CHEST

Official publication of the American College of Chest Physicians

Sleep-Disordered Breathing Is a Risk Factor for Community-Acquired Alveolar Pneumonia in Early Childhood

Aviv D. Goldbart, Asher Tal, Noga Givon-Lavi, Jacob Bar-Ziv, Ron Dagan and David Greenberg

Chest 2012;141;1210-1215; Prepublished online November 17, 2011; DOI 10.1378/chest.11-1998

ISSN:0012-3692

CHEST

Original Research

SLEEP DISORDERS

Sleep-Disordered Breathing Is a Risk Factor for Community-Acquired Alveolar Pneumonia in Early Childhood

Aviv D. Goldbart, MD; Asher Tal, MD; Noga Givon-Lavi, PhD; Jacob Bar-Ziv, MD; Ron Dagan, MD; and David Greenberg, MD

Background: **Data are scarce with regard to risk factors for acute community-acquired alveolar pneumonia (CAAP) in children, but it is known that children with sleep-disordered breathing (SDB) experience more respiratory infections. We aimed to assess whether SDB is a risk factor for CAAP in early childhood.**

Methods: **We conducted a prospective, nested, case-control study assessing children < 5 years old who had been given a diagnosis of CAAP based on World Health Organization radiographic criteria. Demographic and clinical data were collected. SDB symptoms were documented using a structured questionnaire. CAAP study and retrospective sleep laboratory databases were compared. SDB presence and severity were determined by questionnaire and polysomnography (PSG).**

Results: **A total of 14,913 children underwent chest radiography during the study period; 1,546 children with radiographically proven CAAP (58% boys) and 441 control subjects (54% boys) were prospectively enrolled. Frequent snoring was reported in 18.6% vs 2.9% subjects with CAAP and control subjects, respectively (*P* < .001). The respective figures for subjects with CAAP and control subjects for restless sleep, nocturnal breathing problems, abnormal behavior, and chronic rhinorrhea were 21.6% vs 5.3%, 5% vs 1.4%, 6.4% vs 0.2%, and 12.9% vs 1.8%, (*P* < .001 for each). Fifty children (3.3%) with CAAP vs three control subjects (0.7%) underwent adenoidectomy (*P* < .001). PSG diagnosis of obstructive sleep apnea had been established previously in 79 patients (5%) with CAAP vs six (1.3%) of the control subjects (OR, 3.7 [95% CI, 1.6-10.0]; *P* < .001), with higher severity in patients with CAAP than in control subjects.**

Conclusions: **SDB is common in children with CAAP and is possibly a predisposing risk factor for CAAP in children < 5 years old. We recommend considering SDB in young children who are given a diagnosis of CAAP.**

CHEST 2012; 141(5):1210–1215

Abbreviations: CAAP = community-acquired alveolar pneumonia; GA = gestational age; OSA = obstructive sleep apnea; PSG = polysomnography; SDB = sleep-disordered breathing; WHO-SICR = World Health Organization Standardization of Interpretation of Chest Radiographs

It is estimated that > 150 million episodes of pneumonia in children occur yearly worldwide, causing 11 to 20 million hospitalizations, accounting for approximately 7% to 13% of all new cases worldwide and > 2 million deaths.[1] Little is known about the risk factors for acute community-acquired pneumonia in children, although anatomic and physiologic abnormalities of the respiratory, GI, and neuromuscular systems are associated with recurrent lower respiratory tract infections.[2]

Sleep-disordered breathing (SDB) comprises a spectrum of disorders associated with increased upper-airway resistance during sleep, including obstructive sleep apnea (OSA). It affects up to 12% of prepubertal children.[3] This condition, characterized by repeated airway closures, often includes night and day symptoms and may result in a variety of cognitive, behavioral, cardiovascular, and metabolic consequences.[4] Pediatric patients with SDB are heavy consumers of health-care services, mainly pulmonary and otolaryngology consultations, respiratory medications, ED visits, and hospital admissions. This may occur even before OSA is diagnosed.[5] SDB can be screened for by a questionnaire, whereas the diagnosis of OSA is performed by a sleep study (polysomnography [PSG]).[6]

We have reported previously that children who suffer from SDB experience higher rates of lower respiratory tract infections than do those without SDB, especially during the first 4 years of life.[7] However, the prevalence of SDB in community-acquired alveolar pneumonia (CAAP) in children <5 years old and whether SDB is an independent risk factor for CAAP have never been assessed, to the best of our knowledge.

