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STI prevalence among women at risk for HIV exposure initiating safer conception care in rural, southwestern Uganda

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Abstract

Background: Knowledge of STI prevalence and risk factors is important to the development of tenofovir-based pre-exposure prophylaxis (PrEP) and safer conception programming. We introduced STI screening among women at risk for HIV exposure, participating in a safer conception study in southwestern Uganda.

Methods: We enrolled 131 HIV-uninfected women, planning for pregnancy with a partner living with HIV or of unknown HIV-serostatus (2018–2019). Women were offered comprehensive safer conception counseling, including PrEP. Participants completed interviewer-administered questionnaires detailing socio-demographics and sexual history. We integrated laboratory screening for chlamydia, gonorrhea, trichomoniasis, and syphilis as a substudy to assess STI prevalence. Multivariable logistic regression was used to determine correlates.

Results: Ninety-four women completed STI screening (72% of enrolled). Median age was 30 (IQR 26–34) years, and 94% chose PrEP as part of safer conception care. Overall, 24% had STIs: 13% chlamydia, 2% gonorrhea, 6% trichomoniasis, 6% syphilis, and 3% ≥2 STI. STI prevalence was associated with younger age (adjusted odds ratio [AOR] 0.87, 95% confidence interval [CI] 0.77–0.99), prior stillbirth (AOR 5.04, 95% CI 1.12–22.54), and not feeling vulnerable to HIV (AOR 16.33, 95% CI 1.12–237.94).

Conclusion: We describe a 24% curable STI prevalence among women at risk for HIV exposure, planning for pregnancy. These data highlight the importance of integrating laboratory-based STI

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screening into safer conception programs to maximize the health of HIV-affected women, children, and families.

SHORT SUMMARY:

This study describes a 24% curable sexually transmitted infection prevalence among HIV-affected women planning for pregnancy in Uganda, highlighting the importance of integrating STI screening into safer conception care.

Keywords

Sexually transmitted infection; women; PrEP; periconception; Uganda

Introduction

Sub-Saharan Africa (SSA) carries a high burden of sexually transmitted infections (STIs). In 2016, there were 376 million new cases of the four, major, curable STIs: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, and *Treponema pallidum,* and SSA had the highest global incidence of gonorrhea and trichomoniasis among men and women[1]. STIs can cause adult morbidity, increase HIV transmission and acquisition risk[2], and cause neonatal morbidity and mortality if transmitted perinatally[3].

For people in HIV serodifferent relationships, tenofovir-based pre-exposure prophylaxis (TDF/FTC PrEP) is recommended by the World Health Organization (WHO) and many countries (including Uganda) to reduce HIV infection risk by up to 90%[4]. Additionally, the WHO and others emphasize the potential value of PrEP for HIV-exposed women planning for pregnancy as an efficient strategy to prevent perinatal transmission and promote women's health[4,5]. In Uganda, the total fertility rate is 5.1 children per woman, and adult HIV-prevalence is approximately 7% [6,7]. Thus, many women with personal and/or partner pregnancy plans may be exposed to HIV. Additionally, women are at increased risk for HIV acquisition: in Eastern and Southern Africa, young women acquire HIV at twice the rate of their male peers[8]. The 2016 Ugandan Ministry of Health (MoH) first recommended TDF/FTC PrEP to prevent HIV acquisition, and the Mbarara Regional Referral Hospital began offering PrEP in late 2017[9].

STI prevalence among many key populations at risk for HIV exposure and considering PrEP has been shown to be high[10,11]. The majority of this work has focused on gay, bisexual, and men who have sex with men populations in North America and Europe[10,11]. There is, however, scant data on PrEP and STIs among women at risk for HIV acquisition in SSA. Additionally, we are not aware of data on STI prevalence in the context of safer conception programming.

To our knowledge, no studies have determined STI prevalence through laboratory-screening in rural Uganda among women planning for pregnancy and considering PrEP as a part of safer conception care. As PrEP is disseminated across Uganda and SSA, knowledge of STI prevalence and associated risk factors will help to inform PrEP programming. In this study, we assessed STI prevalence and associated risk factors for chlamydia, gonorrhea,

trichomoniasis, and syphilis among a cohort of women at-risk for HIV acquisition and seeking safer conception care.

