INTRODUCTION

Maternal and congenital syphilis cause substantial pregnancy and neonatal morbidity worldwide, affecting approximately 1 million pregnancies annually and contributing to preterm birth, low birth weight, and stillbirth, as well as congenital infection and its sequelae. The prevalence of syphilis in people living with HIV is substantially higher than in the general population, with a recent review reporting a worldwide 9.5% co-infection rate of syphilis in those with HIV infection. In addition to increased risk of pregnancy morbidity, HIV co-infection in pregnant women with syphilis presents unique diagnostic and treatment challenges. Previous studies suggest that HIV co-infection may lead to a delayed serologic response to syphilis treatment and increased rates of treatment failure.

Seroreduction of syphilis non-treponemal titers during pregnancy for women with and without HIV co-infection

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Abstract
Objective: To evaluate the effect of HIV co-infection on non-treponemal titers during pregnancy in women with syphilis.
Methods: This is a secondary analysis of pregnant women with syphilis in the prospective, observational Zambian Preterm Birth Prevention Study (ZAPPS). Treponemal (Treponema pallidum particle agglutination) and non-treponemal (rapid plasma reagin; RPR) testing were performed on serum biospecimens, resulting in 47 participants with serologically confirmed syphilis (27 HIV-positive, 20 HIV-negative). The primary outcome, achievement of RPR titer seroreduction during pregnancy, was analyzed by logistic regression. Secondary outcomes included overall titer reduction, seroreduction rate, serologic cure, and adverse pregnancy outcomes.
Results: Seroreduction of RPR titer occurred in 78% (21/27) of women with HIV versus 45% (9/20) of women without (adjusted odds ratio 4.66; 95% confidence interval [CI] 1.14 – 19.08). Overall RPR titer reduction, rate of seroreduction per week, and the proportion achieving serologic cure each trended higher among women with HIV compared with those without HIV. There was a trend toward decreased stillbirth incidence in participants achieving seroreduction (odds ratio 0.15, 95% CI 0.01–1.58).
Conclusion: HIV co-infection in this cohort of Zambian women with syphilis was associated with greater odds of RPR titer seroreduction during pregnancy. Pregnant women with syphilis and HIV may not be at increased risk for a delayed syphilis treatment response compared with women without HIV.

KEYWORDS
HIV, pregnancy, rapid plasma reagin, serology, stillbirth, syphilis, Treponema pallidum, Zambia
Despite the scientific advances of the last half century, syphilis diagnosis and treatment monitoring remain challenging. Serologic diagnosis of syphilis requires both *Treponema*-specific and non-specific testing; however, only non-treponemal serologies are effective at monitoring syphilis treatment efficacy. Serologic cure following adequate treatment is defined as a four-fold decline in non-treponemal titer (equivalent to reduction by two dilutions) or seroreversion to a negative titer. Hence, serial monitoring of non-treponemal titers is required to assess treatment efficacy, diagnose cure, and assess for re-infection.

Following treatment, the rate of titer reduction varies based on a variety of factors, including starting titer, stage of disease, and previous infection. Hence, achievement of cure may take 12–24 months, although many patients with primary, secondary, or early late-stage disease achieve cure by 6 months. In non-pregnant patients, HIV co-infection has been associated with reduced rates of seroreduction; however, supporting data are older, limited, and not inclusive of pregnant patients.

Although normative values and prediction of seroreduction rates remain elusive, guidelines for serologic monitoring and diagnosis of treatment failure outside pregnancy are well established and usually occur at 6-month intervals (3-month intervals for those with HIV). In pregnant patients, however, no optimal interval has been identified, and indications for re-treatment are less clear. Recommendations for timing of repeat titers in pregnancy differ and range from monthly to every 6 months. Even less information is available to guide obstetric providers regarding when to re-treat based on these repeat serologies, particularly for patients with HIV. Given concerns for delayed response time in HIV-co-infected patients, providers are left with the clinical dilemma of interpreting frequent repeat serologies with few data to guide decision making.

In order to better inform this decision making, we sought to evaluate the effect of HIV co-infection on non-treponemal titers during pregnancy. We hypothesized that HIV co-infection in women with syphilis is associated with decreased odds of seroreduction of non-treponemal titers during pregnancy.

