Epidemiological and Clinical Characteristics of All-age Population with Human Respiratory Syncytial Virus, Beijing, 2015–2019

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Abstract

Background We investigate the epidemiological and clinical characteristics of respiratory infections with respiratory syncytial virus (RSV) among the entire population in Beijing, China. Methods All-age patients with respiratory infection between 2015-2019 were enrolled from 35 sentinel hospitals in Beijing. Their respiratory specimens were obtained for testing of 11 respiratory pathogens, including RSV. Their demographic data and medical record were collected in standardized forms. Results The RSV epidemic season approximately occurred between October to March with a peak in December or January and covered 90% of RSV infections with RSV-A dominated in each year. Children aged 5 years were at the highest risk of RSV infection (52.2%), followed by the elderly adults aged [?]60 years (25.2%). While the elderly patients with RSV were prone to develop dyspnea and lymphocytopenia than other population segments. Moreover, they had an elevated rate of hospitalization, an increased rate of ICU admission, an extended length of hospital stay, and elevated mortality compared to the <5 years children with RSV infection. Conclusions The young children was the population with the highest risk for RSV infection followed by the elderly adults. While the later easily developed a severe infection and need full consideration when making policy.

Introduction

Respiratory syncytial virus (RSV) is one of the most important pathogens leading to severe lower respiratory tract infection in children. It causes 2.7–3.8 million hospitalizations and 94,600–149,400 deaths in children under five years of age each year[1]. It can also result in severe respiratory infections in high-risk adults or elderly healthy persons. Therefore, RSV has been raising concern[2] and RSV surveillance is being conducted in many countries. The United States has included RSV in the National Respiratory and Enteric Virus Surveillance System since 1989[3, 4]. Japan has used the National Epidemiological Surveillance System for Infectious Diseases to monitor RSV since 2003[5]. The European Union has initiated RSV surveillance using the existing influenza surveillance network since 2003[6, 7]. The United States also launched the Global Disease Detection project in 2004, which monitored influenza virus and RSV in several countries world[8]. Likewise, the World Health Organization began monitoring RSV using the global influenza network in 2017[9]. However, so far, a nationwide RSV surveillance network has not been established in China.

China has a heavy burden of RSV infection. Several studies have reported that the RSV detection rate in pneumonia cases in Chinese children could reach 17%–33% during the RSV epidemic season[10, 11]. However,

these studies rarely cover RSV infections in adults (particularly in elderly persons). Given that China is the most populous country globally and its aging population problem is becoming more serious, we can speculate that the proportion of Chinese elderly adults with RSV should not be small. Therefore, more attention should be paid to RSV infections among Chinese adults, especially Chinese elderly adults.

Up to now, there is no licensed RSV vaccine available. Palivizumab is the only prophylaxis biological product approved by the Food and Drug Administration in the USA for use in infants at high risk of severe RSV infection[12], but it is expensive and was not approved by the Chinese Food and Drug Administration. In addition, there is still no specific therapy drug for RSV, and only symptomatic and supportive treatments for RSV infection are available. Thus, it is urgent to establish an effective RSV surveillance system that covers all age groups (particularly the population with a high risk of severe respiratory infection) in China, which would contribute to a better understanding of the epidemiological and clinical characteristics of RSV infection in different ages groups, a better controlling the RSV epidemic and a better administration of severe RSV infection cases.

Our research team has established the Respiratory Pathogen Surveillance System (RPSS) in Beijing since 2014, which consists of 17 Centers for Disease Control and Prevention (CDCs) and 30 sentinel hospitals. Using this surveillance system, we have monitored the 11 most common respiratory pathogens, including RSV, influenza virus, and adenovirus. In this study, we systematically investigated the prevalence of RSV in Beijing for four consecutive years from March 2015 to February 2019, and compared the clinical characteristics of RSV infection among people of different age groups, with a focus on children under five years of age and elderly adult over 60 years of age.

Population and Methods1.1 Ethics statement

This study was approved by the Ethics Committees at Beijing Center for Disease Prevention and Control. Enrollees (or their guardians if appropriate) were told the nature, purpose, procedures, and potential health impact regarding this study, and written informed consent was obtained from each one. Patients were required to provide consent by themselves if their age and medical condition were appropriate.

