Measuring Epidemiology and Sero-Correlates of Protection Against Severe Respiratory Syncytial Virus (RSV) Associated Hospitalisation in HIV Exposed and Unexposed South African Children

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Abstract:

Introduction: RSV is a leading cause of respiratory related hospitalisations in children less than five years globally. The majority of the morbidity and mortality of RSV disease occurs in lower and middle income countries. Decades of epidemiological work have demonstrated that the risk for RSV hospitalisation is highly concentrated in the first six months of life, when infants' immune systems are immature and the protective effects of maternally derived antibody are waning. The South African paediatric population is comprised of a significant percentage of HIV exposed uninfected (HEU) infants who reportedly have higher risk for infectious morbidity and mortality.

Methods: This thesis utilized a prospective, inpatient paediatric surveillance program; and a prospective birth cohort to describe RSV hospitalisations, maternally derived immunity and explore for a sero-correlate of protection against RSV LRTI hospitalisation among HIV unexposed and HEU infants.

Results: RSV hospitalisation incidence was 21.4 per 1000 live births among Sowetan infants. A peak of disease occurred in the first month of life and constituted a large percentage (53%) of all-cause LRTI hospitalisation during the RSV epidemic period. The majority of hospitalisations (69%) occurred among infants in their first six months of life. RSV hospitalisation incidence of HIV unexposed and exposed infants did not differ significantly (21 vs 20 per 1000 live births, respectively). Most RSV hospitalisation cases were discharged home, with a low cases fatality risk (0.002). The majority of RSV-associated hospitalisations received antibiotics (69%). Infants without and with HIV exposure acquired maternally derived neutralizing RSV antibody via transplacental transfer (HUU 0.82 vs HEU 0.67, p_{adj} 0.1222). The cord to maternal blood ratio (CMR) of RSV neutralizing antibody was 0.74. The CMR was significantly associated with maternal hypergammaglobulinemia. Cord blood titres demonstrated an inverse relationship between maternally derived neutralising RSV antibody and risk of RSV hospitalisation in infants up to six months of age. While a definitive threshold of protection was not identified, it was observed that for every unit rise in $\log_2$ titre, there was a 43% reduction in odds for hospitalisation

Conclusion: RSV hospitalisation among Sowetan infants represents a significant burden of disease that is highly concentrated within the first six months of life. Maternally derived neutralising RSV antibody is present in infants at the time of birth, albeit at levels lower than what has been described in other parts of the world. Maternally derived neutralising RSV

antibody is associated with protection against disease but a definitive correlate of protection has not yet been identified.