

Adverse Pregnancy Outcomes Among HIV-Positive Women in the Era of Universal Antiretroviral Therapy Remain Elevated Compared with HIV-Negative Women in Lesotho

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IAS July 23 2019, Mexico City, Mexico



Background

- Unclear whether adverse pregnancy outcomes in HIV-positive women remain higher than HIV-negative women in the era of antiretroviral treatment (ART).
- Lesotho IMPROVE study* provided an opportunity to evaluate this.
- HIV prevalence is 30.4% in women aged 15–59 years in Lesotho. Lifelong ART for pregnant women started 2013, and ART for all in 2016.
- IMPROVE is a cluster randomized study of facility-based interventions to improve PMTCT/MCH services.
 - HIV-positive and -negative pregnant women attending 1st antenatal visit enrolled 2016–17 from 12 health facilities in Maseru District.
 - Women/infants enrolled in intervention and comparison arms and followed regularly for 12–24 months after delivery.



*“A Multidisciplinary ‘Integrated Management Team to Improve Maternal-Child Outcomes (IMPROVE)’ Intervention to Improve Maternal and Child Outcomes and HIV Service and Antiretroviral Therapy Uptake and Retention”

Methods

- Data collected by trained study nurses through participant interviews and medical record abstraction.
- Pregnancy and HIV data analyzed from enrollment and antenatal visits.
- Delivery and birth information collected prior to discharge if possible.
 - Data could be collected at any visit if missed at the time of delivery.
 - Additional data on certain outcomes (such as pregnancy loss) also obtained by phone.
- Pre-conception ART was defined as date of ART initiation ≥ 42 weeks prior to date of delivery (or ≥ 30 weeks prior to date of a miscarriage).



Data Analysis

- Data from intervention and control groups combined for analysis.
- Analysis of delivery outcomes limited to singleton pregnancies: excludes 17 twin deliveries.
- Descriptive statistics used for demographics and selected health/HIV history and pregnancy outcomes.
- Statistical tests (Fisher's exact, student's t-test) used to assess differences in characteristics and outcomes between HIV-positive and HIV-negative women.
 - Miscarriages excluded from analysis of other outcomes.
- Generalized estimating equations used for multivariable analysis, accounting for correlation between participants by site. The Tukey-Kramer method was used to adjust for multiple comparisons.

Study Population

- 1,004 pregnant women enrolled in the study:
 - 614 HIV-positive women
 - 390 HIV-negative women
- At enrollment, 72% of HIV-positive women already aware of their HIV-positive status, and 28% newly diagnosed as HIV-positive.
- All women received ART; most (89%) received TDF/3TC/EFV during pregnancy with 3% receiving TDF/3TC/NVP, 2% AZT/3TC/EFV, 2% AZT/3TC/EFV, and 4% other or unknown.
- Delivery outcome data available for 906 women:
 - 564 (92% of enrolled) HIV-positive women
 - 342 (88% of enrolled) HIV-negative women



Baseline Characteristics

HIV-negative and HIV-positive pregnant women

Baseline Characteristics	HIV-negative (N=390)	HIV-positive (N=614)	P value
Age at 1 st antenatal visit (ANC)	23, 14-42	28, 16-48	<0.0001
(Years; median, range)			
<19 years	48 (12.3)	24 (3.9)	
19-24 years	198 (50.8)	153 (25.0)	
>24 years	144 (36.9)	434 (71.0)	
Gestational age at 1 st ANC	21, 5-29	20, 5-40	0.018
(Weeks; median, range)			
Education			
No secondary education	89 (22.8%)	221 (36.1%)	<0.0001
Any secondary education	262 (67.2%)	347 (56.7%)	
Beyond high school	39 (10.0%)	44 (7.2%)	
Gravidity			
1 st pregnancy	182 (47.5%)	130 (21.5%)	<0.0001
2-3 pregnancies	177 (46.2%)	365 (60.3%)	
≥ 4 pregnancies	24 (6.3%)	110 (18.2%)	
+ syphilis test (of those tested)	3/295 (1.0%)	16/493 (3.3%)	0.055

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Adverse Pregnancy Outcomes

HIV-negative and HIV-positive pregnant women

Adverse pregnancy outcome	HIV-negative (N=342)	HIV-positive (N=564)	P value
Composite: Any adverse outcome (intrauterine loss, preterm, low birth weight, birth defect)	37/342 (10.8%)	117/564 (20.7%)	<0.001
Intrauterine death	8/342 (2.3%)	44/564 (7.8%)	<0.001
Miscarriage (<28 weeks)	2/342 (0.6%)	21/564 (3.7%)	0.004
Stillbirth (≥28 weeks)	6/338 (1.8%)	23/543 (4.2%)	0.052
Any birth defect	4/337 (1.2%)	6/538 (1.1%)	1.000

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Adverse Pregnancy Outcomes, Liveborn Infants

