSSION

The present study used prospective administration of an OSA screening tool with retrospective chart review to report the prevalence of positive OSA screening in a large cohort of children with nonsyndromic CL/P. The prevalence of children with a positive screen was 14.7%. Thus, relative to their unaffected peers, children with CL/P may be seven times more likely to develop OSA symptoms (1-3). Our findings are consistent with the well-documented under-recognition of OSA in children with clefts (13,14). Because pediatric OSA is linked to delays in growth (4), neurodevelopment (15) and adverse metabolic effects (16), it is plausible that delayed recognition of OSA is responsible for increased morbidity in children with CL/P. The majority of studies investigating OSA in children with cleft are limited through the use of heterogeneous cohorts of craniofacial patients and patients undergoing specific surgical interventions (17-19). The present study is the first to report the prevalence of positive OSA screening in a large cohort of children with isolated, nonsyndromic CL/P.

TABLE 5
Patient presentation of positive obstructive sleep apnea (OSA+) screening according to age and cleft type

Cleft type	OSA+ screen, n	Age at Pediatric Sleep Questionnaire, years, n (%) 2–4	5–9	10–13	14–18
Submucous cleft palate	0	0 (0)	0 (0)	0 (0)	0 (0)
Cleft lip	4	1 (25.0)	1 (25.0)	2 (50.0)	0 (0)
*Veau I	4	1 (25.0)	2 (50.0)	1 (25.0)	0 (0)
*Veau II	5	1 (20.0)	3 (60.0)	1 (20.0)	0 (0)
*Veau III	28	7 (25.0)	12 (42.9)	7 (25.0)	2 (7.1)
*Veau IV	13	3 (23.1)	7 (53.8)	2 (15.4)	1 (7.7)

*There were no significant differences between type of cleft and OSA+ screening.*Veau classifications: Veau I – cleft of the soft palate only; Veau II – cleft of the soft and hard palate; Veau III – unilateral complete cleft lip and palate; Veau IV – bilateral complete celft lip and palate*

TABLE 6
Frequency of individual obstructive sleep apnea symptoms in patients with cleft lip and palate

Symptom	Frequency of symptoms, % All patients	Positive screeners	Negative screeners
Snores more than one-half the time	21.9	61.1	13.7
Always snores	9.7	29.2	5.3
Snores loudly	13.1	45.8	6.2
'Heavy' or loud breathing during sleep	23.5	59.7	15.6
Trouble breathing during sleep	4.1	16.7	1.4
Stops breathing during the night	3.7	19.4	1.0
Mouth breather during the day	29.5	69.4	21.3
Wakes in the morning with a dry mouth	22.1	58.3	14.1
Occasionally wets the bed	20.0	33.3	17.0
Wakes up feeling unrefreshed	14.7	38.9	9.1
Problem with sleepiness during the day	9.7	27.8	6.5
Others comment on child appearing sleepy	2.5	9.7	1.2
Hard to wake in the morning	15.4	38.9	10.3
Wakes in the morning with a headache	4.1	16.7	1.7
Ever stopped growing at a normal rate	4.4	15.3	2.2
Overweight	3.2	6.9	2.4
Does not seem to listen when spoken to directly	16.6	59.7	8.6
Difficulty organizing tasks	12.2	47.2	5.5
Easily distracted	22.8	69.4	14.6
Fidgets with hands or feet	25.6	73.6	17.3
'On the go' or 'driven by a motor'	24.7	62.5	17.3
Interrupts others	27.2	69.4	19.4

A PSG can distinguish between OSAs and central sleep apneas, and recognize periodic limb movements and other sleep abnormalities that may mimic OSA symptoms. As such, it remains the gold standard in the diagnosis of OSA; however, in cases in which OSA is well documented clinically, PSG may not always be absolutely indicated (4). In addition to its cost, inconvenience and lack of availability, PSG has numerous limitations that undermine its utility. Although PSG can be used to detect sleep abnormalities related to airway obstruction, gas exchange and disturbances in sleep architecture, it has never been validated to predict adverse clinical sequelae or response to medical treatment (20). Thus, even in the absence of PSG confirmation, symptoms of sleep-disordered breathing commonly result in adverse neurocognitive and behavioural consequences. Furthermore, the lack of consistent acquisition between sleep laboratories and standard

TABLE 7
Surgical procedures affecting the upper airway according to age at time of surgery

Age, years	Tonsillectomy + adenoidectomy	Adenoidectomy	Tonsillectomy	PPF	SPP
2–4	9	4	5	9	3
5–9	5	5	2	14	6
10–13	0	1	1	8	2
14–18	0	0	1	1	1
Total	14	10	9	32	12

Data presented as n. PPF Posterior pharyngoplasty; SPP Sphincter pharyngoplasty

criteria for abnormal sleep studies further limits the utility of PSG as a diagnostic tool (21).

