Eczema Is Associated with Childhood Speech Disorder: A Retrospective Analysis from the National Survey of Children's Health and the National Health Interview Survey

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Objective To determine if eczema is associated with an increased risk of a speech disorder.

Study design We analyzed data on 354 416 children and adolescents from 19 US population-based cohorts: the 2003-2004 and 2007-2008 National Survey of Children's Health and 1997-2013 National Health Interview Survey, each prospective, questionnaire-based cohorts.

Results In multivariate survey logistic regression models adjusting for sociodemographics and comorbid allergic disease, eczema was significantly associated with higher odds of speech disorder in 12 of 19 cohorts ($P < .05$). The pooled prevalence of speech disorder in children with eczema was 4.7% (95% CI 4.5%-5.0%) compared with 2.2% (95% CI 2.2%-2.3%) in children without eczema. In pooled multivariate analysis, eczema was associated with increased odds of speech disorder (aOR [95% CI] 1.81 [1.57-2.05], $P < .001$). In a single study assessing eczema severity, mild (1.36 [1.02-1.81], $P = .03$) and severe eczema (3.56 [1.70-7.48], $P < .001$) were associated with higher odds of speech disorder. History of eczema was associated with moderate (2.35 [1.34-4.10], $P = .003$) and severe (2.28 [1.11-4.72], $P = .03$) speech disorder. Finally, significant interactions were found, such that children with both eczema and attention deficit disorder with or without hyperactivity or sleep disturbance had vastly increased risk of speech disorders than either by itself.

Conclusions Pediatric eczema may be associated with increased risk of speech disorder. Further, prospective studies are needed to characterize the exact nature of this association. *(J Pediatr 2016;168:185-92)*.

Eczema is a chronic inflammatory skin disorder with highest prevalence in childhood,[1] which causes significant suffering because of itch, sleep disturbance,[2] and decreased quality of life.[3] Eczema is accompanied by profound systemic inflammation with activation of T-helper 2, 17, and 22 pathways.[4-7] Systemic inflammation and/or the strong burden of atopic dermatitis may contribute toward a variety of health conditions. Indeed, we and other investigators have previously found childhood eczema to be associated with multiple comorbidities, including obesity,[8-10] hypertension,[10] low bone mineral density,[11] increased risk of warts and extra-cutaneous infections,[12] asthma,[13] allergic rhinitis,[13] attention deficit disorder (ADD)/attention deficit hyperactivity disorder (ADHD),[14,15] anxiety, depression, and conduct disorder.[16,17]

Many studies have reported on the negative neurocognitive outcomes of various chronic diseases of childhood, particularly language ability. For example, chronic otitis media,[18,19] congenital heart disease,[20] and chronic kidney disease[21,22] have all have been associated with poor language and verbal performance in children. However, few studies have examined the neurocognitive ability of pediatric patients with eczema. Recently, we found that pediatric patients with eczema reported higher levels of contact with therapists, including speech therapists[23] suggesting that eczema affects in some way the functional speech capability of children. Children with eczema have multiple risk factors for speech and language disorders, including sleep disturbance[24,25] and ADHD.[26] We hypothesized that eczema is independently associated with increased risk of speech problems in children, particularly in severe eczema, sleep disturbance, and comorbid ADHD. The present study analyzed 19 US population-based cohorts to determine whether there is an association between eczema and speech disorders.

Methods

Data were assessed from 19 different cohorts including the National Survey of Children's Health (NSCH) 2003-2004 and 2007-2008 and the National Health Interview Survey (NHIS) from the years 1997-2013. All surveys are collected by the National Center for Health Statistics, and the specific characteristics of

ADD	Attention deficit disorder
ADHD	Attention deficit hyperactivity disorder
NHIS	National Health Interview Survey
NSCH	National Survey of Children's Health

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each are reviewed (**Table I**; available at www.jpeds.com). In sampled households with multiple children, 1 child was randomly chosen to be the subject of the interview. Common to all samples is a multistage area probability sampling design that factors in age, sex, race, ethnicity, household size, and educational attainment of the most educated household member, using data from the US Census Bureau. Sample weights were created by the National Center for Health Statistics allowing for frequency and prevalence estimates that are representative of each state's population of noninstitutionalized children. In this study, frequency and prevalence estimates presented in analyses of single samples reflect this complex weighting process. The similar sampling methodologies across the sample years allowed for weighted analysis of pooled results for NHIS (n = 17) and NSCH (n = 2), respectively. However, because of the differences in sampling methodology between NHIS and NSCH, sample weights for all 19 samples could not be combined in pooled analyses. Thus, in analyses of pooled weighted data of all 19 samples, meta-analysis of multivariate regression analysis effects were performed using a robust variance estimation method.[27] This study was approved by the institutional review board at Northwestern University.