The aim of the present study was to prospectively determine if SDB is more frequent in children with CAAP than in healthy control subjects. The specific end point of alveolar pneumonia was selected in this study because it is radiologically distinct and the easiest to reach a consensus on when used for the radiologic diagnosis of pneumonia.[8,9]

Materials and Methods

Study Design and Setting

This prospective, population-based, case-control study was conducted from March 2006 through September 2008. The Soroka University Medical Center is the only hospital in southern Israel. The region had 520,000 inhabitants in 2006-2008. During the study period, children <5 years old in the region accounted for 67,300 to 74,000 annually.[10] Medical insurance for children in Israel is universal and is provided free of charge. There are no financial or other barriers to health-care service use in the region. The 7-valent pneumococcal conjugate vaccine was not widely used in Israel during the study period, and <5% of the region's children received the vaccine during the period.

Patients

The study was approved by the Soroka University Medical Center institutional review board (FWA00000721). Children <5 years of age, who were seen at the pediatric ED or were hospitalized, were enrolled after their parents signed an informed consent, if they met the criteria set for alveolar pneumonia by the World Health Organization Standardization of Interpretation of Chest Radiographs (WHO-SICR) Working Group.[9] Chest radiographs were obtained at the ED or within <48 h of hospitalization. Only one episode per child could be included. The control subjects were children <5 years old, seen in maternal-child health clinics for routine vaccination or admitted to the pediatric surgery department for an elective surgery. The presence of SDB was ruled out based on response to a questionnaire (see "SDB Evaluation" for details). Subjects were enrolled daily (Sunday to Thursday from 8:00 AM to 4:00 PM, except for holidays). Patients with underlying neuromuscular disorders were excluded. The inclusion criteria for cases and control subjects were similar, and included the following: geographic area, age range, and study period.

Prospective Data Collection

The data gathered during the study period included demographic characteristics (ie, prematurity, daycare center attendance, previous pneumonia, and asthma), clinical variables (ie, respiratory rate, oxygen saturation, heart rate,) and laboratory data (ie, complete blood count, erythrocyte sedimentation rate/C-reactive protein, serum electrolytes). Clinical data were obtained from the medical charts.

SDB Evaluation

Parents were interviewed by research coordinators at the ED or pediatric ward or by telephone interview. The telephone interview was conducted immediately after the ED visit. If the immediate contact attempt failed, further attempts were made four to five times a week, for up to 1 month.

We used a questionnaire (in both Hebrew and Arabic depending on the spoken language), representing the significant questions in the questionnaire the group was using, that addressed classic symptoms referring to the 12 months preceding the subject's ED visit and was validated in young children.[6] Symptom frequency ranged from 1 to 5 (5 being the most severe) based on the number of positive symptoms. The following symptoms were included: snoring, nighttime breathing problems (witnessed apnea and breathing difficulty), restless sleep, chronic rhinorrhea, and daytime abnormal behavior (tiredness or irritability). In addition, in order to evaluate the presence of SDB before CAAP, we added two more variables: (1) previous PSG; and (2) previous adenoidectomy with or without tonsillectomy.

OSA Evaluation by PSG

The Soroka University Medical Sleep Center is the only pediatric sleep center in the southern region of Israel; it conducts ~1,000 sleep studies annually. In order to define OSA severity, we used the severity definitions that are used most commonly in pediatric sleep medicine, taking the apnea-hypopnea index of 1 as the cutoff for the definition of OSA, apnea-hypopnea index of 1 to 5 as mild OSA, >5 as moderate OSA, and >10 as a severe disorder.[11] We retrospectively matched the identity numbers of the study patients and control subjects to the Sleep-Wake Disorders Center database for the previous 6 years. None of the children underwent their PSG during an acute disease. The results of matched identity numbers of the children undergoing overnight PSG conducted at the center were then compiled into the study database.

