

PEDIATRIC ASTHMA

Factors Associated with the Development of Severe Asthma Exacerbations in Children

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Background. Asthma exacerbations are one of the most common causes of hospitalization in children and account for approximately 10,000 intensive care unit (ICU) admissions per year in the United States. Despite the prevalence of this disease in children, the factors associated with the development of these severe exacerbations are largely unknown. **Methods.** A retrospective case–control study was conducted involving all eligible children admitted to the hospital with asthma for a 1-year period. Potential associated factors and outcomes of children admitted to the ICU with a severe exacerbation (cases) were compared to those of children with acute asthma admitted to the ward (controls). **Results.** A total of 188 children were hospitalized with asthma during the study period, 57 (30%) of whom required admission to the ICU. There were no differences in age, gender, or race between cases and controls. Children admitted to the ICU were significantly more likely to have an allergy or irritant-triggered exacerbation than children admitted to the ward (OR 3.9; 95% CI 1.9–8.2; $p = .0003$). Additionally, children in the ICU had a significantly shorter duration of illness before being admitted to the hospital compared to those admitted to the ward (1.7 ± 2.3 vs. 3.4 ± 4.8 days; $p = .002$). **Conclusions.** In this retrospective review, severe asthma exacerbations in children are associated with a more rapid onset of symptoms and are more likely to be associated with allergens or irritants, supporting the importance of atopy in this population.

Keywords allergen, asthma exacerbation, atopy, children, intensive care unit

INTRODUCTION

Severe asthma exacerbations are one of the most common causes of critical illness in children, accounting for approximately 10,000 intensive care unit (ICU) admissions per year in the United States (1–6). Although the prevalence of this disease is high in children, the risk factors for the development of severe asthma exacerbations are not well established (1–6).

In adults, a number of studies exploring the factors associated with severe asthma exacerbations have helped guide clinicians in the management of patients at risk for these attacks. Severe exacerbations have been associated with increased asthma medication use, moderate-to-severe asthma severity, a previous history of mechanical ventilation, and previous admissions to the hospital and/or ICU (2, 3, 7–9). However, the factors associated with the development of severe asthma exacerbations in children have not been well examined.

We conducted a retrospective case–control analysis in order to investigate the factors associated with the development of severe asthma exacerbations in children. Our hypothesis was that there are allergic or environmental triggers associated with the development of these near-fatal attacks in this population. Expanding our current knowledge of these associations may offer

valuable insight into the prevention of severe asthma exacerbations in children.

METHODS

This retrospective case–control study was conducted at Connecticut Children's Medical Center and involved children admitted to the hospital with asthma between July 2008 and June 2009. Potential associated factors and outcomes of children with a severe asthma exacerbation requiring admission to the ICU (cases) were compared to children with acute asthma admitted to the ward (controls). A severe asthma exacerbation was defined as one requiring admission to the ICU. This study was approved by Connecticut Children's Institutional Review Board and informed consent was waived due to its retrospective nature.

At the study institution, hospital admission guidelines for acute asthma are based on a patient's Modified Pulmonary Index Score (MPIS). The MPIS is an adapted form of the Pulmonary Index (10), with additional components of room air oxygen saturation and heart rate, and adjustment of heart rate and respiratory rate for patient age (11). This pediatric asthma severity of illness score contains six categories for evaluation, which are scored from 0 to 3, resulting in a total score of 0–18 (Table 1) (11). The MPIS has been found to be highly reproducible across groups of healthcare professionals, as evidenced by high degrees of interrater reliability among physicians, nurses, and respiratory therapists (physician to nurse: $r = 0.98$; 95% confidence interval [CI] > 0.96 ; physician to respiratory therapist: $r = 0.95$; 95%

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TABLE 1.—The Modified Pulmonary Index Score.

Category	Score			
	0	1	2	3
Oxygen saturation (%)	>95	93–95	90–92	<90
Accessory muscle use	None	Mild	Moderate	Severe
Inhalation–exhalation ratio	2:1	1:1	1:2	1:3
Wheezing	None	End expiratory	Inspiratory and expiratory wheeze, good aeration	Inspiratory and expiratory wheeze, decreased aeration
Heart rate (per min)				
<3 years old	<120	120–140	141–160	>160
≥3 years old	<100	100–120	121–140	>140
Respiratory rate (per min)				
<6 years old	≤30	31–45	46–60	>60
≥6 years old	≤20	21–35	36–50	>50

