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SCIENTIFIC INVESTIGATIONS

Dysphagia severity is associated with worse sleep-disordered breathing in infants with Down syndrome

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Study Objectives: Hypotonia, commonly seen in infants with Down syndrome (I-DS), can contribute to masticatory and oropharyngeal muscle weakness, increasing the risk for dysphagia and sleep-disordered breathing. Data describing the occurrence of dysphagia and sleep-disordered breathing in I-DS are limited. This study aims to determine the frequency and severity of dysphagia and its relationship to polysomnogram parameters in I-DS.

Methods: We included I-DS who underwent polysomnography at a single academic center over a 6-year period. Data collected included sex, age, presence of dysphagia (low suspicion of dysphagia vs dysphagia vs feeding tube), and polysomnographic data. Dysphagia was determined by a video fluoroscopic swallow study in the presence of clinical suspicion.

Results: A total of 40 I-DS were identified (mean age 6.6 months ± 3; male 65%). There were 11, 13, and 16 I-DS with low suspicion of dysphagia, dysphagia, and feeding tube, respectively. Obstructive sleep apnea was more severe in I-DS in the feeding tube group when compared with the group with a low suspicion of dysphagia and (apnea-hypopnea index mean [standard error] = 49.3 [7.6] vs 19.2 [9.2] events/h; $P = .016$). Dysphagia severity was positively correlated with a higher obstructive apnea-hypopnea index ($r = .43$, $P = .006$).

Conclusions: There is a high incidence of dysphagia and sleep-disordered breathing in I-DS. Dysphagia severity correlated with obstructive apnea-hypopnea index severity. Our results suggest that I-DS need early evaluation of both sleep-disordered breathing and dysphagia.

Keywords: dysphagia, Down syndrome, infants, obstructive sleep apnea, sleep-disordered breathing

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Hypotonia, commonly seen in infants with Down syndrome, can contribute to masticatory and oropharyngeal muscle weakness, increasing the risk of dysphagia and sleep-disordered breathing. Data describing the occurrence of dysphagia and sleep-disordered breathing in infants with Down syndrome are limited.

Study Impact: Our study shows a high incidence of dysphagia and sleep-disordered breathing in infants with Down syndrome. Current guidelines suggest screening at school age or when there are clinical symptoms of obstructive sleep apnea in Down syndrome; however, our results suggest earlier evaluation and intervention in patients with dysphagia, especially if this is severe.

INTRODUCTION

Down syndrome is the most common genetic disorder, affecting approximately 1 in 800 children.[1] Children with Down syndrome have physical and physiologic characteristics that place them at higher risk of gastrointestinal disorders, metabolic abnormalities, cardiovascular complications, and early feeding problems,[2–4] which also places them at risk of frequent hospitalization.[5–7] Studies have demonstrated that up to 80% of infants with Down syndrome (I-DS) can present with early feeding difficulties, weak sucking, problems with mastication, and late transitioning to solid foods.

Up to 25% of normally developing infants will also present with dysphagia, with a higher prevalence in those born prematurely. For infants to have adequate nutrition, it is imperative to have a healthy synchronous interaction between sucking, swallowing, and breathing.[8] In order to have effective sucking, adequate negative intraoral pressure must be generated with the soft palate closing the nasal passages, lips tightening, and lower displacement of the jaw.[9,10] Swallowing, on the other hand, is divided into 3 phases: oral, pharyngeal, and esophageal. For these 3 steps to be successful, neuromuscular and neurophysiologic functions need to be mature and any abnormalities along the way can produce delays, residual liquid, and aspiration.[10] Finally, the respiratory phase must be coordinated with the swallowing phase. Infants breathe at a rate of 1–1.5 breaths per second or approximately 40–60 breaths per minute. The process of swallowing in infants may last from 0.35 to 0.75 seconds. Therefore, time for breathing may be compromised, particularly considering that, during feeding, minute ventilation decreases, exhalation is prolonged, and inhalation is shortened.[11] Coordination between these processes ends in successful feeding. Immaturity, muscle weakness, and poor neuromuscular control[12] in any of the phases of swallowing will lead to dysphagia.

Sleep-disordered breathing (SDB) is common in I-DS due to unique anatomical features in the facial structure including adenotonsillar hyperplasia, midfacial and mandibular hypoplasia, and macroglossia.[2–4] Moreover, general hypotonia including upper airway muscles particularly contributes to the functional susceptibility to obstructive sleep apnea (OSA). Hypotonia also compromises swallowing, making I-DS susceptible to dysphagia.

