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Comparative Clinical Analysis of Respiratory Viruses in Pediatric Community-Acquired Pneumonia

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ABSTRACT

Background: Community-acquired pneumonia (CAP) continues to be one of the most significant reasons for hospital admissions and serious health issues for children all over the world. One reason for the rise in detection of respiratory viruses as an important cause of pediatric CAP is the enhancement of molecular diagnostics. Nevertheless, there are only a few local studies from Pakistan that provide information on the prevalence, clinical features, and age-related trends of viral pathogens among children hospitalized with radiographically confirmed CAP.

Objective: To determine the prevalence and clinical impact of respiratory viruses in children hospitalized with radiologically confirmed CAP.

Methodology: This study was conducted in the Department of Pediatrics at Sahara Medical College, Narowal from January 2022 to June 2023. Patients aged 14 years or younger with radiographic signs of community-acquired pneumonia (CAP) were enrolled in the study. Nasopharyngeal swabs were collected within 24 hours of admission and subsequently analyzed by multiplex RT-PCR for the detection of the following viruses: RSV, rhinovirus (RV), human metapneumovirus (HMPV), human bocavirus (HBoV), adenovirus, influenza, parainfluenza, and seasonal coronaviruses.

Results: Out of the total 315 children, the detection rate of respiratory viruses was 72.4%. RSV, which was responsible for 24.8% of the cases, was the leading pathogen and mainly affected infants less than 18 months old, and there were quite high rates of hypoxia (75%) and wheezing (94%) among these children. RV, which accounted for 18.1% of cases, and HBoV, which accounted for 14.9%, were the viruses associated with the strongest inflammatory reactions and the most antibiotic prescriptions. The rate of viral co-infections was 30.3%, which was significantly higher in the younger age group (P = 0.03). Blood cultures showed bacterial growth in 4.4% of the children, with Streptococcus pneumoniae as the most common isolate.

Conclusion: Respiratory viruses, particularly RSV, RV, and HBoV, constitute a major burden in pediatric CAP. Age-specific differences and frequent co-infections highlight the need for improved viral diagnostics and targeted management strategies to optimize care and reduce unnecessary antibiotic use.

Keywords: Respiratory Viruses; Community-acquired Pneumonia; Pediatric Infections

Introduction

Community-acquired pneumonia (CAP) is still considered one of the major reasons for children's illnesses and hospital admissions globally, especially in developing countries where the burden of the disease is disproportionately high.[1,2] The situation is such that, even with the implementation of vaccination programs and the facilitation of antimicrobial use, CAP remains a major cause of respiratory illness in children, particularly those below 5 years of age.[3] Bacterial pathogens were previously considered the main cause of pneumonia in children, but with the increased use of molecular diagnostic techniques particularly multiplex polymerase chain reaction (PCR), the role of respiratory viruses in pediatric pneumonia etiology has been clarified.[4]

Respiratory syncytial virus (RSV) is the most commonly identified cause of lower respiratory tract infections in babies and young children, and it is often associated with bronchiolitis, wheezing, and severe hypoxic disease.[5] Over the last few years, among the viruses that cause respiratory infections, RV, HMPV, and HBoV have been the major contributors in pediatric community-acquired pneumonia (CAP).[6,7] Understanding the clinical relevance of HBoV and HMPV, which are relatively recent discoveries, is still ongoing; studies have shown that these viruses can be present either as sole pathogens or together with other viral agents, complicating diagnosis and clinical interpretation.[8] RV, which was previously thought to be a pathogen causing diseases only in the upper respiratory tract, is now more and more often associated with cases of lower respiratory tract infection, asthma, and even CAP.[9]

Viral coinfections are an emerging challenge that is being addressed in studies reporting the concurrent presence of two or more respiratory viruses in about 33% of pediatric CAP cases.[8] The clinical significance of multiple viral infections remains disputed; some studies report an additive effect on severity, while others report illnesses that are comparable or even less severe than with single infections. In addition, distinguishing viral from bacterial pneumonia clinically or radiologically is difficult and often leads to the frequent, and sometimes unnecessary, administration of antibiotics. This situation is particularly concerning in countries like Pakistan, where resistance to antimicrobial agents is worsening.

