Original Article

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Paediatrics Section

# Viral Aetiology of Severe Acute Lower Respiratory Tract Infection in Children from the Paediatric Intensive Care Unit at a Tertiary Care Hospital, Eastern India- A Retrospective Study

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## ABSTRACT

**Introduction:** Viral infections are the common source of lower respiratory tract infection worldwide. Rapid and accurate detection of viral infections is important that can prevent antibiotic abuse. However, there are few studies determining viral etiologies in paediatric subjects in Eastern India.

**Aim:** To study viral aetiology in children hospitalised with severe Acute Lower Respiratory Tract Infection (ALRTI) over a period of two years and to detect the impact of co-infection on severity and duration of hospitalization.

**Materials and Methods:** This was a retrospective study based on electronic database in a tertiary care Paediatric Intensive Care Unit (PICU) of Bhagirathi Neotia Women and Child Care Hospital, Kolkata, West Bengal, India. Data were collected for all the patients who fulfilled the selection criteria and were admitted to PICU with ALRTI from March 2018 to March 2020. The medical records were reviewed in 51 patients with positive viral Reverse Transcription Polymerase Chain Reaction (RT-PCR). Data was collected for the type of viruses infecting the subjects and whether there were single infection or co-infection. Co-infection is simultaneous infection with more than one virus. Statistical analysis was done using the IBM Statistical Package for Social Sciences (SPSS) Statistics for Windows, version 24.0 (Armonk, NY: IBM Corp). Student's t-test and Chi-square test were used to compare single infection and co-infection. A p-value <0.05 was considered significant assuming the confidence interval of 95% as the level of significance.

**Results:** The highest positivity rate was 66.6% (34/51) observed in children in the age group 1-12 months. The common viruses detected were adenovirus seen in 51% of samples, Respiratory Syncytial Virus (RSV) in 31.3% and rhinovirus in 11.8%. Clustering of cases was observed for RSV and influenza A in the colder months of the year. Single infection was seen in 74.5% of samples and co-infection in 25.5%. Comparison between single and co-infection with two viruses in terms of complications (p-value=0.163), average duration of PICU stay (p-value=0.70), C-reactive protein (p-value=0.952), procalcitonin (p-value=0.198), white blood cell count (p-value=0.737), absolute neutrophil count (p-value=0.612) were not significant.

**Conclusion**: This present study found that adenovirus and RSV were the leading viral pathogens for ALRTI in the PICU. Co-infection with multiple viruses compared with a single viral infection in a patient did not impact severity.

**Keywords:** Adenovirus, Co-infection, Respiratory syncytial virus, Reverse transcription polymerase chain reaction, Viral infection

## INTRODUCTION

Acute Lower Respiratory Tract Infections (ALRTIs) are among the three major causes of death in children less than 5 years worldwide with around 0.74 million under 5 deaths annually, accounting for 14% of all deaths of children under five years old but 22% of all deaths in children aged 1 to 5 [1]. In India, Pneumonia is the leading cause of death accounting for 19.7% of the proportion of deaths in the age group 1-4 years followed by injuries (19.3%) [2]. Viruses accounted for 30-70% of ALRTI in many studies, the common ones being respiratory syncytial virus (RSV), rhinovirus, influenza A virus and parainfluenza virus [3-5]. Globally, the human respiratory syncytial virus is one of the main viruses causing lower Acute Respiratory Infections (ARI) and attributes to approximately 45% of the hospitalisations and deaths in children over 6 months old [3]. The commonly used diagnostic methods for virus detection in the past were viral culture, rapid antigen test and immunofluorescence assays but molecular assays, specifically multiplex Polymerase Chain Reaction (PCR) has gained attention nowadays due to high sensitivity, specificity and ability to detect a broad range of viruses [6]. Reverse Transcription Polymerase Chain Reaction (RT-PCR) has also gained attention in the recent era because of its ability to detect newly emerging viruses like Coronavirus Disease 2019 (COVID-19) [7].

