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Comparable pregnancy outcomes for HIV-uninfected and HIV-infected women on antiretroviral treatment in Kenya

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Abstract

Background—The impact of Human Immunodeficiency Virus (HIV) on pregnancy outcomes for women on antiretroviral therapy (ART) in sub-Saharan Africa remains unclear.

Methods—Pregnant women in Kenya were enrolled in the second trimester and followed up to delivery. We estimated effects of treated HIV with three pregnancy outcomes: loss, premature birth, and low birthweight and factors associated with HIV-positive status.

Results—Of 2,113 participants, 311 (15%) were HIV-infected and on ART. Ninety-one of 1,762 (5%) experienced a pregnancy loss, 169/1,725 (10%) a premature birth (<37 weeks), and 74/1,317 (6%) had a low birthweight newborn (<2500g).

There was no evidence of associations between treated HIV infection and pregnancy loss (adjusted relative risk [aRR]: 1.19 [95% confidence interval: 0.65–2.16], p=0.57), prematurity (1.09 [0.70–1.70], p=0.69) and low birthweight (1.36 [0.77–2.40], p=0.27). Factors associated with an HIV-positive status included older age, food insecurity, lower education level, higher parity, lower gestation at first antenatal clinic, anemia, and syphilis. Women who were overweight or underweight were less likely to be HIV infected compared to those with normal weight.

Conclusion—Currently treated HIV was not significantly associated with adverse pregnancy outcomes. HIV-infected women, however, had a higher prevalence of other factors associated with adverse pregnancy outcomes.

Summary

We estimated the effect of currently treated HIV on pregnancy loss, prematurity and low birthweight. We found no differences in the risk of the three adverse pregnancy outcomes between pregnant HIV-uninfected women and HIV-infected women on antiretroviral treatment.

Keywords

HIV; antiretroviral therapy; test and treat; pregnancy loss; prematurity; low birthweight; sub-Saharan Africa

Introduction

In 2019, more than 1.3 million women living with HIV gave birth worldwide, and 85% of these happened in sub-Saharan Africa. [1] The recent global scale-up of test and treat programs for HIV has resulted in >85% of HIV-infected pregnant women having access to antiretroviral therapy (ART) globally and >88% in high-burden countries in sub-Saharan Africa like Kenya. [1] In the general population, prematurity, birth asphyxia and congenital malformations are prevalent among newborns in this region. [2]

Studies conducted before the wide availability of ART showed that compared to HIV-uninfected women, HIV-infected women were at an increased risk of adverse pregnancy outcomes, including preterm delivery, low birthweight, miscarriages and stillbirths. [3, 4] Existing literature shows a conflicting picture on the impact of ART on the incidence of adverse pregnancy outcomes. While some studies show comparable risk of adverse pregnancy outcomes between HIV-uninfected women and HIV-infected women on ART, [5, 6] others report an increased risk among HIV-infected women on ART. [4, 7] This could be due to persisting effect of HIV infection or the effect of antiretroviral drugs. Some antiretroviral drugs including protease inhibitors have been associated with increased risk of preterm delivery and low birthweight, [8] while dolutegravir was associated with increased risk of neural tube defects, [9] though this risk is considered much lower compared to the benefits. [10] The 2021 World Health Organization (WHO) guidelines recommend that all HIV-infected adolescents and adults, including pregnant women are started on a dolutegravir-based regimen. [10] This is a departure from the previous guidelines that recommended an efavirenz-based regimen, [11] which appears not to be associated with adverse pregnancy or neonatal outcomes. [12] The effect of viral load on the incidence of pregnancy loss, preterm delivery and low birthweight is also not clear. [13] Apart from HIV, other characteristics associated with adverse pregnancy outcomes include low socio-economic status, poor nutrition and poor access to care, [14] anemia, [15] infections such as syphilis, [16] hypertensive diseases in pregnancy, [17] smoking and alcohol use. [18] Some of these factors are more prevalent among HIV-infected persons compared to HIV-uninfected persons. [19] While the HIV programs across sub-Saharan Africa may have reduced these disparities, studies have not been done to confirm their impact.

