

Clinico-virological Profile, Intensive Care Needs, and Outcome of Infants with Acute Viral Bronchiolitis: A Prospective Observational Study

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ABSTRACT

Objectives: The objective of the study was to describe the clinico-virological profile, treatment details, intensive care needs, and outcome of infants with acute viral bronchiolitis (AVB).

Methodology: In this prospective observational study, 173 infants with AVB admitted to the pediatric emergency room and pediatric intensive care unit (PICU) of a tertiary care teaching hospital in North India during November 2019 to February 2020 were enrolled. The data collection included clinical features, viruses detected [respiratory syncytial virus (RSV), rhinovirus, influenza A virus, parainfluenza virus (PIV) 2 and 3, and human metapneumovirus (hMPV)], complications, intensive care needs, treatment, and outcomes. Multivariate analysis was performed to determine independent predictors for PICU admission.

Results: Most common symptoms were rapid breathing (98.8%), cough (98.3%), and fever (74%). On examination, tachypnea (98.8%), chest retractions (93.6%), respiratory failure (84.4%), wheezing (49.7%), and crepitations (23.1%) were observed. RSV and rhinovirus were the predominant isolates. Complications were noted in 25% of cases as encephalopathy (17.3%), transaminitis (14.3%), shock (13.9%), acute kidney injury (AKI) (7.5%), myocarditis (6.4%), multiple organ dysfunction syndrome (MODS) (5.8%), and acute respiratory distress syndrome (ARDS) (4.6%). More than one-third of cases required PICU admission. The treatment details included nasal cannula oxygen (11%), continuous positive airway pressure (51.4%), high-flow nasal cannula (14.5%), mechanical ventilation (23.1%), nebulization (74%), antibiotics (35.9%), and vasoactive drugs (13.9%). The mortality was 8.1%. Underlying comorbidity, chest retractions, respiratory failure at admission, presence of shock, and need for mechanical ventilation were independent predictors of PICU admission. Isolation of virus or coinfection was not associated with disease severity, intensive care needs, and outcomes.

Conclusion: Among infants with AVB, RSV and rhinovirus were predominant. One-third infants with AVB needed PICU admission. The presence of comorbidity, chest retractions, respiratory failure, shock, and need for mechanical ventilation independently predicted PICU admission.

Keywords: Acute bronchiolitis, Bronchiolitis, Intensive care, Mechanical ventilation, Respiratory syncytial virus.

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INTRODUCTION

Acute viral bronchiolitis (AVB) is the leading cause of hospitalization among infants in developed and developing countries and associated with significant morbidity.¹⁻⁵ The typical presentation of AVB includes a young child presenting in the winter months with 2–4 days history of low-grade fever, nasal congestion, rhinorrhea, and symptoms of lower respiratory tract illness, including cough, tachypnea, and increased respiratory effort in form of grunting, nasal flaring, and intercostal, subcostal, or supraclavicular retractions.^{4,5} Expiratory wheezing and inspiratory crackles may be heard on auscultation. Several definitions of AVB have been proposed, but the term is generally applied to a first episode of wheezing in infants younger than 12 months of age. In preterm infants, apnea may be an early manifestation of AVB.^{3,4,6} Chest radiograph may show lung hyperinflation with patchy atelectasis. Respiratory syncytial virus (RSV) is the main cause of AVB worldwide and accounts for 30–80% of cases. Other viruses implicated are influenza viruses, parainfluenza viruses (PIV 1–3), human metapneumovirus (hMPV), rhinovirus, enterovirus, adenovirus, and bocavirus.^{2,4,7-13} AVB is characterized by acute inflammation, edema, and necrosis of epithelial cells lining of small airways, increased mucus production, and bronchospasm.^{4,14} The severity of AVB varies from asymptomatic exposures to severe lower respiratory

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tract infection leading to emergency room (ER) visit, pediatric intensive care unit (PICU) admission, and sometimes mortality.⁴ The reason for variable course in children is not well understood but it is believed that in children with severe disease, the enhanced inflammatory response may be a contributing factor rather than

virus-induced cytopathy.¹⁵ Children with RSV infection in early life have a higher risk of developing asthma and recurrent wheezing in later childhood.^{4,16,17}

The literature on clinical characteristics, viral profile, intensive care needs, and outcome of infants with AVB from India is limited. Therefore, this prospective observational study was planned to investigate clinico-virological profile, treatment details, intensive care needs, outcomes, and predictors of PICU admission in infants with AVB.

