

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

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## 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 ante-mortem clinical data to determine the causal pathway to death.

## Results

- Of the 205 children aged less than 6 months of 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 1-6months infants between 28 to 182 days age (17 [39.5%] HEU and 26 [60.5%] HIV-unexposed).

## Neonatal deaths

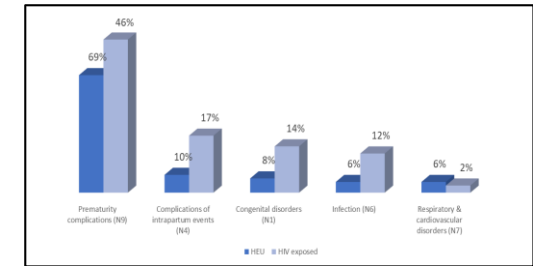
- HEU neonates were more likely to have been born at  $\leq 32$  weeks gestational age (62.5% vs 53.8%) and to have a birth weight  $\leq 1500$  grams (62.5% vs 52.7%) compared with HIV-unexposed neonates.
- Prematurity was more common as an underlying CoD in HEU (68.8%) than HIV unexposed neonates (46.2%).
- 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.

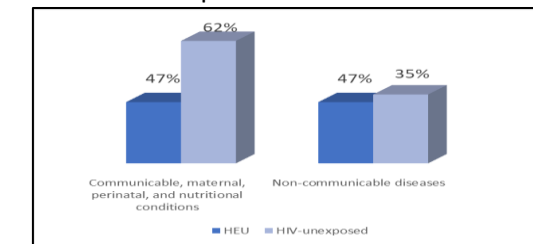
## Early infants (1-6 months) deaths

- The median age of the early-infant deaths were 2.6 and 2.2 months in the HEU and HIV-unexposed early infants, respectively.
- 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.

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



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



## 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.