To determine the need for interventions or policy changes, continued evaluation of pregnancy outcomes among HIV-infected and uninfected women, determination of whether ‘treated HIV’ remains an important cause for adverse pregnancy outcomes, and assessment of other factors that may yet keep HIV-infected women at a higher risk of adverse pregnancy

outcomes despite treatment is necessary. Thus in this study, we conducted an exploratory analysis to estimate associations between HIV status and socio-demographic, obstetric and clinical characteristics known to be associated with adverse pregnancy outcomes, and estimate the effect of currently treated HIV by comparing HIV-uninfected and HIV-infected women on ART on adverse pregnancy outcomes (pregnancy loss, prematurity and low birthweight).

Methods

Study design

Between October 2017 and August 2019, we conducted a prospective cohort study of pregnant women in Mombasa, Kenya (KenZik), with the primary objective to assess the association of Zika infection of pregnant women with adverse pregnancy outcomes. As part of their routine antenatal care, women who had not previously tested HIV positive were tested for HIV in their first antenatal clinic visit. In this study, we analyzed a subset of women enrolled in the KenZik study with known HIV status, ART status and pregnancy outcomes.

KenZik study population

The KenZik study enrolled 2,312 pregnant women at the first antenatal care visit (≤ 28 weeks gestational age) at the Coast General Teaching and Referral Hospital (public referral hospital), Port Reitz Sub-County Hospital (public hospital), and Bomu Hospital (private hospital) and conducted follow-up until delivery. In addition to other services, Bomu hospital provides free HIV care to a large number of patients from underprivileged communities. As the main referral hospital in the region, Coast General Hospital manages a high proportion of pregnant women at a higher risk of adverse pregnancy outcomes. To be included in this study, pregnant women had to be aged 15 years or older with gestational age ≤28 weeks, attending antenatal care and planning to deliver at one of the three hospitals.

Study procedures

Recruitment and enrollment—Recruitment was conducted in general and high-risk antenatal clinics, and prevention of mother to child transmission clinics. Participants completed an enrollment questionnaire with socio-demographic information including their age, education level, and food security, previous pregnancy information including previous pregnancy losses and premature deliveries, and anthropometric measurements including weight, height and mid upper-arm circumference. To determine eligibility, gestational age was determined using dating ultrasounds performed before recruitment or the last normal menstrual period date (LNMP). Those without a dating ultrasound had one done by a study sonographer at enrollment. In addition, antenatal clinic records including their HIV status, ART status, hemoglobin level, hypertension, and syphilis test was abstracted at enrollment.

Follow up and study exit—Participants were followed up monthly during antenatal clinic visits until delivery. After delivery, they completed a questionnaire collecting information on delivery outcomes including premature delivery, birthweight, stillbirth/ miscarriage, and pregnancy-related complications before, during and after delivery.

Anthropometric measurements for neonates were done soon after delivery or abstracted from the newborn nursery records.

Ethical considerations—The KenZik study was approved by the University of Nairobi/Kenyatta National Hospital Ethics Review Committee (P71/02/2017) and Washington State University Institutional Review Board (#15897) with the U.S. Centers for Disease Control and Prevention (#7021) and Kenya Medical Research Institute relying on the local UoN/KNH Ethics Review Committee. Participants provided informed written consent at recruitment.

Statistical Analysis

Descriptive analysis—Among enrolled participants with an HIV status during enrollment, we established the proportion with a record of antiretroviral therapy (ART) use at enrollment. We defined variables as follows: pregnancy loss (miscarriage, defined as intrauterine fetal demise before 22 weeks gestation or stillbirth, defined as intrauterine fetal demise after 22 weeks gestation), low birthweight (birthweight <2500g), premature delivery (gestation at delivery <37 weeks based on ultrasound), primigravid (no previous pregnancy), previous pregnancies (1, 2–3, >3), and anemia (<10.5 g/dl). [20] We summarized the maternal sociodemographic and obstetric characteristics, anthropometric measurements in the current pregnancy, and current pregnancy outcomes using counts, proportions, median and interquartile range (IQR) as appropriate, for HIV-uninfected women, HIV-infected women on ART, and overall.