MATERIALS AND METHODS

This prospective study was conducted in pediatric ER and PICU of a tertiary care teaching hospital in North India during the season of AVB for the year 2019–2020 (November 2019 to February 2020). The study protocol was approved by the Institute Ethics Committee, and the final manuscript was approved by the Departmental Review Board. The patients were enrolled after receiving written informed consent from the parents or legal guardians. All infants (<12 months of age) admitted to ER and PICU with AVB were included. The AVB was defined as a young child presenting in the winter months with 2–4 days history of low-grade fever, nasal congestion, rhinorrhea; symptoms of lower respiratory tract illness, including cough, tachypnea, and increased respiratory effort in form of grunting, nasal flaring, and intercostal, subcostal, or supraclavicular retractions; expiratory wheezing, inspiratory crackles on auscultation; apnea especially in preterm neonates; or first episode of wheezing in infants younger than 12 months of age.^{3,4,6} Tachypnea was defined as respiratory rates >60/min in infants <2 months of age and >50/min in infants 2–12 months of age. Respiratory failure was defined as oxygen saturation (SpO₂) at room air <92% or PaO₂ <60 mm Hg or PaCO₂ >50 mm Hg.^{18–20} Patients were managed following the protocol for AVB in ER and PICU.^{3,5} The admitted infants underwent complete blood count, renal and liver function tests, blood culture, chest radiograph (case-to-case basis), and blood gas analysis. The treatment included humidified oxygen by nasal prongs, trial of bronchodilators and/or hypertonic (3%) saline, intravenous fluids, and early initiation (within 24 hours) of enteral feeding. In case of nonimprovement, the respiratory support was escalated to nasal continuous positive airway pressure (nCPAP), high-flow nasal cannula (HFNC), or invasive mechanical ventilation.^{3,5} Other treatments (case-to-case basis) included antibiotics (in case of suspicion of bacterial infection), inhaled or parenteral steroids, vasoactive drugs (in presence of shock), and intravenous immunoglobulin (in cases with myocarditis).^{3,5} The infants with respiratory failure; clinical worsening and escalation of respiratory support to HFNC/CPAP; mechanical ventilation; need of vasoactive drugs; extrapulmonary complications; and underlying comorbidity were considered for PICU transfer. However, not all infants fulfilling PICU admission criteria were shifted to PICU and were managed in ER.

In the pediatric ER, there are 20–30 admissions per day. The 24-bedded ER is manned 24 × 7 by 6–8 junior residents (undergoing MD pediatrics training), 2–3 senior residents (undergoing pediatric critical care fellowship), and one pediatric critical care consultant. The 15-bedded PICU is manned 24 × 7 by 4–5 junior residents, 2–3 pediatric critical care senior residents, and one pediatric critical care consultant. For the management of AVB, there are facilities for administration of heated humidified oxygen, CPAP, HFNC, nebulization, and multipara monitors at both the places. The facility for noninvasive and invasive ventilation is available only in PICU. In the pediatric ER, children in need for positive pressure ventilation were kept on manual ventilation by self-inflating bags till they get bed in PICU or extubated.

The data were collected on a predesigned study proforma. Clinical features, chest radiograph findings, extrapulmonary manifestations or complications [myocarditis, encephalitis/encephalopathy, transaminitis, shock, acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), and multiple organ dysfunction syndrome (MODS), pulmonary artery hypertension (PAH)], treatment details [oxygen support, mechanical ventilation, nebulization, antibiotics, steroids, vasoactive agents, intravenous immunoglobulin (IVIG)], and outcomes (duration of PICU and hospital admission, and mortality) were noted.