In this study, we aimed to determine the frequency and severity of dysphagia and its relationship to SDB severity in I-DS. We hypothesized that dysphagia severity would be correlated with OSA severity.

METHODS

Subjects

We reviewed consecutive I-DS (< 12 months old) who underwent polysomnography at Seattle Children's Hospital over a 6-year period (October 1, 2015–August 23, 2021). Data collected included the following: sex, age, presence of dysphagia through a video fluoroscopic swallow study, recommended thickener type, and polysomnographic data. The study was approved by the Institutional Review Board at Seattle Children's Hospital (study number 00003376).

Polysomnography

Polysomnography data were recorded using the (Sandman Elite Natus system, Middleton, Wisconsin). Parameters included a standard pediatric montage, which includes electroencephalograms (2 frontal, 2 central, and 2 occipital channels, referred to the contralateral mastoid), electromyograms (submental and anterior tibialis), electro-oculograms (right and left), nasal pressure transducer, oronasal airflow (thermistor), effort signals for thorax and abdomen, oximetry, capnography, a single lead electrocardiogram, and video and audio recording. Calibrations were performed per routine standard by a technician. A Dymedix oronasal sensor was used if the patient did not tolerate nasal cannulas. All patients were studied on room air.

The studies were scored by sleep laboratory technicians and were reviewed and interpreted by a board-certified sleep physician. Scoring was per current American Academy of Sleep Medicine guidelines. Obstructive apneas were defined as a ≥ 90% decrease in airflow from baseline with continued respiratory effort for a minimum of 2 breaths. Hypopneas were defined as a 30–89% decrease in airflow from baseline with continued respiratory effort for a minimum of 2 breaths, associated with a ≥ 3% desaturation, an electroencephalogram arousal, or both. Central apneas were defined as a ≥ 90% decrease in airflow from baseline that lasts at least the duration of 2 breaths with lack of respiratory effort, associated with a ≥ 3% desaturation, an electroencephalogram arousal, or both. Central apnea was also scored if there was a ≥ 90% decrease in airflow from baseline and the duration of the event lasted more than 20 seconds. OSA severity was determined by the obstructive apnea-hypopnea index (oAHI). Mild OSA was defined by an oAHI greater than 1 but less than 5 events per hour. Moderate OSA was defined by an oAHI greater than 5 but less than 10 events per hour. Severe OSA was defined by an oAHI greater than 10 events per hour. Central sleep apnea is common and the reference range for central sleep apnea is unclear for infant age. For the purpose of this study, central sleep apnea was defined by a central apnea index more than 5 events/h. The presence of sleep hypoxemia was determined if time spent with oxygen saturation equal or below 88% was greater than 5 minutes during sleep. Sleep hypoventilation was defined as the percentage of time spent with CO_2 levels > 50 mmHg for more than 25% of sleep time as measured by either end-tidal CO_2 or transcutaneous CO_2.

Other data and dysphagia evaluation

Demographics and other medical history were obtained by reviewing electronic medical records. For those with clinical concerns for dysphagia, a video fluoroscopic swallow study was obtained for confirmation. When there was no report of any signs of aspiration during feeding by a caregiver or clinical providers, a speech evaluation was not pursued. Infants were then classified into 3 groups for comparison: (1) low suspicion of dysphagia group, (2) dysphagia not requiring a feeding tube (on thickeners; "dysphagia" group), and (3) dysphagia requiring a feeding tube (unable to tolerate thickeners; "feeding tube" group).

Statistical analysis

Baseline characteristics are summarized by mean (standard deviation) or number (frequency), as appropriate. The outcome of interest was severity of OSA by oAHI and the presence of sleep-related hypoxemia and hypoventilation. The oAHI (mean [standard error]) was compared among 3 groups: (1) low suspicion of dysphagia vs (2) dysphagia vs (3) feeding tube. Due to the small sample size and nonparametric distribution of the oAHI, we performed Kruskal–Wallis test for the 3 group comparisons. Subsequently, pairwise 2-sided multiple-comparison analysis was performed using the Dwass-Steel-Critchlow-Fligner procedure. Given the similar characteristics between the 3 groups, multivariable analysis was not performed. However, as a sensitivity analysis, regression was performed adjusting for age and airway abnormality. *P* values for linear trend across the 3 groups in the order of (1, 2 and 3) was obtained using a multiple regression. *P* values less than .05 were considered statistically significant. SAS version 9.3 (SAS Institute, Cary, NC) was used.

