Elevated immunoglobulin E (IgE) levels are associated with emergency care and other healthcare utilization among asthma patients in a real-world data setting

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RATIONALE

- Immunoglobulin E (IgE) marks allergic status in asthma.[1]
- Little is known about how increased IgE might be associated with health outcomes (clinical and economic), especially in a real-world setting.
- Our objective was to study whether IgE is associated with clinical and economic outcomes in asthma.

METHODS

- This cross-sectional analysis used Humedica SmartFile™: a database containing electronic medical records (EMR) linked with administrative claims.
- We identified ≥ 18 years old asthma patients with ≥ 1 asthma diagnosis claims, ≥ 2 asthma medications, and ≥1 IgE level recorded, enrolled for ≥ 1 year during 01/01/2007 – 08/31/2013.
- The first eligible IgE measurement was the index date.
- Patients were followed from the index date for at least 1 year and up to the end of available data.
- IgE was classified as:
  - **Study group: Evidence of elevated IgE** with IgE >75 IU/ml **at least once** in follow-up period
  - **Comparison group: No-evidence of elevated or unknown IgE status** with IgE >75 IU/ml never in follow-up period.
- Outcomes of interest included asthma exacerbations and asthma-related healthcare use (medications, office and ED visits, hospitalizations).
- Asthma exacerbations were defined by any asthma-related ED visit, hospitalization, or a burst of OCS (≤15-day supply).
- Exacerbations and resource use are reported per thousand patient years (PTPY).

Statistical Analysis

- T-test and Chi-square tests were used for inferential analyses. Linear and negative binomial regressions were used for multivariable analyses. Data transformations and statistical analyses were performed using SAS® 9.4.

RESULTS

- 1,659 asthma patients had ≥1 eligible IgE value record; among them, 652 were continuously enrolled for ≥1 year and were included in the study.
- 286 (43.9%) patients had evidence of elevated IgE and formed the study group. The remaining patients – comparison group.
- The groups were balanced on age, but slightly misbalanced by sex: (62.9% vs. 76.8% female; p<0.001); Table 1.

Table 1. Patient Characteristics and Medication Use

	Study[a] N = 286; 43.9%	Comparison[b] N = 366; 56.1%	*P* Value
Age, year, mean (SD)	52.0 (15.0)	52.7 (14.8)	0.544[c]
Female, no. (%)	180 (62.9)	281 (76.8)	<0.001[d]
Charlson Comorbidity Index, mean (SD)	2.7 (2.5)	3.0 (2.7)	0.124[c]
Asthma Medications Use[e]			
High dose ICS, no (%)	105 (36.7)	130 (35.5)	0.753[d]
LABA, no. (%)	183 (64.0)	205 (56.0)	0.040[d]
OCS with days of supply > 15, no. (%)	96 (33.6)	95 (26.0)	0.034[d]
Omalizumab, no. (%)	25 (8.7)	13 (3.6)	0.005[d]
No. of doses of omalizumab per year among omalizumab users, mean (SD)	5.6 (4.0)	6.1 (4.2)	0.677[c]
LTRA use, no. (%)	148 (51.7)	190 (51.9)	0.967[d]
Theophylline use, no. (%)	17 (5.9)	14 (3.8)	0.207[d]
Total prednisone-equivalent dose, (mg) per year, mean (SD)	738.3 (1,395)	494.4 (1,024)	0.013[c]

[a] Evidence of IgE > 75 IU/ml at least once; [b] No-evidence of IgE >75 IU/ml; [c] t-test; [d] Chi-square test; [e] filled at any time during follow-up

- Neither Charlson Comorbidity Index (Table 1) nor frequency of most respiratory-related comorbidities (e.g., COPD, rhinitis, sinusitis) (not shown) showed statistically significant differences between groups.
  - 18.2% of study-group patients used allergen immunotherapy, compared to 10.9% for comparison group (p=0.008).
- Among 286 patients with elevated IgE, 25 [8.7%] used omalizumab. Among 366 patients without evidence of elevated IgE, 13 [3.6%] used omalizumab.
- Patients in the study group more likely to have used chronic OCS, LABA, and omalizumab than those in the comparison group; and to have received a higher total annual prednisone-equivalent dose (Table 1).
  - High-dose ICS usage did not differ between the groups (Table 1).
- In unadjusted analyses:
  - Patients in the study group had fewer overall office visits than patients in the comparison group (19,200 vs. 22,977 PTPY; p=0.012).
  - Groups did not have statistically significantly different exacerbation rates (1,393 vs low-IgE 987 exacerbations PTPY; p=0.144).
  - Patients in the study group had more asthma-related office visits (2,197 vs. 1,575 PTPY; p=0.008) and ED visits (62 vs. 5 PTPY; p= 0.002) than those in the comparison group.

Table 2. Adjusted[a] Means and Healthcare Utilization (95% CI)

Per Thousand Patient Year (SD)	Study N = 286; 43.9%	Comparison N = 366; 56.1%	*P* Value
No. of office visits[b]	19,790 (18,060 - 21,510)	21,600 (20,080 – 23,120)	0.127
No. of hospitalizations[c]	172 (132 – 224)	173 (137 – 218)	0.977
No. of ED visits[c]	1,073 (810 – 1,423)	1,045 (814 – 1,341)	0.889
No. of asthma-related office visits[b]	2,280 (1,840 – 2,710)	1,540 (1,150 – 1,920)	0.013
No. of asthma-related hospitalizations per year[c]	19 (9 – 38)	9 (4 – 19)	0.147
No. of asthma-related ED visits[c]	30 (14 -62)	3 (1 – 11)	0.002
No. of asthma-related exacerbations[c]	1,331 (1,149 – 1,542)	989 (866 – 1,131)	0.004

[a] Adjusted by age group, gender, race (Caucasian vs other), region, and Charlson comorbidity index; [b] linear regression model; [c] binomial regression model

- Adjusted for demographics and clinical characteristics (Table 2):
  - Study-group patients had more asthma-related office visits (2,280 vs. 1,540; p=0.013), exacerbations (1,331 vs. 989; p=0.004), and asthma-related ED visits (30 vs. 3; p=0.0002) than their counterparts in the comparison group.
  - Hospitalizations (overall and asthma-related) and any-cause office visits were not statistically significantly different between groups.

LIMITATIONS

- These data were derived from a subset of insurance claims linked with EMR data and may not be representative of patients without commercial insurance, or of insured patients without EMR data.
- Because IgE data came from EMR, it is subject to testing bias. The fact that no elevated IgE has been recorded in the database does not mean that patients in the comparison group, in fact, did not have it. It is not possible to know how many patients in the comparison group in fact did have it elevated.
- Omalizumab is known to reduce IgE, and it was used by 25 patients who had evidence of elevated IgE and by 13 patients in the comparison group. Therefore, the allocation to the comparison group could have been affected by omalizumab use.
- As with all claims studies, miscoding may affect accuracy.
- This study presents the first known analysis of IgE data in real-world settings as reported in EMR. More research (supported by more accurate testing) is needed to confirm findings of this study.

CONCLUSIONS

- Although evidence of elevated IgE does not appear to be associated with increased overall healthcare utilization in patients with asthma, it appears to be associated with increases in some categories of asthma-specific utilization.
- In adjusted analyses, patients with evidence of elevated IgE had statistically significantly more exacerbations, asthma-related office visits, and asthma-related ED visits than patients without elevated IgE.

REFERENCES

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