Sex differences in the risk of hospitalization among patients presenting to US emergency departments with asthma exacerbation, 2010-2012

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Clinical Implications

- Using a nationally representative sample of 4.3 million emergency department visits for asthma exacerbation during 2010-2012, we found that women had a higher risk of hospitalization compared with men. This national sex disparity remains unexplained and merits further study.

TO THE EDITOR:

In the USA, asthma continues to be a major health burden, affecting 26 million Americans in 2010.[1] Asthma exacerbations contribute to a substantial portion of the burden, accounting for 2 million emergency department (ED) visits and 330,000 hospitalizations annually.[1] Previous studies have reported considerable sex differences in asthma prevalence and several measures of chronic and acute morbidity—for example, higher risks of hospitalization in women with asthma exacerbation.[2-4] Although national surveys have reported the sex differences in asthma,[1,5] there have been no recent nationwide studies that examine sex differences in hospitalization risk in ED patients. In this context, we used a nationally representative database to investigate sex differences in the risk of hospitalization in children and adults presenting to US EDs with asthma exacerbation.

We analyzed data from the 2010-2012 Nationwide Emergency Department Sample (NEDS). Details of the study design, setting, measured variables, and analysis may be found in this article's Online Repository at www.jaci-inpractice.org. Briefly, the NEDS represents all ED visits regardless of disposition and contains information on short-term outcomes for patients admitted through all nonfederal hospital-based EDs in the USA. The NEDS is the largest all-payer ED and inpatient database in the USA. In 2012, the NEDS contained 31 million records of ED visits from 950 hospitals; this provided nationally representative data on approximately 134 million ED visits.

In this study, we identified all ED visits for younger children (aged 4-11 years), older children (aged 12-17 years), and adults (aged 18-54 years), who had an *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) code for asthma (493.xx) in the primary diagnosis field during 2010-2012. Details of the study design, setting, data collections, and analysis may be found in this article's Online Repository at www.jaci-inpractice.org. We excluded patients with chronic obstructive pulmonary disease. To examine the association of sex (female vs male) with risk of hospitalization, we constructed 2 logistic regression models for 3 age groups separately. First, we fitted an unadjusted model that included only sex as the independent variable, with male sex as the reference. Next, we constructed multivariable logistic models adjusting for patient-level characteristics and calendar year, with the generalized estimating equations to account for potential clustering of patients within EDs. All analyses used SAS-callable SUDAAN, version 11.0 (Research Triangle Institute, Research Triangle Park, NC) to obtain proper variance estimations that accounted for the complex sampling design. The institutional review board of Massachusetts General Hospital approved this analysis.

During 2010-2012, we identified a total of 966,676 ED visits for asthma exacerbation in the USA, corresponding to a weighted estimate of 4,286,701 visits. Both in younger and older children, patient characteristics were similar between girls and boys. In adults, women were more likely to have public health insurance and chronic comorbidities (Table E1, available in this article's Online Repository at www.jaci-inpractice.org).

In younger children presenting to the ED with asthma exacerbation, the hospitalization rate was higher in girls than boys (10.8% vs 10.3%; $P = .003$). By contrast, in older children, the hospitalization rate was lower in girls than boys (6.5% vs 6.9%; $P = .04$). These results did not change materially in the multivariable models. In adults, the hospitalization rate was higher in women than men (13.6% vs 10.1%; $P < .001$). After adjustment for patient-level characteristics and calendar year, this association was meaningfully attenuated but remained statistically significant (OR, 1.07; 95% CI, 1.02-1.11; $P = .004$; Table I). Across all age groups, private insurance status as compared with self-pay, presence of comorbidities, and metropolitan residence as compared with rural residence were associated with a higher risk of hospitalization. Among adults, older age and higher income were also associated with a higher risk of hospitalization.

To our knowledge, this is the first national study to investigate sex differences in risk of hospitalization among ED patients with asthma exacerbation. During 2010-2012, we found that women had a 35% higher hospitalization rate compared with men; however, much of this difference was attributable to patient-level characteristics that were associated with both sex and hospitalization risk. For example, women had more comorbidities on average than men and were more likely to have health insurance. Interestingly, there were disparities in magnitude of sex differences compared with previous studies.[2-4] However, direct comparisons of these disparities in magnitude are challenging because of the difference in study design (eg, an analysis of administrative dataset vs chart review study[4]), setting, and patient population (eg, a nationally representative ED sample vs urban, academic EDs[2,3]). Notwithstanding with the differences in study design, these data collectively indicate a disproportionate burden in acute asthma morbidity among US female adults.

