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A M E R I C A N C O L L E G E O F
 C H E S T
P H Y S I C I A N S

Sex Differences in the Presentation and Course of Asthma Hospitalizations*

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Objective: To distinguish between differences in prevalence, asthma severity, and treatment to explain sex-related differences in hospitalized asthma patients.

Design: Medical record review.

Setting: Thirty US hospitals as part of the University HealthSystem Consortium Asthma Clinical Benchmarking Project.

Patients: A random sample of patients aged 2 to 54 years and admitted to the hospital for acute asthma from 1999 to 2000.

Measurements: Demographics, medical history, initial oxygen saturation, initial peak expiratory flow (adults), initial pulmonary index (children), emergency department course, length of hospital stay, and discharge plans.

Results: The cohort included 606 pediatric (aged 2 to 17 years) and 680 adult (aged 18 to 54 years) inpatients. The sex ratio varied significantly by age: 40% were girls 2 to 17 years of age, and 68% were women 18 to 54 years of age ($p < 0.001$). Among children, girls did not differ from boys according to asthma history, pulmonary index scores, or hospital length of stay. Among adults, women were more likely to have a primary care provider (90% vs 73%, $p < 0.001$) but did not differ according to asthma history or recent medication use. Women had a higher mean initial PEF compared to men (43% of predicted vs 36% of predicted, $p < 0.001$) and higher median initial oxygen saturation (95% vs 93%, $p = 0.002$) but did not differ by hospital length of stay. No sex differences in discharge regimens were identified in children or adults.

Conclusions: Among US inpatients with acute asthma, male children are more common than female children, while women are more common in adults. The results in children are probably explained by prevalence differences, since no sex differences were seen in markers of asthma severity or treatment. In adults, increased symptoms in response to a given level of airway obstruction in women may contribute to the female predominance in asthma hospitalizations.

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Key words: acute asthma; gender; hospitalizations; management; prevalence; severity; sex differences

Abbreviations: CI = confidence interval; ED = emergency department; IQR = interquartile range; PCP = primary care provider; PEF = peak expiratory flow; UHC = University HealthSystem Consortium

Age-related differences in sex prevalence have been consistently reported in hospitalized asthma patients. While up to twice as many inpatients < 15 years old are male,^{1–10} up to three times as many hospitalized patients > 15 years old are

female.^{4,6–8,10–20} These inpatient sex differences could be due to age-related differences in overall asthma prevalence or sex differences in asthma severity or treatment. The prevalence of asthma has been reported to be higher in male children < 15

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years old and female patients > 15 years old.^{5,12,13,17,21–23} The purpose of this study was to try to identify sex differences in asthma severity or treatment in hospitalized asthma patients.

MATERIALS AND METHODS

This retrospective study was performed from January 1999 to May 2000 as part of the University HealthSystem Consortium (UHC) Asthma Clinical Benchmarking Project. Using a standardized protocol, investigators at 30 UHC hospitals in 22 states performed data abstraction from randomly selected medical records to collect information about patients admitted to the hospital for acute asthma (International Classification of Diseases, Ninth Revision code 493). Exclusion criteria were diagnosis of cystic fibrosis, discharge against medical advice, transferred from another hospital or emergency department (ED), and repeat admissions by individual subjects. Inclusion criteria were physician diagnosis and hospital admission for acute asthma and age 2 to 54 years. Of the 1,318 cases identified, 24 were excluded because they did not meet the inclusion criteria and 8 were excluded due to pregnancy, leaving 606 children (age 2 to 17 years) and 680 adults (age 18 to 54 years). The Institutional Review Board at each of the 30 participating hospitals approved the study.

Data Collection

Data were collected on patient demographic characteristics, medical history, emergency and inpatient course, and discharge plan. All data were submitted to the UHC via on-line data entry. Medical history assessed whether or not the patient reported a primary care provider (PCP), history of hospitalizations for asthma, recent asthma medication use, and smoking status. Smoking status was assigned as never-smoker, former smoker, current smoker, and exposure to passive smoke in the home.

