Respiratory viruses in adults with acute respiratory tract infections

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Abstract

Background: Respiratory viruses are the main pathogens of acute respiratory infections. Viral respiratory pathogens in children are well studied, but the study on adults are limited. So we design this subject to determine viral respiratory pathogens in patients with acute respiratory tract infections of adults.

Methods: We conducted a retrospective study for the patients with acute respiratory infections from June, 2017 through July, 2018 at Fever Clinic in Peking University Third Hospital. We collected throat swab from the patients diagnosed with acute upper respiratory tract infections and sputum or throat swab diagnosed with community-acquired pneumonia. RT-PCRs were performed to detect infection with the following virus: human rhinovirus, influenza A virus, influenza B virus, human coronavirus 229E/HKU1, Coronavirus OC43/NL63, ADV, RSV, PIV1-4, hMPV and EV. **Results:** 185 throat swabs and sputum were collected from outpatients. Overall, 23.8% (44/185) were found to be positive for at least one respiratory virus. The virus detection rate for AURTIs and CAP was 23.3% (14/60) and 24.0 % (30/125), respectively. The most prevalent viruses detected were IFVs (13.5%, 25/185), PIVs (3.24%, 6/185) and HRVs (2.70%, 5/185). In the Influenza Virus, the highest positive detection rate is 21.4% (6/28) in the group >60 years old, while 11.0% (14/127) in the group <40 years old and 13.3% (4/30) ($P<0.05$). **Conclusion:** In one-year study, IFVs were the dominant pathogens both in acute upper respiratory tract infections and community-acquired pneumonia, followed by PIVs and HRVs. The patients in the group >60 years old had a higher rate of influenza infection

Background

Acute respiratory infections (ARIs) are a major global public health problem, and lead to frequent morbidity, and sometimes cause severe outcomes including death. Respiratory viruses (RVs) are the main pathogens of ARIs. The most common viral causes of ARIs respiratory are respiratory syncytial virus (RSV), parainfluenza viruses (PIVs), influenza viruses (IFVs), adenoviruses (ADVs), human rhinoviruses (HRVs), enteroviruses (EVs), human metapneumovirus (hMPV), human coronaviruses, and human bocavirus. RVs are implicated in 50% of community-acquired pneumonia (CAP) in young children, and over 90% of bronchiolitis cases in infants and young children [1, 2]. In adults, 15-56% of CAP are associated with RVs. About 200 million cases of viral community-acquired pneumonia occur every year [3, 4]. Viral respiratory pathogens in children are well studied, but the study on adults are limited. So we design this subject to determine viral respiratory pathogens in patients with acute respiratory tract infections of adults in Beijing, China.

Methods

Study Patients

Respiratory etiological surveillance monitoring system of Centers for Disease Control (CDC) of Beijing is designed to monitor respiratory pathogens in Beijing. Peking University Third hospital is a sentinel hospital and responsible for routine surveillance of respiratory tract infection. We conduct a retrospective

study for the patients in routine surveillance with acute respiratory infections from June 2017 through July 2018 at Fever clinic. The patients were enrolled according to the following criteria.

1. CAP are diagnosed according to the diagnostic criteria of Chinese adult community acquired pneumonia (2016 edition) developed by Chinese society of respiratory medicine: (1) fever (a body temperature > 38.0 °C) or hypothermia (a body temperature < 35.5 °C), (2) leukocytosis (a white blood cell count > 10,000/ml) or leukopenia (a white blood cell count < 4000/ml); (3) had signs/symptoms of cough, sputum, [respiratory symptom aggravation](#), With or without purulent sputum, chest pain, dyspnea and hemoptysis. (4) chest radiological imaging features are patchy infiltration, leaf segment consolidation shadow, leaf segment consolidation shadow, interstitial inflammation change, with or without [pleural effusion](#) (5) Signs of lung consolidation or rales of lung auscultation. CAP can be established when tuberculosis, pulmonary tumor, non-infectious pulmonary interstitial disease, pulmonary edema, pulmonary atelectasis, pulmonary embolism, pulmonary eosinophil infiltration and pulmonary vasculitis are excluded.

2. Acute upper respiratory tract infections (AURTIs) are [diagnosed](#) according to following criteria: 1. symptoms of acute infection, defined as fever (a body temperature > 38.0 °C) with sore throat, runny nose, cough, [nasal obstruction](#), rhinorrhea, cough and other upper respiratory symptoms.

