Published in final edited form as:

J Allergy Clin Immunol Pract. 2015 ; 3(4): 602–603.e1. doi:10.1016/j.jaip.2015.01.014.

Hospital admission associates with higher total IgE level in pediatric patients with asthma

Michael G. Sherenian, MD¹, Yu Wang, MS, MAS², and Patricia C. Fulkerson, MD, PhD¹

¹Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH 45229

²Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229

Keywords

IgE; asthma; clinical setting; season

TO THE EDITOR

Most of the over 10 million children in the United States with asthma suffer from at least one disease exacerbation per year. [1,2] Yet, no confirmed predictors or biomarkers exist for asthma exacerbations. [3,4] Studies implicate immunoglobulin E (IgE) as a significant mediator of exacerbations in pediatric patients since patients with asthma, compared to those without, have elevated serum IgE levels. [5,6] Furthermore, serum IgE levels directly correlate with asthma disease severity in younger patients. [5] Despite these findings, it is unknown whether serum IgE levels increase prior to or during asthma exacerbations. [5,7] Our objective was to determine whether hospitalization for pediatric asthma exacerbations was associated with elevated total serum IgE levels.

This retrospective study extracted de-identified clinical data from the Informatics for Integrating Biology and the Bedside (I2B2) Database at Cincinnati Children's Hospital Medical Center (CCHMC). Pediatric patients with asthma (ages 3 – 17 years) who were admitted to the hospital for asthma exacerbation (Inpatient cohort) were compared with patients evaluated in an outpatient setting (Outpatient cohort). The Inpatient cohort included patients admitted to CCHMC for an asthma exacerbation between November 2009 and May 2011; the Outpatient cohort included patients with asthma that presented to a CCHMC outpatient clinic between June 2009 and May 2011. The Inpatient cohort inclusion criteria were a current diagnosis of asthma, an acute asthma exacerbation as the reason for

Correspondence should be addressed to: Patricia C. Fulkerson, MD, PhD, Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, ML 7028, Cincinnati, OH 45229, Patricia.Fulkerson@cchmc.org, Phone: 513-803-0973, Fax: 513-636-3310.

Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

hospitalization, and a total serum IgE level drawn during hospitalization. The Outpatient cohort inclusion criteria were a current diagnosis of asthma and an associated total serum IgE level drawn at the time of the outpatient visit. We extracted data on patient gender, race, visit date, age at visit, and total serum IgE level.

After excluding patients with total serum IgE level < 1 IU/mL, 227 patients (89 hospitalized inpatients, 138 clinic outpatients) remained for analysis (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). Only the first visit was included in the analysis if patients had multiple encounters. We obtained characteristics (age, gender, race) for all the inpatient asthma admissions from 2009 – 2011 to determine if our inpatient cohort was representative of the CCHMC hospitalized asthma population (Table E1).

The distribution of total serum IgE levels was summarized in intervals (1–200, 200–499, 500–999, 1000–2999, 3000+ IU/mL) by visit site (Inpatient versus Outpatient; Figure 1A). Due to some extreme values, log transformation was applied to IgE levels to investigate the effects of age, gender, parent/self-identified race, and season on total serum IgE levels based on linear regression analysis. The distribution of log(IgE) by visit site is shown in Figure 1B. Age in a continuous scale and in stratified groups (3–4, 5–11, 12–17 years) was used, as specified, in the analysis. Spring was defined as March through May, Summer as June through August, Autumn as September through November, and Winter as December through February.

Inpatients, compared to Outpatients, had a greater percentage (81% vs 33%) of individuals with total serum IgE levels > 200 IU/mL (Figure 1A) and a higher median log(IgE) level (6.54 vs 4.26, Figure 1B), regardless of age group (Figure 2A), race (Figure 2B) or season (Figure 2C).

Simple linear regression analysis indicated that visit site, age, gender, race and season had individually significant effects on total serum IgE levels (Table E2). No significant interactions were found between visit site and age, gender, race or season. Thus, only the main effects of all the factors were included in the multiple regression model (Table E2), where the effects of gender and season were no longer significant. Adjusting for the effects of the covariates age, gender, race and season, the Inpatients had a 3.7-fold higher IgE levels than Outpatients ($P = 0.0001$). Older pediatric patients had higher IgE levels ($P = 0.006$), with each 5-year increase in age leading to a 1.5-fold higher IgE level. African Americans had 2.7-fold higher IgE levels than Caucasians ($P = 0.007$).

Across all age groups (Table E3), Inpatients had significantly higher IgE levels than Outpatients. Inpatients had significantly higher IgE levels than Outpatients in Caucasians ($P < 0.0001$, Table E3), but only a marginal significance was shown for African Americans ($P = 0.098$), which may be due to the smaller sample of African Americans in the outpatient cohort. Moreover, Inpatients had significantly higher IgE levels than Outpatients during all seasons; the greatest difference was during Summer (Table E3). This lack of seasonality may be explained if most patients admitted during seasons with overall low asthma admission rates have more severe phenotypes.