Viral Testing

For viral testing, nasopharyngeal aspirates (NPA) were taken by a trained health personnel within 12 hours of admission by passing 6–8 Fr feeding tube into the nasopharynx and applying gentle suction with a syringe. The secretions were rinsed into viral transport medium (VTM) and transported under cold chain to the regional viral research and diagnostic laboratory (VRDL), the Department of Virology for testing of RSV, rhinovirus, influenza A, PIV 2, PIV 3, and hMPV. The samples were subjected to nucleic acid extraction using QIAamp Viral RNA Mini Kit (Qiagen, Heidelberg) and extracted RNAs were reverse transcribed utilizing high capacity cDNA reverse transcription kits (Applied Biosystems). Matrix gene of influenza A and nucleocapsid gene of RSV, PIV 2, and PIV 3 were targeted to screen the respective RNA according to the protocol by Bharaj et al.⁷ The amplification of influenza A and RSV was done on monoplex single tube format whereas for the amplification of PIV 2 and PIV 3, multiplexing polymerase chain reaction (PCR) was used. Viral genome of hMPV was detected in clinical samples by using primers as described by Bouscambert-Duchamp et al.²¹ For the detection of human rhinovirus, highly conserved 5' untranslated region of the genome was amplified using a previously described nested PCR strategy according to Wisdom et al.²² The amplified DNA fragments were identified on a 2% agarose gel with ethidium bromide and visualized under UV transilluminator. For the confirmation, PCR-amplified products were purified and sequenced bidirectionally using BigDye Terminator v3.1 Cycle sequencing kit (Applied Biosystems, Foster, California) with an ABI 3500 × L genetic analyzer (PE Applied Biosystems Inc., Foster City, California) and further checked by basic local alignment search tool (BLAST) with already available reference database of National Center for Biotechnology Information (NCBI) website.

This study was carried out with the aim to describe the clinical and virological profile, treatment details, intensive care needs, outcomes, and predictors of PICU admission in infants with AVB. We planned to include all infants admitted with AVB during the study period.

Statistical Analysis

Appropriate data entry and statistical analysis were performed on Microsoft Excel 2010 (Microsoft, Redmond, Washington) and SPSS software version 20 (SPSS, Inc, Chicago, Illinois). Descriptive statistics [number (percentages) and median (interquartile range, IQR)] was used for baseline variables. The infants admitted to PICU were compared with those who do not required PICU admission by using the Chi-square test for categorical variables and Mann–Whitney *U* test for continuous variables. Multivariate analysis was done to find out independent predictors of PICU admission. All tests were two-tailed and *p* value <0.05 was taken as significant.

RESULTS

A total of 173 infants with AVB were enrolled with median age of 3 (2–7) months with male preponderance (65.9%, *n* = 114). The number of infants with AVB admitted during the months of November,

December, January, and February were 54 (31.2%), 70 (40.5%), 29 (16.8%), and 20 (11.6%), respectively. Majority (75.7%, $n = 131$) were born by vaginal delivery, 13.3% ($n = 23$) were preterm, 28.9% ($n = 50$) were low birth weight, and median birth weight was 2.6 (2.3–3) kg. The median duration of illness was 4 (3–7) days, and common clinical features were rapid breathing (98.8%), cough (98.3%), and fever (74%). One-third of cases ($n = 59$) had one or another underlying comorbidity. Before referral, 56.1% ($n = 97$) of cases were admitted at local hospitals for 24 (24–72) hours where they received oxygen support (51.4%) and antibiotics (50.3%). The examination findings at admission were tachypnea (98.8%), chest retractions (93.6%), respiratory failure (84.4%), wheezing (49.7%), crepitations (23.1%), and oxygen saturation on room air was 88% (82–91%). The chest radiographs were performed in 65.3% ($n = 113$) of cases, and common abnormalities included hyperinflation (75.2%), microatelectasis (54.9%), and parahilar infiltrates (13.3%) (Table 1).

All infants with clinical diagnosis of AVB underwent virological testing for RSV, rhinovirus, influenza A, PIV 2, PIV 3, and hMPV, and 75% ($n = 128$) of cases were tested positive for one or more viruses with a total of 166 virus isolates. The most common viruses identified were RSV (51.2%, $n = 85$), rhinovirus (39.7%, $n = 66$), influenza A virus (5.4%, $n = 9$), and PIV 3 (3%, $n = 5$), and hMPV (0.6%, $n = 1$). PIV 2 was not isolated in any case. One-fifth of infants (20.8%, $n = 36$) had >1 virus isolated (coinfection) and common combinations were RSV with rhinovirus (14.5%, $n = 25$) and RSV with influenza A virus (2.3%, $n = 4$) (Table 2).

