

Respiratory Failure in Children with Status Asthmaticus: A Review of the VPS Database

Kathleen A. Sala, M.P.H.,¹ Laurie Karamessinis, CCRC,¹ Aaron R. Zucker, M.D.,¹
and Christopher L. Carroll, M.D., M.S.¹

Status asthmaticus is a frequent cause of admission to a pediatric intensive care unit (ICU). Children requiring intubation and mechanical ventilation for respiratory failure during these exacerbations comprise the most severely ill population of this cohort. The purpose of this study was to use a large multicenter database to determine the incidence of respiratory failure in children with acute asthma and to characterize clinical predictors associated with its occurrence. We conducted a retrospective data analysis of pediatric asthmatic patients included in the Virtual PICU Systems (VPS) database between January 2007 and December 2008. Patients requiring mechanical ventilation with cuffed or uncuffed nasotracheal or orotracheal tubes were characterized as having respiratory failure. Three thousand three hundred eighteen children were admitted with status asthmaticus during this study period, of which 201 (6.1%) had respiratory failure. There were no differences in age, male gender, or BMI between those with and those without respiratory failure. However, African-American children were significantly more likely to be intubated for status asthmaticus (OR 1.4; 95% CI 1.0–1.9; $P=0.03$) compared with the children of other races/ethnicities. Children with respiratory failure had significantly longer ICU lengths of stay, higher pediatric index of mortality (PIM2) scores, and higher pediatric risk of mortality (PRISM III) scores than children without respiratory failure. While respiratory failure occurs infrequently in children with status asthmaticus, it is associated with substantial hospitalization burden. In this large multicenter cohort, respiratory failure was not associated with age, gender, or obesity. However, African-American children were significantly more likely to be intubated for status asthmaticus.

Introduction

CHILDHOOD ASTHMA CONTINUES to be a significant public health problem in the United States, and it is a frequent admission diagnosis at many children's hospitals.¹ Approximately 200,000 children are admitted to the hospital with asthma each year in the United States, and ~10,000 of these children have a severe and potentially fatal asthma exacerbation requiring admission to an intensive care unit (ICU).²

Despite extensive advances in pharmacologic treatments and mechanical interventions, asthma continues to be a life-threatening disease that is associated with significant morbidity.^{3–7} During a severe asthma exacerbation, if the patient does not respond to medical therapy, endotracheal intubation and mechanical ventilation may be required, which can lead to serious adverse effects.^{1,3,5,6,8,9} The presence of an endotracheal tube can aggravate bronchospasm or lead to other severe complications, including hypotension, hypoxemia, and cardiac arrest.^{3,6,8–12}

Regardless of the high burden of morbidity in children with status asthmaticus, there is a considerable lack of

research describing the incidence of respiratory failure leading to endotracheal intubation in this population or the characteristics associated with mechanical ventilation in pediatric asthmatics. We have begun examining the incidence and factors associated with respiratory failure within our own institution. In a study looking at the use of noninvasive positive pressure ventilation in the treatment of pediatric patients with asthma, we found that 10% of children admitted to the ICU for status asthmaticus between October 2002 and April 2004 required intubation.¹³ Moreover, in another study exploring the frequency of intubation and mechanical ventilation in children with asthma, we found that those presenting to a community hospital were more likely to be intubated than those presenting to a children's hospital.¹⁴ However, these studies are limited by fairly small sample sizes, and they cannot be generalized to the larger population.

Virtual PICU Systems (VPS) is a national, multi-institutional database, created for the purpose of clinical quality improvement and outcomes research, with daily data provided from ~100 pediatric ICUs (PICUs) around the United States. Previous investigators have used this database to analyze

Abstract presented at the American Thoracic Society International Conference, Denver, Colorado, May 2011.

¹Department of Pediatrics, Connecticut Children's Medical Center, Hartford, Connecticut.

large cohorts of children and to determine potentially generalizable associations. In this study, we conducted a retrospective data analysis of children with status asthmaticus included in the VPS database to describe the incidence of respiratory failure in children with acute asthma and to characterize any demographic factors or clinical predictors that may be associated with its occurrence.