Data and specimen collection

Detailed demographic information was documented, and laboratory data were collected from the patients' medical files. We collected throat swab from the patients diagnosed with acute upper respiratory tract infections within one week after onset of disease, and sputum diagnosed with CAP, or throat swab if there is no sputum. Specimen were transported to CDC laboratory for pathogen nucleic acid amplification test by reverse transcription-polymerase chain reaction (RT-PCR).

The test includes the following virus: human rhinovirus (HRV), influenza A virus (Flu A), novel influenza A (H1N1), seasonal H3 influenza (H3N2), influenza B virus (Flu B), human coronavirus (HCoV) 229E/HKU1, HCoV OC43/NL63, ADV, RSV, PIV1-4, hMPV and EV.

Statistics

All analyses were performed with the Statistical 18.0 and Microsoft Excel 2007.. General data are presented as a percentage (P), or mean $\pm$ SD. Differences in categorical variables between groups were compared by the χ^2 test. A single-tailed P value of <0.05 was considered to be statistically significant.

Experimental methods

1. [Nucleic Acid Extraction](#): Total nucleic acids including DNA and RNA were extracted from 200 μ L of each specimen using magnetic bead nucleic acid Extraction Kit (Thermo Fisher, American, NO.KFR-

805496) by ABI Mag MAX express 96 according to the manufacturer's instructions.

2. RT-PCR Screening for Respiratory Viruses. For all collected specimens, RT-PCRs were performed to detect infection with ADVs, HBoV, HCoV, hMPV, IFVs, RSV, PIV, EV, and HRV. RT-PCR was performed using a RT-PCR Taq kit (HeChuang, JiangSu, China) by ABI 7500 (real-time PCR) instrument.

3 .Results determination: The following conditions should be simultaneously met the following three standards: 1. sleek S-Curve, 2. $CT \leq 35$, 3. $\Delta Rn \geq 1 \times 10^4$

Results

1. Characteristic of patients with acute respiratory infection

Of all the enrolled patients, 93 (50.3%) were male and 92 (49.7%) were female, the age of the patients ranged from 18.5 to 84.2 years, with a median of 37.9 years. The patients enrolled are all with fever and body temperature ranged from 37.5 to 41 degree centigrade, with a median of 38.8 degree centigrade. In the 185 patients, 135 patients (73.0%) are with cough, 75 (40.5%) with expectoration, 12 (6.5%) are with nasal congestion, 24 (13.0%) are with nasal discharge, and 98 (53.0%) are with sore throat (Table 1).

2. Prevalence of respiratory viruses.

From July 2016 to June 2017, 185 throat swabs and sputum were collected from outpatients. Overall, 44 out of 185 samples (23.8%) were found to be positive for at least one respiratory virus. The virus detection rate for AURTIs and CAP was 23.3% (14/60) and 24.0 % (30/125), respectively. There were 2 samples (10.4%) contained two viruses **respectively** in one AURTI and one CAP. The most prevalent viruses detected were IFVs (13.5%, 25/185), PIVs (3.24%, 6/185) and HRVs (2.70%, 5/185). In the IFVs-samples, there are **respectively** 12 samples with Influenza A Virus and 13 samples with Influenza B Virus. In single infection of IFA -new H1N1 influenza virus and influenza A (H3N2) virus are **respectively** 6 and 5 (Table 2).

3. Seasonality of respiratory virus infection distribution

In one-year study, the top three months of viral isolation are January, **February** and July (53.3%, 33.3%, and 33.3%). **Influenza virus** was highest in January and February which were in flu season. In July, PIVs were the main virus. IFV A was detected at the highest frequency and throughout the year. There were three peak of IFV A in December, January and **February**. IFV B was almost in winter. PIVs and HRVs were not detected in winter. EVs were existed in summer and autumn. RSV, ADVs and hMPV were only existed in winter, autumn and spring **respectively** (Table 3, Figure 1 and 2).