## 2 MATERIALS AND METHODS

This is a secondary analysis of the first phase of an ongoing prospective observational cohort, the Zambian Preterm Birth Prevention Study (ZAPPS; ClinicalTrials.gov Identifier: NCT02738892). The University of Zambia Biomedical Research Ethics Committee and the University of North Carolina Institutional Review Board each approved the initial ZAPPS protocol and its subsequent revisions, which included consented permission for secondary laboratory studies. The study also received approval from the Zambian Ministry of Health National Health Research Authority.

The ZAPPS cohort was established at the Women and Newborn Hospital of the University Teaching Hospitals (WNH-UTH), the primary referral hospital in Lusaka, Zambia. In phase 1 of ZAPPS (August 2015 to September 2017), women were recruited from the WNH-UTH and nearby primary health centers and provided individual written informed consent in a language of their choice (English, Bemba, or Nyanja) before undergoing study procedures. Participants received routine obstetrical care, including laboratory tests and ultrasound scans. Blood, urine, and vaginal specimens were collected at scheduled antenatal visits and at delivery and stored in an on-site biorepository.

All ZAPPS participants were screened for syphilis and HIV at enrollment. Syphilis screening was conducted using the rapid point-of-care serologic test SD Bioline Syphilis 3.0 (Standard Diagnostics, Inc.), which is a qualitative test for treponemal-specific immunoglobulin G (IgG), IgA, and IgM antibodies. Owing to resource limitations, non-treponemal titers are not routinely performed in Zambia for either diagnosis or treatment monitoring, which is supported by the World Health Organization for low-income countries. In ZAPPS, participants who tested positive for syphilis were referred for presumptive treatment at WNH-UTH, which includes three weekly intramuscular injections of Penicillin G regardless of suspected stage of disease, prior infection, or HIV status.

Inclusion criteria for this secondary analysis included women with positive syphilis testing at enrollment who had at least one additional serum specimen from later in pregnancy available for testing.

Demographics and clinical characteristics collected during the original study were available for analysis, including maternal age, marital status, education, body mass index (calculated as weight in kilograms divided by the square of height in meters; BMI), parity and obstetric history, and gestational age at enrollment. Available pregnancy outcomes included stillbirth, birth weight, delivery gestational age, basic perinatal phenotype (spontaneous vs. provider-initiated), and pre-eclampsia.

Serum biospecimens used for this secondary analysis were tested at a single university-affiliated laboratory in March 2020. All enrollment serum biospecimens underwent two types of testing: (1) qualitative treponemal-specific testing via *Treponema pallidum* particle agglutination (TPPA) assay and (2) quantitative non-treponemal testing via rapid plasma reagin (RPR) titers. Final serum biospecimens for each participant also underwent RPR testing, which allowed for comparison of RPR titer between the initial (enrollment) and final specimens.

The TPPA results were reported as nonreactive or reactive. RPR results were reported as either nonreactive or reactive with a corresponding titer. Titer results were reported in the standard exponential fashion (1:1, 1:2, 1:4, 1:8, 1:16, etc.) and recorded for analysis in both this raw exponential form and in a corresponding linear form, representing the number of serial dilutions for each titer. For example, a 1:1 titer is reactive at zero dilutions, a 1:2 titer is reactive at one dilution, a 1:4 titer is reactive at two dilutions, and so on. The difference in the number of dilutions between the two samples was then calculated for each participant. Women with reactive TPPA testing but nonreactive initial RPR testing were presumed to represent previously treated infection and excluded from analysis. Women with nonreactive TPPA testing and nonreactive RPR testing were presumed to represent false positive point-of-care results and were also excluded.
Our primary outcome was achievement of seroreduction in RPR titer between the initial and final samples, defined as a reduction in the number of dilutions from the first to the final sample or by seroconversion from any reactive RPR titer to nonreactive titer. Secondary outcomes included achievement of serologic cure (a reduction of two or more dilutions or seroconversion to nonreactive titer), RPR titer reduction (difference in dilutions between samples), rate of RPR seroreduction (dilution reduction per week), and frequency of adverse pregnancy outcomes, including stillbirth, small-for-gestational-age (birth weight less than the 10th centile), spontaneous preterm birth, and pre-eclampsia.

Demographics, clinical characteristics, and outcomes were evaluated for those with and without HIV co-infection with bivariable analysis, using χ² or Fisher exact test for categorical variables and Student t test or Mann–Whitney U test for continuous variables, as appropriate. Logistic regression was used to evaluate our primary outcome by HIV status, generating unadjusted and adjusted models. Our final model was adjusted for initial RPR titer and maternal age. We performed all analyses using STATA SE, Version 15.1 (StataCorp, College Station, TX, USA) and used a value of P less than 0.05 to determine statistical significance.

