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Case Series

Advocacy for neonates: Will respiratory syncytial virus monoclonal antibodies and maternal vaccine be made available in India?

Mohamed Muneer Varikkottil[1], Divya Ajith[1], Femitha Pournami[1], Jyothi Prabhakar[1], Naveen Jain[1]

[1]Department of Neonatology, KIMS Health, Trivandrum, India.

***Corresponding author:**
Femitha Pournami,
Department of Neonatology,
KIMS Health, Trivandrum,
India.

femi_shifas@yahoo.com

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ABSTRACT

Respiratory syncytial virus (RSV)-related morbidity in children has been widely described. Research has led to the availability of palivizumab for decades in high-income countries. Ongoing research underlines the high priority given to this conundrum. Nirsevimab, a long-acting monoclonal antibody, and a maternal vaccine have been developed and approved for RSV. Neither of these are available in India. Improving the survival of extreme preterm neonates in our country should parallel other strategies to protect them from diseases that affect these high-risk neonates. This case series comprises sick RSV-infected infants from our centre over a single season. Of 187 young infants who presented to the Neonatology Department with features of viral lower respiratory infections, 9 (4.8%) required intensive care. All of them were positive for RSV by nasopharyngeal polymerase chain reaction. A total of 25 (13%) required hospitalisation. Preterm infants presented with apnea or severe respiratory distress. All 9 in the intensive care unit required respiratory support, and 8 needed invasive ventilation. The median duration of hospital stay for these infants was 18 (7–37) days. This report is an appeal to stakeholders towards making these evidence-based prophylactic methods available in India. A preventable problem in high-risk neonates could be reduced. Improving neonatal survival and outcomes calls for our country to be at par with high-income countries for RSV prevention. RSV-related morbidity is an endemic conundrum with a high disease burden. We could take prompt action, akin to efforts taken during the COVID-19 pandemic.

Keywords: Respiratory syncytial virus, Nirsevimab, Palivizumab, F Protein maternal vaccine

INTRODUCTION

This case series is representative of a sincere request towards procurement of the recently approved maternal vaccine and monoclonal antibody against respiratory syncytial virus (RSV) in India. The burden of RSV-related morbidity is globally high.[1] Ongoing research to develop prevention methods has led to the approval of two evidence-based strategies that are yet to enter this country.[2,3] We describe here our experience with infected neonates who required intensive care through the season of RSV in 2023. To re-admit neonates who have gone home after several weeks of intensive care only to acquire a severe RSV lower respiratory infection (LRI) is heart-wrenching.

Epidemiological studies describe several million RSV-related lower respiratory infections.[1] In a recent review of 12 studies, including 5969 children, that analysed risk factors for LRI in low-middle income countries (LMIC), authors reported a significantly higher risk of respiratory infections requiring in-hospital care (0.5%–27.7%) in preterm neonates.[4] There were no studies from India included in this report. Other authors, too, highlight that preventive strategies for RSV must be given high priority.[5,6] We audited the de-identified data of affected neonates retrospectively. Therefore, no informed consent was sought.

CASE REPORT

From August 2023, among the 187 young infants who presented to the Neonatology outpatient services or emergency room with features suggestive of viral respiratory illnesses, we admitted nine neonates to the ICU. Sixteen others were admitted to non-ICU rooms for symptomatic treatment since they required monitoring for feeding and posttussive vomiting. The others were managed on an outpatient basis with close follow-up, either physically or by synchronous video teleconsultation. Fifteen infants' families preferred to follow up and receive therapy in hospitals close to their homes.

Polymerase chain reaction (PCR) for respiratory viruses in a nasopharyngeal swab is sent only for those requiring intensive care (unit protocol). This allows for optimised use of antibiotics and reduces the cost of additional testing. In the admitted cohort, all nine tested positive for RSV. Two were extreme preterm with bronchopulmonary dysplasia and 6 were late preterm. Six had predominantly severe cough and chest signs; 5 preterm neonates presented with apnea as well.