Materials and Methods

Study design and participants

The Healthy Families PrEP Study (NCT03832530) is a mixed-methods, prospective, cohort study that assessed PrEP uptake and adherence among women at risk for HIV exposure with personal or partner plans to have a child in rural, southwestern Uganda. Inclusion criteria consisted of being an HIV-uninfected woman, 18–40 years old, fluent in the local language (Runyankole) or English, in a partnership with a man living with HIV (MLWH) or unknown HIV-serostatus, personal or partner desire to conceive a child in the coming year, and not currently pregnant. Participants attended study visits at enrollment, three, six, and nine-months. Participants exited the study if they completed nine months of follow-up or tested positive for HIV. Those with incident pregnancy were followed to the end of pregnancy.

Recruitment was conducted primarily through the Healthy Families Clinical Program, a safer conception counseling program for couples and individuals affected by HIV, housed within the HIV clinic at the Mbarara Regional Referral Hospital (MRRH)[12]. Additional recruitment measures included approaching women accessing HIV counseling and testing at the Mbarara Municipal Council, Bwizibwera, Kinoni, Kakoba, and MRRH outpatient clinics.

Study procedures

Counseling and questionnaires—All participants were offered quarterly safer conception counseling visits, completed a sexual behavior diary, and completed a face-to-face questionnaire administered at study enrollment and exit. A separate STI questionnaire with questions regarding STI symptoms, medical/STI history, and sexual/relationship history was administered to participants who completed enrollment STI testing[13]. Questionnaires were administered by research assistants in Runyankole or English. Data were collected and managed using REDCap electronic data capture tools hosted at Partners Healthcare[14].

Laboratory testing—STI laboratory screening began in June 2018 as a substudy, and all new enrollees to the parent study were invited to participate. Participants provided blood to screen for *Treponema pallidum* via a rapid immunochromatographic test (ICT) confirmed by rapid plasma reagin (RPR). They had the option of self-collected or nurse-collected vaginal swabs to screen for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* via nucleic acid amplification testing with GeneXpert. All participants completed beta HCG-urine pregnancy testing and rapid HIV testing.

STI treatment—Participants with positive STI testing were notified and treated the same day or within days (same-day testing was not always feasible given power instability and participant time constraints). Participants with STI symptoms alone were not treated. All STI treatment was in accordance with Ugandan MoH STI treatment guidelines[9]. Participants with positive syphilis ICT received treatment regardless of RPR due to its variability in

different conditions[15] and were given partner notification (PN) cards outlining the need for presumptive partner treatment with Benzathine penicillin. Participants with chlamydia, gonorrhea, and trichomoniasis diagnoses received patient-delivered partner medications (PDPM) to give to sexual partner(s) and PN cards which outlined the partner exposure, need for medical evaluation, and the purpose of PDPM.

Measures—The primary measure of interest of this substudy was the laboratory diagnosis of at least one STI. Pertinent covariates included age, number of sexual partners in the past three months, condom use at last sexual encounter, number of stillbirths, and a history of prior STIs, which were obtained from the questionnaires.

Statistical analysis—Descriptive statistics were calculated by median (inter-quartile range (IQR)) or mean (standard deviation (SD)). We used Fisher's exact test to assess the association between categorical variables and STI. In constructing the multivariable logistic model, we initially included all variables with a univariable p-value ≤0.20. We then removed the variable with the highest p-value > 0.05, reran the reduced model, and repeated this process until all remaining variables had a p-value ≥ 0.05. We considered this approach with the goal of maximizing the parsimony of our model in the setting of low absolute numbers of STI from the limited sample size[16]. Data were analyzed with STATA V15.

Ethics—All participants provided voluntary informed consent at enrollment. Ethical approval was provided by the research ethics boards of Massachusetts General Hospital, University of Alabama at Birmingham, and Mbarara University of Science and Technology. Consistent with national guidelines, approvals were obtained from the Uganda National Council for Science and Technology and the Research Secretariat in the Office of the President.

