Comparative outcomes of severe obstructive sleep apnea in pediatric patients with Trisomy 21

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ABSTRACT

Objectives: To analyze the outcomes of severe obstructive sleep apnea (OSA) in pediatric patients with Trisomy 21 compared with non-syndromic patients.
Methods: A retrospective chart review was performed for patients with a diagnosis of severe obstructive sleep apnea, (defined as, Apnea–Hypopnea index (AHI) of $\geq$10) in a tertiary children's hospital. Data were analyzed for subjective and objective outcomes along with perioperative care and health care utilization. Patients with Trisomy 21 were compared with non-syndromic patients.
Results: A total of 230 patients with severe OSA were included in the study. Eighteen of these patients had Trisomy 21. Adenotonsillectomy was the most common surgical intervention in both groups. There was no statistical difference in the preoperative AHI between groups. Post treatment AHI in the Trisomy 21 group changed from an average of 26.6 to an average of 11.6 as compared with 24.5 to 3.6 in the non-syndromic group. The average perioperative hospital stay was 3.8 days in Trisomy 21 group compared to 1.7 days for the non-syndromic group ($p < 0.001$, Mann–Whitney U test). Complete resolution was seen in 35% of the Trisomy 21 group versus 75% in the non-syndromic group.
Conclusions: A majority of Trisomy 21 patients with severe OSA had residual symptoms following surgical intervention. There is also an increased risk of post-operative airway intervention and increased length of hospital stay in these patients.

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1. Introduction

Obstructive sleep apnea (OSA) is a common condition affecting 2–5% of the general pediatric population [1]. The American Academy of Pediatrics defines OSA as disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation and sleep patterns [2]. The causes of this condition are numerous; the most common of these are adenotonsillar hypertrophy and obesity [3]. Hypotonic neuromuscular conditions, dental problems and congenital cranio-facial abnormalities which cause reduced airway size or increased airway collapsibility, can additionally contribute to the pathogenesis of OSA [4,5]. Snoring and poor sleep quality are the most common symptoms of OSA however, the clinical presentation can vary depending on the patients' age [6]. Symptoms common in younger children include, enuresis, somnambulism and hyperactivity. Poor academic achievement, emotional instability and cognitive defects are more apparent in older children [7]. Physical sequelae, though rare, can include mild pulmonary hypertension and cardiovascular complications as well as failure to thrive and delayed development in untreated patients [8]. Compared with the general population, children with Trisomy 21 have a significantly higher prevalence of OSA [9,10]. A recent study showed some degree of obstructive sleep apnea in 28/29 8-year-old children with Trisomy 21, and a 59% prevalence of moderate–severe OSA in that cohort of patients, highlighting the prevalence of OSA in this subset of patients [11]. The pathophysiological reasons for this are related to both the cranio-facial features of this syndrome; mid-face hypoplasia and relative macroglossia, as well as generalized hypotonia, lymphoid hyperplasia and preponderance towards obesity [12,13]. A raised BMI appears to correlate strongly with OSA in both groups of patients [14].

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Adenotonsillectomy (AT) is the most common treatment for OSA in patients with and without Trisomy 21 [15]. Thus far, studies reporting outcomes of treatments for patients with Trisomy 21 have not been encouraging, with some reports describing rates of successful treatment, as measured by polysomnography (PSG), at 50% following AT [16,17]. The reasons for poorer outcomes in Trisomy 21 patients after AT have been primarily associated with higher frequency of co-morbidities and synchronous airway pathology [15]. With the above in mind, the specific post-operative findings with regards to post-operative airway intervention, hospital length of stay, and symptomatology have not been examined in depth. Below we describe the results of a retrospective, case controlled study examining the outcomes following surgical treatment for severe OSA in pediatric patients with Trisomy 21 compared to non-syndromic patients.

