

Multicenter Study of Clinical Features of Sudden-Onset Versus Slower-Onset Asthma Exacerbations Requiring Hospitalization

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BACKGROUND: Asthma exacerbations differ in their speed of symptom onset. **OBJECTIVE:** To characterize and compare demographic factors, clinical risk factors, and clinical outcomes among hospitalized patients who presented with sudden-onset (≤ 3 h) versus slower-onset asthma exacerbations, across a wide age range. **METHODS:** We reviewed the medical records of a random sample of 1,294 patients, ages 2–54 years, admitted in 30 United States hospitals, for acute asthma from January 1999 to May 2000. **RESULTS:** Data on duration of symptoms were available for 1,260 (97%) of the patients. Seventy-two patients (6%) had sudden-onset exacerbations. Sudden-onset patients were older than slower-onset patients (30 y vs 19 y, $p = 0.03$) but did not differ by other sociodemographic characteristics. Markers of chronic asthma severity were similar between the groups. The sudden-onset patients were more likely to present to the emergency department between midnight and 8:00 AM, to require intubation, and to be admitted to the intensive care unit (all $p < 0.01$). The higher risk of intensive care unit admission remained significant even after adjustment for 6 potential confounders (odds ratio 2.5, 95% confidence interval 1.3–4.9). However, hospital stay was shorter in the sudden-onset patients (2.0 d vs 2.7 d, $p = 0.01$). There was no difference in peak expiratory flow at hospital discharge. **CONCLUSIONS:** The sudden-onset patients were older and they more commonly presented to the emergency department between midnight and 8:00 AM with severe exacerbations that required intubation and intensive care unit admission. However, the sudden-onset group was discharged from the hospital earlier. *Key words:* sudden-onset asthma, emergency department, intensive care unit, intubation. [Respir Care 2007;52(8):1013–1020. © 2007 Daedalus Enterprises]

Introduction

Asthma is a chronic inflammatory airway disease that has been on the rise over the last several decades and is a major health problem in the United States. Race/ethnicity, sex, genetics, and socioeconomic factors have been implicated to explain worsening asthma symptoms.^{1–8}

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Prior studies have found 2 main variations in presentation of asthma exacerbations to the emergency department (ED): sudden-onset and slower-onset.^{9–13} Sudden-onset exacerbations have been identified as a separate clinical syndrome, characterized by severe airflow obstruction within 1–3 hours of symptom onset. Barr et al⁹ reported that ED visits for sudden-onset exacerbations were distinctly associated with exposure to respiratory allergens and/or tobacco smoke, exercise, and psychological stress. Compared to patients with slower-onset exacerbations, those with sudden-onset exacerbations showed trends toward less ED treatment with medications, fewer hospitalizations, shorter stay for those hospitalized, higher final mean peak expiratory flow (PEF), and higher absolute percentage change in PEF with treatment, though only adults were included in that study.⁹ Emerman et al found that slower-onset exacerbations (eg, duration of symptoms 1–7 d) are more likely to result in relapse than are exacerbations that last less than 1 day.⁵ Further evidence of the heterogeneity of asthma exacerbations is derived from findings of lower eosinophil counts and higher neutrophil counts in airway

submucosae of patients who died of sudden-onset exacerbations, as well as inverted CD4:CD8 ratio.^{14,15}

Though there are notable clinical and physiologic differences between the sudden-onset and slower-onset groups, prior studies have examined relatively small samples and limited age ranges (eg, older children and adults). The objective of the current analysis was to characterize and compare demographic factors, clinical risk factors, and clinical outcomes from more than 1,200 hospitalized patients who presented with either sudden-onset or slower-onset asthma exacerbations, across a wide age range.

Methods

In this retrospective study we collected data from the period January 1999 to May 2000, as part of the University HealthSystem Consortium Asthma Clinical Benchmarking Project. Using a standard protocol, investigators at 30 University HealthSystem Consortium hospitals in 22 states performed data abstraction from randomly identified charts to collect information about patients admitted to the hospital for acute asthma. Exclusion criteria included cystic fibrosis, leaving against medical advice, transfer from another hospital or ED, and repeated admissions of individual subjects. Inclusion criteria were: physician diagnosis of acute asthma, hospital admission for acute asthma, and age 2–54 years. Of the total 1,318 cases, 24 were excluded because they did not meet the inclusion criteria, yielding a total of 606 children (ages 2–17 y) and 688 adults (ages 18–54 y), or a total of 1,294 patients. The institutional review board at each of the 30 participating hospitals approved the study.

