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Sexually transmitted infections and bacterial vaginosis among adolescent girls and young women in the early postpartum period: a cross-sectional study

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Abstract

Background Universal antiretroviral treatment (ART) for pregnant women has reduced mother-to-child transmission risk significantly. However, not all women on ART are virally suppressed during pregnancy and lactation. In addition to poor adherence to ART, co-infections particularly other sexually transmitted infections (STIs) are known to increase the risk of HIV acquisition and HIV transmission. While the prevalence of STIs during pregnancy has been well studied, the prevalence of STIs in the postpartum period and its association with HIV viral suppression are underreported.

Methods In this cross-sectional study, we determined the prevalence of STIs among adolescent girls and young women (AGYW) living with HIV (WLHIV) and without HIV (WNLHIV) at their 6–14 week postnatal clinic visit in a high HIV prevalence district in South Africa. All women were examined for STI-related symptoms and had vaginal swabs collected and stored for later STI testing. Vaginal swabs were tested for *Trichomonas vaginalis (T.vaginalis)*, *Chlamydia trachomatis (C. trachomatis)*, *Neisseria gonorrhoeae (N. gonorrhoea)* and herpes simplex virus-2 (HSV-2) using PCR. All women were tested for bacterial vaginosis (BV) using the Nugent scoring criteria. WLHIV had a blood sample collected for HIV viral load, Hepatitis B and syphilis.

Results Included in this analysis were 82 WLHIV and 102 WNLHIV. Between 6 and 14 weeks postpartum, 40 (21.7%) AGYW tested positive for any STI and among these 15 (37.5%) were symptomatic and received empirical treatment. *C. trachomatis* was most commonly detected (10.9%), followed by HSV-2 (7.7%), *T. vaginalis* (3.8%) and *N. gonorrhoea* (1.6%). WLHIV were more likely to test positive for an STI (OR 2.0; 0.96–3.96) and BV (OR 4.2; 95%CI 2.1–8.1) compared to WNLHIV. Among WLHIV on ART, 70.5% had an undetectable plasma viral load (PVL) and 20.5% had a PVL > 1000 copies/ml. Testing positive for any STI or BV at the postpartum visit was not associated with PVL > 1000 copies/ml (OR 1.33; 95%CI 0.38–4.64).

Conclusion We report a high prevalence of largely asymptomatic STIs and BV in the early postpartum period and STIs in WLHIV were not associated with unsuppressed PVL.The high STI positivity rate among WNLHIV has implications for HIV risk during the postpartum period, and subsequently breastfeeding transmission.

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Keywords Postpartum, Sexually transmitted infections, Bacterial vaginosis, HIV-1, Plasma viral load

Introduction

In 2022, KwaZulu-Natal province in South Africa remained the HIV epicentre with the highest antenatal HIV prevalence in the country (37.1%, 95% CI: 35.8–38.5) [1]. Nationally, 98.8% of pregnant women living with HIV had been initiated on ART and 74.1% were virally suppressed, however, only 46% of 15-19-year-old women were virally suppressed during pregnancy [1]. In addition to poor ART adherence, co-infections particularly other sexually transmitted infections (STIs) are known to induce HIV viral replication and increase susceptibility to HIV infection through the release of cytokines and inflammatory agents [2, 3]. In a cohort study of pregnant women in Umlazi, a high HIV prevalence setting in Durban, South Africa, 38% (571/1480) of pregnant women tested positive for HIV at their first antenatal visit and the prevalence of gonorrhoea (9.8% vs. 4.4%) and trichomoniasis (22.6% vs. 10.5%) during pregnancy was significantly higher in women living with HIV [4]. Furthermore, the incidence of gonorrhoea and trichomoniasis was 5.5 times and 1.8 times higher in women living with HIV during pregnancy [4]. In a subset analysis of the same cohort, genital HSV-2 shedding during pregnancy was detected in 8% of pregnant women; and 1.5 and 2.5 times more likely to occur among young (<24 year) women and women living with HIV [5]. Bacterial vaginosis (BV) and STIs such as trichomoniasis and herpes simplex virus type 2 (HSV-2) in pregnancy are associated with increased HIV shedding and may consequently increase the risk of mother-to-child transmission (MTCT) [6]. In utero MTCT has also been associated with chorioamnionitis caused by ascending lower genital tract infections such as *N. gonorrhoea*, *C. trachomatis*, and *T. vaginalis* [7].

