Clinical Outcomes Associated with Sleep-Disordered Breathing in Caucasian and Hispanic Children—the Tucson Children’s Assessment of Sleep Apnea Study (TuCASA)

James L. Goodwin, PhD1; Kris L. Kaemingk, PhD2,3; Ralph F. Fregosi, PhD4; Gerald M. Rosen, MD5; Wayne J. Morgan, MD1,3; Duane L. Sherrill, PhD1; Stuart F. Quan, MD1,4,6

1Arizona Respiratory, 2Children’s Research, and 4Sleep Disorders Centers, Department of 3Pediatrics and 5Department of Medicine, University of Arizona College of Medicine, Tucson, AZ; 6Department of Pediatrics, University of Minnesota School of Medicine, Minneapolis, MN

Study Objectives: This report describes clinical outcomes and threshold levels of respiratory disturbance index (RDI) associated with sleep-disordered breathing in children participating in the Tucson Children’s Assessment of Sleep Apnea study.

Design: A community-based, prospective cohort study designed to assess the severity of sleep-related symptoms associated with sleep-disordered breathing in children aged 6 to 11 years.

Setting: Students attending elementary school in the Tucson Unified School District.

Participants: Unattended home polysomnograms were completed on 239 children—55.2% boys, 51% Hispanic, and 55% between the ages of 6 and 8 years.

Measurements and Results: Based on full home polysomnography, levels of RDI that correspond to a higher prevalence of clinical symptoms of sleep-disordered breathing in children aged 6 to 11 were observed. An RDI of at least 5 was associated with frequent snoring (20.3% vs 9.1%, P<.01), excessive daytime sleepiness (22.9% vs 10.7%, P<.01), and learning problems (8.5% vs 2.5%, P<.04) when no oxygen desaturation accompanied the respiratory event. An RDI of at least 1 was associated with these symptoms when a 3% oxygen desaturation was required, snoring (24.0% vs 10.4%, P<.006), excessive daytime sleepiness (24.0% vs 13.4%, P<.04), and learning problems (10.7% vs 3.0%, P<.02). Hispanic or Caucasian ethnicity, sex, age category, obesity, insomnia, and witnessed apnea were not associated with RDI regardless of event definition.

Conclusions: The Tucson Children’s Assessment of Sleep Apnea study has shown that there are values of RDI based on polysomnography that correspond to an increased rate of clinical symptoms in children ages 6 to 11 years.

Key Words: sleep, children, sleep-disordered breathing, sleep apnea, RDI

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INTRODUCTION

SLEEP DISORDERED-BREATHING (SDB), INCLUDING OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS), IS INCREASINGLY ACKNOWLEDGED AS AN IMPORTANT CAUSE OF MORBIDITY IN CHILDREN, WITH BEHAVIORAL AND NEUROCOGNITIVE ABNORMALITIES OCCURRING 3 TIMES MORE COMMONLY IN CHILDREN WITH SDB THAN IN THOSE WITHOUT SDB.1 Clinical symptoms associated with SDB in children include frequent snoring (SN), excessive daytime sleepiness (EDS), hyperactivity, and nocturnal arousals.2,3 Prevalence rates of habitual SN generally range from 3% to 17% in population-based samples of children;4,5 however, the degree to which SN is associated with SDB in children has not been determined. Reports of EDS are less consistent but, nevertheless, are present in 8% to 62% of children with SDB.1,5,6 Recently, several studies in a large population of children have shown that learning problems (LP) are associated with symptoms of SDB.1,11,12 Although these studies suggest that there are important behavioral and neurocognitive consequences to SDB, the PSG correlates to these findings are not well established because normative standards relating to SDB are yet to be defined.13 Use of adult standards is ill-advised because clinical manifestations of childhood OSAS or SDB differ from their adult counterparts.14 However, there is a paucity of evidence indicating what severity of SDB must be present in a child to be an “abnormal” finding. Published standards are empirically derived, are based on studies with a small sample size, or use clinical populations.15 Furthermore, appraisal of existing data is made difficult by the lack of standardization in PSG technique and scoring of SDB events among studies. Thus, no epidemiologic study in a normative population has been conducted to determine the relationship between clinical symptoms and polysomnographic severity of SDB.

