Obstructive sleep apnoea in children with Down syndrome

Ng D K, Hui H N, Chan C H, Kwok K L, Chow P Y, Cheung J M, Leung S Y

ABSTRACT

Introduction: Children with Down syndrome (DS) are prone to develop obstructive sleep apnoea (OSA) for a combination of reasons, including small upper airway, midfacial hypoplasia, micrognathia and muscular hypotonia. The objective of this study was to compare the prevalence of OSA in DS children, with or without snoring, with snoring children matched for gender, age and weight for height.

Methods: DS children were prospectively recruited from the Hong Kong Down Syndome Association. All recruited DS children underwent a sleep polysomnography (PSG) in our sleep laboratory. The same number of patients without DS who underwent sleep PSG in the same period were enrolled as controls after they were matched for gender, age and weight for height. OSA was defined as apnoea-hypopnoea index (AHI) greater than 1.5.

Results: 22 DS patients and 22 snoring controls completed the overnight PSG. The mean age of DS children and snoring controls was 10.82 +/- 5.93 and 10.27 +/- 5.68 years, respectively. The prevalence of OSA was 59 percent in DS children and 32 percent in snoring controls. Median and interquartile range (IQR) of AHI of DS children (median 1.80, IQR is 0.40 to 7.10) were significantly higher than those of controls (median 0.50, IQR is 0.00 to 2.03, p-value equals 0.041). Out of 13 DS children with OSA, eight of them (61.5 percent) had no habitual snoring.

Conclusion: 59 percent of DS children in the current series were found to have OSA and they were more likely to develop OSA than controls. Nearly 40 percent of DS children with OSA did not have habitual snoring.

Keywords: apnoea-hypopnoea index, Down syndrome, obesity, obstructive sleep apnoea, polysomnography, snoring

Singapore Med J 2006; 47(9):774-779

Department of Paediatrics
Kwong Wah Hospital
Waterloo Road
Kowloon
Hong Kong

Ng D K, FRCP, FHKAM
Consultant

Chan C H, BSc
Research Assistant

Kwok K L, FRCP, FKHAM
Senior Medical Officer

Chow P Y, MRCP, FHKAM
Specialist

Cheung J M, MNurs, RPSGT
Nurse Specialist

Leung S Y
Research Assistant

Department of Paediatrics and Adolescent Medicine
United Christian Hospital
Hong Kong

Hui H N, MRCPCH, FKHAM
Medical Officer

Correspondence to:
Dr Daniel K Ng
Tel: (852) 3517 5055
Fax: (852) 3517 5261
Email: dkkng@ha.org.hk

INTRODUCTION

Children with Down syndrome (DS) are prone to develop obstructive sleep apnoea (OSA) syndrome for a combination of reasons, including small upper airway, midfacial hypoplasia, micrognathia and muscular hypotonia[1,2]. Frequent upper airway infections with the associated adenotonsillar hypertrophy aggravate the obstruction further[3-5]. Untreated OSA results in serious morbidities including failure to thrive, cor pulmonale, hypertension, poor academic performance, and deterioration in mental function[6]. Untreated OSA may further impair the mental function in children with DS. The objective of this study was to compare the prevalence of OSA in DS children, with or without snoring, with snoring children matched for gender, age and weight for height.

METHODS

384 invitation letters were sent to parents of all members of the Hong Kong Down Syndrome Association under 18 years of age, inviting them to join the study. No reference was made to snoring in the letter. All DS children who agreed to this study were called for a detailed clinical evaluation and overnight polysomnography (PSG). The same number of controls were selected from those non-DS snoring children referred to our department for PSG. The controls were matched with DS children by age, gender and weight for height.

Nutritional data and tonsil size were obtained by one paediatrician (HHN). Tonsil size in children were graded as suggested by Brodsky[7]. The grading was summarised as follows: 0 = no enlargement; 1 = tonsils occupy less than half of the transverse diameter of the oropharynx; 2 = tonsils occupy half of the transverse diameter of oropharynx; 3 = tonsils occupy more than half of the transverse diameter of oropharynx; 4 = tonsils occupy whole of the transverse diameter of oropharynx, i.e. kissing tonsils.