3 RESULTS

Phase 1 of ZAPPS enrolled 1450 women with an overall seroprevalence of HIV of 24% (350/1447). The prevalence of syphilis at enrollment was 5.2% (70/1342). Of these, seven women did not have serum samples available from two different time points in pregnancy, leaving 63 women meeting our study inclusion criteria (Figure 1). Serologic testing was performed for these 63 women. Of these, 16 (25%) were subsequently excluded for RPR nonreactive results on the enrollment specimen: seven with nonreactive TPPA results (presumed false-positive point-of-care testing) and nine with reactive TPPA results, and of these, 57% (27/47) were HIV positive and 43% (20/47) were HIV negative. There were no cases of RPR reactive results with TPPA nonreactive results.

In the final study population, most women were 20–34 years old, normal weight, multiparous, married, and had less than 10 years of formal education (Table 1). The average gestational age at enrollment was 16 weeks (standard deviation [SD] 4 weeks), and the mean number of weeks between the enrollment sample and the final sample was 19 weeks (SD 6 weeks). The final sample was taken at delivery for approximately half of participants, and for the remainder, the average duration between final sample collection and delivery was 3 weeks. Baseline characteristics were similar for women with and without HIV co-infection, with the exception of maternal age, which was lower in the HIV-negative group (Table 1).

Two-thirds of women with HIV co-infection were on antiretroviral therapy before pregnancy (18/27, 67%), and all but two of these had an undetectable viral load. Among the 11 women with detectable viral loads (11/27, 41%), the RNA copies/ml of plasma ranged from 126 copies/ml to 89 366 copies/ml. No HIV-negative women seroconverted during pregnancy.

RPR testing revealed an average starting titer of 3.8 dilutions (SD 2.8), corresponding to a mean raw titer of 1:110. The primary outcome, seroreduction in RPR titer, was achieved by more than half of participants (30/47, 64%), the majority of whom (20/30, 67%) decreased by one dilution (range 1–6). Most women who did not achieve the primary outcome had no change in titer (15/47, 32%). Two women had an increase in titer of one dilution (2/47, 4%).

The only clinical characteristic that differed between women who achieved a reduction in RPR titer and those who did not was HIV status (Table 2). The mean starting titer was higher among women who achieved seroreduction than those who did not (4.1 versus 3.2), but this association did not achieve statistical significance. Among HIV-infected women, use of preconceptional antiretroviral therapy was not associated with achieving a reduction in titer.

Our primary outcome, reduction of RPR titer, occurred in 78% (21/27) of women in the HIV-positive group versus 45% (9/20) of women in the HIV-negative group (odds ratio [OR] 4.28; 95% confidence interval [CI] 1.21–15.15) (Table 3). After adjusting for initial raw RPR titer and maternal age, this remained statistically significant (adjusted OR 4.66; 95% CI 1.14–19.08) (Table 3). Change in RPR titer is shown for individual participants in Figure 2, grouped by HIV status.

Analysis of our secondary outcomes revealed that the proportion of women achieving serologic cure was higher in women with HIV co-infection (8/27, 30%) than those without (3/20, 15%), but this did not achieve statistical significance (Table 3). The mean RPR titer reduction (1.3 vs. 0.8 dilutions) as well as the mean rate of reduction (0.07 vs. 0.04 dilutions per week) were higher among women with HIV compared with those without, but these comparisons achieved only borderline statistical significance. There were no significant associations between adverse pregnancy outcomes and achievement of RPR seroreduction, although there was a trend toward decreased incidence of stillbirth in those achieving seroreduction (OR 0.15, 95% CI 0.01–1.58) (Table 4). HIV co-infection was associated with higher incidence of small for gestational age, which was statistically significant and remained so after excluding stillbirths (Table 4).

4 DISCUSSION

Our hypothesis that seroreduction of RPR titers during pregnancy is less likely to occur in pregnant women with HIV co-infection than in those without was not supported by our results. Instead, HIV co-infection in this cohort of Zambian women was associated with greater odds of titer seroreduction in pregnancy.

