BMC Pulmonary Medicine

RESEARCH

Open Access

Clinical characteristics of severe community-acquired pneumonia in children with virus mono-detection versus co-detection with bacteria

Qian Chen[1], Yuejie Zheng[1], Heping Wang[1*], Xiaonan Li[1], Jiali Gu[1] and Zihao Liu[1]

Abstract

Backgroud By analyzing the etiological distribution and clinical characteristics of severe community-acquired pneumonia in children with virus mono-detection and co-detection with bacteria and other pathogens, to explore the clinical characteristics that can help identify mixed infections, thereby providing a basis for the more precise use of antimicrobial drugs.

Methods A retrospective study was conducted on hospitalized children aged 1 month to 14 years with severe community-acquired pneumonia who underwent bronchoscopy in Shenzhen Children's Hospital from January to December 2018. The distribution of 19 pathogens detected by nucleic acid detection in bronchoalveolar lavage fluid was analyzed. Clinical data of children were obtained from the hospital electronic patient dossiers. Data were analyzed to describe the difference between viral mono-detection and co-detection.

Methods A retrospective study was conducted on hospitalized children aged 1 month to 14 years with severe community-acquired pneumonia who underwent bronchoscopy in Shenzhen Children's Hospital from January to December 2018. The distribution of 19 pathogens detected by nucleic acid detection in bronchoalveolar lavage fluid was analyzed. Clinical data of children were obtained from the hospital electronic patient dossiers. Data were analyzed to describe the difference between viral mono-detection and co-detection.

Results A total of 479 children with severe community-acquired pneumonia were enrolled from January to December 2018, at least one pathogen was detected in 375 cases (78.3%), including 247 cases (51.6%) of viruses, 111 cases (23.2%) of atypical pathogens, and 98 cases (20.5%) of bacteria. Among all positive cases, 274 cases (73.1%) had a single pathogen detected, and 101 cases (26.9%) had co-detection (≥ 2 pathogens). Among these co-detection, 51 cases (50.5%) were virus-bacteria co-detection, and 20 cases (19.8%) were virus-atypical pathogens co-detection. There was no significant difference in the detection rates of different types of pathogens between male and female patients ($p > 0.05$). There were no significant differences in clinical presentation, signs, inflammation and organ function indicators, pulmonary complications, antibiotic use, glucocorticoid use, intravenous immunoglobulin use,

*Correspondence:
Heping Wang
szetgmy@163.com

Full list of author information is available at the end of the article

PICU admission rate, need for mechanical ventilation, and length of hospital stay among children with virus-bacteria co-detection, virus-atypical pathogens co-detection, and virus mono-detection ($p > 0.05$).

Conclusion Virus-bacteria co-detection or virus-atypical pathogens co-detection are common in children with severe community-acquired pneumonia. Clinical features alone cannot distinguish between viral mono-infection and mixed bacterial or atypical pathogen infections.

Keywords Children, Community-Acquired pneumonia, Severe, Co-detection, Clinical characteristics

Background

Community-acquired pneumonia (CAP) is one of the leading causes of death in children under the age of 5, accounting for 12.8% of deaths, second only to neonatal diseases [1–3]. Although the incidence and mortality rates of CAP have been effectively reduced by improving medical standards, empirical use of antibiotics, effective vaccination against major pathogens, and widespread improvement in living conditions and nutrition, statistical data from developing countries between 2000 and 2015 shows a 30% reduction in the incidence rate and a 51% reduction in the mortality rate of CAP in children under 5 years old [4, 5]. However, the widespread use of antibiotics has led to an increase in antibiotic-resistant strains, and the current coverage rate of vaccines in some areas is still low, and there is a lack of vaccines against other common pathogens. Therefore, further efforts to strengthen the management and prevention of CAP, especially early identification of the pathogen causing severe CAP and early antimicrobial treatment, are crucial to further reduce the mortality rate of children with CAP.

This study focused on severe CAP children who require bronchoscopy to explore the pathogen distribution and clinical characteristics of children with severe CAP with a single viral detection or co-detection with other pathogens. The aim is to provide a basis for early clinical recognition of mixed pathogen infections and to use antimicrobial drugs more accurately.