Materials and Methods

This retrospective data analysis of the VPS database was conducted at Connecticut Children's Medical Center and was approved by the Institutional Review Board at our institution and the VPS Research Committee. All patients < 18 years of age included in the VPS database with a primary diagnosis of asthma between January 2007 and December 2008 were included in the analysis. Specific patient data obtained from VPS included demographics (age, gender, race/ethnicity, and BMI) and clinical outcomes [respiratory interventions, pediatric index of mortality (PIM2) score,¹⁵ pediatric risk of mortality (PRISM III) score,¹⁶ and length of stay]. Both validated tools, the PIM2 score estimates mortality risk using clinical data from the first hour of admission to the ICU, while the PRISM III score uses physiologic data from the first 24 h of ICU admission to determine risk of mortality. Patients requiring mechanical ventilation with cuffed or uncuffed nasotracheal or orotracheal tubes in this database were characterized as having respiratory failure. Each center that participates in the VPS database uses its own criteria for intubating and mechanically ventilating a patient, and therefore the definition of respiratory failure may vary across institutions.

The VPS program is dedicated to standardized data sharing and benchmarking among pediatric ICUs. All participants collect information on patient and hospital measures, diagnoses, interventions, discharge, organ donation, and pediatric severity of mortality scores. Currently, there are 98 participating centers in the United States and 1 center in Saudi Arabia and more than 500,000 cases in this database. The total number of admissions was determined using data from centers that participated in full data collection during that quarter.

Data were analyzed using SPSS statistical software (version 17.0; Chicago, IL). Demographic and clinical characteristics of patients with and without respiratory failure 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 respiratory failure were examined using logistic regression analyses. The Kolmogorov-Smirnov statistic and the Shapiro-Wilk test were used to

assess the normality of continuous variables. Distributions of the data are presented as mean $\pm$ standard deviation or median and 25%–75% interquartile range for continuous variables and as frequencies (%) for categorical variables. Frequencies are rounded to the nearest whole number, and *P*-values < 0.05 are considered statistically significant.

Results

Three thousand three hundred eighteen children were admitted to an ICU with status asthmaticus during the study period, of which 201 (6%) had respiratory failure. The mean age of patients was 6.8 ± 4.6 years, and the majority (61%) were male children. The average length of ICU stay was 1.9 ± 2.1 days, with a median of 1.3 days (range 1 h–36 days). Heliox was administered to 5% of children, and noninvasive bilevel positive airway pressure (BiPAP) or continuous positive airway pressure (CPAP) was utilized in 7% of patients. A total of 5 children (0.2%) expired before discharge from the ICU.

A total of 48 centers were included in our analysis, and the median number of asthma admissions per center during the study timeframe was 35 (25%–75% IQR 11–85). The proportion of asthma admissions ranged from 0.5% to 17% of total admissions. These centers had a range of percentages of intubations out of total asthma admissions with a median of 6% (0%–11%). They also had a range of percentages of BiPAP with a median of 1.5% (0%–7%). Due to the large number of centers and the considerable ranges of intubation and BiPAP, we were unable to determine associations.

The demographic characteristics of patients with and without respiratory failure are presented in Table 1. There were no significant differences in age, gender, or BMI between the 2 groups. However, African-American children were significantly more likely to be intubated for status asthmaticus (OR 1.4; 95% CI 1.0–1.9; *P* = 0.03) compared with the children of other races/ethnicities. Moreover, African-Americans had significantly worse PIM2 scores compared to the other children [−6.27 (−6.38 to −6.07) versus −6.29 (−6.39 to −6.14); *P* = 0.002].

Table 2 displays the clinical characteristics and outcomes of study patients. As expected, children with respiratory failure had significantly longer ICU lengths of stay than children without respiratory failure. A Mann-Whitney *U* test revealed a significant difference in the length of stay between those with respiratory failure [3.8 days (2.0–6.5)] and those without respiratory failure [1.3 days (0.8–2.1)] (*P* < 0.001). In addition, there were significant differences in PIM2 and PRISM III scores between the 2 groups. Compared to children without respiratory failure, those with respiratory

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF THE STUDY POPULATION

	Respiratory failure (n = 201)	No respiratory failure (n = 3,117)	<i>P</i> value	OR (95% CI)
Age (years)	7.5 $\pm$ 5.1	6.7 $\pm$ 4.5	0.05	
Male Gender	58% (n = 117)	61% (n = 1,897)	0.50	0.9 (0.7–1.2)
Race/ethnicity				
Caucasian	32% (n = 57)	34% (n = 1,013)	0.50	0.9 (0.6–1.2)
African-American	49% (n = 88)	41% (n = 1,198)	0.03	1.4 (1.0–1.9)
Hispanic	12% (n = 21)	15% (n = 453)	0.21	0.7 (0.5–1.2)
Other	8% (n = 14)	10% (n = 279)	0.53	0.8 (0.5–1.4)
BMI	17.3 (15.4–20.8)	17.1 (15.4–20.1)	0.86	