Tonsil size graded larger than 2 were defined

Table I. Demographical, anthropometrical and clinical data of Down syndrome children and controls.

	Down syndrome (n=22)	Controls (n=22)	p-value
Sex (M/F)	15/7	15/7	1.000
Mean age ± SD (years)	10.82 ± 5.93	10.27 ± 5.68	0.755
Mean weight for height ± SD	121.78 ± 24.90	120.41 ± 24.78	0.855
Obesity	7 (31.2%)	7 (31.2%)	1.000
Allergic rhinitis	5 (22.7%)	15 (68.2%)	0.006*
Asthma	4 (18.2%)	8 (36.4%)	0.310
Nocturnal enuresis	2 (9.1%)	6 (27.3%)	0.240
Bruxism	5 (22.7%)	5 (22.7%)	1.000
Episodes of witnessed apnoea	4 (18.2%)	2 (9.1%)	0.664
Habitual snoring	8 (36.4%)	22 (100.0%)	<0.001*
Tonsillar size			0.683
- Grade 0	1	1	
- Grade 1	9	9	
- Grade 2	8	6	
- Grade 3	4	4	
- Grade 4	0	2	
Tonsillar hypertrophy	4 (18.2%)	6 (27.3%)	0.721

* Statistically significant

Table II. PSG values of Down syndrome children and controls.

	Down syndrome (n=22)	Controls (n=22)	p-value
Total recording time (minutes)	393 (112.17)	450 (71.77)	0.050
Time asleep (%)	71.98 (19.69)	79.09 (13.25)	0.168
Arousal index	14.80 (8.99)	21.01 (11.60)	0.054
Median AHI (IQR)	1.80 (0.40-7.10)	0.50 (0.00-2.03)	0.041*
Median DI (IQR)	2.75 (0.65-14.18)	0.30 (0.00-0.53)	0.001*
Median SaO_2 nadir (IQR) (%)	87.00 (73.50-89.50)	89.00 (85.75-90.25)	0.138

* Statistically significant

Data are presented as mean (SD) unless otherwise indicated.

as tonsillar hypertrophy. Obesity was defined as weight greater than 120% of their median weight for height[8]. An attended overnight PSG with real-time video recording was offered in the paediatric sleep laboratory with Compumedics' Siesta Physiological Monitoring System (Compumedics Limited, Abbotsford, VIC, Australia) which has standard channels, viz. four electroencephalogram (EEG), two electrooculogram (EOG), one nasal cannula, one oral thermistor, one end-tidal CO_2 monitor with pulse oximeter (CO_2SMO, Novametrix, Wallingford, CN, USA), one submental eletromyogram (EGM), two leg EMG, and one chest belt (Piezoelectric bands), one abdominal belt, and one microphone. The children were continuously observed by a nurse trained in PSG during the study. An acceptable sleep study is one with a recording time of at least four hours.

All results were manually scored according to standard criteria and standard definitions for apnoea and hypopnoea[9]. An obstructive apnoeic episode was defined as a decrease of airflow by more than 80% for more than two respiratory cycles in the presence of respiratory effort, while hypopnea was defined as a decrease in airflow by 50 to 80% in the

Table III. Comparison of DS children with or without OSA.

	DS with OSA (n=13)	DS without OSA (n=9)	p-value
Mean age ± SD (years)	13.30 ± 5.91	7.24 ± 3.94	0.014
Mean weight for height ± SD	132.52 ± 26.07	106.28 ± 12.25	0.005
Male	9 (69.2%)	6 (66.7%)	1.000
Allergic rhinitis	5 (38.5%)	0 (0.0%)	0.054
Asthma	2 (15.4%)	2 (22.2%)	1.000
Nocturnal enuresis	0 (0.0%)	2 (22.2%)	0.156
Bruxism	3 (23.1%)	2 (22.2%)	1.000
Witnessed apnoea	2 (15.4%)	2 (22.2%)	1.000
Habitual snoring	5 (38.5%)	3 (33.3%)	1.000
Tonsillar hypertrophy	3 (23.1%)	1 (11.1%)	0.616

