

High Morbidity and Mortality in Adults Hospitalized for Respiratory Syncytial Virus Infections

N. Lee, G. C. Y. Lui, K. T. Wong, T. C. M. Li, E. C. M. Tse, J. Y. C. Chan, J. Yu, S. S. M. Wong, K. W. Choi, R. Y. K. Wong, K. L. K. Ngai, D. S. C. Hui, and P. K. S. Chan
CID 2013:57; 1069-1077

Background

- important cause of lower respiratory tract infections in infants and young children, leading to hospitalizations and deaths
- impact in adults only appreciated in recent years
- RSV estimated to infect 3-10% of adults annually
- most infections mild, but severe lower respiratory tract infections can occur (older adults, underlying conditions)
- RSV may account for 5-15% of community-acquired pneumonia, 9-10% of hospital admissions for acute cardiorespiratory diseases, and excessive deaths during seasonal peaks
- disease burden can approach that of influenza
- little is known about the clinical manifestations, complications, and outcomes of severe RSV infections in adults; factors associated with severe and fatal infections are largely unknown

Aim of the study

- to describe RSV infections in adults, identify factors associated with development of pneumonia, respiratory failure, and death and to compare RSV infections with influenza infections

Methods

- *Study population and case finding*
 - o retrospective cohort study on adults (> 18 years) hospitalized with RSV infections between January 2009 and 31 December 2011 in 3 participating hospitals in Hong Kong, with laboratory confirmed RSV infections
 - o RSV and influenza infections prospectively diagnosed (reasons for admittance: potentially serious medical conditions and/or exacerbation of chronic illness not manageable at home)
 - o in all patients: collection of nasopharyngeal aspirates, tested for RSV and influenza antigens using an immunofluorescence assay, chest X-ray, sputum samples for bacterial culture
- *Data collection and definition of variables*
 - o clinical data: demographics, co-morbidities, illness onset time, presenting symptoms, cardiorespiratory complications, requirement for supplemental oxygen therapy and/or ventilator support, antibiotic use, use of systemic corticosteroids, hospitalization duration, and all-cause death
 - o laboratory data: routine blood tests, bacterial pathogens from respiratory and/or blood samples
 - o Definitions
 - pneumonia: physician diagnosed pneumonia based on symptoms and signs of acute lower respiratory tract infections together with new pulmonary infiltrate
 - acute respiratory failure requiring ventilatory support: persistent respiratory failure despite supplemental oxygen therapy which necessitated noninvasive positive pressure ventilation or invasive mechanical ventilation
- *Main outcome*: all-cause death
- *Secondary outcome*: development of acute respiratory failure requiring ventilatory support and total duration of hospitalization

- *Additional analysis:* Comparison of patients with RSV infections and patients with influenza infection during the same period
- *Virological investigations:* viral antigen detection for a panel of respiratory viruses using an immunofluorescence assay
- *Radiographic assessment:* radiographic review by two independent radiologists (blinded to all clinical information and outcomes)
- *Statistical analysis:*
 - o Univariate analysis with Student t, Mann-Whitney U, and Chi-square test; multivariate Cox proportional hazard model

Results:

- 607 RSV cases among hospitalized patients
- patients' baseline characteristics and clinical manifestations (Table 1)
 - o mean age 80 years
 - o 87.3% with one or more coexisting medical conditions
 - o mean time of admission 2.6 days
 - o symptoms: fever (75%), cough (87.5%), sputum production (81.2%), and wheezy breathing and dyspnea (68.9%)
- complications: lower respiratory tract complications (pneumonia, COPD exacerbation): 71.9%, bacterial superinfection 12.5%, cardiovascular complications 14.3%
- 38.9% systemic corticosteroids, 94.7% antibiotics, 67.9% supplemental oxygen therapy, 11.1% ventilatory support (NIPPV 9.1%, invasive ventilation 2.0%)
- risk factor for acute respiratory failure requiring ventilatory support (table 2): chronic lung disease, pneumonia, elevated serum urea concentration, elevated liver enzymes
- crude all-cause mortality within 30 days and 60 days was 9.1 and 11.9%, respectively (direct cause of death: pneumonia, COPD exacerbation, acute cardiovascular events and underlying medical conditions complicated by pneumonia/sepsis)
- mean duration of hospitalization: 12 days
- comparison with seasonal influenza: patients similar in age, but RSV more frequently with underlying chronic lung disease and major systemic co-morbidities; use of supplemental oxygen and assisted ventilation higher in RSV patients; no significant difference in overall outcome

Discussion:

- RSV can cause severe lower respiratory complications in older adults with underlying diseases
- Severe lower respiratory complications common with potentially fatal outcome
- Clinical manifestation, complications, and outcomes of RSV infections comparable to those of seasonal influenza
- no antiviral treatment or vaccination for RSV infections available, not much data on the use of Ribavirin and immunoglobulins available

Strengths and limitations

- strengths: largest adult cohort of hospitalized RSV patients, multicenter design, virological confirmation of cases
- limitations: retrospective approach; use of IFA instead of PCR (lower sensitivity -> less severe cases probably not detected)

Conclusion:

- Adults hospitalized for RSV infection have high morbidity and mortality