Analysis of Clinical Characteristics of Severe Pneumonia in Children Under Regular COVID-19 Outbreak Prevention and Control

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Abstract: Objective — To investigate the clinical characteristics of severe pneumonia in childhood under the regular prevention and control of the COVID-19 epidemic in 2021. Methods — The clinical data of 132 children with severe pneumonia in our pediatric intensive care unit from January 1, 2021, to December 31, 2021, were counted. Results: There were 132 children diagnosed with severe pneumonia, including 49 with different underlying diseases: 12 with airway dysplasia, 13 with genetic metabolic diseases, 11 with congenital heart disease, 10 with malnutrition, 2 with drowning, and 1 with insecticide poisoning. Pathogenesis includes viruses: 33 cases of respiratory syncytial virus, 10 cases of influenza virus, 5 cases of cytomegalovirus, 3 cases of human rhinovirus, 2 cases of bocavirus, 1 case of adenovirus; 19 cases of Mycoplasma pneumoniae. Bacteria: 7 cases of Pseudomonas aeruginosa, 6 cases of Escherichia coli, 4 cases of Klebsiella pneumoniae, 3 cases of Staphylococcus aureus, including 1 case of methicillin-resistant Staphylococcus aureus, 2 cases of Streptococcus pneumoniae, 2 cases of Haemophilus influenzae, 2 cases of Acinetobacter baumannii, 1 case of Cattamora, and 1 case of Serratia marcescens. There were 6 cases of fungi, and 107 strains were detected, with a detection rate of 81.0%. Conclusion — Children with combined underlying diseases are more likely to develop severe pneumonia, such as malnutrition, congenital heart disease, airway malformations, and congenital inherited metabolic diseases. The top three pathogens are respiratory syncytial virus, Mycoplasma pneumoniae, Mycoplasma pneumoniae, and influenza virus, and the top three bacterial infections are Pseudomonas aeruginosa, Escherichia coli, and Klebsiella pneumoniae. Among them, small infants are mainly respiratory syncytial virus, older children are mainly Mycoplasma pneumoniae, and those who are positive for bacterial infections are mostly mixed infections. After active standardized treatment, the cure rate of severe pneumonia in infants and children is high. Keywords: infants and children, severe pneumonia, normalization, prevention and control, basic diseases

1. Introduction
Severe pneumonia in children ranks first in morbidity and mortality in China [1,2], mainly due to severe hypoxia and sepsis resulting in severe dysfunction of the cardiovascular system, digestive system, and nervous system in addition to respiratory failure. The mortality rate of severe pneumonia in children has decreased as the medical environment has improved [3,4], where early recognition and precise treatment of severe pneumonia play an important role in reducing the risk of death. Early identification requires close clinical monitoring of the disease, and precise treatment requires timely and accurate pathogenic testing and targeted treatment for complications. The incidence of hospitalization for pneumonia in children has decreased significantly under the regular control of the COVID-19 epidemic. Moreover, the incidence of severe pneumonia has also decreased accordingly. We now summarize the clinical characteristics of children hospitalized with severe pneumonia in our hospital in the past year to better guide our work.

2. Clinical information
2.1 General information
From January 1, 2021, to December 31, 2021, there were 132 cases, 44 females and 88 males, aged 30 days to 10 years, including 47 cases from 30 days to March 30 days, 34 cases from April to December, 31 cases from December to 3 years, 10 cases from 3 years to 1 month, 6 years, and 10 cases from 6 years to 10 years. The diagnosis of severe pneumonia was in accordance with the Ninth Edition of Pediatric Internal Medicine, and the diagnosis was clear. The PICU was given continuous cardiac and oxygen monitoring, and respiratory support (nasal cannula oxygenation, non-invasive respiratory support and tracheal intubation assisted ventilation) was given in conjunction with the specific condition. Those with combined bacterial infections are given antibiotics, and those who are young, have a long course of disease, or have poor treatment results are given immune support with human immunoglobulin, and symptomatic support treatment with...
nutrition, blood transfusion, and anticoagulation, respectively. Children with combined sepsis or fluid overload were treated with hemodialysis, and children with prolonged illness and difficult coughing were given supportive treatment such as bronchoalveolar lavage. 128 cases were cured and discharged, 1 case died, and 3 cases were discharged automatically.