Simultaneous infection with multiple viruses at one point in time i.e coinfection is also not uncommon. There are some suggestions that the presence of more than one type of virus in the respiratory specimen may also affect the clinical presentation of respiratory tract infection and in turn, impact the severity and the hospital stay [8,9]. However, the relationship between co-infection and the severity of illness remains unclear.

There are many studies based on identifying the viral aetiology of ALRTI in the community [3,5] and in overall hospitalised patients [4,10-12] but, very few of them were studied solely in PICU patients [13]. Also, there is hardly any epidemiological study on the ALRTI-related viral etiologies in Eastern India due to diagnostic limitations and the cost of Viral RT-PCR. The aim of this study is to detect the viral aetiology of severe ALRTI in children of Eastern India, aged 1 month-5 years leading to PICU admission and to detect the impact of co-infection on severity and duration of PICU stay when compared with single infection.

## MATERIALS AND METHODS

The present study was conducted retrospectively based on the electronic database for a duration of two years from March 2018 to March 2020 in a tertiary care hospital in Eastern India, Bhagirathi

Neotia Women and Child Care Centre, New Town, Kolkata, West Bengal, India. The electronic medical records of the subjects fulfilling selection criteria with documented etiological, demographic, clinical, laboratory and imaging data were entered in an MS excel sheet followed by review and analysis for a period of 6 months from July 2021 to December 2021. A total of 51 eligible children's records found with positive viral RT-PCR belong to the age group of 1 month to 60 months i.e. 5 years, admitted with severe Acute Lower Respiratory Tract Infection (ALRTI) in the Paediatric Intensive Care Unit (PICU) were retrospectively investigated. The term severe ALRTI was used for the ALRTI fulfilling our PICU admission criteria. The sample size was taken as total eligible study subjects within the said study period based on the records available.

The Institutional Ethics Committee (IEC) approval from the IEC of Bhagirathi Neotia Women and Child Care Centre, New town, Kolkata, India, was taken on 30th March 2021. As this was a record-based study, informed consent was not a possibility.

**Inclusion criteria:** All patients aged 1 month to 5 years who were admitted to the PICU and had positive viral respiratory panel were included in the study. Admission to the PICU was guided by the local PICU admission policy after assessing children according to the Paediatric Assessment Triangle (PAT) [14] and that includes

1. Critically ill and unstable patient
2. Patient requiring continuous monitoring
3. Respiratory failure or impending respiratory failure, severe respiratory distress
4. Requirement of high flow nasal cannula, invasive and noninvasive ventilation for maintaining target saturation
5. Need for inotropic support
6. Children with multiorgan dysfunction

**Exclusion criteria:** Children with nosocomial infections, positive blood culture in admission samples, bacterial and viral coinfection, previous recurrent episodes of ALRTI, chronic illness (neurological disorder, heart conditions, chromosomal disorders and immunodeficiency) and other co-morbidities were excluded from the study. Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) (COVID-19) infection was also not included.

### Sample Collection and Processing

In this healthcare setting, each and every subject was clinically assessed by an on-duty paediatric intensivist and admitted according to the hospital PICU admission criteria. The nasopharyngeal swab was routinely collected by a qualified paediatrician (on-call) within 24 hours of admission and used to send for all the patients presenting to the PICU with severe respiratory symptoms. The real-time RT-PCR used in the institution can detect 10 viruses after processing the nasopharyngeal samples. In this present study, the length of PICU stay, inflammatory markers and associated complications as the surrogate marker was considered for assessing the severity between viral co-infection and single infection. The parameter, 'co-Infection' was defined as the simultaneous detection of more than one virus in one clinical specimen. In this study, a comparison was made between the 'co-infection with two viruses' and 'single viral infection'. The differences between 'single infection' and 'co-infection with two viruses' were studied in terms of duration of PICU stay, survival, inflammatory markers, presence of complications like Acute Respiratory Distress Syndrome (ARDS), Pleural effusion, septic shock, Multiorgan Dysfunction Syndrome (MODS), chronic lung disease, hepatitis, Haemophagocytic Lymphohistiocytosis (HLH), pneumothorax, empyema and encephalopathy.

