Maternal HIV is associated with lower risk of preeclampsia among Zambian women

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BACKGROUND

- Preeclampsia is an important cause of maternal and fetal morbidity and may be caused by an abnormal maternal immune response to the fetal allograft.
- The immunodepressive effects of HIV have been hypothesized to lower the risk of preeclampsia.
- We examined the association between HIV infection and preeclampsia in a well-characterized urban population of pregnant women in Zambia.

METHODS

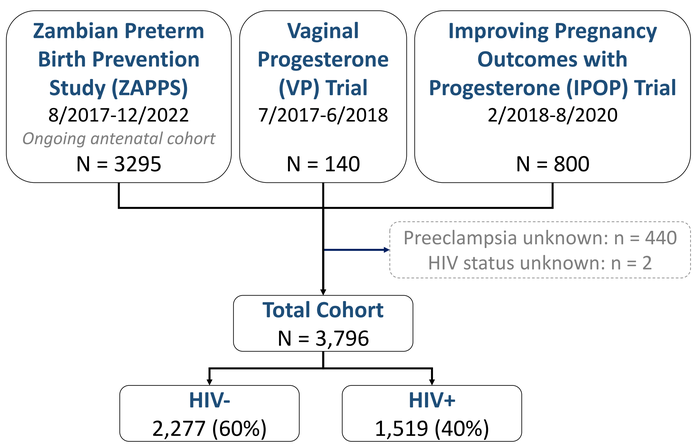
- We combined three contemporaneous studies conducted at two facilities in Lusaka between 2015-2022: the IPOP trial, VP trial, and ZAPPS cohort.
  - Each study drew from the same population and shared most protocol elements, including antenatal assessments, visit timing, and a standardized procedure for phenotyping adverse birth outcomes.
- Using marginal probabilities from logistic regression, we estimated the crude and adjusted risk of preeclampsia (primary outcome) and severe preeclampsia (secondary outcome) associated with HIV infection.

Definitions:

Preeclampsia:
- New-onset (≥20wks) hypertension (≥140 systolic or ≥90 diastolic) with concurrent proteinuria (≥1+)
- Severe preeclampsia diagnosis

Severe Preeclampsia:
- New-onset severe-range BP (≥160 systolic or ≥110 diastolic)
- Eclamptic seizure
- Provider-initiated preterm delivery (<37wks) for preeclampsia

Cohort Flowchart



HIV INFECTION IS ASSOCIATED WITH DECREASED RISK OF PREECLAMPSIA AMONG PREGNANT WOMEN IN LUSAKA, ZAMBIA

Association between Preeclampsia and HIV Positive Populations

Exposure	Total N	PEC n (%)	RR (95%CI)	ARR (95%CI)	ARD (95%CI)	Severe PEC n (%)	RR (95%CI)	ARR (95%CI)	ARD (95%CI)
HIV negative	2,277	110(4.8%)	1.00 (Referent)	1.00 (Referent)	0.00 (Referent)	75 (3.3%)	1.00 (Referent)	1.00 (Referent)	0.00 (Referent)
HIV positive	1,519	30 (2.0%)	0.41 (0.27,0.61)	0.37 (0.25,0.59)	-0.03 (-0.04, -0.02)	24 (1.6%)	0.48 (0.31,0.76)	0.45 (0.28,0.72)	-0.02 (-0.03,-0.01)
HIV positive on preconception ART	1,097	22 (2.0%)	0.42 (0.26,0.65)	0.36 (0.23,0.57)	-0.03 (-0.05,-0.02)	17 (1.6%)	0.47 (0.28,0.79)	0.47 (0.24,0.69)	-0.02 (-0.03,-0.01)
HIV positive on postconception ART	385	7 (1.8%)	0.38 (0.18,0.80)	0.37 (0.17,0.80)	-0.03 (-0.05,-0.01)	6 (1.6%)	0.47 (0.21,1.08)	0.53 (0.23,1.22)	-0.02 (-0.03,0.00)
HIV positive with detectable VL	577	13 (2.3%)	0.47 (0.26,0.82)	0.44 (0.25,0.77)	-0.03 (-0.05,-0.02)	10 (1.7%)	0.53 (0.27,1.01)	0.51 (0.26,0.98)	-0.02 (-0.03,-0.01)
HIV positive with undetectable VL	755	15 (2.0%)	0.41 (0.24,0.70)	0.36 (0.21,0.62)	-0.03 (-0.05,-0.02)	12 (1.6%)	0.48 (0.26,0.88)	0.43 (0.23,0.79)	-0.02 (-0.03,-0.01)
HIV positive with CD4>500 cells/mm^3	688	13 (1.9%)	0.41 (0.22,0.79)	0.36 (0.19,0.69)	-0.03 (-0.05,-0.02)	11 (1.6%)	0.42 (0.19,0.91)	0.39 (0.18,0.86)	-0.02 (-0.03,-0.01)
HIV positive with CD4≤500 cells/mm^3	500	10 (2.0%)	0.39 (0.22,0.69)	0.35 (0.20,0.62)	-0.03 (-0.05,-0.02)	7 (1.4%)	0.49 (0.26,0.91)	0.42 (0.22,0.79)	-0.02 (-0.03,-0.01)

