Original Research

Analysis of polysomnogram findings in children with concurrent obstructive and central sleep apnea

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Abstract

Objective: Increasing evidence suggests overlap in mechanisms of obstructive and central sleep apnea. Our objective was to compare the patient characteristics and polysomnographic findings of children with concurrent obstructive and central sleep apnea (obstructive sleep apnea + central sleep apnea [OSA + CSA]), to those with OSA only.

Methods: A retrospective case series of polysomnogram (PSG) from 30 June 2013 to 30 June 2018 of patients 18 years and younger was performed. PSG parameters were analyzed per standard protocol. There were two groups, OSA only group and OSA + CSA group. OSA + CSA was subdivided into groups of central apnea index (CAI) ≤ 5, and CAI > 5. Differences in the age, sex, body mass index (BMI) percentile, prevalence of medical conditions, and PSG parameters between OSA only and OSA + CSA were assessed for statistical significance.

Results: The mean age of the OSA only group was 8.2 years, significantly higher than that of the OSA + CSA group, 5.0 years, P < .00001. The proportion of underweight, normal weight, overweight, and obese patients according to BMI percentiles was not statistically significantly different between the two groups, P > .05. Most common comorbidity in the two groups was pulmonary conditions, which included asthma. Of the PSG parameters, arousals due to respiratory events and obstructive apnea hypopnea index of all OSA + CSA groups were significantly higher than those of the OSA only group, P < .05. Rapid eye movement (REM) sleep was significantly higher in total OSA + CSA group and OSA + CSA subgroup with CAI ≤ 5, P < .05, compared to OSA only.

Conclusion: Children with concurrent OSA + CSA are younger, but there appears to be no difference in BMI percentiles between OSA only and OSA + CSA. Compared to OSA only group, children with concurrent OSA + CSA have significantly different sleep architecture—higher REM %—and experience significantly higher respiratory arousals and obstructive events, especially in the subgroup with CAI > 5. There appears to be overlap in mechanisms of CSA and OSA in this cohort.

Level of Evidence: 4.
1 | INTRODUCTION

Obstructive sleep apnea (OSA) affects 1.2% to 5.7% of the pediatric population. Long-term consequences of obstructive sleep apnea include neurocognitive deficits, cardiovascular abnormalities, and impairments in behavior. Additionally, children with OSA are at risk for impairments in verbal and nonverbal reasoning, executive functioning, language, verbal fluency, school performance, and analytical thinking.

Central sleep apnea (CSA) is known to affect 4% to 6% of children. Existing research regarding CSA in the pediatric population suggests that the actual prevalence of CSA in children may be higher than expected. The long-term sequelae of CSA in children include but are not limited to sympathetic nervous system activation, oxidative stress, and systemic inflammation due to pathologic effects of multiple episodes of hypoxia, reoxygenation, apnea, and arousals. Maladaptive changes to the heart due to variations in the heart rate and blood pressure have been implicated in children with CSA.

Considerable overlap exists in the development of obstructive and CSA, making this distinction somewhat difficult. Children may have CSA, OSA, or both CSA and OSA. Although OSA and CSA are distinct entities, each with its own risk factors, one can affect the other through pathologic cycles of hypoxia, reoxygenation, apnea, and arousals.

The gold standard for diagnosing OSA and CSA is polysomnogram (PSG). American Academy of Sleep Medicine (AASM) scoring guidelines are used to score the severity of the conditions. Although central apnea index (CAI) greater than or equal to 1 is considered diagnostic of CSA, a study has suggested that CAI of greater 5 is considered clinically significant CSA. Furthermore, it has been shown in literature that in children with OSA, it is common to present with CAI greater than or equal to 1, but rare to present with CAI greater than 5.

Previous retrospective studies of pediatric OSA patients have shown resolution of CSA after adenotonsillectomy, especially for those with CAI between 1 and 5. What remains unknown is why CSA resolves with adenotonsillectomy, and what the relationship between OSA and CSA is.

Therefore, together with the observation that children with OSA often present with CSA as well as the evidence for CSA resolution after adenotonsillectomy, it is reasonable to assume there is an interdependency in development of OSA and CSA. Our goal was to define the patient characteristics of the two groups, OSA only and those with OSA and CSA, and to compare their PSG parameters to better understand similarities and differences in the two conditions.

