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Epidemiology characteristics of respiratory viruses found in children and adults with respiratory tract infections in southern China

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SUMMARY

Background: The World Health Organization (WHO) ranks respiratory tract infection (RTI) as the second leading cause of death worldwide for children under 5 years of age. The aim of this work was to evaluate the epidemiology characteristics of respiratory viruses found in children and adults with RTI from July 2009 to June 2012 in southern China.
Methods: In this work, a total of 14 237 nasopharyngeal swabs (14 237 patients from 25 hospitals) were analyzed, and seven respiratory viruses (influenza virus, respiratory syncytial virus, parainfluenza virus, adenovirus, human metapneumovirus, human coronavirus, human bocavirus) were detected using PCR/RT-PCR from nasopharyngeal swabs.
Results: The demographic characteristics, viral prevalence, age distribution, seasonal distribution, and pathogen spectrum of the patients with RTIs were analyzed. Co-infection was observed in 483 specimens, but it was more common in male patients, inpatients, children, and young adults. It varied by season, being more prevalent in the spring and summer and less so in the winter. Human coronavirus and human bocavirus were the most common pathogens, tending to occur in co-infection with other respiratory viruses.
Conclusions: This work adds to our knowledge of the epidemiology characteristics of these seven common respiratory viruses among patients with RTI in southern China. The detection of the specific viral causes of infection provides a useful starting point for an understanding of illness attributable to respiratory infection, and might also provide data relevant to the development of prevention strategies.

1. Introduction

Respiratory tract infections (RTI) are a significant health burden for children. The World Health Organization (WHO) estimates that 1.9 million children die each year as a result of the complications of acute RTIs, mainly pneumonia,[1] and 70% of RTI deaths occur in Africa and southeast Asia.[2] The major viral agents of RTI include influenza A, B, and C viruses (Flu), respiratory syncytial virus (RSV), parainfluenza virus (PIV), adenovirus (ADV), human metapneumovirus (hMPV), human coronavirus (HCoV), and the newly discovered human bocavirus (HBoV). Flu, RSV, and PIV are often associated with pneumonia, especially in children under 5 years of age and those living in developing countries.[3–8] In one study of hospitalized children, RSV was identified in 15–40% of cases, PIV in 6.8–7%, and Flu in 3%.[9] ADV, HCoV, and HBoV are associated with a substantial proportion of RTI in infants and young children;[7,10–12] hMPV has been detected in up to 10% of respiratory specimens.[13] RSV and PIV may also contribute substantially to mortality among the elderly, and the annual outbreaks and recurrent infections suggest that RSV and PIV may contribute to the burden of disease throughout life.[14,15]

The acquisition and spread of RTIs is known to vary among different study populations in different countries. These variations may be due to cultural and socioeconomic factors, geographical or climatic differences, or variations in health care systems. A clear understanding of the local epidemiology of RTI and the identification

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of risk factors is critical to the successful implementation of a prevention and control program. Southern China is believed to be the origin of some important respiratory viruses, such as severe acute respiratory syndrome coronavirus (SARS-CoV)[16] and influenza virus.[17] Southern China has large populations of humans and domestic and wild animals, as well as a large transient population that includes laborers and business people from different provinces of China and from other countries. The mixing of these large regional populations may favor the transmission of respiratory viruses.

The prevalence and clinical presentation of human viral infections in China have been reported previously.[8,10,18–20] However, there are no previously published reports describing the etiology of the seven common respiratory tract viruses of inpatient and outpatient RTI across the seasons among the various age and gender categories. Information on RTI from southern China is also sparse. To directly address this situation, nasopharyngeal swabs were collected continuously from children and adults seeking medical attention for RTI from a total of 25 hospitals in southern China between July 2009 and June 2012. Seven respiratory viruses were detected by PCR/RT-PCR and their epidemiological characteristics were analyzed.

2. Materials and methods

2.1. Ethics issues

All research involving human participants was approved by the Institutional Review Board of Zhongshan School of Medicine, Sun Yat-sen University, in accordance with the guidelines for the protection of human subjects. Participants provided written informed consent after being briefed on the purpose of the study and of their right to keep information confidential. Written consent was obtained from all study participants or their guardians.