Although data from around the world are available, there is a lack of local evidence on the viral epidemiology of radiologically confirmed CAP in Pakistani children, especially regarding new viruses such as HMPV and HBoV. It is crucial to understand not only the types and numbers of viral pathogens but also the clinical scenarios of patients with CAP admitted to hospitals, so that appropriate diagnostic strategies, judicious antibiotic use, and public health interventions can be planned accordingly.

The high burden of CAP in children in Pakistan, along with the increasing consideration of respiratory viruses as the primary causes, led to this study that aimed to find out the frequency and clinical importance of the main respiratory viruses RSV, RV, HMPV, and HBoV in children with radiologically confirmed CAP. Furthermore, our study aims to comprehensively investigate the clinical behavior of various viral pathogens and thus contribute to the development of more rational, evidence-based management strategies by comparing virus-positive and virus-negative cases and single and multiple viral infections.

Objective

This study aims to determine the prevalence of respiratory viruses, including rhinovirus (RV), human metapneumovirus (HMPV), and human bocavirus (HBoV) in respiratory specimens of children diagnosed radiologically with community-acquired pneumonia (CAP). Additionally, the study compares demographic, clinical, and laboratory characteristics between (i) virus-positive and virus-negative CAP cases, (ii) single versus dual/multiple viral infections, and (iii) CAP caused by different respiratory viruses versus respiratory syncytial virus (RSV).

Methodology

This study was an observational study conducted in the Department of Pediatrics, Sahara Medical College, Narowal from January 2022 to August 2023. The medical staff screened all children aged 14 years or less admitted one after the other for participation in the study, provided they had a clinical diagnosis of community-acquired pneumonia (CAP) and had their pulmonary infiltrates confirmed by radiology. Community-acquired pneumonia was identified if there were acute respiratory symptoms (cough, fever, difficulty breathing, tachypnea, or wheezing) together with new infiltrates or consolidation on chest radiograph, and these were not linked to hospital-acquired or aspiration events. A pediatric radiologist, unaware of the clinical and laboratory data, reviewed all chest radiographs and confirmed the diagnosis according to the WHO standardized criteria for pediatric pneumonia.

Children diagnosed with hospital-acquired pneumonia (≥48 hrs after admission), chronic respiratory illness (aside from asthma), congenital heart disease with decreased blood flow requiring surgery, immunosuppressed status, thoracic surgery within the last two weeks, or those who were admitted within the last two weeks were not considered for the study. Parents or legal guardians were required to sign a consent form before the child was enrolled in the study.

Using a structured clinical proforma, each child's demographic data (age, sex, prematurity), clinical symptoms (fever, respiratory distress, oxygen saturation, wheezing), comorbidities, and need for oxygen or

intensive care were recorded. Fever was defined as a temperature≥38 °C, and hypoxia was defined as oxygen saturation <95% in room air. The duration of fever, oxygen therapy, and length of hospital stay were also documented. Blood was collected at admission for complete blood count (CBC), C-reactive protein (CRP), and blood culture, as clinically indicated.

Nasopharyngeal swab specimens were collected from each subject within the first 24 hours of admission to the hospital and then subjected to various tests. Sterile flocked swabs were used for collection, and the samples were immediately placed in viral transport medium. In accordance with institutional biosafety protocols, the samples were sent to the virology laboratory. All samples were kept at −70 °C until analysis. A multiplex RT-PCR (reverse transcription polymerase chain reaction) test was carried out to identify the presence of a respiratory viral panel that included respiratory syncytial virus (RSV), rhinovirus (RV), human metapneumovirus (HMPV), human bocavirus (HBoV), seasonal coronaviruses, influenza A/B, adenovirus, and parainfluenza viruses. Viral assays were performed using commercially validated multiplex RT-PCR kits supplied by the manufacturer, which included internal positive and negative controls to maintain assay quality and prevent contamination.

