

Clinico-Etiological Spectrum of Acute Respiratory Illness in Pediatric Population

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Abstract

Background: Acute respiratory illness (ARI) is a major cause of pediatric hospitalization and mortality. Identification of respiratory pathogens and associated clinical outcomes is essential for effective management.

Aim: To evaluate the clinico-etiological spectrum, disease severity, and hospital outcomes of acute respiratory illness among children admitted to a tertiary care hospital.

Materials and Methods: This prospective observational study included 255 children aged 2 months to 18 years admitted with ARI at Indira Gandhi Institute of Child Health, Bengaluru, over 18 months. Clinical characteristics, multiplex RT-PCR findings, disease severity, and hospital outcomes were evaluated. Statistical significance was defined as $p < 0.05$.

Results: Children younger than two years constituted 55.7% of participants, and 57.3% were male. RSV was the predominant pathogen (34.5%), followed by *Streptococcus pneumoniae* (11.8%) and Influenza B (6.7%). Severe pneumonia was observed in 12.2% of children. Respiratory etiology was significantly associated with disease severity ($p < 0.001$). Overall mortality was 6.3%, with ARDS being the strongest predictor of mortality (OR = 89.82; $p < 0.001$).

Conclusion: RSV was the leading identified cause of pediatric ARI, while Influenza A and SARS-CoV-2 were associated with greater disease severity. Early pathogen identification and timely management of respiratory complications may improve clinical outcomes.

Keywords: Acute respiratory illness; Respiratory syncytial virus; Pediatric pneumonia; Multiplex RT-PCR; Respiratory pathogens; ARDS; Mortality.

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Introduction

Acute respiratory illness (ARI) is one of the leading causes of morbidity, hospitalization, and mortality among children worldwide, particularly in developing countries. It encompasses a broad spectrum of infections affecting the upper and lower respiratory tracts, ranging from mild respiratory symptoms to severe pneumonia and acute respiratory distress syndrome (ARDS). Respiratory syncytial virus (RSV) remains a major contributor to acute lower respiratory tract infections among children younger than five years, accounting for a substantial proportion of hospital

admissions and respiratory-related deaths globally.[1] The global burden of pediatric respiratory infections remains considerable despite improvements in vaccination, nutrition, and healthcare accessibility. Epidemiological studies have demonstrated significant age-related variations in respiratory infection burden, with infants and younger children experiencing greater susceptibility to severe disease.[2] The Pneumonia Etiology Research for Child Health (PERCH) study identified RSV as a major pathogen associated with severe childhood pneumonia, highlighting the

importance of identifying specific etiological agents for appropriate clinical management.[3] Respiratory pathogens responsible for ARI include viruses such as RSV, influenza viruses, adenovirus, rhinovirus, and human metapneumovirus, along with bacterial organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Shi et al. demonstrated the substantial global burden of RSV-associated acute lower respiratory infections, particularly among infants in low- and middle-income countries.[4] Similarly, McAllister et al. reported that childhood pneumonia continues to contribute significantly to under-five mortality, particularly in South Asia and sub-Saharan Africa.[5]

The clinical presentation of ARI varies according to the causative pathogen, age, nutritional status, immune response, and associated comorbidities. Severe respiratory infections may result in hypoxemia, respiratory failure, intensive care admission, and mortality. Troeger et al. emphasized the importance of understanding the etiological distribution of lower respiratory infections to develop effective preventive and therapeutic strategies.[6] Furthermore, Bénet et al. demonstrated the diverse microbial causes of childhood pneumonia, supporting the need for comprehensive microbiological investigations.[7]

Recent advances in molecular diagnostic techniques, particularly multiplex real-time reverse-transcriptase polymerase chain reaction (RT-PCR), have improved the identification of respiratory pathogens. However, regional data regarding the clinico-etiological spectrum of pediatric ARI remain limited. Therefore, the present study was undertaken to evaluate the clinical characteristics, etiological agents, disease severity, and hospital outcomes among children with acute respiratory illness admitted to a tertiary care hospital.

