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Case Series

Paediatrics Section

Respiratory Syncytial Virus-related Lower Respiratory Tract Infections in Neonatal and Post-neonatal Babies: A Series of Four Cases

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ABSTRACT

Respiratory Syncytial Virus (RSV) is a highly contagious seasonal virus that is the leading cause of acute Lower Respiratory Tract Infections (LRTI) in the paediatric age group and is one of the leading causes of death in children under five in developing countries. There is evidence that severe RSV infection and hospitalisation in early life increase the risk of recurrent wheezing, childhood asthma, and allergic sensitisation. Even though RSV being a major global health concern, very few papers concentrate on the neonatal period in India. The present case series presents four cases (three females and one male baby) highlighting the impact of RSV in neonatal and post-neonatal infants in India. The cases highlight the diversity of presentation; one infant required prolonged High-flow Nasal Cannula (HFNC) support, while two needed just symptomatic care. The importance of Polymerase Chain Reaction (PCR) in resource-constrained situations is highlighted as diagnostic issues are examined. Treatment focuses on supportive care; oxygen and respiratory support are provided in more severe cases. The present study emphasises the need for early detection and preventative measures, such as using novel treatments like nirsevimab. The present case series advocates for focused therapies and additional research in the Indian paediatric environment, adding insightful perspectives to the expanding body of knowledge on RSV.

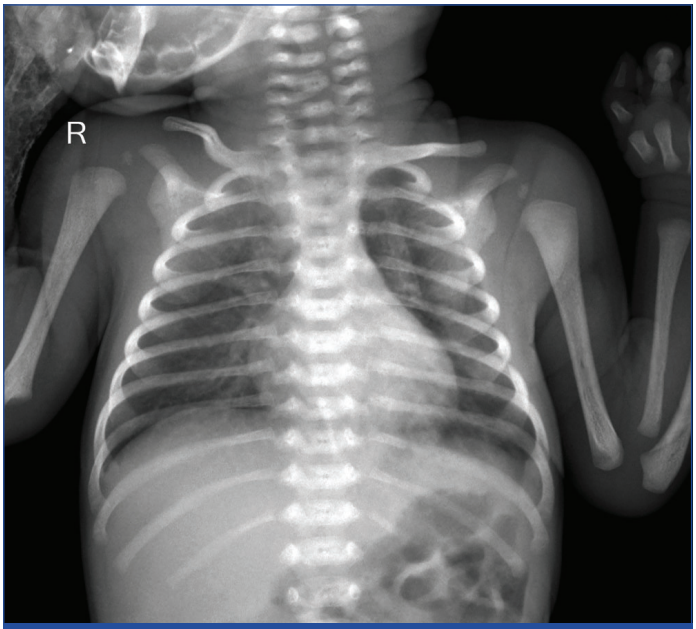
Keywords: High flow nasal cannula, Neonatal intensive care unit, Newborn, Pneumonia

INTRODUCTION

The Respiratory Syncytial Virus (RSV) is the most common viral pathogen identified in children with acute LRTI [1]. In 2020, it was estimated that the disease burden associated with RSV among children under five years in low and lower-middle-income countries was 20.8 million cases, 1.8 million hospital admissions, and 40,000 deaths [2]. Despite the significant burden, severity, and complications associated with RSV infections, there is a lack of reports in the immediate post-neonatal period in India. Here, four cases of RSV infection among infants in their neonatal and immediate post-neonatal period have been reported.