1.2 Study population

The patients with acute upper respiratory tract infection (AURTI) or community-acquired pneumonia (CAP) were enrolled with the RPSS network every month. AURTI patients were included if they presented with fever and/ or respiratory symptoms, e.g., cough, sputum production, and sore throat. Pneumonia patients were included if they had evidence of CAP according to Guidelines of Diagnosis and Treatment for Community-Acquired Pneumonia among Adults in China (released in 2013 by Chinese Thoracic Society, Chinese Medicine Association)[13-15], and further classified as severe community-acquired pneumonia (SCAP) and non-severe community-acquired pneumonia (NSCAP) based on illness severity according to the guidelines described previously[16].

1.3 Specimen and data collection

Respiratory tract samples were collected from the enrolled patients upon hospital visit, including oropharyngeal swabs, sputum specimens, endotracheal aspirates, or bronchoalveolar-lavage specimens. For inpatients, only specimens obtained within 72 hours before or after hospital admission were included. Demographic, epidemiological, and clinical data were collected systematically using standardized forms.

1.4 Laboratory examinations

Total nucleic acids were extracted and tested for the respiratory syncytial virus. Other eight respiratory viruses (influenza virus A and B [FLU A, FLU B], influenza virus AH1N1 2009 pandemic and AH3N2 [AH1N1 2009, AH3N2], parainfluenza virus 1, 2, 3, 4 [PIV 1, 2, 3, 4], adenovirus [AdV], human rhinovirus [HRV], human metapneumovirus [HMPV], human coronavirus 229E/NL63, OC43/HKU1 [CoV 229E/NL63, OC43/HKU1], human bocavirus [HBoV], and human enterovirus [EV]), *M. pneumoniae* (MP), and*Chlamydophila pneumoniae* (CP) were also identified according to the design of this study using a real-

time PCR-based approach (Multiplex Combined Real-time PCR Detection Kit for Respiratory Viruses, Jiangsu Uninovo Biological Technology Co. Ltd., China). RSV-positive samples were further identified into RSV group A (RSV-A) and RSV group B (RSV-B) (Duplex Real-Time PCR Kit for RSV, Beijing Kinghawk Pharmaceutical Co., Ltd., China).

1.5 Statistical analysis

Continuous variables were presented as median (interquartile range, IQR) and compared with the Kruskal-Wallis test between different groups; categorical variables were presented as numbers (%), and comparisons between different groups were done by the χ^2 test or Fisher's exact test. A two-sided α of less than 0.05 was considered statistically significant. Statistical analysis was done using SPSS statistical software version 19.0 (SPSS Inc., Chicago, IL, USA).

2. Results

2.1 Demographic characteristics and RSV detection

From March 1, 2015, to February 29, 2019, a total of 29,923 cases were included in this study, of whom 8,586 (29%) were with AURTI, 16,121 (54%) were with non-severe community-acquired pneumonia (NSCAP), 4,139 (14%) were with severe community-acquired pneumonia (SCAP), and 1074 (4%) were with bronchitis (3 had missing final diagnostic information). Male (16, 668; 56%) and female (13,162; 44%) patients were included in this study (93 missing gender information). The youngest was 1 month old, and the oldest was 104 years old with a median age of 38 years old (120 patients missing age information).

Of all included patients, RSV was detected in 623 (2%), including 92 (15% of 623 RSV infections) patients with AURTI, 429 (69%) with NSCAP, and 92 (15%) with SCAP (diagnostic information was not found for 10). Among these patients with RSV, 352 (57%) were male, 267 (43%) were female (4 missing gender information), the minimum age was 1 month old, and the maximum was 101 years old with a median age of 4 years old (age information was not found for three).

Of the 623 RSV-positive cases, 391 (62.8%) were identified as RSV-A, 126 (20.2%) as RSV-B, and 106 (17.0%) were not identified successfully.