Results

Participant socio-demographic characteristics

All 131 women who met parent study inclusion criteria and all 94 participants who were offered STI substudy participation consented. Among the 94 study participants who completed enrollment STI screening, the median age was 30 (IQR 26–34) years. The majority of participants, 87 (93%) were married or living as married with their primary pregnancy partner. Twenty-six women (28%) reported a prior sexual partner with STI. Among 92 women reporting sexual intercourse in the prior three months, 59 (64%) reported condom use at last sexual encounter with her primary partner. Almost all women in this sample (94%) chose to initiate PrEP. Most participants, 91 (97%), chose to self-collect vaginal swabs (Table 1).

STI participant prevalence and treatment

Among the 94 women screened for STI, 23 (24%) had at least 1 STI including 12 (13%) with chlamydia, 2 (2%) with gonorrhea, 6 (6%) with trichomoniasis, 6 (6%) with syphilis, and 3 (3%) with STI co-infection (Figure 1). All participants with STI received treatment at the study-site.

STI partner notification and treatment

Among the 23 participants with STI, 22/23 (96%) were provided with PN cards and 16/19 (84%) eligible participants were given PDPM.

Factors associated with STI

In the adjusted model, younger age ([AOR]: 0.87 for each year; 95%CI: 0.77– 0.99), prior stillbirth (AOR: 5.04; 95% CI: 1.12–22.54), and not feeling vulnerable to HIV (AOR: 16.33, 95% CI: 1.12–237.94) remained significantly associated with having a current STI (Table 2).

Discussion

To our knowledge, this is one of the first studies in SSA to demonstrate STI prevalence among women desiring pregnancy, at risk for HIV exposure, and seeking safer conception care. We describe a high, 24% STI burden among a population of women at risk for HIV with plans for pregnancy. Given the implications of undiagnosed STI for maternal and child health, these data highlight the importance of implementing STI screening for women and partners as part of safer conception care.

Our data demonstrate a high STI prevalence in Uganda similar to that of other areas in Eastern and Southern Africa. The VOICE trial, assessing topical and oral PrEP among 4,843 women, found a 20% prevalence of chlamydia, gonorrhea, trichomoniasis, and syphilis in South Africa, Uganda, and Zimbabwe[17]. Additionally, the ECHO trial, assessing HIV risk among women using contraception, found an 18% chlamydia and 5% gonorrhea prevalence across South Africa, Zambia, and Kenya[18].

We found several factors associated with STI prevalence. We observed an association between STI and prior stillbirth, despite women with STI being younger, with fewer pregnancies, fewer livebirths, and fewer miscarriages. Syphilis accounts for 11% of stillbirths in SSA[19], and though our cohort was small and not powered to determine the effect of any one STI, our findings support the correlation between stillbirth and syphilis as well as adverse pregnancy outcome and STI found across the world[20]. Uganda has a high prevalence of both syphilis and stillbirth, and while Ugandan clinical guidelines include antenatal syphilis point-of-care (POC) screening and treatment, in 2018 only 57% of antenatal clinic attendees received first-visit, laboratory screening for syphilis[9,21]. The profound impact of stillbirth, precipitated in part by curable STIs, strongly argue for the prioritization of antenatal and pre-conception STI screening.

A history of STI is a strong predictor of future STI[22,23], but in our cohort, prior self-reported STI was significantly associated with a lack of current STI. The Carraguard study, a prospective HIV-prevention trial of nearly 15,000 South African women found that baseline STI was significantly associated with incident STI[23]. Reasons for our differing results may include misdiagnosis with the STI syndromic approach, protective immunity secondary to chlamydia[24], and women with prior STI receiving effective counseling to prevent STI recurrence.

This analysis is limited by a small, cross-sectional dataset, though it is strengthened by high quality laboratory assessment.

Our findings highlight a high STI burden not previously described among Ugandan women at risk for HIV exposure and planning for pregnancy. Rapid advancements in STI POC technology provide hope for appropriate STI diagnoses, but as demonstrated by syphilis, even when POC testing is available, implementation can lag. Thus, we need to prioritize both the development and dissemination of POC diagnostics. Laboratory-based STI diagnostics will allow a greater emphasis on PN and a better understanding of how to break the transmission cycle. Understanding STI epidemiology and risk factors is the first step towards designing interventions for STI screening and treatment, especially as safer conception and PrEP programs expand across SSA.

