Original Article

Self-Reported Stressful Life Events During Adolescence and Subsequent Asthma: A Longitudinal Study

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What is already known about this topic? Adolescents exposed to stressful life events have been shown to be at increased risk for poor health as well as concurrent asthma.

What does this article add to our knowledge? This study provides prospective evidence that objectively defined life events in adolescence were associated with new active asthma diagnosed between ages 18 and 29.

How does this study impact current management guidelines? Major stressful events in adolescence are associated with future asthma in a general population sample and may represent an additional risk factor associated with susceptibility for the development of adult-onset asthma.

BACKGROUND: Although exposure to stressful life events in adolescence has been associated with poor health as measured by number of physicians' visits and symptom scores, little is known regarding stress in adolescence and either concurrent or subsequent asthma.
OBJECTIVE: The objective of this study was to explore whether life events in adolescence are associated with either concurrent or new active asthma.
METHODS: The Tucson Children's Respiratory Study, a prospective population-based birth cohort, surveyed participants at 10 ages between 6 and 29 years regarding respiratory health. Asthma was defined as a physician-diagnosis of asthma with symptoms during the previous year. At age 16, participants (n = 318) were queried regarding stressful life events using the 67-item Life Events Questionnaire for Adolescents (LEQA). LEQA scores were examined in relation to both concurrent and new active asthma. Estimates were obtained with logistic regression and mixed models.
RESULTS: There was no relation between asthma prevalence at age 16 and LEQA scores in the overall sample, although males with high LEQA scores had higher prevalence of asthma compared with males with low scores (relative risk [RR]: 3.03; 95% confidence interval [CI]: 1.37, 6.69; $P = .006$). Among adolescents with no asthma through age 16, risk of new asthma was greater for those with high LEQA scores (adjRR: 4.07; 95% CI: 1.33, 12.43; $P = .014$), after adjustment for potential confounders including smoking. Emotional support from family and friends slightly diminished the relation of stress to new asthma.
CONCLUSIONS: Stressful life events during adolescence are associated with subsequent new asthma. Additional biological and psychological measures of stress would complement these findings. **Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;5:427-34)**

Key words: *Adolescence; Asthma; Stress*

Factors that determine new onset of asthma during adult life have not been extensively studied. Both environmental factors such as occupational exposures,[1,2] smoking, and particulate exposure[3] and host factors such as depression[4] have been associated with risk of incident asthma in adults. There is also increasing evidence that childhood factors, including infections, obesity, and allergic phenotypes,[5] may impact risk for adult asthma, suggesting that new onset asthma may have its roots well before symptoms develop.

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Abbreviations used
BMI- Body mass index
CI- Confidence interval
GEE- Generalized estimating equations
HPA- Hypothalamic-pituitary-adrenal
LEQA- Life Events Questionnaire for Adolescents
PCA- Principal component analyses
RR- Relative risk
SES- Socioeconomic status
TCRS- Tucson Children's Respiratory Study

The role of stress as a potential risk factor for adult-onset asthma has been minimally studied. Longer term chronic stressors such as job insecurity[6] have been associated with a higher risk of self-reported asthma incidence among those with higher compared with lower levels of stressors.[7,8] In particular, the Copenhagen City Heart Study showed perceived stress to be strongly associated with asthma incidence and hospitalizations in a cohort of adults free of atopic disorders at baseline.[7] In contrast, other studies found no effect of daily stress on incidence of self-reported asthma.[9] However, prospective studies on the association between stress before adulthood and adult-onset asthma do not, to our knowledge, exist.

In childhood, stress has been identified as a risk affecting onset, progression, and severity of asthma. Adolescents reporting 2 to 3 stressful events are 1.5 times as likely to have asthma as those with 0 to 1 event.[10] Among asthmatic children, high levels of chronic stress increase the risk for an asthma attack within 2 weeks of a time-limited negative life event.[11] Extreme stressors, such as community violence, are also associated with increased asthma risk.[12] This is of particular interest given high levels of stress reported by teenagers[13] and increasing trends in adolescent asthma prevalence worldwide.[14] However, little is known regarding the effect of stress in adolescence on the development of asthma.

