Predictors for Asthma at Age 7 Years for Low-Income Children Enrolled in the Childhood Asthma Prevention Study

Grace P. Tamesis, MD, MPH[1], Ronina A. Covar, MD[2,3], Matthew Strand, PhD[2,3], Andrew H. Liu, MD[2,3], Stanley J. Szefler, MD[2,3], and Mary D. Klinnert, PhD[2,3]

Objective To identify the predictive factors of early childhood wheezing in children of low socioeconomic status.
Study design The Childhood Asthma Prevention Study enrolled 177 low-income children (9-24 months old) with frequent wheezing. At age 7 years, presence of asthma was assessed through caregiver reports of physician diagnosis of asthma (CRPDA) and corroborated by assessment of bronchial hyperresponsiveness (BHR). Lung function, inflammatory markers, and asthma symptom severity were compared for children with ±CRPDA, ±BHR, and asthma. Baseline predictors for CRPDA, BHR, and asthma at 7 years of age were examined.
Results Maternal symptom report strongly differentiated children with +CRPDA (49%) despite comparable airflow measurements ($P < .0001$), and spirometric lung function measurements were different for +BHR (65%) versus −BHR ($P < .005$). Univariate analyses revealed different baseline predictors of +CRPDA and +BHR for children at age 7 years. Higher levels of maternal psychological resources were associated with +CRPDA, but not +BHR. Only 39% of children with a history of frequent wheezing met the conservative definition of asthma at age 7 years, with the following significant predictors found: low birth weight, baseline symptom severity, and maternal psychological resources.
Conclusions This low-income, multi-ethnic group of wheezing infants represents a unique population of children with distinct characteristics and risks for persistent asthma. Determination of asthma status at 7 years of age required objective measurement of BHR in addition to CRPDA. The association of maternal psychological resources with +CRPDA may represent a previously unrecognized factor in the determination of asthma status among low-income groups. *(J Pediatr 2013;162:536-42)*.

Elevated asthma prevalence and morbidity among low-income minority children remain a significant public health problem in the US.[1] Low-income children with persistent wheezing have been found to have recurrent asthma symptoms since early infancy. Because most prospective studies of early asthma onset have enrolled families from middle to higher socioeconomic status (SES), risk factors for early childhood wheezing and persistent asthma in low-income children remain unclear, and may be quite different.

Multiple prospective birth cohort studies have shown that low birth weight is associated with higher risk for persistent wheezing in early childhood[2]; however, findings are inconsistent.[3] Other variables associated with low birth weight, such as prematurity, maternal smoking, and low SES have been implicated as risk factors for early onset of asthma symptoms, confounding the complex interrelationship between birth weight and infantile wheezing.[3,4] Social risk variables associated with low SES have been shown to be as important as biomedical risk factors in affecting child health and health-seeking behavior.[5]

The Childhood Asthma Prevention Study (CAPS) was a prospective, controlled study of wheezing infants from low-income families designed to assess the efficacy of a multifaceted nurse home visitor/environmental intervention in reducing asthma onset, morbidity, and severity at 4-year and 7-year follow-ups.[6,7] This report focuses on biomedical and psychosocial predictors from the first 2 years of life in relation to caregiver reports of physician diagnosis of asthma (CRPDA), quantified bronchial hyperresponsiveness (BHR), and asthma status at age 7 years. Results of the intervention will be reported separately.

Methods

Eligible infant participants were between the age of 9 and 24 months, with medical record (MR) documentation of ≥3 wheezing episodes observed, and were from low-income families (Medicaid eligible [ie, family income < 1.5 times the annualized federal

BHR	Bronchial hyperresponsiveness
CAPS	Childhood Asthma Prevention Study
CRPDA	Caregiver reports of physician diagnosis of asthma
FeNO	Fractional exhaled nitric oxide
FEV_1	Forced expiratory volume in 1 second
IgE	Immunoglobulin E
MR	Medical record
SES	Socioeconomic status

From the [1]Children's Hospital of the King's Daughters, Norfolk, VA; [2]National Jewish Health, Denver, CO; and [3]University of Colorado Denver, Aurora, CO

Supported by National Institute of Allergy and Infectious Diseases/(R18-AI-41137) and National Center for Advancing Translational Sciences (UL1 TR000154). The authors declare no conflicts of interest.

 http://dx.doi.org/10.1016/j.jpeds.2012.08.023

poverty level; in 1997 the federal poverty level was $13 330 for a 3-person family]). Infants were excluded if they were <34 weeks gestation, had postnatal oxygen requirement >48 hours, or complicating medical conditions. Families were recruited from pediatric departments of local hospitals and clinics between January 1998 and March 2000. Consent forms approved by the institutional review boards of participating institutions were signed by caregivers during enrollment, and by both caregivers and children at the follow-up assessment. Following baseline evaluations, families were assigned randomly to the year-long nurse home visitor intervention or control group, and 1- and 4-year follow-up assessments have been reported.[6,7] Data for this report were derived from a final assessment to determine the children's asthma status at age 7 years.