Case 1

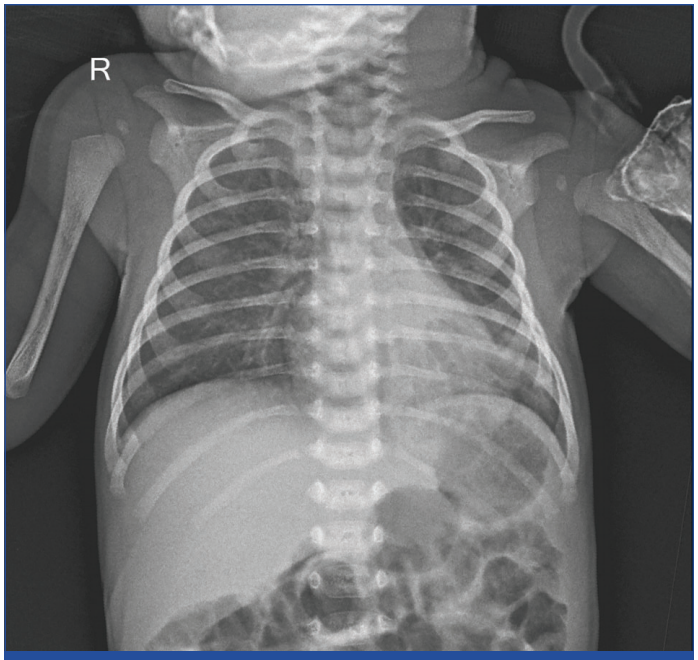
A 19-day-old female neonate with no significant antenatal history and a history of Neonatal Intensive Care Unit (NICU) admission due to low birth weight (birth weight of 1900 g) was admitted to the NICU with a history of fever, cough, and a runny nose for the past six days, and rapid breathing for the past one day. There was a history of similar complaints in an elder sibling. The baby had a room air Peripheral Saturation of Oxygen (SPO_2) of 88% and Downe's score of 5; hence, O_2 by prongs was started, but as the child's condition deteriorated on the third day of admission, respiratory support was escalated to High-flow Nasal Canula (HFNC) with a maximum Fraction of inspired oxygen (Fio_2) of 55%. Considering pneumonia, intravenous (i.v.) antibiotics were started. The chest X-ray taken on the first day of admission showed bilateral perihilar infiltrates [Table/Fig-1]. The X-ray on the third day of admission revealed a worsening picture with bilateral confluent reticulonodular opacities [Table/Fig-2]. The sepsis screen was negative, and considering the clinicoradiological features of viral aetiology, a throat swab Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) was done using the RealStar® RSV RT-PCR Kit 3.0, which showed RSV type B positivity. Hence, i.v. antibiotics were stopped. The baby required eight days of respiratory support with HFNC, along with supportive management. After ten days, the baby was discharged with a good outcome and was doing well on weekly follow-up for a month.



[Table/Fig-1]: Chest X-ray showing bilateral perihilar infiltrates on day one.

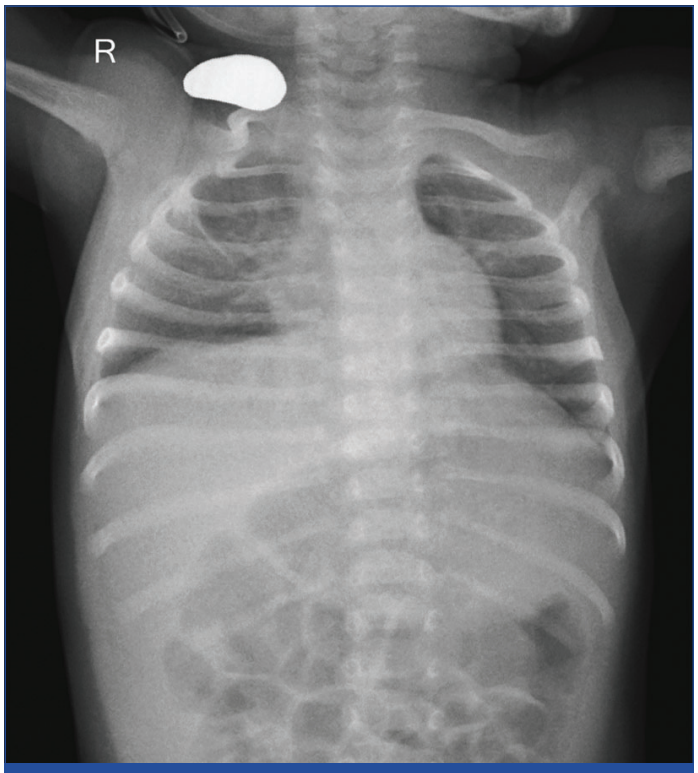
Case 2

A 21-day-old female baby, born as a late preterm at 2.3 kg with no significant perinatal history, was brought in with complaints of a runny nose for the previous week and a cough for two days, which was associated with noisy and hurried breathing. The baby also had a fever for one day just before admission. The baby was admitted with respiratory distress in the form of chest retractions, an SpO_2 of



[Table/Fig-2]: Chest X-ray showing bilateral confluent reticulonodular opacities on day three.