Data Collection

Data were collected on patient demographics, medical history, emergency and in-patient course, and discharge plan. All data were submitted to University HealthSystem Consortium via online data entry. Location of initial patient assessment was recorded as either “ED only,” “office/clinic only,” “office/clinic then ED,” “ED then office/clinic,” “other,” or “not recorded.” To determine the timing of symptom onset, patient responses to the following question were collected: “When did the current asthma attack begin: ≤ 3 hours ago, 4–12 hours ago, 13–23 hours ago, 1–3 days ago, 4–7 days ago, ≥ 8 days ago, unknown?” Duration of symptoms, defined as the time between symptom onset and pre-admission assessment, was the main factor of interest, and was classified into 2 groups: sudden-onset (≤ 3 h) and slower-onset (> 3 h). Demographic characteristics included age, sex, insurance status, race, living situation, and residential ZIP code.

Medical history included the patient’s primary care providers, history of hospitalizations for asthma, past and current medications, and comorbid conditions. Smoking status was

assigned as follows: never smoker, ex-smoker, current smoker, and exposure to passive smoke in the home.

The ED and in-patient course section assessed the patient’s in-hospital asthma management. In adults, initial PEF was expressed as percent of predicted, based on race, age, sex, and height.¹⁶ If height was not known, it was imputed by best subset regression, based on age, sex, race, and weight. In children, a pulmonary index score, ranging from 0 (least severe) to 12 (most severe), was created, with the following factors: respiratory rate, wheezing assessment, inspiratory-expiratory ratio, and accessory muscle use.¹⁷ Any single missing value was imputed by best subset regression, based on the values of the 3 remaining factors; thus, the final pulmonary index scores could contain (at most) one imputed factor.

Statistical Analysis

All analyses (Stata 9.0, StataCorp, College Station, Texas) are presented as either proportions with 95% confidence intervals (CIs), ratios with 95% CI, or means with standard deviations. The association between duration of symptoms and other factors was examined with chi-square tests, Student’s *t* tests, binomial tests of proportions, and Wilcoxon rank tests, where appropriate. Each factor was assessed for inclusion in the multivariate model if the factor was considered clinically important or was found to be a significant predictor in univariate analysis with a *p* value ≤ 0.10. Odds ratio (OR) values are presented with 95% CI. A 2-tailed *p* < 0.05 was considered statistically significant.

Results

Demographics

Among the 1,294 patients, 1,260 (97%) had data available on duration of symptoms: 72 (6%, 95% CI 4–7) presented with sudden-onset exacerbations, and 1,188 (94%) had slower-onset exacerbations. Seventy-nine percent of the patients received pre-admission assessment in the ED. The other pre-admission assessment locations were office/clinic only (12%), office/clinic then ED (7%), and other (2%). Sudden-onset exacerbations were more common among adults than among children (Fig. 1), but other sociodemographic factors did not differ between the 2 groups (Table 1). Sociodemographic factors were similar between the sudden-onset and slower-onset patients when looking only at children (< 18 y) and only at adults (age 18–54 y) in the 2 groups (data not shown). When analyses performed with imputed PEF or pulmonary index scores were compared to those with complete data sets, there were no material differences (data not shown).

