

Analysis of Incidence and Clinical Characteristics of RSV Infection in Hospitalized Children: A Retrospective Study

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Objective: To investigate the incidence and clinical characteristics of hospitalized children with respiratory syncytial virus (RSV) infection, and to provide evidence for the importance of preventive strategies and improvements in supportive care of RSV infection.

Methods: This retrospective study included children under 14 years who received throat swab test and were diagnosed with RSV infection from January 2019 to December 2020. Throat swabs and intravenous blood were the main sources of samples, which were obtained within 24 hours of hospitalization. Direct immunofluorescence assay was used to diagnose RSV infection.

Results: Among the 448 hospitalized children with RSV infection, males (71.9%) showed the highest proportion, the highest incidence was found in children <6 months old (45.3%), and 76.6% of them had pneumonia. Pharyngeal redness, cough, expectoration, and mental fatigue were the most common symptoms in hospitalized children of all ages. More than 60% of hospitalized children had increased lymphocyte count, aspartate aminotransferase, creatine kinase-MB form, lactate dehydrogenase, and α -HBDH levels. The rates of myocardial damage, respiratory failure, stay in the intensive care unit (ICU), use of mechanical ventilation, and absorption of oxygen were higher in children <6 months old. Except for children who were 37–60 months old, the percentage of length of hospital stay ≥ 7 days in the other age groups was greater than 62.0%. Except for children who were 0–28 days old and >61 months old, the other age groups showed a re-hospitalization situation due to re-infection with RSV. In hospitalized children diagnosed with RSV infection from throat swabs, we also performed the RSV IgM test and found that 59.2% of them were positive, 8.0% of them were weakly positive, and 32.8% of them were negative.

Conclusion: This study analyzes the incidence and clinical characteristics of hospitalized children with RSV infection, which provides evidence for the importance of preventive strategies and improvements in supportive care of RSV infection.

Keywords: hospitalized children, respiratory syncytial virus infection, incidence, clinical characteristics

Introduction

Respiratory syncytial virus (RSV) is a negative-sense and single-stranded RNA virus with a filamentous envelope.¹ RSV is the main cause of lower respiratory tract infections, such as bronchiolitis and pneumonia,² in infants and young children worldwide, causing over 3.4 million severe infections annually.^{3,4} In children younger than 6 months, about 45% of hospital admissions and in-hospital deaths were due to RSV infection.³ In low- and middle-income countries, more than 80% of RSV-related acute

lower respiratory tract infections and more than half of RSV-related deaths occur in infants older than 6 months.⁵ In children younger than 5 years, about 54% of deaths are also attributable to RSV infection.⁶ Therefore, RSV is the second leading aetiology of lower respiratory tract infection deaths in children.⁶ The cause of death due to RSV infection is usually apnoea or sepsis.³ At present, there is no generally effective treatment and vaccine to prevent the infection.^{7,8} RSV infection leads to hospital admission of children, which causes serious global clinical burden and financial burden.⁹

Therefore, we need to analyze and summarize the incidence and clinical characteristics of hospitalized children with RSV infection to provide evidence for the early preventive strategies and symptomatic treatment. To address the above questions, we retrospectively collected RSV-infected children who were hospitalized in the Third Affiliated Hospital of Zunyi Medical University from January 2019 to December 2020, and we analyzed the incidence and clinical characteristics of RSV infection.

Methods

Study Population and Data Collection

This retrospective study included children under 14 years of age who received throat swab test and were diagnosed with RSV infection in the Third Affiliated Hospital of Zunyi Medical University from January 2019 to December 2020. Exclusion criteria are shown in Figure 1. Before the start of the study, the parents or legal guardians of all hospitalized children (0–14 years old) included in the study provided written informed consent, and this study was approved by the Ethics Committee of the Third Affiliated Hospital of Zunyi Medical University and was conducted in accordance with the Declaration of Helsinki-1964.