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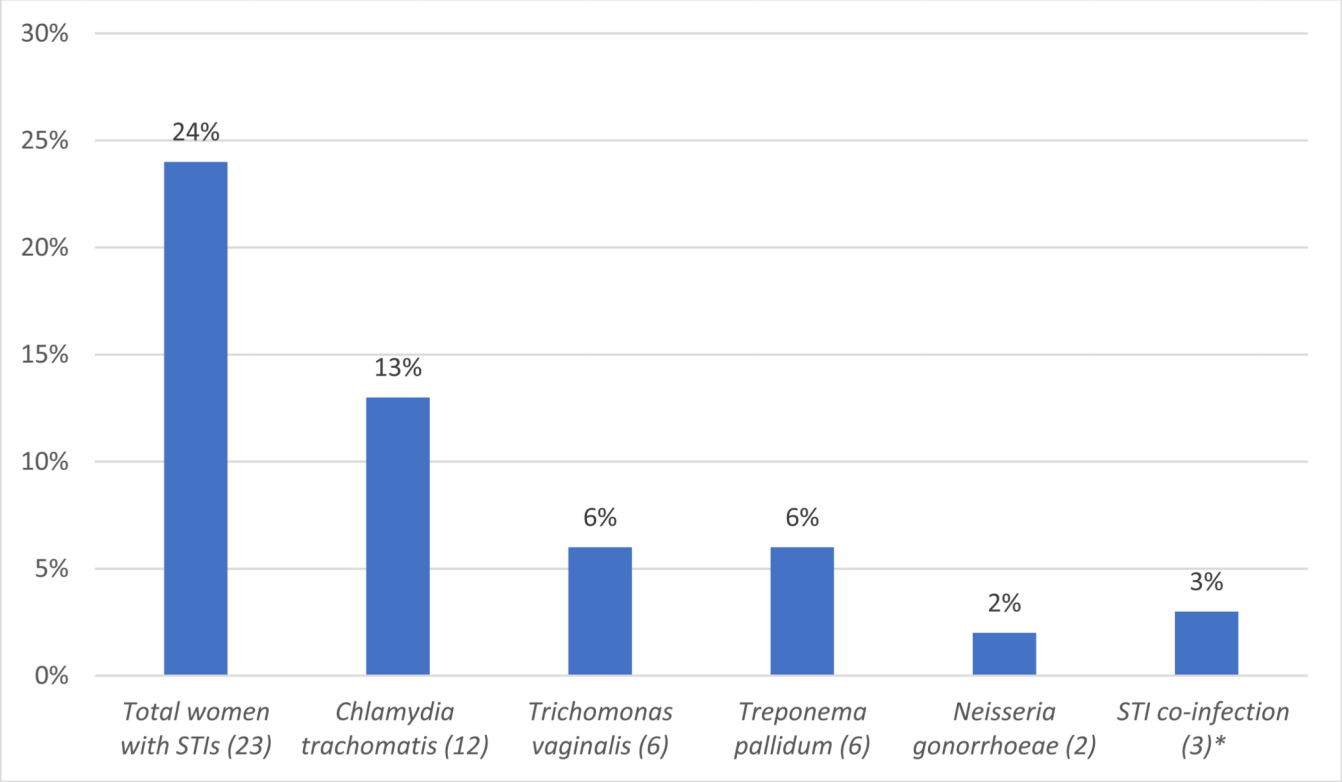

Figure 1:

STI prevalence among 94 women at-risk for HIV exposure, considering PrEP, and seeking safer conception care

*Two participants with chlamydia/syphilis coinfection and one participant with chlamydia/trichomoniasis coinfection

Table 1:

Demographics among 94 women at-risk for HIV acquisition, considering PrEP, and seeking safer conception care - with STI compared to those without STI