For adults, severity of the acute episode was based on initial peak expiratory flow (PEF), expressed as percentage of the predicted value based on race, age, sex, and height.²⁴ For the patients missing a height measurement, height was imputed by best subset regression based on age, sex, race, and weight. For children, the severity of the acute episode was based on the pulmonary index score, calculated using respiratory rate, wheezing, inspiratory/expiratory ratio, and accessory muscle use,²⁵ ranging from 0 (mild) to 12 (severe). For children missing only one of the factors used to compute the pulmonary index score, the missing value was imputed using best subset regression based on the remaining three factors. Information on initial blood gases, oxygen saturation, admission location (regular unit, critical care unit, or observation unit), length of stay, discharge medications prescribed, and discharge follow-up plans also were collected from patient charts.

Statistical Analysis

Children and adults were analyzed separately. All analyses were performed using statistical software (STATA 7.0; StataCorp; College Station, TX). Data are presented as proportions (with 95% confidence interval [CIs]), ratios (with 95% CI), means (with SD), or medians (with interquartile range [IQR]). The associations between sex and other factors were examined using χ^2 test, Fisher Exact Test, Student *t* test, and Wilcoxon rank test, as appropriate. Adjustments for severity of the episode (pulmonary index for children, PEF for adults) were accomplished using

analysis of covariance methods after appropriate interactions were assessed. All tests of equality between sexes for continuous variables are two tailed with *p* values < 0.05 considered statistically significant.

RESULTS

In the pediatric sample, 40% were female; in the adult sample, 68% were female (*p* < 0.001). A further age breakdown of the sample is shown in Figure 1. The female-to-male ratio is approximately 0.60 in children 2 to 9 years old, approximately equal in children aged 10 to 19 years, and ≥ 1.5 thereafter.

Demographic factors and medical history data are shown in Table 1. Girls were somewhat older, but girls and boys did not differ by race or by insurance status. Women also were older than men and did not differ by race. Insurance status differed among adults, with women more likely to have Medicaid and less likely to have no insurance. There were no sex differences with respect to prior hospitalizations for children or adults. Although girls and boys did not differ according to PCP status, adult women were more likely than men to have a PCP. There were no sex differences between controller medications (inhaled corticosteroids, cromolyn, or leukotriene modifiers) used within the 4 weeks prior to the current exacerbation for children or adults. Boys were slightly more likely to be never-smokers, but smoking status did not differ between women and men.

Presentation and ED and hospital course are shown in Table 2. There were no sex differences for duration of symptoms or treatment with systemic steroids in the ED for either children or adults. Mean initial percentage of predicted PEF was significantly higher in women compared to men, and median initial oxygen saturation was also significantly higher in women compared to men. No significant differences were seen between boys and girls regarding oxygen saturation or pulmonary index score. Women stayed longer in the ED compared to men, but no significant gender difference in ED length of stay was seen for children. Admission location did not differ by sex for children or adults. Hospital length also did not differ by sex for children or adults.

Documentation of an action plan or a follow-up appointment with a PCP at hospital discharge was low for both children and adults. While documentation of an action plan did not differ by sex among children, girls were more likely to receive a follow-up appointment with a PCP. Documentation of an action plan and follow-up appointment with a PCP did not differ by sex among adults. Discharge prescriptions for systemic corticosteroids, inhaled corti-