Evaluation of Chest Radiographs

Chest radiographs were analyzed according to the WHO-SICR Working Group[9]: Alveolar pneumonia was defined as dense opacity that may be a fluffy consolidation of a portion, the whole lobe, or the entire lung, often containing air bronchogram and sometimes associated with pleural effusion. All radiographs were processed and visualized in Hipax 3.27.1 radiographic image processing software (Ateinhart Medizinsysteme) and were stored for future

Manuscript received August 15, 2011; revision accepted November 1, 2011.
Affiliations: From the Sleep-Wake Disorders Unit (Drs Goldbart and Tal), the Department of Pediatrics (Drs Goldbart and Tal), and the Pediatric Infectious Disease Unit (Drs Givon-Lavi, Dagan, and Greenberg), Soroka University Medical Center and the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva; and the Department of Radiology (Dr Bar-Ziv), Hadassah University Medical Center, Jerusalem, Israel.
Funding/Support: This study was funded in part by Wyeth [Grant 0887X-101801 to R. D.] and by the Israel Science Foundation [Grant ISF 753/11 to A. D. G.].
Correspondence to: Aviv D. Goldbart, MD, Department of Pediatrics, Sleep-Wake Disorders Unit, Soroka University Medical Center and the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel; e-mail: avivgold@bgu.ac.il

DOI: 10.1378/chest.11-1998

analyses. Two pediatric infectious disease specialists (D. G. and R. D.), who participated in the WHO-SICR group, read separately the chest radiographs of all children. When a diagnosis of alveolar pneumonia was determined by one or both of the pediatric infectious disease specialists, a case was labeled "tentative pneumonia case." For each radiograph defined as "tentative pneumonia case," a control radiograph defined as "no pneumonia" was selected from among all successive chest radiographs for an age-matched child. The chest radiographs were sent periodically to the study radiologist (J. B.-Z.), who was also a member of the WHO-SICR group, after being mixed at random. The study radiologist read the radiographs, unaware of the other investigators' reading results and of the clinical diagnosis. The final diagnosis of alveolar pneumonia was determined solely for the cases confirmed both by the radiologist and at least one pediatric infectious disease specialist.

Statistical Analysis

Data were recorded using Access Microsoft software. Statistical analysis was conducted using SPSS software (version 15.0; SPSS Inc). Contingency table analysis between unmatched samples was performed using the χ^2 tests or Fisher exact test. The Student *t* test was used to compare continuous variables. A multivariate logistic regression model was used for symptoms of SDB, controlling for age and ethnic origin. Statistical significance was defined as $P < .05$. Stratified analysis for age was conducted.

Results

A total of 14,913 children underwent chest radiography during the study period. Radiographically proven community-acquired pneumonia was diagnosed in 2,558 (17.2%) episodes. Of these, alveolar pneumonia was diagnosed in 2,465 subjects (95.7%) and nonalveolar pneumonia in 93 (4.3%). The final study group included 2,465 children (58% males), and 441 control subjects (54% boys) were prospectively enrolled. Of those 2,465 eligible cases, 1,546 (62.7%) were eventually enrolled, because the rest were not available during working hours and could not be reached by telephone. Children with CAAP were older (age 22.2 ± 15.6 months vs 16.4 ± 11.1 months) and were more frequently Jewish children than were control subjects (Table 1). Among children with CAAP, there was a significantly higher prevalence of prematurity, daycare center attendance, previous episodes of pneumonia, and previous diagnosis of asthma than in control subjects. No differences between the CAAP and control groups were found with regard to overall previous acute otitis media episodes, previous episodes of acute otitis media with tympanocentesis, number of siblings, or antibiotic treatment in the 3 months preceding enrollment. Breastfeeding was significantly more common in control subjects than in children with CAAP (Table 1).