2.2 Pathogenetic specimens

All children were admitted to the hospital to complete eight tests for respiratory pathogens in serology, sputum bacterial culture in children under 1 year of age, laryngeal secretion bacterial culture in children over 1 year of age, and alveolar lavage fluid bacterial, viral, and fungal pathogens in those who underwent bronchoscopy [5,6], and brush bacteria and other pathogen check in children who could not undergo lavage. Specimens were collected, stored, transferred, and tested in accordance with the standards. Efforts also was made to improve blood tests such as routine blood, liver and kidney function, coagulation function, blood culture (in febrile children), inflammatory factors, and other imaging tests such as chest X-ray and chest CT as appropriate. Medical history was questioned and recorded in detail.

2.3 Results

There are 11 cases with congenital heart disease, including 7 cases of ventricular septal defect, including 1 case with combined right ventricular double outlet, 1 case of congenital heart conveancy block, 1 case of congenital pulmonary valve closure insufficiency, and 1 case of postoperative congenital heart disease: 10 cases of malnutrition, 6 cases of moderate and 4 cases of severe. 12 cases of congenital airway dysplasia, including 4 cases of congenital laryngeal cartilage dysplasia, 3 cases of laryngopharyngeal reflux, 2 cases of pulmonary dysplasia, 1 case of stenosis of the right main bronchial opening, 1 case of right upper lobe tracheal bronchus, and 1 case of dysphagia. There were 13 cases of inherited metabolic diseases, 3 cases of cerebral palsy, 2 cases of epilepsy, 2 cases of chromosomal abnormalities, 2 cases of thyroid abnormalities, 1 case of myasthenia gravis, 1 case of infantile hepatitis syndrome, 1 case of perianal abscess (immunodeficiency to be excluded), and 1 case of primary carnitine deficiency; 2 cases of drowning and 1 case of insecticide poisoning.

Severe comorbidities during the disease: respiratory failure in 18 cases, septic shock in 6 cases, heart failure in 4 cases, pulmonary atelectasis in 2 cases, pulmonary hemorrhage in 1 case, pneumothorax with mediastinal emphysema in 1 case, emphysema in 1 case, acute respiratory distress syndrome (ARDS) in 1 case, and pulmonary hypertension (severe) in 1 case.

Pathogenesis: viruses: 33 cases (25%) of respiratory syncytial virus, 10 cases (7.5%) of influenza virus, 5 cases of cytomegalovirus, 3 cases of human rhinovirus, 2 cases of bocavirus, 1 case of adenovirus; 19 cases (14.3%) of Mycoplasma pneumoniae (MP). Bacteria: Pseudomonas aeruginosa in 7 cases (5.3%), Escherichia coli in 6 cases (4.5%), Klebsiella pneumoniae in 4 cases (3.0%), Staphylococcus aureus in 3 cases, including methicillin-resistant Staphylococcus aureus in 1 case, Streptococcus pneumoniae in 2 cases, Haemophilus influenzae in 2 cases, Acinetobacter baumannii in 2 cases, Moraxella catarrhalis in 1 case, and Serratia marcescens in 1 case; Six cases (4.5%) of fungi were detected, with a total of 107 strains and a detection rate of 81.0%.

| Table 1. Gender and age distribution of severe pneumonia (number of cases (%)) |
|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                          | Males     | Females    | Within 3 months | 4 months to 1 year | 1 month of 1 year to 3 years | 1 month of 3 years to 6 years | 6 years to 10 years |
|----------------|----------|------------|----------------|--------------------|--------------------------|-------------------------------|-------------------|
| 88 (66.7)     | 44 (33.3)| 47 (35.6)  | 34 (25.8)       | 31 (23.5)          | 10 (7.6)                 | 10 (7.6)                      |

| Table 2. Distribution of underlying diseases in patients with severe pneumonia (number of cases (%)) |
|-----------------------------------|----------|----------------|-------------------|----------------------|-------------------|
|                                    | Congenital Metabolic diseases | Congenital heart disease | Abnormal airway development | Malnutrition | Accidents |
|-----------------------------------|----------------|-------------------|--------------------------|----------------|-----------|
| Severe pneumonia (n=132)           | 13 (9.8)  | 11 (8.3)          | 12 (9.1)                 | 10 (7.6)      | 2 (1.5)   |

| Table 3. Distribution of severe complications in patients with severe pneumonia (number of cases (%)) |
|-------------------------------------------------|----------|----------------|-------------------|----------------------|-------------------|
| Respiratory failure | Shock | Heart Failure | Air leakage | Pulmonary atelectasis | Pulmonary emphysema | Pulmonary hemorrhage | Pulmonary arterial hypertension (severe) | ARDS |
|---------------------|-------|---------------|-------------|-----------------------|---------------------|-----------------------|------------------------------------------|-----|
| 18 (13.6)           | 6 (4.6) | 4 (3.0)       | 2 (1.5)     | 2 (1.5)               | 1 (0.8)             | 1 (0.8)               | 1 (0.8)                                  | 1 (0.8) |