This observed sex disparity is consistent with previous single center studies and our recent multicenter study of ED patients with asthma exacerbation. Thus, multiple studies arrived at a similar conclusion despite different study designs, settings, and

TABLE I. Unadjusted and adjusted associations of female (vs male) sex with hospitalization in children and adults presenting to emergency department with asthma exacerbation

Variables	Younger children (age 4-11 y) OR (95% CI)	*P* value	Older children (age 12-17 y) OR (95% CI)	*P* value	Adults (age 18-54 y) OR (95% CI)	*P* value
Univariable model						
Sex						
Male	Reference		Reference		Reference	
Female	1.05 (1.02-1.08)	.003	0.94 (0.89-1.00)	.04	1.40 (1.34-1.47)	<.001
Multivariable model*						
Sex						
Male	Reference		Reference		Reference	
Female	1.04 (1.01-1.07)	.02	0.91 (0.85-0.96)	.002	1.07 (1.02-1.11)	.004
Age						
18-29 y	–	–	–	–	Reference	
30-39 y	–	–	–	–	1.20 (1.16-1.25)	<.001
40-54 y	–	–	–	–	1.71 (1.62-1.80)	<.001
Primary health insurance						
Public	0.91 (0.84-0.99)	.02	1.01 (0.92-1.11)	.88	1.10 (1.04-1.16)	.004
Private	Reference		Reference		Reference	
Self-pay	0.44 (0.36-0.53)	<.001	0.45 (0.36-0.56)	<.001	0.72 (0.65-0.78)	<.001
Other	0.84 (0.72-0.97)	.02	0.83 (0.60-1.03)	.08	1.28 (1.14-1.43)	<.001
Median household income						
$1-$38,999	0.90 (0.75-1.07)	.21	1.12 (0.93-1.34)	.24	0.78 (0.71-0.86)	<.001
$39,000-$47,999	0.86 (0.75-1.00)	.04	0.88 (0.75-1.03)	.10	0.80 (0.74-0.87)	<.001
$48,000-$63,999	0.86 (0.77-0.97)	.02	0.88 (0.75-1.03)	.10	0.87 (0.82-0.93)	.001
$64,000 or more	Reference		Reference		Reference	
Elixhauser comorbidity†	4.67 (4.13-5.29)	<.001	5.61 (4.99-6.31)	<.001	10.42 (9.85-11.02)	<.001
Patient residence						
Rural area	Reference		Reference		Reference	
Metropolitan area	1.44 (1.26-1.65)	<.001	1.64 (1.36-1.97)	<.001	1.28 (1.17-1.41)	<.001
Calendar year						
2010	Reference		Reference		Reference	
2011	1.06 (0.85-1.32)	.60	1.01 (0.81-1.26)	.94	0.87 (0.80-0.95)	.003
2012	1.11 (0.92-1.33)	.29	1.11 (0.90-1.38)	.33	0.85 (0.77-0.93)	<.001

CI, Confidence interval; *OR*, odds ratio.

*Multivariable logistic models with the generalized estimating equations, adjusting for age, primary payer, quartiles for median household income, Elixhauser comorbidity measures, patient location, and calendar year.

†Comorbidity was defined as at least 1 Elixhauser comorbidity measure.

populations (eg, urban, academic EDs vs nationally representative ED sample). Along with the female predominance in asthma-related ED visits, these data collectively indicate a disproportionate burden in acute asthma morbidity among US female adults.

We also found that the association of female sex with higher risks of hospitalization attenuated with multivariable adjustment. Indeed, the sex difference was partially explained by patients' demographics, insurance status, socioeconomic status, and comorbidities, as reported in the previous studies.[6,7] However, the reasons for the residual sex-related difference after multivariable adjustment are unclear and likely multifactorial. Prior studies have suggested several potential mechanisms—for example, potential influence of estrogen and progesterone,[8] altered bronchial hyperresponsiveness, and perception of airway obstruction in women with asthma.[5]

We acknowledge several potential limitations to this study. First, as with any studies using administrative data, misclassification of ED visits is possible. Nevertheless, the Healthcare Cost and Utilization Project data are accurate and widely used to estimate diagnoses and visit frequency.[9] Second, the NEDS data do not include some clinical covariates and socioeconomic factors that might have confounded our findings (eg, asthma controller medications, education, access to ambulatory health care). Finally, our study focused on patients presenting to the ED with asthma exacerbation; many individuals might have presented to non-ED settings. Nevertheless, our observations are highly relevant to the millions of children and adults presenting to the ED with asthma exacerbation in the USA each year.

In summary, using a nationally representative sample of 4.3 million ED visits for asthma exacerbation, we found material unadjusted sex differences among adults such that women are disproportionately hospitalized following ED visits for asthma exacerbation. However, this burden appears to be largely explained by patient characteristics that are associated with both sex and hospitalization risk. Once patient-level characteristics were accounted for, the impact of sex on hospitalization risk was similar in magnitude across the age groups but inconsistent in direction. Young girls and adult women