Methods

Patients

The inclusion criteria for hospitalized children with severe CAP are based on the 2013 edition of the Management Guidelines for CAP in Children [6], including: (1) Children aged 1 month to 14 years old; (2) Onset of illness occurred outside the hospital, including those who developed symptoms after being infected with a pathogen with a clear incubation period outside the hospital; (3) Having respiratory infection symptoms, such as fever, cough, wheezing, dyspnea, and cyanosis; (4) Confirmed by pulmonary imaging as pneumonia; (5) Meeting the diagnostic criteria for severe pneumonia; (6) Undergoing bronchoscopy and obtaining BAL fluid. Exclusion criteria: (1) Hospitalized children with pneumonia caused by nosocomial infection; (2) Patients with incomplete medical dossier. This study was approved by the Ethics Committee of Shenzhen Children's Hospital in accordance with the Declaration of Helsinki, and its later amendments or comparable ethical standards, with registration number 2,016,013. From January to December 2018, severe CAP hospitalized children who met the inclusion criteria were retrospectively analyzed.

Data collection

A data collection form was developed for clinical data collection, including demographic characteristics, clinical symptoms and signs, laboratory results, treatment processes and outcomes. The collected data encompassed: (1) demographic characteristics: gender and age; (2) clinical information: fever, cough, sputum production, wheezing, shortness of breath, vomiting, and lung rales; (3) laboratory results: WBC increase (WBC > 12 × 10^9/L), WBC decrease(WBC<4 × 10^9/L), Increased neutrophils ratio (GR%>70%), CRP increase (CRP > 10 mg/L), PCT increase (PCT > 0.5ng/mL), ALT increase (ALT > 80IU/L), AST increase (AST > 80IU/L), LDH increase (LDH > 240IU/L), CK increase (CK > 200 IU/L), and CK-MB increase (CK-MB > 6.8ng/mL); (4) complications: pleural effusion, atelectasis, respiratory failure, and plastic bronchitis; and (5) treatment and outcomes: antibiotics, antiviral drugs, glucocorticoids, intravenous immunoglobulin, oxygen therapy, mechanical ventilation, admission to the PICU, and length of hospitalization.

Pathogen detection

Bronchoalveolar lavage (BAL) fluid was collected via bronchoscopy from the severely affected bronchi of the patient and transported to the clinical laboratory within 2 h for standardized diagnostic analysis.

Respiratory pathogens, including common viruses and atypical pathogens, were detected using a respiratory pathogen multiplex PCR kit (Ningbo Haier Biomedical Technology Co., Ltd.) and GeXP system software. The 11 pathogens included adenovirus(ADV), influenza A virus(FluA), influenza B virus(FluB), human bocavirus(HBoV), human coronavirus(HCoV), human metapneumovirus(HMPV), human rhinovirus(HRV), parainfluenza virus(PIV), respiratory syncytial virus(RSV), *Chlamydia pneumoniae*(CP), and

Mycoplasma pneumoniae (MP). Bacteria were detected by real time PCR, including *Streptococcus pneumoniae*(Sp), *Haemophilus influenzae*(Hi), *Staphylococcus aureus*(Sa), *moraxella catarrhalis*(Mc), *Klebsiella pneumoniae*(Kp), *Acinetobacter baumannii*(Ab), *Pseudomonas aeruginosa*(Pa) and *Escherichia coli*(Ec). PCR cycle threshold (Ct) < 30 was judged to be positive.

Statistical analysis

Based on the etiological detection results of the BAL fluid, the patients were categorized and analyzed according to the following groups: viruses, bacteria, atypical pathogens (MP/CP), virus-bacteria, and virus-atypical pathogens.

SPSS 27.0 software was used for statistical analysis. Categorical variables were presented as counts with percentages, and analyzed using the chi-square test or Fisher's exact test, as appropriate. Quantitative variables were represented as medians. Comparisons between two groups were conducted using the Wilcoxon rank-sum test, while comparisons among multiple groups were performed using the Kruskal-Wallis test. A P-value of < 0.05 was considered statistically significant. For pairwise comparisons among multiple groups, the Bonferroni correction method was applied, and a corrected P-value of < 0.005 was considered statistically significant.

