

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

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Clinical Implications

- Total serum IgE levels were significantly greater in pediatric patients admitted for asthma exacerbation than in 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.

TO THE EDITOR:

Most of the more than 10 million children in the United States with asthma suffer from at least 1 disease exacerbation per year.^{1,2} Yet, no confirmed predictors or biomarkers exist for asthma exacerbations.^{3,4} Studies implicate IgE as a significant mediator of exacerbations in pediatric patients because patients with asthma, compared with 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 before 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 deidentified clinical data from the Informatics for Integrating Biology and the Bedside 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 the CCHMC for an asthma exacerbation between November 2009 and May 2011; the outpatient cohort included patients with asthma who presented to a CCHMC outpatient clinic between June 2009 and May 2011. Inclusion criteria for the inpatient cohort were a current diagnosis of asthma, an acute asthma exacerbation as the reason for hospitalization, and a total serum IgE level drawn during hospitalization. Inclusion criteria for the outpatient cohort 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 sex, race, visit date, age at visit, and total serum IgE level.

After excluding patients with total serum IgE level of less than 1 IU/mL, 227 patients (89 hospitalized inpatients and 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, sex, race) for all the inpatient asthma admissions from 2009 to 2011 to determine whether our inpatient cohort was representative of the CCHMC hospitalized asthma population (Table E1).

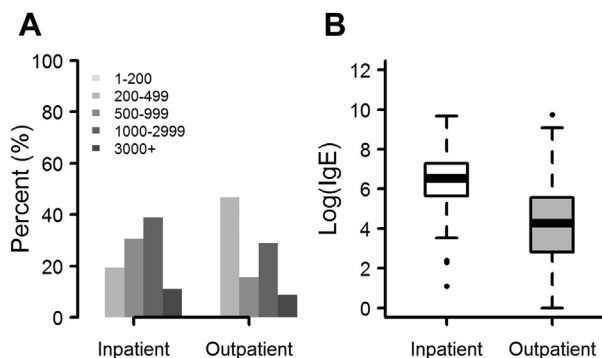


FIGURE 1. Patients in the inpatient cohort have higher IgE levels than do patients in the outpatient cohort. **A**, Percentage of patients within each IgE level category in the study cohorts (inpatient vs outpatient). **B**, Distribution of log-transformed IgE level—log(IgE), median with interquartile ranges—by study cohorts.

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 vs outpatient; Figure 1, A). Because of some extreme values, log transformation was applied to IgE levels to investigate the effects of age, sex, 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 1, B. 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 with outpatients, had a greater percentage (81% vs 33%) of individuals with total serum IgE levels of more than 200 IU/mL (Figure 1, A) and a higher median log(IgE) level (6.54 vs 4.26; Figure 1, B), regardless of age group (Figure 2, A), race (Figure 2, B), or season (Figure 2, C).

Simple linear regression analysis indicated that visit site, age, sex, race, and season had individually significant effects on total serum IgE levels (see Table E2 in this article's Online Repository at www.jaci-inpractice.org). No significant interactions were found between visit site and age, sex, race, or season. Thus, only the main effects of all the factors were included in the multiple regression model (Table E2), in which the effects of sex and season were no longer significant. On adjusting for the effects of the covariates age, sex, race, and season, it was found that inpatients had a 3.7-fold higher IgE levels than did outpatients ($P = .0001$). Older pediatric patients had higher IgE levels ($P = .006$), with each 5-year increase in age leading to a 1.5-fold higher IgE level. Blacks had 2.7-fold higher IgE levels than did whites ($P = .007$).

Across all age groups (see Table E3 in this article's Online Repository at www.jaci-inpractice.org), inpatients had significantly higher IgE levels than did outpatients. Inpatients had significantly higher IgE levels than did outpatients for whites ($P < .0001$; Table E3), but only a marginal significance was shown for blacks ($P = .098$), which may be due to the smaller sample of blacks in the outpatient cohort. Moreover, inpatients

