Epidemiology of Viral Pneumonia

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KEYWORDS

• Respiratory viruses • Pneumonia • Epidemiology

KEY POINTS

- The burden of pneumonia, including that due to respiratory viruses, is markedly higher in the very young (<5 years) and older adults (≥50 years).
- Respiratory viruses substantially contribute to pneumonia in both adults and children, and when systematically tested for, are more commonly detected than bacteria in both adults and children.
- The most commonly detected respiratory viruses in adults and children are adenoviruses, coronaviruses, human metapneumovirus, human rhinoviruses, influenza viruses, parainfluenza viruses, and respiratory syncytial virus.
- It is difficult to distinguish between viruses by clinical presentation, and the exact clinical implication of viral detections among patients with pneumonia depends on the pathogen detected; however, there is increasing evidence of their importance in pneumonia.
- The circulation of respiratory viruses varies from region to region around the world, demonstrating seasonal variation in different parts of the world, which affects the prevalence and incidence of viral pneumonia globally.

INTRODUCTION

Worldwide, 900,000 children aged less than 5 years die from pneumonia every year.[1] Pneumonia is a leading infectious cause of hospitalization and death among US adults, resulting in more than $10 billion annual expenses.[2] Despite advances in clinical diagnostic methods, especially molecular-based methods, a cause is not always ascertained in a patient with pneumonia. Recent prospective pneumonia etiology studies have failed to detect a pathogen in greater than 50% of adults and approximately 20% of children hospitalized with pneumonia.[3–7] In these same studies, viruses were more commonly detected than bacteria in both adults and children, accounting for greater than 25% of detections in adults and greater than 70% in children.[3,7] The exact implications of viral detections among patients with pneumonia depend on the pathogen detected, but there is increasing evidence of their importance in pneumonia.[8]

US PREVALENCE/INCIDENCE

The Etiology of Pneumonia in the Community (EPIC) study was a large prospective multicenter US population-based active surveillance study in which viruses were more commonly detected than bacteria in both adults and children hospitalized with community-acquired pneumonia when systematic testing was used.[3,7] Detailed study details have been previously described,[3,7] but in brief, community-acquired pneumonia was defined as evidence of acute infection, acute respiratory illness, and radiographic evidence of pneumonia; patients with severe immunosuppression and recent hospitalization were excluded. Multiple modalities for pathogen detection of bacteria and viruses were used, including culture, polymerase chain reaction (PCR), serology, and antigen-based diagnostic assays.[3,7]

The results of the EPIC study demonstrated that prevalence and incidence of different pathogens varied by age. Among children less than 18 years

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old enrolled in the EPIC study, 70% of pneumonia hospitalizations occurred among children less than 5 years old.[7] Overall annual incidence of community-acquired pneumonia hospitalization in children was 15.7/10,000 children, and incidence was highest in children less than 2 years old (62.2/10,000 children), decreased in children 2 to 4 years old (23.8/10,000), and further decreased with increasing age. These rates were slightly lower than the 2009 national Kids' Inpatient Database, which reported 22.4 hospitalized pneumonia cases per 10,000 children less than 18 years old.[9] There are methodologic differences that likely explain these differences, including nonoverlapping years of analysis, distinctions between the populations studied, and varying case definitions, including exclusion of the severely immunocompromised in the EPIC study. Nonetheless, there were similar trends indicating that pneumonia burden is highest among the youngest children.

In the EPIC study, among 2222 children with clinical and radiographic pneumonia who had specimens available for bacterial and viral diagnostic testing, a pathogen was detected in 1802 (81%) children with one or more viruses in 1472 (66%), bacteria in 175 (8%), and both bacteria and viruses in 155 (7%). Among these 2222 children, the most commonly detected viruses were respiratory syncytial virus (RSV, 28%), human rhinoviruses (HRV, 27%), human metapneumovirus (HMPV, 13%), adenoviruses (AdV, 11%), parainfluenza 1 to 3 viruses (PIV, 7%), influenza A and B viruses (7%), and coronaviruses (CoV, 5%) (**Fig. 1**B, codetections are indicated by the lighter shading).[7] Compared with older children, RSV, AdV, and HMPV were all more commonly detected among children less than 5 years old (**Fig. 1**C). The incidence of RSV, HRV, HMPV, AdV, influenza viruses, PIV, and CoV was all higher among children less than 5 years old than among older children but was highest among children less than 2 years old.[7]

In adults enrolled in the EPIC study, overall annual incidence of community-acquired pneumonia hospitalization was 24.8/10,000 adults.[3] The overall and pathogen-specific incidences increased with age with rates highest among adults 50 years of age and older. The EPIC study rates and trends are similar to previous pneumonia etiology studies conducted in the 1990s despite methodologic differences,[10] but the EPIC study hospitalization rates were lower than more recent estimates based on hospitalization claims data likely due to certain excluded groups in the EPIC study, including those with severe immunosuppression.[11]

Among the 2259 adults enrolled in the EPIC study with clinical and radiographic pneumonia who had specimens available for bacterial and viral diagnostic testing, a pathogen was detected in 853 (38%) with one or more viruses in 530 (23%), bacteria in 247 (11%), bacteria and viruses in 59 (3%), and a fungal or mycobacterial pathogen in 17 (1%). Among the 2259 adults, the most commonly detected viruses were HRV (9%), influenza A and B viruses (6%), HMPV (4%), RSV (3%), PIV (2%), CoV (2%), and AdV (1%) (**Fig. 1**A).[3] Importantly, the incidence of pneumonia hospitalization with influenza was almost 5 times higher among adults 65 years and older than among younger adults, and the incidence of HRV was almost 10 times as high. Interestingly, the overall incidence of pneumonia hospitalization with influenza (1.5/10,000) was similar to that of pneumococcus (1.2/10,000), a well-known bacterial cause of community-acquired pneumonia.

WORLDWIDE/REGIONAL PREVALENCE, INCIDENCE, AND MORTALITIES

It is well known that respiratory viruses contribute to acute respiratory infections, including those involving the lower respiratory tract and leading to bronchiolitis, pneumonia, and other complications. Although some global estimates of respiratory virus burden have been derived, including some from low- and middle-income countries, these data remain sparse because little surveillance for respiratory viruses is systematically carried out in many countries. In addition, most surveillance and thus estimates are not specific to pneumonia, and definitions of pneumonia vary widely between studies, making comparisons difficult.

In a 2005 study, RSV was associated with 22% of acute lower respiratory infections in children less than 5 years old worldwide with 3.4 (2.8–4.3) million hospitalizations and 66,000 to 199,000 deaths; 99% of deaths occurred in developing countries.[12] Data from this same analysis demonstrated that most RSV deaths in high-income countries were in children less than 1 year old, whereas in low- and middle-income countries, these deaths extended into the second year of life.

Similar analyses have been done for the burden of influenza virus infection, again not necessarily limited to pneumonia. According to the World Health Organization (WHO), influenza occurs globally with an annual attack rate estimated at 5% to 10% in adults and 20% to 30% in children.[13] Worldwide, these annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 250,000 to 500,000 deaths. Although hospitalizations and deaths occur in