Thus, an important area of research is the development of effective OSA screening tools, thereby obviating the need for PSG clinically. While initially developed for research, the Chervin Pediatric Sleep Questionnaire (PSQ) is among the best screening tools for pediatric OSA (22) and, as such, is often used in the clinic (23). The PSQ is a 22-question survey that asks questions related to snoring and troubled breathing, daytime sleepiness, inattentiveness and other common symptoms of pediatric OSA. This instrument has not been adequately studied in children with orofacial clefts and our study is the first to report PSQ findings in a large cohort of children with nonsyndromic CL/P. While unique in this homogenous population, several studies have reported PSQ findings from other craniofacial settings. MacLean et al (19) reported an incidence of positive OSA screening in 31.4% in a cohort of children with Pierre Robin sequence and underlying chromosomal abnormalities.

There were many items on the PSQ that were frequently underreported in the study cohort despite the high prevalence of positive OSA screening. There are several reasons to explain these differences and it must be emphasized that the PSQ was designed and validated for healthy children without CL/P. Children with these disorders have different etiologies for upper airway obstruction that may manifest as differences in 'normal' breathing. These differences can significantly alter the PSQ because symptoms of day- and night-time breathing account for approximately one-third of all questions. Additionally, families of children with CL/P may have an altered sensitivity to OSA symptoms as they are exposed to a lifetime of medical and surgical interventions that may alter their expectations. Furthermore, children with CL/P commonly demonstrate increased risk for impairments in neurocognitive function (24,25), which may be less likely related to OSA than in the general pediatric population. Similarly, factors in the general pediatric population commonly associated with increased risk for OSA failed to demonstrate a statistical correlation in our cohort, such as obesity, a well-established and increasingly common risk factor for OSA (26). Additionally, some studies have shown increased prevalence and severity of OSA among African American children relative to their Caucasian peers (27,28). Finally, pediatric OSA has classically been described to exhibit male predominance (28); however, several large studies have found no significant difference in OSA prevalence according to sex (29,30). Again, differences in our results may be due to complex underlying medical conditions unique to this patient population.

OSA is a well-described complication of surgical interventions for the treatment of velopharyngeal insufficiency (17,31,32). Despite possessing normal mandibular architecture, children with CL/P are at greater risk for upper airway obstruction. A deviated nasal septum is common in children with unilateral CL, and often results after surgical intervention (6). Furlow palatoplasty can both lengthen and thicken the palate, and has a tendency to decrease airway space. Additionally, acute airway obstruction is well documented in patients undergoing PPF and SPP. This chronic obstruction can compromise the nasal airway and manifest as OSA. Interestingly, our study did not find an association between these interventions and increased risk for positive OSA screening. This could be secondary to the relatively small cohort of children with nonsyndromic cleft requiring these complex procedures or length of follow-up.

Combined adenotonsillectomy is the most common surgical procedure to address pediatric OSA (33), with more than a half-million surgeries performed annually in the United States alone (34). For children with CL/P, a partial instead of full adenoidectomy is frequently performed to prevent future velopharyngeal insufficiency. While common in the pediatric population, only 2.9% of children in our cohort underwent this procedure. Despite demonstrated benefits of a recent randomized control trial (35), we did not find a protective effect of adenotonsillectomy from positive OSA screening.

There were some limitations to the present study and, thus, future areas for investigation. The first is the nature of the screening tool we used to determine the prevalence of positive OSA screening. The PSQ validated by Chervin et al (12) had a reported sensitivity and specificity of 0.83 and 0.87, respectively, for the diagnosis of moderate to severe OSA in children two to 18 years of age. To validate the PSQ, overnight PSG was used. The American Academy of Pediatrics recognizes that, despite a lack of consensus, PSG is currently the best available tool for the diagnosis of OSA (9). Until better tools are developed, PSG and screening questionnaires based on its reliability must be used in the diagnosis and treatment of OSA. Second, parents commonly omitted questions from the PSQ that did not pertain to their child. For example, the symptom of 'occasionally wets the bed' has limited applicability to a child still wearing diapers. This may compromise the utility of the PSQ and is a limitation of paper administration of the PSQ. Additionally, the present study was limited in the fact that a control group was not included for comparison and, as such, current published data were used. A control group would have increased the strength of our study by providing an objective benchmark for questionnaire results specific to our practice. With any retrospective study, our analysis was susceptible to inherent biases in patients presenting to clinic, transfer of care issues and different follow-up periods. Thus, we cannot draw strong conclusions regarding PSQ correlations with clinical variables.

CONCLUSIONS

One of seven children with isolated CL/P screened positively for OSA using PSQ. This is out of proportion to the general pediatric population, and highlights the potential importance of routine screening in this high-risk group. Future work will correlate these findings with diagnostic tests for OSA to determine true prevalence of the disease.

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