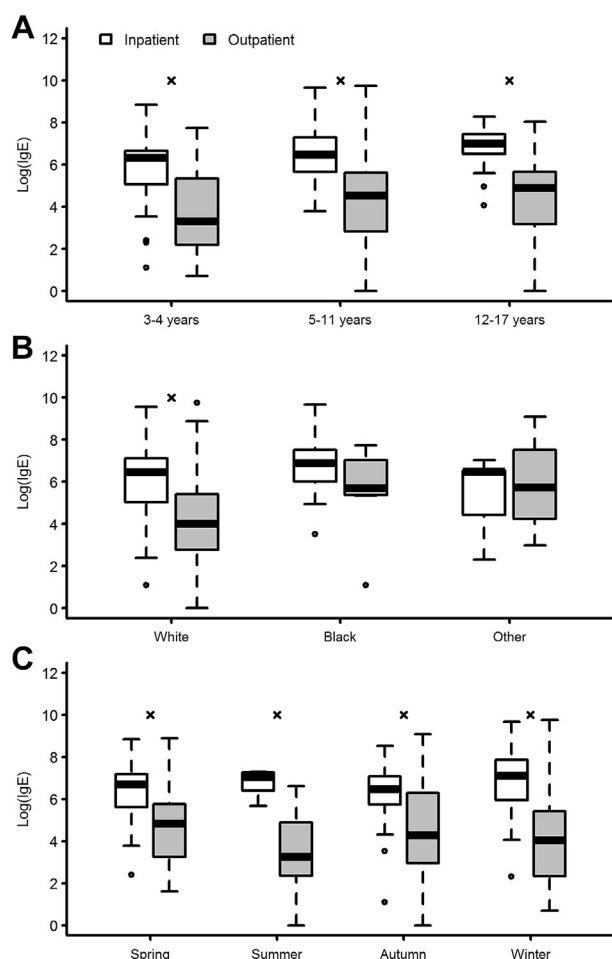


FIGURE 2. Inpatient cohort has higher IgE levels regardless of age group, race, or season. Log-transformed IgE level—log(IgE), median with interquartile ranges—for the inpatient and outpatient cohorts separated by age group (A), parent/self-reported race (B), and season (C). Symbol “x” means significant difference in the medians between inpatients and outpatients based on Wilcoxon rank sum test at a significance level of .05.

had significantly higher IgE levels than did 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 because we included only 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, with most of these patients not having an IgE level drawn. On the basis of the distribution of age, sex, and race in our study’s inpatient cohort and the total inpatient population (Table E1), we found that a higher percentage of older and a higher percentage of black patients were included in our study’s 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

than in those seen in our outpatient clinics. The difference was significant regardless of the season and is consistent with previous 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 sex.^{7,9} However, in our study, sex’s effect on IgE level was influenced by race because there was significant association between the 2 variables ($P = .005$).

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.

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TABLE E1. Patients' demographic characteristics by visit site

Characteristic	Study		<i>P</i> value*	Population inpatients (N = 1335)
	Inpatients (N = 89)	Outpatients (N = 138)		
Age (y), mean ± SD years	8.83 ± 4.03	7.47 ± 3.88	.01	7.51 ± 3.89
Age (y), n (%)			.07	
3-4	17 (19)	36 (26)		378 (28)
5-11	46 (52)	79 (57)		724 (54)
12-17	26 (29)	23 (17)		233 (17)
Sex, n (%)			.09	
Male	58 (65)	74 (54)		823 (62)
Female	31 (35)	64 (46)		512 (38)
Race, n (%)			<.0001	
Black	53 (60)	8 (6)		628 (47)
White	23 (26)	126 (91)		572 (43)
Other	13 (14)	4 (3)		135 (10)
Season, n (%)			.09	
Spring	39 (44)	40 (29)		†
Summer	5 (6)	19 (14)		†
Autumn	29 (33)	43 (31)		†
Winter	16 (18)	36 (26)		†

P < .05 means statistically significant.

*Two-sample *t* test for continuous age; χ^2 test for categorical variables (age group, sex, race, season).

†Data unavailable.

TABLE E2. Regression analyses for each variable's effect on log(IgE)

Variable	Simple regression		Multiple regression	
	Effect estimate (SE)	<i>P</i> value	Effect estimate (SE)	<i>P</i> value
Visit site		<.0001		.0001
Inpatient vs outpatient	2.15 (0.25)		1.31 (0.34)	
Age (y)*		.0006		.006
1 y older	0.12 (0.03)		0.09 (0.03)	
Age group (y)†		.0025		
5-11 vs 3-4	0.76 (0.34)			
12-17 vs 3-4	1.44 (0.41)			
Sex		.033		.188
Male vs female	0.61 (0.28)		0.33 (0.25)	
Race		<.0001		.025
Black vs White	2.19 (0.29)		1.00 (0.37)	
Other vs White	1.27 (0.48)		0.40 (0.50)	
Season		.015		.146
Spring vs winter	0.67 (0.37)		0.27 (0.32)	
Summer vs winter	−0.84 (0.51)		−0.70 (0.44)	
Autumn vs winter	0.36 (0.38)		0.11 (0.33)	

All variables had a significant effect on total serum IgE levels by simple regression analysis. Only visit site, age, and race remained significant with multiple regression analysis. *P* < .05 means statistically significant.

*Continuous age in years.

†Age in stratified groups. The results using age group instead of continuous age in multiple regression are not reported, where *P* = .0001, .013, .329, .020, and .149 for visit site, age group, sex, race, and season, respectively.

TABLE E3. Visit site differences in log(IgE) by age group, race, and season

Variable	Difference* (SE)	95% CI	<i>P</i> value
Age group (y)			
3-4	1.77 (0.54)	0.71-2.83	.001
5-11	2.15 (0.34)	1.48-2.82	<.0001
12-17	2.11 (0.52)	1.08-3.14	<.0001
Race			
Black	1.14 (0.69)	−0.21 to 2.49	.098
White	1.93 (0.41)	1.12-2.73	<.0001
Other	−0.23 (1.03)	−2.27 to 1.80	.821
Season			
Spring	1.64 (0.41)	0.83-2.45	<.0001
Summer	3.44 (0.92)	1.63-5.25	.0002
Autumn	1.71 (0.44)	0.84-2.57	.0001
Winter	2.82 (0.55)	1.74-3.91	<.0001

Inpatients had significantly elevated IgE levels compared with outpatients in all age groups and seasons and in whites. *P* < .05 means statistically significant.

*Difference = Inpatient log(IgE) − Outpatient log(IgE).

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