Exploratory analysis: factors associated with an HIV-positive status—To determine socio-demographic, obstetric and clinical characteristics associated with HIV status, we used generalized linear model procedures (family = ‘binomial’, link = ‘log’) to fit bivariate regression models. For these analyses, mid upper-arm circumference was categorized in 3 levels, underweight (<23 cm), normal weight (23–31 cm), and overweight (>31 cm). Body mass index (BMI) was similarly categorized in 3 levels, underweight (<18 kg/m^2), normal weight (18–30 kg/m^2), and overweight (>30 kg/m^2). [21] We reported prevalence ratios (*PR*), 95% confidence intervals (95%CI) and p values from Wald tests.

Effect of treated HIV on pregnancy outcomes—We assessed differences in pregnancy outcomes – pregnancy loss, prematurity, low birthweight – between HIV-uninfected women and HIV-infected women on ART. We performed single imputation of missing data for gestation at first antenatal clinic visit and gestation at delivery, by ultrasound. All participants had a record for the LNMP, with 11% of the study population missing an ultrasound record. Though considered less accurate, estimating gestation using LNMP is closely related to the estimation by ultrasound. [22] We established the mean difference in gestation using ultrasound and LNMP among participants with complete records, which was then added to the LNMP value to impute the missing gestation by ultrasound values. Due to high levels of missingness of the outcome data (pregnancy loss-17%, prematurity- 18%, low birthweight - 38%), we used multiple imputation by chained equations techniques for imputation of missing data in variables included in each outcome’s model. This included 25 imputations and 10 iterations using the default method in R, which

includes a predictive mean matching for numeric data and regression-based imputation for binary and categorical data. Generalized linear model procedures (family = 'binomial', link = 'log') were applied for unadjusted and adjusted models using complete cases and the imputed datasets to provide risk ratios (*RR*) and adjusted risk ratios (*aRR*), while Rubin's rules for multiple imputation standard errors were used to generate 95%CI. We conducted sensitivity analyses using extreme case scenarios for the missing outcome data, that is, with all missing outcome data considered non-events or events. The p-values were derived from Wald tests. We report results from the imputed datasets and sensitivity analyses in the text but present the results from both complete case analysis and imputed datasets in tables.

The following covariates were considered potential confounders for the three models due to their known association with the pregnancy outcomes and HIV status: age (including a quadratic term), education, syphilis infection, and food security. [16, 23–26] It was expected that the public referral hospital had poorer pregnancy outcomes since it received referrals from the other hospitals of patients with high-risk pregnancies and complicated deliveries, while the gestation at first antenatal clinic visit influenced identification and care for high-risk pregnancies. Site, gestation at first antenatal clinic and pre-eclampsia [23] were considered precision variables. Previous pregnancy loss was considered a precision variable in the pregnancy loss model, previous premature/low birthweight was considered in the prematurity and low birthweight models, while prematurity in the current pregnancy was considered in the low birthweight model. Anemia [27, 28] and BMI [29] have potential mediating roles on the effect of treated HIV on pregnancy outcomes though no studies were found quantifying this relationship. In the results (table and text), we report the estimates from the models that excluded the two variables. Inclusion of anemia attenuated the estimates by 2%−7% while the inclusion of BMI attenuated the estimates by 2.5%−14% in the three models. Though considered potential confounders, we excluded the smoking, alcohol use and twin gestations variables due to their low prevalence in the dataset (<1% each). Zika positivity was not included since only ~300 participants had been tested for Zika virus by the time this analysis was conducted.

Power calculations were done with the assumption that at least 10%−15% of the 2,312 participants enrolled in the KenZik study were HIV-infected. Assuming a prevalence of 5% −15% of any of the outcomes, we had 80% power to detect a relative risk of 1.5–2.0 at alpha 0.05. All analyses were completed using R studio (R Foundation for Statistical Computing, Vienna, Austria).