HIV-negative and HIV-positive pregnant women

Adverse pregnancy outcomes, liveborn infants	HIV-negative (N=332)	HIV-positive (N=520)	P value
Premature (<37 weeks)*	10/330 (3.0%)	25/517 (4.8%)	0.220
Low birth weight (<2500 g)	22/304 (7.2%)	61/477 (12.8%)	0.017
Term low birth weight (≥37 weeks and <2500 g)	13/293 (4.45)	44/453 (9.7%)	0.007

*prematurity live-born infants, excludes stillbirth

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Multivariate Analysis[†]

Adjusted odds of adverse outcome for HIV-positive vs HIV-negative pregnant women

Adverse Pregnancy Outcome	N	Adjusted Odds Ratio (95% CI)	P value
Composite: Any adverse pregnancy outcome	873	2.29 (1.41–3.72)	0.001
Intrauterine loss (miscarriage or stillbirth)	873	2.86 (1.25–6.53)	0.013
Prematurity*	816	1.41 (0.57–3.49)	0.454
Low birth weight	755	2.29 (1.34–3.90)	0.002
Term low birth weight	721	2.99 (1.49–6.03)	0.002

[†]Model adjusted for maternal age, estimated gestational age at enrollment, gravidity, and education

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Multivariate Analysis⁺ in Subset with Syphilis Data

Adjusted odds of adverse pregnancy outcomes remain higher in HIV-positive women after adjustment including syphilis infection

Adverse Pregnancy Outcome	N	Adjusted Odds Ratio (95% CI)	P value
Composite: Any adverse pregnancy outcome	691	2.14 (1.23-3.71)	0.007
Intrauterine loss (miscarriage or stillbirth)	691	2.39 (1.35-4.23)	0.003
Prematurity*	647	1.34 (0.42-4.29)	0.625
Low birth weight	591	2.61 (1.45-4.69)	0.001

⁺Model in subset adjusted for maternal age, estimated gestational age at enrollment, gravidity, education, and syphilis

*prematurity live-born infants, excludes stillbirth

No Significant Difference in Any Adverse Outcomes Between ART Started Preconception vs During Pregnancy

Adverse pregnancy outcome	Pre-conception (N=282)	During pregnancy (N=268)	P value
Miscarriage (<28 weeks)	14/282 (5.0%)	7/268 (2.6%)	0.184
Stillbirth (\geq 28 weeks)	11/268 (4.1%)	11/261 (4.2%)	1.000
Prematurity (<37 weeks)*	12/256 (4.7%)	13/248 (5.2%)	0.839
Low birth weight (<2500 g)*	34/232 (14.7%)	25/233 (10.7%)	0.213
Any birth defect ⁺	2/267 (0.8%)	4/258 (1.6%)	0.443

*Excludes stillbirths

⁺Includes stillbirths

Women without data on timing of initiation (N=34) excluded from this analysis

Conclusions

- Despite improvements in maternal health and decreased perinatal transmission with universal life-long ART in pregnant HIV-positive women, adverse birth outcomes remain 2-3 times higher among HIV-positive women on ART compared to HIV-negative women.
- Similar findings of elevated adverse outcomes in HIV-positive women on ART vs HIV-negative women have been reported from high and low income countries
 - UK/Ireland ↑ risk stillbirth, *Favarato JAIDS 2019*;
 - South Africa ↑ risk composite adverse perinatal outcome, *Santosa AIDS 2019*;
 - Botswana ↑ stillbirth, PTD, LBW in HIV+ vs HIV- women with and without syphilis coinfection, *Shava JAIDS 2019*.

Conclusions

- Data are conflicting regarding an association of adverse pregnancy outcome in HIV-positive women, particularly preterm delivery, with preconception ART compared to starting ART during pregnancy. In our study the timing of ART initiation among HIV-positive women was not associated with any measured adverse outcomes.

Acknowledgments

- USAID
- Population Council
- Lesotho Ministry of Health
- District Health Management Team—Maseru
- Christian Health Association of Lesotho (CHAL)
- Study participants
- IMPROVE study team



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Project SOAR (Cooperative Agreement AID-OAA-A-14-00060) is made possible by the generous support of the American people through the President's Emergency Plan for AIDS Relief (PEPFAR) and United States Agency for International Development (USAID). The contents of this presentation are the sole responsibility of Project SOAR and Population Council and do not necessarily reflect the views of USAID or the United States Government.

Through operations research, Project SOAR will determine how best to address challenges and gaps that remain in the delivery of HIV and AIDS care and support, treatment, and prevention services. Project SOAR is producing a large, multifaceted body of high-quality evidence to guide the planning and implementation of HIV and AIDS programs and policies. Led by the Population Council, Project SOAR is implemented in collaboration with Avenir Health, Elizabeth Glaser Pediatric AIDS Foundation, Johns Hopkins University, Palladium, and The University of North Carolina.

