



Clinical Profile of Neonatal RSV Bronchiolitis - A Descriptive Study

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Abstract

Introduction: Newborns with viral bronchiolitis may have a turbulent clinical course and Respiratory syncytial virus (RSV) is the most common viral agent causing bronchiolitis in childhood.

Methods: This ambispective study was conducted in the outborn nursery of a tertiary care Government Medical College in neonates who were admitted with a working diagnosis of acute bronchiolitis or respiratory tract infection. A retrospective chart review was done for the cases admitted during the outbreaks of August to November 2022 and a prospective study was done from September to December 2023.

Results: During the study period, a total of 100 neonates (60 cases in 2022 and 40 cases in 2023) were admitted with respiratory tract infection or bronchiolitis. 75% of the babies had moderate to severe bronchiolitis. Thirteen babies with severe bronchiolitis required invasive ventilation. The most common virus detected was RSV followed by Rhino virus. Among the neonates with RSV infection, 65.71% were term babies. There was no mortality. The most common clinical presentation was cough (N = 89) (89%) and the threatening symptom was apnea with cardiorespiratory arrest. Remdesivir, an antiviral agent, was given to two babies with severe RSV bronchiolitis on compassionate ground.

Conclusions: Apnea and cardiorespiratory arrest should be anticipated in neonatal bronchiolitis. Remdesivir is an antiviral agent which can be life saving in severe RSV bronchiolitis.

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Introduction

Bronchiolitis is a virus induced injury characterized by acute inflammation, edema, and necrosis of epithelial cells lining of small airways (bronchioles), and increased mucus production. Respiratory syncytial virus (RSV) is the most common viral agent isolated in about 75% cases of bronchiolitis (30-70% in Indian studies). Rhinovirus, parainfluenza, adenovirus, human metapneumovirus, and bocavirus are the other viruses commonly causing this condition. Signs and symptoms typically begin with rhinitis and cough, which may progress to tachypnea, wheezing, rales, and use of accessory muscles. Newborns with viral bronchiolitis may have a turbulent and uncertain clinical course.¹⁻³

Any viral respiratory infection in the NICU has the potential to cause nosocomial outbreaks and may be associated with severe pneumonia, the need for escalated



respiratory support, antimicrobial therapy and prolonged hospital stays.⁴ The impact of RSV on healthy neonates remains unclear and data on respiratory outcomes and other morbidities related to RSV infection in healthy neonates requiring admission from the community are scarce.⁵ There is no definitive therapy, but recently Remdesivir has been used on compassionate ground in severe RSV bronchiolitis with suspected associated pneumonia.

Study of neonatal bronchiolitis is relatively sparse, especially in the resource limited set up. This descriptive study has been thus conceptualized to study the clinical profile of neonates admitted with RSV bronchiolitis during the season in two consecutive years.

Methods

This ambispective study was conducted in neonates with bronchiolitis admitted in the outborn unit of a tertiary care level III Neonatal Intensive Care Unit (NICU) of a Government Medical College in south Kerala, India. The research was commenced after getting ethical clearance from the Human Ethics Committee of the institute with the permission number: HEC NO: 09/05/2024/MCT. A retrospective chart review was done among neonates with bronchiolitis during the outbreaks of August to November 2022 and a prospective study was done from September to December 2023. The data was systematically collected from the hospital medical records. Patient confidentiality was maintained. The authors certify that we have obtained all appropriate patient consent forms. The parents understood that their baby's name would not be published and due efforts would be made to conceal their identity. Diagnosis of acute bronchiolitis was made when the neonate presented with coryzal prodrome lasting one to three days, followed by persistent cough, either tachypnoea or chest recession (or both) and either wheeze or crackles on chest auscultation (or both). Those neonates who presented with apnea and who had a history of contact with URTI or LRTI in the family was also taken as bronchiolitis in this study. The severity was assessed by the standard treatment guidelines on bronchiolitis by Indian Academy of Paediatrics in 2022. Chest X-ray was taken for all. Nasopharyngeal swabs were collected on the first day of hospitalization using a sterile flocked swab for viral PCR. This was done only for those neonates with moderate to severe bronchiolitis who needed respiratory support more than Heated Humidified High Flow Nasal Cannula (HHHFNC). A panel of reverse transcriptase (RT) PCR assays were used to detect respiratory viruses like RSV, Rhinoviruses (RV), influenza virus (IV), Para influenza virus 1-4, SARS CoV2 Coronavirus, Enterovirus, Parecho virus, Human metapneumovirus, Mycoplasma pneumoniae, Human bocavirus and Human adenovirus. Statistical analysis was performed using SPSS version 27. 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 100 neonates (60 cases in 2022 and 40 cases in 2023) were admitted with symptoms of bronchiolitis or upper respiratory tract infection (URTI). URTI was admitted either because of parental anxiety or concerning symptoms. The mean gestational age was 37.67 weeks (SD 1.71) and mean birth weight was 2821grams (SD 496). Moderate to severe bronchiolitis was present in 75 babies (75%). Among these, 13 babies (13%) were having severe bronchiolitis. Oseltamivir was started in neonates requiring noninvasive ventilation (NIV) and above till NP swab results were available. Nasopharyngeal swab real-time PCR was carried out in 54 babies and viruses were detected in 75.92% (N = 41). RSV was detected in 64.8% (N = 35) and Rhinovirus in 11.11 % (N = 6). Among these, dual RSV and Rhinovirus were there in three cases (5.5%). The median (IQR) postnatal age at the time of admission was 17 (4) days.