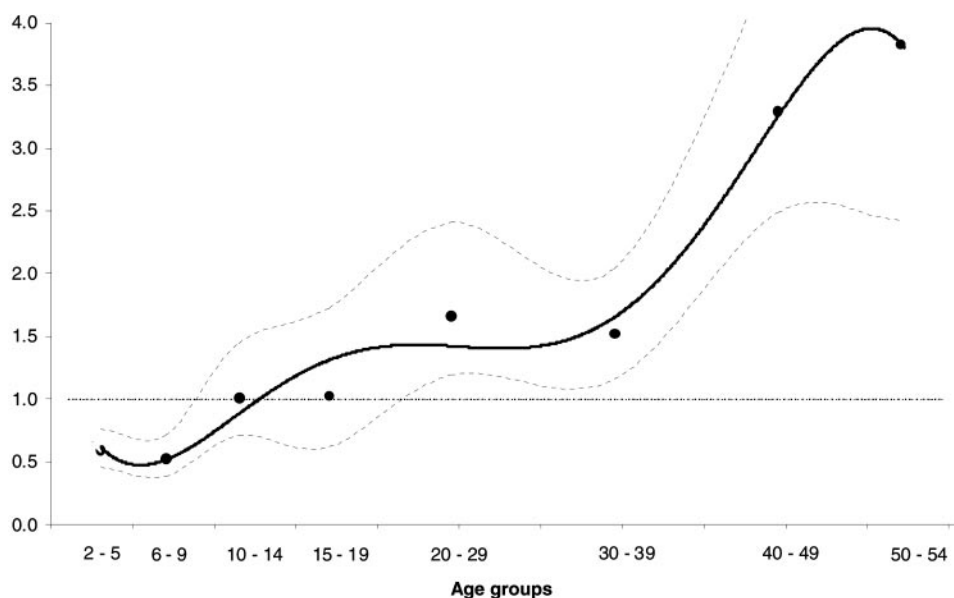


FIGURE 1. Ratio of female to male inpatients for asthma, by age group, with a smoothed polynomial curve (fifth degree) connecting the points. Ratios are presented with 95% CIs represented by dashed intervals.

costeroids, cromolyn, or leukotriene modifiers also did not differ by sex for children or adults. These results did not change when looking only among patients who were not previously using a controller medication.

DISCUSSION

Age-related sex differences in asthma hospitalization rates have been reported, but whether this reflects differences in prevalence, severity, or treatment has not been established. This study confirms previously reported age-related sex differences in hospitalized patients. It shows no important sex differences in asthma history, severity of this episode, or response to therapy in children. In contrast, the episodes requiring hospitalization appear to be less severe in women compared to men based on initial PEF and oxygen saturation levels. No important sex differences were found in history of treatment or discharge therapy in either age group. These results suggest that sex prevalence differences in hospitalized asthmatic children are due to the increased prevalence of asthma in boys but are not associated with sex differences in severity or treatment of those hospitalized. However, these data suggest that, along with an increased prevalence of asthma in adult women, increased symptoms in response to a given level of airway obstruction may contribute to the female predominance in asthma hospitalizations.

This study has a number of strengths. It includes a relatively large, randomly chosen sample of hospitalized asthmatic patients, which provides a valid and relatively unique sample to study for sex differences. Because there is geographic diversity, the findings should be generalizable, at least in the United States and to patients receiving care in academic medical centers. In addition, many important aspects of asthma history, acute episode characteristics, and discharge regimens were captured. Finally, because the physicians caring for the patients and the data extractors were not aware of this purpose of the data collection, there should be no substantial observer bias.

This study does have a number of potential limitations. It was hospital based, not population based, although we did find similar gender prevalence ratios to other population-based and ED-based studies. Insufficient blood gas data were available for analysis. However, at the levels found in this study, oxygen saturation is a good reflection of PO_2 ,²⁶ and carbon dioxide retention is uncommon in patients presenting with acute asthma.²⁷ Data on inpatient therapy were not collected in sufficient detail for further analysis. However, there is no reason to expect sex-related differences in acute inpatient therapy; and prior studies^{14,15,28} in the ED found no significant treatment differences. Adults were insured differently by sex, but this difference should not explain the current results. COPD was not specifically excluded or evaluated. However, the age group

Table 1—Demographic Characteristics and Asthma History of Patients Admitted to the Hospital for Acute Asthma, According to Sex*