Results

Overall description of the study population

Overall, 2,145 participants enrolled had a recorded HIV diagnosis, with 1802 (84%) HIV-uninfected at enrollment. Of 343 HIV-infected pregnant women enrolled, 311 (91%) were on ART at enrollment, while for 32 (9%), we could not establish from their record whether they were on ART during pregnancy and were excluded from the analysis. Of 2,113 participants included in the analysis, the median gestational age at their first antenatal clinic visit was 18 weeks (IQR: 13–22), 1402 (66%) were enrolled in public facilities, and 640 (30%) were ≤24 years old (adolescents and young adults). Six hundred and twenty-one (30%)

were overweight (BMI>30 or mid upper-arm circumference >31cm), while 128 (6%) were underweight (BMI<18 or mid upper-arm circumference <23 cm) at enrollment in the second trimester. Of the 1,480 with a previous pregnancy, 480 (32%) had a previous pregnancy loss, and 142 (10%) had a previous premature/low birthweight neonate. Sixty-nine of 1,402 (5%) developed pre-eclampsia/eclampsia, 33/1,762 (2%) experienced a miscarriage, 58/1,762 (3%) experienced a stillbirth, 169/1,725 (10%) had a premature delivery, and 74/1,317 (6%) had low birthweight neonate (Table 1). The denominators are <2,113 due to missing data.

Factors associated with an HIV-positive status

Socio-demographic characteristics associated with an HIV positive status included older age (PR: 1.10 [95%CI: 1.08–1.11], p<0.001), being currently married (0.58 [0.45–0.74], p<0.001), higher monthly family income (0.99 [0.98–0.99], p=0.001), and being food insecure (4.94 [4.08–5.97], p<0.001). Compared to women with a primary education or lower, those with a secondary education or a tertiary education were less likely to be living with HIV (0.59 (0.48–0.74) and 0.32 (0.23–0.44) respectively, p<0.001). Obstetric factors associated with an HIV positive status included being a primigravida (0.29 [0.20–0.40], p<0.001) and having a previous low birthweight/premature (1.73 [1.32–2.28], p<0.001). Clinical factors associated with an HIV positive status included higher gestation at first antenatal clinic (0.93 [0.91–0.95], p<0.001), having anemia (1.62 [1.31–1.99], p<0.001) and having syphilis (3.41 [2.32–5.02], p<0.001). Compared to women with a normal BMI, those categorized as overweight or underweight were less likely to be living with HIV (0.65 [0.49–0.86] and 0.40 [0.10–1.53] respectively, p=0.005), (Table 2).

Effect of treated HIV on pregnancy outcomes

There were no significant differences in pregnancy outcomes between HIV-uninfected and HIV-infected women on ART. While in bivariate analysis HIV-infected women had a 62% higher risk of pregnancy loss (*RR*: 1.62 [1.01–2.61], p=0.04), the association was not significant after adjusting for confounders (*aRR*: 1.19 [0.65–2.16], p=0.57). In addition, there were no significant differences in prematurity between HIV-infected on ART and uninfected women in bivariate and adjusted analyses (1.17 [0.82–1.67], p=0.39 and 1.09 [0.70–1.70], p=0.69 respectively). Similarly, there were no significant differences in low birthweight between HIV-infected and uninfected women in bivariate and adjusted analyses (1.45 [0.92–2.31], p=0.11 and 1.36 [0.77–2.40], p=0.27 respectively), (Table 3).

In the extreme-case sensitivity analyses, the effect of treated HIV on pregnancy loss was stronger in the bivariate analysis with all missing data considered non-events (1.85 [1.16–2.94], p=0.01) but not significant in the bivariate analysis with all missing data considered events (0.81 [0.62–1.04], p=0.1). The results were similar to the complete case analysis when adjusted for confounders in the two extreme case scenarios. None of the bivariate or adjusted extreme-case sensitivity analyses for the effect of treated HIV on prematurity or low birthweight were significant.

Discussion

This study demonstrated that comparing HIV-infected women on ART to HIV-uninfected women, there was no difference in adverse pregnancy outcomes. A strength of this study was the large sample size, which provided the statistical power to assess differences in risk of adverse pregnancy outcomes between HIV-uninfected and HIV-infected women on ART, and determine differences in the prevalence of other known characteristics associated with adverse pregnancy outcomes. The participants were enrolled at a median of 18 weeks gestational age, which allowed adequate follow-up of participants to observe the pregnancy outcomes.