Materials and Methods

Study Design and Setting: This prospective cross-sectional observational study was conducted in the Department of Paediatrics, Indira Gandhi Institute of Child Health (IGICH), Bengaluru, Karnataka, over 18 months, from April 2024 to November 2025.

Study Population and Sample Size: A total of 255 children aged 2 months to 18 years admitted with acute respiratory illness were enrolled using consecutive sampling.

The sample size was calculated using the formula:

$$n = \frac{Z_{\alpha/2}^2 \times p(1 - p)}{d^2}$$

Considering a previously reported viral etiology prevalence of 18.5%, a 95% confidence level, and

an absolute precision of 5%, the minimum sample size was estimated to be 232. After accounting for approximately 10% attrition, the final sample size was 255.

Inclusion Criteria: Children aged 2 months to 18 years admitted with acute respiratory illness to the pediatric wards or Pediatric Intensive Care Unit (PICU) whose parents or guardians provided written informed consent were included. Assent was obtained from children older than 12 years.

Exclusion Criteria: Children with pre-existing chronic respiratory diseases, including bronchiectasis, cystic fibrosis, and structural lung abnormalities, were excluded. Children with confirmed primary or secondary immunodeficiency, including HIV infection or immunosuppressive therapy, were also excluded.

Data Collection and Clinical Assessment: Demographic details, clinical history, presenting symptoms, immunization status, nutritional status, and associated comorbidities were recorded using a structured proforma. Clinical examination included assessment of respiratory rate, oxygen saturation, chest indrawing, wheezing, crepitations, and other signs of respiratory distress.

Routine laboratory investigations included complete blood count, C-reactive protein, serum electrolytes, and chest radiography, as clinically indicated. Disease severity was assessed using World Health Organization Integrated Management of Neonatal and Childhood Illness (IMNCI) criteria.

Microbiological Investigations: Nasopharyngeal and oropharyngeal swab samples were collected and transported in viral transport medium to the Virology Laboratory, Department of Neurovirology, NIMHANS, and Bengaluru.

Respiratory pathogens were identified using multiplex real-time RT-PCR targeting common viral, bacterial, and atypical respiratory organisms, including RSV, influenza viruses, adenovirus, SARS-CoV-2, and *Streptococcus pneumoniae*.

Outcome Assessment: The primary outcome was the distribution of respiratory pathogens identified through multiplex RT-PCR. Secondary outcomes included clinical severity, respiratory complications, oxygen requirements, PICU admission, duration of hospitalization, and in-hospital mortality.

Statistical Analysis: Data were analyzed using appropriate statistical software. Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized using mean $\pm$ standard deviation or median with interquartile range.

Associations between categorical variables were assessed using the Chi-square test. The Kruskal–Wallis test was applied for comparisons of non-normally distributed continuous variables, and binary logistic regression was used to identify predictors of in-hospital mortality. A p-value <0.05 was considered statistically significant.

Ethical Considerations: The study was conducted after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from parents or guardians, and assent was obtained from eligible children. Confidentiality of participant information was maintained throughout the study.

Results

The present prospective observational study included 255 children aged 2 months to 18 years admitted with acute respiratory illness (ARI) at Indira Gandhi Institute of Child Health, Bengaluru, over 18 months. The median age was 17 months (IQR: 7–48 months), with a male predominance of 57.3%. Respiratory syncytial virus (RSV) was the most frequently identified pathogen (34.5%), followed by *Streptococcus pneumoniae* (11.8%) and Influenza B (6.7%). The overall mortality rate was 6.3%, with acute respiratory distress syndrome (ARDS) emerging as the strongest predictor of mortality.

Table 1: Demographic and Clinical Characteristics of Children with Acute Respiratory Illness (N = 255)

Parameter	Frequency (n)	Percentage (%)
Age group		
<2 years	142	55.7
2–5 years	56	22.0
>5 years	57	22.3
Gender		
Male	146	57.3
Female	109	42.7
Clinical manifestations		
Nasal discharge	235	92.2
Cough	230	90.2
Fast breathing	229	89.8
Wheezing	135	52.9
Fever	108	42.4
Chest indrawing	31	12.2
Hospital characteristics		
PICU admission	237	92.9

Median age: 17 months (IQR: 7–48 months); mean hospital stay: 8.76 ± 4.79 days.