Variables	Children Aged 2 to 17 yr			Adults Aged 18 to 54 yr		
	Boys (n = 362)	Girls (n = 244)	p Value	Men (n = 215)	Women (n = 465)	p Value
Demographic factors						
Age, yr	7.0 ± 3.8	8.1 ± 4.3	0.002	35.7 ± 9.6	39.4 ± 9.9	> 0.001
Race, %			0.49			0.64
White	39	33		41	43	
African American	38	41		46	42	
Hispanic	17	20		12	13	
Other	7	6		1	3	
Insurance, %			0.81			> 0.001
Private/commercial	19	21		21	18	
Managed care	42	45		21	27	
Medicaid/Medicare	27	22		17	35	
Other insurance	5	4		3	2	
None	7	8		38	18	
Medical history						
Primary care physician	96	95	0.70	70	89	> 0.001
Prior hospital admission for asthma	60	63	0.49	72	74	0.51
Hospital admission for asthma during past year	51	56	0.42	59	62	0.56
Documented medications within past 4 wk						
Systemic corticosteroids	18	19	0.62	25	32	0.08
Inhaled corticosteroids	23	26	0.44	42	45	0.42
Cromolyn	11	9	0.52	0.5	2	0.14
Leukotriene modifier	9	7	0.37	12	11	0.79
Smoking status			0.04			0.39
Never-smoker	97	94		42	42	
Former smoker	0	3		17	22	
Current smoker	3	3		41	36	
Exposure to passive smoke in home	33	37	0.26	3	3	0.66

*Data are presented as mean ± SD or % unless otherwise indicated.

of the current population (2 to 54 years) and similar smoking histories between male and female patients suggest this is not likely to affect the findings. Moreover, data analysis excluding the 12% of patients with International Classification of Diseases, Ninth Revision code-documented concomitant

COPD did not materially affect the findings (data not shown). Finally, indicators of chronic disease severity, other than prior hospitalizations and use of controller medications, were not captured in this study.

There are several possible hypotheses to explain

Table 2—Presentation and Management of Patients Admitted to the Hospital for Acute Asthma*

Variables	Children Aged 2 to 17 yr			Adults Aged 18 to 54 yr		
	Boys (n = 362)	Girls (n = 244)	p Value	Men (n = 215)	Women (n = 465)	p Value
Presentation and ED course						
Duration of symptoms ≤ 24 h	40	38	0.68	37	33	0.25
Given systemic steroids in ED	77	78	0.88	80	75	0.15
Pulmonary index score	6.0 ± 1.8	6.2 ± 1.8	0.38			
Initial peak flow, % predicted				36 ± 16	43 ± 18	< 0.001
Initial oxygen saturation, %	93 (90–96)	92 (89–96)	0.84	93 (90–96)	95 (91–97)	0.002
ED length of stay, h	4.3 ± 2.4	4.5 ± 2.5	0.49	5.1 ± 3.1	5.7 ± 3.5	0.03
Inpatient course						
Admission location			0.34			0.17
Regular medical/surgical unit	72	71		77	76	
Critical care or stepdown unit	24	23		22	20	
Other (eg, observation status)	4	6		1	4	
Hospital length of stay, d	2.8 ± 1.9	3.0 ± 1.7	0.18	3.2 ± 3.0	3.4 ± 3.1	0.62

*Data are presented as %, mean ± SD, or median (IQR) unless otherwise indicated.

the age-related sex differences in asthma hospitalizations. First, it may be just a reflection of overall age-related disease prevalence—*ie*, among those with the disease, the proportion of those severe enough to be hospitalized does not differ between male and female patients. Several articles^{3,12,13,17,21,23} have reported the prevalence of asthma to be greater in male patients < 15 of age and female patients > 15 years of age. In addition, bronchial hyperresponsiveness has been reported to be more frequent in women than men.^{29–31} Our large study²² of sex differences in asthmatic patients showed female-to-male ratios of 35:65 for ages 2 to 13 years and 65:35 ages 23 to 64 years. These results are similar to the age-related sex ratios found in the current cohort. This supports the hypothesis that sex differences in baseline prevalence explain the sex-based hospitalization rate differences. However, this study explored two other potential factors that could contribute to these differences: sex differences in asthma severity or treatment.

