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Prevalence of rhinovirus in wheezing children: a comparison with respiratory syncytial virus wheezing



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ABSTRACT

Objective: To explore the distribution and clinical manifestations of rhinovirus infection in wheezing children, and compare the clinical differences between rhinovirus- and respiratory syncytial virus-induced wheezing.

Materials and methods: This prospective cohort study was carried out in Children's Hospital of Soochow University from Dec 2012 to Nov 2014. We enrolled consecutive hospitalized children <60 months of age presented with wheezing. Clinical data including cough, fever, dyspnea, crackles were recorded by pediatricians on the first day of admission. Meanwhile, nasopharyngeal aspirates were obtained to test for respiratory viruses, by using polymerase chain reaction method for rhinovirus, human bocavirus, and human metapneumovirus, and direct immunofluorescence assay to test for respiratory syncytial virus, adenovirus, parainfluenza virus types 1–3, and influenza virus types A and B.

Results: Rhinovirus was a main causative agent isolated in 14.7% of the hospitalized wheezing children in Suzhou, China, being second to respiratory syncytial virus (21.0%). Different from respiratory syncytial virus infection, which peaked in winter months, rhinovirus could be detected all year round, peaked between July and September, and in November. Children with rhinovirus infection were older and presented with more often allergic sensitizations, blood eosinophilia, and leukocytosis than those of respiratory syncytial virus infection. Logistic regression analysis revealed that rhinovirus-infected children experienced earlier wheezing more often than respiratory syncytial virus children (odds ratio, 3.441; 95% confidence interval, 1.187–9.979; $p = 0.023$).

Conclusion: Rhinovirus was a main viral pathogen in wheezing children, especially in summer time. Rhinovirus-induced wheezing was different from respiratory syncytial virus, apart from seasonal epidemics; these two groups differed with regard to age, allergic sensitizations, laboratory test, and history of wheezing episodes.

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Introduction

A range of respiratory viruses is known to cause acute wheeze, including bronchiolitis and asthma exacerbations. The most frequently reported viral pathogen has been respiratory syncytial virus (RSV) in children less than two years. Other viruses included adenovirus, influenza virus (FLU), parainfluenza virus (Pinf), rhinovirus (RV), human metapneumovirus (hMPV), adenovirus (ADV), and human bocavirus (HBoV). RV caused a wide range of respiratory diseases ranging from common cold to life-threatening pneumonia, and was popular as a major cause of common colds. By the age of two years, about 91.3% of the children once had RV infection.¹

Over the past years, the role of RV in wheezing patients might have been underestimated since the detecting technology for RV was less sensitive. From 2006, with the development of PCR methods, RV was recognized as an important cause of lower respiratory infections in young children, with a detection rate ranging from 5% to 40%.¹⁻⁶ In addition, RV could trigger acute wheezing and was highly prevalent in asthma exacerbations.⁷ Moreover, childhood RV induced wheezing may be more closely related to adult asthma than RSV.^{8,9}

The clinical association of wheezing illness with RV has not been well described in China. Herein, we conducted a prospective cohort study of virus induced wheezing in children, aimed to analyze the distribution and clinical manifestations of RV and compare with RSV-induced wheezing.

Materials and methods

Patient enrollment and data collection

We conducted a prospective cohort study at the Children's Hospital of Soochow University from Dec 2012 to Nov 2014. This study was approved by the Institutional Review Board of Children's Hospital of Soochow University. A standardized protocol was used to enroll a target number of consecutive patients from the inpatient wards of pulmonology. Children aged <60 months who presented with wheezing were included. The exclusion criteria were preterm birth ≤ 37 weeks of gestation, history of a diagnosis of chronic lung disease, congenital heart disease, and immunodeficiency.

After obtaining informed consent from the parents, clinical-epidemiological information was collected by pediatricians on admission. Nasopharyngeal samples were taken within 24 h of admission by trained researchers.

Laboratory analysis

RT-PCR methods were applied to test RNA of RV and hMPV, and DNA of HBoV. Direct immunofluorescence assay was performed on nasal aspirates by using murine monoclonal antibodies (Chemicon) to test RSV, FLU A, FLU B, and Pinf 1, 2, 3.

Statistical analysis

All of the statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS; version 19.0). Categorical variables were compared using chi-square test. Multivariate analysis was performed using logistic regression to determine odds ratios (OR). p -Value <0.05 was considered statistically significant.

Results

Study cohort

Seven hundred and fourteen patients were enrolled in the study. Five enrolled patients were excluded because of incomplete data, leaving a total of 709 subjects in the study cohort. Enrolled and non-enrolled children were similar in age and gender (both $p > 0.05$). Among the 709 children, 277 children were under six months old, 335 aged 6–24 month, and 97 aged 24–60 months. The male to female ratio was 2.4.

Distribution of respiratory viruses in wheezing children

Among the 709 wheezing children, 371 (52.3%) were positive for any of the viruses tested. In order of frequency, RSV (21.0%) and RV (14.7%) were the most frequently detected viruses, followed by HBoV (8.0%), Pinf-3 (6.1%), Pinf-1 (1.0%), FLU-A (0.7%), ADV (0.6%), and hMPV (0.4%). Co-infections were observed in 32 (4.5%) patients, with RV as the most frequently recovered pathogen accounting for 21 (65.6%) patients of co-infections,

Table 1 – Distribution of respiratory viruses in wheezing children.

	RV	RSV	FLU-A	Pinf-1	Pinf-2	Pinf-3	ADV	HBoV	hMPV	Total
RV	83	7	0	0	0	2	0	12	0	104
RSV		134	2	0	0	1	1	4	0	149
FLU-A			2	0	0	1	0	0	0	5
Pinf-1				6	0	0	0	1	0	7
Pinf-2					0	0	0	0	0	0
Pinf-3						37	0	1	0	42
ADV							3	0	0	4
HBoV								39	0	57
hMPV									3	3

Number of samples containing each set of viruses, in boldface, simple infections, no influenza virus B was detected. RV, rhinovirus; RSV, respiratory syncytial virus; FLU, influenza virus; Pinf, parainfluenza virus; ADV, adenovirus; hMPV, human metapneumovirus; HBoV, human bocavirus.

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