Children identified with at least one respiratory virus were considered virus-positive; those without viral detection were categorized as virus-negative. Viral infections were then divided into single infections (one virus detected) or dual/multiple infections (≥2 viruses detected). Clinical and laboratory features were studied in these groups, and subgroup analyses were performed for children <18 months and ≥18 months of age, mirroring the established age-related differences in viral epidemiology and immune response.

The data were securely recorded in an electronic database and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were shown as mean ± standard deviation or median (interquartile range), depending on the distribution, and were compared using either the Student's t-test or Mann–Whitney U test. Categorical variables were related in terms of frequencies and percentages, and compared by means of the chi-square test or Fisher's exact test if applicable. A P-value <0.05 was taken to indicate statistical significance. The study protocol was approved by the Institutional Review Board (IRB) of Sahara Medical College, Narowal, and was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

Results

A total of 315 hospitalized children (<14 years) with radiologically confirmed community-acquired pneumonia (CAP) were included. The mean age was 26.8 ± 21.3 months (median: 17 months); 53% were males. Prematurity was reported in 10.2%. Fever ≥38 °C was present in 82% of patients, with a mean admission temperature of 38.9 °C.

Antibiotics were administered in 57.5% of cases. Blood culture was performed in 178 patients (56.5%), of which 8 (4.4%) were positive (Streptococcus pneumoniae = 7; Moraxella catarrhalis = 1). A total of 168 children (53.3%) required supplemental oxygen for an average of 2.9 ± 2.1 days. The overall mean hospital stay was 4.6 ± 2.4 days (range: 1–19 days). Among the study cases, 9 (2.9%) required PICU admission, and none died.

Results showed that at least one respiratory virus was detected in 228 of 315 children (72.4%). Viral detection was significantly higher in children <18 months (82.6%)

Table 1. Respiratory viruses detected in 315 hospitalized children with CAP

Virus	n (%) of total	Single infection n (%)
RSV	78 (24.8%)	68 (87.1%)
Rhinovirus	57 (18.1%)	49 (86.0%)
Human bocavirus	47 (14.9%)	16 (34.0%)
Adenovirus	40 (12.7%)	19 (47.5%)
HMPV	21 (6.6%)	13 (61.9%)
Parainfluenza	14 (4.4%)	8 (57.1%)
Influenza	12 (3.8%)	7 (58.3%)
Coronavirus	4 (1.3%)	2 (50.0%)

Table 2. Etiology of CAP in virus-positive children stratified by age

Virus	<18 months (n=138)	≥18 months (n=90)	P-value
RSV	54 (39.1%)	24 (26.6%)	<0.01
Rhinovirus	27 (19.6%)	30 (33.3%)	0.02
HBoV	25 (18.1%)	22 (24.4%)	0.18
Adenovirus	18 (13.0%)	22 (24.4%)	0.04
HMPV	8 (5.8%)	13 (14.4%)	0.03
Parainfluenza	7 (5.1%)	7 (7.7%)	0.36
Influenza	6 (4.3%)	6 (6.6%)	0.42

compared with older children (63.8%) (P < 0.001) (Table 1).

When the viral etiology was analyzed by age groups, distinct patterns emerged. RSV was markedly more frequent among infants <18 months, accounting for the highest proportion of detections in this age group, whereas rhinovirus (RV) predominated among children ≥18 months. Overall, of the 228 virus-positive samples, 159 (69.7%) represented single viral infections, while 69 (30.3%) involved dual or multiple viruses. Co-infections were significantly more common in younger children (34.8%) than in older children (24.2%; P = 0.03). Among the detected pathogens, HBoV showed the strongest association with mixed infections (68.1% of HBoV cases occurred as co-infections), followed by adenovirus (51.4%) and RV (44.7%), indicating that these viruses frequently co-occur with other respiratory pathogens (Table 2).

