



Letter

Sex differences in risk of hospitalization among emergency department patients with acute asthma

Asthma remains an important public health problem in the United States, accounting for 1.8 million emergency department (ED) visits and 440,000 hospitalizations annually.¹ Its prevalence is higher in women (9.2%) than in men (7.0%).¹ Prior studies have reported sex differences in quality of life, health care use, and morbidity in patients with asthma.^{2–4} Our previous multicenter study, conducted in the late 1990s, found that women presenting to the ED with acute asthma had higher risks of hospitalizations compared with men.⁵ Despite the substantial burden of asthma-related ED visits and hospitalizations, there have been no recent efforts to examine sex differences in acute morbidity in this population. To address this knowledge gap, we investigated sex differences in patient characteristics and risk of hospitalizations in 2,000 ED patients with acute asthma.

This article presents the results of a secondary analysis of data from a multicenter chart review that characterized adult ED patients with acute asthma, as part of the Multicenter Airway Research Collaboration (MARC). The study setting, participants, methods of measurement, and measured variables have been reported previously.^{6,7} Briefly, we recruited 48 academic and community EDs across 23 states in the United States. Using a primary discharge diagnosis of asthma, we identified all ED visits for asthma exacerbations from 2011 through 2012 in adults 18 to 54 years old with a history of physician-diagnosed asthma. After being trained (lecture, practice charts, and certification), chart abstractors reviewed 40 randomly selected ED charts. Two hospitals each examined an additional 40 charts, yielding a total of 2,000 charts. Using a standardized form, evaluators abstracted data, including patients' demographics, asthma history, presentation, and asthma management in the ED. To examine the association of sex with risk of hospitalization for asthma exacerbation, we constructed a series of logistic regression models. Initially, we fitted an unadjusted model that included only sex as the independent variable, with male sex as the reference. Next, we fitted 4 multivariable logistic regression models adjusting for potential confounding factors (age, race or ethnicity, body mass index status, insurance, household income, primary care physician status, smoking, history of hospitalization for asthma, ED visits for asthma in past year, current use of oral corticosteroids, current use of inhaled corticosteroids,

respiratory rate and peak expiratory flow at ED presentation, and comorbidities) and clustering of patients within EDs.

Of the 2,000 enrolled adults with acute asthma, 814 (41%) were men and 1,186 (59%) were women. Patient demographics differed between groups (Table 1). For example, women were more likely to have health insurance (public or private) and a primary care physician ($P < .001$ for the 2 comparisons). Several chronic asthma factors also differed between groups. For example, women were less likely to have an ED visit for acute asthma in the past year but more likely to be seen by an asthma specialist and treated with long-term control medications ($P < .001$ for all comparisons). However, the proportions of patients who had been seen by an asthma specialist and who had used control medications were small between groups (eg, 31% of men and 39% of women were treated with inhaled corticosteroids).

Most ED presentations and ED treatment did not differ between groups. However, compared with men, women were more likely to be categorized as having acute asthma of mild or moderate severity as opposed to severe or very severe based on their initial peak expiratory flow value ($P = .02$). In contrast, women had a higher risk of hospitalization (12% vs 20%, odds ratio 1.92, 95% confidence interval 1.48–2.48, $P < .001$; eTable 1). This association remained significant in multivariable models adjusting for potential confounders ($P \leq .001$ for all comparisons).

This multicenter study of adults presenting to 48 EDs with acute asthma demonstrated that, compared with men, women were more likely to have outpatient management by asthma specialists and guideline-recommended long-term control management, although the proportions who received this recommended care were small. Furthermore, we found that women had higher risks of hospitalizations even after adjusting for multiple potential confounders (eg, markers of chronic and acute asthma severity).

Our findings are similar to those of our previous multicenter study of 1,228 adult ED patients with acute asthma.⁵ Although the study design was different (eg, chart review in the present study vs interview in the previous study), the previous study found that, compared with men, women were more likely to be insured and have a primary care physician and that women had a higher risk of hospitalization despite a higher mean peak expiratory flow in the ED. Likewise, another analysis of administrative data in Canada reported that women presenting to an ED with acute asthma were more likely to be hospitalized, despite their apparently less severe asthma.³ We suspect that the reasons for these findings are multifactorial, such as altered perception of airflow obstruction, potential influences of the female sex hormones, differences in bronchial hyperresponsiveness, and health behaviors.^{2,8,9} Awareness of the aspects of asthma unique to women should stimulate collaborative research to determine the underlying mechanisms

Disclosure: Dr Camargo has provided asthma-related consultation for GlaxoSmithKline, Novartis, and Teva. The other authors have no relevant financial relationships to disclose.

Disclaimer: The sponsor had no role in the conduct of the study or in the collection, management, or analysis of the data.

Funding: This study was funded by a grant from Novartis Pharmaceuticals Corporation to Massachusetts General Hospital (principal investigator, Carlos A. Camargo, Jr, MD, DrPH).