The medical records of children were retrospectively reviewed, and the following data were recorded: gender, age, body temperature, pulse, respiratory rate, clinical manifestations (including pharyngeal redness, cough, expectoration, rhinobyon, runny nose, shortness of breath, mental fatigue, lack of appetite, vomiting, drowsiness, and dyspnea), laboratory data (including white blood cell count, neutrophil percentage, lymphocyte count, platelet count, C-reactive protein, serum creatinine, aspartate aminotransferase, alanine aminotransferase, creatine kinase-MB form, creatine kinase, lactate dehydrogenase, and α -HBDH), chest CT examination, serum RSV IgM test, intensive care unit (ICU) stay, mechanical ventilation, oxygen absorption, length of hospital stay, complications, ≥ 2 episodes of hospitalization due to RSV infection.

Specimen Collection and Detection

Throat swabs and intravenous blood were the main sources of samples, which were obtained within 24 hours of hospitalization. Throat swabs were collected from all hospitalized children by trained nurses using a COPAN flocced swab (FLOQSwabs; Copan Flock Technologies S. r. l., Brescia, Italy), according to the standard protocols.

The child's name and bed number were checked, and the sampling process and purpose were explained to the child's parents. The parents were asked to help in fixing the child's upper limbs and head. After disinfecting the hands, a COPAN flocced swab was quickly inserted and slightly rotated over the posterior pharyngeal wall for about 5 times, and then it was removed. The tip of the swab was broken off and put into a sampling tube containing 3 mL of virus preservation solution. The cap of the virus collection tube was tightened, the information of the child was checked again, the label was affixed, and the tube was transferred to the laboratory for

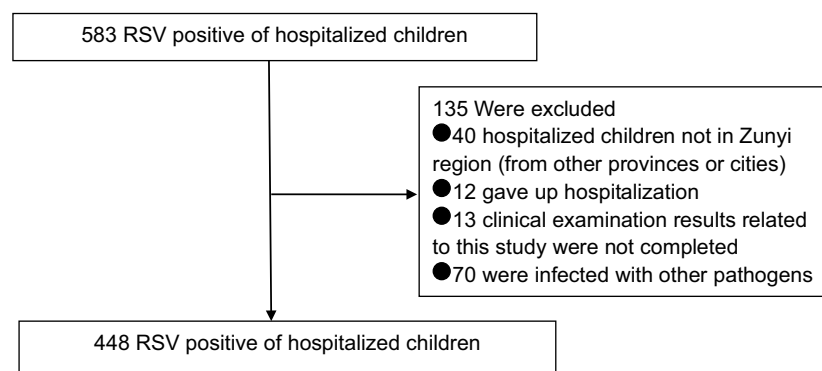


Figure 1 Exclusion criteria of hospitalized children with RSV infection.

nucleic acid testing as soon as possible. RSV was detected in children's samples using a commercially available D³ Ultra DFA Respiratory Virus Screen and ID Kit (Diagnostic Hybrids, Inc, Athens, Ohio), according to the manufacturer's instructions.

Statistical Analysis

Data were processed and analyzed using Microsoft Excel 2010 and SPSS statistical software package (version 19.0; SPSS, Inc., Chicago, IL, USA). All categorical variables were reported as frequency and percentage. Quantitative data were reported as median with interquartile range.

Results

A total of 583 hospitalized children aged 0 day to 14 years who were diagnosed with RSV infection were initially enrolled. Based on to the inclusion and exclusion criteria, 448 hospitalized children were finally enrolled, and 71.9% of hospitalized children (N=448) were male. According to the statistics of different age groups, we found that the three age groups with a higher incidence of RSV infection were 29 days–6 months old (43.1%), 7–12 months old (25.6%), and 13–36 months old (20.8%) age groups (Table 1). Moreover, most of the hospitalized children with RSV infection were 29 days-6 months old (Table 1).

