Recognising RSV infection in adults: The role of recently-developed vaccines

Respiratory syncytial virus (RSV) was previously thought largely to cause infection in infants and children. Only recently has there been increasing awareness of its importance as a cause of infection in adults, sometimes with significant consequences.[1] RSV infection was initially overlooked in adults because of lack of knowledge that it could occur in this age group, and because of infrequent testing for it, at least partly due to cost as well as the belief that in any case there was very little one could do on making the diagnosis, in terms of treatment or prevention. However, more recently, significant advances have occurred in the prevention of this infection, which have led to a change in clinicians' perception.[1]

Several studies have documented the incidence and burden of RSV infection in adults and children and also described its impact on patient morbidity and mortality.[2-6] What the data have shown is that: (*i*) estimates of RSV incidence are highly variable across populations and within and between different geographical areas;[2] (*ii*) the disease burden of RSV-associated acute respiratory infection among adults with comorbidity is substantial;[3] (*iii*) the disease burden of RSV in adults aged >60 years in high-income countries is even higher than previously estimated;[4] (*iv*) RSV infection in hospitalised older adults can manifest as a severe, life-threatening lower respiratory tract illness, with high rates of pneumonia, requirements for ventilatory support, and short- and long-term mortality;[5] and (*v*) future studies with well-defined case definitions and surveillance strategies are needed to determine accurate and comparable estimates of RSV incidence in regions where such information is lacking, with more research needed, particularly in older adults, in Africa, Asia, Latin America and the Middle East.[6]

In this issue of *AJTCCM* there is a timely article by Goolam *et al.*[7] describing the clinical features, radiographic changes and outcomes of adult patients with severe respiratory infection due to RSV admitted to two urban medical centres in Cape Town, South Africa (SA). While some of the findings were similar to other studies from high-income countries, some of which are mentioned above, there were also some unique findings. Overall, 18/916 (2%) of adults admitted with severe respiratory infection tested positive for RSV, with a median (range) age of 50 (35 - 75) years, of whom 12 (67%) were female. All the patients had at least one comorbidity, including immune-compromising conditions (described as living with HIV in 11/18 (61%), diabetes mellitus in 3/18 (17%), and active tuberculosis (TB) co-infection in 2/18 (11%)). In addition, metabolic conditions (*n*=8/18; 44%), structural lung disease (*n*=12/18; 66%) and cardiovascular conditions (*n*=3/18; 16%) were noted. Of the chronic lung conditions, post-TB lung disease was documented in 9/18 patients (50%) and polysubstance lung damage (with the use of mandrax and/or cannabis) in 7/18 (39%). The median (range) length of hospital stay was 4.5 (1 - 15) days, with both in-hospital and 3-month mortality rates of 17% (*n*=3/18). The authors concluded that the findings indicate that there may be a need to expand RSV vaccination recommendations in SA to include younger adults, especially those with HIV and post-TB lung disease.

Previous studies from SA confirmed that adult patients with HIV and RSV-related severe acute respiratory infection (SARI) had greater odds of being in the age groups 18 - 44 years and 45 - 64 years (odds ratio (OR) 26.3; 95% confidence interval (CI) 6.2 - 112.1 and OR 11.4; 95% CI 2.6 - 50.0, respectively) compared with those aged >65 years, and of being female (OR 2.7; 95% CI 1.4 - 5.4),[8] compatible with the findings in the present study. The relative risk of hospitalisation with RSV-associated SARI was 12 - 18 times higher in HIV-infected individuals compared with those who were uninfected,[8] similar to the findings in other studies from SA.[9] The importance of post-TB lung disease and/or polysubstance abuse-associated lung disease as a risk for RSV infection in the present study appears to be unique, requiring further investigation.

As indicated by the authors, three vaccines have already been licensed internationally for the prevention of RSV infection in adults.[10] The first of these is a vaccine from GlaxoSmithKline, RSVPreF3 OA (Arexvy), an adjuvanted (AS01E) RSV prefusion F protein-based candidate vaccine shown to have an acceptable safety profile and to prevent RSV-related acute respiratory infection and lower respiratory tract infection (LRTI), including severe LRTI, in adults aged ≥60 years (AReSVi-006 Study Group[11]). The second vaccine is from Pfizer, RSVpreF (Abrysvo), a bivalent RSV prefusion F protein-based vaccine that prevented RSV-associated lower respiratory tract illness and RSV-associated acute respiratory illness in adults >60 years of age without any safety concerns (RENOIR Clinical Trial[12]). This latter vaccine was also studied when administered during the third trimester of pregnancy, and found to be effective against medically attended severe RSV-associated lower respiratory tract infection in infants with no safety concerns (MATISSE Clinical Trial[13]). Lastly, there is the vaccine from Moderna, mRNA-1345 (mResvia), which is an mRNA-based RSV vaccine encoding stabilised prefusion F glycoprotein (Conquer RSV Study Group[14]). A single dose of this vaccine resulted in no significant concerns and led to a reduced incidence of RSV-associated lower respiratory tract infection and RSV-associated acute respiratory disease among adults >60 years of age. The initial dosing recommendation for all these vaccines in Europe was a single injection in adults >60 years of age.[10] In the USA, the initial indications were for adults aged ≥75 years, or those aged 60 - 74 years with an increased risk of RSV infection.[10] Subsequent recommendations saw a progressive decrease in age recommendations in those adults at high risk of RSV. In the case of RSVpreF (Abrysvo), other than being recommended for older adults, a single dose in pregnant women in their third trimester, between 32 and 36 weeks, was an additional recommendation.

Regarding these vaccines, Abrysvo is licensed in SA, but only available in the private sector. Fortunately, based on recent study results and a strong motivation from the National Advisory Group on Immunisation, licensing of Abrysvo for routine use in pregnant women as well is currently being considered in SA.[15]

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