## STATISTICAL ANALYSIS

As per selection criteria, the data were collected, collated and entered in an Microsoft Excel sheet and analysed using the data (both variables and their values) were coded into an alpha-numeric format for concealment with few designated persons having the coding key. Categorical variables are presented as percentages and continuous variables are presented as mean with standard deviation or median with interquartile range. Student's t-test and Chi-square test were used to compare clinical and laboratory parameters between single infection and co-infection. The confidence interval of 95% was assumed as the level of significance so that the p-value<0.05 was considered statistically significant.

## RESULTS

[Table/Fig-1] shows the patient's demographic and clinical data of total 51 subjects, in which the mean age was 15±16.3 months and the median age was 10 (IQR 6,14.5) months. [Table/Fig-2]

| Variables | Result (n,%) |
|---|---|
| **Gender** | |
| Male | 32 (62.7) |
| Female | 19 (37.3) |
| **Age group (months)** | |
| 1-12 | 34 (66.6) |
| 13-24 | 8 (15.7) |
| 25-36 | 4 (7.84) |
| 37-48 | 3 (5.88) |
| 49-60 | 2 (3.92) |
| **History obtained** | |
| History of malnutrition | 34 (66.6) |
| History of absent or deficient breastfeeding | 39 (76.4) |
| History of prematurity | 8 (15.65) |
| History of low birth weight | 8 (15.65) |
| Not completed vaccination for their age | 15 (29.4) |
| History of atopy | 9 (17.6) |
| History of siblings or any close relative with symptoms | 22 (43.0) |
| **Final diagnosis** | |
| Bronchiolitis | 25 (49) |
| Bronchopneumonia | 8 (15.6) |
| Pneumonia | 12 (23.5) |
| Wheezing associated lower respiratory infection | 3 (5.9) |
| Acute Respiratory Distress Syndrome | 3 (5.9) |
| Median duration of illness before admission (Inter quartile range) | 5 days (3-8 days) |
| Median duration of paediatric intensive care unit stay (Inter quartile range) | 8 days (4-10 days) |
| **Support needed** | |
| High flow nasal cannula | 39 (76%) |
| Non invasive ventilation | 4 (7.8%) |
| Invasive ventilation | 8 (16%) |
| **Complications** | |
| Acute Respiratory Distress syndrome (ARDS) | 3 |
| Pleural effusion | 2 |
| Septic shock | 2 |
| Multiorgan Dysfunction Syndrome (MODS) | 1 |
| Chronic Lung Disease | 3 |
| Hepatitis | 4 |
| Hemophagocytic lymphohistiocytosis (HLH) | 1 |
| Pneumothorax | 1 |
| Empyema | 1 |
| Encephalopathy | 1 |
| **Final outcome** | |
| Cured and discharged | 43 (84.3%) |
| Died | 2 (3.9%) |
| Leave against medical advice | 6 (11.8%) |

**[Table/Fig-1]:** Demographic and clinical profile of the patients (N=51).

demonstrates the number of different types of viruses detected in the nasopharyngeal RT-PCR samples.

| Virus | Nasopharyngeal swab |
|---|---|
| Adenovirus | 26 |
| RSV | 16 |
| Metapneumovirus | 3 |
| Rhino/Enterovirus | 12 |
| Influenza A | 7 |
| Parainfluenza | 2 |
| Influenza B | 1 |
| Human coronavirus | 1 |