Data are presented as number (%) unless otherwise indicated.

presence of respiratory effort with the presence of desaturation ≥4% or EEG arousal. The cut-off point of apnoea-hypopnoea index (AHI) for OSA in children is controversial and the cut-off value for OSA in the current study was an obstructive AHI of more than 1.5[10]. Other polysomnographical parameters, i.e. arousal index, desaturation index (DI, defined as ≥4% drop in SpO_2), SaO_2 nadir, total sleep time and sleep efficiency were analysed.

Data were analysed by the Statistical Package for Social Science (SPSS) version 10.0 for Windows (Chicago, IL, USA). Normality of continuous data was assessed by the Kolmogorov-Smirnov Test. Continuous data with normal distribution were reported as mean with standard deviation (SD). For continuous data with asymmetric distribution, median with interquartile range (IQR) were reported. Student's t-test was used to compare means. For variables distributed asymmetrically, the Mann-Whitney U test was used for comparison. Correlation between two continuous variables was assessed by Pearson's correlation. Categorical data were compared by Fisher exact test. A two-tailed p-value of less than 0.05 was considered significant. The ethics committee of Kwong Wah Hospital approved the protocol of this study.

RESULTS

22 DS children were recruited from the Hong Kong Down Syndrome Association which had 384 members, giving a participation rate of 5.73%. All DS participants were confirmed by karyotype to be non-disjunction. All DS children completed the overnight PSG successfully. The demographical data, anthropometrical data and results from physical examination of DS children and controls

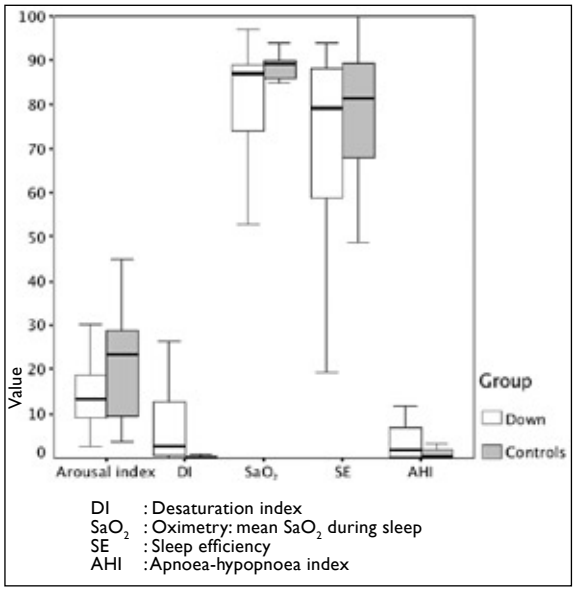

Fig. 1 Box plot of various PSG parameters.

are shown in Table I. Children in the control group had a significantly higher rate of allergic rhinitis and habitual snoring. The two groups had comparable tonsil size. No children had prior adenoidectomy or tonsillectomy before the PSG study.

The polysomnographical findings of the two groups are shown in Table II and Fig. 1. DS children had a significantly higher AHI and DI than controls. No significant difference was found between the prevalence of OSA between DS children and controls when different AHI cut-off values were used, i.e.: AHI>1.5 (DS: 13/22, controls: 7/22, p=0.129), AHI>2 (DS: 10/22, controls: 5/22, p=0.203), AHI>5 (DS: 7/22, controls: 2/22, p=0.132) or AHI>10 (DS: 2/22, controls: 1/22, p=1.000). The comparison of children as stratified by OSA is shown in Tables III

Table IV. Comparison of controls with or without OSA.