Table 1
Characteristics of 2,000 emergency department patients with acute asthma, according to patient's sex^a

Patient characteristics	Men (n = 814, 41%)	Women (n = 1,186, 59%)	P value
Demographics			
Age (y), median (IQR)	33 (24–45)	35 (25–45)	.11
18–29	322 (40)	422 (36)	.15
30–39	188 (23)	307 (26)	
40–54	304 (37)	457 (39)	
Race or ethnicity			
Non-Hispanic white	151 (19)	233 (20)	.03
Non-Hispanic black	432 (53)	584 (49)	
Hispanic ethnicity	134 (17)	251 (21)	
Others	97 (12)	118 (10)	
Primary health insurance ^b			<.001
Private	230 (28)	402 (34)	
Public	267 (33)	508 (43)	
No insurance	285 (35)	236 (20)	
Median household income estimated from ZIP code, median (IQR)	35,664 (25,991–51,034)	35,319 (27,263–48,113)	.67
Having primary care physician	382 (47)	788 (66)	<.001
Active smoker	293 (36)	356 (30)	.003
Body mass index, median (IQR) ^c	28 (24–33)	32 (26–39)	<.001
Chronic asthma factors			
Ever intubated for asthma	102 (13)	142 (12)	.71
Ever hospitalized for asthma	259 (32)	421 (36)	.07
Hospitalization for asthma in past 12 mo	106 (13)	188 (16)	.08
ED visit for asthma in past 12 mo	373 (46)	490 (41)	.02
Seen by asthma specialist in past 12 mo	43 (5)	113 (10)	<.001
Total IgE checked in past 12 mo	11 (1)	37 (3)	.03
Allergen-specific IgE checked in past 12 mo	2 (<1)	17 (1)	.02
Skin prick test reaction checked in past 12 mo	2 (<1)	6 (1)	.49
Current asthma medications			
Oral corticosteroids	77 (10)	172 (15)	<.001
Inhaled corticosteroids	252 (31)	460 (39)	<.001
Long-acting β -agonist	153 (19)	332 (28)	<.001
Leukotriene modifiers	60 (7)	161 (14)	<.001
ED presentations			
Vital signs			
Initial respiratory rate (breaths/min), median (IQR)	20 (18–22)	20 (18–22)	.002
Initial oxygen saturation (%), median (IQR)	97 (95–98)	98 (96–100)	<.001
Severity based on initial PEF ^d			.02
Mild	60 (17)	114 (24)	
Moderate	138 (39)	194 (41)	
Severe	117 (33)	131 (28)	
Very severe	40 (11)	36 (8)	
Change in PEF (%) ^e , median (IQR)	41 (14–82)	35 (13–67)	.048
Concomitant medical disorders	87 (11)	186 (16)	.001
ED treatment			
Inhaled β -agonists	808 (99)	1,175 (99)	.81
Inhaled anticholinergics	568 (70)	849 (72)	.38
Systemic corticosteroids	612 (75)	920 (78)	.11
Intravenous magnesium	72 (9)	107 (9)	.89
Mechanical Ventilation	8 (1)	19 (2)	.23
ED disposition			<.001
Admitted to hospital ^f	94 (12)	237 (20)	<.001
Sent home	706 (87)	928 (78)	
Other (eg, left against medical advice)	14 (2)	21 (2)	

Abbreviations: ED, emergency department; ICU, intensive care unit; IQR, interquartile range; PEF, peak expiratory flow.

^aData are expressed as number (percentage) unless otherwise indicated.^bPercentages are not equal 100 because of missing data.^cAnalyzed for 1,227 patients (61%) with body mass index available. Severity of acute asthma was classified according to the initial PEF as mild (≥ 400 L/min for men and ≥ 300 L/min for women), moderate (250–399 L/min for men and 200–299 L/min for women), severe (150–249 L/min for men and 120–199 L/min for women), and very severe (< 150 L/min for men and < 120 L/min for women). The absolute PEF values represented approximately 70%, 40%, and 25% of predicted value, respectively, for a typical woman and man.^dAnalyzed for 830 patients (42%) with initial PEF available.^eAnalyzed for 609 patients (31%) with change in PEF available.^fDefined as hospital admission to an observation unit, inpatient unit, or intensive care unit.

and establish effective, individualized asthma management strategies.

The study has potential limitations. First, the data relied on medical record review of patient characteristics and outcomes; thus, measurement error is possible. However, previous studies have demonstrated excellent inter-rater agreement in ED disposition (eg, hospitalization) in patients with acute asthma.¹⁰ Second, this observational study did not use standard

criteria for hospitalization across the EDs; therefore, institutional variability in ED hospitalization is possible (we addressed this concern by accounting for patient clustering within EDs). Third, the sample consisted mainly of urban academic EDs; therefore, our findings might not be generalizable to other populations (eg, non-ED setting, rural community EDs, or states without a participating ED). However, in the present study, we enrolled EDs mainly by inviting the sites that had participated

in the previous MARC study,⁵ which made this study setting comparable.