**[Table/Fig-2]:** Total number of viruses detected in all the nasopharyngeal swab samples.

Out of a total of 51 study samples, 38 (74.5%) children had single infection and 13 (25.5%) had co-infection with multiple viruses. Co-infection with two viruses was seen in 10 (19.6%) samples, three viruses in 2 (4%) samples and four viruses in 1 (2%) samples. [Table/Fig-3] shows the distribution of single viral infection and co-infection patterns amongst the study population. Adeno viral aetiology was the most common single infection whereas Adenovirus plus RSV (respiratory syncytial virus) and Adeno with Influenzae A were common amongst co-infections with two pathogens. The present study just compared single infection with co-infection with two viruses as the co-infection with two viruses was the most commonest co-infection found in the samples. [Table/Fig-4] demonstrates the differences between single infection and co-infection with two viruses in terms of duration of stay, inflammatory markers, and presence of complications like Acute Respiratory Distress Syndrome (ARDS), pleural effusion, septic shock, Multiorgan Dysfunction Syndrome (MODS), chronic lung disease, hepatitis, Haemophagocytic Lymphohistiocytosis (HLH), pneumothorax, empyema and encephalopathy. Statistical analysis of our data showed no statistical significance in terms of severity (which was measured as the duration of PICU stay, Infection markers like absolute neutrophil count, CRP, procalcitonin and complications seen) between single infection and co-infection.

| Single infection | | Co-infection | |
|---|---|---|---|
| Adenovirus | 15 | Adenovirus+RSV | 3 |
| RSV | 9 | Adenovirus+Influenza A | 3 |
| Metapneumovirus | 1 | Adenovirus+Metapneumovirus | 2 |
| Rhinovirus | 7 | RSV+Rhinovirus | 2 |
| Influenza A | 3 | Adenovirus+RSV+ Rhinovirus | 2 |
| Influenza B | 1 | | |
| Parainfluenza | 1 | Adenovirus Influenza A+Rhinovirus+ Parainfluenza | 1 |
| Human coronavirus | 1 | | |

**[Table/Fig-3]:** Distribution of single viral infection and co-infection/s pattern (N=51).

| Parameters | Co-infection (n=10) (Mean±SD) | Single infection (n=38) (Mean±SD) | p-value |
|---|---|---|---|
| Age (months) | 12.3±8.1 | 14.2±7.6 | 0.490* |
| Duration of stay in PICU (days) | 8.2±4.2 | 8.8±4.7 | 0.70* |
| White blood cell count (/cu mm) | 10350±5568 | 11050±5890 | 0.737* |
| Absolute neutrophil count (/cu-mm) | 5678±4605 | 6470±4306 | 0.612* |
| C-reactive protein (mg/dL) | 2.13±3.1 | 2.20±3.3 | 0.952* |
| Procalcitonin (ng/mL) | 0.62±0.21 | 0.48±0.32 | 0.198* |
| Complications (n,%) | 6 (60%) | 13 (34%) | 0.163# |

**[Table/Fig-4]:** Comparison of clinical characteristics of single pathogen and co-infection.
*Independent t-test; # Chi-square test

## DISCUSSION

This study was conducted to find out the viral aetiology of severe ALRTIs in children admitted to the PICU and to identify the effect of co-infection on severity. The median age of presentation was 6 months and the incidence of severe ALRTI decreased with age being more in infancy and then decreasing as the age increased. This may be because infancy is a time of increased disease susceptibility and severity. Of the patients 62.7% were male and 37.3% were females; the reason for this discrepancy is unclear but may be due to a reporting bias where parents seek care for boys more than girls. Almost 3/4 of the infants admitted were not having proper breastfeeding and that could be a predisposing factor for infection [15,16]. The common presentations of these ALRTIs were bronchiolitis and pneumonia. This classification is sometimes difficult because X-ray findings can vary due to interobserver bias in clinicians. In our study clustering of cases was seen in the winter months and that can be due to a decrease in innate immunity defence mechanisms such as mucociliary clearance, leading to increased susceptibility to viral infections [17-19].