2 | MATERIALS AND METHODS

A retrospective review of patients presenting to the Robert Wood Johnson Comprehensive Sleep Center for PSG was conducted. We obtained approval from the Institutional Review Boards of The Rutgers Biomedical Health Sciences, New Brunswick, NJ (IRB Pro2019000908), and Robert Wood Johnson University Hospital Somerset, NJ (IRB19-13). The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration.

2.1 | Study population and variables

Patients 18 years old and younger who had PSG done between 30 June 2013 and 30 June 2018 were included. Data were extracted from the electronic medical records of PSG parameters. The following PSG parameters were collected and analyzed: % in rapid eye movement (REM); % in N1 and N2 sleep; % in N3 sleep; end tidal CO2 (ETCO2); % oxygen saturation (O2 sat.); number of arousals; number of arousals due to respiratory events; awake ETCO2; nonrapid eye movement (NREM) ETCO2; REM ETCO2; % total sleep time with ETCO2 > 5 mm Hg; awake % O2 sat.; NREM % O2 Sat.; REM % O2 sat.

Patients were divided into two groups: OSA only group, and concurrent OSA and CSA group (OSA + CSA). Obstructive apnea hypopnea index (oAHI) is the number of obstructive apneas, mixed apneas, and hypopneas per hour of sleep. Mixed apnea is a unique combination of OSA and CSA, where apneic episode begins as central apnea and progresses into obstructive apnea. CAI is the number of central apneas per hour of sleep, and it includes central and hypopneic events.

The inclusion criteria for OSA only group were oAHI >1 and CAI <1. For OSA + CSA group, the inclusion criteria were oAHI >1 and CAI >1. Patients with normal PSG findings, incomplete study, or pure CSA (CAI >1 and oAHI <1), were excluded. Age and sex of each patient were recorded. Body mass index (BMI) of each patient was converted to BMI percentile adjusted for sex and age, according to Centers for Disease Control and Prevention (CDC) guidelines for pediatric patients.

While there is no consensus on the CAI cutoff to define pathologic CSA in literature, we performed a subgroup analysis to evaluate the effect of various CAI cutoffs on the study outcomes. In doing so, our goal was to evaluate for patterns of changes in PSG parameters with increased severity of CAI. OSA + CSA group was further subdivided into groups of abnormal CAI values: CAI ≤5, and CAI >5; although CAI greater than or equal to 1 is considered diagnostic of CSA, a study has suggested that CAI of greater 5 is considered clinically significant CSA. Subsequently, the PSG parameters of each OSA + CSA subgroup was compared to those of the OSA only group to analyze patterns of differences in PSG parameters.
2.2 | Statistical analyses

Mann-Whitney U test was used to assess for statistically significant differences in PSG parameters between OSA only and OSA + CSA groups, as well as to assess for statistically significant difference in oAHI in OSA only and OSA + CSA groups. A P value <.05 was considered significant.

Mann-Whitney U test was used to assess for statistically significant differences between the mean ages of OSA and OSA + CSA, as well as BMI of the two respective groups. Pearson’s chi-squared test was used for statistical comparison of proportions of coexisting medical conditions of patients in OSA and OSA + CSA groups, proportions of BMI percentile groups, and for proportion of male and female. Microsoft Excel version 16.44 (Redmond, WA), Social Science Statistics, 2021 (https://www.socscistatistics.com/), and MedCalc Software version 19.6.1 (Ostend, Belgium) were used for statistical analyses.

3 | RESULTS

3.1 | Patient population

There were a total of 426 OSA only patients and 158 OSA + CSA patients between 30 June 2013 and 30 June 2018. Within the OSA + CSA group, there were 142 patients with CAI ≤5, and 16 with CAI >5, totaling 158 OSA + CSA patients. The prevalence of OSA only within this study population was 50.1%, and the prevalence of OSA + CSA within this study population was 18.6%. Both OSA only and OSA + CSA groups had higher proportion of males than females with statistical significance: 58.0% to 42.0% respectively for OSA only group, P < .0001; and 62.7% and 37.3% respectively for OSA + CSA group, P < .0001. The mean age of the OSA only group was 8.2, which was statistically significantly greater than that of the OSA + CSA group, whose mean age was 5.0, P < .00001. The percent of patients within each BMI percentile category, underweight (<5th percentile), normal (≥5th to <85th percentile), overweight (≥85th to <95th percentile), and obese (≥95th percentile), was not statistically significantly different between OSA only and OSA + CSA groups, P > .05 (Table 1).