2.2 Epidemiological characteristics of RSV infections

From March 2015 to February 2019, we observed a yearly RSV epidemic around Winter as expected. RSV detection rate began to rise in October, peaked in December or the following January, and fell to an ordinary level in April, with about 90% of RSV infections occurring during the epidemic season (from October to the following March) (Fig. 1A, B). In different years, the RSV epidemic season may advance or be delayed by about one month. Two groups of RSV (RSV-A and RSV-B) were prevalent each year, but RSV-A remained predominant from March 2015 to February 2019. The proportion of RSV-A infection among total RSV-positive cases was 62.8%. (Fig. 1C)

RSV detection rate was the highest in the 0-year-old group (9.98%), followed by the 1-year-old group (6.18%), and the 2–4-years-old group (4.92%); it decreased significantly to a low level in 5–44 years group (5–13 yr: 1.68%; 14–17 yr: 0.61%; 18–44 yr: 0.57%), and increased in the 45–59 years of age adults (1.15%), and more obviously in the elderly persons with 60 years of age or older (1.57%) (Fig. 2A). Both RSV-A and RSV-B were detected in all age groups, with RSV-A a dominant proportion (Fig. 2A). For further analysis, the above mentioned nine age groups were incorporated into four age groups as 0–4 years (subtotal of detection rate: 6.07%), 5–17 years (subtotal of detection rate: 1.51%), 18–59 years (subtotal of detection rate: 0.76%), and 60 years or older (subtotal of detection rate: 1.57%). The proportion of RSV infections under five years old (52%) among the total RSV infections was the greatest, followed by that of the elderly adults with 60 years of age or older (25%); the top two groups accounted for 77% of RSV infections (Fig. 2B).

The RSV detection rate of pneumonia cases (NSCAP and SCAP) was higher than that of AURTI cases by age group, which showed that RSV was more prone to cause acute lower respiratory tract infection. However, the RSV detection rate of NSCAP cases was slightly higher than that of SCAP cases despite no significant

difference observed. Although RSV-A and RSV-B were both detected among each class of RSV infection in each age group, RSV-A approximately dominated in each group (Fig. 3).

The most common co-existing pathogen identified from RSV-positive cases was the influenza virus (10.2%), followed by *M. pneumoniae*(4.1%; Fig. 4).

2.3 Clinical characteristics of RSV infections

2.3.1 Clinical manifestations and laboratory findings

Among the 623 patients with RSV infection identified in this study, the medical data of 597 were collected successfully and analyzed. The comorbidity rate was 2.9% in the 0–4 years old group, 0% in 5–17 years old group, 22.4% in 18–44 years old group, and 57.2% in [?]60 years old group; and presented an approximately rising trend as age increasing ($p < 0.001$). Among the children with 0 to 4 years of age, the most common symptoms were cough (95.8%), fever (87.8%), sputum production (61.0%), rhinorrhea (42.9%), nasal congestion (33.5%), dyspnea (12.3%), and sore throat (11.6%), whereas among the adults 60 years of age or older, the most common symptoms were cough (88.8%), sputum production (82.9%), fever (74.8%), dyspnea (52.6%), sore throat (18.4%), and rhinorrhea (17.1%). Notably, almost more than half of patients with RSV infection aged [?]60 years eventually developed dyspnea in their clinical course (52.6%; Table 1).

There were some differences in blood analysis observed between the younger children and the elderly adults with RSV. The elderly patients frequently developed lymphopenia (5.1% for 0–4 yr, 41.5% for [?]60 yr, $p<0.001$), neutrophilia (15.1% for 0–4 yr, 71.2% for [?]60 yr, $p<0.001$), and elevated C-reactive protein (CRP; 23.2% for 0–4 yr, 73.6% for [?]60 yr, $p<0.001$), which indicated that there might be co-existing bacterial infection in these elderly patients besides RSV infection. However, the younger child patients were more likely to develop elevated aspartate aminotransferase (AST) levels (34.9% for 0–4 yr, 13% for [?]60 yr, $p<0.001$) and/or an elevated creatine kinase MB fraction (CKMB; 30.4% for 0–4 yr, 2.5% for [?]60 yr, $p<0.001$), which suggested that acute heart injuries may have occurred (Table 2).

Radiographic findings showed that the older the age of the patients with RSV infection was, the larger the proportion of pneumonia (23.2% for 0–4 yr, 59.2% for [?]60 yr, $p<0.001$). Furthermore, about 50% of the abnormal radiographic findings involved bilateral lung in children and adults (Table 2).