As shown in Table 2, we counted the rate of abnormal pulse and respiratory rate of hospitalized children with RSV infection in different age groups. Children of different ages have different ranges of normal pulse and respiratory rate. Considering the normal range of pulse as the reference, we found that 50% of children (N=10) with

abnormal pulse were 0 day-28 days old, 75.1% of children (N=378) with abnormal pulse were 29 days–23 months old, 65.8% of children (N=38) with abnormal pulse were 24–47 months old, 85.7% of children with abnormal pulse (N=14) were 48–84 months old, and 100.0% of children (N=8) with abnormal pulse were >85 months old. Therefore, hospitalized children with RSV infection generally had an abnormal pulse. Considering the normal range of respiratory rate and the number of people >50% as the reference, we found that the three age groups with a higher abnormal respiratory rate were 0–28 days old (100.0%), 48–84 months old (64.3%), and >85 months old (75.0%) age groups.

As shown in Table 3, we counted the rate of clinical symptoms of hospitalized children with RSV infection in the different age groups. Considering the number of people >50% as the reference, pharyngeal redness, cough, expectoration, and mental fatigue were the most common symptoms, but the rate of expectoration in children 37–60 months old was slightly less than 50%. Rhinobyon, runny nose, vomiting, drowsiness, and dyspnea were the least common symptoms. Compared with the other age groups, shortness of breath was the most common symptom in children who were 29 days–6 months old (52.3%), and lack of appetite was the most common symptom in children who were 0–28 days old (60.0%) and 29 days-6 months old (64.3%).

As shown in Table 4, we counted the rate of fever and analyzed the laboratory test results of hospitalized children with RSV infection. We found that 79.7% of hospitalized children (N=448) had no fever. Further, 8.9% of hospitalized children had fever in the range of 37.3°C-38°C, 7.8% had fever in the range of 38.1°C-39°C, 3.4% had fever in the range of 39.1°C-41°C, and 0.2% had fever >41°C. There was no important clinical significance in some baseline laboratory test results, such as white blood cell count, neutrophil percentage, platelet count, serum creatinine, alanine aminotransferase, and creatine kinase. The proportion of lymphocyte count >4.0 × 10⁹/liter in hospitalized children was 67.2%, and the median lymphocyte count was 5.3 × 10⁹/liter (IQR, 3.5 to 7.7 × 10⁹/liter). The proportion of aspartate aminotransferase >40 U/liter in hospitalized children was 68.8%, and the median aspartate aminotransferase level was 45.8 U/liter (IQR, 37.7 to 58.7 U/liter). The proportion of creatine kinase-MB form >25 U/liter in hospitalized children was 64.1%, and the median level of creatine kinase-MB form was 28.5 U/liter (IQR, 22.9 to 35.2 U/liter). The proportion

Table 1 Demographic Characteristics of Hospitalized Children with RSV Infection

Characteristics	Total (N=448) n (%)
Sex	
Male	322 (71.9)
Female	126 (28.1)
Age (days and months)	
0 d-28 d	10 (2.2)
29 d-6 mo	193 (43.1)
7 mo-12 mo	115 (25.6)
13 mo-36 mo	93 (20.8)
37 mo-60 mo	21 (4.7)
>61 mo	16 (3.6)

Table 2 Characteristics of Abnormal Pulse and Respiratory Rate in Hospitalized Children with RSV Infection

Age	Normal Range of Pulse (per Minute)	n (%)	Normal Range of Respiratory Rate (per Minute)	n (%)
0 d–28 d (N=10)	120–140	5 (50.0)	40–45	10 (100.0)
29 d–23 mo (N=378)	110–130	284 (75.1)	30–40	165 (43.7)
24 mo–47 mo (N=38)	100–120	25 (65.8)	25–30	10 (26.3)
48 mo–84 mo (N=14)	80–100	12 (85.7)	20–25	9 (64.3)
>85 mo (N=8)	70–90	8 (100.0)	18–20	6 (75.0)