The proportion of participants with pregnancy loss (5%) in our study was higher than what was reported in a recent cross-sectional analysis of facility registers for pregnancy and neonatal outcomes in Kenya (<4%). [30] However, our study had a slightly lower proportion of premature births (10% versus 14%), and low birthweight (6% versus 13%). [30] This may indicate differences in the prevalence of adverse pregnancy outcomes by region, since our study was confined to the population located in the Coastal region of Kenya, and probably due to lower recruitment from the high-risk antenatal clinics compared to the usual clinics in the three facilities. Other studies in the region report similar proportions of premature births (11%−13%). [31]

This study demonstrated that treated HIV does not significantly influence the incidence of three pregnancy outcomes - pregnancy loss, premature delivery and low birthweight. The results are consistent with studies showing an overall protective effect of ART on the risk of miscarriages and stillbirths, [5, 7, 32] prematurity [32, 33] and low birthweight [7, 32, 33] among HIV-infected women. However, a few previous studies in sub-Saharan Africa showed a persisting negative impact of HIV status on premature delivery [4, 7] and low birthweight [4] despite ART use. While showing that HIV-infected women had ~2-fold increase in the risk of low birthweight and premature delivery even with ART use, the meta-analysis by Xiao et al., [4] highlighted that this effect was largest for women in sub-Saharan Africa compared to women in developed countries. Possible explanations for the differing results from the different studies could be the effects of ART regimen and duration of ART use on low birthweight and premature delivery. Protease inhibitors for example are independently associated with premature delivery and low birthweight. [34–36] Further, the use of ART during pregnancy has rapidly evolved in the last decade. Women who used a single drug regimen at the time of birth in the earlier years, were changed to the use of a triple drug regimen for the duration of pregnancy, and now with the ‘test and treat’ era, newly-diagnosed women are immediately started on triple drug ART regimen. [37, 38] In our study, we ascertained that >90% of HIV-infected women were on ART, though this is a lower figure than the >95% reported in routine data from Kenya. [30, 39] ‘Test and treat’ [38] ensures that for the majority of pregnancies, HIV-infected women are on treatment for the full duration of the pregnancy. This likely has an impact on viral loads during pregnancy and other health indicators including pre-pregnancy weight and weight gain during pregnancy, which have an impact on pregnancy outcomes. [40] Unadjusted analyses suggested an association between treated HIV (versus no HIV infection) and pregnancy loss. However, after adjusting for other factors associated with pregnancy loss, the association

was not significant, suggesting that an apparent link between treated HIV and pregnancy loss is driven by other factors. The results are reassuring for HIV-infected women, who can expect that when on ART, their HIV status does not negatively affect their risk of pregnancy loss, premature delivery, or the birthweight of their neonate.

We found several characteristics associated with adverse pregnancy outcomes to be significantly more common among HIV-infected women on ART than HIV-uninfected women. They, for example, had >50% higher prevalence of anemia, a difference previously demonstrated across sub-Saharan Africa despite the wider access to ART and demonstrated impact of ART in reducing anemia prevalence. [41] While studies have previously demonstrated the effect of anemia on premature delivery [42] and low birthweight [27], the link to pregnancy loss is not clear. One study in-fact reported a protective effect of mild anemia. [43] Our study also shows that HIV-infected women had a higher prevalence of food insecurity, lower income and lower education. Poverty, through multiple mechanisms, including poorer nutrition and poorer access to healthcare is linked to adverse pregnancy outcomes. [44] Additionally, syphilis, >3 times more prevalent among HIV-infected women in our study has previously been associated with pregnancy losses, prematurity and low birthweight. Obesity, on the other hand, could counterbalance the overall risks of adverse pregnancy outcomes for HIV-infected and uninfected women with the lower prevalence of obesity among HIV-infected women (25% vs. 30%) being protective. The other protective factor could be closer monitoring during pregnancy. We found that HIV-infected women attended antenatal clinic an average of 4 weeks earlier. Earlier studies have found that lower numbers of antenatal clinic visits attended are associated with a higher risk of adverse pregnancy outcomes. [45] The older age and higher parity of HIV-infected women may be an important factor when comparing pregnancy outcomes between HIV-infected and uninfected women due to the progressively lower incidence of HIV among younger women. [46] Increased survival of HIV-infected women due to effective ART will continue to increase the number of older HIV-infected women who become pregnant. [47]