Among neonates with RSV infection, 65.71% were term babies and only 34.29% (N = 12) were born preterms (< 37 weeks of gestation). Among that only five (14.28%) were less than 34 weeks and none were less than 32 weeks at birth. The median age of starting illness was 14.5 days (IQR 7). The lowest age seen was three days. The most common clinical presentations were cough (N = 89) (89%), respiratory distress (N = 75) (75%), rhinitis (N = 56) (56%), fever (N = 38) (38%), irritable cry (N = 10) (10%) and aspiration of feeds (N = 9) (9%). Five neonates among moderate to severe illness (6.67%) presented to the emergency room with cardiorespiratory arrest. Among these, four (80%) were RSV positive (11.4% of RSV cases) and for the remaining one baby nasopharyngeal swab was negative for COVID-19, RSV and Influenza. Other viral panel were unavailable in the centre at that time. Five babies had a history of poor activity and developed encephalopathy at or after admission. Among this one baby had NEC like features as well.

Out of the 13 babies who required invasive ventilation, 10 were positive for RSV (28.6% of RSV cases), one was positive for rhino virus and two were not positive for any. Out of these ventilated babies, eight babies were ventilated because of worsening respiratory distress and five babies were ventilated because of apnea or poor respiratory efforts. Among the babies who were ventilated, 75% of the babies had recurrent collapse after ventilation and most of them required prolonged ventilation with a median duration of six days (IQR 9).

Out of the 13 babies who got ventilated, nine were during first season and four were during second season. As many ventilated babies had recurrent collapse and difficult extubation during the first season, the unit followed a restrictive ventilation policy for the babies during second season. Even if there was

significant oxygen requirement on NIV, if the work of breathing was controlled on NIV, intubation was not done. Out of the 35 RSV positive neonates, six (15.4%) experienced hypotension requiring inotropic support. One neonate had superadded bacterial culture-positive sepsis. In 2022 outbreak, 60% babies were started on empirical antibiotics at admission but during second year (2023), only 20% of the babies were started on antibiotics at admission.

Among the four ventilated neonates in 2023, all were intubated for refractory apnea and encephalopathy and among them two had cardiac arrest. They were twins who presented one after the other within an interval of three days. After ventilation their oxygen requirement started increasing and required high ventilator settings (required above 50% oxygen with high pressures). When the second twin also got intubated, as per the decision by infectious disease specialist Remdesivir was given to both the babies on compassionate ground. There was improvement in sensorium and babies were extubated within the next few days. For the other two babies, there was no significant oxygen requirement on ventilator and they were extubated within 48 hours. The baseline laboratory parameters including hemoglobin, total leukocyte count, and platelet count were within normal limits in all cases. All neonates were discharged well. The mean duration of hospital stay among RSV bronchiolitis babies were 12 days (7.4 days).

Discussion

In this study, the authors have tried to highlight the complexities that has to be anticipated in bronchiolitis. 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 from September to November. Typically, there is seasonal variation in infectivity that is highest during the winter months in temperate zones, with less variability in tropical zones.^{6,7} This variation occurs because RSV favors cool temperatures and high humidity, meaning cool and dry winters have less illness related to RSV than warmer, wetter conditions.⁸ In tropical areas, large aerosol droplets are formed due to higher humidity and stable temperatures resulting in less variability across the year. There are two possible explanations for variations in viral circulation over time: either the transmission of distinct viral genotypes or "herd immunity. Virus subtypes was not tested in this study. However, varying hospitalization rates during different epidemic seasons can be explained by the alternating circulation of RSV types A and B.