Results

Pathogen detection in children with severe CAP

According to the inclusion and exclusion criteria, a total of 479 children were enrolled in the study, including 299 males and 180 females, with a gender ratio of 1.7. The minimum age was 1 month, the maximum age was 14 years, and the median age was 29.0 months (12.0, 58.0). Among them, 133 cases (15%) were aged between 1 month and ≤ 1 year, 143 cases (26%) were aged between 1 and 3 years, 113 cases (16%) were aged between 4 and 6 years, and 90 cases (11%) were aged between 7 and 14 years.

Of the 479 cases, 375 cases (78.3%) had pathogen detection, including 247 cases (51.6%) with viral detection, 98 cases (20.5%) with bacterial detection, and 111 cases (23.2%) with detection of atypical pathogens. The pathogen detection rates were followed: ADV 117 cases (24.4%), MP 109 cases (22.8%), HRV 62 cases (12.9%), *Sp* 37 cases (7.7%), FluB 40 cases (8.4%), RSV 23 cases (4.8%), CP 20 cases (4.2%), FluA (H3N2) 13 cases (2.7%), HBoV 13 cases (2.7%), PIV 19 cases (4.0%), HMPV 18 cases (3.8%), Sa 7 cases (1.5%), HCoV 4 cases (0.8%), CP 4 cases (0.8%), Pa 4 cases (0.8%), Kp 3 cases (0.6%), and Ec 1 case (0.2%).

Among the 375 cases with pathogen detection, single-pathogen detection was found in 274 cases (73.1%), while mixed pathogens were detected in 101 cases (26.9%), including 15 cases (4.0%) of virus-virus co-detections, 7 cases (1.9%) of bacteria-bacteria co-detections, 2 cases (0.5%) of MP-CP co-detections, 51 cases (13.6%) of virus-bacteria co-detections, 20 cases (5.3%) of virus-atypical pathogens co-detections, 2 cases (0.5%) of bacteria- atypical pathogens co-detections, and 4 cases (1.1%) of virus-bacteria-atypical pathogens co-detections. Among the co-detections, the most frequently detected viruses were PIV (11/19, 57.9%), rhinovirus (32/62, 51.6%), and RSV (10/23, 43.5%). Bacteria were mostly co-detected with other pathogens, with a co-detection rate of 65.3% (64/98) for bacteria, 85% (17/20) for CP, 75.7% (28/37) for Sp. The co-detection rate of Hi was 55.0% (22/40), while that of Sa was 57.1% (4/7). Pa, Ab, Kp, and Ec were only detected with other pathogens (Fig. 1).

Among them, 232 cases of pathogens were detected in male children (77.6%), while 143 cases were detected in female children (79.4%). However, the difference in pathogen detection between male and female children was not statistically significant ($\chi^2 = 0.227$, $P = 0.634$).

Clinical characteristics of severe CAP with single or mixed pathogen detections

Based on the pathogen detection for all cases of severe CAP, we divided the patients into the following 5 groups: virus group (172 cases), bacteria group (41 cases), atypical pathogen (MP/CP) group (85 cases), virus mixed with bacteria group (51 cases), and virus mixed with atypical pathogen group (20 cases). The clinical manifestations, laboratory examination results, treatment, and outcomes were presented in Table 1. Due to the small number of cases, 4 cases of bacterial mixed with atypical pathogen and 2 cases of virus mixed with bacteria and atypical pathogen were not included in the statistics.

Clinical characteristics of severe CAP with single pathogen detection

Compared with bacteria mono-detection, patients with virus mono-detection had a higher fever rate, a higher likelihood of elevated procalcitonin, and a greater need for oxygen therapy ($P < 0.05$). Compared with atypical pathogen mono-detection, patients with virus mono-detection had a lower fever rate, a lower incidence of pleural effusion, a smaller likelihood of elevated neutrophil percentage and C-reactive protein (CRP), and a higher likelihood of wheezing, dyspnea, leukocytosis, and a greater need for intravenous immunoglobulin and oxygen therapy ($P < 0.05$).