All required non-invasive respiratory supports at some point during hospital stay. All of the preterm infants were ventilated, 2 of these needed high-frequency ventilation for up to 3 weeks. Median Interquartile range (IQR) age at presentation and duration of hospital stay was 30 (24–58) days and 18 (7–37) days, respectively. One infant was readmitted for the resurgence of a worrying cough. We had treated 4 with oral ribavirin and inhaled steroids, as there was a very slow response to supportive measures. Fortunately, all survived.

DISCUSSION

We report a rate of 4.8% requirement for intensive care and a 13% hospitalisation rate in infants <2 months of age for viral respiratory illness in 3 months. Indian hospital and community-based reports of RSV infection rates in children range up to 54% and 15%, respectively.[7] Seasonal variations are known, these are, however, spread over several months. Other authors from different regions of India showed an incidence rate of up to 62.5%, with a high disease burden in children under five years.[5] We describe nine neonates who were seriously ill and needed intensive care. Kalane *et al.* has reported 14 neonates who required hospitalisation related to RSV.[8]

RSV infection has been implicated in LRI, neurological complications, and long-term predilection to asthma.[9] Basic science research from 10 states in India has identified genotypes through phylogenetic analyses. In spite of the authors describing the very high burden of RSV disease in the country, we have no methods of prevention available here yet. Palivizumab is a short-acting monoclonal antibody derived from recombinant technology. This has been in use for several decades in high-income countries. The hospitalisation rate decreased significantly in those with comorbidities. Problems identified were low compliance due to the need for monthly injections and prohibitive costs.[10] Gupta *et al.* concluded that infants at high risk of RSV pneumonia would still be at risk of acquiring other more common viral and bacterial infections and deemed the intervention cost-ineffective in India.[11] Times have changed since, and we beg to differ. With the improved survival of extreme preterm neonates and the approval of effective methods of prevention, we would have to re-consider this statement.

Nirsevimab, a recently developed recombinant monoclonal antibody, can be given as a single intramuscular dose for preterm infants at high risk of RSV. Approved in 2023, the three amino acid substitutions in fragment crystallisable (FC) region increase Immunoglobulin G (IgG) affinity for the human Fc receptor, allowing recirculation. This results in a longer half-life and high potency. The safety profile is good, and evidence supports reduced medically attended RSV in term and high-risk preterm infants.[2]

One can understand the scientific logic that supports vaccination during pregnancy for the passive transfer of antibodies to infants who are too young to receive vaccines themselves for diseases like influenza, pertussis, and COVID-19. A vaccine for RSV based on glycoprotein F has been approved for pregnant mothers. Since administration is recommended between 32 and 36 weeks gestation, extreme preterms would miss out.[3] Moreover, with larger households having potential contacts for infection (elder siblings), maternal vaccination would not be wholly preventive.[12]

Hence, the neonatology community might strategize a staged implementation. For high-risk infant groups like preterm and those with chronic cardiorespiratory illnesses, Nirsevimab would be required as a single dose (duration of action of 5 months) given at birth or before the baby's first RSV season. If the baby remains "susceptible" or at high risk, another dose is advisable before the second season he/she is exposed to.[13] It would mean that a schedule of 1 or 2 doses is advised for high-risk infants.

The costs vary based on the strategies used. In some countries, universal prophylaxis is given. Others are based on the severity of the RSV season or in high-risk neonates only. A recent cost-based review concluded that compared to placebo or palivizumab, nirsevimab was consistently less costly and more clinically efficacious (in terms of hospital admissions and in-patient/ICU care). However, the results varied depending immunisation program, parameters used to assess clinical efficacy, and the local price of nirsevimab.[14]

Hence, generalising the findings may not be prudent. Local or regional data of efficacy and costs may be required to

systematically assess cost–effectiveness. If indeed we were to study immunogenicity, efficacy, and clinical protection aspects systematically, the products would have to first be made available in the country. There would be a compelling reason to work towards maternal vaccination for wider protection.

CONCLUSION

RSV poses a risk to neonates, and some require prolonged intensive care support.

It is time we are at par with high-income countries with regard to the availability of advanced medications, along with increasing expertise and improved outcomes in neonatal care. Implementation of evidence-based measures for RSV infection would require cognizance of disease burden and preventive strategies. Programmatic changes and coordination with the pharmaceutical industry are necessary. We appeal that the near future will hold hope for these drugs to be available in India.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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