RSV bronchiolitis babies presented with apnea and encephalopathy indicating potential neurological involvement, possibly due to transient cytotoxic edema associated with RSV infections.⁹ Apnea and encephalopathy may be the first manifestation. If there is a contact with a case of URTI, the condition should be suspected in an unexplained case of apnea. A significant proportion of ventilated neonates experienced a

more severe clinical course and maximum days of ventilation needed was 17 days. In 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 duration of 4, 3, and 4 days, respectively.¹⁰ In a study conducted by Venkat M et al on 37 neonates with RSV bronchiolitis, a significant proportion of neonates experienced a more severe clinical course as indicated by the need for respiratory support with almost 78% requiring assistance and 48.7% required mechanical ventilation, while the majority of others required non-invasive ventilation for a median duration of five days.¹¹

As viral detection improves, infants with bronchiolitis may present with multiple viruses simultaneously. Studies have shown strict infection control practices, including hand hygiene and use of personal protective equipment can reduce nosocomial RSV infection rates by 50%.¹² Recommended treatment for viral bronchiolitis includes mainly supportive measures in terms of respiratory support, nebulization with 3% saline, temperature, fluid, and nutritional management.

Management that includes chest physiotherapy, Monteleukast, Ipratropium bromide and steroids do not have a validated role in neonatal bronchiolitis. Possible interventions which may show good response in neonates with bronchiolitis includes intravenous immunoglobulin, Aerosolised Ribavirin, Remdesivir, surfactant, and Heliox.¹³ Nebulized or oral Ribavirin is a nucleoside analogue with good in vitro activity against RSV, however neither it is readily available, nor did it show a reduction in mortality rates or duration of mechanical ventilation. Remdesivir is a novel nucleoside analogue and its active metabolite is remdesivir triphosphate which acts selectively as the substrate for viral RNA-dependent RNA polymerase (RdRp) causing delayed chain termination to reduce viral load, and became well known in COVID era. For COVID positive babies with severe respiratory distress, it is recommended to start Remdesivir within five days of symptom onset (maximum nine days) for a period of five days, or till symptom recovery whichever earlier. The dosing of Remdesivir recommended was loading dose of 5 mg / kg over 1 hour, followed by maintenance dose 24 hours later as 1.25 mg / kg once daily for the next four days. Same guidelines were followed for two cases in this study. Our babies did not encounter the reported side effects of Remdesivir therapy which include bradycardia, transaminitis, acute kidney injury, and hypersensitivity reactions. Palivizumab is a humanized mouse immunoglobulin G1 (IgG1 j) monoclonal antibody produced by recombinant DNA technology, used as a prophylaxis for RSV bronchiolitis. The antibody is directed against a conserved epitope, site II of the prefusion and postfusion (F) protein of respiratory syncytial virus (RSV) and demonstrates both neutralizing and fusion inhibitory activity.^{14,15} Palivizumab is administered intramuscularly at a dosage of 15 mg / kg once a month.¹⁶ It may be required for five to six months. Cost

hinders its usage. It is mostly recommended for preterms and at risk babies.

In this study, virus subtypes were not checked. About 65% of the affected neonates with bronchiolitis were term babies without any risk factors. The lessons learned during first outbreak helped to streamline the management during second outbreak. As there is high chance of apnea and cardiorespiratory arrest due to RSV, the hospital protocol was changed during the RSV season to keep the neonates with URTI symptoms under observation for initial 48 hours anticipating adverse events. Empirically antibiotics can be avoided in a viral infection unless localized collapse or significant infiltrates in X ray or the baby get ventilated. As recurrent collapse was an important issue after ventilation, a higher threshold can be kept for invasive ventilation.

Conclusions

RSV bronchiolitis is a common problem for neonates. Complications like apnoea and cardiorespiratory arrest expected in neonatal bronchiolitis. Oxygen support, along with non invasive ventilation may be required. Rarely, mechanical ventilation may be necessary. Remdesevir can be used in severe RSV bronchiolitis to improve the outcome.

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