RESULTS

We identified 40 I-DS (mean age: 6.6 months [3.0]; male: n = 26 [65%]). There were 11 infants (27.5%) with a low suspicion of dysphagia, 13 infants (32.5%) with dysphagia through a swallow study but who did not require a feeding tube, and 16 infants (40%) requiring a feeding tube. In those in the "dysphagia" group, 36% could tolerate thin liquids, 47% were prescribed nectar-thick, 17% prescribed honey-thick, and 57% were feeding tube dependent. Baseline characteristics were similar between the 3 groups (**Table 1**). There was no association between age and apnea-hypopnea index (AHI; $r = -.1$, $P = .5$).

oAHI increased across the 3 dysphagia groups (19.2 [9.2], 29.5 [8.4], and 49.3 [7.6] events/h, respectively; group

Table 1—Characteristics of infants with Down syndrome included in the study.

	Low Suspicion for Dysphagia (n = 11)	Dysphagia without Feeding Tube (n = 13)	Dysphagia with Feeding Tube (n = 16)	*P*
Age, mo	6.5 (3.7)	6.7 (2.9)	6.6 (2.8)	NS
Gestational age, wk	37.5 (1.4)	38.9 (1.3)	37.6 (1.6)	.02
Sex, male	8 (72.7%)	10 (76.9%)	8 (50%)	NS
Ethnicity (White)	8 (72.7%)	11 (84.6%)	11 (68.8%)	NS
Hypothyroidism	1 (9.1%)	3 (23.1%)	4 (25%)	NS
Congenital heart disease	8 (72.7%)	9 (69.2%)	11 (68.8%)	NS

Age and gestational age are expressed as mean (standard deviation). Other categorical variables are expressed as n (%). Analysis of variance (ANOVA) was used for comparing means across the groups. Chi-square test or Fisher's exact test were performed for comparing frequency across the groups. NS = not significant.

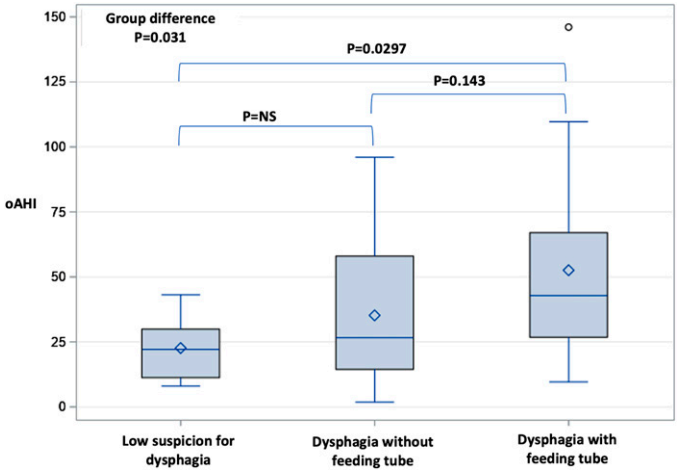
difference $P = .04$, P for trend = .0127). Pairwise comparisons showed a significant difference between the low suspicion of dysphagia and feeding tube groups ($P = .016$) (**Figure 1**). Sensitivity analysis adjusting for age yielded similar results (data not shown). The frequency of hypoxemia also increased across the 3 groups (0 [0%], 3 [23.1%], and 8 [50%]; $P = .015$). The frequency of hypoventilation was similar across the 3 groups (3 [27.3%], 3 [23.1%], and 4 [25%]; P = not significant). Dysphagia severity was positively correlated with a higher oAHI ($r = .43$, $P = .006$) (**Figure 2**).

DISCUSSION

This study demonstrates that there is a high prevalence of dysphagia and SDB in I-DS. Furthermore, we demonstrated our hypothesis that dysphagia severity is correlated with oAHI severity. To our knowledge, this represents the first study describing the occurrence of dysphagia and OSA exclusively in I-DS.

