Acute lower respiratory infections in children

In this *South African Journal of Child Health* issue, we publish an article from Nigeria on the association of hypoxaemia with the outcome in children under the age of 5 years admitted with pneumonia.[1] In this study, children with hypoxaemia (pulse oximetry SpO_2 <90%) were 48 times more likely to die, and those who survived were likely to spend almost twice as long in hospital as those who were not hypoxaemic. The overall mortality rate of admitted children with pneumonia was 8.5%, but all the deaths occurred in those who were hypoxaemic on admission (giving a mortality rate of 20% in that group). In a very recent systematic review of risk factors for mortality from acute lower respiratory infections (ALRIs) in <5-year-old children in low- and middle-income countries[2] (95% of all deaths from ALRIs occur in these countries), the major risk factors were the diagnosis of very severe pneumonia using the World Health Organization (WHO) definition, being <2 months of age, and having underlying chronic disease, HIV or severe malnutrition. The usual socioeconomic and environmental factors also contributed, namely young maternal age, low maternal education, second-hand smoke exposure and indoor air pollution.

The most common bacterial causes of pneumonia have typically been *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Staphylococcus aureus*;[3] however, the increasing use of *Haemophilus influenza* type b and pneumococcal vaccines in the Expanded Programme of Immunization in many countries has dramatically reduced the role of the latter two organisms in the pathogenesis of the disease, and has also reduced the importance of bacterial pathogens as a cause of ALRI. In HIV-negative children, the 9-valent pneumococcal vaccine has reduced invasive pneumococcal disease by 83% and ALRIs by 20%.[4]

In a study conducted in South Africa and published this year, viral pathogens were found in 78% of children <5 years of age with ALRIs.[5] As expected, the most common viruses were rhinovirus (37%), respiratory syncytial virus (RSV) (26%), adenovirus (26%) and influenza virus (7%). As an aside, the actual role of rhinovirus and adenovirus in the pathogenesis of ALRI is unclear, as the two viruses are frequently found in healthy controls. The case fatality rate in the cohort of children with ALRIs was 2%, but it is difficult to draw comparisons with the Nigerian study quoted above. HIV-infected children had up to a three-fold greater incidence of ALRIs than HIV-negative children, but this increased risk appears to have declined over the years of the study, from 3.7 in 2009 to 1.8 in 2012, possibly because of the greater use of highly active antiretroviral therapy. The mortality among HIV-positive children was 7% compared with 1% in HIV-negative children.

These figures highlight the urgent need for effective interventions against respiratory syncytial and influenza viruses, not only to reduce mortality but also hospital admissions from ALRIs. RSV infection is the major cause of ALRI globally and of morbidity especially in infants <1 year of age[6] and those with underlying chronic diseases or a history of prematurity. Anecdotally, RSV infections account for the large upsurge in admissions to the paediatric wards at Chris Hani Baragwanath Academic Hospital during the autumn and winter months. Some 80% of children at 2 years of age have been infected with RSV, of whom one-third will have developed an ALRI, usually bronchiolitis. Vaccines have been developed but have yet to be proven efficacious in preventing RSV infections in infants and young children. The reason is that the natural immune response to RSV is complex. After an infection, protection against repeat infection is short-lived and incomplete, so that infants may be reinfected with the same RSV strain within the same year. Reinfections with antigenically similar strains of RSV occur throughout life, despite there being relative antigenic stability.[7] Maternal IgG antibodies against RSV do cross the placenta and are present in the neonate, but levels decline rapidly. The presence of sufficient levels of antibodies in the young infant does help to protect the infant from severe infection, but these do not last. As RSV disease is most severe in infants <12 months of age, any effective vaccine is going to have to ensure that it stimulates adequate antibody levels in this age group, and this is currently a challenge. It appears that we still have a long way to go before we see an effective RSV vaccine available to protect young infants from the most common cause of bronchiolitis and severe lower respiratory infection globally.

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