The American Thoracic Society13 and the American Academy of Pediatrics16 have recently convened subcommittees to examine current practice guidelines and to make recommendations for the direction of future research into childhood OSAS. Among the areas requiring additional investigation that have been identified include 1) obtaining accurate prevalence data, 2) identifying risk factors for complications resulting from OSAS, and 3) delineating the natural history of treated and untreated primary SN and OSAS. The Tucson Children’s Assessment of Sleep Apnea (TuCASA) study is a prospective cohort study designed to determine the prevalence of objectively documented SDB in preadolescent children and to investigate its relationship to symptoms, performance on neurobehavioral measures, and physiologic and anatomic risk factors. This report describes the association between objective PSG assessment of SDB and the prevalence of reported symptoms in Hispanic and Caucasian children.

METHODS

The design of the TuCASA study specified recruitment of Hispanic and Caucasian children aged 6 through 11 years to undergo an unattended home polysomnogram (PSG), complete a pediatric sleep habits questionnaire, and have a neurocognitive assessment.17 The TuCASA protocol was approved by both the University of Arizona Human Subjects and the Tucson Unified School District Research Committees. Subjects were
recruited through the Tucson Unified School District, a very large district with an elementary school population representative of children living in southern Arizona. Typically, parents were asked to complete a short sleep-habits screening questionnaire and to provide their contact information if they would allow study personnel to call and schedule a PSG for their child.

The screening questionnaire consists of a 1-page, 13-item survey designed to assess the severity of OSAS-related symptoms in children. Questions such as “How often does your child snore loudly?” “Does your child stop breathing during sleep?” and “Does your child have learning problems?” were evaluated by the parent on the scale of Never, Rarely, Occasionally, Frequently, Almost Always or Don’t Know. Additional questions were asked on the night of the PSG with a more extensive sleep-habits questionnaire. Composite variables were created based on a combination of selected survey items. Subjects were classified as having EDS if the parents reported that their child had any of the following frequently or almost always: child was sleepy in the daytime, fell asleep while watching TV or in school, or had problems falling asleep during the day. Witnessed apnea was present if the parents reported that their child stopped or struggled to breathe, their child’s lips turned blue, or they shook their child because they were worried about their child’s breathing during sleep frequently or almost always. Snoring was defined as occurring if parents reported their child snored loudly frequently or almost always. Insomnia was present if the parents reported that their child had trouble falling asleep, staying asleep, had not enough sleep, or was troubled by waking up too early and not being able to get back to sleep. The child was classified as having LP if the parent reported this at least as frequently.

The overall response rate on the screening questionnaire was 30.6%. The return rate was similar for boys and girls (49.7% and 49.4%), and was higher for Hispanics than Caucasians (45.4% and 38.1%, respectively). Other ethnicities comprised 16.6% of the surveys. We encouraged maximum participation through recruitment incentives for the school and also allowed parents to return the survey anonymously. Parents were called regarding the possibility of a PSG for their child if they indicated their willingness to participate further. Children were excluded if they had a history of asthma, OSAS, tonsillectomy, attention-deficit hyperactivity disorder, other chronic respiratory problems, or mental retardation. The profile of children who participated in the sleep study was similar to that of nonparticipants in terms of symptoms; however, Hispanic parents were more likely than Caucasian parents to complete the survey but opt out of having a PSG for their child.

