20 Self-reported HIV risk in Kenyan pregnant and breastfeeding women compared to non-pregnant, non-breastfeeding women seeking HIV pre-exposure prophylaxis

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OBJECTIVES: In 2016, WHO recommended HIV pre-exposure prophylaxis (PrEP) for women who are pregnant or breastfeeding (PBF) and at substantial risk of HIV infection (defined as HIV incidence >3/100 person-years in absence of PrEP). This analysis compared self-reported HIV risk factors at baseline between PBF versus non-PBF women seeking PrEP in Kenya, and explored differences in continuation in PrEP services at 1, 3, and 6 months between these groups.

METHODS: Data were collected on women served by a PrEP rollout project implemented in 10 counties in Kenya, including both public and private sector service delivery sites. All sites received provider training and support for client records and commodities management. Baseline self-reported HIV risk factors and continuation at 1, 3, and 6 months were compared for PBF vs. non-PBF women (control). Continuation in PrEP services was defined as receipt of PrEP refill at that months visit.

RESULTS: Between March 2017 and February 2019, 16,472 women sought PrEP at project-supported sites, including 474 PBF women. PBF and non-PBF women reported similar proportions of inconsistent condom use at baseline. PBF women were less likely to report engagement in transactional sex (33.3% vs. 58.3%, OR 0.36, 95% CI [0.29-0.43]), sex under influence of alcohol/drugs (17.5% vs. 31.9%, OR 0.45, 95% CI [0.36-0.58]), or recurrent use of HIV post-exposure prophylaxis (1.5% vs. 3.3%, OR 0.44, 95% CI [0.21-0.94]), but more likely to report having a known HIV positive partner (27.6% vs. 8.2%, OR 4.26, 95% CI [3.46-5.25]), compared to control. Continuation in PrEP services at 1, 3, and 6 months post-initiation of PrEP was similarly low for PBF and non-PBF women (40.7% vs. 42.6%, 14.3% vs. 13.6%, and 6.1% vs. 4.6%, respectively).

CONCLUSION: This analysis found differences in baseline self-reported HIV risk between PBF and non-PBF women seeking PrEP in Kenya, but similar patterns of PrEP continuation at 1, 3, and 6 months post-initiation of PrEP. Results, while limited by small numbers of pooled pregnant and breastfeeding women (who may differ in HIV risk), contribute data to the limited evidence base on PrEP delivery for PBF women in low resource settings. Findings suggest PBF women, who are known to be at higher risk for HIV acquisition vs. non-PBF women, may be similarly challenging to retain in large-scale PrEP programs. Additional data are needed to understand motivations for discontinuation and strategies for improving continuation and adherence among PBF PrEP users.

LEARNING OBJECTIVES: Describe differences in at least one self-reported measure of HIV risk between women who are pregnant or breastfeeding compared to non-pregnant, non-breastfeeding women seeking HIV pre-exposure prophylaxis in Kenya.

21 The association between cervical cytokines and HIV acquisition in pregnant and postpartum women

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OBJECTIVES: We evaluated relationships between concentrations of cervical cytokines and HIV acquisition in pregnant and postpartum Kenyan women.

METHODS: A nested case-control study was performed utilizing data collected from the Mama Salama Study, a prospective cohort study that enrolled pregnant, HIV-uninfected women in Kenya. Cervical swab collection and HIV testing using nucleic acid amplification testing (NAAT) were performed at 1-3-month intervals through nine months postpartum. Concentrations of 9 cytokines (IFNγ, IL-1β, IL-6, IL-8, IL-10, TNFα, IP-10, MIP-1α, and MIP-1β) were measured from cervical swabs collected at the visit prior to detection of HIV. Cases were defined as women who acquired HIV during follow-up, and had a cervical swab collected within 12 weeks of diagnosis. Controls were matched 3:1 based on age, marital status, partner HIV status, transactional sex, and gestational age or weeks postpartum at cervical swab collection. Cytokine concentrations were measured using electrochemiluminescence immunoassays, and compared between cases and controls using Wilcoxon rank sum tests. Principal component analysis was used to create a summary score for closely correlated cervical cytokines. Associations between this principal component score, the remaining uncorrelated cytokine (IP-10), and HIV acquisition were evaluated using conditional logistic regression analysis.