Limitations of this study included lack of information on when the HIV positive participants were diagnosed, started ART, their ART regimen, ART adherence and viral load. [8, 34] This information would have enabled more rigorous analyses, accounting for possible mediating or interactive effects on the impact of HIV on pregnancy outcomes. To mitigate for potential confounding due to ART use, we excluded the small population of HIV positive women without information on ART. There was potential for misclassification of HIV status for some women classified as HIV negative at enrollment since they could have become HIV infected later in pregnancy. Future studies looking at potential causes of adverse pregnancy outcomes in areas with high HIV prevalence could look at mediating and possible interactive effects of long-term use of ART, pre-and post-conception viral loads, and ART regimen. Further, little is known on how acute HIV infection affects pregnancy outcomes, since increasingly, a higher proportion of HIV diagnoses during pregnancy are acute infections during pregnancy. [48] Lastly, making a causal claim on the effect of treated HIV is challenging since randomization of the combined exposure of HIV and HIV treatment is not possible in the real world. One of the assumptions we made was that at the time the participants conceived (became at risk of pregnancy outcomes), their exposure status was

well defined. [49] The high rates of HIV testing and ART coverage especially for pregnant women in Kenya gives us some confidence that this assumption has some basis. [39]

Conclusions

This study demonstrated that when on ART, the risk of adverse pregnancy outcomes among HIV-infected women is similar to that of HIV-uninfected women. However, the study showed a higher prevalence of other characteristics associated with adverse pregnancy outcomes including anemia, syphilis, higher parity, older age and proxy factors for poverty including lower monthly income, food insecurity and lower education among HIV-infected women. Possible mitigating factors for HIV-infected women include closer monitoring due to earlier antenatal care attendance and lower prevalence of obesity.

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Table 1:

socio-demographic characteristics, obstetric history, anthropometric and other pregnancy characteristics, and pregnancy outcomes for pregnant women

	N	Overall	HIV-uninfected (N=1802)	HIV-infected on ART (N=311)
Socio-demographic Characteristics			n (%)/ Median (IQR)	
Site	2113			
Private hospital		711 (34%)	468 (26%)	243 (78%)
Public referral hospital		632 (30%)	605 (34%)	27 (9%)
Public hospital		770 (36%)	729 (40%)	41 (13%)
Age (years)	2099	28 years (24–32)	27 years (23–31)	31 years (27–36)
Employed	2112	858 (41%)	726 (40%)	132 (42%)
Education level started	2083			
<Primary/ primary		536 (26%)	410 (23%)	126 (42%)
Secondary/vocational training		931 (45%)	801 (45%)	130 (43%)
Tertiary		616 (29%)	570 (32%)	46 (15%)
Monthly family income ($)	1620	$196 (98–294)	$196 (98–294)	$118 (49–245)
Food insecure	2107	115 (5%)	46 (3%)	69 (22%)
Currently married	2113	1833 (87%)	1587 (88%)	246 (79%)
Previous pregnancy characteristics				
Primigravida	2113	633 (30%)	599 (33%)	34 (11%)
Previous pregnancies	1480			
1		608 (41%)	539 (45%)	69 (25%)
2–3		687 (46%)	529 (44%)	158 (57%)
>3		185 (13%)	135 (11%)	50 (18%)
Previous pregnancy loss	1480	480 (32%)	387 (32%)	93 (34%)
Previous low birthweight/ Premature	1465	142 (10%)	99 (8%)	43 (16%)
Previous caesarian section	1477	247 (17%)	203 (17%)	44 (16%)
Current pregnancy characteristics				
Gestation at first antenatal clinic (weeks)	2107	18 (13–22)	19 (14–23)	15 (10–20)
Folic acid use during pregnancy	2060	502 (24%)	435 (25%)	67 (23%)
Chronic hypertension	2112	41 (2%)	32 (2%)	9 (3%)
Pre-eclampsia/ eclampsia	1402	69 (5%)	62 (5%)	7 (3%)
Anemia	2075	549 (26%)	435 (25%)	114 (37%)
Syphilis (VDRL) positive	2008	28 (1%)	14 (1%)	14 (5%)
Body Mass Index (Kg/m^2)	2096	26 (23–30)	26 (23–30)	25 (22–28)
Mid-Upper Arm Circumference (cm)	2102	28 (26–31)	28 (26–31)	28 (25–30)
Current pregnancy outcomes				
Pregnancy loss	1762	91 (5%)	69 (5%)	22 (8%)
Miscarriages	1762	33 (2%)	22 (1.5%)	11 (4%)
Stillbirths	1762	58 (3%)	47 (3.5%)	11 (4%)
Premature birth	1725	169 (10%)	141 (10%)	28 (10%)
Low birth weight newborn	1317	74 (6%)	58 (5%)	16 (7%)