90% at room air, and a Downe's score of 5. The infant was brought to the NICU with a tentative diagnosis of pneumonia and began on blended oxygen at an Fio_2 of 40%. The sepsis screen performed as part of the late-onset sepsis protocol was positive. Thus, the neonate was started on i.v. antibiotics. The clinical examination and X-ray indicated viral aetiology [Table/Fig-3]; therefore, a throat swab for RSV and influenza was found positive for RSV-B, after which the antibiotics were discontinued since the blood culture was sterile. Oxygen was weaned down by fourth day. Throughout the hospitalisation, the baby remained afebrile. She was sent home in good condition after six days and is doing well on weekly follow-ups for a month.



[Table/Fig-3]: Chest X-ray showing bilateral perihilar infiltrates.

Case 3

A 29-day-old male baby, born at term weighing 3.9 kg, with transient tachypnoea of the newborn at birth, was brought in with complaints of breathing difficulty during feeds. The baby had hurried and noisy breathing for 20 days, and chest indrawing was noted for the last four days. At admission, he had chest retractions and tachypnoea, but his SpO_2 was maintained at room air. Bilateral wheezing on auscultation was noted, and the Downe's score was 4. The baby, however, did not have any other features of sepsis, and his cardiac examination was unremarkable, so he was managed symptomatically. The clinical examination indicated viral aetiology; therefore, a throat swab for RSV and influenza was performed and found positive for RSV-B. The distress settled with hypertonic saline nebulisations. Throughout the hospitalisation, the baby remained afebrile and haemodynamically stable. After two days, he was sent home in good condition and was doing well on weekly follow-ups for a month.

Case 4

A three-month-old female baby, born at term weighing 2.7 kg, with no significant perinatal history, was brought in with complaints of a runny nose, noisy breathing for two days, and cough for one day associated with post-tussive vomiting. The baby was admitted with respiratory distress in the form of chest retractions and tachypnoea; however, her SpO_2 was maintained at room air. Bilateral wheezing and crepitations on auscultation were noted, and the Downe's score was 4. The baby, however, did not have any other features of sepsis, and her cardiac examination showed a systolic murmur for which 2D echocardiography was done and revealed a patent foramen ovale. Hence, she was managed symptomatically. The clinical examination indicated viral aetiology; therefore, a throat swab for RSV was performed and found positive for RSV-B. The distress resolved with hypertonic saline nebulisations. Throughout the hospitalisation, the baby remained afebrile and haemodynamically stable. After three days, she was sent home in good condition and did well on weekly follow-ups for a month. The relevant case details are summarised in [Table/Fig-4].

Parameters	Case 1	Case 2	Case 3	Case 4
Age	19 days	21 days	29 days	3 months
Gender	Female	Female	Male	Female
Term/preterm	Term	Preterm	Term	Term
Birth weight (kg)	1.9	2.3	3.9	2.7
Small for gestational age at birth	Yes	No	No	No
Fever	Yes	Yes	No	No
Cough	Yes	Yes	No	Yes
H/o Hurried breathing	Yes	Yes	Yes	Yes
Respiratory distress score at admission (Downe's score)	5	5	4	4
Contact history with possible family members	Yes	No	No	No
Duration of symptoms (days)	1	2	20	2
Respiratory support	HFNC	Oxygen	None	None
Chest X-ray findings	B/l confluent reticulonodular opacities	B/l perihilar infiltrates	-	-
Respiratory failure	No	No	No	No
Duration of hospitalisation (days)	11	8	2	3

[Table/Fig-4]: Characteristic features of RSV positive neonatal and post neonatal babies.

DISCUSSION

The RSV is a member of the *Paramyxoviridae* family and contains a continuous, single-stranded, negative-sense Ribonucleic acid (RNA) genome [3]. Human RSV (hRSV) is the most common cause of bronchiolitis and pneumonia in children under 12 months of age [4]. More severe disease in the youngest infants is thought to be related to decreased levels of maternally derived RSV-specific antibodies and physical, immune, and viral factors. The severity of RSV infection in a young infant with augmented disease induced by

the inactivated RSV vaccine developed in the 1960s first suggested the role of the immune response in the pathogenesis of RSV in infants [5]. The potential importance of the host's immune response to the disease has been supported by the observation that RSV is not generally invasive or cytopathic [5].

