Community-Acquired Pneumonia Hospitalization among Children with Neurologic Disorders

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Objective To describe and compare the clinical characteristics, outcomes, and etiology of pneumonia among children hospitalized with community-acquired pneumonia (CAP) with neurologic disorders, non-neurologic underlying conditions, and no underlying conditions.

Study design Children <18 years old hospitalized with clinical and radiographic CAP were enrolled at 3 US children's hospitals. Neurologic disorders included cerebral palsy, developmental delay, Down syndrome, epilepsy, non-Down syndrome chromosomal abnormalities, and spinal cord abnormalities. We compared the epidemiology, etiology, and clinical outcomes of CAP in children with neurologic disorders with those with non-neurologic underlying conditions, and those with no underlying conditions using bivariate, age-stratified, and multivariate logistic regression analyses.

Results From January 2010-June 2012, 2358 children with radiographically confirmed CAP were enrolled; 280 (11.9%) had a neurologic disorder (52.1% of these individuals also had non-neurologic underlying conditions), 934 (39.6%) had non-neurologic underlying conditions only, and 1144 (48.5%) had no underlying conditions. Children with neurologic disorders were older and more likely to require intensive care unit (ICU) admission than children with non-neurologic underlying conditions and children with no underlying conditions; similar proportions were mechanically ventilated. In age-stratified analysis, children with neurologic disorders were less likely to have a pathogen detected than children with non-neurologic underlying conditions. In multivariate analysis, having a neurologic disorder was associated with ICU admission for children ≥2 years of age.

Conclusions Children with neurologic disorders hospitalized with CAP were less likely to have a pathogen detected and more likely to be admitted to the ICU than children without neurologic disorders. *(J Pediatr 2016;173:188-95)*.

Pneumonia is a leading cause of pediatric hospitalization in the US.[1-3] Although children with neurologic disorders—a diverse spectrum of conditions including epilepsy, neurodevelopmental disorders, and neuromuscular disorders—comprise a small proportion of the US pediatric population,[4-6] this group is particularly vulnerable to severe complications and death from respiratory failure.[7-13] Causes of respiratory failure in these children are multifactorial and include pulmonary scarring from recurrent aspiration, ineffective cough, and chest wall or spinal abnormalities prohibiting maximal chest expansion.[9,11,14,15] Specifically, children with neurologic disorders also are at increased risk of complications and death from influenza virus and respiratory syncytial virus (RSV) infection.[16-21] However, data from prospective clinical studies describing community-acquired pneumonia (CAP) in children with neurologic disorders are limited.

We used data from the Centers for Disease Control and Prevention Etiology of Pneumonia in the Community (EPIC) study,[3] a prospective, multicenter, population-based, active surveillance study, to describe and compare the clinical characteristics, outcomes, and pneumonia etiology among children hospitalized with CAP with neurologic disorders, non-neurologic underlying conditions, and no underlying conditions.

CAP	Community-acquired pneumonia
EPIC	Etiology of Pneumonia in the Community
ICU	Intensive care unit
LOS	Length of stay
RAD	Reactive airway disease
RSV	Respiratory syncytial virus

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Methods

From January 1, 2010 to June 30, 2012, children <18 years old were enrolled in the EPIC study at Le Bonheur Children's Hospital (Memphis, Tennessee), Monroe Carell Jr Children's Hospital at Vanderbilt (Nashville, Tennessee), and Primary Children's Hospital (Salt Lake City, Utah).[3] Informed consent was obtained before enrollment. The study protocol was approved by the institutional review boards at each institution and the Centers for Disease Control and Prevention.

Children admitted to the study hospitals with signs of acute infection, respiratory symptoms, and chest radiography consistent with pneumonia within 72 hours of admission were eligible for enrollment.[3] A dedicated study radiologist at each study hospital independently reviewed chest radiography for final determination of radiographic pneumonia.[3] Children were excluded if they were recently hospitalized (<7 days for immunocompetent children, <90 days for immunosuppressed children), enrolled in the EPIC study <28 days earlier, resided in an extended care facility, had a clear alternative respiratory diagnosis, were newborns who never left the hospital, or had any of the following conditions: tracheostomy, cystic fibrosis, cancer with neutropenia, solid organ or hematopoietic stem cell transplant ≤90 days earlier, active graft vs host disease or bronchiolitis obliterans, or HIV with CD4 cell count <200 cells/mm^3 (or CD4% <14%).

