Maternal vaccination: a promising preventive strategy to protect infants from respiratory syncytial virus

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Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory tract infection (ALRTI) in early childhood.[1,2] In most patients, RSV infection is self-limiting and manifests as an upper respiratory illness.[1] However, in high-risk infants and young children, RSV infection can manifest as bronchiolitis, pneumonia, and acute respiratory failure; it may require hospitalisation or mechanical ventilation and potentially result in death.[1] Risk factors for severe illness in early childhood include prematurity, young age, and underlying conditions (ie, congenital heart disease, chronic lung disease, and neurodevelopmental conditions).[1,3]

Respiratory syncytial virus circulates year-round globally but peaks during the winter months in temperate regions and the rainy season in tropical climates.[4] In Hong Kong, RSV activity peaks from March to August, when relative humidity is elevated and wind speed is low.[5,6] An understanding of RSV seasonality facilitates effective public health planning and resource allocation.

Whereas the implementation of infection control measures during the coronavirus disease 2019 (COVID-19) pandemic effectively flattened the infection curve, the subsequent relaxation of such measures had severe impacts on RSV epidemiology and its seasonal patterns.[7] Studies in multiple countries revealed an off-season RSV epidemic among children aged <5 years after the peak of the COVID-19 pandemic,[8-10] indicating a major shift in seasonality and the need for continuous RSV surveillance.

Although RSV is a well-recognised threat in early childhood,[2] local data concerning RSV epidemiology and disease burden remain scarce due to the lack of systematic collection methods.[5,6] The under-recognition of RSV as a substantial contributor to morbidity and mortality among children might also explain the scarcity of local prevalence data. In Hong Kong, RSV currently is not considered a notifiable communicable disease. Most patients with clinical features of acute respiratory infection are offered laboratory testing, particularly in clinics with access to point-of-care testing facilities. Because respiratory viruses cause nonspecific symptoms, laboratory testing to identify the infectious agent is essential for guided management strategies.[1,11] Both rapid antigen diagnostic tests and nucleic acid assays are common laboratory tests for RSV detection, although nucleic acid assays have higher diagnostic accuracy than rapid antigen diagnostic tests.[12] The development of multiplex nucleic acid assays and rapid antigen diagnostic tests has allowed for the simultaneous detection of various respiratory pathogens[13]; however, the lack of access to subsidised diagnostic tests often limits their clinical utility.

In the absence of sufficient local prevalence data, it is important to prioritise the implementation of territory-wide RSV surveillance and promote the use of laboratory testing for patients with suspected acute respiratory infection. Surveillance data can help understand local RSV epidemiology and disease burden (particularly among infants aged ≤6 months); it can also inform local vaccination policy.

Globally, there were approximately 33.0 million cases of RSV-related ALRTI among children aged <5 years in 2019, including 3.6 million hospitalisations.[2] Notably, there were 101 400 RSV-attributable deaths; of these, 97% occurred in low- and middle-income countries, and 45% occurred in children aged <6 months.[2] In 1999, the estimated annual incidence of RSV-related hospitalisation in Hong Kong was 2.5 cases per 1000 children aged <5 years, with a mortality rate of 0.15% among hospitalised children.[5]

The economic burden of RSV infection is substantial. The estimated global medical cost of RSV

infection in young children was EUR€4.82 billion in 2017; hospitalisation costs constituted 55% of the global RSV economic burden, and high-income countries carried 35% of the burden.[14] In Hong Kong, the estimated annual healthcare expenditure for RSV-related ALRTI was HK$6.67 million.[5]

Multiple studies have shown that severe RSV infection in early childhood is associated with long-term respiratory sequelae (ie, decreased pulmonary function,[15] wheezing,[16,17] and the development of atopic asthma and clinical allergy[18,19]), emphasising the high actual disease burden.