	Control with OSA (n=7)	Control without OSA (n=14)	p-value
Mean age ± SD (years)	8.14 ± 6.59	11.27 ± 5.15	0.239
Mean weight for height ± SD	122.45 ± 26.52	119.45 ± 24.83	0.799
Male	6 (85.7%)	9 (64.3%)	0.350
Allergic rhinitis	4 (57.1%)	11 (78.6%)	0.630
Asthma	2 (28.6%)	6 (42.9%)	1.000
Nocturnal enuresis	3 (42.9%)	3 (21.4%)	0.334
Bruxism	3 (42.9%)	2 (14.3%)	0.274
Witnessed apnoea	2 (28.6%)	0 (0.0%)	0.091
Habitual snoring	7 (100%)	14 (100%)	1.000
Tonsillar hypertrophy	2 (28.6%)	4 (28.6%)	1.000

Data are presented as number (%) unless otherwise indicated.

and IV. Unlike controls, DS children with OSA were significantly older and more obese than DS children without OSA. Only 15.4% and 38.5% of DS children with OSA had observed apnoea and habitual snoring, respectively.

Two variables were significantly correlated with log AHI in DS children: weight for height (r=0.477, p=0.039) and age (r=0.477, p=0.055). For controls, only one positive correlation between age and log AHI was found (r=0.547, p=0.008), but not weight for height (r=0.253, p=0.345). Multivariate analysis of the risk factor for OSA in DS children was not done because of insufficient sample size.

DISCUSSION

In the current study, we found the prevalence of OSA in DS children and non-DS habitual snorers to be similar. However, we found that children with DS had a significantly higher AHI than paediatric habitual snorers without DS. Moreover, 38.5% DS children with OSA had no habitual snoring. DS is a common chromosomal abnormality occurring in about 1 in 961 live births[11], and OSA is common in patients with DS[4]. Marcus et al and Southall et al reported the prevalence of OSA in children with DS to be 45%[12] and 50%[5], respectively. de Miguel-Diez et al reported that the prevalence of OSA, defined as ≥2 per hour, in a community sample of children with DS, was 65%[13]. Dyken et al reported that OSA, defined as obstructive apnoea index >1, affected 79% in a group of 19 American DS children (aged 3-18 years) recruited from the outpatient population[14].

Dahlqvist et al recruited Swedish DS children at a younger age (2-10 years) from the community and reported a much lower prevalence of OSA (24%), defined as AHI>1[15]. Stebbens et al reported a slightly higher prevalence (31%) in a group of community-based sample of younger DS children. (0-5 years)[16]. In our series, 59% of 22 children with DS recruited from the community were found to have OSA, defined as AHI>1.5. The difference in the prevalence of OSA in the published series could be explained by different methodologies including different diagnostic criteria, source of recruitment of DS children, age group and proportion of obesity. Prevalence of OSA in DS children in the current series was similar to the prevalence reported by de Miguel-Diez et al[13], who used a similar diagnostic criteria and source of recruitment as the current study.

In the current study, we found that DS children with OSA were older than those DS children without OSA, and this was similar to the findings of Dyken et al[14]. It was different from the study by de Miguel-Diez et al who found a negative correlation between AHI and age[13]. In addition, de Miguel-Diez et al found that DS children younger than eight years of age was an independent risk factor for OSA[13], which was not the case in the current study. A longitudinal study is required to shed more light on the relationship between age and AHI in DS children. In the current study, tonsils hypertrophy was not found to be a risk factor for OSA in children, DS or otherwise. This was in line with the review by Uong et al who showed adenoidectomy, tonsillectomy, or other surgical modalities (eg. uvulopalatopharyngeoplasty) corrected only 30-50% of cases of OSA in DS children[17].

Uong et al also found that DS children had

a significantly smaller upper airway volume compared to non-DS children. They reported that the difference in upper airway volume was not likely to be mediated by tonsillar hypertrophy or adenoid hypertrophy as the adenoid and tonsil volumes in DS children were significantly smaller than non-DS children as shown by magnetic resonance imaging. The same study also demonstrated that DS children had a significantly smaller mid- and lower-facial skeleton, shorter mental spine-clivus distance, hard palate length and mandible volume compared to non-DS children. However, the size of tongue, soft-palate, pterygoid and parapharyngeal fat pads were similar in DS children and non-DS children[17]. Donnelly et al found that 25% of OSA in DS children were caused by glossoptosis during sleep[18]. The site of airway obstruction during sleep was not investigated in the current study. Further study should identify the site of obstruction during sleep, as suggested by Guilleminault et al[19].