Total participants (n=94)	Total	Total		Women with STI (n=23)		Women without STI (n=71)		p-value
		N Median	(%) [IQR]	N Median	(%) [IQR]	N Median	(%) [IQR]	
Median age [IQR]	**94**	**30**	**(26–34)**	**27**	**(24–31)**	**30**	**(27–34)**	**0.02**
Education	94							1.00
no school or primary school		47	(50%)	12	(52%)	35	(49%)	
secondary school or above		47	(50%)	11	(48%)	36	(51%)	
Employment	94							0.18
part-time, full-time, or self-employed		68	(72%)	14	(61%)	54	(76%)	
not employed		26	(28%)	9	(39%)	17	(24%)	
Relationship status	92							0.60
Married or living as married		87	(95%)	21	(91%)	66	(96%)	
Has boyfriend		5	(5%)	2	(9%)	3	(4%)	
Median age difference between primary partner and participant in years [IQR]	92	6	(2–11.5)	7	(2–11)	6	(2–12)	0.96
Median household monthly income $USD [IQR]	94	$40	($16 – $81)	$27	($13 – $81)	$40	($22 – $81)	0.41
Home ownership	94	38	(40%)	6	(26%)	32	(45%)	0.14
Median number of pregnancies	94	3	(2 – 4)	2	(2 – 3)	3	(2 – 4)	0.21
Median number of livebirths	87*	2	(1 – 3)	2	(1 – 2)	2	(1 – 3)	0.26
Prior miscarriage	87*	38	(44%)	6	(32%)	32	(47%)	0.30
Prior stillbirth	**87***	**10**	**(11%)**	**5**	**(26%)**	**5**	**(7%)**	**0.04**
Median total fertility score[14]**	94	1	(0 – 2)	1	(0 – 3)	1	(1 – 2)	0.57
Prior STI	**94**	**32**	**(34%)**	**3**	**(13%)**	**29**	**(41%)**	**0.02**
Partner with prior STI	93							0.19
Yes		26	(28%)	3	(13%)	23	(31%)	
I don’t know		11	(12%)	3	(13%)	8	(11%)	
No		56	(60%	17	(74%)	40	(58%)	
History of exchanging sex for goods	88	18	(20%)	6	(30%)	12	(18%)	0.34

Total participants (n=94)	Total	Total		Women with STI (n=23)		Women without STI (n=71)		p-value
		N Median	(%) [IQR]	N Median	(%) [IQR]	N Median	(%) [IQR]	
Current primary partner physically hurts or threatens	88	13	(15%)	4	(20%)	9	(13%)	0.48
≥2 sexual partner in the past 3 months	**94**	**8**	**(9%)**	**5**	**(22%)**	**3**	**(4%)**	**0.02**
Condomless sex during last sexual encounter with primary partner	92***	59	(64%)	18	(78%)	41	(59%)	0.13
Knowledge of primary partner's HIV status****	92***	70	(76%)	18	(78%)	52	(75%)	1.00
Feel vulnerable to HIV	**94**	**89**	**(95%)**	**19**	**(83%)**	**70**	**(99%)**	**0.01**
Started PrEP	94	88	(94%)	21	(91%)	67	(94%)	0.63
Sexual and relationship power scale[16]*****	94							0.34
Low score		47	(50%)	14	(61%)	33	(46%)	
Medium/high score		47	(50%)	9	(39%)	38	(54%)	

* Seven women reported no prior pregnancies

** The total fertility score is based on a summation of eight questions on menses, pelvic pain/surgery, and STI. The higher number indicates more risk of infertility.

*** Two women reported no sexual activity in the past three months

**** All participants who knew their primary partner's HIV status had partners living with HIV

***** The sexual and relationship power scale is a summation of 23 questions.

Table 2:

Factors associated with enrollment STI using unadjusted and adjusted multivariable linear regression among 94 women at-risk for HIV exposure, considering PrEP, and seeking safer conception care

Covariate	Unadjusted analysis			Adjusted analysis		
	Crude Odds Ratio	(95% CI)	p-value	Adjusted Odds Ratio	(95% CI)	p-value
Age	0.89	(0.78 – 1.02)	0.105	0.87	(0.77 – 0.99)	0.029
Employed	0.33	(0.77 – 1.37)	0.127	--		--
Home ownership	0.53	(0.13 – 2.06)	0.355	--		--
Prior stillbirth	4.28	(0.77 – 23.70)	0.096	5.04	(1.13 – 22.54)	0.034
Prior STI	0.35	(0.07 – 1.67)	0.186	--		--
Partner with prior STI	0.82	(0.32 – 2.10)	0.675	--		--
≥2 sexual partner in the past 3 months	2.51	(0.33 – 19.14)	0.374	--		--
Condomless sex during last sexual encounter with primary partner	2.58	(0.58 – 11.58)	0.215	--		--
Do not feel vulnerable to HIV	17.85	(1.17 – 273.12)	0.038	16.33	(1.12 – 237.94)	0.041