**Adenovirus as the leading viral pathogen causing severe ALRTI hospitalisation in Eastern India:** While studying the retrospective data for 2 years we clarified the burden of virus infection causing PICU admission. The most commonly detected virus in our study was adenovirus followed by RSV and influenza A. This was in contrast to the study conducted by Duyu M and Karakaya Z on critically ill 115 children in the PICU unit of a tertiary care hospital in Istanbul where they found RSV as the most common virus (36.5%) followed by hRV and hBoV sharing equal frequency (27%) [13]. Other hospital-based studies also showed RSV as the most common pathogen detected [3,4,10-12] [Table/Fig-5]. This can be explained by the local topographic and latitude location of Kolkata where the study took place. Kolkata because of its high average humidity level may give a favourable environment for adenoviruses as this virus is much more stable in areas with high humidity levels [18].

**Respiratory virus co-infections and their interaction in the development of LRTIs:** The co-infection rate in this study was 25.5% and there was no statistical difference between co-infection with two viruses and single infection in terms of inflammatory markers, duration of PICU stay and complications which were comparable to the study by Lin CY et al., which was conducted in MacKay Memorial Hospital, Taipei, Taiwan, where a co-infection rate of 25.8% was found and they further compared the clinical manifestations of patients in which either no viruses, a single infection or co-infections were detected [20]. The age, body weight, duration of hospitalisation, Intensive Care Unit (ICU) stay, White Blood Cell (WBC) counts, and C-Reactive Protein (CRP) levels were not significantly different. A meta-analysis and systematic review for clinical disease severity of respiratory viral Co-infection versus single viral infection which was concluded over 21 studies involving 4,280 patients showed no significant differences in Length Of Hospital stay (LOS) (mean difference-0.20 days, 95% CI-0.94- 0.53, p-value=0.59), or mortality (RR 2.44, 95% CI 0.86, 6.91, p-value=0.09) in subjects with viral co-infections compared to those with a single viral infection [16]. The present study was not be able to compare mortality in single versus co-infection as some of the patients who took Leave Against Medical Advice (LAMA) were in critical condition, therefore, the outcome in that respect was inconclusive. A study by Yoshida LM et al., which was conducted in Vietnam found that co-infection of RSV with certain respiratory viruses increased the risk for LRTIs that is due to synergistic interactions of viruses [8]. Another study by Semple MG et al., was conducted on children less than 2 years with bronchiolitis and found to have a 10-fold increase in Relative Risk (RR) of admission to a paediatric ICU for mechanical ventilation [9]. Different study designs, detection methods and population diversity may be the reason behind this inconclusiveness.