There was no significant difference ($P > 0.05$) in the comparison of cough, sputum, vomiting, diarrhea, ALT levels, AST levels, LDH levels, CK and CK-MB levels, pulmonary atelectasis, respiratory failure, bronchiolitis obliterans, antibiotic use, antiviral medication use, corticosteroid use, PICU admission rate, mechanical

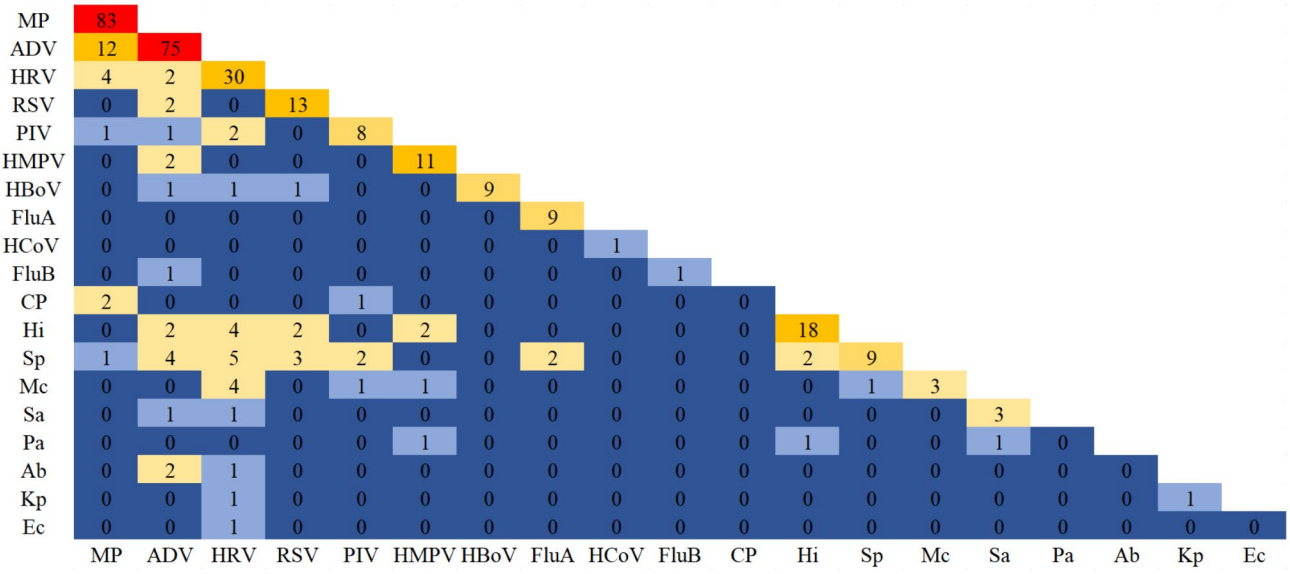

Fig. 1 Specific combinations of pathogens identified in BAL fluid from severe CAP patients with lower respiratory tract infections

ventilation requirement, and length of hospital stay among severe CAP children with different types of pathogen mono-detection or co-detections.

Clinical characteristics of patients with co-detection

Compared with virus mono-detection, patients with virus-bacteria co-detections or virus-atypical pathogens co-detections showed no significant differences in terms of wheezing, fever, pulmonary rales, dyspnea, white blood cell count, CRP level, neutrophil ratio, procalcitonin level, and pleural effusion, as well as the use of intravenous immunoglobulin and oxygen therapy ($P>0.05$). Compared with bacteria mono-detection, patients with virus-bacteria co-detections were more likely to present pulmonary rales ($P<0.05$), but showed no significant differences in other aspects mentioned above ($P>0.05$). Compared with atypical pathogen mono-detection, patients with virus-atypical pathogens co-detections showed no significant differences in terms of wheezing, fever, dyspnea, pulmonary rales, white blood cell count, CRP level, neutrophil ratio, procalcitonin level, pleural effusion, and the use of intravenous immunoglobulin and oxygen therapy ($P>0.05$).

