Journal of Microbiology, Immunology and Infection (2016) 49, 737—742

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com

ORIGINAL ARTICLE

Risk factors associated with death in patients with severe respiratory syncytial virus infection

Yen-I Lee [a], Chun-Chih Peng [a,b], Nan-Chang Chiu [a,c], Daniel Tsung-Ning Huang [a,d], Fu-Yuan Huang [a], Hsin Chi [a,b,c,d,*]

[a] *Department of Pediatrics, Mackay Memorial Hospital, Taipei, Taiwan*
[b] *Department of Medicine, Mackay Medical College, New Taipei City, Taiwan*
[c] *Mackay Junior College of Medicine, Nursing and Management, Taipei, Taiwan*
[d] *Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan*

Received 28 April 2014; received in revised form 29 August 2014; accepted 29 August 2014
Available online 31 October 2014

KEYWORDS
Down's syndrome;
mortality;
nosocomial infection;
respiratory syncytial virus;
risk factors

Background: Respiratory syncytial virus (RSV) infection is an important cause of viral respiratory tract infection in children. This retrospective study describes the clinical characteristics of severe RSV infection and determines the risk factors for death.
Methods: Patients were identified through a review of all patients discharged with a diagnosis of RSV lower respiratory tract infection and admitted to hospital in the pediatric intensive care unit (PICU) of a tertiary medical center between July 1, 2001 and June 30, 2010. The medical and demographic variables were recorded and analyzed.
Results: The 186 RSV-positive patients admitted to the PICU had a median age of 5.3 months (interquartile range 2.3—12.4 months) and included 129 boys and 57 girls. Among them, 134 had at least one underlying disease: prematurity in 92, neurological disease in 57, bronchopulmonary dysplasia in 40, congenital heart disease in 26, hematological malignancies in 11, and Down's syndrome in nine patients. The 10 patients who died from RSV-related causes had a median age of 20.8 months (interquartile range 6.6—89.2 months) and all had a comorbidity. In multivariate analysis, the risk factors for death in severe RSV infection were Down's syndrome (odds ratio 7.20, 95% confidence interval 1.13—45.76; $p = 0.036$) and nosocomial RSV infection (odds ratio 4.46, 95% confidence interval 1.09—18.27; $p = 0.038$).
Conclusion: Down's syndrome and nosocomial RSV infection are significantly associated with death in severe RSV infections. Clinicians should be alert to these conditions.

* Corresponding author. Department of Pediatrics, Mackay Memorial Hospital, 92, Section 2, Zhongshan North Road, Taipei 10449, Taiwan.
E-mail address: chi.4531@mmh.org.tw (H. Chi).

http://dx.doi.org/10.1016/j.jmii.2014.08.020

Introduction

Respiratory syncytial virus (RSV) is an important cause of acute lower respiratory tract infection (LRTI) in children younger than 5 years of age. In 2005, RSV was estimated to be responsible for at least 3.4 million episodes of severe LRTI requiring admission to hospital in children worldwide and caused 66,000—199,000 deaths in children younger than 5 years old.[1] In Switzerland, RSV infections cause intermediate or intensive care unit (ICU) admissions of approximately 1—2% of each annual birth cohort.[2] In a retrospective study in Hong Kong, the rate of RSV-associated ICU admissions was 2.4% among 4912 RSV-positive pediatric patients.[3]

Many studies have shown that patients at high risk of severe RSV disease include premature infants,[4,5] children with hemodynamically significant congenital heart disease (CHD),[4,6,7] patients with bronchopulmonary dysplasia (BPD),[4,5,8] and those who are immunocompromised.[6,9—11] However, data regarding risk factors for death in severe RSV infection remain limited. The aim of this retrospective study was to identify the clinical characteristics of patients admitted to the pediatric intensive care unit (PICU) with RSV infection and the risk factors for death.

Materials and methods

Ethics statement

The Ethics Committee of Mackay Memorial Hospital, Taipei, Taiwan approved this study (Institute Review Board number MMH-I-S- 627, protocol title "Clinical Features of Pediatric Respiratory Syncytial Virus Infections: Risk Factors and Outcome").

Patient inclusion

Patients were identified through a review of medical records from July 1, 2001 to June 30, 2010. This study used data from a 12-bed PICU in a tertiary medical center.

Patients aged $\leq$18 years and discharged with a diagnosis of RSV LRTI were evaluated. The diagnosis was confirmed by an RSV antigen immunofluorescence test and/or culture from specimens taken from nasopharyngeal or throat swabs. Patients who were admitted to the PICU and were labeled as "severe" were enrolled into this study.

The general policy was that patients who required mechanical respiratory support or intensive care were transferred to the PICU. In the PICU, respiratory support included mechanical ventilation (conventional and high frequency), nasal intermittent positive pressure ventilation, nasal continuous positive airway pressure, and supplemental oxygen only.

Virology sampling and investigations

Diagnostic samples, including nasopharyngeal aspirates for the RSV antigen test and throat virus cultures, were obtained by residents, nurses, or PICU staff members. The RSV was identified using IMAGEN Respiratory Syncytial Virus (Oxoid Ely Ltd, Hampshire, UK), a qualitative immunofluorescence test for the direct detection of RSV in clinical specimens. Throat swabs for viral culture used standard cell culture methods.

Treatment with ribavirin

Ribavirin treatment was used for PICU patients younger than 6 years of age who had RSV LRTI and least one of the following: (1) high-risk for RSV infection, including immunocompromised patients, prematurity, or patients with CHD, BPD, or a malignancy being treated with chemotherapy; (2) severe respiratory distress ($Pao_2 \leq 65$ mmHg or $Sao_2 \leq 90\%$); and (3) requiring ventilator support. Ribavirin (20 mg/mL) was given via continuous aerosol administration for 12—18 hours daily for 3 days. However, ribavirin became unavailable in Taiwan from February 2009.

Definitions of variables

Children with gestational age <37 weeks were regarded as preterm. Hemato-oncological diseases included acute lymphocytic leukemia, acute myeloid leukemia, chronic myeloid leukemia, and lymphoma. Congenital hemodynamically significant heart diseases or cyanotic heart diseases were defined as CHD. Patients with atrial septal defect were excluded from the study. Neurological diseases included cerebral palsy, neuromuscular diseases, or other central nervous system abnormalities. Patients with seizures were excluded from this category. Nosocomial RSV infection was defined as symptoms or signs of RSV infection developing 72 hours or more after admission for other diagnoses.

Statistical analysis

Frequency distribution analysis was used to describe the patients' baseline characteristics. Median and interquartile ranges (IQRs) were used to interpret the demographic distributions. Continuous variables were expressed as a median with IQR and were compared using the Student *t* test or the Mann—Whitney *U* test. Categorical variables were presented as frequencies and percentages and were compared using the χ^2 or Fisher's exact test as appropriate. Univariate analysis was performed to evaluate the relationship between the variables and death. The factors were also analyzed using a multivariate model built by backwards elimination (a significance level of 5%) to assess the