An unattended home PSG was scheduled as soon as possible after recruitment. Methods for obtaining PSG data have been described previously. Briefly, a 2-person, mixed-sex team arrived at the home approximately 1 hour prior to the child’s normal bedtime. Informed consent was obtained from the parent, and an Institutional Review Board-approved assent form was obtained from the child. Questionnaires were administered, and anthropometric and other physiologic measurements were completed. Unattended overnight PSGs were obtained using the Compumedics PS-2 system (Abbotsford, Victoria, Australia). The following signals were acquired as part of the TuCASA montage: Cz/A1 and C3/A1; electroencephalogram, right and left electrooculogram, a bipolar submental electromyogram, thoracic and abdominal displacement (inductive plethysmography bands), airflow (nasal/oral thermistor), nasal pressure cannula, finger pulse oximetry, electrocardiogram to detect major arrhythmias (single bipolar lead), SN microphone, body position (mercury gauge sensor), and ambient light to determine sleep period time (sensor attached to the vest to record on/off). Studies were done on both weekdays and weekends depending upon parent preference.

The Compumedics software system was used to process all PSG data. Scoring has been described in detail previously. Briefly, sleep stages were scored according to Rechtschaffen and Kales criteria. Arousal events were identified using criteria published by the American Academy of Sleep Medicine. Apneas were scored if the amplitude (peak to trough) of the airflow signal using the thermistor decreased below at least 25% of the amplitude of baseline breathing (identified during a period of regular breathing with stable oxygen levels), if this change lasted for more than 6 seconds or 2 breath cycles. Hypopneas were designated if the amplitude of any respiratory signal decreased below (approximately) 70% of the amplitude of baseline and if the thermistor signal did not meet the criterion for apnea. Central events were marked if no displacement was noted on both the chest and abdominal inductance channels. However, central hypopneas were marked if no displacement occurred for at least 3% oxygen desaturation, as well as with or without arousal. Summary measures of desaturation, sleep stages, arousal frequencies, and heart rate variation also were computed.

All studies were scored by a single registered polysomnographic technologist who was required to demonstrate a complete understanding of the study’s scoring rules and to articulate reasons for assigning epoch by epoch codes for sleep and respiratory scoring. Approximately 5% of studies were rescoring by the same scorer on a blinded basis to determine consistency in scoring. No systematic differences were observed between initial and rescored studies.

Statistical analysis was done using SPSS 11.0 for Windows (SPSS®, Inc; Chicago, IL, 2001). We used contingency tables to examine bivariate relationships between the symptoms associated with SDB with each definition of RDI. For these analyses, we did a bivariate analysis using sex, Caucasian or Hispanic ethnicity, obesity, SN, EDS, witnessed apneas, insomnia, LP, and age against various RDI definitions. Statistical significance (P<0.05) was determined using the Pearson χ² test statistic.

Table 1—Baseline characteristics of 239 children completing polysomnography in the TuCASA study

<table>
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<th>Ethnicity</th>
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<th>Girls (44.8%)</th>
<th>Total</th>
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<th>% of total*</th>
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<td>% of total*</td>
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* may not sum to 100% due to rounding. BMI >95%, defined as obese because body mass index exceeded the 95th percentile for the child’s age, sex, and ethnicity; SN, snoring; EDS, excessive daytime sleepiness; WITAP, witnessed apnea; LP, learning
RESULTS

A total of 239 PSGs were completed on a sample that included 55.2% boys and 51.0% Hispanic children (Table 1). Approximately 55% of the children were between the ages of 6 and 8 years, and 11.7% were classified as obese because their BMI exceeded the 95% percentile for their age, sex, and ethnicity.20 Parental report of symptoms showed that 14.6% of these children snored, 16.7% had reported EDS, 6.7% had witnessed apnea, 25.5% had insomnia, and 5.4% had reported LP.