In the current study, weight for height was significantly correlated with AHI in DS children, in contrast to the non-significant correlation reported by Marcus et al[12] and de Miguel-Diez et al[13]. BMI is not an ideal yardstick for adiposity in children[20] but it was used in the study by de Miguel Diez et al[13]. Weight for height, or BMI corrected for age, are better methods for quantifying adiposity in children. Weight for height was used to quantify adiposity in the study by Marcus et al[12], but correlation between weight for height and AHI was not established. Obesity is considered to be a risk factor of OSA in children but the evidence on the correlation between the AHI and adiposity remained inconclusive even in non-DS children[21]. Further study with a larger sample of DS children and an acceptable way to quantify adiposity in DS children, should be performed to confirm the correlation found in the current study.

In the current study, the success rate of PSG in DS children was 100%, although children with developmental disability may have more problems tolerating electrode applications which may lead to a failed PSG. Dahlqvist et al reported that DS children in their series removed electrodes during the PSG session[15]. The reasons for the high success rate of PSG in our DS children were most likely due to a sleep technologist who was also a qualified experienced paediatric nurse, a child-friendly environment, and presence of a parent during the PSG study.

A review by Hatipoglu and Rubinstein suggested that local, e.g. allergic rhinitis, or systemic inflammation might amplify upper airway narrowing, and thus worsen OSA[22]. However, allergic rhinitis and asthma were not found to be a risk factor of OSA in both DS children and controls in the current study. Moreover, the difference in the prevalence of OSA between DS children and controls was not significant, most likely due to the small sample size of the current study. Further paediatric studies with larger sample size are warranted. The current study design did not allow for analysis of reasons behind the refusal to participate in the current study.

The participation rate of this study, 5.73%, is quite low and may reflect a potential selection bias. Unfortunately, the reason for refusal was not known due to the constraint of the study design. In this study, the only possible selection bias may be attributed to the fact that parents of DS children who were more likely to have OSA, might be more likely to consent to participation in this study. This selection bias might be partially balanced by the fact that control children, who were referred for suspected OSA, had higher risks for OSA than non-DS children in the community.

Only 38.5% of all recruited DS children had habitual snoring suggestive of OSA, and this was less than that obtained in a previous study[12]. This suggested against any selection bias of the current study in favour of recruiting DS with OSA. The fact that 61% of DS children with OSA had no habitual snoring nor observed apnoea in the current study highlighted the difficulty of screening OSA in DS children by clinical history. Moreover, AHI in DS children were positively correlated to age. We suggest that routine PSG should be offered to all DS children from the ages of four to six years for early diagnosis of OSA.

The current study confirms that DS children are more prone to have higher AHI than snoring, non-DS children. It is important to note that this group of snoring children might not be healthy children[23]. It is expected that the risk of DS children to develop OSA when compared to non-snoring, non-DS children would probably be even higher. Further studies which include non-snoring children, are warranted. In conclusion, 59% of DS children in the current series were found to have obstructive sleep apnoea, and only 38.5% DS children with OSA had habitual snoring.

REFERENCES

1. Fink GB, Madaus WK, Walker GF. A quantitative study of the face in Down's syndrome. Am J Orthd 1975:67:540-53.
2. Allanson JE, O'Hara P, Farkas LG, Nair RC. Anthropometric craniofacial pattern profiles in Down Syndrome. Am J Med Genet 1993; 47:748-52.

