Steroid Requirements and Immune Associations With Vitamin D Are Stronger in Children Than Adults With Asthma


PURPOSE OF THE STUDY. To compare the age-specific relationship between serum vitamin D (25-OH-D) levels and allergic sensitization, vitamin D receptor (VDR) activation pathways, peripheral blood mononuclear cell (PBMC) steroid responsiveness, and inhaled corticosteroid (ICS) requirements in children and adults with asthma.

STUDY POPULATION. One hundred three patients with asthma (53 children, 50 adults) and 102 healthy control subjects (51 children, 51 adults) were matched for age, gender, race, and BMI.

METHODS. Serum 25-OH-D levels were checked during the winter in all subjects. Inducible markers of VDR activation (cytochrome P450 family 24 [cyp24a] mRNA and plasma cathelicidin [LL-37]) were measured. Tumor necrosis factor (TNF)-α and interleukin (IL)-13 were measured after in vitro stimulation of PBMC with dexamethasone.

RESULTS. Although there was great overlap in 25-OH-D levels between groups, asthmatics had a higher rate of vitamin D deficiency (<20 ng/mL) than healthy control subjects (56.8% vs 47.6%). The level of vitamin D–regulated targets (cyp24a and LL-37) correlated with 25-OH-D level in children, but only cyp24a had a similar correlation in adults. There was a significant inverse correlation between 25-OH-D and serum immunoglobulin (Ig) E in children but not adults. Dust mite–specific IgE was associated with lower 25-OH-D levels, but there was no such association in adults or to specific IgE levels for other allergens. In children, but not adults, 25-OH-D levels had a significant inverse correlation with ICS requirement in the patients with asthma. A similar inverse correlation between 25-OH-D level and cyp24a and LL-37 was seen only in children. Cyp24a expression by PBMC correlated with the degree of TNF-α and IL-13 suppression by dexamethasone only in children. All of these associations were stronger in children aged 6 to 12 years than those aged 13 to 17 years. In the older children, the associations did not reach statistical significance.

CONCLUSIONS. There are significant associations between serum vitamin D level, inhaled corticosteroid requirement for asthma, and in vitro responsiveness to corticosteroids in children (particularly 6– to 12-year-olds) but not in adults.

REVIEWER COMMENTS. There has been a surge of interest in vitamin D and its effects on numerous biological functions. Many associations are based on epidemiologic studies, including the role of vitamin D in atopic diseases. It is not clear if the rate of vitamin D deficiency and insufficiency has increased or if there is just greater awareness of the problem. This study demonstrates the association of 25-OH-D levels with biologic function, particularly in school-age children. Because the study was done in the winter, it is not clear if the same associations would be found in the summer when endogenous 25-OH-D levels are likely to be higher. It is also not clear why the associations were strongest in the youngest subjects. Finally, it is not clear if vitamin D supplementation would change the results or improve asthma outcomes in the study population. Nonetheless, this study suggests the opportunity for early intervention in young children with asthma. At the very least, it is another reason to recommend that children “turn off the screens” and go outside to play.


Sleep-Disordered Breathing Is Associated With Asthma Severity in Children


PURPOSE OF THE STUDY. To examine the association between obesity, sleep-disordered breathing, and asthma severity in children.

STUDY POPULATION. The study included 108 asthmatic children, aged 4 to 18 years, 45.4% African American and 67.6% male subjects, enrolled in an asthma specialty clinic at Rainbow Babies and Children’s Hospital, Cleveland, Ohio.
METHODS. Sleep-disordered breathing was measured by a written questionnaire to assess snoring, as well as by 2 nights of home pulse oximetry. The duration of the study was 1 year, and participants were prospectively followed every 6 months. Data collected at these visits included current asthma and allergy medications. Asthma Control Test score to determine asthma symptom burden, asthma-related missed school days, number of prednisone courses, number of unscheduled physician and emergency department visits, and number of hospitalizations since the previous visit.

RESULTS. Of the 108 children, 29 were diagnosed with severe asthma, and the remaining 79 had mild/moderate asthma. The severe asthmatics were more likely to be male, African American, and of lower socioeconomic status. Sleep-disordered breathing was strongly associated with asthma severity (P < .01). Obesity, as measured by BMI z scores, did not have a significant association with asthma severity (P = .31). However, extreme obesity was more prevalent in severe asthmatics than nonsevere asthmatics (20.7% vs 10.1%, P = .20). Also, increases in BMI strengthened the association between sleep-disordered breathing and severe asthma.

CONCLUSIONS. Sleep-disordered breathing correlates with asthma severity. Obesity and asthma severity were not significantly associated.

REVIEWER COMMENTS. Previous studies have demonstrated parallels among obesity, sleep-disordered breathing, and asthma (Sulit LG, Storfer-Iseer A, Rosen CL, et al. Am J Respir Crit Care Med. 2005;171[6]:659–664). However, the association of these disorders to asthma severity, particularly in the pediatric population, has not been thoroughly investigated. This study discovered an important association between severe asthma and sleep-disordered breathing. Future studies are required to examine these interactions in a broader population and to determine whether management of sleep-disordered breathing and/or obesity has the potential to ameliorate asthma prevalence and severity in children.

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Evidence for a Causal Relationship Between Allergic Sensitization and Rhinovirus Wheezing in Early Life

PURPOSE OF THE STUDY. To determine if there is a temporal relationship in the development of allergic sensitization and rhinovirus-induced wheezing.

STUDY POPULATION. There were 289 children studied who were part of a group of children at high risk for asthma and allergies who were enrolled at birth and followed prospectively in the Childhood Origins of Asthma (COAST) study.

METHODS. Children were followed for the first 6 years of life. Specific viral pathogens were identified in 90% of wheezing episodes during the first 3 years of life (nearly all outpatient illnesses). Peripheral blood was drawn annually to assess for aeroallergen sensitization.

RESULTS. Sensitized children were at significantly greater risk for viral wheeze than nonsensitized children (hazard ratio [HR] 1.9; 95% confidence interval [CI], 1.2–3.1). Looking at specific viral infections, allergic sensitization was associated with increased risk of wheezing from human rhinovirus (HR 2.3; 95% CI, 1.4–4.0) but not respiratory syncytial virus (HR 1.6; 95% CI, 0.87–2.9). Conversely, viral wheezing was not associated with increased risk of allergic sensitization (HR 0.76; 95% CI, 0.5–1.1).

CONCLUSIONS. Allergic sensitization increases the risk for all viral wheezing, especially for human rhinovirus wheezing but not respiratory syncytial virus wheezing.

REVIEWER COMMENTS. Allergic sensitization and viral wheezing early in life have both been associated with increased risk for child-onset asthma. This study is novel in that it is the first prospective cohort to identify allergic sensitization preceding viral wheezing. However, there are some previous data from another study finding severe respiratory syncytial virus bronchiolitis to be a risk factor for subsequent wheezing. If allergic sensitization is a primary event in the pathway to childhood asthma, it then would become a primary target for prevention.


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Preschool Asthma After Bronchiolitis in Infancy

PURPOSE. To evaluate the outcome of asthma in preschool-age children who were hospitalized at <6 months of age for bronchiolitis. Other predictors of childhood asthma were collected about parental risk factors and atopic dermatitis in children.

STUDY POPULATION. Full-term infants (n = 166) <6 months of age were enrolled upon hospitalization for bronchiolitis and were followed up at 5 to 6 years of age.

METHODS. From participant nasopharyngeal aspirates, 7 viruses including respiratory syncytial virus (RSV) and rhinovirus were assessed for the bronchiolitis etiology. At follow-up, questionnaires identified doctor-diagnosed
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