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Respiratory

Understanding the Under-Recognised Burden and Unmet Needs in Infants and Children with Respiratory Syncytial Virus



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Interview Summary

For this article, an interview was conducted by EMJ in June 2023 with key opinion leader, Lindsay Broadbent, Lecturer (Assistant Professor) in Virology in the Faculty of Health and Medical Sciences at the University of Surrey, Guildford, UK. Broadbent specialises in respiratory virus–host interactions and subsequent innate immune responses, and the role of respiratory viruses in longer-term lung damage and the development of chronic lung disease.

In this interview, Broadbent discussed the global burden of respiratory syncytial virus (RSV), a virus spread by micro-droplets. Broadbent highlighted RSV as a major cause of hospitalisations, particularly in children under the age of 1 year, which can impose a significant burden on health, particularly in infants, and healthcare systems globally. Broadbent provided insights into the leading risk factors of RSV, and emphasised the need for preventative measures to mitigate severe infections. Additionally, Broadbent highlighted the importance of improving the diagnosis and treatment options to address the unmet medical needs related with RSV. They called for increased awareness of RSV, and understanding of why certain infants are more susceptible to severe disease.

INTRODUCTION

Lower respiratory tract infections (LRTI) are a leading cause of hospitalisations, particularly in infants under 1 year of age. Among these infections, RSV is the primary cause,¹ resulting in approximately 3 million RSV-related hospitalisations worldwide each year in children under 5 years.² Broadbent noted that worldwide, RSV infections in infants account for approximately 50–90% of bronchiolitis cases,³ and around 31% of cases present as childhood pneumonia.⁴

Broadbent noted that RSV primarily affects the upper respiratory tract, and is typically self-limiting and mild for the majority of individuals, with recovery occurring within 1 week. However, they identified that infants under 1 year of age, “especially those between 6 weeks and 6 months old,” are at higher risk of developing severe LRTIs.⁵ This susceptibility is due to the loss of initial protection from maternal antibodies following birth, their immature immune systems, and the tendency of mucus buildup and “sloughing of cells that line the airways,” stated Broadbent. These factors can lead to the formation of mucus plugs that may block their tiny airways. Severe RSV infections are associated with signs and symptoms, such as fever, shortness of breath, wheezing, coughing, lethargy, and difficulties in feeding. These symptoms can result in lower blood O₂ saturation.

THE BURDEN OF RESPIRATORY SYNCYTIAL VIRUS IN INFANTS

Broadbent emphasised that while the “rate of RSV infection is similar across the world, and in fact, that almost every child before the age of 2 is infected with RSV,”⁶ the severity of the disease and access to healthcare resources impact the disease outcomes. The estimated global mortality rate attributed to RSV varies between studies. Broadbent highlighted a large 2015 study that estimated approximately 60,000 in-hospital deaths in infants under the age of 5 years worldwide were attributed to RSV.² The total increases to 100,000–150,000 deaths per year if deaths in the community and at home are also considered.² Broadbent noted the majority of these cases occur in lower- and

middle-income countries, where factors such as limited healthcare resources, transportation costs, parental/carer work commitments, and healthcare accessibility could contribute to poorer outcomes.^{1,2} However, they emphasised that RSV is a global problem, and that severe disease can be seen worldwide.

When considering disease severity, the focus is often on hospitalisations. Based on their experience in the UK, Broadbent highlighted the impact of RSV on the healthcare system. Annually, there are around 30,000 RSV-related hospitalisations in children under 5 years,⁷ with an estimated 83 deaths in the UK for children and adolescents <18 years.⁵ Moreover, the burden is also seen in terms of primary care visits, where approximately 450,000 general practitioner visits per year, in children under 5, are attributed to RSV.⁷

While data on hospitalisations globally is relatively accessible, information on general practitioner visits and community-based cases can be more challenging to obtain, particularly in the absence of “sentinel swabbing schemes,” stated Broadbent. This can lead to potential gaps in the data. However, Broadbent emphasised that current preventative efforts primarily focus on hospitalisations. They stressed that prevention of hospitalisation and mortality is crucial, not only for the health of infants, but also for the overall burden on the healthcare system, the economy, and the wellbeing of parents and carers.^{7,8}

Broadbent also acknowledged the potential for misunderstanding or coding disparity in the reporting of RSV infections in hospital settings. RSV is often not tested or, when testing does take place, it is often for the purpose of ruling out bacterial infections (e.g., pneumonia), which can be effectively treated with antibiotics, rather than specifically identifying RSV. Broadbent explained that diagnosing RSV can be challenging, since symptoms overlap with other respiratory viruses and bacterial infections. These include symptoms such as low-grade fever, runny nose, cough, and sore throat. Therefore, timely testing and diagnosis can be used to differentiate RSV from other potential causes. Broadbent identified that testing is also important for wider patient management, as it plays a crucial role in preventing the spread of RSV within hospital settings. They, however, highlighted that testing

does not matter, as the treatment options available for RSV are “incredibly limited.”

