Published in final edited form as:

Int J STD AIDS. 2010 August ; 21(8): 549–552. doi:10.1258/ijsa.2010.010005.

Diagnosis of sexually transmitted infections and bacterial vaginosis among HIV-1-infected pregnant women in Nairobi

G Marx, MPH^{*}, G John-Stewart, MD, PhD^{*,†,‡}, R Bosire, MBChB, MPH[§], D Wamalwa, MBChB, MMed, MPH^{**}, P Otieno, MBChB, MMed, MPH^{**}, and C Farquhar, MD, MPH^{*,†,‡}

^{*} Department of Medicine, University of Washington, Seattle, USA

[†] Department of Epidemiology, University of Washington, Seattle, USA

[‡] Department of Global Health, University of Washington, Seattle, USA

[§] Kenya Medical Research Institute, Nairobi, Kenya

^{**} Department of Paediatrics, University of Nairobi, Nairobi, Kenya

Summary

HIV-infected women with sexually transmitted infections (STIs) or bacterial vaginosis (BV) during pregnancy are at increased risk for poor obstetric outcomes. In resource-limited settings, diagnostic testing for STIs and BV is often not available and most pregnant women are managed using syndromic algorithms. As part of a Nairobi perinatal cohort, HIV-1-infected pregnant women were interviewed and samples were collected for STIs and BV testing. Diagnostic accuracy of STIs and BV by syndromic algorithms was evaluated with comparison to the reference standard. Among 441 women, prevalence of BV was 37%, trichomoniasis 16%, chlamydia 4%, syphilis 3% and gonorrhoea 2%. Significantly more women with STIs were aged 21-years-old, had not attended secondary school and had a history of STIs. Syndromic diagnosis of STIs and BV demonstrated a sensitivity of 45% and 57%, and positive predictive value of 30% and 42%, respectively. Among these HIV-infected, pregnant women, STIs and vaginal infections were common and syndromic diagnosis was insensitive, resulting in missed opportunities to intervene and improve infant and maternal health.

Keywords

syndromic diagnosis; STIs; BV; HIV; pregnancy

INTRODUCTION

Sexually transmitted infections (STIs) and bacterial vaginosis (BV) cause high rates of morbidity in the developing world, with women and their offspring bearing the majority of the disease burden.¹ STIs have been strongly associated with infertility, septic abortion, ectopic pregnancy and congenital infection² and a small to moderate association has been found between BV and adverse pregnancy outcomes such as low birthweight infants and preterm delivery.² In human immunodeficiency virus (HIV)-infected women, STIs may also increase the risk of mother-to-child transmission (MTCT) of HIV.³ Women in Tanzania who were co-infected with HIV and gonorrhoea were found to have a 5.5 times increased risk of intrauterine HIV transmission compared with women with HIV who did not have

gonorrhoea.⁴ Furthermore, women with HIV and either herpes simplex virus (HSV) or syphilis have also been found to be two to five times more likely to pass HIV to their infants during pregnancy or delivery, compared with HIV-infected women without HSV or syphilis.^{5,6}

The Centers for Disease Control and Prevention recommends that pregnant women be screened at their first antenatal visit for STIs, including chlamydia, gonorrhoea, HIV and syphilis, and that women at high risk undergo rescreening during the third trimester.⁷ Screening for BV is not currently recommended for asymptomatic women of either high- or low-risk for preterm labour;⁸ however, symptomatic women at high-risk should have access to BV diagnosis, as treatment may be indicated. In many resource-poor areas, limited access to laboratory facilities and lack of accurate, cheap diagnostic testing is a significant obstacle to the prompt recognition and treatment of STIs and most pregnant women never receive screening. Presently, when STI laboratory testing is not available, syndromic diagnostic algorithms advocated by the World Health Organization (WHO) are used, which assign diagnoses to women with symptoms and clinical signs consistent with STIs.¹ A major challenge to syndromic diagnosis of STIs in women is that many women with STIs are asymptomatic or do not seek treatment, rendering a clinical approach for STI detection exceptionally difficult.

In this study, we evaluated the prevalence and presentation of STIs and BV in a cohort of pregnant women infected with HIV-1 in Nairobi, Kenya. We also compare sociodemographic characteristics, symptoms and clinical signs in women with one or more STIs to women without STIs and BV. After identifying significant risk factors for STIs and BV, we developed syndromic diagnosis algorithms in this population. Our research aim was to determine the diagnostic validity of these algorithms in our study population of pregnant women infected with HIV-1.