Baseline Evaluation at 9-24 Months

Interviews were conducted with the infants' primary caregivers in their homes to obtain baseline demographic, medical, environmental, and psychosocial information. We obtained infant urine specimens for cotinine analysis and household dust samples to determine allergen content (cockroach, cat and dog dander). Consistent with the symptom report dimension of the National Heart, Lung, and Blood Institute asthma severity classification available at the time of study implementation,[8] caregivers reported infantile wheezing frequency/severity for the past 6 months using a modified check-list,[9-11] with 5-point scales for daytime, nighttime, and following physical activity, and a yes/no rating for occurrence of severe breathing difficulty. Caregiver psychosocial measures that assessed mental health,[12] cognitive functioning,[13,14] and sense of mastery,[15] were *z*-score standardized and combined to indicate caregivers' personal psychological resources.[16] In clinic following enrollment, infants underwent venipuncture for total serum immunoglobulin E (IgE) and prick skin testing to common indoor inhalant allergens (*D. pteronyssinus*, *D. farinae*, American and German cockroach mix, cat dander, dog dander, indoor molds) and food allergens (egg, milk, soybean). MRs were obtained and abstracted for child's birth weight, history of respiratory syncytial virus bronchiolitis, physician documented wheezing episodes, emergency department visits, and hospitalizations.

Evaluation at 7 Years

Of the 177 children randomized to nurse home visitor/environmental intervention or control groups at baseline, 140 (79%) families participated in follow-up at age 7 years. 128 (72%) children were evaluated in clinic and 125 (71%) children had complete spirometric lung function measurement data for this report (**Figure**; available at www.jpeds.com). Seven-year evaluations took place from November 2002 through June 2006. Age at follow-up was an average of 7.15 years (SD = 0.28, range = 6.7-8.3 years). During the clinic visit, caregivers were interviewed regarding child's asthma status, symptoms, medications, and health care utilization and were asked "Has a doctor told you in the past year that your child has asthma?" Interview-embedded questions included the Pediatric Asthma Symptom Scale regarding symptoms that occurred in past 4 weeks[17] and the Asthma Functional Severity Scale regarding frequency and severity of symptoms over the past year.[9]

Prior to pulmonary function testing, fractional exhaled nitric oxide (FeNO) was measured using NIOX (Aerocrine, Inc, Stockholm, Sweden). Pulmonary function testing included: (1) baseline spirometry; (2) 10-minute treadmill exercise challenge with spirometry at 1, 5, and 10 minutes post-exercise; (3) followed by bronchodilator administration; and (4) post bronchodilator spirometry measurement (Jaeger MasterScreen Spirometry System, Jaeger Co, Hoechberg, Germany). Children were instructed to refrain from taking controller medication and bronchodilator medication for 24 hours and 6 hours prior to testing, respectively. Children were considered to have +BHR if there was a decrease in forced expiratory volume in 1 second (FEV_1) of 10% from baseline to post-exercise, or an increase in FEV_1 of 12% from baseline to post-bronchodilator measurement, based on National Heart, Lung, and Blood Institute/National Asthma Education and Prevention Program guidelines.[18] BHR data were analyzed for 107 children (**Figure**). If the pre- post-bronchodilator measurement failed to meet criteria for BHR and the exercise challenge was not conducted, data was excluded from BHR analyses (n = 10; **Figure**). Children did not receive the exercise challenge if: (1) baseline FEV_1 values were below 80% predicted; (2) challenge was contraindicated due to asthma symptoms; or (3) caregivers declined the challenge. Because exposure to corticosteroid medication reduces airway reactivity,[19] for analyses where BHR was the outcome variable, children with +CRPDA/−BHR but documented prescription of controller medication were excluded (n = 8; **Figure**). Children underwent prick skin testing for inhalant allergens using the Colorado Panel (24 antigens, 3 mm wheal bigger than the negative saline control read as positive). The occurrence of American Thoracic Society-B[20] symptoms within the past year was queried: (1) wheeze with colds; (2) wheeze without colds; (3) shortness of breath with wheeze; (4) cough, wheeze, or shortness of breath after exercise; or (5) persistent cough without colds. MRs were obtained and abstracted for documentation of asthma medication prescriptions.

Outcome Measures

The primary outcome measures for this report are CRPDA, evidence of BHR, and asthma at age 7 years. Asthma was defined as +CRPDA corroborated by +BHR. In addition, children with +CRPDA but negative BHR challenges (−BHR) or no BHR data, but who had MR documentation of controller medication were included in the final asthma group (**Figure**).

Statistical Analyses

Data with right-skewed distributions were log transformed for analyses, then back-transformed for presentation, yielding geometric means. Unadjusted comparisons of baseline predictor variables and concurrent measures of asthma