ORIGINAL ARTICLE

Clinical Profile and Short-Term Outcomes in Neonates with Respiratory Syncytial Virus Infection: A Single-Center Study

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ABSTRACT

Objective: To explore the clinical profile and outcomes in neonates hospitalized with respiratory syncytial virus (RSV) infection.

Methods: Clinical features, respiratory support, pharmacological treatment, complications and outcomes of neonates admitted to the neonatal intensive care unit with RSV infection between January 2018 and March 2023 were recorded. Descriptive statistics were employed for analysis.

Results: Thirty-seven neonates with RSV infection were analyzed. The most common presenting features were cough (*n* = 29, 74.4%), refusal to feed (*n* = 29, 74.4%) and apnea (*n* = 7, 17.9%). 19 (48.7%) neonates were mechanically ventilated, 28 (71.8%) required non-invasive respiratory support and 13 (35.1%) required bronchodilator therapy. All neonates were discharged after a median (IQR) duration of 14 (9, 23.5) days.

Conclusion: Neonates with RSV infection requiring hospitalization have considerable respiratory morbidity requiring prolonged respiratory support and pharmacological therapy.

Keywords: *Bronchodilator, Infant, Lower respiratory tract infection, Respiratory viral infection, RSV*

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INTRODUCTION

Respiratory syncytial virus (RSV) infection commonly presents with acute lower respiratory tract infection (ALRI) in children and carries a high morbidity and mortality [1,2]. An estimated 33 million cases occur globally every year, resulting in nearly 1.4 million hospital admissions and 118,200 deaths in under-5 children. Notably, low-income countries (LICs) and lower-middle-income countries (LMICs) bear a substantial burden of RSV, with approximately 22 million cases and 103,000 deaths occurring in these regions [2,3].

In recent years, there has been a growing recognition of ALRI due to RSV in neonates, with reported rates of RSV isolation in neonatal intensive care units (NICUs) ranging from 1 to 4% during winter epidemics [4]. However, there is a lack of comprehensive data on RSV occurrences in neonates from LICs and LMICs, where the prevalence is presumed to be higher due to several factors.

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Any respiratory infection in NICU has a potential for nosocomial outbreak and may be associated with prolonged hospital stay, need for escalated respiratory support and antimicrobial therapy [5]. Further, RSV infection in neonates is associated with increased risk for morbidities like bronchopulmonary dysplasia and higher mortality [6]. While most of these effects have been primarily observed in high-risk preterm infants, the impact of RSV on healthy neonates is still elusive.

Despite the significance of these outcomes, data on respiratory outcomes and other morbidities related to RSV infection in healthy neonates requiring admission from the community are scarce. Moreover, only one study from the Indian subcontinent has reported outcomes of fourteen neonates [7]. Therefore, our study aims to explore the clinical profile and outcomes in neonates with documented RSV infection. To our knowledge, this is one of the few datasets from India offering insights into the outcomes of previously healthy neonates admitted with community-acquired RSV ALRI.

METHODS

A single-site retrospective study was conducted in a tertiary care level III NICU from January 2018 to March 2023. Outborn neonates with clinical features suggestive

of ALRI requiring NICU admission with laboratory confirmation of RSV infection were included. Admission criteria to NICU included age of less than 30 days, or a postnatal age of more than one month but with a postmenstrual age (PMA) of less than 44 weeks, or admission weight of less than 2,500g. The data was systematically collected from the hospital medical records and relevant data variables were entered in a predesigned proforma. These variables included demographic information, clinical presentation, comorbidities, respiratory support, morbidities, laboratory test results, treatment modalities and outcomes. All patient information was anonymised to maintain confidentiality of participants.

Neonates who presented with respiratory distress were initially received in the emergency room and were subsequently admitted to the NICU after stabilization. As part of the ALRI evaluation, all neonates underwent chest X-ray. Nasopharyngeal swabs or respiratory secretions (in the case of intubated neonates) were collected and transported in viral transport media. Laboratory confirmation of RSV infection was performed using the reverse transcription polymerase chain reaction (RT-PCR) technique. The management was as per unit protocol; nebulized salbutamol was the preferred bronchodilator. Oseltamivir was administered to neonates with confirmed influenza infection by RT-PCR, if they required non-invasive respiratory support and above. Neonates with ALRI symptoms were isolated by admitting them in a separate block within the NICU complex.

Statistical analysis: Statistical analysis was performed using SPSS version 16. Descriptive statistics were used. Categorical variables were presented as frequencies and percentages, while continuous variables were reported as means with standard deviations (SD) or medians with interquartile ranges (IQR), depending on the distribution of the data.