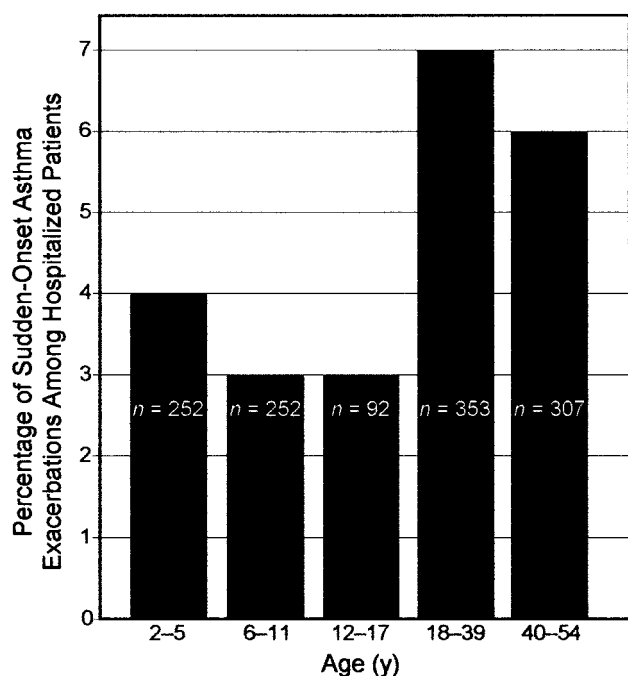


Fig. 1. Percentage of sudden-onset asthma exacerbations among hospitalized patients, by age group. The *n* values are the number of patients in each age group.

Chronic Asthma Severity

As seen in Table 2, markers of chronic asthma severity (eg, asthma admissions, recent medications) were comparable between the sudden-onset and slower-onset patients. Over half of the patients (675, 53%) had a concomitant medical disorder. The presence of a concomitant medical disorder was similar between the sudden-onset and slower-onset patients. Hypertension was significantly more common (14% vs 6%, $p = 0.01$) in the sudden-onset group. Other concomitant medical disorders were not appreciably different between the 2 groups, including allergies, chronic obstructive pulmonary disease, obesity, gastroesophageal reflux disease, pneumonia, illicit inhalation drug use, psychiatric disorder, presence of respiratory syncytial virus, sinusitis, congestive heart failure, and other chronic lung disease (Table 3). When assessing the children and adults separately, the presence of concomitant medical disorders remained similar in the sudden-onset and slower-onset groups: adults 73% vs 65%, $p = 0.25$, and children 38% vs 41%, $p = 0.77$. Smoking status also was similar between the sudden-onset and slower-onset groups. In multivariate analysis, controlling for sex, race/ethnicity, and concomitant medical disorder, age was significantly associated with sudden-onset exacerbation: with the 2–11-year-old group as the reference group, age 12–17 years group OR 0.9, 95% CI 0.2–3.0; age 18–54 years group OR 2.1, 95% CI 1.2–3.7.

Acute Asthma Severity

The sudden-onset patients were more likely to present to the ED between midnight and 8:00 AM than were the slower-onset patients (see Table 2). Prior to admission, 33 (3%) patients were intubated; among these, the sudden-onset patients were more likely to require intubation (14% vs 2%, $p < 0.001$). The sudden-onset patients were also more likely to present to the ED with more severe wheezing. In the ED, there was a trend toward greater administration of inhaled and systemic corticosteroids in the slower-onset patients. There were no significant differences in frequency of accessory muscle use, initial respiratory rate, PEF, median pulmonary index score, or oxygen saturation between the 2 groups.

In-Patient Course

The sudden-onset patients were 3 times as likely to be admitted to the intensive care unit (ICU) than were the slower-onset patients (OR 3.1, 95% CI 1.9–5.0, $p < 0.001$). Even after adjustment for 6 potential confounders (age, sex, race/ethnicity, history of hospital admission for asthma, present concomitant medical disorders, and smoking status), the sudden-onset patients remained significantly more likely to be admitted to the ICU (OR 2.5, 95% CI 1.3–4.9, $p = 0.007$). However, despite the higher ICU admission rate, hospital stay was 0.7 days shorter in the sudden-onset patients. There was no difference in PEF at hospital discharge between the 2 groups.