The methods for data collection, specimen collection, laboratory testing, and definitions for pathogen detection have been previously described.[3] Data on underlying medical conditions, including neurologic disorders, were collected through a patient/caregiver interview and medical chart review. Blood and respiratory samples were collected from patients and tested for bacterial and viral pathogens by multiple modalities including bacterial culture, real-time polymerase chain reaction, and serology with methods as previously described.[3]

We identified 3 distinct groups for analysis: children with neurologic disorders, children with non-neurologic underlying conditions, and children with no underlying conditions. We categorized disorders as neurologic disorders based on literature review.[16,22] In addition, we consulted with a behavior-development pediatrician (G.P.) to assist with categorizing neurologic disorders. Only those with possible neurologic sequelae attributable to the neurologic disorder as indicated from the literature were categorized as neurologic disorders. We defined neurologic disorders as a diagnosis of cerebral palsy, developmental delay, Down syndrome and non-Down syndrome chromosomal abnormalities, epilepsy, spinal cord abnormalities, and other neurologic disorders; if a child had a neurologic disorder and another non-neurologic underlying condition, he or she was categorized as having a neurologic disorder. Non-neurologic underlying conditions included asthma/reactive airway disease (RAD), other chronic lung disease, chronic kidney disease, chronic liver disease, congenital heart disease, diabetes mellitus, immunosuppressive conditions (either because of chronic conditions, medication use, HIV-infection with CD4 cell count >200 cells/mm^3, and nondermatologic malignancies), and pre-term birth (in those aged <2 years old, defined as born at <37 weeks gestation). Those with no underlying conditions were defined as not having a neurologic disorder or a non-neurologic underlying condition.

Statistical Analyses

We describe the type and frequency of neurologic disorders occurring among children hospitalized with CAP and enrolled in the EPIC study. We compared epidemiologic and clinical characteristics, outcomes, and pathogens detected among children with neurologic disorders, non-neurologic underlying conditions, and no underlying conditions. Our primary outcome of clinical severity was intensive care unit (ICU) admission. We also examined other clinical outcomes including hospital length of stay (LOS), ICU LOS, invasive mechanical ventilation requirement and duration, receipt of vasopressors within 72 hours of ICU admission, and death. We performed bivariate and separate age-stratified analyses comparing the characteristics between children with neurologic disorders vs non-neurologic underlying conditions, and neurologic disorders vs no underlying conditions. In addition, we conducted subgroup analyses comparing the clinical outcomes of the subset of children with neurologic disorders and no other non-neurologic underlying conditions to the outcomes of children with non-neurologic underlying conditions and no underlying conditions; however, for our primary analysis, the neurologic disorders group includes children with a neurologic disorder who may also have non-neurologic disorders because there were few differences in the outcomes between these groups and because of sample size. We performed multivariable logistic regression using stepwise elimination to further investigate clinical outcomes found to be more common among children with neurologic disorders; covariates for the regression models were based on significance on bivariate analysis and epidemiologic or biological plausibility.

Data were analyzed using SAS version 9.3 (SAS Institute, Cary, North Carolina). The χ^2 or Fisher exact tests were used to compare proportions and the Wilcoxon rank sum test was used to evaluate distribution differences between continuous variables. All comparisons were 2-sided, and P values of <.05 was considered significant.

Results

Over the 2.5-year study period, 2638 (69.4%) of 3803 eligible children were enrolled; among which, 2358 (89.4%) children had radiographic CAP. Two hundred eighty (11.9%) of 2358 children had a neurologic disorder, 934 (39.6%) had non-neurologic underlying conditions only, and 1144 (48.5%) had no underlying conditions. Among the 280 children with neurologic disorders, 146