2.3.2 Treatments and outcomes

Approximately 65% (390/597) of RSV infections identified in this study were inpatients. The median time from illness onset to hospital admission was 3.5 days (IQR 2–5 days) in 0–4 years old group, 3 days (IQR 1–6 days) in 5–17 years old group, 2.5 days (IQR 1–6 days) in 18–44 years old group, and 3 days (IQR 1–6 days) in [?]60 years old group with no significant difference observed. The hospitalization rates in the four age groups were different significantly as follows: 65.5%, 52.5%, 48.7%, and 78.3% ($p<0.001$). As age increased, the median length of hospital stay extended significantly as follows: 7 days (IQR 6–9 days), 8 days (IQR 5–11 days), 10 days (IQR 7–15 days), and 12 days (IQR 8.5–16 days) ($p<0.001$). The rate of ICU admission among the four age groups differed obviously as follows: 0.6%, 0.0%, 10.5%, 15.1% ($p<0.001$). Taken together, the patients with [?]60 years old were all the highest in the rate of hospitalization, the length of hospital stay, or the rate of ICU admission among the four age groups (Table 3).

Compared with children aged 0–4 years, the rates of antibiotic use (60.7%, 74.4%, $p<0.001$), oxygen support therapy (12.6%, 62.5%, $p<0.001$), and mechanical ventilation (8.4%, 12.5%, $p=0.035$) among the elderly patients aged [?]60 years were all significantly increased. However, the rates of vasoactive drug administration, corticosteroid use, and antiviral therapy among the four age groups were similar. Eight (8/597) patients with RSV infection were treated with extracorporeal membrane oxygenation (ECMO), and one case, a 63-year-old man, died (Table 3).

The most frequent complications among RSV-infected patients were acute myocardial injury in children (9% in 0–4 yr group, 6.8% in 5–17 yr group), respiratory failure in adults (11.8% in 18–59 yr group, 15.8% in [?]60 yr group). The RSV infections in adults with [?]60 years of age resulted more frequently in organ

failures than in the other three younger age groups, and heart failure (13.2%) and renal failure (5.9%) were also commonly observed besides respiratory failure (15.8%). Five adults with RSV infection (0.8%, 5/597) developed acute respiratory distress syndrome (ARDS), two in the 18–59 age group and three in the [?]60 age group. (Table 3)

The median time from onset to discharge was 11 days (IQR 9–14 days) in 0–4 years old group, 13 days (IQR 10–17 days) in 5–17 years old group, 13 days (IQR 11–18 days) in 18–44 years old group, and 16 days (IQR 12–20 days) in [?]60 years old group, and extended significantly as age increased ($p<0.001$). The mortality of 597 RSV infections was 1.7%. No death was observed in the patients of 0–4 years and 5–17 years of age. Two deaths in the hospital occurred in the 18–49 age group (mortality 6.7%) and 8 deaths in the [?]60 age group (mortality 7.8%). From onset to death of these two age groups, the median times were 10.5 days (IQR 2–19 days) and 15.5 days (9.3–21.8 days), respectively (Table 3).

3.Discussion

Using hospital-based and multicenter surveillance for RSV infection among the all-age population in Beijing for four years, this study revealed the epidemiological characteristics of RSV in Beijing from 2015 to 2019: The RSV was prevalent in the all-age population in Beijing with only one annual epidemic season. Moreover, the RSV season started in October, ended in March of the following year with a single peak in Winter, and covered about 90% of RSV infections. The epidemic season's onset and offset times in different years may advance or be delayed by about one month. However, the offset time of the RSV epidemic season we observed was not consistent with Yu et al.'s report[17]. The reason may be that they adopted the definition of the RSV epidemic season described previously by CDC in the U.S.[18], the consecutive weeks during which the RSV detection rate per week exceeds a threshold of 10%, which might be appropriate for RSV infections among children but not applicable in this study due to the inclusion of adults. Yu et al. also reported that RSV-A and RSV-B dominated alternatively in different years in Beijing from 2007 to 2015[17], but we observed that RSV-A has remained dominant in Beijing since 2015.