Table 3 Clinical Symptoms of Hospitalized Children with RSV Infection

Symptoms	0 d–28 d (N=10) n (%)	29 d–6 mo (N=193) n (%)	7 mo–12 mo (N=115) n (%)	13 mo–36 mo (N=93) n (%)	37 mo–60 mo (N=21) n (%)	>61 mo (N=16) n(%)
Pharyngeal redness	10 (100.0)	193 (100.0)	111 (96.5)	88 (94.6)	21 (100.0)	15 (93.8)
Cough	9 (90.0)	191 (99.0)	109 (94.8)	79 (85.0)	15 (71.4)	13 (81.3)
Expectoration	9 (90.0)	186 (96.4)	100 (87.0)	63 (67.7)	10 (47.6)	11 (68.8)
Rhinobyon	1 (10.0)	32 (16.6)	9 (7.8)	15 (16.1)	0 (0.0)	1 (6.3)
Runny nose	1 (10.0)	42 (21.8)	23 (20.0)	32 (34.4)	7 (33.3)	4 (25.0)
Shortness of breath	4 (40.0)	101 (52.3)	39 (33.9)	30 (32.3)	1 (4.8)	0 (0.0)
Mental fatigue	9 (90.0)	149 (77.2)	85 (73.9)	56 (60.2)	15 (71.4)	9 (56.3)
Lack of appetite	6 (60.0)	124 (64.3)	57 (49.6)	45 (48.4)	8 (38.1)	6 (37.5)
Vomiting	2 (20.0)	45 (23.3)	13 (11.3)	14 (15.1)	3 (14.3)	3 (18.8)
Drowsiness	2 (20.0)	17 (8.8)	4 (3.5)	2 (2.2)	0 (0.0)	0 (0.0)
Dyspnea	3 (30.0)	28 (14.5)	8 (7.0)	2 (2.2)	0 (0.0)	0 (0.0)

of lactate dehydrogenase >245 U/liter in hospitalized children was 97.5%, and the median level of lactate dehydrogenase was 332.6 U/liter (IQR, 291.8 to 382.1 U/liter). The proportion of α -HBDH >180 U/liter in hospitalized children was 79.0%, and the median α -HBDH level was 213.7 U/liter (IQR, 183.5 to 241.7 U/liter). Chest CT examination of hospitalized children with RSV infection revealed pneumonia in 76.6% of children. In hospitalized children diagnosed with RSV infection from throat swabs, we also performed the RSV IgM test and found that 59.2% of them were positive, 8.0% of them were weakly positive and 32.8% of them were negative.

As shown in Table 5, we counted the rate of status and treatments of hospitalized children with RSV infection in the different age groups. The 0–28 days old and 29 days–6 months old children had higher rates of stay in the ICU, use of mechanical ventilation, and absorption of oxygen than hospitalized children in the other age groups. Except for the 37–60 months old age group, the percentage of length of hospital stay ≥ 7 days in the other age groups was greater than 60.0%. Complications found in all age groups

were myocardial damage, respiratory failure, and sepsis. The rates of myocardial damage and respiratory failure in the 0–28 days old and 29 days–6 months old age groups were higher than those in the other age groups. Secondary granulocytopenia, liver function damage, and kidney function damage were uncommon complications. Except for the 0–28 days old and >61 months old age groups, the other age groups had a re-hospitalization situation due to re-infection with RSV.

Discussion

The present study promotes our understanding of incidence and clinical characteristics of hospitalized Chinese children under 14 years of age with RSV infection, and it provides epidemiological data from a population in Zunyi, a developing city in Southwest China.