Our study cohorts may be biased because of our inclusion criteria as we only included those patients who had an IgE level drawn during their clinic visit or hospitalization. Our institution admits approximately 850 patients every year for asthma exacerbations, most of those patients do not have an IgE level drawn. Based on the distribution of age, gender and race in our study Inpatient cohort and the Total Inpatient population (Table E1), we found that a higher percentage of older and a higher percentage of African American patients were included in our study Inpatient cohort. Differences in baseline disease severity between the Inpatient and Outpatient cohorts may contribute to the differences in the observed IgE levels.

In our study, total serum IgE level was significantly elevated in children during asthma exacerbations requiring hospitalization compared to those seen in our outpatient clinics. The difference was significant regardless of the season and is consistent with prior studies that associate IgE levels with asthma severity and not season. [7,8]. Our study is also consistent with findings that total serum IgE levels increase with age and vary with race and gender. [7,9] However, in our study, gender's effect on IgE level was influenced by race since there was significant association between the two variables ($P = 0.005$).

To our knowledge, this is the first study to specifically investigate total serum IgE levels in association with asthma exacerbation at one institution. Our results highlight the potential of using IgE elevations as a biomarker for asthma exacerbation. A prospective study is needed to determine whether significant changes in an individual's total IgE levels can predict asthma exacerbations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We are grateful to Lijuan Gu and Dr. Sheharyar Durrani for their assistance in data retrieval. This work was supported in part by the NIH grants K08 AI093673 (P.C.F.) and by an Institutional Clinical and Translational Science Award, NIH/NCRR Grant Number 5UL1RR026314-3.

Abbreviations

IgE	immunoglobulin E
CCHMC	Cincinnati Children's Hospital Medical Center

References

1. Akinbami L. The state of childhood asthma, United States, 1980–2005. *Adv Data*. 2006;1–24. [PubMed: 17180851]
2. CDC. 2012 National Health Interview Survey (NHIS) Data. *Cent Dis Control Prev Asthma*; 2012.
3. Forno E, Celedon JC. Predicting asthma exacerbations in children. *Curr Opin Pulm Med*. 2012; 18:63–9. [PubMed: 22081091]
4. Robroeks CMHHT, van Vliet D, Jöbsis Q, Braekers R, Rijkers GT, Wodzig WKWH, et al. Prediction of asthma exacerbations in children: Results of a one-year prospective study. *Clin Exp Allergy*. 2012; 42:792–8. [PubMed: 22515395]

5. Chipps BE, Zeiger RS, Borish L, Wenzel SE, Yegin A, Hayden M, Lou, et al. Key findings and clinical implications from The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study. *J Allergy Clin Immunol*. 2012; 130:332–42.e10. [PubMed: 22694932]
6. Busse WW, Morgan WJ, Gergen PJ, Mitchell HE, Gern JE, Liu AH, et al. Randomized trial of omalizumab (anti-IgE) for asthma in inner-city children. *N Engl J Med*. 2011; 364:1005–15. [PubMed: 21410369]
7. Borish L, Chipps B, Deniz Y, Gujrathi S, Zheng B, Dolan CM. Total serum IgE levels in a large cohort of patients with severe or difficult-to-treat asthma. *Ann Allergy Asthma Immunol*. 2005; 95:247–53. [PubMed: 16200815]
8. McNichol KN, Williams HE. Spectrum of asthma in children. II. Allergic components. *Br Med J*. 1973; 4:12–6. [PubMed: 4755206]
9. Wittig HJ, Belloit J, De Fillippi I, Royal G. Age-related serum immunoglobulin E levels in healthy subjects and in patients with allergic disease. *J Allergy Clin Immunol*. 1980; 66:305–13. [PubMed: 7419833]

Clinical Implications

Total serum IgE levels were significantly greater in pediatric patients admitted for asthma exacerbation compared to children who had an outpatient asthma visit, provoking future studies focused on evaluating elevations in total serum IgE levels as a predictor or biomarker for exacerbations.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1. Patients in the Inpatient cohort have higher IgE levels than patients in the Outpatient cohort

A) Percentage of patients within each IgE level category in the study cohorts (Inpatient vs. Outpatient) is shown. B) Distribution of Log-transformed IgE level [Log(IgE), median with interquartile ranges] by study cohorts is shown.

Figure 2. Inpatient cohort has higher IgE levels regardless of age group, race or season
Log-transformed IgE level [Log(IgE), median with interquartile ranges] for the Inpatient and Outpatient cohorts separated by age group (A), parent/self-reported race (B) and season (C). Symbol “x” means significant difference in the medians between inpatients and outpatients based on Wilcoxon rank sum test at significance level of 0.05.