A high prevalence of largely asymptomatic STIs in pregnant women has been commonly reported in several studies in sub-Saharan Africa [8]. In addition, a more recent study also demonstrated that pregnant women remain at high risk of incident STIs throughout pregnancy, which may go undetected if aetiological screening is not repeated during antenatal care [9]. Studies reporting the prevalence of STIs in the postpartum period are sparse.

In this cross-sectional study, we compared the prevalence of STIs and bacterial vaginosis in AGYW living with HIV and not living with HIV in the early postpartum period. Among AGYW living with HIV, we further explored the impact of STIs on maternal viral load in the presence of antiretroviral treatment.

Methods

For this cross-sectional postpartum epidemiological study, AGYW not living with HIV who previously participated in an HIV incidence cohort study (CAP 088 study) were included in this sub-study analysis and served as a control group. In the the CAP 088 study, antenatal clinic attendees in the Umlazi area in Durban, South Africa, who tested negative for HIV were enrolled between Feb 2017 and Mar 2018 [9]. Pregnant women who were in their third trimester of pregnancy (>28 weeks), in labour or with obstetric complications that required referral to the regional hospital were excluded from the study. Women meeting eligibility criteria were asked to provide written informed consent for participation in the study and storage of biological specimens for future research. Women enrolled in the CAP 088 study were seen at two antenatal visits prior to delivery and thereafter had scheduled appointments at 14, 26, and 38 weeks post delivery. Women attending the 14 week postpartum visit were included in this substudy analysis. Institutional regulatory oversight for the CAP 088 study was provided by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BE 194/18).

For the comparator group, young women (<25 years of age) living with HIV and having delivered 6–14 weeks prior, were recruited from a postnatal clinic between July 2017 and April 2020 in the Umlazi area, Durban, the same study area as for the CAP 088 study. These participants constituted the Women living with HIV (WLHIV) group. Women without evidence of a positive HIV test, or who delivered less than 6 weeks ago or more than 14 weeks ago were excluded from enrolment. Institutional regulatory oversight was provided by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BE 482/17).

After providing written informed consent, WLHIV and WNLHIV completed demographic and behavioural questionnaires with the assistance of the research nurse. The research nurse then examined all participants for symptoms suggestive of a STI such as abnormal vaginal discharge, genital blisters or sores and subsequently collected three vaginal swabs for BV and STI testing. Vaginal swabs were transported to the central lab for Gram staining to diagnose BV with Nugent's criteria (a score of 0–3 was considered BV negative, 4–6 intermediate BV, and 7–10 BV positive) and the remaining swabs were stored at -70°C until the end of the respective studies. a stored vaginal swab was tested for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* using the Roche Light Cycler 480 and Roche STI kits (Roche Diagnostics, USA). A second vaginal swab

was tested for herpes simplex virus-2 (HSV-2) using the Roche Light Cycler 480 and HSV-1/2 detection kit (Roche Diagnostics). Participants who were symptomatic for STIs were treated empirically with single doses of azithromycin (1 g oral dose), ceftriaxone (250 mg intramuscular injection) and metronidazole (2 g oral dose) as per the National Department of Health Guidelines for STI Management. For WLHIV, a blood sample was collected for HIV viral load, Hepatitis B surface antigen (HepBsAg) and Syphilis testing. The HIV RNA PCR was performed using the NucliSENS EasyQ® HIV-1 v2.0 assay to determine HIV-1 plasma viral load. The same blood sample was also used to test for HepBsAg using the ARCHITECT HBsAg Confirmatory V1 assay and for syphilis using the BD Macro-Vue™ RPR Card Test. Samples that were positive for syphilis on the RPR test were retested using a TPHA test to confirm positive status. All investigations for both cohorts were performed at a central commercial laboratory (Global Clinical Virology, Durban, South Africa).

Statistical analyses

Socio-demographic (age and occupation), relationship characteristics (partner's age and relationship status) and recent obstetric characteristics and outcomes were compared between WLHIV and WNLHIV using Chi Square tests for categorical data and t-tests or Mann-Whitney for numeric data. Positivity rate of STIs and BV was calculated as the proportion (%) of women who tested positive for each of the STIs and BV separately and as a composite number of pregnant women with a positive test for any STI. Using binary logistic regression to estimate odds ratio and 95% CI, we compared the positivity rate of STIs between WLHIV and WNLHIV and then compared the positivity rate of STIs in WLHIV with plasma viral load < 1000 copies/ml versus plasma viral load > 1000 copies/ml.