There are several possible explanations for these unexpected results. First, there may be differences between the two groups in stage of disease, although there was no significant difference in starting titer (which has been shown to be associated with disease stage), and results remained significant even when adjusting for
starting titer. Second, adherence to syphilis treatment may have differed between groups. Although the same clinical management was used for all participants, this management included referral for treatment at a partnering clinic, and confirmation of this treatment was not captured in the ZAPPS study data. Additionally, clinicians were not blinded to HIV status during the study, and it is possible that staff or provider bias exists in ensuring treatment follow up for HIV-positive participants, who are often perceived as being at higher risk.

Even taking these possible confounders into consideration, our results should prompt re-evaluation of how HIV co-infection affects syphilis treatment response. Although our results should be interpreted with caution, they suggest that syphilis-infected pregnant women with HIV co-infection may not be at increased risk for delayed treatment response as supported by previous literature.

Our study has several strengths. The original ZAPPS study from which this secondary analysis was performed collected clinical data and biospecimens prospectively. This contemporary cohort of pregnant women with syphilis undergoing serial serologic testing is one of only a few available that contains a substantial number of patients with HIV and is by far the largest. The mean gestational age between initial and final samples (19 weeks) is a longer pregnancy duration than many of the available studies that report non-treponemal titers in pregnancy over time. Additionally, this analysis is strengthened by the use of three separate serologic tests performed for each participant to confirm diagnosis.

Our study also has limitations. These include missing clinical information, such as stage of disease, patient symptoms, confirmation of treatment, and partner treatment status. This cohort is

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**FIGURE 1** Study population. Flowchart of ZAPPS trial participants included in this secondary analysis. Final study population included pregnant women with positive syphilis screening and positive confirmatory testing who had serum specimens available from at least two time points in pregnancy. NR, nonreactive; POC, point-of-care; RPR, rapid plasma reagin; TPPA, *Treponema pallidum* particle agglutination; ZAPPS, Zambian Preterm Birth Prevention Study.

HIV, human immunodeficiency virus; NR, nonreactive; POC, point-of-care; RPR, rapid plasma reagin; TPPA, *Treponema pallidum* particle agglutination; ZAPPS, Zambian Preterm Birth Prevention Study.
a population of women in sub-Saharan Africa where resources are limited and the prevalence of both HIV and syphilis are substantially higher than in developed countries, which may limit the generalizability of these results. Additionally, small sample size limits the analysis of secondary outcomes.

Our results have clinical and research implications moving forward. Currently, ensuring syphilis treatment efficacy for an individual patient is determined by non-treponemal titer response over time. If, as our results suggest, HIV co-infection does not predispose patients to reduced serologic response to treatment, then the

| TABLE 1 | Clinical characteristics of pregnant women with syphilis in ZAPPS, aggregate and by HIV status

| Sub-study cohort (n = 47) | HIV+ women (n = 27) | HIV− women (n = 20) | P valueb |
|-------------------------|---------------------|---------------------|---------|
| Age, years              | 28.8 ± 6.4          | 30.4 ± 6.7          | 26.7 ± 5.3 | 0.044 |
| <20                     | 3 (6%)              | 2 (7%)              | 1 (5%)   |
| 20–34                   | 33 (70%)            | 17 (63%)            | 16 (80%) |
| ≥35                     | 11 (23%)            | 8 (30%)             | 3 (15%)  |
| BMI                     | 23.6 ± 3.9          | 23.6 ± 4.1          | 23.6 ± 3.7 | 0.690 |
| Parity                  | 2 (0–7)             | 2 (0–4)             | 1.5 (0–7) | 0.190 |
| Years of education      | 8.7 ± 2.7           | 8.6 ± 2.6           | 8.7 ± 2.9 | 0.733 |
| Married or living together | 41 (89%)          | 25 (93%)            | 16 (84%) |
| EGA at enrollment, week | 16.4 ± 4.0          | 16.7 ± 4.2          | 16.0 ± 3.7 | 0.445 |
| EGA difference between initial and final specimens, week | 19.2 (6.1) | 19.5 ± 5.8 | 18.9 ± 6.6 | 0.554 |

| HIV parameters | Undetectable VL | Detectable VL | VL, copies/ml |
|----------------|-----------------|---------------|---------------|
|                | 16 (59%)        | 11 (41%)      | 19823 [4135–32101] |

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); EGA, estimated gestational age; HIV+, HIV-positive; HIV−, HIV-negative; RPR, rapid plasma reagin; VL, viral load.

aData are presented as mean ± standard deviation, median (range), median [interquartile range], or as number (percentage).