In summary, this multicenter study of ED patients with acute asthma demonstrated that, similar to our findings published in the 1990s, women have higher risks of hospitalization despite their greater use of asthma specialists and guideline-recommended long-term asthma care. These findings continue to reflect the inadequacy of current clinical and public health measures to manage female patients with asthma. Given the high prevalence of asthma in US women,¹ the higher risk of hospitalization in the ED population should be of interest to many stakeholders, including patients, clinicians, payers, policy makers, and researchers. These findings support further investigation of the mechanisms by which female sex affects acute asthma morbidity and health care use.

Acknowledgments

The authors thank the MARC-36 study hospitals and research personnel for their ongoing dedication to asthma research (eTable 1). The report was copyedited by Linda J. Kesselring, MS, ELS.

Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anai.2015.03.021>.

Rose M. Chasm, MD*
Y. Veronica Pei, MD, MPH, MEd*
Daniel J. Pallin, MD, MPH†
Nathan Shapiro, MD‡
Brian Snyder, MD§
Ashley F. Sullivan, MPH, MS||
Carlos A. Camargo, Jr, MD, DrPH||
Kohei Hasegawa, MD, MPH||
*Department of Emergency Medicine
University of Maryland School of Medicine
Baltimore, Maryland
†Department of Emergency Medicine
Brigham and Women's Hospital
Harvard Medical School

‡Department of Emergency Medicine
Beth Israel Deaconess Medical School
Boston, Massachusetts

§Department of Emergency Medicine
University of California–San Diego Medical Center
San Diego, California

||Department of Emergency Medicine
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts
rchas001@umaryland.edu

References

- [1] Moorman JE, Akinbami LJ, Bailey CM, et al. National surveillance of asthma: United States, 2001–2010. *Vital Health Stat.* 2012;3:1–67.
- [2] Kynnyk JA, Mastrorade JG, McCallister JW. Asthma, the sex difference. *Curr Opin Pulm Med.* 2011;17:6–11.
- [3] Baibergenova A, Thabane L, Akhtar-Danesh N, Levine M, Gafni A, Leeb K. Sex differences in hospital admissions from emergency departments in asthmatic adults: a population-based study. *Ann Allergy Asthma Immunol.* 2006;96:666–672.
- [4] Schatz M, Camargo CA Jr. The relationship of sex to asthma prevalence, health care utilization, and medications in a large managed care organization. *Ann Allergy Asthma Immunol.* 2003;91:553–558.
- [5] Singh AK, Cydulka RK, Stahmer SA, Woodruff PG, Camargo CA Jr. Sex differences among adults presenting to the emergency department with acute asthma. Multicenter Asthma Research Collaboration Investigators. *Arch Intern Med.* 1999;159:1237–1243.
- [6] Hasegawa K, Sullivan AF, Tovar Hirashima E, et al. A multicenter observational study of US adults with acute asthma: who are the frequent users of the emergency department? *J Allergy Clin Immunol Pract.* 2014;2:733–740.
- [7] Hasegawa K, Sullivan AF, Tsugawa Y, et al. Comparison of US emergency department acute asthma care quality: 1997–2001 and 2011–2012. *J Allergy Clin Immunol.* 2015;135:73–80.
- [8] Schatz M, Clark S, Camargo CA Jr. Sex differences in the presentation and course of asthma hospitalizations. *Chest.* 2006;129:50–55.
- [9] Farha S, Asosingh K, Laskowski D, et al. Effects of the menstrual cycle on lung function variables in women with asthma. *Am J Respir Crit Care Med.* 2009;180:304–310.
- [10] Hasegawa K, Chiba T, Hagiwara Y, et al. Quality of care for acute asthma in emergency departments in Japan: a multicenter observational study. *J Allergy Clin Immunol Pract.* 2013;1:509–515.

eTable 1

Association of female (vs male) sex to risk of hospitalization in adults with acute asthma

Model	Odds ratio (95% CI)	P value
Unadjusted model	1.92 (1.48–2.48)	<.001
Adjusted models ^a		
Model 1 ^b	1.72 (1.38–2.14)	<.001
Model 2 ^c	1.47 (1.17–1.84)	<.001
Model 3 ^d	1.59 (1.20–2.09)	.001
Model 4 ^e	1.60 (1.21–2.11)	<.001

Abbreviation: CI, confidence interval.

^aAll adjusted models accounting for clustering of patients within emergency departments using generalized estimating equations.

^bModel adjusting for age and race or ethnicity.

^cModel adjusting for age, race or ethnicity, body mass index status, primary health insurance, estimated household income, primary care physician status, and smoking.

^dModel adjusting for age, race or ethnicity, body mass index status, primary health insurance, estimated household income, primary care physician status, smoking, history of hospitalization for asthma, emergency department visits for asthma in past year, current use of oral corticosteroids, and current use of inhaled corticosteroids.

^eModel adjusting for age, race or ethnicity, body mass index status, primary health insurance, estimated household income, primary care physician status, smoking, history of hospitalization for asthma, emergency department visits for asthma in past year, current use of oral corticosteroids, current use of inhaled corticosteroids, respiratory rate and peak expiratory flow at emergency department presentation, and comorbidities.