RSV was the main virus that caused severe clinical signs in infants with single viral infections who were less than 18 months old. RSV-infected infants had the highest 75% and 94% percentages of hypoxia and wheezing, respectively, confirming the close connection of RSV with the lower respiratory tract during this age period. On the other hand, RV infections accounted for only half of the hypoxia cases (50%) and fewer wheezing episodes (72%), but RV was still linked to the highest white blood cell counts (mean over 20,000/mm^3), which points to a more intense systemic inflammation despite fewer respiratory symptoms. HBoV infection in infants was also associated with high rates of hypoxia (86%) and wheezing (86%), thus making it possible to regard HBoV as another virus with mild RSV-like disease. HBoV and RV infants were more commonly (71% and 50%, respectively) than RSV infants, who required antibiotics (22%). This was probably due to the mimicry of bacterial infection by WBC and CRP elevation. Fever ≥38 °C was seen in all viral groups; however, RSV patients were generally younger, and hypoxia lasted longer. RSV posed the greatest risk of respiratory impairment, while RV and HBoV caused stronger inflammatory responses, which resulted in higher antibiotic usage (Table 3).

In children aged 18 months or older, RSV continued to be associated with significant respiratory involvement and revealed the largest number of hypoxemia cases (69%) compared to RV (35%), HBoV (44%), and HMPV (67%). Fever was reported as very high across all viral groups, but HBoV and HMPV infections had a 100% frequency of fever over 38 °C, suggesting a more febrile presentation in older children. Moreover, RV and HBoV cases presented with remarkably high inflammatory markers of CRP and WBC levels, which were significantly greater than those seen in RSV infections and thus contributed to more frequent antibiotic usage in RV (65%) and HBoV (78%) cases. RSV-infected older children, however, had the longest hospital stay, reflecting the more difficult course of illness, even if there was less intense laboratory inflammation. While the prevalence of wheezing was low and similar across all groups, it was especially rare in HMPV infection, which showed a clinical severity pattern very similar to that of RSV, with high rates of hypoxia and fever but fewer patients requiring antibiotics. These results suggest that in older children, RSV still remains the main culprit for respiratory failure, whereas RV and HBoV cause more inflammation and antibiotic treatment (Table 4).

Discussion

In the present study involving 315 hospitalized children, all of whom had community-acquired pneumonia (CAP) confirmed by radiology, respiratory viruses were identified in 72.4% of cases. This percentage highlights the major role these viruses play in causing pneumonia in young children. The result is consistent with other studies showing that the viral detection rates in children with CAP

Table 3. Clinical characteristics of RSV vs RV vs HBoV vs HMPV in children <18 months (single infections)

Feature	RSV (n=32)	RV (n=18)	HBoV (n=7)	HMPV (n=7)	P-value
Male	17 (53%)	13 (72%)	4 (57%)	3 (43%)	0.18
Temperature >38°C	25 (78%)	12 (67%)	6 (86%)	6 (86%)	0.44
Hypoxia <95%	24 (75%)	9 (50%)	6 (86%)	5 (71%)	0.09
Wheezing	30 (94%)	13 (72%)	6 (86%)	2 (29%)	<0.01
Antibiotics given	7 (22%)	9 (50%)	5 (71%)	2 (29%)	0.03
WBC (mean/mm³)	12,980	20,540	14,210	13,980	<0.01

range from 55% to even 85% globally.[9,10] Likewise, Dandachi et al. reported a 75% viral positivity rate among children hospitalized,[11] which is not far from the burden reported in our group.

Respiratory Syncytial Virus (RSV) was the top pathogen (31.6%) in these cases, especially among infants less than 18 months old. The RSV in these young infants caused sham hypoxia in 75% and wheezing in 94% of the patients. According to the worldwide literature, RSV has consistently been identified as the major virus causing lower respiratory tract infections in infants.[12,13] Hall et al. reported a lot of RSV-related morbidity that led to hospitalization,[14] thus, strengthening the main role of RSV in pediatric CAP, especially in the very young infants age groups, where the problem is much more exacerbated by the narrow airway diameter and the immunological immaturity.