| Author | Type of study | Journal | Year of publication | Major pathogen | Co-infection |
|---|---|---|---|---|---|
| Shi T et al., [3] | Meta-analysis | Lancet | 2017 | 33·1 million (21·6-50·3) episodes of RSV-ALRI, resulted in about 3·2 million (2·7-3·8) hospital admissions, and 59,600 (48,000-74,500) in-hospital deaths in children younger than 5 years | - |
| Singh AK et al., [4] | Prospective study | Indian Journal of Medical Microbiology | 2014 | Out of 86 positive samples, 21.3% RSV positivity followed by measles virus (8.5%), influenza A virus (7.4%), ADV (5.3%), influenza B virus (1.6%), hMPV (1.1%) and HBoV (0.5%). | Only two samples showed co-infection with more than one virus, that is RSV B with hMPV (one case) and Influenza A virus with ADV (one case). |
| Semple MG et al., [9] | Retrospective case incidence study | Journal of Infectious Diseases | 2005 | Out of 196 infants with bronchiolitis, hRSV was found in 174 (89%) and hMPV in 37 (19%). | Dual infection by hMPV and hRSV was demonstrated in 15 (10%) of 149 hRSV-infected infants admitted to the general wards and in 18 (72%) of 25 hRSV-infected infants admitted to the PICU, suggesting a significant association between dual infection and admission to the PICU. |
| Núñez-Samudio V et al., [10] | Retrospective study | BMC Infectious Diseases | 2021 | Out of 216 patients, the most common virus was RSV (25.9%) followed by influenza A virus (10.6%), rhinovirus (10.6%), parainfluenza type 3 (PIV-3; 8.2%) and adenovirus (5.9%). | The test positivity proportion for viral co-infections was 4.7%. All four co-infections included the PIV-3; three were co-infections with RSV and one with adenovirus. |
| Raju AT et al., [11] | Prospective study | Journal of Clinical and Diagnostic Research | 2021 | Out of 185 positive samples, the most common virus detected in the study (including single and co-infection) was RSV in 96/185 (51.9%), followed by HRV 43/185 (23.2%). | Infection with more than one virus were observed only in 67/185 (36.2%) cases. Most co-infections were observed with HRV 36/59. |
| Juliana AE et al., [12] | Prospective surveillance study | PLoS ONE | 2021 | Out of positive 290 samples, Rhinovirus/ enterovirus (43%) and respiratory syncytial virus (34%) were most prevalent. | Two pathogens were found in 85 (29%) of positive patients, three found in 20 (7%) patients and four in 1 (0.3%) patient. |
| Duyu M et al., [13] | Prospective descriptive study | Medicina Intensiva (English Edition) | 2020 | Out of total 63 patients, Respiratory syncytial virus (RSV) was the most frequent causal virus (36.5%). | Multiple viral infection was identified in 20.6% of the patients, the most common in this subgroup being rhinovirus. |

**[Table/Fig-5]:** Major pathogen detected and co-infection rate in various other paediatric studies [3,4,9-13].

Viral infections are ubiquitous and there is no clear-cut clinical difference between viral and bacterial infection leading to unwarranted use of antibiotics in all cases presented with ALRTI and antibiotic treatment does not help in patients having primarily viral ALRTI. Moreover, correct diagnosis of viral agents can lead to effective therapy in cases of certain viral infections like, oseltamivir in influenza infection; also contributes to effective infection control measures and isolation care. Also, detection of the respiratory virus could enable estimation of local epidemiology, therefore, help in clinical judgements of practitioners.

### Limitation(s)

Firstly, this study has limitations due to the small sample size. Secondly, the multiplex RT-PCR was used here to detect nine viruses, which may have chances that some of the viruses which were not detected may be missed. Lastly, respiratory viral infections are known to predispose to secondary bacterial pulmonary infections, and thus can result in substantial confounding when comparing a single viral infection with viral co-infection.

## CONCLUSION(S)

This study provides an overview of viral causes of severe ALRTI as awareness of pathogen leads to accurate diagnosis and management; however, a large multicentre study is required for determining the causative viral agents leading to PICU admission as a clear picture of their prevalence in PICU can help to reduce unnecessary antibiotic abuse. Adenovirus is one of the most common viral cause of ALRTI in PICU and need specific attention for the development of any vaccine or antiviral agent against it. Also, the presence of co-infection with two viruses did not have any impact on the severity when compared with single viral infection. Future studies should employ stratified analysis where the effects of specific pairs of viruses are studied so as to find the type of virus pairs which increase or decrease disease severity.

## REFERENCES


[1] "Pneumonia." Key Facts World Health Organization, 11 Nov. 2021, Retrieved from https://www.who.int/news-room/fact-sheets/detail/pneumonia.

[2] Cause of Death in India 2015-2017,Sample Registration System (SRS)-Reference ID: SRS_COD-STATISTICS_2015-2017, Office of the Registrar General & Census Commissioner, India (ORGI): March 2022 Page 31. Retrieved from https:// censusindia.gov.in /nada/ index.php/ catalog/ 42519/ #metadata.

[3] Shi T, McAllister DA, O'Brien KL, Simoes EAF, Madhi SA, Gessner BD, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: A systematic review and modelling study. Lancet. 2017;390(10098):946-58.