Discussion

Given the presence of colonized bacteria and non-pathogenic viruses in the human oral/nasopharyngeal region, pathogen detection in BAL fluid is considered more reliable for etiological diagnosis and provides more accurate indications of pathogens causing lower respiratory tract infections compared to oral/nasopharyngeal swabs [7–9]. In this study, we utilized nucleic acid amplification technology to detect a spectrum of pathogens, including 9 viruses, 8 bacteria, and 2 atypical pathogens, in BAL fluid from hospitalized children with severe CAP. The detection was facilitated through multiplex PCR. We identified at least one pathogen in 375 cases, a total detection rate of 78.3%, which exceeded the 58.13% previously reported by Huang et al. for severe CAP patients in Suzhou [10]. This detection rate is notably higher than the 29.7% by culture and PCR in BAL fluid observed in a large-scale study of severe CAP pathogens in children across Africa and Asia [1]. Additionally, Khai reported a 90.5% positive rate for pathogen detection in nasopharyngeal aspirates from severe CAP patients using RT-PCR [11]. Eva demonstrated that the application of multiplex PCR technology on BAL fluid from pneumonia patients significantly improved the pathogen detection rate compared to traditional culture methods [12]. These findings showed the importance of the sample type and detection methodology in determining the detection rate of severe CAP pathogens.

Among the positive cases, the detection rate of mixed pathogens reached 26.9%, with virus-bacteria co-detection being the most prevalent, followed by virus-mixed MP/CP. This suggested that co-detection with other pathogens play a significant role in severe CAP in children. Ding Lin reported a 38.4% co-detection rate in childhood severe CAP in Suzhou in 2018, with virus-bacteria co- detections accounting for 55.8% [13]. Khai's study in Japan showed a higher proportion of co-detection, with virus-bacteria co-detections making up 43.1% of positive cases, involving mainly Sp, Hi, methicillin-resistant Sa, and Kp [11]. Study on severe pneumonia in Malaysian children under 5 years old reported a 13.3% mixed pathogen in 2020 [14]. The variability in mixed pathogen detection rates across studies was closely

Table 1 Comparison of clinical features in detection with different types of pathogens and co-detection