Associations with Eczema and Speech Disorder

Associations of both pediatric eczema and speech disorder were examined in children aged 3-17 years from NHIS 1997-2013 and NSCH 2003 and children aged 2-17 years from NSCH 2007 including sex, age, race, household income, highest level of household/parental education, birthplace in the US, and insurance coverage.

Associations between caregiver-reported history of eczema (19 samples) and eczema severity (1 sample) and speech disorder were examined both for each individual cohort and in pooled analyses. Interactions between eczema and several comorbidities including ADD/ADHD, sleep disturbance, fatigue, and depression were examined for their effect on speech disorders. Contrast statements were used to determine the differential effect of each on the risk of speech disorder.

Statistical Analyses

All data analyses and statistical processes were performed using the SURVEY procedures in SAS v 9.4 (SAS Institute, Cary, North Carolina). Weighted population-based frequencies and prevalences were assessed for each study (PROC SURVEYFREQ). Multivariate survey logistic regression models were constructed for individual samples and pooled years of NSCH or NHIS accounting for the surveys' complex weighting. The dependent variable in each model was the history of speech disorder in the past year. The independent variables were either 1-year history of eczema (ie, active eczema in the past year [yes/no] or eczema severity [no eczema/mild/moderate/severe]). Age (2-6/7-11/12-17 years), sex (male/female), race/ethnicity (non-Hispanic Caucasian/non-Hispanic African American/Hispanic/multiracial or other), household income (0%-99%/100%-199%/200%-399%/400%+ federal poverty level), level of education of the highest member of the family/highest level of parental education (less than high school/high school or graduate equivalence degree/more than high school), insurance status (yes/no), birthplace (US/outside US), lifetime history of asthma (yes/no), and 1-year history of hay fever (yes/no) and digestive allergy (yes/no) were included as covariates. In addition, there was concern that diagnosis of comorbidity was related to overall increased healthcare utilization. Thus, a second multivariate model was created to examine the effect of eczema on speech disorder when controlling for number of outpatient visits per year. The aOR and 95% CI were determined. Two-way interactions between covariates were assessed and noted if significant ($P < .01$) and modified the effect size by ≥20%.

Our a priori hypothesis was that psychological and sleep dysfunction occurring in eczema is particularly associated with speech disorder. History of ADD/ADHD was assessed in all samples, whereas depression and number of nights of adequate sleep per week were assessed in NSCH 2007-2008. Fatigue and insomnia were assessed in NHIS 2007 and 2012, and daytime sleepiness was assessed in NHIS 2012 only. These variables and interaction terms with history of eczema were included in multivariate models. Estimates of effect size for significant interactions between the 2 variables were conducted for each level of the covariates using contrast statements. The various questions used in this study to assess eczema, speech disorder, depression, ADD/ADHD, and sleep disturbance are presented (**Table II**; available at www.jpeds.com).

Complete data analysis was performed in that subjects with missing data were excluded. The frequency of missing values from each study is presented (**Table III**; available at www.jpeds.com). Analysis of missing value patterns for speech disorder found that missing values were not more likely to occur in various age groups, racial and ethnic groups, family income levels, or education levels.

Results

Data were analyzed on 354 416 US children and adolescents age 2-17 years, including those of all racial/ethnic groups, sex, levels of household income, and birthplaces. The pooled prevalence of eczema from all 19 samples was 10.1% (95% CI 10.0%-10.2%) (**Table IV**; available at www.jpeds.com). In pooled, bivariate logistic regression models, eczema was positively associated with female sex, and African American and multiracial race. In contrast, eczema was inversely associated with older age (7-11 years, 12-17 years), Hispanic ethnicity, less than high school level of household education, foreign birthplace, and lack of insurance coverage.

The US pooled prevalence of speech disorder was found to be 2.4% (95% CI 2.4%-2.5%; **Table IV**). In bivariate logistic regression models, speech disorder was positively associated with African American race, Hispanic ethnicity, lower