This study compared the prevalence of RSV infections among the populations of different age groups and found that the detection rate of RSV was highest in children under five years of age (6.07%), followed by people aged [?]60 years (1.57%). Ren et al[19] reported that the RSV detection rate in patients aged [?]66 years was 2% in Beijing during 2005–2007, the same percentage Feng et al.[10] reported for the average of RSV detection rates in patients aged [?]65 years from 22 provinces in China from 2009 to 2013. These two estimates are slightly higher than ours, probably due to the inclusion of the 60–64 years of age population in our study. However, our findings confirmed that the elderly people aged [?]60 years were another RSV infection susceptible population, accounting for 25.2% of total RSV infections, besides the expected children under five years of age, who accounted for 52.0%. Given that China is the world's largest population country and its population is aging, it can be speculated that the proportion of RSV-infected patients with 60 years of age or older will increase continuously shortly. So, the elderly population, 60 years of age or older, should receive full consideration when the RSV prevention and control policy is made.

This study also found that co-infection of multiple pathogens was common in RSV-infected cases. The most frequently identified pathogens was the influenza virus, followed by *M. pneumoniae* , which might be due to a certain overlap of the epidemic seasons of RSV, influenza virus, and*M. pneumoniae* in Beijing[16].

Another contribution of this study was that we described and compared the clinical characteristics of patients with RSV infection from different age groups in Beijing, particularly patients 60 years or older. We found that the many key indicators of the patients with RSV infection among the elderly adult aged [?]60 years were significantly higher than those among the populations of any other age group, namely, the rate of hospitalization, the rate of ICU admission, and the rate of death in hospital. However, the RSV detection rate of the elderly adult aged [?]60 years was lower than that of children under five years old.

As to clinical manifestations, the most outstanding for RSV-infected patients with [?]60 years of age was dyspnea followed by lymphocytopenia, which was more common compared to other age groups, and occurred at a significantly higher frequency than the RSV-infected patients under five years of age. Regarding com-

plications, there was an obvious difference in the different age groups. RSV infections in elderly adults aged [?]60 years were frequently complicated by respiratory failure, heart failure, and kidney failure compared to other populations, while acute myocardial injury was more common in RSV infections in children under five years of age. Notably, a total of eight RSV-infected patients with severe pneumonia were given ECMO therapy in this study, and finally, seven cases were cured, and one died. This favorable ratio suggests that there may be a chance to improve the hospitalization mortality of RSV-infected adults further and needs to be confirmed by collecting more cases.

Several studies reported the RSV infection in elderly adults focusing on different aspects, and considered that the RSV infection led to a heavier health burden and more severe illness in the elderly adults than influenza[2, 20, 21]. In this study, the hospital length of stay of patients with RSV infection was elevated as the age of the patients increased, the hospital length of stay in RSV-infected patients with [?]60 years was 12 days, and was longer than that of any other age group, but was shorter than the hospital stay of 20 days reported by Jin et al[20] for RSV-infected elderly adults in South Korea. The hospitalization mortality of RSV-infected patients aged [?]60 years is 7.8%, which was also significantly higher than that of children with RSV infection under five years of age (0%), and approximately consistent with the study of Falsey et al. [2] on American healthy elderly adults (mortality of 8% among RSV-infected patients aged [?]65 years), but lower than Jin's[20] study on the elderly adults in South Korea (mortality of 12% among RSV-infected patients aged [?]65 years).

In conclusion, The RSV season in Beijing usually began in October and ended in March of the following year and covered approximately 90% of RSV infections. The RSV infection in the elderly aged [?]60 years old, the second most susceptible population, usually developed more severe outcomes than in children under five years of age, with dyspnea and lymphocytopenia as important clinical characteristics.These findings can promote the comprehensive understanding of the illness course and contribute to the policy-making on RSV prevention and control in China, particularly in Beijing.

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Contributions

LM, GC and ZY did data analysis and prepared the manuscript. HF and XWB conducted the study design and reviewed the manuscript. LM, GC, WX, LY, LQ, LAH, WYT, LMZ and DM tested the specimens.

Figure 1. RSV seasonality in Beijing.