Data from this study do not show any sex-related severity differences in children. Similarly, data from other studies have not shown sex differences in hospitalization rate in children, adjusting for prevalence²² or sex-related severity differences in children presenting to EDs with acute asthma.²⁸

In contrast, our prior study²² found an increased hospitalization rate in women, even after accounting for prevalence and adjusting for prior utilization and inhaled steroid treatment. The current data show that even though more adult inpatients with asthma were women than men, the women on average had less severe episodes, based on initial PEF and oxygen saturation. These data suggest that women may experience increased symptoms and distress in re-

sponse to a given level of reduced pulmonary function compared to men. Several other studies support this hypothesis as well. In a study¹¹ of patients aged 18 to 54 years presenting to the ED with moderate-to-severe exacerbations, women were more likely to report “severe” complaints in terms of symptom frequency, intensity, and activity limitation, but men had a lower average percentage of predicted PEF. In a cohort of patients with physician-diagnosed asthma in an health maintenance organization, women had increased symptoms and decreased quality of life but demonstrated a higher mean FEV₁ than men.³² Finally, among 967 asthmatic patients > 16 years old recruited from general practice in the Netherlands, women reported poorer quality of life but had higher levels of pulmonary function.³³ The current data suggest that this increased symptomatic response to airway obstruction may contribute to the sex difference in adult asthma hospitalizations but does not lead to a sex difference in length of stay, confirming the results of other studies.^{16,20,22}

Another theoretical explanation for differential hospitalization rates in male vs female patients could be sex-related treatment differences. However, no evidence for sex differences in prehospital treatment regimens was observed in this study for children or adults. A study³⁴ also found no sex difference in the use of optimal inhaled steroid therapy in a managed-care population of children and adults. The proportion of patients discharged with an action plan, a follow-up appointment, or receiving controller medication was disappointingly low (Table 3) but did not differ by sex.

In summary, this study confirms the male predominance among hospitalized asthmatic children and the female predominance in adults. It suggests that

Table 3—Discharge Treatment for Patients Admitted to the Hospital for Acute Asthma*

Variables	Children Aged 2 to 17 yr			Adults Aged 18 to 54 yr		
	Boys (n = 362)	Girls (n = 244)	p Value	Men (n = 215)	Women (n = 465)	p Value
Received asthma action plan	57	54	0.44	34	40	0.16
Follow-up appointment made before discharge	44	53	0.04	46	48	0.67
Discharge medications						
Systemic corticosteroids	88	88	0.92	86	84	0.57
Inhaled corticosteroids	57	58	0.70	69	64	0.18
Cromolyn	8	8	0.83	1	2	0.43
Leukotriene modifier	15	13	0.50	19	15	0.21
Discharge medications if not receiving controller medications before hospital admission†						
Systemic corticosteroids	86	89	0.36	81	80	0.85
Inhaled corticosteroids	47	46	0.90	55	53	0.73
Cromolyn	4	4	0.89	0	0.4	0.48
Leukotriene modifier	7	7	0.79	6	4	0.46

*Data are presented as % unless otherwise indicated.

†Include inhaled corticosteroids, cromolyn, and leukotriene modifiers during the 4 weeks prior to hospital admission.

in children, this is due to the increased disease prevalence in boys, rather than due to sex-based differences in inherent severity or treatment. In contrast, the current and prior data suggest that increased symptomatic distress in response to a given level of airway obstruction may contribute to the increased proportion of women vs men who are hospitalized for asthma. Further studies will be necessary to define the mechanism of this observation.

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