3. Lefaivre JF, Cohen SR, Burstein FD, et al. Down syndrome: identification and surgical management of obstructive sleep apnea. Plast Reconstr Surg 1977; 99:629-37.
4. Strome M. Obstructive sleep apnea in Down syndrome children: a surgical approach. Laryngoscope 1986; 96:1340-2.
5. Southall DP, Stebbens VA, Mirza R, et al. Upper airway obstruction with hypoxaemia and sleep disruption in Down syndrome. Dev Med Child Neurol 1987; 29:734-42.
6. Schechter MS. Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome. Technical report: diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2002; 109:e69.
7. Brodsky L. Modern assessment of tonsils and adenoids. Pediatr Clin North Am 1989; 36:1551-69.
8. Leung SS, Lau JT, Tse LY, Oppenheimer SJ. Weight-for-age and weight-for-height references for Hong Kong children from birth to 18 years. J Paediatr Child Health 1996; 32:103-9.
9. Rechtschaffen A, Kales A. A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Bethesda: US Department of Health, Education, and Welfare, 1968.
10. Witmans MB, Keens TG, Davidson Ward SL, Marcus CL. Obstructive hypopneas in children and adolescents: normal values. Am J Respir Crit Care Med 2003; 168:1540. Comment on: Am Rev Respir Dis 1992; 146:1235-9.
11. Olsen CL, Cross PK, Gensburg LJ, Hughes JP. The effects of prenatal diagnosis, population ageing, and changing fertility rates on the live birth prevalence of Down syndrome in New York State, 1983-1992. Prenat Diagn 1996; 16:991-1002.
12. Marcus CL, Keens TG, Bautista DB, von Pechmann WS, Ward SL. Obstructive sleep apnea in children with Down syndrome. Pediatrics 1991; 88:132-9.
13. de Miguel-Diez J, Villa-Asensi JR, Alvarez-Sala JL. Prevalence of sleep-disordered breathing in children with Down syndrome: polygraphic findings in 108 children. Sleep 2003; 26:1006-9. Comment in: Sleep 2004; 27:1023-5.
14. Dyken ME, Lin-Dyken DC, Poulton S, Zimmerman MB, Sedars E. Prospective polysomnographic analysis of obstructive sleep apnea in Down syndrome. Arch Pediatr Adolesc Med 2003; 157:655-60.
15. Dahlqvist A, Rask E, Rosenqvist CJ, Sahlin C, Franklin KA. Sleep apnea and Down's syndrome. Acta Otolaryngol 2003; 123:1094-7.
16. Stebbens VA, Dennis J, Samuels MP, Croft CB, Southall DP. Sleep related upper airway obstruction in a cohort with Down's syndrome. Arch Dis Child 1991; 66:1333-8.
17. Uong EC, McDonough JM, Tayag-Kier CE, et al. Magnetic resonance imaging of the upper airway in children with Down syndrome. Am J Respir Crit Care Med 2001; 163:731-6. Comment in: Am J Respir Crit Care Med 2002; 165:1187.
18. Donnelly LF, Strife JL, Myer CM III. Glossoptosis (posterior displacement of the tongue) during sleep: a frequent cause of sleep apnea in pediatric patients referred for dynamic sleep fluoroscopy. AJR Am J Roentgenol 2000; 175:1557-60. Erratum in: AJR Am J Roentgenol 2001; 176:548.
19. Guilleminault C, Li K, Quo S, Inouye RN. A prospective study on the surgical outcomes of children with sleep-disordered breathing. Sleep 2004; 27: 95-100. Comment in: Sleep 2004; 27:1218.
20. Pietrobelli A, Faith FS, Allison DB, et al. Body mass index as a measure of adiposity among children and adolescents: A validation study. J Pediatr 1998; 132:204-10. Comment in: J Pediatr 1998; 132:191-3. J Pediatr 1999; 134:522-3.
21. Ng DK, Lam YY, Kwok KL, Chow PY. Obstructive sleep apnoea syndrome and obesity in children. Hong Kong Med J 2004; 10:44–8. Comment in: Hong Kong Med J 2004; 10:144.
22. Hatipoglu U, Rubinstein I. Inflammation and obstructive sleep apnea syndrome pathogenesis: a working hypothesis. Respiration 2003; 70:655-71.
23. Guilleminault C, Lee JH. Does benign "primary snoring" ever exist in children. Chest 2004; 126:1396-8. Comment on: Chest 2004; 126:1467-72.