The average percentage of RSV-positive cases per month among the tested cases in Beijing from March 2015 to February 2019. Gray bars denote the tested cases per month, blue bars denote the RSV-positive cases per month, and the brown line denotes the average percentage of RSV-positive cases per month among the tested cases. B) Average proportion of RSV-positive cases per month among the total RSV-positive cases in Beijing from March 2015 to February 2019. C) RSV detection rate by month in Beijing from March 2015 to February 2019. The bars represent the RSV detection rate per month. Blue denotes RSV group A, orange denotes RSV group B, gray denotes untyped RSV. RSV, respiratory syncytial virus.

Figure 2. Distribution of RSV infections by age group in Beijing from March 2015 to February 2019. A) RSV detection rate by age group. The bar represents the RSV detection rate per age group. Blue denotes RSV group A, orange denotes RSV group B, and gray denotes untyped RSV. RSV, respiratory syncytial virus. B) Proportion of RSV-positive cases per new-age group (9 age groups were combined into 4 new-age groups).

Figure 3. RSV detection rates andproportions of RSV subgroups by age group and illness severity in Beijing from March 2015 to February 2019. A) RSV detection rate by age group and

illness severity. The bar represents RSV detection rate per age group and illness severity. B) Proportion of RSV groups per age group and illness severity. Blue denotes RSV group A, orange denotes RSV group B, and gray denotes untyped RSV. RSV, respiratory syncytial virus. AURTI, Acute upper respiratory tract infection. NSCAP, non-severe community-acquired pneumonia. SCAP, severe community-acquired pneumonia.

Figure 4. Co-existing pathogens identified in RSV-positive cases. The blue bars denote the positive cases of co-existing pathogens identified in RSV-positive cases. The orange line denotes the positive rates of co-existing pathogens identified in RSV-positive case (the data are represented in the second Y-axis). Here, AdV denotes adenovirus, CoV coronavirus, Flu influenza A or B virus, HMPV human metapneumovirus, HRV human rhinovirus, PIV parainfluenza virus, RSV respiratory syncytial virus, HBoV human bocavirus, EV enterovirus, MP *M. pneumoniae* , and CP *Chlamydophila pneumoniae* .

Table 1 Demographic and clinical characteristics of 597 patients infected with RSV.

	0–4 yr. n=310	5–17 yr. n=59	18–59 yr. n=76	[?]60 yr. n=152	P-value
Demographics and clinical characteristics					
Female	124 (40%)	26 (44.1%)	36 (47.4%)	70 (46.1%)	0.506
Inpatient	203 (65.5%)	31 (52.5%)	37 (48.7%)	119 (78.3%)	<0.001
Time from illness onset to hospital admission, days	3.5 (2–5)	3 (1–6)	2.5 (1–6)	3 (1–6)	0.065
Comorbidity	9 (2.9%)	(0%)	17 (22.4%)	87 (57.2%)	<0.001
Asthma	1 (0.3%)	0 (0%)	6 (7.9%)	7 (4.6%)	<0.001
Bronchitis/bronchiolitis	1 (0.3%)	0 (0%)	1 (1.3%)	12 (7.9%)	<0.001
Chronical Obstructive Pneumonia disease	0 (0%)	0 (0%)	3 (3.9%)	13 (8.6%)	<0.001
Diabetes	1 (0.3%)	0 (0%)	5 (6.6%)	24 (15.8%)	<0.001
Hypertension	2 (0.6%)	0 (0%)	9 (11.8%)	52 (34.2%)	<0.001
Heart disease	4 (1.3%)	0 (0%)	1 (1.3%)	35 (23%)	<0.001
Chronical renal disease	1 (0.3%)	0 (0%)	2 (2.6%)	2 (1.3%)	0.143
Chronical liver disease	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)	0.481
Malignancy	2 (0.6%)	0 (0%)	0 (0%)	6 (3.9%)	0.034
Stroke	0 (0%)	0 (0%)	1 (1.3%)	16 (10.5%)	<0.001
Symptoms and signs					
Fever (temperature [?]37.3°C)	267/304 (87.8%)	57/58 (98.3%)	67/75 (89.3%)	113/151 (74.8%)	<0.001
Temperature, °C					
<37.3	37/304 (12.2%)	1/58 (1.7%)	8/75 (10.7%)	38/151 (25.2%)	<0.001