The following symptoms were significantly more common in children with CAAP than in control subjects: frequent (> 3 nights per week) snoring; restless sleep; nocturnal breathing problems; abnormal behavior; and chronic rhinorrhea (Table 1). More children in the CAAP group underwent previous PSG and previous adenoidectomy than in the healthy control group.

The proportion of children with one or more symptoms (1 to 5) was significantly higher in the CAAP group than in the healthy control subjects after adjustment for age, prematurity, and ethnicity (Fig 1). To assess whether the various respiratory symptoms were more frequent in the CAAP group than in the control group, multivariate logistic regression models, adjusted for age, prematurity, and ethnicity, showed the following variables to be significantly more common in children

Table 1—*Demographics, Risk Factors, SDB Characteristics, and Medical History of Children With CAAP vs Healthy Control Subjects*

Characteristic	Control Children (n = 441)	Children With CAAP (n = 1,546)	*P* Value
Demographics and risk factors			
Age, mean ± SD, mo	11.1 ± 16.4	22.2 ± 15.6	< .001
Male	254 (57.9)	893 (57.8)	.982
Jewish	34 (7.7)	696 (45)	< .001
Bedouin	407 (92.3)	849 (55)	< .001
Prematurity (< 36 gestational wk)	27 (6.1)	197 (12.9)	< .001
Attending daycare center	43 (9.8)	682 (44.5)	< .001
Previous pneumonia	34 (7.7)	333 (21.7)	< .001
Breastfeeding	419 (95)	1,304 (85.5)	.001
Previous diagnosis of asthma	22 (5.0)	230 (15.0)	.003
SDB characteristics and medical history			
Snoring > 3 nights per wk	13 (2.9)	288 (18.6)	< .001
Nighttime breathing problems	6 (1.4)	78 (5.2)	.001
Restless sleep	23 (5.3)	328 (16.8)	< .001
Daytime abnormal behavior	1 (0.2)	97 (6.3)	< .001
Rhinorrhea	8 (1.8)	194 (12.5)	< .001
Previous adenoidectomy	3 (0.7)	50 (3.3)	.003
Previous polysomnography	1 (0.2)	55 (3.6)	< .001

Data are presented as No. (%) unless indicated otherwise. CAAP = community-acquired alveolar pneumonia; SDB = sleep-disordered breathing.

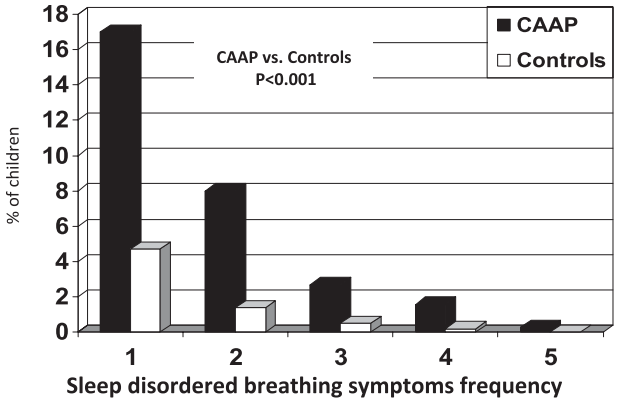

FIGURE 1. Sleep-disordered breathing (SDB) symptoms frequency in children with CAAP vs control subjects <5 years of age. CAAP = community-acquired alveolar pneumonia.

with CAAP than in healthy control subjects: chronic rhinorrhea, restless sleep, and daytime abnormal behavior (Table 2). Snoring (>3 nights a week) also showed a trend for significance but did not reach statistical significance.

Previous PSG performed before enrolment indicated the presence of SDB in 79 (5%) of the children with CAAP vs six (1.3%) of the control subjects (OR, 3.7; 95% CI, 1.6-10.0; $P < .001$) (Fig 2). SDB severity according to PSG was significantly higher in CAAP patients: 80% of the children with CAAP who underwent PSG had moderate or severe OSA, vs only 66% of the control subjects ($P < .001$) (Fig 3).