Rhinovirus (RV), observed in 25.0% of children, ranked second among the most prevalent pathogens. Infections with RV in our group were characterized by very high WBC counts (>20,000/mm³) and a significant increase in antibiotic use (50% in infants), indicative of a strong systemic inflammatory response. The same was also noted by Papadopoulos et al., who showed RV's ability to infect the lower respiratory tract and cause large-scale inflammation.[15] RV, previously thought to be a mild upper respiratory virus, is now recognized as a major player in pneumonia and asthma attacks, in line with our results.[16,17]

Human bocavirus (HBoV), found in 11.8% of viral cases, was strongly associated with co-infections; 68.1% of HBoV-positive children had at least 2 viruses detected. This is similar to the findings of earlier studies, which indicated that HBoV is often detected as a co-pathogen rather than a primary pathogen.[18,19] Nevertheless, the HBoV in our group was associated with high fever, elevated inflammatory markers, and a total antibiotic prescription rate of 71–78%, suggesting that its presence, in combination with other viruses, could clinically escalate the situation. These results agree with those characterizing HBoV-associated pneumonia as difficult to differentiate from bacterial infection.[18,20]

Human Metapneumovirus (HMPV) was detected in 9.6% of children and was responsible for serious respiratory distress in older children and hypoxia in 67% of the total cases. Marinari et al. have also reported that HMPV causes the same clinical manifestations as RSV, albeit more often and to a lesser degree.[21] In the group we studied, HMPV infections manifested with high fever and moderate hypoxia, but with less antibiotic use, suggesting a less intense inflammatory signature than RSV and HBoV infections.

Viral co-infections were found in 30.3% of the cases that were positive for the virus. Infants under 18 months had co-infection rates of 34.8%, compared with 24.2% in older children (P = 0.03), a significant difference. Different studies have reporting similar co-infection rates of 20% to 45%.[22-24] The issue of co-infections and their clinical relevance has not yet been settled, but our results clearly indicate that co-infected children, especially those infected with HBoV, adenovirus, or RV, had stronger inflammatory responses and greater antibiotic exposure than non-infected or mono-infected children. This supports the idea that multiple viruses may act together to increase the severity of diseases in infants.

The comparison between virus-positive and virus-negative cases indicated significant relationships between viral infections and wheezing as well as hypoxia, while the opposite was true for the virus-negative group, where higher levels of CRP and WBC were reported these findings being in accord with previous reports that inflammatory markers are usually more pronounced in bacterial than in viral pneumonia.[25] Antibiotic use, however, remained high in viral CAP cases, an indicator of real-world diagnostic confusion and a problem that needs to be addressed through the availability of better laboratory and point-of-care instruments for antimicrobial stewardship. The data from our study showed a distinct wintertime peak, with the highest virus activity around February, a pattern resembling the RSV and RV global seasonality patterns as well as regional respiratory virus

Table 4. Clinical characteristics of RSV vs RV vs HBoV vs HMPV in children ≥18 months (single infections)

Feature	RSV (n=36)	RV (n=31)	HBoV (n=9)	HMPV (n=6)	P-value
Temperature >38°C	31 (86%)	23 (74%)	9 (100%)	6 (100%)	0.09
Hypoxia	25 (69%)	11 (35%)	4 (44%)	4 (67%)	<0.01
Wheezing	9 (25%)	8 (26%)	2 (22%)	1 (17%)	0.77
Antibiotics	16 (44%)	20 (65%)	7 (78%)	2 (33%)	0.04
CRP (mg/L)	34 ± 40	92 ± 98	88 ± 70	50 ± 42	<0.01

surveillance reports from South Asia.

All in all, our findings point out the large number of respiratory viruses, namely RSV, RV, HBoV, and HMPV, that are primarily responsible for children being hospitalized with CAP in Pakistan. The high rate of coinfections, the strong inflammatory responses caused by RV and HBoV, and doctors prescribing antibiotics for viral infections underscore the need for molecular diagnostics for proper case management. Being aware of these epidemiological and clinical patterns is crucial for developing preventive strategies, including RSV vaccination, improved diagnostic algorithms, and more precise interventions to reduce unnecessary antibiotic exposure.

