Background

- HIV and ART have been associated with preterm birth (PTB) and other adverse birth outcomes (ABOs).
- The underlying mechanisms may be related to timing of antiretroviral therapy (ART) relative to conception, specific drug exposures, or both.
- Many studies do not differentiate between deliveries that occur spontaneously and those that are medically indicated and/or initiated by a provider.

Objectives

- To assess the effect of HIV and ART on PTB in an ongoing Zambian pregnancy cohort, accounting for known obstetric risk factors.
- To determine whether the effect of HIV and ART on PTB is amplified when analysis is limited to those births that occur spontaneously (i.e., spontaneous labor or membrane rupture prior to delivery).

Methods

The Zambia Preterm Birth Prevention Study (ZAPPS) is an ongoing prospective cohort at the Women and Newborn University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; 2 University of Zambia School of Medicine, Lusaka, Zambia; 3 UNC Global Projects Zambia, Lusaka, Zambia; 4 Seattle Children’s Hospital, Seattle, WA.

- Pregnant women ≥18 years with a viable singleton or twin pregnancy enrolled at ≥20 weeks of gestation (<37 weeks if HIV-infected) confirmed by ultrasound, are followed through pregnancy, delivery, up to 42 days postpartum.
- Participants receive early ultrasonic gestational dating, lab testing, midtrimester cervical length measurement, serial fetal growth monitoring, and phenotyping of each adverse birth outcome.

Timing of ART exposure among HIV+ women was confirmed by testing drug concentrations at first antenatal care visit with liquid chromatography/mass spectrometry.

Results

- Between August 2015 and September 2017, we enrolled 1,450 pregnant women, of whom 929 have delivered.
- At enrollment, median maternal age was 27 years (IQR: 23,32); median BMI was 24 kg/m² (IQR: 21,27); 24% were nulliparous; 35% had a ≤3 prior PTB; 2.5% had short cervix (<2.5cm); and 23% were HIV+.
- Of 946 infants born to date (17 sets of twins), 153 (16%) were small for gestational age (<10%ile) and 27 (23%) were ≥2 prior miscarriages.
- In the ZAPPS cohort, 1.2% (95% CI: 0.7 – 2.1) of deliveries were spontaneous PTB, 1.5% (95% CI: 1.0 – 2.3) were preterm premature rupture of membranes (PPROM), 5.1% (95% CI: 3.2 – 7.8) were spontaneous preterm labor (sPTL), and 2.3% (95% CI: 1.0 – 2.6) were twin gestations.
- Among the spontaneous preterm births, the primary conditions present at the time of delivery were: HIV (11%), other infection (4%), 5% (of the remaining), and twins (13%).

- Of 129 (14%) preterm births:
  - 70 (54%) were spontaneous
  - 27 (21%) were indicated (i.e., provider-initiated), and
  - 22 (17%) could not be definitively classified.

- Among the preterm births, 9% (11%) of infants were born to mothers who were ART-exposed, and 8% (9%) of infants were born to mothers who were ART-naive. The ART-exposed group had a significantly lower risk of spontaneous PTB (aRR: 0.7, 95% CI: 0.4 – 1.1) and a higher risk of twin gestation (aRR: 2.3, 95% CI: 1.0 – 5.0) compared to the ART-naive group.

- Preconceptional ART was not statistically associated with preterm birth (<37 weeks), asymmetric fetal growth restriction at 32 weeks, small for gestational age, or stillbirth.

Conclusions

- In our African cohort established specifically to study preterm birth in which the predominant ART exposure is TDF/3TC/EFV, women continuing preconceptional ART appear to be at higher risk of PTB than HIV-negative women and those initiating ART during pregnancy.
- The risk of preconceptional ART may be amplified when analyses are limited to the spontaneous PTB phenotype.
- Future studies should account for known obstetrical risks of PTB, phenotype characteristics of PTB, as well as factors associated with HIV and treatment including timing of ART initiation in relation to conception, specific ART regimen, and HIV disease characteristics.