DISCUSSION

This study reveals that SDB serves as a risk factor for CAAP in young children. We now report that SDB is significantly more common and is clinically present at least 12 months prior to the infectious event. Furthermore, a direct correlation exists between the severity of SDB and the chances of receiving a diagnosis of pneumonia.

Childhood community-acquired infections are a frequent cause of physician visits, antibiotic and over-the-counter drug consumption, work loss, and reduction of quality of life.[12] There are some hints that anatomic and functional abnormalities can lead to CAAP, such as in the case of neurologically impaired children who suffer more episodes of aspiration pneumonia.[13]

Although no data exist in children, it appears that pneumonia is also prevalent in adults who have a diagnosis of SDB. A retrospective analysis was conducted on data from 371,000 discharges of hospitalized adult patients from the 2004 National Hospital Discharge Survey. One of the most common diagnoses in hospitalized patients with sleep apnea was pneumonia.[14]

Several risk factors for CAAP were observed in this study: prematurity (<36 wk), daycare center attendance, previous pneumonia, and asthma. Indeed, some of these risk factors were also reported previously. Prematurity is a very important risk factor for respiratory morbidity during infancy and early childhood.[15] In fact, very preterm infants (<32 weeks' gestational age [GA]), as well as preterm infants born at 32 to 36 weeks' GA, are particularly vulnerable to developing severe lower respiratory tract infections that require frequent hospitalizations.[15] Even infants born at 33 to 36 weeks' GA had substantially higher rates of admission when compared with full-term infants.[16] The investigators at Rainbow Babies and Children's Hospital (Cleveland, Ohio) found that 21% of children born prematurely were habitual snorers and had three- to five-times-higher rates of SDB than did full-term infants.[17] In addition, prematurity has been linked to severe CAAP in children <5 years of age.[18] We, therefore, took into account prematurity, in addition to age and ethnicity, in the multivariate logistic regression model (Figs 1-3).

Daycare center attendance is a well-known risk factor for several infectious conditions, such as otitis media.[19] Asthma is frequently found in the differential diagnosis of recurrent chest infections in children. The most common explanation is that mucus plugging causes microatelectasis, which eventually gets infected and leads to subsegmental and later to lobar consolidation.[20]

To the best of our knowledge, the association between SDB and CAAP in children has not been described previously. In our study, we found that SDB symptoms and previous SDB PSG diagnoses were more prevalent in children with CAAP than in control subjects. Moreover, we found an association between SDB severity in a previous PSG and the frequency of CAAP in these children.

We have reported a study[7] in which we looked at the medical files of young children who had been given a diagnosis of OSA at the age of 4 years. We found that, indeed, the respiratory morbidity and symptoms of SDB had already started during their first year of life. Interestingly, a major finding was increased incidence of lower respiratory tract infections and pneumonia from the first year of life.

Table 2—*ORs and 95% CIs for SDB Symptoms in Children With CAAP vs Healthy Control Subjects (Multivariate Logistics Regression Analysis, Adjusted for Age and Ethnicity)*

Variable	OR	95% CI	*P* Value
Rhinorrhea	3.24	1.54-6.83	.002
Snoring > 3 nights per wk	2.11	0.94-4.78	.070
Nighttime breathing problems	1.76	0.79-4.29	.208
Restless sleep	1.68	1.04-2.73	.035
Daytime abnormal behavior	11.06	1.51-81.26	.018
Previous adenoidectomy	2.21	0.65-7.51	.202

See Table 1 for expansion of abbreviations.

