Minimally Invasive Tissue Sampling to Compare the Cause of Death Among HIV Exposed Uninfected and HIV Unexposed Uninfected Children in South Africa

Sana Mahtab1, Richard Chawana1, Vicky L. Baillie1, Nana Bukwwe Thwala1, Fatima Solomon2, Peter Swartz3, Martin Hale3, Sithembiso Velaphi3, Shabir A. Madhi2
1South African Medical Research Council Vaccines and Infectious Diseases Analytics Research Unit, University of the Witwatersrand, Johannesburg, South Africa

Background
• HIV-exposed uninfected children (HEU) are at greater risk of death compared with HIV-unexposed children in the first six months of life.
• We investigated the causes of death (CoD) between HEU and HIV-unexposed children using post-mortem minimally invasive tissue sampling.

Methods
• We enrolled children under 60 months of age from Chris Hani Baragwanath Academic Hospital, Soweto, South Africa.
• Post-mortem sampling included blood, brain, cerebrospinal fluid, liver and lung.
• Tests included tissue histopathology, molecular organism detection and bacterial culture.
• Expert panels used MITS and antemortem clinical data to determine the causal pathway to death.

Results
• Of the 205 children aged less than 6 months of age who were enrolled, 184 were included in this analysis.
• Excluded were 10 children who had a reactive HIV-1 PCR result, and 11 in whom the HIV infection or exposure status was not ascertainable.
• Overall, included in the analysis were 141 neonates (48 [34%] HEU, and 93 [66%] HIV-unexposed) and 43 1-month infants between 28 to 182 days of age (17 [39.5%] HEU and 26 [60.5%] HIV-unexposed).

Neoatal deaths
• HEU neonates were more likely to have been born at ≤32 weeks gestational age (62.5% vs 53.8%) and to have a birth weight ≤1500 grams (62.5% vs 52.7%) compared with HIV-unexposed neonates.
• Prematurity was more common as an underlying CoD in HEU (68.8%) than HIV-unexposed neonates (46.2%).
• Respiratory and cardiovascular disorder were more common in the HEU (6.3%) than HIV-unexposed neonates (2.1%).
• Complication of intrapartum events (17.2% vs 10.4%) and congenital malformations (14.0% vs 8.3%) as underlying causes were more common in HIV-unexposed than HEU neonates.
• Sepsis in the causal pathway of death was more common among HEU than HIV-unexposed neonates (45.8% vs 38.7%).

• Acinetobacter baumannii (22.9% vs 10.8%), Staphylococcus aureus (8.3% vs 5.4%), and Escherichia coli (6.3% vs 2.2%) were the common pathogens for sepsis among HEU vs HIV-unexposed neonates.

Early infants (1-6 months) deaths
• The median age of the early-infant deaths were 2.6 and 2.2 months in the HEU and HIV-unexposed early infants.
• The HIV-unexposed compared with HEU infant deaths were more likely to be malnourished (weight for age Z-scores < -2; 88.9% vs 53.8%).
• For early infants, non-communicable disease was the most common underlying CoD; and more so in the HEU (47.1%) than HIV-unexposed early infants (34.6%), and particularly congenital anomalies (41.2% vs 23.1%).
• Sepsis in the causal pathway of death was more common among HEU than HIV-unexposed early infants (47.1% vs 38.5%).
• HEU compared with HIV unexposed early infants were more likely to have Klebsiella pneumoniae (17.6% vs 3.8%) and RSV (17.6% vs 11.5%) attributed as a cause for community acquired pneumonia.

Conclusion
• HIV-exposed uninfected neonatal deaths were mainly attributable to complications of prematurity.
• Deaths in HEU compared with HUU within 0-6 months from birth, were more likely to include sepsis in the causal pathway.
• Community-acquired pneumonia was more prevalent in the causal pathway to death in HEU infants.

Figure 2: Leading cause of the deaths in neonates by HEU & HIV-unexposed

Figure 3: Global burden of disease by HEU and HIV-unexposed

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CHAMPS

Prematurity
Sepsis
Community Acquired Pneumonia
HIV
HIV-unexposed
Non-communicable disease
Communicable, maternal, perinatal, congenital anomalies
HIV
HIV-unexposed

Deaths in HEU & HIV unexposed

Deaths in HEU & HIV unexposed