RESULTS

During the study period, a total of 145 neonates had symptoms of ALRI of which 37 (25%) neonates tested positive for RSV. Neonates with RSV infection were observed to be more frequently admitted during the months of October (13/37; 35%), November (13/37; 35%), and September (3/37; 8%). The median (IQR) postnatal age at the time of admission was 25 (16, 35) days. The mean (SD) gestational age and birth weight were 36 (3.3) weeks and 2,361 (718) g, respectively. Among the 37 neonates with RSV infection, 17 (46%) were born preterm (< 37 weeks of gestation) and 9 (24%) had a birth weight less than 2000g (**Table I**). The most common clinical presentations were cough (*n* = 29, 74.4%), refusal to feed (*n* = 29, 74.4%), noisy breathing (*n* = 24, 61.5%) and lethargy (*n* = 21, 53.8%). Seizures and apnea were presenting symptoms in five (12.8%) and seven (17.9%) neonates, respectively. Cerebrospinal fluid (CSF) examination was unremarkable in all the neonates with seizures. The neonates exhibited respiratory distress, with a median (IQR) Downe's score of 5 (4, 7) upon admission. Among the 37 neonates included in the study, 19 (48.7%) required mechanical ventilation. Non-invasive respiratory support was provided to 28 (71.8%) neonates. The median (IQR) duration of mechanical ventilation and non-invasive respiratory support were 5 (3, 9) and 5 (3, 11.7) days, respectively. Pharmacological therapy included nebulization with beta-2 agonists (*n* = 12, 30.8%) and inhaled steroids (*n* = 5, 12.8%) (**Table II**). Chest radiographs of neonates revealed consolidation (*n* = 9, 23.1%), patchy infiltrates (*n* = 6, 15.4%), interstitial infiltrates (*n* = 4, 10.3%) and hyperinflation (*n* = 13, 33%) (**Table I**). The baseline laboratory parameters including hemoglobin,

Table I Baseline Characteristics of Neonates Admitted with RSV Acute Lower Respiratory Tract Infection

Gestational age (wk)	36 (3.3)
28-32[a]	5 (13.5)
32-37[a]	12 (32.4)
>37[a]	20 (54)
Birth weight (g)	2361 (718)
< 1000[a]	3 (8.1)
1000 -2000[a]	6 (16.2)
> 2000[a]	28 (75.6)
Postnatal age at presentation (days)[b]	25 (16, 35)
Intrauterine growth restriction[a]	9 (23.1)
Male[a]	18 (46.2)
Chest X-ray findings[a]	
Consolidation	9 (23.1)
Patchy infiltrates	6 (15.4)
Interstitial infiltrates	4 (10.3)
Hyperinflation	13 (33)
Laboratory parameters	
Hemoglobin (g/dL)[b]	13 (11, 15)
Total leukocyte count (mm^3)	11,156 (4,703)
Neutrophil/lymphocyte ratio	1.19 (1.3)
Platelet count (x 10^3)[b]	299 (192, 452)
C-reactive protein positive (>6 mg/dL)[a]	6 (15.4)
Transaminitis[a]	6 (16)
Clinical presentation	
Pneumonia[a]	7 (17.9)
Need for inotropes[a]	6 (15.4)
Anemia requiring PRBC transfusion[a]	7 (17.9)
Myocarditis[a]	3 (7.7)
Blood stream sepsis[a]	4 (10.3)
Duration of hospital stay[b]	14 (9, 23.5)

All values are mean (SD), [a]n (%) or [b]median (25th centile, 75th centile)

total leukocyte count, platelet count, and C-reactive protein were within normal limits. Transaminitis was observed in six (16%) of the cases.

Out of the 37 neonates, six (15.4%) experienced hypotension requiring inotropic support and seven (17.9%) required packed red blood cell (PRBC) transfusion. Four (10.3%) neonates had culture-positive sepsis. Three neonates were found to have associated myocarditis. Reduced cardiac contractility was identified in one neonate who was managed with dobutamine infusion for 24 hours, while the other two neonates did not require additional medication. All 37 neonates were discharged home with a median (IQR) duration of hospital stay of 14 (9, 23.5) days (**Table II**).

DISCUSSION

In this retrospective study, we aimed to assess the clinical characteristics and outcomes of neonates admitted to the NICU who were tested positive for RSV. During the five-year study period, we identified a total of 37 neonates with confirmed RSV ALRI infections. The pattern of occurrence of RSV infection aligned with the peak incidence of RSV infections in India, i.e., during the winter months, with a higher frequency of admissions in September to November [8]. The study primarily focused on healthy term infants who acquired infections from the community. The median postnatal age at the time of admission was 25 days. Our results were similar to the study by Alan et al where neonates presented at a comparable postnatal age of 24 days and the infections were predominantly acquired from the community [9]. Our study largely included neonates (86%) born after 32 weeks of gestation with no underlying comorbidities.