Selected characteristics of sleep in these children are shown in Table 2. The mean sleep time was approximately 490 minutes, with sleep efficiency of 90%. In general, there was little distortion in sleep architecture,21,22 However, mean sleep and rapid eye movement latencies were slightly prolonged at 17 and 131 minutes, respectively.23,24

A description of the RDI distribution, calculated using various levels of associated oxygen desaturation, is shown in Table 3. In the event that no associated oxygen desaturation was required, the median RDI was 3.5% and ranged from 0 to 48.4. If an associated 3% desaturation was required, the median RDI dropped again to 0.65 and ranged from 0 to 29.1.

Cut points of RDI using an index calculated without any associated oxygen desaturation were examined against the prevalence of OSAS-related symptoms reported by parents (Table 4). Snoring was reported in 18.5% of children with an RDI of 4 events or more versus those with an RDI of less than 4 (P<.04). Excessive daytime sleepiness (19.9% vs 11.8%, P<.11) and LP (7.5 vs 2.2, P<.07) were also reported more frequently for those children with an RDI of 4 or greater, although neither were statistically significant. However, when an RDI of 5 events per hour or greater was used as a cut point, SN (20.3% vs 9.1%, P<.01), EDS (22.9% vs 10.7%, P<.01), and LP (8.5% vs 2.5%, P<.04) were all statistically significantly different. Each of these symptoms were highly significant across cut points of RDI at 6, 7, and 8 events per hour when no associated oxygen desaturation was linked to the event (Table 4, data for RDI cut points of 7 and 8 not shown).

A similar analysis was done for cut points of RDI when the event was required to be associated with at least a 2% oxygen desaturation (Table 5). Children with an RDI of 1 were significantly more likely to have reports of SN (18.9% vs 6.3%, P<.009) and LP (7.5% vs 1.5%, P<.05) than were children with an RDI of less than 1. Excessive daytime sleepiness was not significant at this cut point of 1 (17.6% vs 15.0%); however, EDS was significant at the RDI cut point of 2 (23.3% vs 12.8%, P<.03). Snoring and LP remained highly significant at higher cut points of RDI for those children classified with the higher RDI based on 2%
oxygen desaturation-related events, whereas EDS did not.

When a 3% oxygen desaturation was required for an event to be included in the calculation of RDI, a similar pattern was seen (Table 6). At an RDI of 1 or greater, SN (24.0% vs 10.4%, $P<.006$), EDS (24.0% vs 13.4%, $P=.04$), and LP were (10.7% vs 3.0%, $P<.02$) were all significantly more likely to be reported than for those children with an RDI less than 1. This remained true at an RDI cut point of 2; however, the number of children who had events associated with a 3% desaturation was not sufficient in this population-based study to test statistical significance.

Regardless of the cut point of RDI or oxygen desaturation criteria that were used to define events, neither ethnicity nor sex altered these associations. This was also true for age category, obesity, insomnia, and witnessed apnea.

**Discussion**

The TuCASA study has documented the relationships between RDI values based on PSG and clinical symptoms of SDB in children aged 6 to 11 years. At an RDI of at least 5, when no oxygen desaturation accompanied the respiratory event, there was a significantly higher prevalence of SN, EDS, and LP. Similarly, an RDI of at least 2 was associated with an increased prevalence of these symptoms when a 2% oxygen desaturation was required, and an RDI of at least 1 was associated with these symptoms when a 3% oxygen desaturation was required. Hispanic or Caucasian ethnicity, sex, age category, obesity, insomnia, and witnessed apnea were not associated with RDI, regardless of event definition.

The principal findings of this study are that there are values of RDI ascertained by PSG associated with an increase in prevalence of clinical symptoms of SDB or OSAS. Heretofore, data linking objective indexes of RDI severity to the presence of clinical symptoms have been lacking. Currently used RDI thresholds are derived empirically from clinical experience or are based on statistical inference.1,15 Alternatively, values that are used for adults are applied to children, although evidence shows that OSAS or SDB is a different disease in children than in adults.14 Children may develop clinical sequelae with what appears to be relatively mild SDB. Thus most pediatric pulmonologists consider an apnea index of 10 in children to be severe, whereas it is considered only mildly abnormal in adults.15 No previous studies have linked values for RDI based on full PSG to clinical symptoms in a population-based sample. Nevertheless, our findings are similar to a previously published standard suggesting that an apnea index greater than 1 is abnormal.20 However, our data extend these observations by indicating that hypopneas are equally important in defining SDB severity. Therefore, these findings represent an important step toward examining the relationship between SDB severity and specific clinical outcomes.