This study examines the role of stressful life events in adolescence (age 16) on concurrent asthma and newly diagnosed asthma from ages 18 to 29 within the population-based Tucson Children's Respiratory Study (TCRS) cohort. We hypothesize that having additional stressful life events is associated with new active asthma diagnoses. We further examine the differential effects of these stressors on adolescent girls and boys as well as the potential mediating effects of emotional support. Some of the results of these studies have been previously published in the form of an abstract.[15]

METHODS

Study population

Participants were enrolled as newborns in the TCRS, a prospective, longitudinal study of the risk factors for acute and chronic respiratory illness in childhood and adult life, described previously.[16,17] A total of 1246 healthy newborns and their families were enrolled at birth between 1980 and 1984. All participants were English speaking. Shortly after the child's birth, parents completed a questionnaire reporting a history of physician-diagnosed asthma, ethnicity, and other demographics. They subsequently completed up to 7 questionnaires on their child's respiratory health approximately every 2 years until the child was 16 years old. Active asthma was defined as physician diagnosis of asthma plus active symptoms in the previous year at any survey.

Asthma diagnosed before age 18 was determined from questionnaires completed at ages 6, 8, 11, 13, and 16. If active physician-diagnosed asthma was reported on any questionnaire, the participant was considered to have asthma. If the participant had 3 or more completed questionnaires without a report of active asthma, then they were considered nonasthmatic. Participants with less than 3 completed questionnaires were excluded (n = 8, Figure 1). Starting at age 18, participants completed questionnaires themselves, answering questions on asthma diagnoses and symptoms. Newly diagnosed asthma was defined as physician-diagnosed active asthma with symptoms reported on questionnaires in adult life (ages 18-29) among subjects who did not report asthma by age 16 ("new active asthma"). Parental smoking, education level, ethnicity, and self-reported smoking were determined by questionnaire; body mass index (BMI) was determined from nurse-measured height and weight.

Informed consent was obtained from the parents for their children, or from the enrollees themselves as appropriate and the Institutional Review Board of the University of Arizona approved and monitored the study.

Exposures—stressful life events and emotional support

At age 16, participants who had an in-depth evaluation after July 1998 (n = 530) were eligible to complete the Life Events Questionnaire for Adolescents (LEQA)[18] and the Emotional Support Scale.[19] The LEQA consists of 67 items regarding potentially stressful events occurring in the past year. The number of events reported was summed to create a total life events score, and 10 subscale scores were created pertaining to particular domains (family, friends, physical, accomplishments, failures, medical, legal, safety, finance, and conflict) based on independent scoring of the 67 items by the study authors.

One-year test-retest correlations for the original LEQA version among adolescents have been moderately high and statistically significant. For negative, ambiguous, and total life events categories, correlations ranged from 0.53 to 0.64.[20] Permission was obtained from the publisher (Wiley) for the use of the instrument.

The Emotional Support Scale asks whether the respondent feels comfortable speaking with parents, siblings, and friends on a range of issues. The scale is designed for ages 11-16 and questions show high internal consistency. Answers from questions were scored from 1 (no support) to 10 (high support) and then summed to create 3 indices measuring support from parents, siblings, and friends. These indices were also added to create a total support score (range: 0-150).

Statistical analysis

For demographic and exposure variables, differences in medians or proportions between adolescents with and without both concurrent (age 16) and new (ages 18-29) asthma were evaluated using χ^2 or Student's *t*-tests, as appropriate. Associations of stressful life events with demographic and exposure variables and the asthma outcomes were modeled with generalized estimating equations (GEE), using an independent correlation structure for concurrent asthma models and an exchangeable correlation structure for longitudinal models, as well as a log link function and a binomial distributional family with robust standard errors (STATA v.13). GEE allows for subjects to have missing data at any time point, accommodates correlated data by including an appropriate within-subject covariance structure, and can adjust for covariates. Exchangeable correlation structures were used assuming intrasubject