CI > 0.92; nurse to respiratory therapist: $r = 0.94$; 95% CI > 0.90) (11). The MPIS has also been shown to be a valid indicator of severity of illness in children with asthma, as it was found to be highly correlated with clinically relevant outcomes including durations of continuous albuterol and supplemental oxygen, as well as hospital length of stay (11). Children are admitted to our general hospital ward when they have an MPIS greater than or equal to 7 after treatment in the emergency department (ED), or when they require supplemental oxygen therapy to maintain saturation at or above 94%. Patients on the ward can receive up to 20 mg/hour of continuous albuterol. Admission to the ICU requires an MPIS greater than 12 after at least 2 hours of continuous albuterol therapy (20 mg/hour) or an FIO₂ of greater than 40% to keep saturation at or above 94%.

Queries of electronic medical records and admission databases identified patients admitted to the hospital with asthma during the study period. Children aged 2–18 years with an ICD-9 code of 493.0X (extrinsic asthma), 493.1X (intrinsic asthma), and 493.9X (asthma unspecified), including fifth digit subclassifications of 0 (unspecified), 1 (status asthmaticus), and 2 (acute exacerbation), were included in the analysis. Patients with any pulmonary comorbidities including prematurity, bronchopulmonary dysplasia, tracheomalacia, and chronic lung disease were excluded from the study. Data were collected by chart and data review using a standardized extraction tool, and audits for uniformity were performed. Demographic variables of interest included age, gender, race, zip code, and insurance status. Asthma history, controller medications used, and pre-hospitalization duration of illness were ascertained from parent interviews as reported in the medical chart. Asthma severity classification and asthma triggers were determined based on attending notes made by board-certified pulmonologists and intensivists describing physician impression and parental report. Clinical data regarding length of stay, admission MPIS, and duration of oxygen and continuous albuterol therapy were collected as well.

Data were analyzed using SPSS Statistical Software (version 17.0; Chicago, IL, USA). Demographic and

clinical characteristics of the two groups were compared using Student's t -tests or Mann–Whitney U -tests for continuous variables and chi-square tests for categorical variables. Factors associated with severe asthma exacerbations were examined using univariate and multivariate logistic regression analyses. Calculations are presented as mean $\pm$ standard deviation or median and 25–75% interquartile range for continuous variables and as frequencies (%) for categorical variables. Frequencies were rounded to the nearest whole number and p -values of <.05 were considered statistically significant.

RESULTS

A total of 188 children were hospitalized with asthma during the study period, 57 (30%) of whom required admission to the ICU. Six of these patients required intubation for respiratory failure (Figure 1). The mean age of enrolled patients was 8.8 (± 3.7) years and the majority (61%) were male. The demographic characteristics of cases and controls are shown in Table 2. There were no significant differences in age, gender, race, insurance, or asthma severity between the two groups. Children with a severe asthma exacerbation requiring ICU admission were no more likely than controls to have been previously hospitalized or admitted to the ICU for

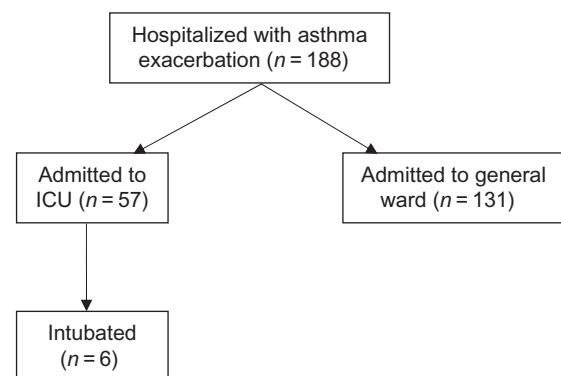


FIGURE 1.—Flowchart of patient population.

TABLE 2.—Demographic characteristics.

