

CDC Influenza Division Key Points

February 26, 2015

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“Community-Acquired Pneumonia Requiring Hospitalization among U.S. Children.” *NEJM* by Seema Jain et al.

Key Points

- Pneumonia is the leading cause of hospitalization among children in the United States with medical costs estimated at almost \$1 billion in 2009.
- The “Etiology of Pneumonia in the Community” (EPIC) multi-center CDC study estimated the incidence and etiologies of community-acquired pneumonia requiring hospitalization in U.S. children.
 - The study was conducted by researchers at CDC, Vanderbilt University School of Medicine, Le Bonheur Children’s Hospital, University of Tennessee Health Science Center, and University of Utah Health Sciences, Northwestern University Feinberg School of Medicine, and St. Jude Children’s Research Hospital.
- This study attempts to fill in gaps in knowledge about pneumonia in children by providing estimates of the incidence of community-acquired pneumonia hospitalizations in U.S. children, as well as its viral and bacterial causes.
- The study was published in the *New England Journal of Medicine* on February 26, 2015, and is available online at <http://www.nejm.org/doi/full/10.1056/NEJMoa1405870>.
- A CDC press release is available at <http://www.cdc.gov/media/releases/2015/p0225-pneumonia-hospitalizations.html>.
- CDC has launched a new website that provides an overview of the EPIC study’s scope and purpose and will provide links to all future publications based on EPIC data. It is available at www.cdc.gov/pneumonia/epic/.

Methods

- As part of the CDC EPIC study, active population-based surveillance was conducted for community-acquired pneumonia hospitalizations among children younger than 18 years of age in three children’s hospitals in Memphis, Nashville, and Salt Lake City.
- Children were included in the study if they
 1. Were admitted to one of the three study hospitals
 2. Resided in one of the 22 counties in the study catchment areas
 3. Had evidence of acute infection defined as reported fever or chills, documented fever or hypothermia, or leukocytosis (high white count) or leukopenia (low white count)
 4. Had evidence of an acute respiratory illness defined as new cough or sputum production, chest pain, shortness of breath, fast breathing, abnormal lung examination, or respiratory failure
 5. Had chest radiography consistent with pneumonia within 72 hours from admission
- Children with recent hospitalization and severe immunosuppression were excluded.

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- Staff obtained blood, acute sera, and naso/oropharyngeal (NP/OP) swabs on all enrolled children as soon as possible after presentation.
- Pleural fluid (PF), endotracheal (ET) aspirates, and bronchoalveolar (BAL) specimens obtained for clinical care were also collected.
- Enrolled children and/or their caregivers were interviewed using a standardized questionnaire and medical charts were abstracted after discharge; demographic, epidemiologic, and clinical data were systematically collected.
- Enrollment was based on clinicians' initial interpretation of chest radiographs obtained within 72 hours of admission. Final inclusion required independent confirmation by the board certified pediatric study radiologist at each study hospital who was blinded to demographic and clinical information.
- Gram stain and bacterial culture were performed on blood, PF and ET aspirates, and BAL specimens using standard techniques. Real-time polymerase chain reaction (PCR) was used to identify respiratory viruses (coronaviruses; human metapneumovirus; human rhinovirus; influenza viruses; parainfluenza viruses; and respiratory syncytial virus) and atypical bacteria (*Chlamydomphila pneumoniae* and *Mycoplasma pneumoniae*) in NP/OP swabs, and *Streptococcus pneumoniae* and *Streptococcus pyogenes* in whole blood and PF specimens. PF was also tested for *Haemophilus influenzae* and other bacteria.

Results

- From January 2010-June 2012, the study enrolled 2,638 (69%) of 3,803 eligible children.
 - Of these, 2,358 (89%) had radiographic pneumonia
 - The median age was 2 years old
 - 497 (21%) of the children required intensive care
 - 3 (<1%) of the children died
- Among 2,222 children with radiographic pneumonia and specimens available for both bacterial and viral testing, a pathogen was detected in 1802 (81%).
 - One or more viruses were detected in 1,472 (66%)
 - Bacteria were detected in 175 (8%)
 - Bacterial and viral co-detected pathogens were identified in 155 (7%)
- Annual pneumonia incidence was 15.7/10,000 children (95% CI: 14.9-16.5), with the highest rates among children younger than 2 years old [62.2/10,000 (CI: 57.6-67.1)]. Rates of pneumonia decreased with increasing age.
- Respiratory syncytial virus (RSV) was the most common pathogen detected (28%), with greatest burden among children <2 years old with pneumonia.
- Other detected pathogens were human metapneumovirus (13%), adenovirus (11%), *Mycoplasma pneumoniae* (8%), parainfluenza viruses (7%), influenza (7%), coronaviruses (5%), *Streptococcus pneumoniae* (4%), *Staphylococcus aureus* (1%), and *Streptococcus pyogenes* (<1%).
- The following viruses were more commonly detected in children younger than 5 compared with older children:

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- Respiratory syncytial virus (37% in children younger than 5 years old compared with 8% in older children)
- Adenovirus (15% vs 3%)
- Human metapneumovirus (15% vs 8%)
- *Mycoplasma pneumoniae* (19% vs. 3%) was more common in children 5 years of age and older.
- Human rhinovirus was detected in 22% of cases, but it also was found in 17% of asymptomatic controls who were enrolled, by convenience sample, at the same sites during the same period. This makes it challenging to interpret the meaning of human rhinovirus detection in children hospitalized with pneumonia.

Conclusions

- The burden of community-acquired pneumonia requiring hospitalization was highest among the children < 5 years old, with respiratory viruses most commonly detected.
- Increasing influenza vaccination coverage and introduction of new anti-viral vaccines or treatments, particularly for RSV, could reduce the burden of pediatric pneumonia.
- The low prevalence of bacterial detections likely reflects both the effectiveness of bacterial conjugate vaccines and suboptimal sensitivity of bacterial diagnostic tests.
- The pediatric community-acquired pneumonia burden was associated with multiple different and co-detected pathogens, underscoring a need for the enhancement of sensitive, inexpensive, and rapid diagnostics to accurately identify pneumonia pathogens and target appropriate treatment.