Limitations

This study has several limitations. First, it was conducted at a single tertiary care center, which may limit the generalizability of findings to other regions of Pakistan with different epidemiological patterns. Second, although multiplex RT-PCR provides high sensitivity, viral detection does not always confirm causation, and the clinical relevance of certain viruses, particularly HBoV, remains uncertain in the presence of co-infections. Third, bacterial diagnostics were limited to blood cultures, which have low sensitivity in pediatric pneumonia; therefore, bacterial co-infection may have been underestimated. Fourth, the study did not evaluate long-term clinical outcomes or follow-up viral shedding, which could provide insight into disease severity and recurrence. Despite these limitations, the large sample size, radiologic confirmation, and comprehensive viral testing strengthen the validity of the findings and provide important local data on the viral etiology of pediatric CAP.

Conclusion

This study demonstrates that respiratory viruses are a major etiological contributor to community-acquired pneumonia in hospitalized children, with 72.4% of cases testing positive for viruses. RSV remained the predominant pathogen, particularly among infants, and was strongly associated with hypoxia and wheezing, highlighting its clinical impact in early childhood. RV and HBoV, although less frequently detected than RSV, were associated with more pronounced systemic inflammatory responses and greater antibiotic use, underscoring the diagnostic challenge of distinguishing viral from bacterial pneumonia in routine clinical practice. The high rate of viral co-infections, especially in younger children, further complicates clinical management and emphasizes the need for enhanced surveillance and improved diagnostic strategies. These findings reinforce the importance of incorporating molecular viral testing into routine evaluation of pediatric CAP to promote evidence-based decision-making, guide antimicrobial stewardship, and support the development of targeted preventive approaches, including RSV immunization strategies.

References

1. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. Bull World Health Organ. 2008;86(5): 408–416. DOI:10.2471/BLT.07.048769.
2. Walker CL, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, et al. Global burden of childhood pneumonia and diarrhoea. Lancet. 2013;381(9875): 1405–1416. DOI:10.1016/S0140-6736(13)60222-6.
3. McIntosh K. Community-acquired pneumonia in children. N Engl J Med. 2002;346:429–437. doi:10.1056/NEJMra011994.
4. Tsolia MN, Psarras S, Bossios A, Audi H, Paldanius M, Gourgiotis D, et al. Etiology of community-acquired pneumonia in hospitalized school-age children. Clin Infect Dis. 2004;39:681–686. doi:10.1086/422996.
5. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. N Engl J Med. 2009;360:588–598. doi:10.1056/NEJMoa0804877.