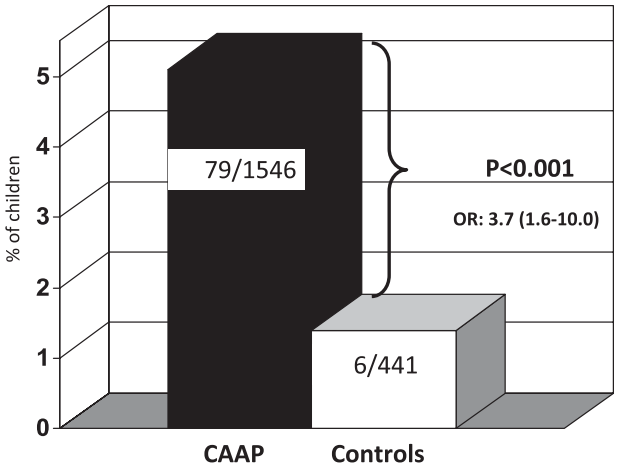

FIGURE 2. Previous polysomnographic diagnosis of SDB in children with CAAP vs control subjects < 5 years of age. See Figure 1 legend for expansion of abbreviations.

There are several mechanisms that may explain, in part, the association between the pathology in the upper airway and the infections of the lower respiratory tract. It was suggested previously that children with adenoid hypertrophy may suffer from recurrent microaspirations to the lungs. The researchers evaluated ventilation during sleep before and after adenotonsillectomy. In all the cases, esophageal pressure during sleep was elevated four- to sixfold above the normal value. This was caused by nasal obstruction due to adenoid hypertrophy and obstruction of the oropharynx by hypertrophied tonsil and collapse of the tongue due to muscular relaxation during sleep. When contrast media were instilled into the nasopharynx, contrast media aspiration to the lung was found significantly more frequently in subjects with upper airway obstruction, suggesting that active aspiration by marked inspiratory negative pressure during sleep may play a major role in causing lower respiratory infections.[21]

In another prospective study, patients with symptoms of OSA aspirated significantly more radiotracer (infused through the nasopharynx), suggesting an apparent risk of increased pharyngeal aspiration in patients with OSA.[22] Moreover, there is ample evidence supporting the existence of inflammation in upper airway surgical specimens obtained from children with SDB.[23] Inflammatory pathways are activated in the lymphatic tissue, that alternatively can induce chemotaxis of preinflammatory cytokines.[24] Furthermore, it was suggested that inflammation can be linked to denervation of the upper airway, leading to its collapsibility and dysfunction.[25] Indeed, the data gathered so far in the field of pulmonary medicine as well as in otolaryngology and anesthesiology support the concept of a nocturnal airway dysfunction in children with SDB. This, in turn, may result in a decrease in the "filtering" ability of the upper airway and an increased likelihood of upper airway microaspirations unopposed by local defense immunologic barriers, ending in alveolar pneumonia.

Because SDB refers to a spectrum of breathing disorders during sleep, a questionnaire can identify the presence of an abnormal breathing pattern to a certain degree of certainty. However, in our setting it was not possible to assess the presence of SDB in 2,000 children during an acute event of pneumonia, other than by questioning them with a well-defined set of questions. We believe that this is perhaps a limitation but also the strength of this study. We decided to take one of the well-accepted questionnaires[6] that showed a significant correlation between specific questions and PSG findings. Another limitation is that PSG data were not collected systematically and were analyzed retrospectively. This was done because this is the only pediatric sleep laboratory in our catchment area. We need to emphasize that this was not a matched-case control study, and differences were noted between the two groups. Therefore, we used multiregression analysis for age and ethnicity when we evaluated the possible risk factors.

The fact that the same proportions of children with SDB were found by the questionnaire and by PSG reinforces the potential correlations between screening instruments and objective findings. However, another limitation was that only 62.7% of all radiographically proven alveolar pneumonia cases were recruited to the study. The main obstacle was communication (phones/cell phones) with parents of children discharged from the ED. However, it is possible that these results underestimate the presence of SDB in patients with CAAP because we gathered data from all control subjects.