2.2. Patients and specimens

Study participants had all been admitted to one of the 25 hospitals covering southern China. Selection criteria included having one or more respiratory symptoms, such as headache, cough, expectoration, and pharyngodynia, combined with a body temperature above 37.5 °C. Symptoms, history of illness, results of a clinical examination and laboratory tests, and demographic data were collected for each patient using a standardized form. Nasopharyngeal swabs were collected according to a standard procedure, kept in viral transport medium, and stored at −80 °C prior to analysis (one swab was collected from each patient). For patients with viral infections, some additional clinical information was abstracted retrospectively from the medical treatment records.

2.3. Nucleic acid extraction and cDNA synthesis

DNA or RNA was extracted from 200 μl of the nasopharyngeal swab specimen using the QIAamp MiniElute Virus Spin kit (Qiagen). Reverse transcription of virus RNA was conducted using SuperScript III RT (Invitrogen, Life Technology) in order to detect RNA viruses (Flu, RSV, PIV, hMPV, and HCoV). DNA samples extracted using the kit were used directly to detect DNA viruses (ADV and HBoV). Both kits were used in accordance with the manufacturer's instructions.

2.4. Pathogen screening

Flu (A, B, C), RSV, PIV, ADV, hMPV, HCoV, and HBoV were detected by standard PCR or reverse transcription PCR (RT-PCR), as described previously, using specific primers listed in the **Supplementary Material** Table S1,[21–25] and amplified products were detected using agarose gel electrophoresis.

2.5. Statistical analysis

Statistical analysis was performed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA). Viral prevalences were compared using the Chi-square test for categorical variables, and the cartogram was drawn using Excel software. A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Demographic characteristics

A total of 14 237 nasopharyngeal swabs were collected from July 2009 to June 2012. In all, 7323 specimens were from outpatients and 6914 specimens were from inpatients. More specimens were collected from males than from females (ratio 1.48). The median patient age was 21 years (range 0–110 years). The number of children (age ≤14 years) was 6117 and the number of other patients (>14 years) was 8120. The seasonal distribution of patients sampled was 3756 in spring (January to March), 2617 in summer (April to June), 3993 in autumn (July to September), and 3871 in winter (October to December). An estimated 99.9% of eligible patients volunteered to participate. Our data showed a significant difference in inpatient proportion by age, and showed the difference in sex distribution by age. They did not show the 20–30 and 50–55 years groups, and the relative numbers of male participants in other age groups were all over 50%.

3.2. Clinical characteristics of the patients

The clinical characteristics of the patients are listed in the **Supplementary Material** Table S2. Most patients presented with symptoms of respiratory tract illness (RTI), including fever (≥37.5 °C; 100.0%), cough (84.1%), expectoration (42.1%), runny nose (36.4%), and sore throat (19.8%).

3.3. Viral prevalence

The total rate of detection of all seven viruses for all specimens was 39.24% (5582/14 237). Flu viruses were detected in 2632 specimens (18.50%), RSV in 1120 (7.86%), PIV in 494 (3.47%), ADV in 493 (3.47%), hMPV in 319 (2.24%), HCoV in 351 (2.47%), and HBoV in 180 (1.26%). The total viral detection rate (all seven viruses) for all inpatients was 40.01% (2772/6914), which was higher than that of outpatients (38.47%, 2817/7323) (Chi-square = 3.937, $p = 0.047$). With the exception of Flu, the viruses were more common in inpatients than in outpatients (Figure 1). The total viral detection rate (all seven viruses) was higher in male patients (40.11%, 3403/8485) than in female patients (37.95%, 2179/5742) (Chi-square = 6.687, $p = 0.010$). The rates of detection of RSV, PIV, and hMPV were higher in male patients than in female patients, and the detection rate of Flu was lower in male patients than in female patients (Chi-square = 19.262, $p < 0.0001$). There was no difference in the detection rates for ADV, HCoV, and HBoV (Figure 2).

3.4. Age distribution

A decline in the incidence of viral infections with age was observed for respiratory viruses, except for Flu. The detection rates of RSV, PIV, ADV, hMPV, HCoV, and HBoV among children (≤14 years) were higher than among adults (>14 years old). The