Our conclusions contribute much-needed information for determining clinically significant levels of RDI based on differing definitions of respiratory events. One of the major hindrances to establishing clinically significant thresholds of RDI is that the metric has been defined differently by each study that has presented RDI data in children. Studies of OSA or SDB in children report a prevalence ranging from 0.7% to 2.9% to 10.3%.6,26 The disparity is due to varying criteria for RDI-event definition. Our findings support those recently reported by Tang et al that the RDI value in children can vary by as much as 20-fold depending upon the definition used for respiratory events.27 A similar analysis in adults found a 10-fold difference in RDI.28 If events are counted regardless of oxygen desaturation, the RDI level associated with a greater prevalence of clinical outcomes is higher than if the event requires a 2% desaturation. This value is gradually reduced as the level of oxygen desaturation required for an event is increased; our results are similar to those found by Redline in both adults and children.26,27 Additionally, our data show a consistent association between RDI values and clinical outcomes. For example, the outcomes that are significant for events associated with a 2% or 3% oxygen desaturation are similar to those found with no desaturation required.

Establishing values for RDI that relate to clinical outcomes not only will be important in allowing consistent estimates of disease, but will permit clinicians to ascertain if clinically significant SDB is present and to assess whether there is a risk for clinical sequelae. The varying approaches for quantification of RDI in the past have led to poor clinical estimates of both the presence and severity of SDB in children. Previously, both limited-channel sleep studies and parent questionnaires have been used as screening measures for clinically important SDB; however, there has been no consensus on a group of symptoms or PSG characteristics to guide treatment decisions pertaining to SDB in children. Thus, our findings may be an important first step in providing such information to clinicians.

Although SN, EDS, and LP were strongly associated with RDI, sex and age were not. This is possibly due to homogenous physical characteristics between prepubescent school-aged children and is consistent with previous reports.28 The relationships in this study between RDI and clinical symptoms were not significantly associated with Hispanic ethnicity, although parental report of symptoms consistent with OSAS or SDB in children are reported at a higher rate in Hispanics.29,30 No epidemiologic studies of SDB have been done in Hispanic children; however, SDB has been found to be more prevalent in a population-based sample of Hispanic adults.31 Children categorized as obese were not more likely to have a higher RDI at any of the listed thresholds. Although previous studies have reported this association, they have used clinical samples with patients referred for a sleep-related problem. Thus, participants were more likely to have OSAS or SDB as well as be obese. It has been reported that SDB in childhood is more prevalent in obese children.15 However, TuCASA is population based and, therefore, not as likely to enroll a high number of children with morbid obesity. This explanation is supported by the recent report of Gozal et al who found that OSAS in children was associated with morbid obesity not with simply being overweight.10 Our analysis did not show insomnia to be associated with increased RDI in these children. This may be due to the very broad definition used to define this symptom, which was based upon questions answered on the Sleep Habits Questionnaire administered on the night of the sleep study. The prevalence of this symptom was 25.5% of the sample. Thus, it is not surprising that there would be no statistical difference between the 2 groups. This high prevalence of insomnia is similar to that recently found by Chervin et al in a general pediatric clinic population.22 Witnessed apnea was also not significantly associated with increasing RDI level. This observation is not necessarily unusual because a parent cannot accurately observe the frequency of apneic events for the entire duration of sleep.