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Table 4. Pathogenic distribution of severe pneumonia (number of cases (%))

| Classification of pathogenic bacteria | Severe pneumonia (n=132) |
|---------------------------------------|--------------------------|
| Respiratory syncytial virus           | 33 (25.0)                |
| Mycoplasma pneumonia                  | 19 (14.4)                |
| Influenza virus                       | 10 (7.6)                 |
| Pseudomonas aeruginosa                | 7 (5.3)                  |
| Escherichia coli                      | 6 (4.5)                  |
| Cytomegalovirus                       | 5 (3.8)                  |
| Staphylococcus aureus                 | 4 (3.0)                  |
| Klebsiella pneumoniae                 | 4 (3.0)                  |
| Human rhinovirus                      | 3 (2.3)                  |
| Streptococcus pneumonia               | 2 (1.5)                  |
| Acinetobacter baumannii               | 2 (1.5)                  |
| Serratia marcescens                   | 1 (0.8)                  |
| Moraxella catarrhalis                 | 1 (0.8)                  |
| Adenovirus                            | 1 (0.8)                  |
| Serratia marcescens                   | 1 (0.8)                  |
| Pneumocystis jirovecii                | 1 (0.8)                  |
| Fungi                                 | 6 (4.5)                  |
| Pneumocystis jirovecii                | 1 (0.8)                  |
| Fungi                                 | 6 (4.5)                  |

3. Discussion

Pneumonia is currently one of the leading causes of death in children under 5 years of age in China, and the morbidity and mortality rates are especially high for the severe pneumonia. Therefore, in childhood pneumonia, we should dynamically assess the severity of the disease and the high-risk factors for severe disease at the first visit and throughout the treatment process and prioritize the management of severe cases promptly. There is no exact definition of severe pneumonia in China or abroad. A child with pneumonia is considered to have severe pneumonia when there is severe ventilation dysfunction or complications within or outside the lungs. According to WHO [7] criteria, i.e., those who present with one of the manifestations of inspiratory depression of the lower chest wall, nasal flapping or moaning are considered to have severe pneumonia; those who present with central cyanosis, severe respiratory distress, refusal to eat or signs of dehydration, and impaired consciousness (drowsiness, coma, convulsions) is considered extremely severe pneumonia. In clinical practice, it should also be analyzed in conjunction with facial color and mental reaction. If there is a pale or grayish face and poor reaction to the surrounding environment, it is also considered a severe manifestation of the disease.