	Admitted to ICU (<i>n</i> = 57)	Admitted to ward (<i>n</i> = 131)	<i>P</i> -value	OR (95% CI)
Age (years)	8.8 ± 4.3	8.8 ± 3.4	.95	
Male gender	70% (<i>n</i> = 40)	57% (<i>n</i> = 75)	.11	1.8(0.9 – 3.4)
Race/ethnicity				
Caucasian	36% (<i>n</i> = 20)	34% (<i>n</i> = 45)	.87	1.1(0.6 – 2.0)
African American	21% (<i>n</i> = 12)	25% (<i>n</i> = 33)	.71	0.8(0.4 – 1.7)
Hispanic	25% (<i>n</i> = 14)	31% (<i>n</i> = 40)	.49	0.8(0.4 – 1.5)
Other	18% (<i>n</i> = 10)	10% (<i>n</i> = 13)	.15	1.9(0.8 – 4.7)
Public insurance	57% (<i>n</i> = 31)	68% (<i>n</i> = 86)	.23	0.6(0.3 – 1.2)
Asthma severity ^a				
Intermittent	45% (<i>n</i> = 17)	30% (<i>n</i> = 16)	.23	1.9(0.8 – 4.5)
Mild persistent	5% (<i>n</i> = 2)	21% (<i>n</i> = 11)	.08	0.2(0.04 – 1.0)
Moderate persistent	24% (<i>n</i> = 9)	25% (<i>n</i> = 13)	1.0	1.0(0.4 – 2.5)
Severe persistent	26% (<i>n</i> = 10)	25% (<i>n</i> = 13)	1.0	1.1(0.4 – 2.9)
Previously hospitalized	53% (<i>n</i> = 30)	54% (<i>n</i> = 71)	.87	0.9(0.5 – 1.8)
Previously admitted to ICU	23% (<i>n</i> = 13)	17% (<i>n</i> = 22)	.41	1.5(0.7 – 3.2)
Previously intubated	11% (<i>n</i> = 6)	3% (<i>n</i> = 4)	.07	3.7(1.0 – 13.8)
Controller medications				
Inhaled corticosteroid	67% (<i>n</i> = 38)	47% (<i>n</i> = 62)	.02	2.2(1.1 – 4.3)
Leukotriene receptor antagonist	33% (<i>n</i> = 19)	22% (<i>n</i> = 29)	.14	1.8(0.9 – 3.5)
Received both ICS and LTRA	30% (<i>n</i> = 17)	17% (<i>n</i> = 22)	.07	2.1(1.0 – 4.4)

Notes: ICU, intensive care unit; ICS, inhaled corticosteroids; LTRA, leukotriene receptor antagonist.

^aData not available on all children (*n* = 38 for those admitted to the ICU; *n* = 53 for those admitted to the ward).

asthma. Additionally, cases were not significantly more likely than controls to have been intubated for mechanical ventilation in the past. There were no differences between the two groups concerning leukotriene receptor antagonist (LTRA) usage or the use of both LTRA and inhaled corticosteroids (ICS). However, children with a severe exacerbation were significantly more likely to use ICS than children admitted to the ward (67% vs. 47%; $p = .02$).

Table 3 displays the clinical characteristics and outcomes of study patients. As expected, children with a severe asthma exacerbation had significantly higher MPISs upon admission to the hospital than controls (13 ± 2 vs. 9 ± 3 ; $p < .001$). Children admitted to the ICU also had significantly shorter durations of illness prior to being admitted to the hospital compared to those with a non-severe exacerbation. A Mann–Whitney *U*-test revealed a significant difference in duration of illness between children with a severe exacerbation [1 day (0–2)] and those with a non-severe exacerbation [2 days (1–4)] ($p < .001$).

In our study population, a total of 142 patients identified at least one identifiable trigger for their current exacerbation: 104 patients reported infectious triggers, 20 reported allergic/irritant triggers, and 18 reported both infectious and allergic triggers. In both groups, the majority of exacerbations were reportedly triggered by infectious agents (60% of cases vs. 67% of controls; $p = .41$); however, children with a severe exacerbation were four times more likely than controls to have an exacerbation that was triggered by allergens or environmental irritants (37% of cases vs. 13% of controls; $p < .001$). Furthermore, among all patients, triggers

from infectious agents exceeded allergic or environmental triggers throughout most months of the year. However, during June, July, and August, there were higher proportions of allergic triggers reported compared to infectious ones. The most common allergic or environmental trigger reported for the current exacerbation was a pet (39%), followed by cold weather, pollen, and smoke (30%, 22%, and 9%, respectively). The majority of infectious triggers reported were upper respiratory infections (56%), while less-frequent infectious triggers included pneumonia, sinusitis, and fever (20%, 15%, 9%, respectively).

Asthmatics admitted to the ICU demonstrated significantly longer durations of hospitalization [72 hours (48–144) vs. 42 hours (33–50), $p < .001$], continuous albuterol therapy [27 hours (17–59.5) vs. 10 hours (6–19), $p < .001$], and oxygen use [38 hours (18–99.5) vs. 5.5 hours (0–16), $p < .001$] compared to children admitted to the ward. During most months of admission, equal percentages of patients were admitted to the ICU versus the general ward. However, in August and October, month of admission was weakly associated with the development of a severe exacerbation, as children were more likely to be admitted to the ICU than the ward (OR 9.8; 95% CI 1.1–89.9 in August; OR 2.7; 95% CI 1.2–6.2 in October).