Discussion

To better understand patients with sudden-onset asthma exacerbations, we analyzed data from 1,260 patients admitted for acute asthma at 30 hospitals. The main findings from this retrospective cohort study are that the sudden-onset patients (1) were older but otherwise sociodemographically similar, (2) were more likely to present between midnight and 8:00 AM, (3) were more often intubated, (4) had a higher rate of ICU admission, and (5) had shorter hospital stay. These findings are similar to those of prior studies, in that they confirm the existence of 2 distinct categories of acute asthma that require hospitalization.^{9–13,18–24} In prior studies, different authors have used different definitions of “sudden onset”; the times between symptom onset and physician presentation have ranged roughly between 30 min and 6 hours.^{18,19,21} We used an intermediate cutoff of 3 hours. Sudden-onset patients composed 6% of our cohort, which is slightly less than the 8.5% found by Kolbe et al.¹⁸ Other studies found a male predominance in the most severe acute asthma,^{10,13,22} whereas we found no significant difference in the number of male and female patients in the sudden-onset and slower-onset groups. However, in accordance with Schatz et al,²⁵ an overall pre-

SUDDEN-ONSET VERSUS SLOWER-ONSET ASTHMA EXACERBATIONS

Table 1. Demographic Characteristics of Patients Hospitalized for Asthma Exacerbations

	Sudden-Onset Exacerbation (≤ 3 h) (n = 72)	Slower-Onset Exacerbation (> 3 h) (n = 1,188)	P
Median age (y) (IQR)	30 (11–44)	19 (7–39)	0.03
Female (%)	63	55	0.19
Race/ethnicity (%)			0.08
White	40	39	
Black	44	41	
Hispanic	7	16	
Asian	8	4	
Estimated median household income (US\$) (IQR)	32,252 (27,574–45,569)	35,750 (26,441–44,365)	0.78
Insurance (%)			0.25
Private/commercial	12	20	
Managed care (HMO/Medicare/Medicaid)	40	34	
Public (Medicare/Medicaid)	23	27	
Other	2	4	
None	23	16	
Has primary care provider (%)	86	89	0.44

IQR = interquartile range
 US = United States
 HMO = health-maintenance organization

dominance of females was seen, which suggests that females may be more symptomatically sensitive to a given drop in pulmonary function than are males. This possibility is supported by Turner and colleagues,²⁶ who found that, among patients admitted for near-fatal asthma, males displayed a higher degree of impairment in sensation of dyspnea.

Age was significantly associated with sudden-onset asthma in our multivariate analysis. Previous studies have had mixed results: many examined either adults or children, and found no difference in age between sudden-onset and slower-onset patients,^{9,13,27} whereas others found a younger age in adults¹⁰ or older age among children^{19,21} with sudden-onset asthma. Our study examined patients with a wider age range, though the minimum and maximum ages in our cohort were selected to reduce overlap with non-asthma conditions and chronic obstructive conditions, respectively. When analyzed separately in our study, children (< 18 y, 47% of the total subjects) and adults (18–54 y, 53% of the total subjects) showed similar occurrences of sudden-onset and slower-onset asthma, in concordance with prior studies.^{9,13,27} The fact that slower-onset patients tended to be younger may suggest a greater tendency of symptoms to progress more rapidly in older patients, due to differences in airway pathophysiology, such as hypersensitivity reactions, which may increase with age. Various authors have described differences in immunohistologic features of sudden-onset and slower-onset asthma, such as airway-related local neutrophil and eosinophil concentrations, mucus gland area, and CD8 lymphocyte numbers.^{14,15,28} Furthermore, genetic factors such as

β-agonist receptor genotypes have been implicated to explain possible differential presentations of acute asthma exacerbations,^{2,3} particularly among black patients.¹ It is conceivable that at certain ages, genetically driven cellular and organ derangement may become manifest as sudden-onset or slower-onset asthma exacerbations, when combined with the correct environmental factors. Thus, the aging process may have direct relevance to the development of sudden-onset or slower-onset asthma, and further investigation is needed to examine this issue.

