Expert Insights on the Complexities of Respiratory Syncytial Virus Infections in Infants

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Interview Summary

For this article, EMJ conducted an interview with key opinion leader Chryssoula Tzialla, paediatrician and Director of the Paediatrics and Neonatology Unit at Voghera Azienda Socio-Sanitaria Territoriale (ASST), Pavia, Italy. Tzialla specialises in the prevention and treatment of respiratory infections in children, with a particular focus on respiratory syncytial virus (RSV), aiming to improve the lives of children globally. She is a member of the Italian Society of Paediatrics, the Italian Society on Neonatology, and its working group on neonatal infections. During this interview, Tzialla provided her insights into the burden of RSV disease in infants, highlighting the clinical presentations, long-term health consequences, and the importance of implementing preventive measures against RSV infection, including educational campaigns and immunisation programmes.

INTRODUCTION

RSV is the most common cause of acute lower respiratory tract infections (LRTI) in children under 5 years of age. An estimated 33 million RSV-associated LRTI episodes occur annually in this age group.[1] This results in over 3.5 million hospital admissions, and over 100,000 deaths, worldwide in a typical year.[1] By the age of 1 year, 60–70% of children have been infected with RSV.[2] Surveillance data acquired from 15 countries identified that 55% of RSV cases occurred in those under 1 year of age.[3]

Tzialla stated that RSV is therefore considered a leading cause of hospitalisation in infants under 1 year of age.[2] She noted that RSV is the second most frequent cause of infant mortality, after malaria, and is the top cause of mortality among respiratory infections.[4]

Real-World Experience of the Burden of Respiratory Syncytial Virus

As a paediatrician based in Italy, Tzialla shared her real-world perspectives on RSV, extrapolating data from other countries to provide insights into the burden of RSV, and highlighting a significant burden to healthcare systems.

Italian data available from a retrospective analysis of hospitalisations in children under 6 years of age, from a population based in the Tuscany region of Italy, identified that, between 2014–2019, 38.4% of hospitalisation cases were found to be RSV-positive (n=624, out of 1,627 investigations).[5] Of note, most of these RSV cases were in infants that were born at term, with 73% of premature infants being late preterm, and born between 34–37 weeks of gestational age.[5]

Tzialla also highlighted the high economic cost of RSV, which is responsible for 58% of bronchiolitis cases, and the associated economic burden, in a study of hospitalisation costs at a paediatric hospital in Rome, Italy.[6] While the case-fatality ratio of RSV infection is less than 1% in children who receive supportive care in a timely manner, it can be as high as 9% in low- to middle-income countries.[7,8] Importantly, more than 97% of RSV-associated deaths occur in low- and middle-income countries.[1] Tzialla highlighted that this disparity demonstrates the importance of implementing preventative measures, and providing timely supportive care.

RESPIRATORY SYNCYTIAL VIRUS DISEASE SEVERITY AND THE NEED FOR INFANT PROTECTION

Symptoms of RSV infection in infants can vary from mild to severe. RSV infection can result in severe lower respiratory illness, including bronchiolitis, which Tzialla stated is the "most common clinical manifestation associated with severe RSV infection."[9] Bronchiolitis, characterised by inflammation of the small airways, can also be associated with symptoms such as coughing and dyspnoea.[10] In addition to these respiratory symptoms, young infants may also experience other clinical signs, including fever, feeding difficulties, and irritability.[11]

Other potential health consequences of RSV infection include pneumonia, as well as a possible association with recurrent wheezing and the development of asthma later in childhood.[10-13] Indeed, RSV accounts for approximately 60–80% of infant bronchiolitis, and 40% of paediatric pneumonia.[11] The consequences of RSV infection can be severe enough to require hospitalisation and the need for intensive care, including intubation and mechanical ventilation.[10]

A recent study from the USA identified an association between non-severe RSV infections in infancy and long-term morbidity. The findings suggested that the prevention of RSV infection during infancy could potentially reduce the proportion of current asthma cases at age 5 by approximately 15%.[14]

The long-term morbidity associated with RSV can also require ongoing paediatric visits in primary care settings.[12] Tzialla indicated that, although it is difficult to determine the true impact due to the relative paucity of community-based viral testing, healthcare utilisation is estimated to be around 97% of cases resulting in outpatient visits.[11] Compared with influenza, RSV infections are responsible for nearly double the number of primary care consultations, resulting in time- and resource-consuming issues for healthcare professionals, and those caring for their children.[11]

As Tzialla reported, "the impact of hospitalisations is just the tip of the iceberg. We have a lot of other problems correlated to RSV infection."