TABLE 2. CLINICAL CHARACTERISTICS OF PATIENTS WITH AND WITHOUT RESPIRATORY FAILURE

	Respiratory failure (n = 201)	No respiratory failure (n = 3,117)	P value	OR (95% CI)
ICU length of stay (days)	3.8 (2.0–6.5)	1.3 (0.8–2.1)	<0.001	
PIM2 score	−4.9 (−5.1 to −4.4)	−6.3 (−6.4 to −6.2)	<0.001	
PRISM III score	5.0 (3.0–9.8)	0.0 (0.0–3.0)	<0.001	
BiPAP/CPAP	18% (n = 37)	6% (n = 185)	<0.001	3.6 (2.4–5.3)
Heliox	14% (n = 29)	4% (n = 131)	<0.001	3.8 (2.5–5.9)

ICU, intensive care unit; PIM2, pediatric index of mortality; PRISM III, pediatric risk of mortality; BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure.

failure had higher PIM2 [−4.9 (−5.1 to −4.4) versus −6.3 (−6.4 to −6.2); $P < 0.001$] and PRISM III [5.0 (3.0–9.8) versus 0.0 (0.0–3.0); $P < 0.001$] scores. There were also significant differences in respiratory interventions utilized among those with and without respiratory failure. Children with respiratory failure were significantly more likely to receive noninvasive BiPAP or CPAP (OR 3.6; 95% CI 2.4–5.3; $P < 0.001$) as well as Heliox (OR 3.8; 95% CI 2.5–5.9; $P < 0.001$) compared to those without respiratory failure.

Discussion

Asthma remains a significant cause of morbidity in children and a potentially life-threatening disease. In this retrospective review of the VPS database, we found that 6% of children admitted to the ICU required mechanical ventilation for respiratory failure. Relatively few authors have explored the incidence of respiratory failure in this population and those who have report a wide range in rates of intubation and mechanical ventilation.^{17–20} At our own institution, ~10% of children admitted to the ICU with asthma were intubated and mechanically ventilated.^{13,14} Roberts et al. conducted an analysis of data from 11 PICUs participating in the Pediatric Intensive Care Evaluation (PICUE) database.¹⁷ The average rate of mechanical ventilation among 1,528 pediatric asthmatics was 17% with a range of 3% to 47% across different institutions.¹⁷ The variation in use of mechanical ventilation in this study was not explained by severity of illness, as children at high-use centers were ~2 times more likely to be intubated compared to children at low-use centers, even after adjustment for degree of hypercarbia, maximal respiratory rate, and PRISM III scores.¹⁷

Another study reporting data from a large, multi-institutional database, the Pediatric Health Information System (PHIS), found that 14% of 7,125 children admitted to the PICU with asthma required intubation and ventilation (range 6%–27%).¹⁸ Although the authors did not collect data using a standardized severity of illness or risk of mortality score, they reported that more than half of patients who were intubated received ventilation for 1 day or less. This finding suggests either expeditious recovery of patients who were intubated or, as the case in Roberts' study, a lower clinical threshold for initiating mechanical ventilation.¹⁸

More recently, Hartman et al. conducted a review of all hospitalizations for pediatric status asthmaticus in New Jersey spanning a 15-year period.¹⁹ Similar to the rate at our own institution, ~10% of the 4,559 children admitted to the PICU were mechanically ventilated during this timeframe.¹⁹

In the current cohort, African-American children were significantly more likely to be intubated for respiratory fail-

ure. African-American children also had significantly worse severity of illness scores, and therefore the association between African-American children and increased risk for intubation was tested in a regression analysis. Intubation and African-American race were no longer significant when accounting for the severity of illness using PIM2 and PRISM III. However, we question the validity of these tools in the current population, as neither are asthma-specific measurements. Additionally, the scores for all patients on both of these tests were very low, which further indicates that the tools may not be reflective or discriminatory in assessing true illness severity in children with asthma. Unfortunately, there were no other severity of illness measurements available in the VPS database, and thus the scores used were our only option.