2. Materials and methods

2.1. Study design

A retrospective chart review was performed for patients with a diagnosis of severe obstructive sleep apnea (defined as, obstructive Apnea–Hypopnea index (AHI) of >9.9) identified between January 2007 and June 2012. Data regarding patient demographics, perioperative hospitalizations and post-operative outcomes were collected from patient charts. Data concerning pre and post-operative symptoms were obtained from responses to routinely asked questions during patient consultations, documented in patient charts. These data were analyzed for subjective and objective outcomes along with perioperative care and health care utilization. Patients with Trisomy 21 were then compared with non-Trisomy 21 patients.

2.2. Subjects

Patient and surgical information of children with and without the diagnosis of Trisomy 21 were collected. A total of 4972 non-Trisomy 21 and 103 Trisomy 21 patients who underwent AT were initially reviewed. Inclusion criteria included children with severe obstructive sleep apnea (obstructive AHI $\geq$10) documented on polysomnogram who underwent adenotonsillectomy. In our practice, all children with documented severe obstructive sleep apnea undergo post-operative polysomnogram 3–4 months postoperatively. Children who did not have both a pre-operative and post-operative polysomnogram were excluded. Children suffering from developmental delays or syndromes other than Trisomy 21 were also excluded.

2.3. Polysomnography

Polysomnography was conducted within an overnight sleep laboratory at the Children's Hospital of Pittsburgh. As per AAO-HNS clinical practice guidelines on polysomnography for sleep-disordered breathing prior to tonsillectomy in children, the physiologic parameters measured included gas exchange, respiratory effort, airflow, snoring, sleep stage, body position, limb movement, and heart rhythm [18]. Apneic events were measured and interpreted as per the recommendations of the AASM Manual for the Scoring of Sleep and Associated Events [19]. AHI was graded as follows, mild (AHI 1–4.9), moderate (AHI 5–9.9) and severe (AHI $\geq$10). Children suffering from primarily central sleep apnea were excluded. The presence of some central apneas in addition to severe obstructive sleep apnea was not an exclusion criteria, however the obstructive AHI rather than the total (obstructive + central) AHI was used for our statistical analysis.

2.4. Data analysis

Comparative analysis was performed both pre and post-operative findings between both groups of patients. This was also conducted on post-operative airway interventions required. Wilcoxon signed rank tests were utilized to examine pre and post-surgical obstructive AHI's between the two groups. While post-operative hospitalization days were analyzed using Mann–Whitney U testing.

The University of Pittsburgh Medical Center institutional review board reviewed the protocol summary and full approval was granted for the collection and reporting of data in this study.

3. Results

3.1. Patient demographics

Two hundred-thirty patients met criteria for this study and of these, 18 had a diagnosis of Trisomy 21. There were approximately equal percentages of male and female patients in each group, 53% male and 47% female in the non-Trisomy 21 group and 56% male, 44% female in the Trisomy 21 group. The mean age of children in the non-Trisomy 21 group, at the time of surgery was 72 months, the Trisomy 21 group mean age was 88 months ($p = 0.2$). Pre-operatively, patients in the non-Trisomy 21 group had a mean BMI of 20, the Trisomy 21 group had a mean BMI of 19.7 ($p = 0.9$). There was an increased incidence of overall previous airway surgery prior to adenotonsillectomy in the Trisomy-21 group compared with non-Trisomy 21, 22% compared with 12%. Previous airway surgeries included supraglottoplasty, septal surgery, partial adenoidectomy, modified palatoplasty.

Polysomnogram data was collected and analyzed for Obstructive-Apnea and Hypopnea Indices (O-AHI) for both groups. As demonstrated in Fig. 1, the post treatment O-AHI in the Trisomy 21 group decreased from an average of 26.6 to an average of 11.6 ($p < 0.015$) while in the non-syndromic group the average O-AHI decreased from 24.5 to 3.6 ($p < 0.001$).