bComputed using Student t test (age), Pearson χ² test (marital status), or Mann–Whitney U test (all other variables).

| TABLE 2 | Clinical characteristics by primary outcome

| RPR seroreduction (n = 30) | No RPR seroreduction (n = 17) | P valueb |
|---------------------------|-------------------------------|---------|
| Age, years                | 28.8 ± 6.5                    | 28.8 ± 6.3 | 0.991 |
| BMI                       | 24.0 ± 3.9                    | 22.8 ± 3.8 | 0.357 |
| Parity                    | 2 (0–7)                       | 2 (0–4)    | 0.991 |
| Years of education        | 8.6 ± 3.1                     | 8.8 ± 1.8  | 0.932 |
| Married or living together | 27 (90%)                      | 14 (82%)   | 0.795 |
| EGA at enrollment, week   | 16.0 ± 4.0                    | 17.1 ± 4.0 | 0.419 |
| EGA difference between initial and final specimen, week | 20.0 ± 5.4 | 17.8 ± 7.1 | 0.278 |
| Initial RPR titer, no. of dilutions | 4.1 ± 2.7 | 3.2 ± 3.0 | 0.162 |
| HIV-positive status       | 21 (78%)                      | 6 (35%)    | 0.021 |

| HIV parameters among HIV-positive women (n = 27) | |
|-----------------------------------------------|---|
| On preconceptional ART                       | 14/21 (67%) | 4/6 (67%) | 0.877 |
| Undetectable VL                              | 12/21 (57%) | 4/6 (67%) | 0.675 |
| VL, copies/ml                                | 19823 [4135–24011] | 50110 [10854–89366] | 0.346 |

Abbreviations: ART, antiretroviral therapy; BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); EGA, estimated gestational age; RPR, rapid plasma reagin; VL, viral load.

aData are presented as mean ± standard deviation, median (range), median [interquartile range], or as number (percentage). Total n = 47.

bComputed by Student’s t test (age), Pearson χ² test (marital status, HIV status, ART, and undetectable VL), or Mann–Whitney U test (all other variables).
relationship between HIV co-infection and treatment failure should be revisited, especially in the context of an older body of literature and the improvements in HIV care over the last two decades.

Additionally, the stillbirth incidence in our final study population (9%) is notable and is more than twice that of the larger ZAPPS cohort (4%). Our results show a trend toward higher

**TABLE 3** Serologic testing results by HIV status

|                     | HIV+ women with syphilis (n = 27) | HIV− women with syphilis (n = 20) |
|---------------------|-----------------------------------|----------------------------------|
|                     | Raw result | Result in no. of dilutions | Raw result | Result in no. of dilutions | P value |
| **Initial RPR titers** |           |                           |           |                           |         |
| Median              | 1:16       | 4                          | 1:4       | 2                          | 0.671a   |
| Mean ± SD           | 1:165 ± 1:434 | 4.1 ± 3.1                   | 1:37 ± 1:64 | 3.4 ± 2.4                  |         |
| Range               | 1:1–2048   | 0–11                       | 1:1–256   | 0–8                        |         |
| **Final RPR titers** |           |                           |           |                           |         |
| Median              | 1:4        | 2                          | 1:4       | 2                          | 0.794a   |
| Mean ± SD           | 1:82 ± 1:266 | 2.6 ± 2.8                   | 1:16 ± 1:30 | 2.7 ± 1.9                  |         |
| Range               | NR–1024    | 0–10                       | 1:1–128   | 0–7                        |         |
| Achieved seroreduction | 21 (78%)   |                             | 9 (45%)   |                             | 0.032b   |
| Achieved serologic cure | 8 (30%)    |                             | 3 (15%)   |                             | 0.310b   |
| **Degree of RPR titer reduction (no. of dilutions)** | | | | | |
| Median              | 1          |                             | 0         |                             | 0.053b   |
| Mean ± SD           | 1.3 ± 1.5  |                             | 0.8 ± 1.3 |                             |         |
| Range               | -1 to 6    |                             | -1 to 4   |                             |         |
| **Rate of RPR titer reduction (reduction per wk)** | | | | | |
| Median              | 0.05       |                             | 0         |                             | 0.046d   |
| Mean ± SD           | 0.07 ± 0.07 |                             | 0.04 ± 0.07 |                             |         |
| Range               | -0.07 to 0.23 |                             | -0.08 to 0.27 |                             |         |
| **Unadjusted analysis** | | | | | |
| Odds of seroreduction | |                             | |                             |         |
| OR (95% CI)         | 4.28 (1.21–15.15) | | | | |
| **Adjusted analysis** | | | | | |
| Odds of seroreduction | |                             | |                             |         |
| aOR (95% CI)        | 4.66 (1.14–19.08) | | | | |

Note: Data are presented as number (percentage) unless otherwise stated; total n = 47.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; HIV+, HIV-positive; HIV−, HIV-negative; OR, odds ratio; RPR, rapid plasma reagin; SD, standard deviation; VL, viral load.