Given the absence of specific treatment for RSV infection, the current approach to managing RSV infection focuses on supportive care.[1,11] Moreover, although monoclonal antibody remains a promising approach for RSV prevention in high-risk paediatric patients,[20] a safe and effective RSV vaccine remains necessary. Considering the naïve immune system and challenges associated with neonatal vaccination, active immunisation of pregnant women during the third trimester is a viable approach to protect neonates from vaccine-preventable diseases.[21]

Previous efforts to develop various types of RSV vaccines have yielded no positive outcomes.[22] Efforts to understand structural differences in the fusion (F) glycoprotein between its pre-F and pro-F conformations have led to the development of an effective RSV vaccine.[22] The RSV pre-F protein (RSVpreF) is the target for vaccine development because it is an immunologically important antigen with high conservation across all known RSV subgroups.[22]

In August 2023, the United States Food and Drug Administration approved the RSVpreF bivalent vaccine as the first and only vaccine for use in pregnant women to protect infants (birth until 6 months of age) from developing RSV-related ALRTI and severe ALRTI. The decision was based on results from the phase III MATISSE study (Maternal Immunization Study for Safety and Efficacy), which showed that the RSVpreF vaccine had efficacies of 81.8% and 69.4% in preventing medically attended severe RSV-related ALRTI among newborns within 3 and 6 months after birth, respectively.[23] No safety signals were detected in maternal participants or their infants up to 24 months of age.[23] Moreover, concurrent administration of RSVpreF with either tetanus, diphtheria, and pertussis or inactivated influenza vaccine was immunogenic and well-tolerated by non-pregnant women and older adults, respectively.[24,25]

In October 2023, the United States Centers for Disease Control and Prevention issued an official recommendation regarding the administration of a single dose of RSVpreF bivalent vaccine to pregnant women at 32 to 36 weeks of gestation for the prevention of RSV-related ALRTI in infants.[26]

Similar to the maternal tetanus, diphtheria, and pertussis vaccination programme, strong government support for including the RSV vaccine in the Vaccination Subsidy Scheme is needed to encourage its uptake. Importantly, RSV vaccination and counselling should be offered by obstetricians during routine prenatal care visits to reduce additional appointments, waiting, and travelling time.[27-29] Strong collaborations between obstetricians and paediatricians allow for effective dissemination of public messaging; obstetricians can counsel expectant mothers about vaccine safety and benefits, while paediatricians can reinforce the messaging to the general public.

Clinicians should be equipped with evidence-based information to effectively advocate for maternal RSV vaccination. Public health agencies and professional bodies should collaborate to develop educational materials for the medical community, such as clinical practice guidelines, consensus recommendations, and continuing medical education materials. Clinical guidelines for simplified immunisation schedules, achieved by combining the administration of two or more vaccines, could address concerns related to vaccine hesitancy.

Government-led public education campaigns should address knowledge gaps concerning the RSV disease burden in the paediatric population to promote vaccine confidence and encourage vaccination uptake. All campaign materials should be developed in multiple languages, made available in various formats, and disseminated through various platforms to maximise the reach of vaccination campaigns.

Additional data are needed to achieve full support for maternal RSV vaccination. Data regarding the duration of protection conferred by maternal vaccination could provide insights into herd immunity and the timing of booster vaccination for children aged ≤2 years. Investigations of whether maternal RSV-specific antibodies are present in the breast milk of RSV-vaccinated mothers could raise the possibility of postnatal RSV vaccination for cases in which the vaccine is not administered during pregnancy.

Author contributions

All authors contributed to the development of the manuscript. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

LC Poon has received speaker fees and consultancy payments from Roche Diagnostics and Ferring Pharmaceuticals. Additionally, she has received in-kind contributions from Roche Diagnostics, Revvity Inc (formerly PerkinElmer Life

and Analytical Sciences), Thermo Fisher Scientific, Ningbo Aucheer Biological Technology Co Ltd, and GE HealthCare. Other authors declare no conflicts of interest.

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