Serious pneumonia has a high mortality rate and can leave sequelae, requiring early recognition and treatment. High risk factors for severe pneumonia [8,9], including pathogenic factors, structural factors of the bronchi or lungs, and systemic factors: (1) Pathogenic factors: pathogenic bacteria such as Staphylococcus aureus, Streptococcus pneumoniae, Pseudomonas aeruginosa, etc.; viruses with high copy numbers such as influenza viruses that correlate with disease severity or specific viruses (adenovirus type 7 often leads to severe cases), mixed infections that often lead to refractory or severe pneumonia; (2) Structural factors of the bronchi or lungs: structural deformities of the respiratory and upper gastrointestinal tracts, foreign bodies, tracheobronchial stenosis, softening, etc; (3) Systemic factors: such as congenital immunodeficiency disorders, precocious heart disease with increased pulmonary blood, gastroesophageal reflux, neuromuscular diseases, genetic metabolic diseases, severe anemia or malnutrition, premature and low birth weight infants; and pneumonia in small infants less than 3 months of age. In children with these conditions, the disease can progress to severe pneumonia within a short period, and those with the combined underlying disease have a high mortality rate. Among our severe pneumonia in infants younger than 3 months of age, severe pneumonia accounted for 47 cases (35.6%), and among the 10 cases (7.5%) of severe pneumonia in older children, covering severe malnutrition, congenital heart disease, chromosomal abnormalities, inherited metabolic diseases and underlying diseases such as neuromuscular diseases and epilepsy, but with a low overall mortality rate, which is significantly related to our early identification and precise treatment relationship.
Various domestic guidelines and consensus have re-emphasized the importance of early identification of the etiology to convert empirical treatment to target therapy as soon as possible to improve prognosis and reduce mortality in severe pneumonia [10]. Early identification of potentially severe bacterial pneumonia, severe refractory mycoplasma pneumonia, adenovirus pneumonia, and influenza virus pneumonia, and implementation of targeted treatment to reduce morbidity and mortality and minimize sequelae. Before the new coronavirus pneumonia, the number of children hospitalized for pneumonia in our hospital before the epidemic 2019 was 2436 cases, including 239 cases of severe pneumonia (9.8%), of which the top three children with severe pneumonia were Mycoplasma pneumoniae, adenovirus and influenza virus. In contrast, the number of children hospitalized for pneumonia in our hospital in 1-year 2021 after normalized epidemic prevention and control was 1553 cases, including 132 cases (8.6%) of severe pneumonia, in which 33 cases (25.0%) of respiratory syncytial virus were predominant, and the proportion of adenovirus pneumonia and influenza virus pneumonia was significantly reduced. This may have an important relationship with the general practice of diligent hand washing, wearing masks to enter and leave crowded places, strengthening indoor ventilation, cleaning and disinfection of the surrounding environment and other preventive measures after the normalization of the prevention and control of the new coronavirus outbreak. Because most of pneumonia is transmitted through respiratory droplets and close contact related, the incidence of pneumonia has decreased significantly due to the strengthening of the above sub-precautions. As in the study of Seilesh Kadambari [11], interventions such as masks, social distancing, school closures, lockdowns, and travel restrictions required for outbreak prevention and control during the Covid-19 pandemic reduced the risk of developing common and severe infections in children while reducing the spread of SARS-CoV-2.

The detection rate of severe bacterial pneumonia (30 cases, 22.7%) contained 7 cases of Pseudomonas aeruginosa (5.3%), 6 cases of Escherichia coli (4.5%), 4 cases of Klebsiella pneumoniae (3.0%), 4 cases of Staphylococcus aureus, including 1 case of methicillin-resistant-Staphylococcus aureus, 2 cases of Streptococcus pneumoniae, 2 cases of Haemophilus influenzae, 2 cases of Acinetobacter baumannii, 1 case of Moraxella catarrhalis, 1 case of Serratia marcescens, 1 case of pneumocystis jirovecii. According to reports [12,13,] Escherichia coli and Klebsiella pneumoniae are not common pathogens but can cause severe pneumonia, mostly in infants, or in those with underlying diseases such as chronic aspiration, congenital heart disease, airway malformations, immunocompromise, and severe viral infections, which are fully compatible with our situation. In our cases, most of the positive bacteria were detected in infants younger than 3 months and in older children with severe underlying diseases, so in childhood pneumonia, we need to identify the pathogenic bacteria more accurately and give sensitive treatment according to the drug sensitivity results to prevent severe pneumonia conditions.

Mycoplasma pneumoniae (MP) is not only a common pathogen of CAP in preschool and school-age children, but in recent years it is also not uncommon in infants and children aged 1 to 3 years, and more refractory mycoplasma pneumoniae have been reported and studied [14], which requires our attention. There were 19 cases (15.4%) of Mycoplasma pneumoniae (MP) with severe pneumonia in our hospital last year, covering children of all ages, but no cases of refractory Mycoplasma pneumoniae pneumonia occurred.

Our overall cure rate for severe pneumonia is 96.9%, which is mainly attributed to the early recognition of severe pneumonia, especially in young infants, close observation, and a timely treatment of children with co-morbid underlying diseases. What’s more, there is timely adjustment of the treatment plan for children with poor outcomes, immune support with gamma globulin, and adjunctive interventions with bronchoscopy [8], including assistance in completing detection of deep pathogens, enabling more precise targeting of bacteria, fungi, and viruses, deep respiratory secretion lavage therapy reducing the occurrence of serious complications of airway obstruction, atelectasis, and pneumothorax, as well as respiratory support and blood purification therapy is very critical cases [15,16], saving more children.

4. Conclusions

The pandemic is not over, but pneumonia in children needs attention regardless of the existence of an epidemic, and the management of children with severe pneumonia [17] is even more significant. And we hope that our good habits will continue to persist, reducing the incidence of pneumonia and severe pneumonia. In addition, more precise treatment requires even more continued efforts.

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