Results

We included a total number of 184 AGYW (82 WLHIV and 102 WNLHIV) in this cross-sectional study. The study groups were comparable in age, number of pregnancies, and not living together with their partner (Table 1). The median (IQR) age in WLHIV was 22 (19;24) ranging from 15 to 25 years and WNLHIV was 21 (19;23) and also ranging from 15 to 25 years ($p=0.241$). WNLHIV included 8 (7.8%) adolescents and WLHIV included 5 (6.1%) adolescents. Women not living with HIV were more likely to be employed (43.1%) compared to WLHIV (9.8%) ($p<0.001$). WNLHIV have had more favourable pregnancy outcomes when compared to WLHIV. WLHIV had a significantly higher rate of preterm births (27.9% vs. 13.9%) ($p=0.024$) and low-birthweight babies (17.6% vs. 6.1%) ($p=0.025$) (Table 1).

Table 1 Sociodemographic Characteristics and recent pregnancy outcomes of AGYW living with HIV in comparison to AGYW not living with HIV

Variable	WLHIV *N* = 82	WNLHIV *N* = 102	*P* Value
Age, median (IQR)	22 (19;24)	21 (19;23)	0.241
Gestational age (weeks) at Delivery, median (IQR)	38 (36;39)	39 (38;40)	< 0.001
Gravidity, mean (SD)	1.6 (0.8)	1.7 (0.8)	0.360
Occupation			
Employed	8 (9.8)	44 (43.1)	< 0.001
Student	26 (31.7)	26 (25.5)	
Unemployed/At Home	48 (58.5)	32 (31.4)	
Partner's age (years), median (IQR)	26 (22;29)	27 (24;32)	< 0.01
Partner > 5 years older *n* (%)	31 (37.8)	61 (59.8)	< 0.01
Relationship status, *n*(%)			
Living together	12 (14.6)	20 (19.6)	0.437
Not Living together	70 (85.4)	82 (80.4)	
Pregnancy Outcome-Livebirth			
Yes	79 (96.3)	99 (97.1)	1.000
No	1 (1.2)	2 (2.0)	
Missing Data	2	1	
Pregnancy Outcome-Preterm birth (live births)			
Yes	22 (27.8)	12 (12.1)	0.012
No	57 (72.2	87 (87.9)	
Pregnancy Outcome-Low Birth Weight			
Yes	13 (17.6)	6 (6.1)	0.025
No	61 (82.4)	93 (93.9)	
Missing Data	5	0	

Between 6 and 14 weeks postpartum, 40 (21.7%) of the 184 AGYW tested positive for any STI and among these 15 (37.5%) were symptomatic and received empirical treatment. *C. trachomatis* was most commonly detected (*n*=20; 10.9%), followed by HSV-2 (*n*=14; 7.7%), *T. vaginalis* (*n*=7; 3.8%) and *N. gonorrhoea* (*n*=3; 1.6%). Of note, *N. gonorrhoea* was only detected among WLHIV (*n*=3) and overall, WLHIV were two times more likely to test positive for any STI when compared to WLNHIV in the postpartum period (Table 2). WLHIV were also four times more likely to test positive for BV in the postpartum period when compared to WNLHIV (51.2% vs. 18.6%) (OR 4.2; 95%CI 2.1–8.1) (*p*<,0.0001).

At the postpartum visit, all 82 WLHIV were on antiretroviral treatment with 75 women with known commencement date of ART. The average duration on ART as at the time of the postpartum visit was 8 months ranging from 1 to 12 months. And four women were on treatment for less than 3 months. Plasma viral load (PVL) results were available for 78 (95.1%) of WLHIV. The mean (SD) PVL was 22 023 (91 077) copies/ml. PVL was undetectable (<50 copies/ml) in 55 (70.5%; 95%CI 59.1–80.3) women at the postpartum visit. Among the 23 women with detectable PVL the mean (SD) was 75 643 (158 648) copies/ml and ranged from 56 to 700 000 copies/ml. Seven (9.0%), four (5.1%) and 12 (15.4%) had PVL in the 50-1000, 1000–10,000, and >10,000 copies/ml respectively. Duration of ART was not associated with viral suppression at the postpartum visit; two (50%) women with shorter duration of ART and 13 (19.4%) with longer duration of ART were not virally suppressed, [OR 0.25 (95%CI 0.03–1.87)] (*p*=0.194). Adherence was not measured in this cohort of women. Testing positive for any STI at the postpartum visit was not associated with PVL>1000 copies/ml (OR 1.33; 95%CI 0.38–4.64) (table 3). Of note, 20.5% of WLHIV on ART had a PVL>1000 copies/ml at the postpartum visit.