	virus[a] *n* = 172(%)	bacteria[b] *n* = 41(%)	MP/CP[c] *n* = 85(%)	virus + bacteria[d] *n* = 51(%)	virus + MP/CP[e] *n* = 20(%)	statistical measure	*P* value
Gender(male)	108(62.8)	30(73.2)	44(51.8)	33(64.7)	14(70.0)	χ2 = 147.9	0.152
Age(month)	20(11,36)[ce]	18(9,47)[ce]	76(53,98)[abd]	18 (11.5,41)[ce]	62.5 (36.25,79.5)[abd]	Z = 125.3*	0.000
Fever	140(81.4)[bc]	24(58.5)[ace]	83(97.6)[abd]	40(78.4)[c]	19(95.0)[b]	χ2 = 33.308	0.000
Cough	166(96.5)	39(95.1)	85(100)	50(98.0)	20(100)	F = 4.158	0.309
Expectoration	134(77.9)	35(85.4)	64(75.3)	43(84.3)	14(70.0)	χ2 = 3.585	0.465
Wheezing	82(47.7)[c]	22(53.7)[ce]	4(4.7)[abd]	26(51.0)[c]	3(15.0)[b]	χ2 = 59.661	0.000
Anhelation	53(30.8)[c]	11(26.8)	8(9.4)[a]	13(25.5)	3(15.0)	χ2 = 15.488	0.004
Vomiting	41(23.8)	8(19.5)	21(24.7)	13(25.5)	4(20.0)	χ2 = 0.688	0.953
Lung rale	71(41.3)	9(22.0)[d]	28(32.9)	27(52.9)[b]	9(45.0)	χ2 = 11.163	0.025
Atelectasis	39(22.7)	9(22.0)	22(25.9)	11(21.6)	5(25.0)	χ2 = 0.514	0.972
Pleural effusion	28(16.3)[c]	5(12.2)	29(34.1)[ad]	2(3.9)[c]	3(15.0)	χ2 = 23.049	0.000
Respiratory failure	6(3.5)	1(2.4)	4(4.7)	1(2.0)	1(5.0)	F = 1.244	0.881
Plastic bronchitis	16(9.3)	1(2.4)	10(11.8)	2(3.9)	4(20.0)	F = 7.233	0.105
WBC increase	76(44.2)[c]	22(53.7)[c]	22(25.9)[abd]	32(62.7)[c]	7(35.0)	χ2 = 20.784	0.000
WBC decrease	23(13.4)	1(2.4)[e]	9(10.6)	3(5.9)	6(30.0)[b]	χ2 = 12.382	0.015
Increased neutrophils ratio	36(20.9)[c]	6(14.6)[c]	38(44.7)[abd]	10(19.6)[c]	7(35.0)	χ2 = 22.26	0.000
CRP increase	90(52.3)[c]	15(36.6)[c]	67(78.8)[ab]	30(58.8)	11(55.0)	χ2 = 25.154	0.000
PCT increase	65(37.8)[b]	5(12.2)[a]	20(23.5)	17(33.3)	6(30.0)	χ2 = 12.906	0.012
ALT increase	4(2.3)	1(2.4)	5(5.9)	2(3.9)	1(5.0)	F = 2.918	0.532
AST increase	25(14.5)	3(7.3)	7(8.2)	4(7.8)	3(15.0)	χ2 = 4.094	0.393
LDH increase	142(82.6)	30(73.2)	68(80.0)	43(84.3)	17(85.0)	χ2 = 2.541	0.637
CK increase	30(17.4)	4(9.8)	16(18.8)	3(5.9)	1(5.0)	χ2 = 7.673	0.104
CK-MB increase	9(5.2)	2(4.9)	0(0.0)	4(7.8)	0(0.0)	F = 7.352	0.075
Antibiotics	166(96.5)	37(90.2)	84(98.8)	49(96.1)	20(100)	F = 5.331	0.192
Antiviral	48(27.9)	7(17.1)	13(15.3)	9(17.6)	7(35.0)	χ2 = 8.503	0.075
Corticosteroid	83(48.3)	19(46.3)	47(55.3)	22(43.1)	14(70.0)	χ2 = 5.54	0.236
Intravenous immunoglobulin	57(33.1)[c]	6(14.6)	12(14.1)[a]	9(17.6)	6(30.0)	χ2 = 15.719	0.003
Oxygen inhalation	96(55.8)[bc]	8(19.5)[a]	22(25.9)[a]	20(39.2)	7(35.0)	χ2 = 31.686	0.000
Mechanical ventilation	1(0.6)	1(2.4)	1(1.2)	0(0.0)	0(0.0)	F = 2.867	0.423
PICU administration	11(6.4)	1(2.4)	3(3.5)	1(2.0)	2(10.0)	F = 3.392	0.441
Duration of hospitalization	9(6,11)	8(6,9)	8(7,10)	9(7,10)	8.5(6.8,12.8)	Z = 5.259*	0.262

a, b, c, d and e represented statistically significant differences between different groups, F refers to Fisher's exact test, * indicated data that is not normally distributed, expressed as median (P25, P75), and the statistical measure was the Z value

related to the sample type, detection method, and timing of testing.

Nolan found that children with viral-bacterial co-infections exhibited a more pronounced increase in white blood cells, a higher likelihood of lung consolidation and pleural effusion, a greater need for ICU admission, mechanical ventilation, and a longer hospital stay compared to those with simple viral infections [15]. Lin's study associated bacterial co-infection with elevated CRP, hyponatremia, PICU admission, and prolonged hospital stay [16]. Choo's research indicated that children with co-infection of respiratory viruses and MP were younger, had a longer fever duration, and were more likely to progress to severe pneumonia and refractory MP pneumonia [17]. Gao's study demonstrated that children with MP co-infection with viruses had a longer hospital stay, longer fever duration, a higher incidence of respiratory distress, and a higher rate of oxygen therapy and non-invasive ventilation use compared to those with a single MP infection [18]. However, Anna Marie Nathan's study showed that mixed infections were only associated with higher CRP levels and did not correlate with other aspects of disease severity [8]. Our study found no significant differences in disease severity indicators, such as the occurrence of pulmonary complications, the use of glucocorticoids or intravenous immunoglobulin, antibiotic use, PICU admission, mechanical ventilation requirement, and hospital stay, among children with virus-bacteria co-detection, virus-atypical pathogen co-detection, and virus mono-detection. This may be due to the inclusion of only severe CAP cases in this study, all of whom required bronchoscopy, indicating an already severe condition. Furthermore, due to the presence of colonizing pathogens, the co-detection of pathogens did not entirely

indicate co-infection, which may introduced bias into the experimental results.