True to our results, previous authors have found that African-American children carry a greater burden of disease with asthma than children of other races and ethnicities.^{20–22} In fact, in the United States, African-American children aged 0–18 years are almost 3 times more likely to be hospitalized for asthma and 4 times more likely to die from asthma compared to white children.²³ Proposed etiologies of these disparities are outside the scope of this retrospective analysis, but include socioeconomic status, preventive care, birth weight, place of residence, and genetic differences such as response to medication and allergic sensitization.^{20–22} Nonetheless, concurrent with these other investigators, our study reinforces the evidence of racial disparities in childhood asthma.

Not surprisingly, children with respiratory failure in our study had significantly worse severity-of-illness scores compared to those without respiratory failure, as well as longer ICU lengths of stay. These findings were similar to those of Hon and colleagues, who conducted a small study of children admitted to the ICU with acute asthma in Hong Kong.²⁴ The authors reported that children who were mechanically ventilated had significantly higher PIM2 scores and longer PICU stays compared to children who did not receive mechanical ventilation.²⁴ Likewise, in a 15-year review of children treated in the PICU for asthma in Taiwan, Chiang found that patients who were intubated had significantly longer ICU lengths of stay than children who did not require mechanical ventilation.²⁵

While the use of a multi-institutional database provides the benefit of a large sample size, it presents several limitations. Each participating center of VPS uses its own criteria for treatment, including the use of respiratory therapies and intubation. Therefore, our main outcome of respiratory failure may have varied across institutions. However, because of the large number of patients in our study, we believe that these variations in practice may not have as much of an effect as they would have in a smaller study. Another limitation is

that data obtained from VPS correspond to hospitalizations rather than individual patients; therefore, it is possible that our analysis includes multiple admissions for the same patient rather than a strictly unique patient population.

Due to the retrospective nature of the study, we were limited to the use of variables collected for general pediatric critical care admissions, rather than specific to asthma. For example, it would have been valuable to stratify our analysis by asthma severity classification as well as patients with and without other chronic diseases. We also would have been interested to examine the use of medications such as steroids and long-acting beta-agonists. Other important factors that would have contributed to our analysis, but were not available in the VPS database, include duration of illness, exposures, triggers, and presence of smokers in the home. Additionally, specific hospital data would have been useful, as previously we have found that the location of presentation may influence a provider's decision to intubate a child with acute asthma.¹⁴ We also would have liked to examine whether significant associations vary by region; however, due to deidentification of the database, we were not privy to information regarding the region or type of hospital. Finally, a child's race/ethnicity determination was made based on each participating hospital's individual protocol, which may be subjective and prone to variation that may have affected the results.

Respiratory failure in acute asthma is a rare, yet potentially life-threatening occurrence. In this large, multicenter study of children admitted to the ICU with status asthmaticus, ~6% required intubation and mechanical ventilation. Respiratory failure was not associated with age, gender, or obesity; however, African-American children were significantly more likely to be intubated. Additional research is needed to further our understanding of potential predictors and etiologies for respiratory failure in this population.

Acknowledgments

VPS data was provided by the VPS, LLC. No endorsement or editorial restriction of the interpretation of these data or opinions of the authors have been implied or stated.

Authors' Contributions

Kathleen Sala contributed to study conception and design; data collection, analysis, and interpretation; and manuscript writing and revision. Laurie Karamessinis contributed to the study conception and design, data collection, and manuscript revision. Aaron Zucker was involved in study conception and design as well as manuscript revision. Christopher Carroll contributed to study conception and design; data collection, analysis, and interpretation; and manuscript writing and revision. All authors have provided final approval of the manuscript.

Author Disclosure Statement

No competing financial interests exist for any of the authors.