Overall, patients with Trisomy 21 experienced increased rates of immediate post-operative airway interventions while in the recovery room. These included the use of oxygen delivered by facemask, heliox, nasal trumpet, and patients who remained intubated or required re-intubation. The incidence of flash pulmonary edema was also examined. Presence of pulmonary edema was diagnoses based on chest X-ray. Fig. 2 is a graphical representation of the percent of patients in each group who experienced post-operative airway intervention following surgery. Twenty-six percent ($n = 55$) of non-Trisomy 21 patients required oxygen delivered by face
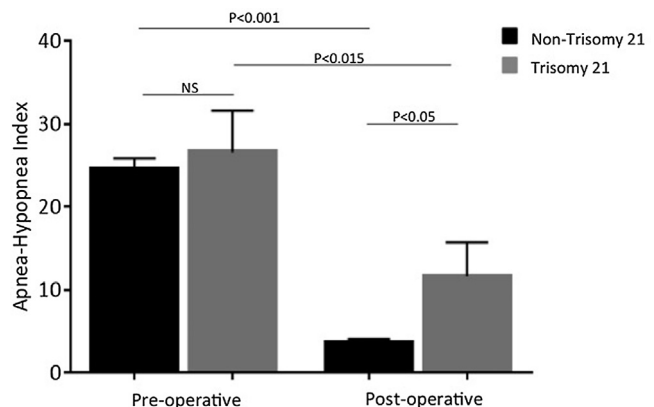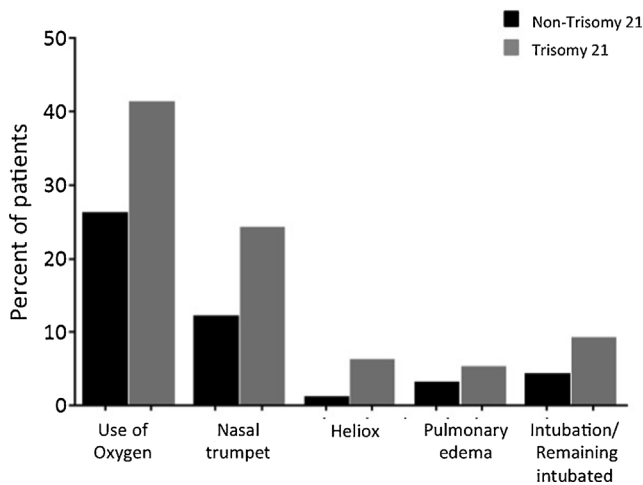

Fig. 1. Pre and post-operative obstructive-AHI of Trisomy 21 and non-Trisomy 21 children.
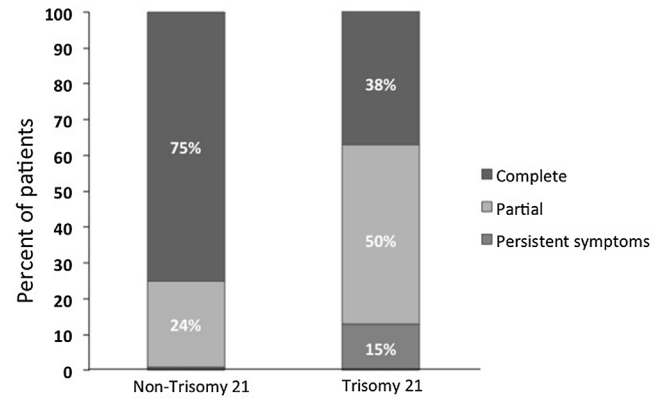
Fig. 2. Children requiring immediate post-operative interventions and/or suffering from pulmonary edema.

Fig. 3. Overall reported resolution of pre-operative symptoms at 3-month post-operative visit.

mask compared to 41% ($n = 7$) of Trisomy 21 patients ($p < 0.0001$). Twenty four percent ($n = 4$) patients with Trisomy 21 required nasal trumpet compared with 12% ($n = 25$) non-Trisomy 21 patients ($p < 0.0001$). One patient (5%) with Trisomy 21 required heliox while no non-Trisomy 21 children needed this intervention ($p < 0.0001$). One patient (5%) with Trisomy 21 patients developed pulmonary edema compared to 3% ($n = 6$) of non-Trisomy 21 patients ($p < 0.0001$). While 9% ($n = 2$) of Trisomy 21 patients remained intubated or had to be reintubated compared with 4% ($n = 8$) of non-Trisomy ($p < 0.0001$).