One-fourth of cases developed one or more complications in the form of encephalopathy (17.3%), transaminitis (14.3%), shock (13.9%), AKI (7.5%), myocarditis (6.4%), MODS (5.8%), and ARDS (4.6%). Only three (1.7%) cases developed healthcare-associated infections and all three had ventilator-associated pneumonia (VAP). All cases were managed with oxygen support. The highest level of oxygen support received was in the form of nasal cannula (11%), CPAP (51.4%), HFNC (14.5%), and mechanical ventilation (23.1%). Other treatments included nebulization (74%, $n = 128$) [3% saline (66.5%), epinephrine (15%), and salbutamol (13.9%)], intravenous fluids (55.5%, $n = 96$), intravenous antibiotics (35.9%, $n = 96$), steroids (11.6%, $n = 20$), vasoactive drugs (13.9%, $n = 24$), and IVIG (1.7%, $n = 3$). The PICU admission was needed in 36.4% ($n = 63$) cases for 3 (2–6) days. The duration of hospital stay was 5 (3–9) days and the mortality was 8.1% ($n = 14$) (Table 2).

On univariate analysis, infants who required PICU admission had higher rates of comorbidity (55.6 vs 21.8%, $p = 0.001$), prereferral admission (68.3 vs 48.2%, $p = 0.01$), fever (84.1% vs 74%, $p = 0.02$), chest retractions (100 vs 90%, $p = 0.009$), respiratory failure at admission (92.1 vs 80%, $p = 0.026$), encephalopathy (25.4 vs 12.7%, $p = 0.03$), transaminitis (22.2 vs 10%, $n = 0.02$), shock (20.6 vs 1%, $p = 0.04$), MODS (11.1 vs 2.7%, $p = 0.029$); requirement of mechanical ventilation (39.6 vs 13.6%, $p < 0.001$), intravenous fluids (71.4 vs 46.4%, $p = 0.001$), and vasoactive drugs (20.6 vs 1%, $p = 0.04$); and had lower SpO₂ at admission [85% (80–90%) vs 88% (84–93%), $p = 0.04$] compared to those who did not require PICU admission (Table 3). The duration of hospital stay was longer in those who required PICU admission (9 vs 3 days, $p = 0.001$). On multivariate analysis, underlying comorbidity ($p < 0.001$), presence of chest retractions ($p < 0.001$), respiratory failure ($p = 0.03$) at admission, presence of shock ($p = 0.02$), and need for mechanical ventilation ($p = 0.04$) were independent predictors of PICU admission. The SpO₂ at admission was not taken into consideration for multivariate analysis, instead respiratory failure at admission was taken as both were judging the same variable.

Table 1: Demographic and clinical characteristics of infants with acute viral bronchiolitis

Characteristics	Total cases ($n = 173$)
Age (months); median (IQR)	3 (2–7)
Males, n (%)	114 (65.9)
Mode of delivery	
Normal vaginal delivery, n (%)	131 (75.7)
Lower segment Cesarean section, n (%)	42 (24.3)
Preterm, n (%)	23 (13.3)
Birth weight (kg), median (IQR)	2.6 (2.3–3.0)
Low birth weight, n (%)	50 (28.9)
Family history of upper respiratory infection, n (%)	13 (7.5)
Duration of illness (days), median (IQR)	4 (3–7)
Clinical features	
Rapid breathing, n (%)	171 (98.8)
Cough, n (%)	170 (98.3)
Fever, n (%)	128 (74)
Lethargy, n (%)	24 (13.9)
Seizure, n (%)	16 (9.2)
Any comorbidity	59 (34.1)
Cardiovascular, n (%)	24 (13.9)
Neurological disorder, n (%)	13 (7.5)
Neuromuscular, n (%)	4 (2.3)
Ventilation in neonatal age-group, n (%)	11 (6.4)
Chronic lung disease, n (%)	3 (1.7)
Failure to thrive, n (%)	4 (2.3)
Prereferral admission, n (%)	97 (56.1)
Length of hospital stay (hours), median (IQR)	24 (24–72)
Received oxygen support, n (%)	89 (51.4)
Received antibiotics, n (%)	87 (50.3)
Examination findings at admission	
Tachypnea, n (%)	171 (98.8)
Chest retractions, n (%)	162 (93.6)
Respiratory failure, n (%)	146 (84.4)
SpO ₂ on room air, median (IQR)	88 (82–91)
Wheeze, n (%)	134 (77.5)
Crepts, n (%)	40 (23.1)
Wheeze + crepts, n (%)	38 (22)
Decrease air entry, n (%)	2 (1.2)
Chest radiographs done, n (%)	113 (65.3)
Hyperinflation, n (%)	85 (75.2)
Microatelectasis, n (%)	62 (54.9)
Parahilar infiltrates, n (%)	15 (13.3)
Normal, n (%)	10 (8.8)
Pneumothorax, n (%)	1 (0.9)

There was no difference in demographic details, clinical features, complications, treatment details, intensive care needs, and outcomes among infants who had at least one virus detected compared to those with no virus and in whom >1 virus detected (coinfection) compared to those in whom no virus or at least 1 virus detected (data not shown).