*Mann–Whitney U test.

+Fisher exact test.

+Multivariable logistic regression.

*Model adjusted for initial titer (raw) and maternal age.

**FIGURE 2** Change in RPR titers of study participants during pregnancy. Graph of RPR titers during pregnancy of study participants, grouped by HIV co-infection status. Each line plots the initial and final RPR titers, in absolute number of dilutions, of an individual participant (n = 47). EGA, estimated gestational age; RPR, rapid plasma reagin.
incidence of stillbirth in those who did not achieve titer seroreduction (19%) compared with those who did (3%). This association did not achieve statistical significance, which is not surprising given sample size limitations. Despite this, this trend is noteworthy and should be considered in future studies. Additionally, this high rate of stillbirth in a cohort without any cases of treatment failure as currently defined by guidelines (a four-fold increase in RPR titer) questions the utility of these guidelines for management in pregnancy. Research is needed to determine what additional clinical factors may be useful in identifying women at elevated risk for perinatal morbidity despite stable or down-trending titers.

Current research is heavily focused on the development of new screening tests and alternative screening algorithms; however, rates of stillbirth and congenital infection remain substantial despite this increased attention on refining diagnostic modalities. Future research on treatment monitoring and its implementation into clinical practice must supplement these efforts to succeed in eliminating this longstanding cause of pregnancy morbidity.

TABLE 4  Pregnancy outcomes by HIV status and RPR seroreduction status for study participants with available pregnancy outcome data

| Sub-study cohort (n = 46) | HIV+ women with syphilis (n = 27) | HIV− women with syphilis (n = 19) | P value | RPR sero-reduction (n = 30) | No RPR sero-reduction (n = 16) | P value |
|--------------------------|-----------------------------------|-----------------------------------|---------|-----------------------------|-------------------------------|---------|
| Stillbirtha | 4 (9%) | 3 (11%) | 1 (5%) | 0.632 | 1 (3%) | 3 (19%) | 0.114 |
| Livebirth | | | | | | | |
| SGA <10th centile | 6 (13%) | 6 (25%) | 0 (0%) | 0.029 | 5 (17%) | 1 (8%) | 0.647 |
| SGA <3rd centile | 1 (2%) | 1 (4%) | 0 (0%) | >0.99 | 1 (3%) | 1 (8%) | >0.99 |
| Spontaneous PTB | 2 (4%) | 2 (8%) | 0 (0%) | 0.498 | 1 (3%) | 1 (8%) | 0.518 |
| Delivery GA, wk | 38.4 ± 2.3 | 38.4 ± 2.3 | 38.5 ± 2.4 | 0.615 | 38.7 ± 2.0 | 38.0 ± 2.9 | 0.678 |
| Pre-eclampsia (n = 31)b | 2/31 (6%) | 1/16 (6%) | 1/15 (7%) | >0.99 | 1/18 (6%) | 1/13 (8%) | >0.99 |

Abbreviations: GA, gestational age; HIV+, HIV-positive; HIV−, HIV-negative; PTB, preterm birth; RPR, rapid plasma reagin; SGA, small for gestational age.

aData are presented as mean ± standard deviation or as number (percentage).

bComputed by Student t test (delivery GA) or Fisher exact test (all other outcomes).

One participant in the HIV-negative group was lost to follow up and did not have delivery data collected.

All stillbirths in this sub-study cohort occurred antepartum (none occurred intrapartum).

Pre-eclampsia outcome was only available for the denominator listed.

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AUTHOR CONTRIBUTIONS

This secondary analysis was conceived by CMW, JSAS, and EMS. Conception, data collection, and analysis of the primary study were performed by MPK, JTP, EMS, BV, and JSAS. Secondary data collection and analysis were performed by CMW with data interpretation by CMW and JTP and statistical analysis review by CAW. The manuscript was drafted by CMW, and all authors have critically appraised the manuscript and approved the final version.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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