Multivariate analysis was conducted using variables that were significantly associated with severe asthma exacerbations in univariate analyses. Results of multiple logistic regression analyses are shown in Table 4. A model containing duration of current illness, having an exacerbation triggered by an allergen or environmental irritant, admission MPIS, duration of oxygen therapy, and duration of hospitalization was statistically significant [χ^2 (6, *N* = 182) = 141.7, $p < .001$] and correctly

TABLE 3.—Clinical characteristics.

	Admitted to ICU (<i>n</i> = 57)	Admitted to ward (<i>n</i> = 131)	<i>P</i> -value	OR (95% CI)
Admission MPIS	13 ± 2	9 ± 3	<.001	
Triggers for this exacerbation				
Allergen/environmental irritant	37% (<i>n</i> = 21)	13% (<i>n</i> = 17)	<.001	3.9(1.9 – 8.2)
Infection	60% (<i>n</i> = 34)	67% (<i>n</i> = 88)	.41	0.7(0.4 – 1.4)
Duration of current illness (days)	1 (0–2)	2 (1–4)	<.001	
Duration of hospitalization (hours)	72 (48–144)	42 (33–50)	<.001	
Duration of continuous albuterol (hours)	27 (17–59.5)	10 (6–19)	<.001	
Duration of oxygen (hours)	38 (18–99.5)	5.5 (0–16)	<.001	
Month of admission				
January	9% (<i>n</i> = 5)	11% (<i>n</i> = 15)	.80	0.7(0.3 – 2.2)
February	7% (<i>n</i> = 4)	9% (<i>n</i> = 12)	.78	0.7(0.2 – 2.4)
March	9% (<i>n</i> = 5)	8% (<i>n</i> = 11)	1.00	1.0(0.3 – 3.2)
April	9% (<i>n</i> = 5)	11% (<i>n</i> = 14)	.80	0.8(0.3 – 2.3)
May	5% (<i>n</i> = 3)	12% (<i>n</i> = 16)	.19	0.4(0.1 – 1.4)
June	5% (<i>n</i> = 3)	5% (<i>n</i> = 7)	1.00	1.0(0.2 – 4.0)
July	5% (<i>n</i> = 3)	2% (<i>n</i> = 2)	.16	5.6(0.6 – 22.1)
August	7% (<i>n</i> = 4)	1% (<i>n</i> = 1)	.03	9.8(1.1 – 89.9)
September	11% (<i>n</i> = 6)	17% (<i>n</i> = 22)	.37	0.6(0.2 – 1.5)
October	23% (<i>n</i> = 13)	10% (<i>n</i> = 13)	.03	2.7(1.2 – 6.2)
November	4% (<i>n</i> = 2)	6% (<i>n</i> = 8)	.73	0.6(0.1 – 2.7)
December	7% (<i>n</i> = 4)	8% (<i>n</i> = 10)	1.00	0.9(0.3 – 3.0)

Note: MPIS, Modified Pulmonary Index Score.

TABLE 4.—Multivariate logistic regression analysis of factors associated with a severe asthma exacerbation.

	<i>B</i>	SE	Wald	<i>P</i> -value	OR (95% CI)
Duration of current illness (days)	−0.31	0.12	6.98	.01	0.73(0.58 – 0.92)
Allergen/environmental irritant	1.84	0.64	8.24	<.001	6.28(1.79 – 22.00)
Admission MPIS	0.62	0.14	18.22	<.001	1.85(1.39 – 2.45)
Duration of oxygen (hours)	0.07	0.02	11.21	<.001	1.07(1.01 – 1.12)
Duration of hospitalization (hours)	0.02	0.01	6.13	.01	1.02(1.01 – 1.04)
Intercept	−10.40	2.04	26.09	<.001	

Note: MPIS, Modified Pulmonary Index Score.

classified 91% of cases. All factors remained statistically significant in the model, yet the strongest predictor of an ICU admission for a severe exacerbation when controlling for other factors was having an exacerbation triggered by an allergen/irritant, with an OR of 6.3 (95% CI 1.8–22.0).