Children younger than two years constituted the largest proportion (55.7%), followed by those older than five years (22.3%). Males accounted for 57.3% of participants. Nasal discharge (92.2%), cough (90.2%), and fast breathing (89.8%) were the

most frequently observed clinical manifestations. Wheezing was present in 52.9% of children, while chest indrawing was documented in 12.2%. PICU admission was required in 92.9% of participants, reflecting the tertiary referral setting.

Table 2: Distribution of Respiratory Pathogens Identified by Multiplex RT-PCR (N = 255)

Etiological agent	Frequency (n)	Percentage (%)
Respiratory syncytial virus (RSV)	88	34.5
<i>Streptococcus pneumoniae</i>	30	11.8
Influenza B	17	6.7
Influenza A	6	2.4
Adenovirus	6	2.4
SARS-CoV-2	5	2.0
Co-infection (RSV + <i>S. pneumoniae</i>)	1	0.4
Negative/No pathogen identified	102	40.0
Total	255	100.0

RT-PCR: reverse-transcriptase polymerase chain reaction.

Multiplex RT-PCR identified RSV as the predominant respiratory pathogen, accounting for 34.5% of cases. *Streptococcus pneumoniae* was detected in 11.8%, followed by Influenza B (6.7%). Influenza A and adenovirus were each identified in 2.4% of cases, while SARS-CoV-2 accounted for 2.0%. A single case of RSV and *S. pneumoniae* co-infection was documented. No pathogen was identified in 40.0% of specimens, highlighting the limitations of the available diagnostic panel.

Table 3: Association between Respiratory Etiology and Disease Severity (N = 255)

Etiological agent	No pneumonia n	Pneumonia n	Severe pneumonia n	Severe pneumonia (%)
RSV	5	77	6	6.8
S. pneumoniae	3	23	4	13.3
Influenza B	1	14	2	11.8
Influenza A	1	2	3	50.0
Adenovirus	1	5	0	0.0
SARS-CoV-2	1	1	3	60.0
Co-infection	0	1	0	0.0
Negative/Undetected	5	84	13	12.7
Total	17	207	31	12.2

Chi-square = 54.50; $p < 0.001$

Disease severity was classified according to WHO IMNCI criteria. Most children (81.2%) were classified as having pneumonia, while 12.2% had severe pneumonia. Severe pneumonia was proportionately most frequent among children with SARS-CoV-2 infection (60.0%) and Influenza A

(50.0%). RSV accounted for the largest absolute number of pneumonia cases ($n = 77$), although severe pneumonia occurred in only 6.8% of RSV-positive children. A statistically significant association was observed between respiratory etiology and disease severity ($p < 0.001$).

Table 4: Clinical Outcomes and Predictors of In-Hospital Mortality

Parameter	Result	p-value
Hospital outcomes		
Total participants	255	—
In-hospital deaths	16 (6.3%)	—
Survivors	239 (93.7%)	—
Mean hospital stay	8.76 $\pm$ 4.79 days	—
Association with outcomes		
Respiratory etiology vs. disease severity	$\chi^2 = 54.50$	<0.001
Respiratory etiology vs. hospital outcome	$\chi^2 = 32.96$	0.003
Predictors of mortality	Odds ratio (95% CI, where available)	
Acute respiratory distress syndrome (ARDS)	89.82 (22.29–361.91)	<0.001
Influenza A infection	15.84 (CI not reported)	0.003
SARS-CoV-2 infection	13.47 (CI not reported)	0.008

OR: odds ratio; CI: confidence interval; ARDS: acute respiratory distress syndrome. Odds ratios are reproduced from the thesis.

The overall in-hospital mortality rate was 6.3% (16/255). Respiratory etiology demonstrated a statistically significant association with clinical outcomes ($p = 0.003$). ARDS emerged as the strongest predictor of mortality (OR = 89.82; 95% CI: 22.29–361.91; $p < 0.001$). Influenza A (OR = 15.84; $p = 0.003$) and SARS-CoV-2 infection (OR = 13.47; $p = 0.008$) were also significantly associated with increased mortality. These findings indicate that although RSV was the most prevalent respiratory pathogen, Influenza A and SARS-CoV-2 were associated with greater disease severity and mortality risk in this cohort.