RESULTS: This analysis included 14 cases and 42 matched controls. Acquisition of HIV was associated only with increased concentrations of IP-10 (p=0.03). Eight cytokines (IFNγ, IL-1β, IL-6, IL-8, IL-10, TNFα, MIP-1α and MIP-1β were found to be highly correlated by principal component analysis (eigenvalue 6.29, explaining 70% of variability). Conditional logistic regression analysis demonstrated no association between the principal component and HIV acquisition (OR=1.75, 95% CI 0.47, 1.93; p=0.893), but did show an association between increased concentrations of the uncorrelated cytokine, IP-10, and HIV acquisition (OR=1.74, 95% CI 1.04, 2.93; p=0.034). This association persisted in multivariable regression adjusting for bacterial vaginosis, vaginal washing, vulvovaginal candidiasis, trichomoniasis, and condomless sex.

CONCLUSION: HIV acquisition was associated with increased concentrations of the pro-inflammatory cytokine IP-10 in pregnant and postpartum women. Further studies are needed to determine how IP-10 may influence HIV pathogenesis.

LEARNING OBJECTIVES: Learners will be able to identify cervical cytokines associated with HIV acquisition in pregnant and postpartum women.

22 Combination antiretroviral therapy and hypertensive disorders of pregnancy at grady memorial hospital

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OBJECTIVES: Our objectives were 1) to compare the incidence of hypertensive disorders of pregnancy (HDP) among pregnant women living with HIV (WLHIV) on combination antiretroviral therapy (cART) to HIV-negative patients, and 2) to discern whether type of cART regimen or timing of cART initiation alters the risk for the development of HDP.

METHODS: We conducted a retrospective cohort study using two pregnancy cohorts at Grady Memorial Hospital (GMH): all pregnant women with deliveries from July 1, 2016 to June 30, 2018 and all deliveries by pregnant WLHIV at GMH from January 1, 2011 to June 30, 2018. The primary outcome was any HDP, including gestational hypertension (gHTN) and preeclampsia; both gHTN and preeclampsia were also examined independently. The primary exposure variables were HIV status, cART regimen [Integrase Strand Transfer Inhibitor (INSTI)-containing, Protease Inhibitor (PI)-containing (no INSTI), or non-nucleoside reverse transcriptase inhibitor (NNRTI)-containing (no INSTI or PI)], and timing of cART initiation (before or during pregnancy). We generated adjusted odds ratios (ORadj) using multivariable general estimated equation models to evaluate the association of the exposures with HDP.

RESULTS: Among 85 deliveries by 80 WLHIV and 3,556 deliveries by 3,465 women without HIV, pregnant WLHIV had no significant differences in odds of any HDP, gestational hypertension, or preeclampsia compared to HIV-negative women. Among 327 deliveries by 265 pregnant WLHIV, taking INSTI-containing regimens increased the odds of having any HDP (ORadj 4.03, 95% CI 1.98-8.19) and gHTN (ORadj 4.02, 95% CI 1.70-9.53) compared to PI-containing regimens. Timing of cART initiation was not associated with HDP.

CONCLUSION: INSTI-containing regimens were associated with increased odds of developing HDP, and specifically gHTN, compared to PI-containing regimens. Although cART initiation timing was not significantly associated with occurrence of HDP, larger studies are needed to confirm these findings.

LEARNING OBJECTIVES: Identify whether HIV seropositivity, cART regimen, or timing of cART initiation is associated with increased risk of HDP in a cohort of women at Grady Memorial Hospital.

23 Characterizing condomless sex among new contraceptive implant users who are living with or at risk for HIV in Kenya

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OBJECTIVES: Since condoms are the only method that prevents both pregnancy and HIV/STI transmission, dual method use of condoms and long-acting reversible contraceptive methods would ideally be used in high HIV prevalence settings. Therefore, our objective was to assess whether self-reported condomless sex differs between HIV-positive and HIV-negative women who recently initiated a contraceptive implant in a high HIV prevalence setting in Kenya.