[4] Singh AK, Jain A, Jain B, Singh KP, Dangi T, Mohan M, et al. Viral aetiology of acute lower respiratory tract illness in hospitalised paediatric patients of a tertiary hospital: one year prospective study. Indian J Med Microbiol. 2014;32:13-18.

[5] Waghmode R, Jadhav S, Nema V. The burden of respiratory viruses and their prevalence in different geographical regions of India: 1970-2020. Front Microbiol. 2021;12:723850.

[6] Mahony JB. Detection of respiratory viruses by molecular methods. Clinical Microbiology Reviews. 2008;21(4):716-47.

[7] Krause JC, Panning M, Hengel H, Henneke P. The role of multiplex PCR in respiratory tract infection in children. Dtsch Arztebl Int. 2014;111:639-45.

[8] Yoshida LM, Suzuki M, Nguyen HA, Le MN, Dinh Vu T, Yoshino H, et al. Respiratory syncytial virus: Co-infection and paediatric lower respiratory tract infections. Eur Respir J. 2013;42(2):461-69.

[9] Semple MG, Cowell A, Dove W, Greensill J, McNamara PS, Halfhide C, et al. Dual infection of infants by human metapneumovirus and human respiratory syncytial virus is strongly associated with severe bronchiolitis. J Infect Dis. 2005;191(3):382-86.

[10] Núñez-Samudio V, Landires I. Epidemiology of viral respiratory infections in a paediatric reference hospital in Central Panama. BMC Infect Dis. 2021;21(1):43.

[11] Raju AT, Das R, Rai N, Kumar A, Gaind R. A prospective study on respiratory viral pathogens causing acute lower respiratory infections in children below five years of age at a tertiary care hospital of India. J Clin Diagn Res. 2021;15(5):DC12-16.

[12] Juliana AE, Tang MJ, Kemps L, Noort AC, Hermelijn S, Plötz FB, et al. Viral causes of severe acute respiratory infection in hospitalised children and association with outcomes: A two-year prospective surveillance study in Suriname. PLoS ONE. 2021;16(2):e0247000.

[13] Duyu M, Karakaya Z. Viral aetiology and outcome of severe lower respiratory tract infections among critically ill children admitted to the PICU. Med Intensiva (Engl Ed). 2020. Doi: 10.1016/j.medin.2020.04.023. Online ahead of print.

[14] Horeczko T, Enriquez B, McGrath NE, Gausche-Hill M, Lewis RJ. The paediatric assessment triangle: Accuracy of its application by nurses in the triage of children. J Emerg Nurs. 2013;39(2):182-89. Doi: 10.1016/j.jen.2011.12.020. Epub 2012 Jul 24. PMID: 22831826; PMCID: PMC4318552.

[15] Breastfeeding protects against illness and infection in infants and children: A review of the evidence. Breastfeeding Review. 2001;9(2):11-18. PMID: 11550600.

[16] Swathi R, Kishore SV, Pradhan M, Champatiray J. Risk factors and outcome of respiratory disease in children aged between 2 months to 5 years: A prospective observational study. J Clin Diagn Res. 2021;15(11):SC19-23.

[17] Asner SA, Science ME, Tran D, Smieja M, Merglen A, Mertz D, et al. Clinical disease severity of respiratory viral co-infection versus single viral infection: A systematic review and meta-analysis. PLoS One. 2014;9(6):e99392.

[18] Giesbrecht GG. The respiratory system in a cold environment. Aviat Space

Environ Med. 1995;66: 890-02.
[19] Price RHM, Graham C, Ramalingam S. Association between viral seasonality and meteorological factors. Scientific Reports. 2019;9:929.
[20] Lin CY, Hwang D, Chiu NC, Weng LC, Liu HF, Mu JJ, et al. Increased detection of viruses in children with respiratory tract infection using PCR. Int J Environ Res Public Health. 2020;17(2):564.

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