Optimum Predictors of Childhood Asthma: Persistent Wheeze or the Asthma Predictive Index?


PURPOSE OF THE STUDY. To determine whether the University of Cincinnati’s Asthma Predictive Index (ucAPI) and/or persistent wheezing by the age of 3 years are able to predict asthma at the age of 7 years, as confirmed by objective measures.

STUDY POPULATION. Five hundred eighty-nine children were recruited from the Cincinnati Childhood Allergy and Air Pollution Study, a prospective birth cohort of children with at least 1 atopic parent: 54.8% were boys, 21.2% were African American, and 16.7% were from a household with yearly income <$20,000. Additionally, 53.1% were breastfed until age 4 months, 52.1% attended day care, and 40.8% had at least 1 parent with asthma.

METHODS. Peripheral blood leukocyte DNA was extracted and bisulphite converted. The extent of DNA methylation was examined by Illumina HumanMethylation27 Arrays. Fitted models were used to identify predictors of IgE concentration with a false discovery rate (FDR) <10^{-4}. Methylation levels of isolated eosinophils were compared among 8 asthmatics with high serum IgE levels, 8 asthmatics with low serum IgE levels, and 8 controls.

RESULTS. The authors identified 36 predictive loci with FDR <10^{-4}. Several of the loci identified are associated with genes that encode proteins important for eosinophil function, including an eosinophil eotaxin receptor, eosinophil granule major basic protein, and an eosinophil transcription factor. In purified eosinophils, the lowest level of methylation was observed in asthmatics with high IgE, whereas the methylation in asthmatics with low IgE was intermediate to controls.

CONCLUSIONS. Methylation status of eosinophils is related to IgE levels. This study also identifies potentially novel biomarkers and therapeutic targets underlying IgE-mediated diseases.

STUDY POPULATION. Studies were performed on samples from 355 subjects recruited to the Medical Research Council Asthma (MRCA) panel. Subjects were between the ages of 2 and 61 (mean age, 28 years) and 175 had doctor-diagnosed asthma. Epigenome-wide association results were validated in 2 replication cohorts of 149 subjects and 160 subjects.

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REVIEVER COMMENTS. This study is the first to perform an epigenome-wide association study on subjects with asthma. Measurement of methylation at loci characterized to eosinophils may help identify patients responsive to therapies directed at eosinophils and or their gene products. Further studies on the relationship between methylation status and gene expression at each identified predictive locus are needed.

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and hay fever, are increasing in prevalence. Previous genome-wide association studies have identified single nucleotide polymorphisms (SNPs) in several loci including STAT6, FCER1A, and IL-4 that correlate with high levels of IgE. However, these genome-wide studies do not include environmental effects and account for only a limited amount of the variation between IgE concentrations. This study uses an epigenome-wide association study to identify therapeutic targets and biomarkers for patients with IgE-mediated diseases.
Development and Internal Validation of a Pediatric Acute Asthma Prediction Rule for Hospitalization


Purpose of the Study. To develop and internally validate an effective clinical prediction rule regarding need for hospitalization in pediatric patients presenting to the emergency department with acute asthma exacerbations.

Study Population. Children (n = 928) aged 5 to 17 years (mean age 8.8 years, 61% boys, 59% African American) presenting to a tertiary children’s hospital emergency department with an acute asthma exacerbation between April 2008 and February 2013 were included using a prospective convenience design.

Methods. Fifteen predictor variables including demographics, asthma symptom history and control, pulmonary examination findings, and measures of lung function and inflammation were evaluated for the development of an asthma prediction rule. Penalized maximum likelihood estimation logistic regression models were used to evaluate the association between the need for hospitalization and hospitalization decision by the clinical team treating the patient. A bootstrapping algorithm was implemented to assess for internal validity.

Results. Of the 15 predictor variables evaluated, oxygen saturation on room air (odds ratio 2.4, 95% confidence interval 1.9–3.1) and inspiratory-to-expiratory ratio (odds ratio 1.9, 95% confidence interval 1.1–3.1) correlated most with need for hospitalization. Oxygen saturation on room air, intercostal retractions, inspiratory-to-expiratory ratio, and wheezing were variables most associated with the hospitalization decision of the clinical team.

Conclusions. The asthma prediction rule is an internally validated model for predicting need for hospitalization in children with acute asthma exacerbations presenting to the emergency department. Further studies are needed to assess the external validity and impact on patient care and clinical outcomes of this tool.

Exhaled Biomarkers and Gene Expression at Preschool Age Improve Asthma Prediction at 6 Years of Age


Purpose of the Study. The objective of this study was to assess whether exhaled biomarkers, expression of inflammation genes, and early lung function measurements can improve early asthma prediction in the wheezing preschool child when used in conjunction with the Asthma Predictive Index (API).

Study Population. The study included 202 children, aged 2 to 4 years, with history of recurrent wheeze who were prospectively followed up yearly until 6 years of age. At age 6, a diagnosis of asthma or transient wheeze was determined on the basis of symptoms, use of asthma medication, and lung function features.
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