DISCUSSION

In this prospective observational study, we enrolled 173 infants with AVB and noted that the common symptoms were rapid breathing, cough, and fever and common findings at admission

Table 2: Details of virological profile, complications, treatment, and outcome of infants with acute viral bronchiolitis

Characteristics	Total cases (n = 173)
Infants with at least one virus isolated, n (%)	128 (74)
Number of viral isolates	166
RSV, n (%)	85 (51.2)
Rhinovirus, n (%)	66 (39.7)
Influenza A virus, n (%)	9 (5.4)
PIV 3, n (%)	5 (3)
hMPV, n (%)	1 (0.6)
PIV 2, n (%)	0
Infants with >1 virus isolated (coinfection), n (%)	36 (20.8)
RSV and rhinovirus, n (%)	25 (14.5)
RSV and influenza A virus, n (%)	4 (2.3)
Rhinovirus and PIV 3, n (%)	3 (1.7)
Rhinovirus and influenza A virus, n (%)	2 (1.2)
RSV and PIV 3 virus, n (%)	1 (0.6)
RSV, rhinovirus, influenza A virus, and PIV 3, n (%)	1 (0.6)
Complications, n (%)	44 (25.4)
Encephalopathy, n (%)	30 (17.3)
Transaminitis, n (%)	25 (14.3)
Shock, n (%)	24 (13.9)
Acute kidney injury, n (%)	13 (7.5)
Myocarditis, n (%)	11 (6.4)
Multiple organ dysfunction syndrome, n (%)	10 (5.8)
Acute respiratory distress syndrome, n (%)	8 (4.6)
Pulmonary artery hypertension, n (%)	1 (0.6)
Oxygen support, n (%)	173 (100)
Nasal prongs oxygen, n (%)	19 (11)
Nasal CPAP, n (%)	89 (51.4)
High-flow nasal cannula, n (%)	25 (14.5)
Mechanical ventilation, n (%)	40 (23.1)
Nebulization, n (%)	128 (74)
3% saline, n (%)	115 (66.5)
Epinephrine, n (%)	26 (15)
Salbutamol, n (%)	24 (13.9)
3% saline + Epinephrine, n (%)	22 (12.7)
3% saline + Salbutamol, n (%)	9 (5.2)
Intravenous fluids, n (%)	96 (55.5)
Antibiotics, n (%)	62 (35.9)
Steroids, n (%)	20 (11.6)
Vasoactive agents; n (%)	24 (13.9)
Maximum vasoactive-inotropic score, median (IQR)	43 (10–76)
IVIG, n (%)	3 (1.7)
PICU admission, n (%)	63 (36.4)
Duration of PICU stay (days), median (IQR)	3 (2–6)
Duration of hospital stay (days), median (IQR)	5 (3–9)
Mortality, n (%)	14 (8.1)

were tachypnea, chest retractions, respiratory failure, low SpO₂, wheezing, and crepitations. RSV and rhinovirus were most commonly detected viruses. The extrapulmonary manifestations were noted in 25% of cases in the form of encephalopathy, transaminitis, shock, AKI, myocarditis, MODS, and ARDS. More than one-third of cases needed PICU admission and common treatment included oxygen support (nasal prong oxygen, CPAP, HFNC), mechanical ventilation, nebulization (3% saline, adrenaline,

and salbutamol), vasoactive drugs, and steroids. One-third of cases also received intravenous antibiotics. The mortality rate was 8%.