Table II Respiratory Profile of Neonates Admitted With RSV Acute Lower Respiratory Tract Infection

Severity of RD at admission (Downe's score > 4)	36 (97)
Invasive ventilation	19 (48.7)
Duration of invasive ventilation (days)[a]	5 (3, 9)
High frequency ventilation	4 (10.3)
Non-invasive ventilation	28 (71.8)
NIMV	21 (53.8)
CPAP	21 (53.8)
HHFNC	17 (43.6)
Pharmacological therapy	13 (35.1)
Bronchodilator therapy	13 (35.1)
Inhaled bronchodilators	12 (30.8)
Inhaled steroids	5 (12.8)
Systemic steroids	10 (25)
Aminophylline	5 (12.8)
SC adrenaline	6 (15.4)
Ketamine infusion	2 (5.1)

CPAP Continuous Positive Airway Pressure, HHHFNC Heated humidified high flow nasal cannula, NIMV Noninvasive mandatory ventilation, PRBC Packed red blood cell components, RD Respiratory distress, SC Subcutaneous
All values are expressed as n (%) or [a] median (IQR)

The primary reason for hospital admission was either respiratory distress or the need for additional respiratory support. The clinical manifestations at presentation were lethargy, refusal to feed and poor cry. This presentation matches the presentation of older infants with severe RSV infection when compared to the upper respiratory tract symptoms seen in toddlers [10]. Additionally, apnea, a notable finding in RSV ALRI, was observed in seven (17.9%) neonates in our study which is within the reported incidence of 1.2 to 23.8% in hospitalized infants [11]. Furthermore five (12.8%) neonates had seizures, indicating potential neurological involvement, possibly due to transient cytotoxic edema associated with RSV infections [12].

Our study primarily investigated short-term respiratory morbidities including the use of respiratory support and pharmacological agents in managing severe ALRI. Although our study cohort consists of previously healthy mature neonates, a significant proportion of them experienced a more severe clinical course as indicated by the need for respiratory support with almost 78% requiring such assistance. Among the 37 neonates admitted, 19 (48.7%) required mechanical ventilation, while the majority of others (n = 28) required non-invasive ventilation for a median duration of 5 days. A study by Goncalves et al in preterm and term infants, 5.4% were mechanically ventilated, 83.8% required oxygen support, and 37% needed respiratory support for median durations of 4, 3, and 4 days, respectively [13]. In studies by Alan et al and Cho et al, mechanical ventilation and oxygen requirement rates were 10.8% and 22%, and 45.7% and 4.4%, respectively [9,14]. A similar study from India described the clinical profile of 14 neonates, among whom 12 required respiratory support for a median (IQR) duration of 7 (3, 12) days. However, this cohort was primarily comprised of preterm neonates who had been discharged from the NICU [7]. Although the need for support aligns with findings from other studies, our study cohort showed a prolonged duration of non-invasive respiratory support, indicating potential differences in disease severity or management practices.

Recommended treatment for viral ALRI includes mainly supportive measures in terms of respiratory support, temperature, fluid and nutritional management. Although no substantial evidence supports the use of

WHAT THIS STUDY ADD?

- Respiratory syncytial virus is a significant cause of acute lower respiratory tract infections in neonates.
- Respiratory syncytial virus in previously healthy neonates can be severe requiring invasive or non-invasive ventilation, prolonged hospital stay and respiratory morbidity.

pharmacological agents, clinicians often tend to use these medications, especially in severe cases. Of 37 neonates, 12 (30.8%), 5 (12.8%) and 10 (25%) infants received beta-2 agonist nebulisation, inhaled and systemic steroids, respectively. In contrast, in a study by Alan et al, the use of inhaled salbutamol (71.2%) was higher, whereas the use of inhaled steroids (6.8%) and systemic steroids (12.4%) was lesser [9]. These differences in the use of pharmacological agents can be attributed to the management practices. ALRI cases are often challenging for clinicians, which was the case in our study cohort, where six infants had severe bronchospasm and wheeze and required either one of the following therapies: subcutaneous adrenaline in six (16.2%), aminophylline infusion in five (13.5%) and ketamine infusion in two (5.4%). These agents are also documented in Alan et al where subcutaneous adrenaline was used in ten (2.5%) infants [9].

The study also highlighted the occurrence of various morbidities. Three (7.7%) neonates were diagnosed with myocarditis. RSV leading to myocarditis was reported in a survey of 22 cases of myocarditis during RSV infection; out of 22 cases, two were infants around one month of age [15]. The median duration of hospital stay in our study was 12 days. Meanwhile, Alan et al reported the median duration of hospital stay as 8 days and Cho et al reported it as 9 days [9,14].

Our study provides valuable insights in the outcomes of previously healthy neonates with community acquired RSV infection. Being a single-site study, it offers a realistic view of clinical practices and outcomes in managing RSV infections in neonates. However, due to a retrospective design, potential selection bias may have influenced our findings. Our sampling was limited to babies with severe ALRI, restricting our outcome data to moderate to severe cases requiring hospital admission and not encompassing all community-acquired infections. Additionally, we did not account for potential confounding factors, such as co-infections with other pathogens or variations in treatment practices over time which could have influenced the observed outcomes.

Neonates with RSV requiring hospitalization have considerable respiratory morbidity requiring prolonged respiratory support, hospital stay and the need for pharmacological agents.

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