DISCUSSION

Severe asthma exacerbations are a significant source of morbidity in pediatric asthmatics, yet little is known about the causes or predictors of these attacks (1–6). Identifying factors associated with the development of severe exacerbations is of particular importance, considering the large number of children who suffer from asthma. This retrospective case–control study identified several factors associated with the development of a severe asthma exacerbation requiring admission to the ICU. Specifically, allergic or irritant triggers and a more rapid onset of illness were associated with more severe disease in this population.

Our results are consistent with the finding by Lyell and colleagues (6) that asthmatics admitted to the ICU were more likely to use ICS to control their disease than those with a less severe exacerbation. The authors also reported that these patients were more likely to use long-acting β_2 -agonists, a factor that was not explored in the current study. Lyell speculated that their results may imply a greater severity of asthma in these children. However, this was not substantiated in our data when comparing asthma severity tiers between these two populations. Moreover, the fact that cases were more likely to use ICS indicates that these children may have had more severe or persistent disease which warranted preventive therapy. This would imply that the cases did indeed have more severe baseline asthma than the control group, despite the fact that this was not reflected in our results. Conversely, it may be possible that, for reasons that are not apparent, controls were less likely to have a primary care provider and thus were less likely than cases to obtain controller medications, regardless of need. Clearly, further exploration is needed to better understand these associations.

However, our results also contrast with those of other investigators in the context of asthma severity. Belessis et al. (5) found that children admitted to the ICU with asthma were more likely than those with a less severe exacerbation to have “frequent episodic” or persistent asthma, multiple prior hospital admissions for asthma, an asthma admission in the past year, and three or more presentations to the ED in the past year, which suggest that these patients have a more severe asthma phenotype. Similarly, in Alvarez et al.’s (9) meta-analysis of risk factors associated with near-fatal and fatal asthma in both adults and children, the authors reported that increased use of asthma medications and a history of hospital and/or ICU admissions and mechanical ventilation due to asthma were significant predictors of near-fatal asthma exacerbations. Mitchell and colleagues (7) also found that patients with near-fatal asthma were more likely to report moderate-to-severe asthma and more frequent symptoms than ED control patients with asthma or asthmatic community controls. Additionally, the authors reported that these severe exacerbations were associated with increased night symptoms, increased use of asthma medications, previous hospitalization for asthma, and previous intubation, all presumed markers of disease severity (7). Inconsistent with these previous findings, our data show no differences between cases and controls in terms of previous hospitalizations, ICU admissions, or intubations suggesting that these two groups are more similar in regard to baseline asthma severity than comparison groups in other studies.

Several possibilities exist that may explain the discrepancy between our findings and those of other authors. Both Mitchell and Alvarez defined their cases as patients requiring assisted ventilation, which limited this group to only the most severe exacerbations (7–9). In contrast, our population of cases included all patients admitted to the ICU, including some children who did not require assisted ventilation. Similarly, the control population used for the current study involved children with an acute exacerbation requiring admission to a general hospital ward, while Mitchell and Belessis categorized their control groups as asthmatics visiting the ED (5, 7). Because asthma exacerbations that require an inpatient stay are more serious than those treated in an ambulatory setting, there may have been less difference in asthma severity between our cases and controls than in those of other authors. These inconsistencies in the definitions of cases and controls among studies limit the generalizability of findings and may contribute to the variations in outcomes.

It may also be possible that differences in the ethnic distributions of patients in the current study versus other studies influenced the findings. Our study was made up of a diverse patient population, consisting of 35% Caucasians, 24% African Americans, 29% Hispanics, and 12% other races. While several authors did not describe the racial/ethnic makeup of their populations, thereby restricting our ability to make direct comparisons,

Belessis and colleagues (5) reported that approximately three quarters of their patient population was Caucasian, a factor that may have contributed to the inconsistencies in findings.

In this study, we found that children admitted to the ICU had more indicators of atopy than children in the control group. Cases were four times as likely to have an exacerbation triggered by an allergen or environmental irritant as children admitted to the ward. However, our indicators for atopy were indirect (based on parent report) and only 76% ($n = 142$) of children in our study population had an identifiable trigger for their exacerbation, a limitation that may have biased our results. Despite this, the association found between allergens/irritants and severity of exacerbation in the current study echoes results reported by other authors, highlighting the contribution of atopy in severe asthma (3, 5–7). Belessis and colleagues (5) found that children admitted to the ICU were more likely than controls to be allergic to three or more allergens and to have higher levels of IgE. Similarly, Lyell et al. (6) reported that hay fever was found to be a predictor of near-fatal asthma in children in their study, again suggesting a link between atopy and more severe asthma (6). In Mitchell et al.’s (7) study of both children and adults, the authors found several markers of atopy that were associated with near-fatal asthma, including a history of food allergies, eczema, and life-threatening allergic reaction.