The impact of AVB on the health of young children is huge and approximately 2–3% of infants require hospitalization due to AVB.⁴ Despite the high burden of disease, there is lack of effective treatment for AVB and none of the commonly practiced modalities shown to shorten the disease course or hastens the resolution of symptoms. With supportive treatment (heated humidified oxygen, adequate hydration, and respiratory monitoring), majority of infants with AVB do well. The American Academy of Pediatrics published clinical practice guidelines based on Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system to standardize the diagnosis and management of AVB.²³ As per the guidelines, the suspicion of AVB should be based on the history and physical examination. There is no need for routine radiographic, laboratory studies, and viral testing. The supplemental oxygen is needed if oxyhemoglobin saturation (SpO₂) falls below 90%. Intravenous or nasogastric fluids are administered to maintain adequate hydration. Epinephrine, short-acting β₂-agonists, systemic glucocorticoids, chest physiotherapy, and antibiotics are not recommended routinely. Nebulization with hypertonic saline may be used as it improves symptoms of mild-to-moderate AVB.²³ The use of antibiotics does not lead to change in course or outcome and are not routinely recommended.^{4,23} Despite these facts, antibiotics have been used in AVB inappropriately.²⁴ Therefore, efforts are needed to reduce inappropriate and unnecessary use of antibiotics in AVB. The use of bronchodilators, hypertonic saline, steroids, and antibiotics in the index study possibly suggests variable practice among treating physicians, inappropriate use of various treatment modalities, discrepancies between evidence-based medicine and routine clinical practice, and substantial variability in the diagnosis and management of AVB as reported in other studies as well.^{25–28}

PICU admission is usually needed in 15–25% of children with AVB and about 25–40% of those admitted to PICU require endotracheal intubation and mechanical ventilation.^{28–31} Various noninvasive modes [CPAP, HFNC, noninvasive positive pressure ventilation (NPPV), and bilevel positive airway pressure (BiPAP)] are increasingly used these days which may obviate the need for invasive mechanical ventilation.^{32–36} The common indications for invasive mechanical ventilation are nonimprovement or deterioration on noninvasive modes, apnea, severe lower airway disease, or ARDS. The duration of mechanical ventilation is usually short (<5 days).^{3,37} In the index study, 36.4% of cases needed PICU admission. Underlying comorbidity; presence of chest retractions, respiratory failure, and lower oxygen saturation at admission; presence of shock; and need of mechanical ventilation were independent predictors of PICU admission.

The mortality observed in PICU and no PICU admission groups was similar (7.9 vs 8.2%) despite the fact that higher proportion of infants in the PICU group had underlying comorbidities, respiratory failure at admission, shock, and MODS; and greater proportion required mechanical ventilation and vasoactive drugs. The reason for same mortality could be due to the optimal level of intensive care and monitoring provided to patients admitted to PICU despite they were being sicker. The higher mortality (8%) in the index study could be attributed to the facts that ours being a tertiary care hospital managing cases referred with more severity of illness; delayed presentation; higher sickness level; and higher proportions with respiratory failure (84%), extrapulmonary complications (25%), requirement of PICU admission (36.4%), mechanical ventilation



Table 3: The predictors of PICU admission among infants with AVB according to univariate and multivariate logistic regression analyses