In this cohort, both sudden-onset and slower-onset patients had similar use of inhaled β agonists (both short-acting and long-acting), inhaled corticosteroids, and systemic corticosteroids prior to admission. Approximately 70% of the patients had used β agonists prior to their asthma hospitalization, of whom 39% were white, 41% black, 15% Hispanic, and 4% other race/ethnicity, which is similar to prior studies.²⁹ This relatively high access to medications argues against gross medication noncompliance to explain sudden presentation to the ED and hospital admission. Verification of appropriate β agonist inhaler technique, daily use statistics, and documentation of differential access to β agonists, compared with inhaled corticosteroids, were not available and might have contributed to the results. Most studies, but not all, have not found an increased risk of severe asthma exacerbation among users of currently available β agonists, after carefully controlling for baseline asthma severity.^{9,30–33} Furthermore, though the number of nighttime ED presentations by sudden-onset patients was higher than among the slower-on-

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Table 2. Chronic and Acute Asthma Characteristics of Patients Hospitalized for Asthma Exacerbations

	Sudden-Onset Exacerbation (≤ 3 h) (n = 72)	Slower-Onset Exacerbation (> 3 h) (n = 1,188)	P
Chronic Asthma (%)			
Ever admitted for asthma	68	68	0.98
Admitted for asthma during past year	59	57	0.88
Medication Use During Preceding 4 Weeks (%)			
Short-acting β agonists	67	71	0.40
Long-acting β agonists	19	14	0.21
Inhaled corticosteroids	36	35	0.79
Systemic steroids	22	24	0.76
Present Concomitant Medical Disorder (%)	63	53	0.12
Smoking Status (%)			
Never smoker	62	63	
Former smoker	10	13	
Current smoker	29	24	
Acute Asthma (%)			
ED triage time between midnight and 8:00 AM	38	23	0.006
Intubation in the ED	14	2	< 0.001
Wheezing (%)			
None	9	6	0.001
End-expiration	11	19	
Entire expiration	30	36	
Inspiration/expiration	28	16	
Inspiration/expiration without stethoscope	8	1	
No air entry	13	22	
Accessory Muscle Use (%)			
None	28	33	0.49
+	31	30	
++	23	26	
++++	18	10	
Initial Respiratory Rate (median and IQR breaths/min)	28 (24–38)	28 (24–36)	0.66
Initial Peak Flow (median and IQR % predicted)	36 (26–52)	38 (28–51)	0.82
Pulmonary Index Score (median and IQR)	6 (5–7)	6 (5–7)	0.86
Initial Oxygen Saturation (median and IQR %)	95 (92–98)	94 (91–97)	0.30
Medications Administered in ED, Clinic, or Office Prior to Admission (%)			
Inhaled corticosteroids	6	10	0.15
Systemic steroids	76	78	0.81
Inhaled β agonists	86	90	0.33
Intubation in the ED	14	2	< 0.001
Medications Administered During In-Patient Stay (%)			
Inhaled corticosteroids	26	39	0.03
Systemic steroids	85	93	0.02
Inhaled β agonists	99	93	0.08

ED = emergency department
IQR = interquartile range

set patients, the ED medical treatment (excluding intubation) was similar between the 2 groups, which is a finding also seen in other studies.³⁴ Taken together, these results support that sudden-onset asthma exacerbations are a distinct asthma presentation that cannot be explained solely by differences in short-term or long-term medication use.

The sudden-onset group had a much higher risk of intubation. The most likely contributors to this higher risk are the time of patient arrival to the ED and the presence of clinical wheezing or absence of air entry on examination, all of which may have raised the physician's concern about rapidly progressing symptoms at a time of day when physician staffing

SUDDEN-ONSET VERSUS SLOWER-ONSET ASTHMA EXACERBATIONS

Table 3. Comorbid Conditions of Patients Hospitalized for Asthma Exacerbations

	Sudden-Onset Exacerbation (≤ 3 h) (n = 72) (%)	Slower-Onset Exacerbation (> 3 h) (n = 1,188) (%)	p
Concomitant medical disorder present	63	53	0.12
Allergies	22	19	0.50
Bronchiolitis	10	6	0.46
Congestive heart failure	4	2	0.53
COPD	16	12	0.46
GERD	10	6	0.19
Hypertension	14	6	0.01
Illicit inhalation drug use	6	8	0.63
Obesity	11	14	0.49
Pneumonia	7	10	0.44
Psychiatric disorder	6	6	0.86
Respiratory syncytial virus	5	2	0.31
Sinusitis	4	4	0.93
Other chronic lung diseases	3	5	0.48