The study also revealed no significant differences in clinical presentations, including wheezing, dyspnea, fever, cough, sputum, vomiting, and lung sounds, between patients with virus-bacteria co-detections, virus-atypical pathogen co-detection, and virus mono-detection. Similarly, there were no significant differences in inflammatory markers such as CRP, white blood cell count, neutrophil ratio, procalcitonin, and organ function markers like alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, creatine kinase, and creatine kinase isoenzymes. Do suggested that clinical symptoms alone were insufficient to diagnose severe RSV pneumonia mixed with bacterial infection, but elevated procalcitonin was associated with mixed bacterial infection [19]. However, Ericksen found that procalcitonin could not be used as a basis for judging virus-induced bronchiolitis complicated by bacterial pneumonia with respiratory failure [20]. Gao's study showed no significant differences in laboratory examinations between single MP infection and its mixed adenovirus infection [18]. Therefore, this study suggested that relying solely on clinical features was not sufficient to distinguish between simple viral infection and mixed viral infections with other pathogens in severe CAP, and targeted antimicrobial therapy still relies on pathogen detection.

This study has several limitations. Firstly, all cases were children who required BAL for diagnosis and/or treatment, which may have certain characteristics that do not represent the general distribution of pathogens in severe CAP. Secondly, some children had received antimicrobial drugs before BAL, which may have selectively affected the detection of bacteria and atypical pathogens, leading to discrepancies between detected pathogens and actual infection status. Thirdly, although the use of BAL fluid for pathogen detection in this study provides more reliable etiological diagnosis compared to oral/nasopharyngeal swabs, it is still challenging to avoid the presence of colonizing pathogens. Additionally, the PCR detection method, with its higher sensitivity, may detect pathogens that are not necessarily indicative of active infections, which could potentially influence the experimental outcomes. Fourthly, as this study was retrospective, there may be biases in the observation of clinical indicators.

Conclusion

The study revealed no significant differences in clinical presentations, including wheezing, dyspnea, fever, cough, sputum, vomiting, and lung sounds, between patients with virus-bacteria co-detections, virus-atypical pathogen co-detections, and virus mono-detection. Similarly, there were no significant differences in inflammatory markers such as CRP, white blood cell count, neutrophil ratio, procalcitonin, and organ function markers like alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, creatine kinase, and creatine kinase isoenzymes. Therefore, this study suggested that relying solely on clinical features was not sufficient to distinguish between simple viral infection and mixed viral infections with other pathogens in severe CAP, and pathogen detection plays a critical role in etiological diagnosis and targeted antimicrobial therapy. However, the presence of respiratory colonizing pathogens cannot be overlooked. In clinical practice, it is essential to integrate microbiological findings with clinical characteristics and laboratory results to achieve a comprehensive and accurate assessment.

Acknowledgements
We appreciate the encouragement from our funders that made this project possible.

Author contributions
HW and QC wrote the main manuscript text. YZ, XL, ZL and JG contributed to analysis and interpretation of the data. YZ and QC prepared Fig. 1; Table 1. All authors reviewed the manuscript.

Funding
The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This research was supported by grants from the Shenzhen Fund for Guangdong Provincial High-level Clinical Key Specialties and Shenzhen Key Medical Discipline Construction Fund (SZGSP012 and SZXK032 to Yuejie Zheng), and the grant from Guangdong Provincial High-level Hospital Construction Special Fund (YNKT2021-ZZ10 to Heping Wang).

Data availability
Data is provided within the manuscript.

Declarations

Ethics approval and consent to participate
The studies involving human participants were reviewed and approved by the Ethical Committee of Shenzhen Children's Hospital (2016013) in accordance with the Declaration of Helsinki and its later amendments or comparable ethical standards. Written informed consent to participate in this study was provided by the participants' legal guardian.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

Author details
[1]Department of Respiratory Medicine, Shenzhen Children's Hospital, Shenzhen 518038, China

Received: 11 September 2024 / Accepted: 10 March 2025
Published online: 21 March 2025

References

1. O'Brien KL, Baggett HC, Brooks WA, et al. Causes of severe pneumonia requiring hospital admission in children without HIV infection from