Another finding from the current study was that children admitted to the ICU with a severe exacerbation had significantly shorter durations of their current illness compared to controls, indicating a rapidly progressing attack, which is a common characteristic of exacerbations triggered by allergens or environmental irritants (3). This supports the theory that atopic disease plays a strong role in the development of severe asthma in children. In contrast, other authors who have investigated near-fatal and fatal asthma in adults propose a difference in atopic status based on timing of attack. Restrepo and Sur both report that patients with sudden-onset attacks have more neutrophils and less eosinophils in the airway submucosa compared to those with slower-onset asthma (12, 13). In addition, patients with rapid-onset, near-fatal, and fatal asthma tend to have a greater proportion of neutrophils than eosinophils in the submucosa (12, 13). These authors suggest that different biological mechanisms may be at play in asthmatics with sudden- versus slow-onset disease and that there may be less of an allergic component to the disease in patients with sudden-onset asthma (12, 13). This difference in findings compared to the current study may reflect differences in adult versus pediatric asthma, as asthma in children has been shown to manifest in different ways than asthma in adults. Clearly this relationship between atopy and severe asthma needs to be explored further.

The difference in monthly admission rates between cases and controls was an unexpected finding. In both August and October, there were higher proportions of

children admitted to the ICU with a severe exacerbation, which may suggest the role of seasonal factors. This association was weak ($p = .03$), however, and given the small numbers of children in each group, especially in August, these findings may simply be statistical noise. Nonetheless, Belessis et al. (5) reported a similar pattern, as cases in this study were significantly more likely than controls to be admitted in the autumn (5). Furthermore, in a study examining 2 years of national hospital discharge data, Pendergraft et al. (14) found a peak in the proportion of ICU admissions for asthma in July and August, despite a decline in general hospital admissions for asthma in the summer months, a finding that further supports the role of seasonal factors. Moreover, our finding that a greater proportion of allergic than infectious triggers were reported in June, July, and August additionally suggests seasonal variations in asthma exacerbations. Larger and more long-term studies are needed to evaluate whether there are true associations between severe asthma exacerbations and month of admission and if so, whether these differences in admission are associated with reactions to allergens or irritants related to seasonal factors.

Due to the retrospective nature of the study, we were unable to obtain complete data for all variables. For example, asthma severity could only be ascertained in approximately 50% of our population, a limitation which may have biased our outcome. A comparison of children with and without asthma severity classification suggested that those with unclassified asthma severity may have less severe asthma, as they were significantly less likely than those with classified asthma severity to have been previously hospitalized, admitted to the ICU, and intubated for asthma. However, subgroup analyses were conducted looking only at patients with or without documented asthma severity classification, which did not change the primary outcomes of the study. Other findings involving variables with incomplete data may be inaccurate and suggest erroneous implications. Conducting a parent interview may have revealed more information than was apparent in the medical record. Unfortunately, due to the transient nature of our study population, conducting retrospective phone interviews or mailed surveys was not a feasible approach.

Another limitation of the current study that is characteristic of retrospective reviews is the lack of availability of certain variables of interest. Specifically, it would be valuable to have data on the dose of steroids received by patients in the ICU to compare to those received by patients admitted to the ward, as well as additional information on controller medication use such as long-acting β -agonists. Moreover, because pets were a commonly reported trigger for patients, it would be important to note the location of these exposures—in the patient's own home or elsewhere—as it is imperative that treating clinicians educate patients in avoiding known triggers and having a plan for unavoidable exposures.

A further limitation was that a few of the variables, including infectious asthma triggers, were not based on

objective assessments. Viral studies during this period were inconsistent and therefore the data from patient charts are not reliable regarding viral exposures. These variables were ascertained from the physician notes in the medical chart based on parental report and provider assessment. Relying on more objective measures would strengthen the validity of this study.

CONCLUSIONS

In this retrospective review, we found that allergic or irritant triggers were associated with more severe exacerbations in children with asthma. The onset of these more severe exacerbations was also more rapid, supporting the significance of atopy. Unfortunately, however, due to the retrospective nature of this study, we were unable to determine the actual incidence of atopy in this population. Additional studies are needed to further examine these relationships and to directly examine influence of atopy on more severe disease. Regardless of a child's risk factors, every effort should be made to avoid possible allergic or environmental triggers and to provide the most rapid care, should an exacerbation occur.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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