4. Age distribution of respiratory virus profiles

The positive detection rates of viruses that corresponded to different age groups. Overall, virus infection rate is 39.3% in the patients >60 years old $\geq$ 18.9% in the patients of the group <40 and 23.3% in the patients of the group 40-60 years old (23.3%) group ($P > 0.05$). In the Influenza Virus, the highest positive

detection rate is 21.4% (6/28) in the group >60 years old, while 11.0% (14/127) in the group <40 years old and 13.3% (4/30) in the group 40-60 years old ($P<0.05$). The major infectious virus in the older patients in the group 40-60 and >60 years old is Influenza Virus B and the positive rates are 10% (3/30) and 14.3% (4/28). Influenza A Virus is the most common virus in the group of <40 years old (7.9%, 10/127). (Table 4 and Figure3)

5. Distribution of respiratory virus profiles in AURTI group and CAP group.

In the AURTI group, the most prevalent viruses detected were IFVs (15.0%, 9/60), HRVs (6.6%, 4/60) and EVs (3.3%, 2/60). In the CAP group, the most prevalent viruses detected were IFVs (12.8%, 16/125) and PIVs (3.2%, 4/125). In our study, IFVs were the dominate virus in the two groups of AURTI and CAP (Table 5).

Discussion

Respiratory viruses are the main pathogens of ARIs, and in our study, we analysis the respiratory viruses in the AURTI and CAP. In one-year-study, we found that

23.8% of the outpatients with AURTI and CAP were found to be positive for at least one respiratory virus. The virus detection rate for AURTIs and CAP was 23.3% and 24.0 %, which was similar with other studies [5]. The most prevalent viruses were IFVs (13.5%), PIVs (3.24%), and HRVs (2.70%). Influenza viruses are significant human respiratory pathogens that cause both seasonal and endemic infections. Influenza viral infections were common in our study and were found almost throughout the year.

We collected the patients with acute respiratory tract infections including the AURTIs and CAP for virological analysis. In the AURTI group and CAP group, IFVs are the main virus, 15.0% (9/60) in AURTI and 12.8% (16/125) in CAP group. IFV-B was dominant in the influenza season, because of the epidemic strain of seasonal influenza virus was B type in 2018. The risk of IFV infection was higher (21.4%) in the group >60 years, and 11.0% in the group <40 years old, 13.3% in the group 40-60 ($P<0.05$). In another study of the Chinese, IFVs was also the most common agent in hospitalized patient ≥ 65 years [6]. In the IFA infection, patients <40 years old took the highest rates of infections (7.8%), while in the IFB infection, patients in the group >60 years old took the highest peak rates of infections (14.3%). In the previous study, patients with age ≥ 65 years take highest case fatality rate but lowest rate of infection [7].

In the seasonal distribution analysis, influenza A was throughout the year and founded in four seasons, while IFV B was almost in winter. In another two-year-study on the Chinese people, influenza A was also the leading virus of ARIs, but there was some difference in IFV B from our study. In the two-year study, influenza B is active in spring in Beijing and rates of influenza B infection were low throughout the study period. The IFV B peaks occurred following IFV A peaks. In our study, influenza B is active in winter and the peaks occurred with the influenza A because of the epidemic strain of the seasonal influenza virus was B type in 2018[8]. In our daily clinical work, we should take emphasis on IFV, especially IFV A for its high incidence and serious consequence.

In the CAP group of our study, IFVs were the most common (12.8%), especially influenza A (7.2%). In a study on the incidence and characteristics of viral community-acquired pneumonia in adults of New Zealand, rhinoviruses (10%) and influenza A (8%) being the most common. Another respiratory Viruses in adults with community-acquired pneumonia of Israel, the results are quite different for the most common virus are [coronaviruses](#)(13.1%), RSV(7.1%), [rhinovirus](#) (4.9%) and influenza virus(4.4%) [9]. So the distribution of respiratory virus profiles differs between different regions for the unique climatic characteristic and [geographical location](#)

In summary, Influenza is a global burden which is associated with significant morbidity and mortality, and it was the main virus of ARIs and founded throughout the year in our study, so it deserves our more attention in the clinical work. It is a vaccine-preventable disease, so our government should pay full attention on the disease prevention to reduce the economic burden and medical burden.

