

HIV exposure as a risk factor for death among neonates with healthcare-associated bloodstream infections in South Africa, 2016-2017

ABSTRACT

Background: Hospitalised neonates (aged 0-28 days) are at high risk of developing bloodstream infections (BSI). Bacterial infections account for 26% of deaths during the neonatal period in low- and middle-income countries. HIV-exposed neonates may have lower specific antibody levels at birth compared to HIV-unexposed neonates, which makes them vulnerable to various infectious agents. We hypothesized that HIV exposure was associated with death among neonates with *Staphylococcus aureus*, carbapenem-resistant Enterobacterales (CRE) or *Candida* BSI.

Methods: A cross-sectional study was conducted at five hospitals participating in GERMS-SA surveillance for culture-confirmed BSIs, 2016-2017. A case was defined as a neonate with isolation of *S. aureus*, CRE or *Candida* from a blood culture specimen. Demographic, clinical and in-hospital outcome was collected by chart review/interview. We defined neonatal exposure to maternal HIV infection as any neonate with an HIV polymerase chain reaction (PCR) test result, assuming that this test would be ordered only if the mother was known to be HIV-seropositive. We used classical and multivariable logistic regression analyses to determine the association between HIV exposure and in-hospital mortality. We adjusted for age, sex, birthweight, gestational age, a central venous catheter (CVC) *in situ*, antimicrobial use and looked for effect modification of HIV exposure on mortality by birth weight in the final adjusted model.

Results: There were 380 cases and 86.8% (330/380) of the cases had a known outcome and HIV status. The percentage of missing information varied across cases and therefore the total for each variable was different. The median age was 11 days (IQR 7-18) and males accounted for 52.3% (195/373). Cases with CRE accounted for 5.2% (20/380), *Candida* 37.4% (142/380) and *S. aureus* cases 57.4% (218/380). The percentage of HIV-exposed neonates was 32.7% (108/330), of these 108 had a known outcome. The overall crude case-fatality ratio (CFR) was 25.4% (84/330). The CFR among HIV-exposed neonates was 26.8% (29/108). HIV-exposed neonates had 14% higher crude odds of death compared to HIV-unexposed neonates (odds ratio [OR] 1.14, 95% CI: 0.68-1.93). After adjustment, the OR for death was 1.19 (95% CI: 0.60-2.37, $p=0.62$). Among babies

with birthweight ≥ 2.5 kg, the adjusted OR for death was 4.01 (95% CI: 0.14-113.86, $p=0.42$) among HIV-exposed versus HIV-unexposed neonates. Among neonates with a low birth weight, the stratum-specific OR for the effect of HIV exposure on mortality was 1.12 (95% CI: 0.55-2.28, $p=0.74$).

Conclusion: HIV-exposed neonates with a BSI had 19% higher adjusted odds of death than HIV-unexposed neonates, though the 95% CI spanned one. Birth weight modified the effect of HIV exposure on mortality and this was stronger among neonates with normal birthweight (≥ 2.5 kg). Our total sample size may not have been sufficiently large. Missing data probably resulted in selection bias. However, we recommend using a prospective cohort study design for the analysis to accurately measure 30-day in hospital mortality from admission date.

Keywords: HIV-exposed, neonate, bloodstream infections, mortality, pathogens, hospital-based surveillance, South Africa