Both Trisomy 21 and non-Trisomy 21 patients were hospitalized in the perioperative period following surgery. The Trisomy 21 group had a statistically significant longer perioperative hospitalization rate compared with non-Trisomy 21 group, with a mean of 3.5 days compared with 1.5 days ($p < 0.001$).

As demonstrated in Table 1, the most common preoperative symptom experienced by both groups was snoring. While, a smaller percentage of patients in both groups demonstrated symptoms of hyperactivity, behavioral changes and enuresis. Post operatively; both groups exhibited a reduction in all symptoms measured, however, patients with Trisomy 21 experienced less symptom resolution (Table 1 & Fig. 3). The three most common symptoms; snoring, mouth breathing and apneic pauses decreased from 99% to 16% ($p < 0.0001$), 66% to 3% ($p < 0.0001$) and 67% to 3% ($p < 0.0001$), respectively in the non-Trisomy 21 group. Although there were fewer patients experiencing these symptoms post operatively in the Trisomy 21 group, the decrease was less marked with percent of patients who experienced these same symptoms.

In addition, parents of patients reported resolution of symptoms at 3 months following intervention. Outcomes were divided into complete resolution (no post-operative symptoms), partial resolution (decrease of one or more symptoms but not all) and

unchanged (symptoms still persist). As illustrated in Fig. 3, our data indicated that 35% of parents of Trisomy 21 patients described complete symptom resolution, compared to 75% of parents of patients who did not have Trisomy 21. Fifty-percent of parents with Trisomy 21 children noted partial resolution of symptom compared with 25% of parents of patients without Trisomy 21 and 15% were described as persistent or unchanged symptoms in the Trisomy 21 group whereas no parents of patients without Trisomy 21 reported persistent or unchanged symptoms 3 months post-surgical intervention.

4. Discussion

Obstructive sleep apnea is an important cause of morbidity in the pediatric population with Trisomy 21. The consequences of severe OSA in patients with Trisomy 21 have not been fully investigated, one explanation for this may be that consequences of Trisomy 21 itself may be difficult to distinguish from consequences specifically related to severe OSA [20]. Nevertheless, given the impact of OSA on the general, non-Trisomy 21 pediatric population, it is reasonable to assume that the impact on cognitive development and quality of life may be increased in the population with Trisomy 21 [21]. Pathophysiological factors which contribute to its increased prevalence in this population include both the cranio-facial features associated with Trisomy 21, as well as generalized physical hypotonia and predisposition towards a raised BMI and obesity. Although it is recognized that poorer outcomes following surgical treatment for OSA is expected in patients with Trisomy 21, patient associated hospital course, and specific outcomes post-tonsillecto-my have not previously been investigated.

Our data indicates that surgical treatment of OSA was successful in significantly improving AHI in both groups of patients ($p < 0.05$). The difference in post-operative AHI between appears to indicate that patients with Trisomy 21 had less of an improvement in AHI compared to non-Trisomy 21 patients

Table 1
Pre and post-operative symptoms of Trisomy 21 and non-Trisomy 21 children.

Symptoms	Pre-operative		χ^2	p	Post-operative		χ^2	p
	Healthy ($n=212$)	Trisomy 21 ($n=18$)			Healthy ($n=212$)	Trisomy 21 ($n=18$)		
Snoring	210 (99%)	16 (89%)	10.04	0.002	34 (16%)	9 (50%)	12.59	<0.001
Mouth breathing	140 (66%)	10 (56%)	0.80	0.370	6 (3%)	2 (13%)	3.39	0.066
Apneic pauses	142 (67%)	8 (44%)	3.71	0.054	6 (3%)	2 (13%)	3.39	0.066
Restless sleep	106 (50%)	9 (50%)	0.00	0.999	13 (6%)	4 (25%)	6.28	0.012
Daytime fatigue	38 (18%)	4 (22%)	0.21	0.651	6 (3%)	3 (19%)	8.49	0.004
Hyperactivity	6 (3%)	0 (0%)	NA	NA	2 (<1%)	0 (0%)	NA	NA
Behavioral changes	17 (8%)	1 (6%)	0.14	0.709	0 (0%)	1 (6%)	NA	NA
Enuresis	11 (5%)	1 (6%)	0.01	0.944	0 (0%)	0 (0%)	NA	NA

