Vaginal Inflammatory Markers Associated with Preterm Birth in Zambian Women with HIV

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BACKGROUND

HIV infection is a known risk factor for adverse pregnancy outcomes, including spontaneous preterm birth (sPTB), yet the maternal biological mechanisms are not well understood.

We performed a targeted proteome analysis of vaginal samples to determine the association between HIV, antiretroviral therapy initiation, and spontaneous preterm birth in pregnant Zambian women.

METHODS

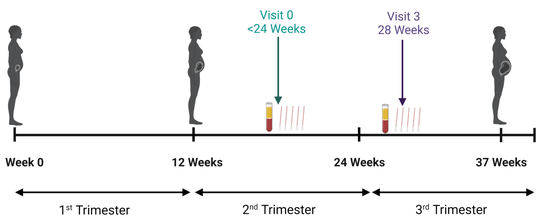

Fig. 1. Visit Timeline of Pregnant Women. Blood and vaginal samples were collected throughout pregnancy and at time of delivery. Pregnant women were seen at The University Teaching Hospital in Lusaka, Zambia.

Sample Collection and Processing:

- Vaginal swabs were collected at an initial enrollment screening between 10-21 weeks gestation (V0), and at the 3rd visit (V3) at weeks 28-29 of gestational age.
- Fluid was eluted and tested by ELISA or multiparameter Luminex analysis for 11 different soluble immune markers.
- Immune mediators included pro- and anti-inflammatory cytokines, anti-viral cytokines, beta defensins, and markers of microbial translocation.

STUDY SAMPLE COMPOSITION

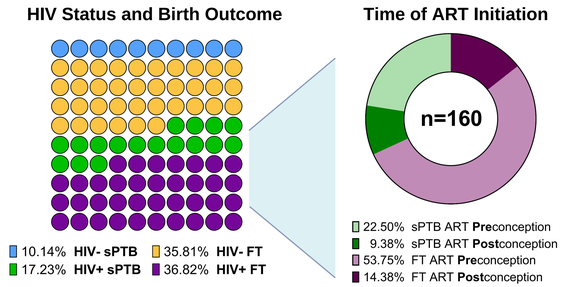

Fig. 2. Case-Cohort. The case-cohort sample consisted of n=136 women without HIV and n=160 women with HIV. The cohort size was selected to include all cases of spontaneous preterm birth (sPTB) and about twice as many women with full term (FT) birth**.** A small number of participants (n=7 HIV+, n=10 HIV-) who had of provider-initiated preterm birth were grouped into the FT group**.** The left graph shows the percentage of pregnant women with sPTB or FT outcome by HIV status as percent of the total cohort size. The right diagram indicates the percentage of women with HIV who initiated ART prior to or post-conception in relation to birth outcome.

RESULTS

Biomarker Concentrations in Vaginal Swabs of Pregnant Women By HIV Status and Birth Outcome

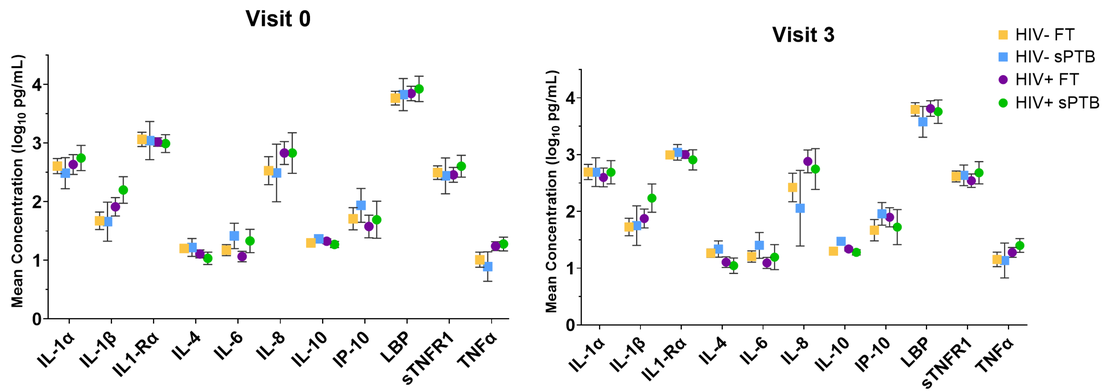

Fig. 3: Biomarker Concentrations in Vaginal Swabs by HIV Status and Birth Outcome. Shown are the mean concentrations of each biomarker with the 95% confidence interval at Visit 0 and Visit 3. HIV status and birth outcome are represented by colored symbols as indicated in the legend.