METHODS: We used data from an ongoing, prospective pharmacokinetic study of HIV-positive and HIV-negative women ages 18-45 in Kisumu, Kenya, who recently initiated a levonorgestrel or etonogestrel implant. HIV-positive women were using efavirenz- or dolutegravir-based antiretroviral therapy (ART) and were virally suppressed at enrollment. At each study visit, women were asked how often they used a male or female condom during sex since the last visit. We used Poisson regression with generalized estimating equations to assess if risk of reporting condomless sex in the 12-week period following implant initiation differed by women's HIV status. In separate models, we tested for differences in trends in reported condomless sex over time using an interaction term for HIV status and study week. Multivariable models adjusted for condomless sex reported at baseline and number of prior pregnancies.

RESULTS: At the time of analysis, 91 HIV-positive and 49 HIV-negative women were enrolled and had reached week 12 of the study. Recent condomless sex was reported by 13% of HIV-positive women and 45% of HIV-negative women at baseline and 42% of HIV-positive women and 94% of HIV-negative women at week 12. Over the first 12 weeks of implant use, the risk of reporting condomless sex was 45% lower among HIV-positive women than HIV-negative women in the adjusted model (RR: 0.55, 95% CI: 0.45, 0.68). We found no evidence that changes in condomless sex reported over time differed between HIV groups (interaction p=0.47).

CONCLUSION: Report of condomless sex increased after implant insertion in both groups. However, in the first 12 weeks of implant use, HIV-positive women were significantly less likely to report condomless sex than HIV-negative women. This may be partly explained by counseling received by HIV-positive women about condom use for dual pregnancy prevention given potential drug interactions between implants and some ART.

LEARNING OBJECTIVES: Learners will be able to describe dual method use by HIV-positive and HIV-negative women newly initiating contraceptive implants in Kenya.

24 Hematopoietic type I interferon signaling controls Zika virus viremia after intravaginal exposure

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OBJECTIVES: We use a mouse model of sexually-transmitted Zika virus (ZIKV) to investigate the mechanisms of systemic and uterine spread after intravaginal exposure to ZIKV.

METHODS: Mice were treated with Depo-provera to synchronize their estrous cycles. Mice were infected intravaginally with Cambodian ZIKV by pipetting 10ul of the virus into the vagina. ZIKV infection was monitored by collecting vaginal washes, blood, and tissues for histology. ZIKV infection was detected by using ZIKV-immune rat serum to stain tissues, and RT-qPCR was used to quantify ZIKV in the blood and vaginal washes. Mice lacking the innate antiviral type I interferon signaling (IFN) are highly susceptible to ZIKV infection. Previous studies have shown that mice lacking different components of the IFN pathway including the anti-viral receptors (toll-like receptor 7 [TLR7] and mitochondrial antiviral signaling protein [MAVS]), the transcription factors upstream of IFN (Interferon regulatory factor 3 [IRF3] and IRF7), and the IFN receptor (IFNAR) were infected. Bone marrow chimeras lacking IFNAR in the stroma or hematopoetic compartment were also infected.

RESULTS: ZIKV infects vaginal epithelial cells in all mice tested, including those with intact IFN signaling which are highly resistant to the virus. It spreads to vaginal submucosal cells in mice lacking IFNAR in the hematopoetic compartment. This spread to the submucosal cells in the vagina correlates with viremia and infection of the uterine submucosa.

CONCLUSION: While ZIKV is primarily a mosquito-borne virus, it can also be transmitted by sexual exposure. We investigate the mechanisms by which interferon signaling restricts ZIKV infection after vaginal exposure. We show that interferon responsiveness of the hematopoietic compartment is essential for blocking ZIKV spread to the vaginal submucosa, uterine submucosa, and blood. These studies provide insight into how sexual exposure to ZIKV leads to systemic infection.

LEARNING OBJECTIVES: Learners will be able to identify the role of interferon signaling in blocking systemic ZIKV spread after vaginal exposure.