References

- Werner HA. Status asthmaticus in children. *Chest* 2001; 119: 1913–1929.
- Centers for Disease Control and Prevention. Asthma Prevalence, Health Care Use and Mortality: United States, 2003–05. NCHS Health E-Stat. <http://www.cdc.gov/nchs/data/hestat/asthma03-05/asthma03-05.htm>
- McFadden ER Jr. Acute severe asthma. *Am J Respir Crit Care Med* 2003; 168:740–759.
- Pendergraft TB, Stanford RH, Beasley R, Stempel DA, Roberts C, McLaughlin T. Rates and characteristics of intensive care unit admissions and intubations among asthma-related hospitalizations. *Ann Allergy Asthma Immunol* 2004; 93: 29–35.
- Phipps P, Gerrard CS. The pulmonary physician in critical care: acute severe asthma in the intensive care unit. *Thorax* 2003; 58:81–88.
- Papiris S, Kotanidou A, Malagari K, Roussos C. Clinical review: severe asthma. *Crit Care* 2002; 6:30–44.
- Maffei FA, van der Jagt EW, Powers KS, et al. Duration of mechanical ventilation in life-threatening pediatric asthma: description of an acute asphyxial subgroup. *Pediatrics* 2004; 114:762–767.
- Cox RG, Barker GA, Bohn DJL. Efficacy, results and complications of mechanical ventilation in children with status asthmaticus. *Pediatr Pulmonol* 1991; 11:120–126.
- Wetzel RC. Pressure-support ventilation in children with severe asthma. *Crit Care Med* 1996; 24:1603–1605.
- Stein R, Canny GJ, Bohn DJ, Reisman JJ, Levison H. Severe acute asthma in the pediatric intensive care unit: six years' experience. *Pediatrics* 1989; 83:1023–1028.
- Shugg AW, Kerr S, Butt WW. Mechanical ventilation of paediatric patients with asthma: short and long term outcome. *J Paediatr Child Health* 1990; 26:343–346.
- Kao CC, Jain S, Guntupalli KK, Bandi V. Mechanical ventilation for asthma: a 10-year experience. *J Asthma* 2008; 45:552–556.
- Carroll CL, Schramm CM. Noninvasive positive pressure ventilation for the treatment of status asthmaticus in children. *Ann Allergy Asthma Immunol* 2006; 96:454–459.
- Carroll CL, Smith SR, Collins MS, Bhandari A, Schramm CM, Zucker AR. Endotracheal intubation and pediatric status asthmaticus: site of original care affects treatment. *Pediatr Crit Care Med* 2007; 8:91–95.
- Slater A, Shann F, Gearson G. PIM2: a revised version of the pediatric index of mortality. *Intensive Care Med* 2003; 29: 278–285.
- Pollack MM, Patel KM, Ruttimann UE. PRISM III: an updated Pediatric Risk of Mortality score. *Crit Care Med* 1996; 24: 743–752.
- Roberts JS, Bratton SL, Brogan TV. Acute severe asthma: differences in therapies and outcomes among pediatric intensive care units. *Crit Care Med* 2002; 30:581–585.
- Bratton SL, Odetola FO, McCollegan J, Cabana MD, Levy FH, Keenan HT. Regional variation in ICU care for pediatric patients with asthma. *J Pediatr* 2005; 147:355–361.
- Hartman ME, Linde-Zwirble WT, Angus DC, Watson RS. Trends in admissions for pediatric status asthmaticus in New Jersey over a 15-year period. *Pediatrics* 2010; 126:904–911.
- Akinbami LJ, Moorman JE, Garbe PL, Sondik EJ. Status of childhood asthma in the United States, 1980–2007. *Pediatrics* 2009; 123:S131–S145.
- McDaniel M, Paxson C, Waldfogel J. Racial disparities in childhood asthma in the United States: evidence from the National Health Interview Survey, 1997 to 2003. *Pediatrics* 2006; 117: e868–e877.
- Joseph CLM, Williams LK, Ownby DR, Saltzgaber J, Johnson CC. Applying epidemiologic concepts of primary, secondary, and tertiary prevention to the elimination of racial disparities in asthma. *J Allergy Clin Immunol* 2006; 117: 233–240.

23. Moorman JE, Rudd RA, Johnson CA, et al. National surveillance for asthma—United States, 1980–2004. *MMWR CDC Surveill Summ* 2007; 56:1–14, 18–54.
24. Hon KL, Tang WSW, Leung TF, Cheung KL, Ng PC. Outcome of children with life-threatening asthma necessitating pediatric intensive care. *Italian J Pediatr* 2010; 36:47–51.
25. Chiang BL, Hsieh CT, Wang LC, et al. Clinical course and outcome of children with status asthmaticus treated in a pediatric intensive care unit: a 15-year review. *J Microbiol Immunol Infect* 2009; 42:488–493.

Address correspondence to:

Kathleen A. Sala, M.P.H.

Department of Pediatrics

Connecticut Children's Medical Center

85 Seymour St., Suite 701

Hartford, CT 06016

E-mail: ksala@ccmckids.org

Received for publication August 23, 2012; accepted after revision September 21, 2012.

This article has been cited by:

1. Harold J. Farber, Stuart L. Abramson. 2012. Highlights from This Issue. *Pediatric Allergy, Immunology, and Pulmonology* **25**:4, 175-176. [[Citation](#)] [[Full Text HTML](#)] [[Full Text PDF](#)] [[Full Text PDF with Links](#)]