Discussion

The present study evaluated the clinico-etiological spectrum of acute respiratory illness (ARI) among 255 hospitalized children at a tertiary care hospital. Children younger than two years constituted the largest proportion (55.7%), with a male predominance of 57.3%. Respiratory syncytial virus (RSV) was the most frequently identified pathogen (34.5%), followed by Streptococcus

pneumoniae (11.8%) and Influenza B (6.7%). These findings highlight the substantial burden of respiratory infections among younger children. RSV was the predominant etiological agent, consistent with the findings of Nair et al., who demonstrated its considerable contribution to acute lower respiratory tract infections and hospitalization among young children.[8] The predominance of RSV emphasizes the importance of early recognition and preventive strategies. Hammitt et al. demonstrated the effectiveness of nirsevimab in preventing RSV-associated lower respiratory tract infections in infants, while Kampmann et al. highlighted the protective role of maternal RSV vaccination.[9,10] In the present study, nasal discharge (92.2%), cough (90.2%), and fast breathing (89.8%) were the most common clinical manifestations. Multiplex RT-PCR identified respiratory pathogens in approximately 60% of cases, demonstrating its usefulness in etiological diagnosis. Huang et al. reported the diagnostic accuracy of multiplex PCR in detecting

respiratory viruses, supporting its application in pediatric respiratory infections.[11]

Influenza B accounted for 6.7% of cases, while Influenza A was detected in 2.4%. Despite its lower prevalence, Influenza A was associated with a higher proportion of severe pneumonia (50.0%) and increased mortality risk (OR = 15.84; $p = 0.003$). Iuliano et al. emphasized the substantial global mortality burden associated with seasonal influenza, highlighting the importance of influenza surveillance and preventive measures.[12]

SARS-CoV-2 was detected in 2.0% of children but demonstrated the highest proportion of severe pneumonia (60.0%). Dong et al. described the variable clinical severity of COVID-19 among children, indicating that severe manifestations may occur despite the generally lower disease burden in pediatric populations.[13] *Streptococcus pneumoniae* was identified in 11.8% of participants, consistent with its established role as an important bacterial cause of childhood respiratory infections, as described by O'Brien et al.[14]

The present study demonstrated a significant association between respiratory etiology and disease severity ($p < 0.001$). These findings are supported by Jain et al., who reported considerable variation in the microbial etiology and clinical manifestations of community-acquired pneumonia among hospitalized children.[15] Similarly, Rhedin et al. highlighted the importance of respiratory viruses in childhood pneumonia, emphasizing the need for accurate etiological identification.[16]

The overall in-hospital mortality rate was 6.3%. Acute respiratory distress syndrome (ARDS) emerged as the strongest reported predictor of mortality (OR = 89.82; 95% CI: 22.29–361.91; $p < 0.001$). Self et al. demonstrated the clinical importance of respiratory viral detection in patients with pneumonia, supporting the role of molecular diagnostics in evaluating respiratory infections.[17] Florin et al. further highlighted the importance of assessing disease severity in children with community-acquired pneumonia.[18] The present findings emphasize the importance of early etiological diagnosis, appropriate severity assessment, and timely intensive care management. However, the single-center design, high proportion of PICU admissions, and absence of pathogen identification in 40% of cases limit the generalizability of the findings. Larger multicenter studies incorporating broader molecular diagnostic panels are recommended.

Conclusion

Acute respiratory illness predominantly affected children younger than two years, with RSV being the most frequently identified pathogen (34.5%),

followed by *Streptococcus pneumoniae* and Influenza B. Although RSV accounted for the largest proportion of infections, SARS-CoV-2 and Influenza A were associated with higher proportions of severe pneumonia. The overall mortality rate was 6.3%, with ARDS emerging as the strongest predictor of in-hospital mortality. These findings emphasize the importance of early clinical assessment, multiplex RT-PCR-based pathogen identification, appropriate respiratory support, and preventive strategies to improve pediatric respiratory outcomes.

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