($p < 0.015$; $p < 0.001$). This is likely due to the multiple factors that are present in Trisomy-21 patients that may also be causing airway obstruction [15]. Not surprisingly, more patients with Trisomy 21 experience ongoing or partially resolved symptoms of OSA compared with non-Trisomy 21 counterparts. These finding were particulary demonstrated in the ongoing complaints of snoring, restless sleep and daytime fatigue in the Trisomy 21 patients post-operatively (Table 1).

Although the demographics of both groups were fairly comparable with regards to breakdown of gender and pre-operative symptomatology our results demonstrated that there were significant differences in outcomes following surgery. Patients with Trisomy 21 experienced increased immediate post-operative associated airway difficulties compared to their counterparts in the non-Trisomy 21 group ($p < 0.0001$). These included correction of hypoxia with oxygen, as well as more invasive airway management such as intubation. We suspect that this may have contributed to Trisomy 21 patients experiencing significantly longer post-operative hospitalization times ($p < 0.001$). These findings suggest that children with Trisomy 21 may require a higher level of care in the immediate post-operative period compared to healthy children, and are also helpful in setting parental expectations regarding hospital length of stay following surgery.

This study was not without limitations, primarily due to its retrospective nature and the small size of our Trisomy 21 population. Although relatively low, the ratio of Trisomy 21 to non-Trisomy 21 groups mirrors that within the general population. The symptomalogical data collected was largely subjective and conveyed through parental observation. Though subjective data is perhaps not ideal, these data do reinforce the objective PSG data, which indicate that children with Trisomy 21 improved less than non-Trisomy 21 children. Objective data was also collected, but again with the limitations inherent to a retrospective study and small Trisomy 21 sample size. For example, although we have data on post-operative intubation rates in the 2 subgroups of patients, the specific details leading to reintubation. Nonetheless, we are able to compare the cohort of Trisomy 21 patients to non-syndromic patients and make some interesting comparisons. These data are also potentially useful for post-operative expectations including facilitating clear and realistic expectations of outcomes post surgery during discussions with patients' families.

Additionally, our study looks only at children with severe obstructive sleep apnea on pre-operative polysomnogram, and cannot be generalized to children with mild and moderate sleep apnea. The retrospective nature of the study limits our analysis to those children on whom we have pre-operative and post-operative polysomnographic data, which is the cohort with severe sleep apnea only. We do not routinely get post-operative sleep studies on children with mild or moderate sleep apnea, therefore these children were excluded from our study. However, the data we have presented does represent valuable information on outcomes in those children with severe disease, but further prospective studies could evaluate those children with mild and moderate disease to determine whether our findings can be generalized to those subgroups as well.

5. Conclusion

Obstructive sleep apnea is a common disorder identified in both Trisomy 21 and non-syndromic children alike. Untreated, obstructive sleep apnea can lead to significant pulmonary and cardiovascular sequelae, particularly in patients with comorbidies such as Trisomy 21. In this study, we examined the effectiveness of adenotonsillectomy in the treatment of both subjective and objective symptoms of severe OSA as well as hospital stay and airway intervention in syndromic and non-syndromic children. Although children with Trisomy 21 demonstrated an improvement of almost all post-operatively measured outcomes, non-syndromic children demonstrated greater levels of improvement. Trisomy 21 children also demonstrated a higher rate of post-operative airway needs and longer hospital stays. Additionally, the presence of persistent sleep apnea symptoms and persistent obstructive sleep apnea on polysomnogram for many of these patients post-operatively highlights the importance of close follow-up and possible need for further intervention in these patients. The authors feel that these data can be utilized to drive further research in pre-operative optimization and post-operative management for this important subset of patients as well as counseling prior to surgery.

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