Africa and Asia: the PERCH multi-country case-control study. Lancet. 2019;394(10200):757–79.
2. Ning G, Wang X, Wu D, et al. The etiology of Community-acquired pneumonia among children under 5 years of age in Mainland China, 2001–2015: A systematic review. Hum Vaccines Immunotherapeutics. 2017;13(11):2742–50.
3. Li Z-J, Zhang H-Y, Ren L-L, et al. Etiological and epidemiological features of acute respiratory infections in China. Nat Commun. 2021;12(1):5026.
4. Li F, Zhang Y, Shi P, et al. Mycoplasma pneumoniae and adenovirus coinfection cause pediatric severe Community-Acquired pneumonia. Microbiol Spectr. 2022;10(2):e0002622.
5. Liu L, Oza S, Hogan D, et al. Global, regional, and National estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: A systematic analysis. Lancet Global Health. 2019;7(1):e47–57.
6. Chinese Medical Association Pediatrics Branch Respiratory Group. Management guidelines for community-acquired pneumonia in children (2013 revision, part 2). Chin J Pediatr. 2013;51(11):856–62. [in Chinese].
7. Nathan AM, Teh CSJ, Jabar KA, et al. Bacterial pneumonia and its associated factors in children from a developing country: A prospective cohort Study[J]. PLoS ONE. 2020;15(2):e0228056.
8. de Benedictis FM, Kerem E, Chang AB, et al. Complicated pneumonia in Children[J]. Lancet (London England). 2020;396(10253):786–98.
9. Diaz-Diaz A, Bunsow E, Garcia-Maurino C, et al. Nasopharyngeal codetection of haemophilus influenzae and Streptococcus pneumoniae shapes respiratory syncytial virus disease outcomes in Children[J]. J Infect Dis. 2022;225(5):912–23.
10. Huang SH, Meng XY. Etiology and clinical characteristics of severe pneumonia in children. Chin J Practical Pediatr. 2021;36(4):262–6.
11. Quang KT, Do HT, Van Pham, Hung, et al. Study on the Co-infection of children with severe community-acquired pneumonia. Pediatr Int. 2022;64(1):e14853.
12. Tschiedel E, Goralski A, Steinmann J, et al. Multiplex PCR of Bronchoalveolar lavage fluid in children enhances the rate of pathogen detection. BMC Pulm Med. 2019;19(1):132.
13. Ding L, Ji W, Zhang XX. Pathogen analysis of 483 cases of severe pneumonia in children from 2012 to 2015 in the affiliated children's hospital of Soochow university. Chin J Practical Pediatr, 2018(06 vo 33): 449–52.
14. Jung J, Seo E, Yoo RN, et al. Clinical significance of viral–bacterial codetection among young children with respiratory tract infections: findings of RSV, influenza, adenoviral Infections[J]. Medicine. 2020;99(2):e18504.
15. Nolan VG, Arnold SR, Bramley AM, et al. Etiology and impact of coinfections in children hospitalized with Community-Acquired Pneumonia[J]. J Infect Dis. 2018;218(2):179–88.
16. Lin H-C, Liu Y-C, Hsing T-Y, et al. RSV pneumonia with or without bacterial Co-infection among healthy Children[J]. J Formos Med Association = Taiwan Yi Zhi. 2022;121(3):687–93.
17. Choo S, Lee YY, Lee E. Clinical significance of respiratory virus coinfection in children with Mycoplasma pneumoniae Pneumonia[J]. BMC Pulm Med. 2022;22(1):212.
18. Gao J, Xu L, Xu B, et al. Human adenovirus coinfection aggravates the severity of Mycoplasma pneumoniae pneumonia in Children[J]. BMC Infect Dis. 2020;20(1):420.
19. Do Q, Dao TM, Nguyen TNT, et al. Procalcitonin identifies bacterial coinfections in Vietnamese children with severe respiratory syncytial virus Pneumonia[J]. Biomed Res Int. 2020;2020(1):7915158.
20. Ericksen RT, Guthrie C, Carroll T. The use of procalcitonin for prediction of pulmonary bacterial coinfection in children with respiratory failure associated with viral Bronchiolitis[J]. Clin Pediatr. 2019;58(3):288–94.

Publisher's note