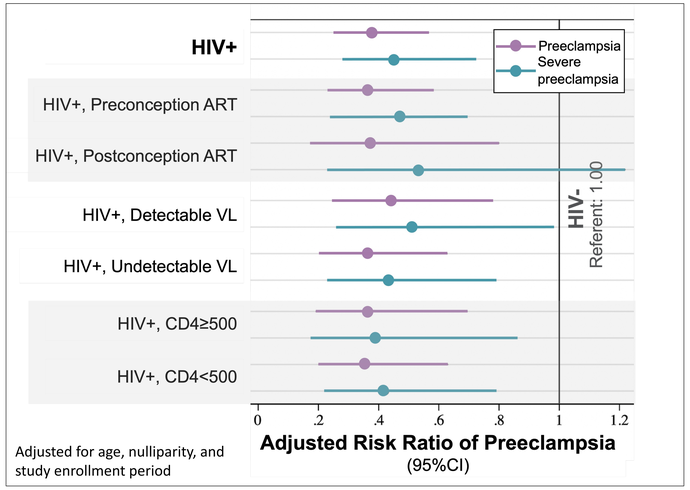
Crude and adjusted risk calculated using marginal probabilities from logistic regression analyses
ARR and ARD adjusted for maternal age, nulliparity, time period at enrollment
PEC: preeclampsia; RR: risk ratio; ARR: adjusted risk ratio; ARD: adjusted risk difference; CI: confidence interval

Baseline Characteristics and Preeclampsia Risk

Maternal Characteristic	Total N	Total PEC Risk, % (n)	HIV- N	HIV- PEC Risk, % (n)	HIV+ N	HIV+ PEC Risk, % (n)
	3,796	3% (140)	2,277	5% (110)	1,519	2% (30)
Age ≥35 years	15% (559)	5% (28)	12% (268)	7% (19)	19% (291)	3% (9)
BMI ≥30 (kg/m2)	18% (687)	6% (39)	19% (430)	7% (29)	17% (257)	4% (10)
Hypertension	5% (190)	7% (14)	6% (133)	10% (13)	4% (57)	2% (1)
Nulliparous	26% (995)	4% (43)	32% (730)	5% (35)	17% (265)	3% (8)
Twin gestation	2% (58)	10% (6)	2% (43)	12% (5)	1% (15)	7% (1)
Education ≥12 yrs	46% (1,751)	5% (79)	54% (1,234)	5% (66)	34% (517)	3% (13)
Living with partner	81% (3,080)	4% (120)	79% (1,804)	5% (98)	84% (1,276)	2% (22)
Home electricity	91% (3,468)	4% (130)	92% (2,090)	5% (102)	91% (1,378)	2% (28)
Piped water	82% (3,099)	4% (120)	87% (1,973)	5% (96)	74% (1,126)	2% (24)
Flush/pour toilet	54% (2,035)	4% (87)	57% (1,305)	5% (70)	48% (730)	2% (17)
Preconception ART					72% (1097)	2% (22)
Detectable VL*					38% (577)	2% (13)
CD4>500cells/mm^3					45% (688)	2% (13)

PEC: preeclampsia; ART: antiretroviral therapy; VL: viral load
*At study enrollment

Adjusted Risk Ratio of Preeclampsia among HIV positive populations



Adjusted for age, nulliparity, and study enrollment period

CONCLUSIONS

- In this large, well-phenotyped pregnancy cohort from Zambia, women living with HIV are less likely to have preeclampsia compared to those without infection.
- Although the association does not appear to be mitigated by maternal disease status, further investigation into whether the relative immune suppression of maternal HIV is protective against preeclampsia is warranted.