Our study found that RSV infection was common in hospitalized children of different ages; the infection most commonly occurred in children <6 months old (45.3%), and the proportion of male children (71.9%) was higher than that of female children (28.1%), which coincides with

Table 4 Characteristics of Body Temperature and Laboratory Test Results in Hospitalized Children with RSV Infection

Characteristics	Total (N=448) n(%)
Body temperature	
<37.2 °C	357 (79.7)
37.3 °C–38 °C	40 (8.9)
38.1 °C–39 °C	35 (7.8)
39.1 °C–41 °C	15 (3.4)
> 41 °C	1 (0.2)
White blood cell count ($\times 10^9$ /liter)–median (IQR)	9.8 (7.4–12.9)
4–10 $\times 10^9$ /liter	219 (48.9)
<4 $\times 10^9$ /liter	14 (3.1)
>10 $\times 10^9$ /liter	215 (48.0)
Neutrophil proportion (%)–median (IQR)	31 (18.8–44.4)
50–70%	66 (14.7)
$\geq 70\%$	25 (5.6)
< 50%	357 (79.7)
Lymphocyte count ($\times 10^9$ /liter)–median (IQR)	5.3 (3.5–7.7)
0.8–4 $\times 10^9$ /liter	144 (32.1)
<0.8 $\times 10^9$ /liter	3 (0.7)
>4.0 $\times 10^9$ /liter	301 (67.2)
Platelet count ($\times 10^9$ /liter) –median (IQR)	386.5 (291–471.8)
$\geq 100 \times 10^9$ /liter	442 (98.7)
<100 $\times 10^9$ /liter	6 (1.3)
C-reactive protein (mg/liter)	
<10 mg/liter	383 (85.5)
≥ 10 mg/liter	65 (14.5)
Serum creatinine ($\mu\text{mol/liter}$)–median (IQR)	20.9 (17.0–25.3)
$\leq 97 \mu\text{mol/liter}$	447 (99.8)
>97 $\mu\text{mol/liter}$	1 (0.2)
Aspartate aminotransferase (U/liter)–median (IQR)	45.8 (37.7–58.7)
≤ 40 U/liter	140 (31.2)
>40 U/liter	308 (68.8)
Alanine aminotransferase (U/liter)–median (IQR)	22.4 (15.8–34.7)
≤ 40 U/liter	359 (80.1)
>40 U/liter	89 (19.9)
Creatine kinase-MB Form (U/liter)–median (IQR)	28.5 (22.9–35.2)
≤ 25 U/liter	161 (35.9)
>25 U/liter	287 (64.1)

(Continued)

Table 4 (Continued).

Characteristics	Total (N=448) n(%)
Creatine kinase (U/liter)–median (IQR)	99.5 (69.5–146.0)
≤ 140 U/L	328 (73.2)
>140 U/L	120 (26.8)
Lactate dehydrogenase (U/liter)–median (IQR)	332.6 (291.8–382.1)
≤ 245 U/liter	11 (2.5)
>245 U/liter	437 (97.5)
α -HBDH (U/liter)–median (IQR)	213.7 (183.5–241.7)
≤ 180 U/liter	94 (21.0)
>180 U/liter	354 (79.0)
Chest CT examination	
Pneumonia	343 (76.6)
Serum RSV IgM test	
Weakly positive	36 (8.0)
Positive	265 (59.2)
Negative	147 (32.8)

the results presented by Kombe et al¹⁰ Li et al¹¹ and Zhu et al.¹² RSV is the most common pathogen causing pneumonia.¹³ Our study found that 76.6% of children with RSV infection had pneumonia. The study by Yu et al¹⁴ showed that the average positivity rate of RSV was 54% in children with pneumonia aged from 28 days to 5 months.

RSV can cause respiratory tract infection in infants, and eventually pneumonia. The main symptoms include fever, cough, rhinobyon, and wheezing.¹⁵ In severe cases, it can lead to apnea or even death, and it can also cause a series of complications, such as bronchitis, laryngitis, otitis media, and myocarditis.¹⁶ However, our findings differed from those of previous studies, and we found that pharyngeal redness, cough, expectoration, and mental fatigue were the most common symptoms in every age group. Moreover, myocardial damage, respiratory failure, and sepsis occurred in children of different ages. The rates of myocardial damage and respiratory failure in the 0–28 days old and 29 days–6 months old age groups were higher than those in the other age groups.