Conclusions

In the analysis of respiratory viruses in adults with acute respiratory tract infections, the positive rate of viral isolation was 23.8%, and in the group of AURTIs and CAP was 23.3% and 24.0%. IFVs were the dominant pathogens both in acute upper respiratory tract infections and community-acquired pneumonia, followed by PIVs and HRVs. The patients in the group >60 years old had a higher rate of influenza infection

Study limitations

There are several limitations that should be stated. First, we chose the data of one year and the sample size is not large enough, so the conclusion may has limitations. Second, the viral respiratory pathogens differ year by year, and especially in 2018, IFV B is active—so the conclusion deserves further studied.

Abbreviations

ARIs: acute respiratory infections

RVs: respiratory viruses

RSV: [respiratory syncytial virus](#)

PIVs: parainfluenza viruses

IFVs: influenza viruses

ADVs: adenoviruses

HRVs: human rhinoviruses

EVs: enteroviruses

hMPV: human metapneumovirus

CAP: community-acquired pneumonia

CDC: Centers for Disease Control

AURTIs: acute upper respiratory tract infections

HRV: human rhinovirus

Flu A: influenza A virus

H1N1: novel influenza A

H3N2: seasonal H3 influenza

Flu B: influenza B virus

HCoV: human coronavirus

Declarations

Ethics approval and consent to participate

The general Ethics approval has been conducted by Centers for Disease Control (CDC) in Beijing and the Respiratory etiological surveillance monitoring system. This study was approved by the Ethics Committee of Centers for Disease Control in Beijing. The patients enrolled had signed the consent to participate.

Availability of data and material

The datasets used in the current study are available from the corresponding author.

Consent for publication

All the authors read and approved the publication.

Funding details

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

CJ, LXG and XJ designed the study, CJ, WW and JY collected the samples

. CJ wrote the manuscript .All the authors read and approved the final manuscript.

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Table

Table 1. Characteristic of patients with acute respiratory infection

age	37.9±18.5-84.2
gender(M/F)	93/92
body temperature (median; range)	38.8(37.5-41)
clinical symptoms	
cough	135
expectoration	75
nasal congestion	12
nasal discharge	24
Sore throat	98

Table 2 The positive rates of respiratory viruses in each month

month	samples	positive samples	Rato%
2017-6	16	3	18.75%
2017-7	9	3	33.3%
2017-8	14	3	21.4%
2017-9	16	2	12.5%
2017-10	15	4	26.7%
2017-11	20	1	5%
2017-12	20	6	30%
2018-1	15	8	53.3%
2018-2	15	5	33.3%
2018-3	25	2	8%
2018-4	15	5	33.3%
2018-5	15	1	6.7%
Sum	185	44	23.8%

Table 3 Distribution of Respiratory Viruses

month	respiratory viruses
17-6	IFB=1
17-7	PIVs=2,PIVs=2, HRVs=1
17-8	IFA=3
17-9	IFA=1, IFA+RSV=1,PIVs=1
17-10	IFA=1,HRVs=1,EVs=1,ADVs=1
17-11	ADVs=1
17-12	IFA=1, IFB=4, RSV=1
18-1	IFA=3, IFB=4, IFA+RSV=1
18-2	IFA=1, IFB=3, RSV=1
18-3	IFA=1, hMPV=1
18-4	IFA=1, PIVS=1
18-5	HRVs=1

Table 4. Age distribution of respiratory virus profiles

Virus	<40 (n=127)	40-60(n=30)	>60(n=28)
Influenza A Virus	10	1	2
Influenza B Virus	4	3	4
PIVs	2	2	1
HRVs	3	0	2
EVs	3	0	0
RSV	0	1	1
ADVs	2	0	0
hMPV	0	0	1
Positive rate	18.9%(24/127)	23.3%(7/30)	39.3% $\square$ 11/28 $\square$

Table 5 Distribution of respiratory viruses in AURTI and CAP group.

Respiratory virus	Subjects (n)	AURTI	CAP
IFVs	24	9	16
Influenza B Virus	12	5	7
new H1N1 influenza virus	7	2	5
influenza A(H3N2) viruse	5	2	3
H3N2+RSV	1	1	0
H3N2+PIV-2	1	0	1
PIVs	5	1	4
HRVs	5	4	1
EVs	3	2	1
RSV	2	1	1
ADVs	2	1	1
hMPV	1	0	1

Figures

Figure 1

Monthly distribution of respiratory virus infection

Figure 2

Seasonality of respiratory virus infection distribution

Figure 3

Age distribution of respiratory virus profiles