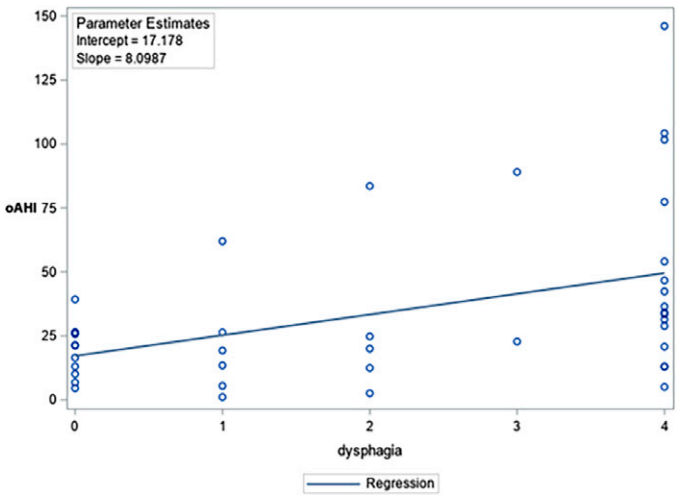
A number of studies have highlighted the high prevalence of dysphagia in I-DS. One prior study including children with Down syndrome, 2–7 years of age, demonstrated problems in the oral phase of swallowing—in particular, an immature chewing pattern in which food was held in the mouth for longer periods of time without chewing. There was a lack of oral anterior seal and poor movement of the tongue, resulting in inefficient bolus transit.[12] Nearly all (96%) of I-DS between the ages of 0 and 6 months were found to have some manifestation of oral or pharyngeal dysphagia with symptoms severe enough to warrant alteration of breast milk, formula, or nonoral feeds in 69%.[13] In another study including I-DS, 90% of them showed oral dysphagia with abnormal sucking in 63.7%, abnormal bolus formation in 62%, and pharyngeal dysphagia was present in 72.4%, with 53.5% of infants demonstrating abnormal swallow. Pharyngeal residue was present in 17.3% and pharyngonasal reflux was present in 27.5%, laryngeal penetration was seen in 52.0% of infants, and tracheal aspiration was seen in 31.5%.[14]

Figure 1—Comparison of oAHI between groups.



NS = not significant, oAHI = obstructive apnea-hypopnea index, Diamond = mean, Box = 25-75th percentile, End lines = maximum and minimum.

Figure 2—Dysphagia severity and oAHI correlation.



oAHI = obstructive apnea-hypopnea index.

These findings have important implications in terms of airway protection and pulmonary complications. In fact, Jackson et al[15] demonstrated that there was a statistically significant association between aspiration and/or deep laryngeal penetration and pulmonary hypertension, congenital heart defects, laryngomalacia, or pneumonia; however, sleep studies and the presence of SDB were not assessed. Although the association between OSA and dysphagia has not been previously established in I-DS, Vielkind et al demonstrated in children aged 1 month to 18 years an increased prevalence of chronic respiratory symptoms and abnormal airway findings. In this study, flexible bronchoscopy, including airway dynamics and bronchoalveolar lavage, demonstrated evidence of increased levels of neutrophilia and airway inflammation in children with dysphagia.[16]

The mechanism behind our findings of a close association of dysphagia and OSA is unclear. One can hypothesize that the increased airway inflammation, chronic sensory and motor changes of the pharynx with an impaired swallow-breathing mechanism, decreased pulmonary reserve due to chronic micro-aspiration, and alveolar simplification could be factors increasing the risk of OSA.[17] Alternatively, impaired muscle tone and neuromuscular control common in I-DS may confer risks for both dysphagia and OSA.[17–19]

Of note, in addition to OSA, other elements of SDB were common. Central sleep apnea was present in nearly one-third of I-DS, although there was no difference by dysphagia group. The frequency of hypoxemia increased across the dysphagia severity groups. Hypoventilation was present in nearly one-quarter of the I-DS, but the frequency of hypoventilation was similar across the 3 groups.

Current guidelines suggest screening at school age or when there are clinical symptoms of OSA in children with Down syndrome. Given these findings, even earlier screening for SDB may be warranted, especially in the presence of dysphagia. Future studies should examine the potential benefit of early intervention of OSA in I-DS. Moreover, studies should examine the evolution of OSA and dysphagia in older children with Down syndrome and how treatment of OSA may impact dysphagia and vice versa in larger multicenter settings.

Some of the limitations of this study include involvement of a single center with a limited number of participants. Since all included infants were referred to a sleep center, there is an inherent referral bias, limiting the generalizability of the study. The normative value for SDB parameters for infant age is not well defined and the AHI may be influenced by age. However, this was not apparent in our study. Not all infants categorized as having a low suspicion of dysphagia underwent clinical evaluation by a speech pathologist; therefore, dysphagia cannot be completely ruled out. In conclusion, we found that there is a correlation between OSA severity and dysphagia. Future directions should include study of the progression of SDB and dysphagia in older children with Down syndrome, evaluation of improvement of OSA with treatment of dysphagia, and larger multicenter studies. Our results suggest the need to evaluate and intervene earlier, especially in I-DS and dysphagia.

ABBREVIATIONS

I-DS, infants with Down syndrome
oAHI, obstructive apnea-hypopnea index
OSA, obstructive sleep apnea
SDB, sleep-disordered breathing

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DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. The authors report no conflicts of interest.