6. Wang X, Li Y, Deloria-Knoll M, Madhi SA, Cohen C, Ali A, B, et al. Global burden of acute lower respiratory infection associated with human metapneumovirus in children under 5 years in 2018: a systematic review and modelling study. Lancet Glob Health. 2021 Jan 1;9(1):e33-43.
7. Don M, Söderlund-Venermo M, Valent F, Lahtinen A, Hedman L, Canciani M, et al. Serologically verified human bocavirus pneumonia in children. Pediatric pulmonology. 2010 Feb;45(2):120-6. DOI:10.1002/ppul.21151.
8. García-García ML, Calvo C, Pozo F, Villadangos PA, Pérez-Breña P, Casas I. High prevalence of viral infections in children with CAP. Pediatr Infect Dis J. 2012;31(8):808–813. DOI:10.1097/INF.0b013e3182568c67.
9. Papadopoulos NG, Bates PJ, Bardin PG, Papi A, Leir SH, Fraenkel DJ, et al. Rhinoviruses infect the lower airways. J Infect Dis. 2000;181:1875–1884. DOI:10.1086/315513.
10. Nair H, Simões EA, Rudan I, Gessner BD, Azziz-Baumgartner E, Zhang JS, et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children. Lancet. 2013;381:1380-90. DOI:10.1016/S0140-6736(12)61901-1.
11. Dandachi D, Rodriguez-Barradas MC. Viral pneumonia: etiologies and treatment. J Invest Med. 2018;66(6):957-65. DOI:10.1136/jim-2018-000712.
12. Leung AK, Wong AH, Hon KL. Community-acquired pneumonia in children. Recent Pat Inflamm Allergy Drug Discov. 2018;12(2):136-44. DOI: 10.2174/1872213X12666180621163821.
13. Shi T, McAllister DA, O'Brien KL, Simoes EA, Madhi SA, Gessner BD, et al. Global disease burden estimates of RSV in young children. Lancet. 2017;390:946–958. DOI:10.1016/S0140-6736(17)30938-8.
14. Heikkinen T, Ojala E, Waris M. Clinical and socioeconomic burden of respiratory syncytial virus infection in children. J Infect Dis. 2016:jiw475. DOI:10.1093/infdis/jiw475.
15. Johnston SL. Natural and experimental rhinovirus infections of the lower respiratory tract. Am J Respir Crit Care Med. 2012. DOI:10.1164/ajrccm/152.4_Pt_2.S46.
16. Nascimento-Carvalho AC, Vilas-Boas AL, Fontoura MS, Vuorinen T, Nascimento-Carvalho CM, PNEUMOPAC-Efficacy Study Group. Respiratory viruses among children with non-severe community-acquired pneumonia: a prospective cohort study. J Clin Virol. 2018;105:77-83. DOI:10.1016/j.jcv.2018.06.003.
17. Wildenbeest JG, van der Schee MP, Hashimoto S, Benschop KS, Minnaar RP, Sprikkelman AB, et al. Prevalence of rhinoviruses in young children of an unselected birth cohort from the Netherlands. Clin Infect Dis. 2016;22(8):736-e9. DOI:10.1016/j.cmi.2016.05.022.
18. Allander T, Tammi MT, Eriksson M, Bjerkner A, Tiveljung-Lindell A. Cloning of human bocavirus. Proc Natl Acad Sci. 2005;102:12891–12896. DOI:10.1073/pnas.0504666102.
19. Mietzsch M, Kailasan S, Garrison J, Ilyas M, Chipman P, Kantola K, et al. Structural insights into human bocaparvoviruses. J Virol. 2017;91(11):10-128. DOI:10.1128/jvi.00261-17.
20. Zhou F, Wang Y, Liu Y, Liu X, Gu L, Zhang X, et al. Disease severity and clinical outcomes of community-acquired pneumonia caused by non-influenza respiratory viruses in adults: a multicentre prospective registry study from the CAP-China Network. Eur Respir J. 2019;54(2). DOI:10.1183/13993003.02406-2018.
21. Marinari LA, Danny MA, Simpson SA, Schmitt JE, Miller Jr WT. Lower respiratory tract infection with human metapneumovirus: chest CT imaging features and comparison with other viruses. Eur J Radiol. 2020;128:108988. DOI:10.1016/j.ejrad.2020.108988.
22. Tran Quang K, Tran Do H, Pham Hung V, Nguyen Vu T, Tran Xuan B, Larsson M, Duong-Quy S, Nguyen-Thi-Dieu T. Study on the co-infection of children with severe community-acquired pneumonia. Pediatr Int. 2022;64(1):e14853. DOI:10.1111/ped.14853.
23. Tsou P, Vadivelan A, Kovvuri M, Garg N, Thangavelu M, Wang Y, Raj S. Association between multiple respiratory viral infections and pediatric intensive care unit admission among infants with bronchiolitis. Arch Pediatr. 2020;27(1):39-44. DOI:10.1016/j.arcped.2019.11.006.
24. Penela-Sánchez D, González-de-Audicana J, Armero G, Henares D, Esteva C, de-Sevilla MF, et al. Lower respiratory tract infection and genus enterovirus in children requiring intensive care: clinical manifestations and impact of viral co-infections. Viruses. 2021;13(10):2059. DOI:10.3390/v13102059.
25. Ito A, Ishida T. Diagnostic markers for community-acquired pneumonia. Ann Transl Med. 2020;8(9):609. DOI:10.21037/atm.2020.02.182.