Timing of ART Initiation - Impact on sPTB

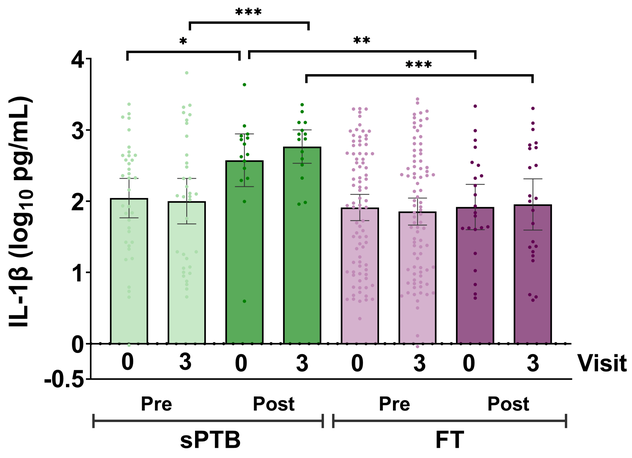

Fig. 4. Impact of ART Initiation Timing on IL-1β Concentrations and Birth Outcome in HIV Positive Women. Vaginal IL-1β concentrations are graphed for each visit in women with sPTB or FT grouped by the time of ART initiation (pre- or post-conception). Each data point within a bar represents an individual woman with the bar height corresponding to the mean of the group; the lines indicate the 95% CI. Group differences were determined by unpaired t tests with Welch's correction using a two-tailed p value with a significance threshold of p<0.05.

Multi-omics Approach

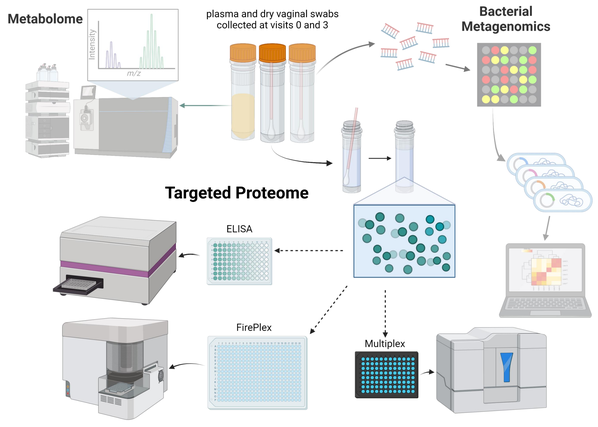

Fig. 5 Multi-omics approach to define risk factors for sPTB. The targeted proteome analysis is part of a larger study that also analyzes the plasma metabolome and metagenomics of the vaginal microbiota.

SUMMARY

HIV and Pregnancy

- Pregnant women with HIV exhibit a more inflammatory vaginal milieu throughout pregnancy.
- Compared to women without HIV, women with HIV trended towards higher concentrations of IL-1β, IL-8, and TNF-α independent of birth outcome and visit time.

Inflammation and sPTB

- Independent of HIV status, increased concentrations of IL-6 and IP-10 appeared to be associated with sPTB, confirming findings by prior studies.

Time of ART Initiation and sPTB

- In women with HIV who began ART during pregnancy, increased IL-1β concentrations were associated with sPTB.

NEXT STEPS

The analysis of additional biomarkers is in progress.

A detailed statistical analysis will be completed with data integration of vaginal metagenomics, proteomics, and plasma metabolomics.

ACKNOWLEDGEMENTS

UNC GLOBAL PROJECTS, LLC ZAMBIA

BILL & MELINDA GATES foundation