COPD = chronic obstructive pulmonary disease
GERD = gastroesophageal reflux disease

is relatively low and diurnal disease severity is known to be high. With regard to wheezing, this clinical examination variable must be viewed with caution, as there is no standardized method of grading severity of wheezing, so the assessment is quite operator-dependent. Furthermore, asthma, which is an obstructive pulmonary disease, is primarily characterized by wheezing during exhalation; similar findings during inhalation are problematic, because they may in some cases represent stridor due to non-asthma conditions such as vocal cord dysfunction.³⁵⁻⁴⁰ Thus, one must be cognizant of the fact that a host of respiratory and nonrespiratory conditions (eg, other obstructive pulmonary disorders, congestive heart failure) may have overlapping clinical features with asthma that may complicate diagnosis of asthma and subsequent therapeutic approaches. The impact of comorbidities is thus an important clinical consideration in both diagnosis and medical management.

Regarding diurnal disease severity and its impact on intubation rate, it may be that the sudden-onset patients actually possess an exaggerated fluctuation in lung function and symptoms that is particularly salient at night, leading to a more intensive therapeutic regimen at that time. Future studies could track PEF values and symptoms at regular intervals before, during, and following asthma exacerbations that require hospitalization, to identify changes in the degree of diurnal variation. The presence of comorbid conditions may have influenced the decision to intubate as well; concurrent active medical problems may act as catalysts in worsening an existing asthma disease

process and/or prolong subsequent recovery, compared to those without such complicating factors.

At the same time, however, it is important to recognize that disease acceleration and clinical decline may be paroxysmal and unpredictable in sudden-onset patients, especially given known alterations in nocturnal responses to hypoxemia and hypercapnia. As noted previously by Kikuchi et al,⁴¹ patients with asthma (and particularly those with a history of “near-fatal” asthma attacks) showed evidence of reduced hypoxic chemosensitivity and perception of dyspnea, so sudden-onset patients may be less likely to detect progressive adverse changes in lung function, and therefore they seek medical attention later, at a more critical level of lung function.²⁵ Symptoms in these patients may appear “sudden” because the time between ultimate symptom onset and the need for medical attention is markedly less than among patients who are better able to recognize a decline in lung function.

Hospital admission was strongly favored toward the ICU in the sudden-onset group, whereas the slower-onset group was more likely to be cared for on the medical service. The higher rate of intubation in the sudden-onset patients, which is clearly a contributor to ICU admission, may be related to differences in relative nighttime insensitivity to hypoxemia and/or hypercapnia, as suggested by Brenner et al.³⁴ Furthermore, Wasserfallen et al¹⁰ found that acutely presenting patients with rapid deterioration (their “group I”), when compared with more slowly progressive respiratory failure, showed a higher intubation rate but better resolution of carbon dioxide abnormalities and shorter duration of mechanical ventilation (mean 34 h vs 91 h), which suggests a different pathophysiologic process in rapid-onset patients, such as heightened sensitivity to airway smooth-muscle contraction. However, Brenner et al³⁴ found that, though the number of nighttime ED presentations and nighttime intubation rate was higher in sudden-onset patients, the hospital admission rate was the same between nighttime and daytime presentation. Thus, the hour of presentation to the ED and intubation rate cannot completely explain the higher hospital admission rate among sudden-onset patients. In this light, especially given the initial similarity in PEF and medication use at presentation to the ED, it is difficult to ignore the importance of comorbid conditions in the decision tree toward ICU admission and intubation. In fact, Weber et al found that severity of chronic illness was independently associated with hospitalization for acute asthma.⁴²