Baseline characteristics	PICU admission (n = 63)	No PICU admission (n = 110)	p value (Univariate analysis)***	p value (Multivariate analysis)***
Age (months), median (IQR)	3 (2–8)	4 (2–7)	0.09	0.13
Male, n (%)	44 (69.8)	70 (63.6)	0.40	
Preterm, n (%)	8 (12.7)	15 (13.6)	0.86	
Comorbidity, n (%)	35 (55.6)	24 (21.8)	0.001	<0.001
Prereferral admission, n (%)	43 (68.3)	53 (48.2)	0.01	0.88
Duration of illness (days), median (IQR)	4 (3–7)	3.5 (2.7–6.6)	0.20	
Fever, n (%)	53 (84.1)	75 (74)	0.02	0.64
Cough, n (%)	62 (98.4)	108 (98.2)	0.911	
Tachypnea, n (%)	63 (100)	108 (98.2)	0.28	
Chest retraction, n (%)	63 (100)	99 (90)	0.009	<0.001
Seizure, n (%)	7 (11.1)	9 (5.2)	0.52	
Lethargy, n (%)	11 (17.5)	13 (11.8)	0.30	
Respiratory failure at admission, n (%)	58 (92.1)	88 (80)	0.026	0.03
Room air SpO ₂ at admission, median (IQR)*	85 (80–90)	88 (84–93)	0.04	
Encephalopathy, n (%)	16 (25.4)	14 (12.7)	0.03	0.53
Transaminitis, n (%)	14 (22.2)	11 (10)	0.02	0.56
Shock, n (%)	13 (20.6)	11 (1)	0.04	0.02
Acute kidney injury, n (%)	8 (12.7)	5 (4.5)	0.051	0.38
Myocarditis, n (%)	5 (7.9)	6 (6.4)	0.532	
MODS, n (%)	7 (11.1)	3 (2.7)	0.029	0.16
ARDS, n (%)	5 (7.9)	3 (2.7)	0.142	
Mechanical ventilation, n (%)	25 (39.6)	15 (13.6)	<0.001	0.04
Nebulization, n (%)	50 (79.4)	78 (70.9)	0.22	
Antibiotic received, n (%)	54 (85.7)	85 (77.3)	0.179	
Intravenous fluid received, n (%)	45 (71.4)	51 (46.4)	0.001	0.12
Steroids, n (%)	13 (20.6)	7 (6.4)	0.005	0.98
Intravenous immunoglobulin, n (%)	2 (3.2)	1 (0.9)	0.30	
Vasoactive drugs, n (%)**	13 (20.6)	11 (1)	0.04	
Maximum VIS score, median (IQR)	50 (10–81)	35 (13–63)	0.83	
Virus detected, n (%)	44 (69.8)	84 (76.4)	0.34	
RSV, n (%)	27 (42.9)	58 (52.7)	0.21	
Rhinovirus, n (%)	22 (34.9)	44 (40)	0.50	
Rhinovirus + RSV, n (%)	7 (11.1)	18 (10.4)	0.34	
Infants with >1 virus isolated, n (%)	9 (14.3)	27 (24.5)	0.08	
Duration of hospital stay (days), median (IQR)	9 (5–16.3)	3 (2–5)	0.001	
Mortality, n (%)	5 (7.9)	9 (8.2)	0.31	

* Not included in multivariate analysis as the presence of respiratory failure was included. **Not included in multivariate analysis as the presence of shock was included. *** Bold numbers indicate significant p-value

(23%), and vasoactive drugs (14%). The rates of these complications and mortality are much higher than reported in the literature.^{38,39}

With the availability of molecular techniques, it has been possible to identify viruses causing AVB including RSV (50–80%), rhinovirus (5–25%), PIV (5–25%), hMPV (5–10%), coronavirus (5–10%), adenovirus (5–10%), and influenza (1–5%).^{4,13,40,41} The proportion of virus causing AVB differ according to geographical location and time of the year. The clinical features of AVB caused by different viruses

are generally indistinguishable. Also, there are not much differences in response to medical treatment among infants with AVB caused by different viruses.⁴ However, it has been noted that AVB caused by rhinovirus may be less severe and associated with shorter duration of hospitalization than RSV.^{4,42} The reported rates of coinfection varied widely among different studies (6 to >30%).^{4,42,43} Among infants with coinfection, few studies noted greater severity of disease, longer hospital stay, more severe hypoxemia, and greater risk of

relapse^{42,44,45} whereas others demonstrated no difference in disease severity and outcome.^{43,46–48} In the index study, at least one virus was isolated in 74% of cases with RSV and rhinovirus as commonest. One-fifth of cases had coinfection with >1 virus. However, isolation of virus or coinfection was not associated with any differences in clinical features, complications, treatment, PICU needs, and outcomes.

The strengths of this study include a prospective study with large sample size. All the enrolled cases underwent viral testing that is important to determine etiology but did not have much significance in determining disease severity, treatment, and short-term outcome. The details of treatment, intensive care needs, and outcomes have been described. The predictors of PICU admission were determined. The limitations included a single-center study and lack of long-term follow-up. The sample size was not calculated for any outcome variable independently, and all infants with AVB were enrolled during one season of AVB.

CONCLUSION

AVB is a common cause of hospitalization among infants, RSV and rhinovirus are commonly detected viruses, and one-third of cases required PICU admission. Underlying comorbidity; presence of chest retractions, respiratory failure at admission, and shock; and need for mechanical ventilation were independent predictors of PICU admission. Isolation of virus or coinfection was not associated with disease severity, PICU admission, or outcome.

DECLARATION

Ethics approval and consent to participate: Yes

Consent for publication: Consent of parents was obtained before enrolment.

Authors' Contributions

SKA conceptualized the study, supervised data collection, and finalized the manuscript; LT collected and analyzed the data. SS, IJ, IB, RKR, Performed laboratory investigations. Muralidharan Jayashree conceptualized and supervised the study and finalized the manuscript. All the authors approved the final manuscript.

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