Patient comorbidities included developmental disabilities, prematurity, asthma, gastroesophageal reflux disease, attention deficit hyperactivity disorder, cardiac disease, neuromuscular disease, and craniofacial abnormalities (Table 1). Within this study population, 57.1% of OSA + CSA patients had greater than one comorbid condition listed in the electronic medical record, and 57.2% of OSA only patients had greater than one comorbid condition. The percent of patients with greater than one comorbid condition was not significantly different between the two groups, P = .98.

The prevalence of each of the comorbid conditions was not statistically significantly different between OSA only and OSA + CSA groups, P > .10, except for history of frequent common colds and ear infections. OSA + CSA had a significantly higher prevalence of history of frequent common colds and ear infections than OSA only, 56.46% and 40.59%, respectively, P = .0009. The most prevalent comorbid condition for both OSA only and OSA + CSA was pulmonary conditions, with 61.61% for OSA only and 63.27% for OSA + CSA (Table 1).

3.2 | PSG parameter analysis

Comparing OSA only group to the total OSA + CSA group (CAI >1), mean % REM, mean % N1 and N2, median number of arousals due to respiratory events, and median number of arousals were the statistically different parameters between the two groups, P < .05 (Table 2). The mean % REM (17.21%), the median total number of arousals during sleep (88 events), and the median number of arousals due to
respiratory events (12 events) of OSA only group were significantly lower than those of the OSA + CSA group (20.42%, 100 events and 18.5 events, respectively). The mean % N1 and N2 (42.27%) was significantly higher in OSA only group than that of the OSA + CSA group (38.49%). The rest of the PSG parameters were not statistically different between OSA only and OSA + CSA.

Comparing OSA only group to the OSA + CSA CAI ≤5 subgroup, the same parameters that were statistically different between OSA and OSA + CSA CAI >1 were also significantly different (Table 2): mean % REM, mean % N1 and N2, median number of arousals due to respiratory events, and median number of arousals, P < .05. The rest of the PSG parameters were not statistically different between OSA only and OSA + CSA subgroups.

Comparing OSA only group to the OSA + CSA CAI >5 subgroup, only the median number of arousals due to respiratory events was statistically different: OSA + CSA group had a statistically significantly higher arousals due to respiratory events (27 events) compared to that of OSA only group (12 arousals), P < .0005. The rest of the PSG parameters, including those that had been statistically significantly different between OSA only and the other subgroup of OSA + CSA, which were % REM, % N1 and N2, and arousals, were not statistically significantly different.

The total OSA + CSA group and each OSA + CSA subgroup had a statistically significantly greater oAHI compared to OSA only group, P < .05. OSA + CSA CAI >5 subgroup had a statistically significantly greater oAHI compared OSA + CSA CAI ≤5 group, P = .02 (Table 2).

In summary, except for OSA + CSA CAI >5 subgroup, the mean % REM sleep was statistically higher for OSA + CSA, compared to that of the OSA only group, P < .05. Additionally, the mean % N1 and N2 sleep was statistically lower for the total OSA + CSA group and OSA + CSA with CAI ≤5 group compared to that of the OSA only group, P < .05. The oAHI was significantly higher across all OSA + CSA groups compared to OSA only group, P < .05.

4 | DISCUSSION

Although it is widely accepted that one of the causes of OSA is anatomical obstruction of the upper airway due to adenotonsillar hypertrophy, other etiologies of OSA exist. Patients may present with poor control of upper airway dilator muscles while others have unstable ventilatory control (high loop gain).7,14,16 Our research has shown there is an overlap in polysomnographic characteristics of OSA only and OSA + CSA, and there also appears to be a compounded worsening of respiratory and obstructive events in patients with concurrent OSA + CSA, demonstrated by significantly higher oAHI and arousals due to respiratory events in OSA + CSA compared to OSA only. As evidenced by preexisting literature showing obstructive components during CSA via collapsible airway,7,14,16 we postulate there is worsening of oAHI and arousals due to respiratory events in OSA + CSA due to the additive effect of CSA.