Table 2 Detection of STIs and BV in Young and adolescent women at the Postpartum visit stratified by HIV Status

	WNLHIV *N*=102 *n* (%)	**WLHIV *N*=82 *n* (%)**	**Odds Ratio (95%CI)**	***P* Value**
Chlamydia				
Negative	94 (92.2)	70 (85.4)	Ref	
Positive	8 (7.8)	12 (14.6)	2.0 (0.8–5.2)	0.159
Gonorrhoea				
Negative	102 (100)	79 (96.3)	-	
Positive	0 (0)	3 (3.7)	-	0.087
Trichomoniasis				
Negative	98 (96.1)	79 (96.3)	Ref	
Positive	4 (3.9)	3 (3.7)	0.9 (0.2–4.3)	1.000
Herpes Simplex Virus-2				
Negative	96 (94.1)	72 (87.8)	Ref	
Positive	6 (5.9)	8 (9.8)	1.8 (0.6–5.4)	0.402
Missing Data	0	2		
Bacterial Vaginosis				
Negative	83 (81.4)	40 (48.8)	Ref	
Positive	19 (18.6)	42 (51.2)	4.2 (2.1–8.1)	<0.0001
HepBsAg				
Negative	ND	77 (97.5)	-	-
Positive	ND	2 (2.5)	-	-
Missing Data	-	3		
Syphilis				
Negative	ND	68 (97.1)	-	-
Positive	ND	2 (2.9)	-	-
Missing Data		12		
Any STI				
Negative	85 (83.3)	59 (72.0)	Ref	
Positive	17 (16.7)	23 (28.0)	2.0 (0.96–3.96)	0.073
Any STI and Symptomatic				
No	10 (58.8)	12 (60.0)	Ref	
Yes	7 (41.2)	8 (40.0)	0.9 (0.3–3.6)	1.000

Table 3 Association of STIs and plasma viral load in AGYW living with HIV at the Postpartum visit

	Plasma Viral Load < 1000 copies/ml ***N*** **= 62** ***n*** **(%)**	**Plasma Viral Load >1000 copies/ml** ***N*** **= 16** ***n*** **(%)**	**OR (95%CI)**	***P*** **Value**
Chlamydia				
Negative	53 (80.3)	13 (19.7)	Ref	
Positive	9 (75.0)	3 (25.0)	0.74 (0.18–3.80)	0.703
Gonorrhoea				
Negative	59 (78.7)	16 (21.3)		
Positive	3 (100)	0	--	0.497
Trichomoniasis				
Negative	60 (80.0)	15 (20.0)	Ref	
Positive	2 (66.7)	1 (33.3)	0.50 (0.04–15.7)	0.503
Herpes Simplex Virus-2				
Negative	53 (76.8)	16 (23.2)		
Positive	8 (100)	0	--	0.193
Bacterial Vaginosis				
Negative	33 (80.5)	8 (19.5)	Ref	
Positive	29 (78.4)	8 (21.6)	0.88 (0.29–2.64)	1.000
HepB sAg				
Negative	61 (80.5)	15 (19.7)		
Positive	1(50)	1 (50)	--	0.370
Syphilis				
Negative	52 (77.6)	15 (22.4)		
Positive	2 (100)	0		
Missing Data	8	1		
Any STI				
Yes	19 (82.6)	4 (17.4)	Ref	
No	43 (78.2)	12 (21.8)	1.33 (0.38–4.64)	0.766
On ARV Treatment				
Yes	62 (79.5)	16 (20.5)		
No	0	0	--	--

Discussion

With limited evidence of the burden of STIs in postpartum women, we report that 40 (21.7%) of 184 adolescent girls and young women tested positive for any STI between 6 and 14 weeks postdelivery. Among these AGYW who tested positive for any STI postdelivery, only 15 (37.5%) were symptomatic and received empirical treatment. Overall, WLHIV were two times more likely to test positive for any STI and four times more likely to test positive for BV when compared to WNLHIV in the postpartum period. Although all WLHIV were on ART at the postpartum visit, 20.5% had PVL>1000 copies/ml and STIs were not associated with unsuppressed viral load.