We must also recognize that practice within and between EDs may differ widely, which may have affected our results. Though wheezing is often a subjective finding and inhaled corticosteroids are not a mainstay of treatment of acute asthma attacks, the observation that sudden-onset patients were more likely to present with severe wheezing but less likely to receive inhaled or systemic corticosteroids during their stay suggests that practice variations may have influenced our

findings. Accordingly, one hypothesis for the shorter stay among sudden-onset patients is that these patients were overcautiously triaged to the ICU (and/or intubated) by ED practitioners, compared to slower-onset patients, when in fact their courses of illness may have been more parallel. In support of this theory, Roberts et al⁴³ found that in pediatric patients admitted to the ICU with severe asthma exacerbations, the decision to intubate, as well as subsequent ICU stay and hospital stay, were largely dependent on the institution's overall usage pattern of mechanical ventilation. When compared to "higher-use" centers (in which > 20% of all asthmatic patients admitted to the pediatric ICU were intubated), "lower-use" centers (< 20% intubation rate among all pediatric ICU asthmatics) had significantly less use of mechanical ventilation (12% vs 27%). The lower-use centers also had shorter ICU stay and hospital stay (regardless of the need for mechanical ventilation), despite similar physiologic measures of illness. That acknowledged, others¹⁸ have found that the higher rate of repeated ICU admissions for severe life-threatening asthma in sudden-onset patients suggests that they are in fact a distinct subgroup, rather than merely one end of a spectrum of disease. Future studies should determine the effects of practice variation on outcomes in sudden-onset versus slower-onset asthma exacerbations.

Regarding hospital discharge, in concordance with the findings of Barr et al,⁹ we found a 0.7-day shorter hospital stay in the sudden-onset group. Without further information on ICU stay or ventilator-free days, however, it is difficult to comment on the impact of intensive care on resolution of an asthma exacerbation and hospital discharge. It seems plausible, however, that with the ICU level of care, the shorter stay might be more related to intensity of multisystem care (including respiratory care), and less related to singular differences in asthma pathophysiology and consequent responsiveness to treatment per se.

The present study has several potential limitations. A prospective study with clear questioning of patients regarding specific symptoms and clinical stability of comorbid conditions would be important to differentiate the validity of a true asthmatic condition from a comorbid state that mimics asthma or complicates a true asthma process. It also would be useful to have a standardized measurement strategy for wheezing (eg, quadrant localizing, gradation on a severity scale). In addition, more objective data regarding lung function (eg, PEF values) and symptoms before, during, and following exacerbations that require hospitalization would be useful to address the degree of fluctuating diurnal features in sudden-onset and slower-onset groups. The influence of comorbidities could be further assessed with information on typical ICU scoring systems (eg, Multiple Organ Dysfunction Score, Acute Physiology and Chronic Health Evaluation scores), ICU stay, and ventilator-free days, which are useful in trials involving patients who require ICU care. More detailed

questioning of patients and objective information regarding onset of asthma symptoms (such as was done by Kolbe et al¹⁸) would be useful to create a clearer temporal demarcation between sudden-onset and slower-onset patients. Furthermore, it would have been advantageous to have had assessments of characteristics that are associated with either sudden-onset (eg, respiratory allergen triggers) or slower-onset asthma (eg, triggers of upper respiratory infection).^{11,44} During ED treatment and subsequent hospitalization, the initial diagnostic criteria and therapeutic approach should be standardized according to a protocol to minimize practice variation,

Regarding the cohort in the present study, our analysis was performed as part of a study on the management of patients with asthma exacerbations that required hospitalization. Although the cohort included more than 1,200 patients, the relatively small number of sudden-onset patients may have limited our ability to detect differences in certain characteristics between sudden-onset and slower-onset exacerbations. Additionally, we were interested in whether similar analyses that focused only on children or only on adults had produced findings similar to the entire cohort of both children and adults, but our relatively small sample size prevented us from examining these groups effectively. Thus, a larger sample size would be advantageous in future work on age-specific characteristics of sudden-onset asthma exacerbations.

Conclusions

This retrospective analysis of 1,260 children and adults hospitalized for asthma exacerbations found that sudden-onset patients were older than those with slower-onset exacerbations. Clinically, more sudden-onset patients presented to the ED between midnight and 8:00 AM, were intubated, and were subsequently admitted to the ICU, but they were discharged from the hospital earlier than the slower-onset patients.

Future studies should clarify the impact of comorbidities, diurnal disease severity variation, and practice variation on the identification, treatment, and clinical outcome of sudden-onset and slower-onset exacerbations. In addition, there should be investigation of the roles of genetic and pathophysiologic profiles of sudden-onset exacerbations in children and adults to explain the observed differences in clinical outcomes.

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