Long-Term Consequences of Respiratory Syncytial Virus

In addition, severe RSV disease in infants may have long-term consequences. Broadbent identified that RSV-related LRTIs can be associated with recurrent wheezing.⁹ They also noted that while an association between RSV infection and childhood asthma has been observed, the exact relationship is not yet fully understood.⁹ It remains unclear whether severe RSV infection directly causes asthma, or if there is an underlying common cause that predisposes children to both conditions. Broadbent noted that ongoing research is needed to investigate the long-term effects of RSV, and how early-life infections can influence lung health and overall wellbeing throughout an individual's life. While it is recognised that early-life childhood infections may have long-term consequences throughout our lives, the specific implications and extent of these potential consequences are still being investigated.

RISK FACTORS AND SEASONALITY OF RESPIRATORY SYNCYTIAL VIRUS

Certain risk factors increase an infant's susceptibility to severe RSV infection. Broadbent mentioned that pre-existing conditions, such as chronic heart disease, lung disease, Down syndrome, and cystic fibrosis, as well as premature birth, are associated with a higher risk of severe RSV disease.¹⁰

Additionally, as RSV is considered a seasonal virus with increased activity during the winter months, the time of year a child is born can also play a role.¹⁰ In the UK, Broadbent noted that RSV activity is typically higher from October through to early March. However, they emphasised that “the majority of children hospitalised with RSV do not have any pre-existing risk factors, so are otherwise healthy.” They highlighted the need for further research to understand why certain infants are more susceptible to severe disease, including potential underlying genetic causes, metabolome mechanisms, or other unidentified risk factors.

The seasonality of RSV infections can also significantly impact the healthcare system and healthcare professionals (HCP). Broadbent stated the high number of RSV infections during the winter months can strain healthcare resources and impact other services, including delays to elective procedures for children, and a shortage of hospital beds.

It is also essential to provide parents and caregivers with information regarding RSV symptoms and risk factors to help them recognise when medical attention is needed. Factors such as smoking in the home, attending daycare, and having school-aged siblings can increase the risk of RSV infection.¹¹

TREATMENT AND PREVENTIVE MEASURES TO REDUCE THE BURDEN OF RESPIRATORY SYNCYTIAL VIRUS

Since there are currently no routinely used specific treatments for RSV, HCPs primarily focus on providing supportive care and medical interventions for severe RSV and LRTIs. This includes administering fluids, O₂, and help with feeding,⁷ while closely monitoring the infants' progress. Higher-income countries with better healthcare resources can provide more effective supportive care.²

While treatment options for RSV remain limited, Broadbent highlighted improvements in testing capabilities, with the availability of accurate PCR testing, and mentioned the ongoing development of rapid tests for point-of-care testing.⁸ They also added the importance of identifying biomarkers or anomalies that could serve as indicators for the risk of severe RSV infection. Such advancements would facilitate early detection and prompt medical care.

Furthermore, protecting infants from RSV infection is of the utmost importance. Considering the risk of high rates of RSV in hospitals, Broadbent indicated that implementing infection control measures within healthcare facilities becomes paramount to prevent the spread of RSV and safeguard vulnerable patients, including other children, such as those with complicated conditions, or undergoing life-saving surgeries.

Broadbent also indicated the importance of simple, non-pharmaceutical, preventative measures, such as regular handwashing, covering the mouth and nose when coughing and sneezing, using tissues, and avoiding contact with at-risk populations, especially very young children, when ill. These measures reduce the risk of RSV transmission via micro-droplets.

ADDRESSING THE UNMET MEDICAL NEEDS IN THE TREATMENT AND PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS IN INFANTS AND CHILDREN

Efforts are being made to address the gap and improve access to preventative options, exploring more affordable alternatives.^{12,13} The availability and accessibility of preventative measures, as well as ongoing research for effective prevention and treatment, are essential areas of focus in addressing RSV. Broadbent stressed the importance of raising awareness of RSV, stating that RSV is often under-recognised. Understanding the impact and the severity of RSV is crucial, as it highlights the need for appropriate preventative measures. Broadbent also suggested that HCPs, researchers, public health agencies, policymakers, and stakeholders

should work together to improve education and awareness regarding RSV.

CONCLUSION

Broadbent highlighted that RSV represents one of the most significant unmet medical needs, calling for increased awareness among the general public, as well as the scientific and medical communities. They emphasised the importance of gaining understanding of why certain children are at a higher risk of severe disease, and exploring the long-term consequences of RSV infection, particularly in relation to lung conditions and lung disease.

Furthermore, Broadbent highlighted the need to continue the research and development of effective treatments, vaccines, and preventative measures for RSV. This requires collaboration, adequate funding, and allocation of resources to drive progress in the field. They highlighted the crucial role of HCPs in actively engaging with research and reporting clinical data to better understand the burden of RSV. Broadbent emphasised the importance of a multidisciplinary approach, involving researchers, clinicians, and industry stakeholders, to advance RSV-related efforts.

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