Postpartum detection of STIs and BV in Sub-Saharan Africa is underreported. In a large population based study in the US in the 1990s, 2.6% tested positive for *C. trachomatis* and 1.3% for *N. gonorrhoea* in the first 3 months after delivery [10]. Another longitudinal study of adolescents in the US, reported STI detection in 7.1% at a 3 month postpartum visit and further reported increased incidence of STIs at subsequent visits in the first year postdelivery [11]. In our South African study, we report a three times higher detection rate of any STI (22%) at the 3-month postpartum visit. Using a cross-sectional design, we were unable to determine if these STIs were new infections or infections acquired during late pregnancy and were untreated due to their asymptomatic nature. In an earlier report, we provided evidence that pregnant women are at continued risk of acquiring incident STIs in late pregnancy and moreover more than 50% of infections are asymptomatic [9]. A recent metanalysis highlighted that more than 50% of postpartum women resume sexual intercourse soon after birth [12] suggesting a heightened risk for unwanted pregnancies, HIV and STI acquisition. Several factors have been identified as risk for unprotected sexual intercourse in the postpartum period in association with unwanted pregnancies, STIs and HIV acquisition, these including disparate age relationships, intimate partner violence, low perception of risk during pregnancy and lactation and resuming sexual intercourse with old or new partners who have been in other relationships [13–15].

Although all WLHIV in our study had initiated ART during pregnancy or at delivery, after a minimum period of 3 months of ART, 20% of the women were not virally suppressed at the 3 month postpartum visit. We were unable to conclude that STIs were likely associated with unsuppressed plasma viral load (>1000 copies). Our findings are similar to a meta-analysis that estimated the average difference in plasma viral load in presence of a STI was 0.11 log higher than in the absence of a STI suggestive that ART is able to maintain HIV VL in the presence of STIs [16]. Although a few studies reported a good correlation between genital viral load and plasma viral load, further studies are needed to examine the effect of STIs on genital HIV viral load [17, 18].

Other possible factors associated with unsuppressed VL could include late initiation of ART in pregnancy and poor adherence to ART during the postpartum period [19]. A South African cohort study of pregnant women reported similar findings of unsuppressed viral load at delivery despite ART initiation during pregnancy [20]. Myer et al. reported 30% of women had a detectable viral load (>50 copies/ml) while 10% were considered virally unsuppressed (>1000 copies/ml). The study also reported an early MTCT risk of 1.3% but more importantly the study confirms that MTCT risk increased with increase in maternal viral load, MTCT risk among women with unsuppressed viral load (>1000 copies) at delivery was 8.5%. Viral load monitoring in other South African studies reported similar results of viral suppression during pregnancy [21, 22]. AGYW were more likely to be virally unsuppressed compared to older women [22].

In conclusion, our study may not have found an association between STIs and HIV viral non-suppression in the early postpartum period, however the high prevalence of largely asymptomatic STIs in WNLHIV has implications for HIV acquisition during the postpartum period and subsequent mother-to-child transmission of HIV during breastfeeding.

While our study is one among a few postpartum STI studies, it has several limitations. With the cross-sectional study design we were not able to verify if STIs were old or newly acquired infections. Furthermore, we did not consider the impact of STIs on viral load beyond the 3 month postpartum visit. Our study was not powered to draw firm conclusions and our findings may not be generalizable to the general population.

Abbreviations

WLHIV	Women living with HIV
WNLHIV	Women not living with HIV
STI	Sexually transmitted infections
PCR	Polymerase chain reaction
GTI	Genital tract infections
CT	Chlamydia trachomatis
TV	Trichomonas vaginalis
NG	Neisseria gonorrhoeae
BV	Bacterial vaginosis
AGYW	Adolescent girls and young women
PVL	Plasma viral load
OR	Odds ratio
CI	Confidence interval

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Author contributions
VG and DM conceptualized this study and drafted the manuscript. MN was the clinician on the study and guided the syndromic management of BV and STIs this study.

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Data availability
The data for this paper is stored with the authors and can be made available upon request and with permission from the funder.

Declarations

Ethics approval and consent to participate
Women meeting eligibility criteria were asked to provide written informed consent for participation in the study and for storage of biological specimens for future research. Institutional regulatory oversight was provided by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BE 194/18) (BE 194/18).

Consent for publication
N/A.

Competing interests
The authors declare no competing interests.

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