ART – Antiretroviral therapy

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Table 2:

Bivariate analysis of socio-demographic, obstetric, anthropometric characteristics, and HIV status among pregnant women

	Bivariate analysis	
	[a]PR (95% CI)	p value
Characteristics		
Site		[b]<0.001
Private hospital	Reference	
Public referral hospital	0.13 (0.09–0.18)	
Public hospital	0.16 (0.11–0.21)	
Age (years)	1.10 (1.08–1.11)	<0.001
Education level		[b]<0.001
< Primary/ primary	Reference	
Secondary/vocational	0.59 (0.48–0.74)	
Tertiary	0.32 (0.23–0.44)	
Employed	1.08 (0.88–1.33)	0.51
Monthly family income ($)	0.99 (0.98–0.99)	0.001
Food insecure	4.94 (4.08–5.97)	<0.001
Currently married	0.58 (0.45–0.74)	<0.001
Primigravida	0.29 (0.20–0.40)	<0.001
Previous pregnancies		[b]<0.001
1	Reference	
2–3	2.03 (1.56–2.63)	
>3	2.38 (1.72–3.30)	
Previous pregnancy loss	1.05 (0.84–1.32)	0.65
Previous low birthweight/premature	1.73 (1.32–2.28)	<0.001
Previous caesarian section	0.94 (0.71–1.26)	0.70
Gestation at first antenatal clinic (weeks)	0.93 (0.91–0.95)	<0.001
Folic acid use during pregnancy	0.93 (0.72–1.20)	0.57
Chronic hypertension	1.51 (0.84–2.71)	0.17
Pre-eclampsia/ eclampsia	0.56 (0.28–1.14)	0.11
Anemia	1.62 (1.31–1.99)	<0.001
Syphilis (VDRL) positive	3.41 (2.32–5.02)	<0.001
Body Mass Index (Kg/m^2)		[b]0.005
Normal weight (18–30)	Reference	
Overweight (>30)	0.65 (0.49–0.86)	
Underweight (<18)	0.40 (0.10–1.53)	
Mid-Upper Arm Circumference (cm)		[b]0.34
Normal weight (23–31)	Reference	
Overweight (>31)	0.86 (0.67–1.11)	

	Bivariate analysis	
	[a]PR (95% CI)	p value
Characteristics		
Underweight (<23)	1.26 (0.73–2.18)	

[a]PR - Prevalence Ratio

[b]Global Wald test at 2 degrees of freedom

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Table 3:

Association between HIV status and pregnancy/neonatal outcomes using imputed and complete case datasets

	Imputed dataset			Complete case dataset		
Pregnancy/neonatal outcome	**[a] RR (95% CI)**	**[b] aRR (95% CI)**	**p value**	**RR (95% CI)**	**aRR (95% CI)**	**p value**
Pregnancy loss	1.62 (1.01–2.61)	1.19 (0.65–2.16)	0.57	1.69 (1.07–2.69)	1.49 (0.60–3.68)	0.39
Prematurity	1.17 (0.82–1.67)	1.09 (0.70–1.70)	0.69	1.07 (0.73–1.57)	1.22 (0.65–2.32)	0.38
Low birthweight	1.45 (0.92–2.31)	1.36 (0.77–2.40)	0.27	1.30 (0.76–2.23)	1.32 (0.62–2.82)	0.47

[a] RR - Risk Ratios

[b] aRR – Adjusted Risk Ratios

Variables included as confounders or precision variables in the models: age, education level, food security (confounders), facility, gestation at first antenatal clinic, parity, previous pregnancy loss, and previous premature or low birthweight (precision variables).