37.3–37.9	21/304 (6.9%)	3/58 (5.2%)	4/75 (5.3%)	21/151 (13.9%)	
38–38.9	129/304 (42.4%)	25/58 (43.1%)	41/75 (54.7%)	59/151 (39.1%)	
[?]39	117/304 (38.5%)	29/58 (50%)	22/75 (29.3%)	33/151 (21.9%)	
Sore throat	36 (11.6%)	20 (33.9%)	27 (35.5%)	28 (18.4%)	<0.001
Cough	297 (95.8%)	52 (88.1%)	66 (86.8%)	135 (88.8%)	0.003
Sputum production	189 (61%)	37 (62.7%)	55 (72.4%)	126 (82.9%)	<0.001
Hemoptysis	2 (0.6%)	0 (0%)	2 (2.6%)	4 (2.6%)	0.138
Chest pain	1 (0.3%)	1 (1.7%)	5 (6.6%)	7 (4.6%)	0.001
Dyspnea	38 (12.3%)	0 (0%)	21 (27.6%)	80 (52.6%)	<0.001
Nasal congestion	104 (33.5%)	18 (30.5%)	9 (11.8%)	12 (7.9%)	<0.001
Rhinorrhea	133 (42.9%)	23 (39%)	22 (28.9%)	26 (17.1%)	<0.001
Headache	1 (0.3%)	4 (6.8%)	8 (10.5%)	7 (4.6%)	<0.001
Fatigue	2 (0.6%)	3 (5.1%)	11 (14.5%)	11 (7.2%)	<0.001
Myalgia	0 (0%)	0 (0%)	3 (3.9%)	5 (3.3%)	0.002
Diarrhea	11 (3.5%)	0 (0%)	1 (1.3%)	4 (2.6%)	0.534
Abdominal pain	6 (1.9%)	0 (0%)	4 (5.3%)	2 (1.3%)	0.175
Nausea or vomiting	14 (4.5%)	1 (1.7%)	2 (2.6%)	4 (2.6%)	0.717
Oliguria	1 (0.3%)	0 (0%)	0 (0%)	1 (0.7%)	0.731
Disturbance of consciousness	0 (0%)	0 (0%)	3 (3.9%)	11 (7.2%)	<0.001
Abnormal respiratory rate, beats/min	116/237 (48.9%)	5/46 (10.9%)	6/65 (9.2%)	10/137 (7.3%)	<0.001

Data are median (IQR) or n (%). p-values were calculated by Kruskal-Wallis test, χ^2 test, or Fisher's exact test, as appropriate.

Table 2 Laboratory andradiographic findings of 597 patients infected with RSV.

	0–4 yr. n=310	5–17 yr. n=59	18–59 yr. n=76	[?]60 yr. n=152	P-value
Laboratory findings					
White blood cell count, ×109 per L	7.98 (6–10.8)	8.0 (6.4–10.4)	7.3 (5.5–10.0)	7.5 (5.9–10.7)	0.485
<4	6/280 (2.1%)	/49 (0%)	7/71 (9.9%)	10/145 (6.9%)	0.037
4–10	189/280 (67.5%)	35/49 (71.4%)	47/71 (66.2%)	92/145 (63.4%)	
[?]10	85/280 (30.4%)	14/49 (28.6%)	17/71 (23.9%)	43/145 (29.7%)	
Lymphocyte count, × 109 per L	3 (2–4.4)	2.05 (1.225–2.875)	1.4 (0.9–2.15)	1.1 (0.7–1.7)	<0.001
<1000	14/277 (5.1%)	8/48 (16.7%)	19/68 (27.9%)	54/130 (41.5%)	<0.001
Neutrophil proportion, %	49 (32.0–62.5)	64.9 (58.1–74.0)	72.8 (57.3–83.3)	76.5 (67.6–84.3)	<0.001
<50	138/271 (50.9%)	7/49 (14.3%)	11/70 (15.7%)	5/139 (3.6%)	<0.001
50%–69%	92/271 (33.9%)	24/49 (49%)	19/70 (27.1%)	35/139 (25.2%)	