Our finding must be qualified: parents of children who had an RDI exceeding any given threshold value were more likely to report that their child had LP. Our assessment of LP was based on the answer to 1 question on the screening survey; therefore, parental report could be subject to interpretation or cultural bias. Furthermore, this question has not been validated in a large sample. Nevertheless, it does have face validity and was consistently associated with threshold values of RDI across all definitions used in this analysis. Although this association was highly significant in our analysis, we were not able to control for variables known to be associated with LP, such as socioeconomic status or parent education. Further prospective studies with objective measures of neurocognitive function should be conducted to confirm this relationship.

Our assessment of RDI was based on a single-night, unattended, ambulatory sleep study. Although laboratory-based PSG is the gold standard, this method is generally not feasible for a large, population-based, epidemiologic study of sleep in children. Other studies have shown that unattended studies are reliable for measuring RDI and have little first-night effect in children.17 The sleep architecture data presented in Table 2 support the concept that sleep in TuCASA children is comparable to the normal sleep architecture in children of this age. It has been reported that SDB in children manifested as hyperventilation may be more accurately assessed by carbon dioxide measurement; however, this was not possible with the limited montage in the home environment.
Recent studies have suggested that it may not be appropriate to include central apneas when calculating the RDI in children. To address this issue, we conducted an analysis of central apneas similar to that used for RDI based on an obstructive apnea-hypopnea index, in which central events were not used in the summary measure of RDI. Our findings were unchanged, most likely because the preponderance of events in TuCASA children were hypopneas, with few obstructive or central apneas contributing to the total RDI. Our mean hypopnea index was 4.6±4.3, and the combined index for obstructive apnea-hypopnea index, which included only apneas that were obstructive, had a mean of 4.7±4.5. This represents approximately 80% of the total events, whereas central events were only 20% of the total.

It has been reported that sleep fragmentation due to SDB-related arousals may be responsible for EDS or LP in children. Using contingency tables, we examined arousal indexes of 3, 4, 5, 6, and 7 arousals per hour against SN, EDS, and LP. No level of arousal index was significantly associated with these symptoms. In this population-based sample, the mean arousal index was 3.4 (range, 8 to 11.1 per hour; SD, 1.27). We did not have a sufficient number of subjects to examine arousal indexes greater than 7 per hour against SN, EDS, and LP. We acknowledge that this observational study design is not without limitations. A very large number of children must be enrolled in order to accumulate an adequate number of symptomatic children with SDB to analyze. We recognize that a limitation of these analyses is our lack of sufficient sample size to control for confounding in RDI by large numbers of multiple covariates. Unfortunately, the prevalence of SDB when RDI is defined using more stringent respiratory-event criteria was not adequate in our population-based sample. Furthermore, recruitment may have incurred a selection bias so that parents who participated might be more likely to have symptomatic children with SDB than those who did not participate. Given that our prevalence of SN is similar to that found in other studies, we do not think that a large amount of selection bias occurred. Although we did record SN with a SN microphone, this measurement of SN with an uncalibrated microphone is an inherently imprecise method of documenting SN.

Our assessment of EDS was based on a subjective report of symptoms by the parent; therefore, our results should be considered in this context. The definition for EDS (frequently or almost always) was consistent with our a priori hypotheses, as well as with our other definitions for LP, SN, and witnessed apnea. However, we did examine less frequent reporting of EDS and other variables as they pertain to RDI since this is another area where a major gap in knowledge exists, as well as allowing us to establish threshold levels.

In summary, the TuCASA study has demonstrated that there are RDI values above which there is a higher prevalence of clinical symptoms of SDB. These findings should assist in determining prevalence rates based on PSG results in epidemiologic studies and assist clinicians by providing more objective criteria for case identification.

ACKNOWLEDGEMENTS

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ABBREVIATIONS

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<th>Definition</th>
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<tr>
<td>BMI</td>
<td>body mass index</td>
</tr>
<tr>
<td>EDS</td>
<td>excessive daytime sleepiness</td>
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REFERENCES