CONCLUSIONS

CAAP in children was found significantly more frequently in children with SDB than in control

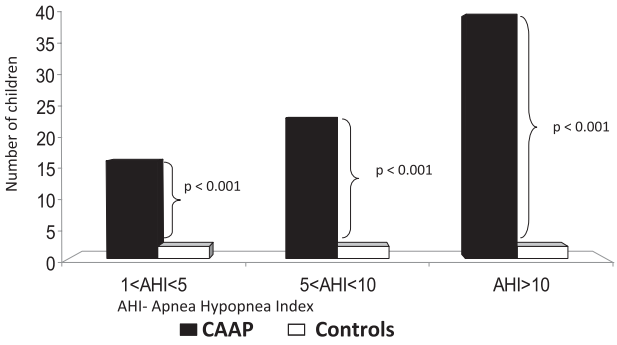

FIGURE 3. Polysomnographic severity of SDB in children with CAAP vs control subjects < 5 years of age. See Figure 1 legend for expansion of abbreviations.

subjects. In addition, a linear association was found between the severity of SDB and the risk of CAAP. Thus, SDB is an independent risk factor predisposing for pneumonia in early childhood. We recommend that SDB presence be ruled out by detailed history and physical examination in young children who receive a diagnosis of CAAP, which may suggest the need to refer the patient to a specialist.

Acknowledgments

Author contributions: Dr Goldbart had full access to all the data in the study and takes responsibility for the integrity and accuracy of the data analysis.
Dr Goldbart: contributed to the study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; obtaining of funding; administrative, technical or material support; and supervision.
Dr Tal: contributed to the study concept and design; analysis and interpretation of data; critical revision of the manuscript for important intellectual content; and administrative, technical or material support.
Dr Givon-Lavi: contributed to the analysis and interpretation of data, drafting of the manuscript, and statistical analysis.
Dr Bar-Ziv: contributed to the acquisition of data, drafting of the manuscript, and supervision.
Dr Dagan: contributed to the study concept and design; acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content; obtaining of funding; administrative, technical or material support; and supervision.
Dr Greenberg: contributed to the study concept and design and critical revision of the manuscript for important intellectual content.
Financial/nonfinancial disclosures: The authors have reported to *CHEST* that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.
Role of sponsors: The sponsors had no role in the design of the study, the collection and analysis of the data, or in the preparation of the manuscript.