Our study found that children in the 0–28 days old and 29 days–6 months old age groups had a higher rate of stay in the ICU, use of mechanical ventilation, and absorption

Table 5 Status and Treatments of Hospitalized Children with RSV Infection

Characteristics	0 d–28 d (N=10) n (%)	29 d–6 mo (N=193) n (%)	7 mo–12 mo (N=115) n (%)	13 mo–36 mo (N=93) n (%)	37mo–60 mo (N=21) n(%)	>61 mo (N=16) n (%)
ICU stay	3 (30.0)	21 (10.9)	9 (7.8)	4 (4.3)	1 (4.8)	1 (6.3)
Mechanical ventilation	3 (30.0)	29 (15.0)	13 (11.3)	6 (6.5)	0 (0.0)	2 (12.5)
Oxygen absorption	7 (70.0)	94 (48.7)	40 (34.8)	21 (22.6)	5 (23.8)	6 (37.5)
Length of hospital stay						
< 7 day	3 (30.0)	48 (24.9)	29 (25.2)	35 (37.6)	12 (57.1)	3 (18.8)
≥ 7 day	7 (70.0)	145(75.1)	86 (74.8)	58 (62.4)	9 (42.9)	13(81.2)
Complication						
Secondary granulocytopenia	0 (0.0)	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function damage	0 (0.0)	10 (5.2)	2 (1.7)	2 (2.2)	0 (0.0)	0 (0.0)
Kidney function damage	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myocardial damage	1 (10.0)	19 (9.8)	12 (10.4)	8 (8.6)	5 (23.8)	2 (12.5)
Respiratory failure	3 (30.0)	30 (15.5)	10 (8.7)	9 (9.7)	1 (4.8)	2 (12.5)
Sepsis	1 (10.0)	3 (1.6)	3 (2.6)	8 (8.6)	2 (9.5)	1 (6.3)
Re-hospitalization situation due to re-infection with RSV	0 (0.0)	9 (4.7)	5 (4.4)	3 (3.2)	1 (4.8)	0 (0.0)

of oxygen than hospitalized children in the other age groups. Arriola et al¹⁷ conducted a study in 1554 children under the age of 2 years who were hospitalized in the community with RSV infection. They found that 27% of children were admitted to an ICU, and 6% of these children needed mechanical ventilation.

Our study found that, with the exception of the 37–60 months old age group, the proportion of length of hospital stay \geq 7 days in the other age groups was greater than 62.0%. However, Papan et al¹⁸ found that the average hospital stay was about 5 days in a study of hospitalized children under 2 years of age with RSV infections.

Our study found that except for the 0–28 days old and $>$ 61 months old age groups, the other age groups had a re-hospitalization situation due to re-infection with RSV. Wong et al¹⁹ conducted a retrospective analysis of hospitalized children with RSV infection in Alberta, Canada over 13 years. They found that a total of 666 children (6.5%) were re-infected with RSV, of whom 433 (4.2%) were re-infected within 30 days of the initial hospital discharge; and in the same RSV season, 36 children (0.35%) had two RSV admissions $>$ 30 days.

There are some limitations to the present study. First, the clinical analysis of hospitalized children with RSV infection in our hospital from January 2019 to December 2020 may not fully reflect the situation and epidemiological characteristics.

Therefore, it is necessary to expand the scope of investigation to accurately reveal the clinical symptoms, treatment, and epidemiological characteristics of hospitalized children with RSV infection. Second, this was a single-center study, and a multicenter study is needed to verify the results. Third, all data were obtained from retrospective analysis.

Conclusion

In summary, our study analyzes the incidence and clinical characteristics of children with RSV infection, which provides evidence for the importance of preventive strategies and improvements in supportive care of RSV infection.

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Disclosure

The authors report no conflicts of interest for this work.

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