The RSV accounts for up to 16% of children hospitalised in India for Acute Respiratory Infections (ARI), with the highest incidence in infants under six months of age [6]. Data from a community-based study in India showed RSV-associated incidence of hospitalisation per 1000 child years was 3.2 among children <5 years of age [6]. In India, almost 2.5 million children die each year, with ARI accounting for one-fifth of these deaths [7]. RSV is mainly spread through aerosols or direct contact with infected surfaces, where the virus can remain virulent for hours. RSV manifests as rhinorrhoea, nasal congestion, cough, sneezing, and occasionally fever and myalgia. After the virus has replicated in the nasopharynx during the first 4 to 5 days of incubation, it can cause LRTI. Three of our four babies had features of upper respiratory tract infection and later developed LRTI signs. Preterm delivery, Chronic Lung Disease (CLD), haemodynamically significant Congenital Heart Disease (CHD), age less than three months, neuromuscular abnormalities, and immunodeficiency are risk factors for severe illness and fatality in RSV infection [8]. In support of this, two of cases, who were preterm and low birth weight, had severe illness. LRTI may develop in upto 40% of infected neonates with features of fast breathing, wheezing, persistent coughing, and difficulty feeding, which was similar to all four cases. Bronchiolitis, the most common LRTI caused by RSV, is characterised by hyperinflation, atelectasis, and wheezing in young infants. In severe cases, it may also manifest as viral pneumonia, hypoxia, lethargy, apnoea, and acute respiratory failure [9]. Wheeze was the predominant finding in three of present cases. Only one baby developed severe illness, needing HFNC support.

Clinical suspicion of RSV-induced LRTI, particularly bronchiolitis, relies on clinical and epidemiological features in infants and young children. Laboratory confirmation and imaging studies are essential to differentiate RSV from other disorders. Specific testing for RSV can be done by rapid antigen testing, PCR-based testing, and viral culture. Although nasal wash yields the best results, a nasopharyngeal swab is commonly used and considered adequate [10,11]. Although viral culture is the standard for definitive diagnosis, it can take up to two weeks. PCR-based testing is increasingly preferred due to its rapid availability of results, ease of testing, and a higher sensitivity rate than rapid antigen testing. PCR-based tests carry the disadvantages of being expensive and requiring specialised equipment to process the sample. Rapid Antigen Detection Tests (RADT) can be an alternative to PCR-based tests when PCR is not feasible. Although RADTs are quick and inexpensive, they are less sensitive and carry a higher false-negative rate [12]. In present cases, authors used a PCR-based test to identify RSV RNA by analysing nasopharyngeal swab samples. Diagnosis of RSV in two of present cases helped in the discontinuation of i,v. antibiotics.

Treating LRTI caused by RSV is primarily supportive, including frequent monitoring and maintaining fluid balance and providing respiratory support as and when needed [13]. Treatment in neonates is extrapolated from the management of infants. In children, not all cases are admitted to the hospital, and only those with severe illness are admitted; however, in neonates, the scenario is different; all babies would need admission for a workup of neonatal sepsis [13].

In non severe cases, maintaining hydration and relieving nasal obstruction are the mainstays of treatment. Two of babies received similar care. However, in severe cases, oxygen and respiratory support are provided based on the child's clinical status to maintain a target SpO_2 of 92% in neonates [14]. Two of present cases needed oxygen support, out of which one had a severe illness requiring HFNC. Hypertonic saline, bronchodilators, and glucocorticoids are not routinely recommended [13,14]. Ribavirin is an Food and Drug Administration (FDA)-approved nucleoside analogue, but it is not recommended for neonates or infants [13,15].

Nirsevimab is a monoclonal antibody recommended for prophylaxis at the beginning of an RSV season, which protects for around five months [16]. It was approved by the United States FDA in 2023 and has been recommended as a preferred choice over palivizumab [17]. It has been intended to be used by the Centre for Disease Control (CDC) and the American Academy of Paediatrics in healthy infants under eight months and those with risk factors. A single 50-milligram intramuscular dose is recommended [18]. However, it has yet to be made available in India. Live attenuated vaccines are under development for infants [15].

CONCLUSION(S)

The present case series highlights the diagnosis and management of RSV-related respiratory infections in neonatal and post-neonatal babies in India. Early detection, prevention, and ongoing research are vital to mitigating the impact of RSV on this vulnerable population.

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