Risks Associated with Respiratory Syncytial Virus Infection

The key risk factors that may increase infant susceptibility to RSV, as well as the risk of severe RSV disease, include low gestational age, low birth weight, chronic lung disease, congenital heart disease, and/or immunological disease, such as immunosuppressive disease.[10]

Although prematurity is an important risk factor for severe RSV disease, most children with LRTI due to RSV are born full-term, and do not have any underlying disease;[15] approximately 75% of

RSV infections occur in healthy, full-term infants.[5] Tzialla also highlighted that full-term, healthy infants without traditional risk factors accounted for the largest proportion of hospitalisations in Italy.[16]

Despite the lack of an Italian national surveillance system, a significant increase in RSV infections, particularly in neonates and children, is apparent during the winter season. Based on her clinical experience, during the RSV season in Italy (from November–April), Tzialla has observed a significant increase in admissions for bronchiolitis or pneumonia in paediatric and neonatal wards, as well as an incremental increase in outpatient visits to emergency departments and primary care facilities.[16]

Tzialla said, "infants born prematurely, under 3 months of age, or 3–6 months of age, in their first season of RSV, are at the greatest risk of infection."

As such, Tzialla highlighted that the main risk factors for RSV infection are young age and seasonality,[11,15,16] indicating that premature infants and those under 6 months of age are considered at greatest risk of severe RSV-associated events.[1]

RESPIRATORY SYNCYTIAL VIRUS PREVENTION STRATEGIES FOR INFANTS

Tzialla emphasised the importance of safeguarding all infants, irrespective of risk factors, against RSV infection. She advocates for the inclusion of all infants in prevention efforts, as they are all susceptible to RSV infection. While the severity of the disease cannot be entirely predicted in full-term infants and those without underlying disease, preventing RSV infection during infancy can prevent long-term health problems, including hospitalisations and outpatient visits.

RSV infection is transmitted through contact with respiratory secretions from infected individuals, either directly, or via contaminated surfaces.[11] RSV can survive for several hours, particularly at lower temperatures and high humidity, and can remain viable for up to half an hour on hands.[11]

Non-pharmacological Interventions of Respiratory Syncytial Virus and Educational Campaigns

Non-pharmacological interventions, such as hand hygiene, handwashing, and social distancing from people who are already infected with a respiratory virus, even if their RSV status is unknown, are essential for RSV prevention.[11]

Tzialla recommended campaigns and educational efforts to raise the awareness of RSV prevention among parents and caregivers, including information delivered during antenatal classes before the birth of the child. She also provided an example of a campaign conducted by the Italian Society of Neonatology, where paediatricians shared brochures with parents in hospitals and birth centres during the RSV season, so that they were aware of the risks of RSV, such as the risk of siblings bringing RSV infection into the homes of newborns.[17]

Tzialla also recommended innovative approaches, such as social media and video streaming campaigns, engaging social media influencers or people who have an impact in society to play a role in addressing RSV awareness, and confidence in immunisation strategies.

Pharmacological Prevention of Respiratory Syncytial Virus: Opportunities and Challenges

Reducing RSV infections can have several benefits from a public health perspective, including alleviating pressure on hospital beds and intensive care units, which can then be used to care for other health conditions and diseases.[18]

Tzialla indicated that, currently, Italy does not have a national surveillance system for suspected RSV infections or RSV-associated hospitalisations, which would be invaluable in helping to establish prevention strategies.

Pharmacological prevention strategies, including monoclonal antibodies and maternal immunisation strategies aimed at the protection of infants, as well as vaccines for older people, are currently available in some countries, and offer potential avenues for global RSV prevention efforts.[19,20]

Universal immunisation of infants could significantly reduce RSV-LRTI medical events.[21]

Among the presently accessible immunisation strategies, maternal vaccination and monoclonal antibodies both offer direct and rapid protection for neonates. Monoclonal antibodies involve the administration of antibodies to the infant, while maternal immunisation involves passive transplacental transfer of maternal antibodies following the administration of a vaccine to the pregnant mother.[16,22] However, with immunisation through maternal vaccination, premature births may result in infants not receiving sufficient protection, due to a lack of time for the antibodies to be transferred, hence the increased risk of RSV; Tzialla stated that this highlighted the need for additional preventative measures, in accordance with national guidelines.[16]

Tzialla also emphasised the importance of adopting national RSV prevention strategies to reduce the burden of RSV disease. However, she said Italy is still facing challenges in terms of healthcare registration and public awareness of RSV. One challenge in immunisation efforts in general is vaccine hesitancy, which has increased due to the COVID-19 pandemic,[23] underlining that awareness, education, and communication, such as through social media influencers, may be of benefit to increase future immunisation acceptance.

CONCLUSIONS

RSV is a leading cause of hospitalisations among infants under 1 year of age, significantly contributing to the global economic and health burden.[1,2,10] All infants are at risk of RSV infection, including healthy, full-term infants.[15,16]

Tzialla concluded that, given the unpredictability of RSV disease severity, prevention of RSV infections is key. She noted that while non-pharmacological strategies like hand hygiene are important, education campaigns and pharmacological strategies need to be adapted to the seasonal patterns of RSV to help protect the most vulnerable against severe disease. Nevertheless, Tzialla said implementing prevention strategies, in general, has proven challenging, partly due to a possible hesitancy toward immunisation strategies. She emphasised the importance of educating parents and caregivers about the burden and impact of RSV infection on both families and national health systems. Ultimately, she hopes for a future without RSV infections.

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