References

1. Rudan I, Tomaskovic L, Boschi-Pinto C, Campbell H; WHO Child Health Epidemiology Reference Group. Global estimate of the incidence of clinical pneumonia among children under five years of age. *Bull World Health Organ*. 2004;82(12):895-903.
2. Sectish T, Prober C. Pneumonia. In: Kliegman R, Behrman R, Jenson H, Stanton B, eds. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia, PA: Saunders; 2007:1795-1800.
3. Rosen CL, Larkin EK, Kirchner HL, et al. Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity. *J Pediatr*. 2003;142(4):383-389.
4. Gozal D, Kheirandish-Gozal L. The multiple challenges of obstructive sleep apnea in children: morbidity and treatment. *Curr Opin Pediatr*. 2008;20(6):654-658.
5. Reuveni H, Simon T, Tal A, Elhayany A, Tarasiuk A. Health care services utilization in children with obstructive sleep apnea syndrome. *Pediatrics*. 2002;110(1 pt 1):68-72.
6. Friedman BC, Hendeles-Amitai A, Kozminsky E, et al. Adenotonsillectomy improves neurocognitive function in children with obstructive sleep apnea syndrome. *Sleep*. 2003;26(8):999-1005.
7. Tarasiuk A, Greenberg-Dotan S, Simon-Tuval T, et al. Elevated morbidity and health care use in children with obstructive sleep apnea syndrome. *Am J Respir Crit Care Med*. 2007;175(1):55-61.
8. Cherian T, Mulholland EK, Carlin JB, et al. Standardized interpretation of paediatric chest radiographs for the diagnosis of pneumonia in epidemiological studies. *Bull World Health Organ*. 2005;83(5):353-359.
9. World Health Organization. Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children: World Health Organization Pneumonia Vaccine Trial Investigators' Group. WHO website. http://www.who.int/vaccine_research/documents/en/pneumonia_children.pdf. Accessed July 2011.
10. The Israel Bureau of Statistics, 2005. Central Bureau of Statistics website. http://www1.cbs.gov.il/shnaton56/st02_10x.pdf. Accessed July 2011.
11. Dayyat E, Kheirandish-Gozal L, Gozal D. Childhood obstructive sleep apnea: one or two distinct disease entities? *Sleep Med Clin*. 2007;2(3):433-444.
12. Shoham Y, Dagan R, Givon-Lavi N, et al. Community-acquired pneumonia in children: quantifying the burden on patients and their families including decrease in quality of life. *Pediatrics*. 2005;115(5):1213-1219.
13. Conley SF, Beecher RB, Delaney AL, Norins NA, Simpson PM, Li SH. Outcomes of tonsillectomy in neurologically impaired children. *Laryngoscope*. 2009;119(11):2231-2241.
14. Spurr KF, Graven MA, Gilbert RW. Prevalence of unspecified sleep apnea and the use of continuous positive airway pressure in hospitalized patients, 2004 National Hospital Discharge Survey. *Sleep Breath*. 2008;12(3):229-234.
15. Colin AA, McEvoy C, Castile RG. Respiratory morbidity and lung function in preterm infants of 32 to 36 weeks' gestational age. *Pediatrics*. 2010;126(1):115-128.
16. Boyce TG, Mellen BG, Mitchel EF Jr, Wright PF, Griffin MR. Rates of hospitalization for respiratory syncytial virus infection among children in medicaid. *J Pediatr*. 2000;137(6):865-870.
17. Hibbs AM, Johnson NL, Rosen CL, et al. Prenatal and neonatal risk factors for sleep disordered breathing in school-aged children born preterm. *J Pediatr*. 2008;153(2):176-182.
18. Mahon BE, Ehrenstein V, Nørgaard M, Pedersen L, Rothman KJ, Sørensen HT. Perinatal risk factors for hospitalization for pneumococcal disease in childhood: a population-based cohort study. *Pediatrics*. 2007;119(4):e804-e812.
19. Greenberg D, Hoffman S, Leibovitz E, Dagan R. Acute otitis media in children: association with day care centers—antibacterial resistance, treatment, and prevention. *Paediatr Drugs*. 2008;10(2):75-83.
20. Couriel J. Assessment of the child with recurrent chest infections. *Br Med Bull*. 2002;61:115-132.
21. Konno A, Hoshino T, Togawa K. Influence of upper airway obstruction by enlarged tonsils and adenoids upon recurrent infection of the lower airway in childhood. *Laryngoscope*. 1980;90(10 pt 1):1709-1716.
22. Beal M, Chesson A, Garcia T, Caldito G, Stucker F, Nathan CO. A pilot study of quantitative aspiration in patients with symptoms of obstructive sleep apnea: comparison to a historic control group. *Laryngoscope*. 2004;114(6):965-968.
23. Goldbart AD, Tal A. Inflammation and sleep disordered breathing in children: a state-of-the-art review. *Pediatr Pulmonol*. 2008;43(12):1151-1160.
24. Goldbart AD, Goldman JL, Li RC, Brittian KR, Tauman R, Gozal D. Differential expression of cysteinyl leukotriene receptors 1 and 2 in tonsils of children with obstructive sleep apnea syndrome or recurrent infection. *Chest*. 2004;126(1):13-18.
25. Boyd JH, Petrof BJ, Hamid Q, Fraser R, Kimoff RJ. Upper airway muscle inflammation and denervation changes in obstructive sleep apnea. *Am J Respir Crit Care Med*. 2004;170(5):541-546.

Sleep-Disordered Breathing Is a Risk Factor for Community-Acquired Alveolar Pneumonia in Early Childhood

Aviv D. Goldbart, Asher Tal, Noga Givon-Lavi, Jacob Bar-Ziv, Ron Dagan and David Greenberg

Chest 2012;141; 1210-1215; Prepublished online November 17, 2011;
DOI 10.1378/chest.11-1998