Although CAI >1 is a commonly used cutoff to define CSA, CAI >5 is considered severe or clinically significant threshold.2,17 Our results suggest that those with more clinically significant CSA as measured by CAI >5 have significantly greater oAHI, adding to the notion of greater obstructive and respiratory distress during sleep for those presenting with concurrent OSA + CSA.

Additional analysis comparing OSA + CSA CAI >5 subgroup with total OSA + CSA group (CAI >1) revealed no statistically significant difference in age and proportion of patients within each BMI percentile category, P = .90 and P > .15, respectively. Surprisingly, the prevalence of preexisting conditions was comparable between OSA + CSA CAI >5 and total OSA + CSA group, with no statistically significant difference between the two groups, P > .10. Future study could expand the analysis on patient characteristics in this subgroup, which would be useful to understand why that is the case.

Camacho and colleagues reported that with increasing severity of OSA, there was an associated increase in CAI.18 Our results show...
there was significantly greater severity of OSA when CAI was greater than 5 in the OSA + CSA group. The key differences between Camacho and colleagues and our study were that we included children with neurological abnormalities, and we had separated our groups into OSA only with CAI <1, and subdivided groups of OSA + CSA into different levels of CAI, because there is not a general consensus in literature on the cutoff for CSA.13-15

In terms of the sleep architecture, majority of obstructive apnea events occur during REM sleep.19,20 The results of this study show that children with OSA + CSA with CAI >1 spend significantly higher percent of sleep in REM, compared to OSA only. Additionally, oAHI in OSA + CSA is significantly greater compared to that of OSA only. These observations are consistent with what is reported in literature in terms of sleep architecture and its correlation with sleep disordered breathing: OSA + CSA children spent higher proportion in REM sleep, and had a significantly greater oAHI, which signify a significantly greater number of obstructive events during sleep. However, because patients with OSA + CSA were significantly younger compared to the OSA only group, this could have contributed to the differences in sleep architecture between the two groups.

Additionally, because of the younger age of OSA + CSA group, this could have contributed to the statistically significant difference in history of frequent ear infections and common cold between OSA + CSA and OSA only groups, because of higher prevalence of such conditions in younger children. However, the percent prevalence of all other medical conditions was not statistically significantly different between the two groups.

Limitations of the study include the fact that this is a retrospective study, subjecting it to biases. We cannot draw causality from this study, and the study provides primarily correlation and association between measurements such as CAI and oAHI, as well as various PSG parameters in OSA only and OSA + CSA groups. Small sample size within OSA + CSA group with CAI >5 may have led to missed results. Additionally, the patient and demographic information can be expanded to include school performance, presenting symptoms, socioeconomic status, race, ethnicity, and insurance status. This information was not incorporated into the electronic medical record and unretrievable at the time of this study. However, our study provides a preliminary demographic information of the female to male ratio, BMI, age, and preexisting conditions for children presenting with pure OSA and OSA + CSA. Additionally, future studies could include more patients to increase the power of the study.

Future direction includes analyzing the current cohort of OSA + CSA and OSA only patients and comparing for successful resolution of symptoms postoperatively on PSG, including what type of treatment was instituted. This could be done to investigate if children with OSA + CSA are more difficult to treat.

In summary, our comparisons of polysomnographic data have shown that OSA and CSA do not appear to be independent events, with increased respiratory obstruction leading to sleep disturbance in children with concurrent OSA + CSA.

5 | CONCLUSION

Our study demonstrates that when compared to patients with pure OSA, children with concurrent OSA + CSA tend to be younger. Children with concurrent OSA + CSA also appear to have different sleep architecture with higher REM percentage and experience significantly higher arousals due to respiratory events as well as significantly greater obstructive events, especially in the subgroup with CAI >5. These findings potentially suggest that, as opposed to being independent events, obstructive apnea and hypopnea during sleep may play an important role in CSA.

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CONFLICT OF INTEREST

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