[?]70%	41/271 (15.1%)	18/49 (36.7%)	40/70 (57.1%)	99/139 (71.2%)	
Platelet count, × 109 per L	294 (225–368.5)	292 (225–355.5)	200 (166.25–260)	197 (154–246)	<0.001
<100	1/285 (0.4%)	/51 (0%)	4/69 (5.8%)	10/154 (6.5%)	<0.001
Creatinine, μmol/L	22 (18.6–26.9)	36.9 (29.7–39.8)	60 (51–78)	69.5 (56.5–87.6)	<0.001
>133	/98 (0%)	/16 (0%)	/25 (0%)	7/94 (7.4%)	0.02
Blood urea nitrogen, mmol/L	2.8 (2.1–3.625)	2.7 (2.3–4)	4.6 (2.95–6.025)	5.1 (3.9–7.55)	<0.001
[?]7.14	2/101 (2%)	1/15 (6.7%)	2/26 (7.7%)	27/90 (30%)	<0.001
Alanine aminotransferase, U/L	20 (14–28)	13 (10–37.5)	22 (11.5–36.5)	16 (11–26)	0.174
Aspartate aminotransferase, U/L	34.5 (28.75–44)	27 (20–31.5)	24 (17–34)	21 (17–32.75)	<0.001
>40	37/106 (34.9%)	2/17 (11.8%)	4/26 (15.4%)	12/92 (13%)	0.001
Creatine kinase, U/L	77 (52.8–119.0)	81 (50.0–105.3)	78 (55.0–131.8)	77 (45.0–134.0)	0.951
Creatine kinase MB fraction, U/L	21 (15.5–29)	19.5 (14–21)	10.5 (2.8–17.3)	10 (5.3–14.0)	<0.001
>25	31/102 (30.4%)	3/17 (17.6%)	2/19 (10.5%)	2/79 (2.5%)	<0.001
Sodium, mmol/L	137.5 (136–139)	139 (136–139.1)	138 (135.5–142)	138 (135–140)	0.619
Erythrocyte sedimentation rate, mm/hour	21 (15.5–29.3)	42 (14–59)	24.5 (15.8–48.8)	35 (25–60)	0.267
C-reactive protein, mg/L	8 (6–8)	9 (8–80)	18.55 (12.25–120.175)	26 (8.5–81.8)	<0.001
[?]10	13/56 (23.2%)	3/7 (42.9%)	14/16 (87.5%)	39/53 (73.6%)	<0.001
Procalcitonin, ng/mL	0.15 (0.1–0.39)	0.39 (0.25–0.64)	0.055 (0.02–0.1675)	0.09 (0.05–0.31)	0.019
The arterial partial pressure of oxygen	97 (77.25–105.25)	96 (91–98)	82 (65–98)	92 (74–96)	0.099
Saturation of arterial blood oxygen, %	97 (92–99)	94.5 (89–97)	94 (88–99)	94 (88–98)	0.135
<90	6/35 (17.1%)	2/8 (25%)	7/23 (30.4%)	33/105 (31.4%)	0.346
Radiographic findings					
Monolateral involvement of chest radiographs	40 (12.9%)	12 (20.3%)	16 (21.1%)	46 (30.3%)	<0.001

bilateral involvement of chest radiographs	32 (10.3%)	4 (6.8%)	19 (25%)	44 (28.9%)

Data are median (IQR) or n (%). As appropriate, p-values were calculated by the Kruskal-Wallis test, χ^2 test, or Fisher's exact test.

Table 3. Treatments and outcomes of 597 patients infected with RSV.

	0–4 yr. n=310	5–17 yr. n=59	18–59 yr. n=76	[?]60 yr. n=152	P-value
Treatments					
Vasoactive drug	6 (1.9%)	1 (1.7%)	1 (1.3%)	6 (3.9%)	0.573
Antiviral treatment	19 (6.1%)	1 (1.7%)	7 (9.2%)	7 (4.6%)	0.288
Antibiotics	188 (60.6%)	30 (50.8%)	35 (46.1%)	113 (74.3%)	<0.001
Corticosteroids	61 (19.7%)	11 (18.6%)	10 (13.2%)	24 (15.8%)	0.509
Oxygen therapy	39 (12.6%)	2 (3.4%)	27 (35.5%)	95 (62.5%)	<0.001
Mechanical ventilation	26 (8.4%)	0 (0%)	6 (7.9%)	19 (12.5%)	0.035
noninvasive	25 (8.1%)	0 (0%)	4 (5.3%)	7 (4.6%)	<0.001

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