METHODS

Study population and follow-up

The study was nested in a prospective cohort study of pregnant HIV-1-infected women who were recruited from antenatal clinics in Nairobi, Kenya from 1999 to 2002. To be eligible for enrolment, women had to be at least 18 years of age, have enzyme-linked immunosorbent assay (ELISA)-confirmed HIV-1 infection and present at less than 32 weeks gestation. Eligible women were enrolled into the cohort after provision of informed consent. The study was approved by the University of Washington Institutional Review Board and the University of Nairobi Ethics Review Committee.

At enrolment, medical history and sociodemographic information were obtained by interview and questionnaire and at 32 weeks gestation, a complete physical exam was performed with collection of blood and cervicovaginal swabs for laboratory STI and BV diagnosis. Women were treated syndromically according to published World Health Organization STI treatment guidelines and any definitive diagnosis of STIs not covered by syndromic treatment was treated at their 34-week gestation study visit. Women were subsequently seen at 36 weeks, then weekly until delivery and monthly for 12 months postpartum with their infants.

Laboratory assays

Reference standards for the diagnosis of syphilis, trichomoniasis, gonorrhoea, chlamydia and BV were standardized and validated laboratory tests. Diagnosis for syphilis was by rapid plasma reagin test (Becton and Dickinson, Franklin Lakes, NJ, USA) with confirmation by *Treponema pallidum* haemagglutination assay (Randox Laboratories Ltd,

Crumlin, UK). *Trichomonas vaginalis* (TV) in-pouch culture testing was performed on vaginal swabs using TV analyte-specific reagents with APTIMA General Purpose Reagents (Gen-Probe, San Diego, CA, USA). Testing of cervical swabs for *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) was performed using polymerase chain reaction nucleic acid amplification and hybridization assay for detection of NG/CT primers (Amplicor® CT/NG test, Roche Molecular Systems Inc, Branchburg, NJ, USA). BV was diagnosed using Nugent criteria, which relies on the identification of categories of vaginal microflora based on quantitative assessment of a Gram-stained vaginal smear. A score of 7–10 on Gram stain smear was considered positive for BV.

Statistical analyses

Data analysis was conducted using the Statistical Package for Social Sciences for Windows (version 10.0; SPSS Inc, Chicago, IL, USA). For this study, STI was defined as one or more of chlamydia, gonorrhoea, syphilis and trichomoniasis. Univariate analysis was conducted using two-tailed *t*-tests, chi-squared tests and Mann-Whitney U tests to identify socio-demographic factors, symptoms and clinical signs significantly associated with the presence of one or more STIs. Crude odds ratios (OR) were determined with corresponding 95% confidence intervals (CI). Variables that were significant at $P < 0.10$ in univariate analyses were selected for multivariate analysis. Based on these significant factors, algorithms for syndromic diagnosis of STIs and BV were developed. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of these algorithms were then determined by comparison to the reference standard outcomes and 95% CI were calculated. For all statistical analysis, a P value of < 0.05 was considered significant.

RESULTS

Cohort description

Of the 463 women enrolled in the parent cohort, 441 (95%) completed microbial exam with either a positive or negative result and were included in the present analysis. Median age was 25 years (interquartile range [IQR] 22–28), with 60 (13%) under 21 years of age. Single relationship status was reported by only 22 (5%) women and 344 (80%) stated they had been in the current relationship for more than one year. Current relationship duration was four years (IQR 2–7) on average and 262 (60%) women had only a primary school education. Median CD4 count was 433 (IQR 306–614) cells/ μ L and CD4 less than 250 cells/ μ L were found in 76 (17%) women.

Sexual history

The median age at sexual debut was 17 (IQR 16–19) and the number of lifetime sexual partners was 3 (IQR 2–4). Of the 398 women who responded, only two ($< 1\%$) reported more than one sexual partner during their current pregnancy. Just over half (55%) recounted prior use of contraception, with only 20 (4%) women reporting prior use of condoms. A history of exchanging sex for material goods was reported by seven (2%) women and a prior STI was reported by 64 (14%).

Clinical signs, symptoms and diagnostic testing results

Of the 441 who underwent the reference standard diagnostic tests, 121 (27%) elected to not answer questions on the health questionnaire regarding symptoms of vaginal discharge. Of the 320 women who responded, 20 (6%) complained of abnormal vaginal discharge. Abnormal vaginal discharge was found on exam in 223 (51%) women. Genital ulcers were detected in 21 (5%) women and BV was identified in 156 (37%). Of the STIs, trichomoniasis was detected in 73 (16%) women, chlamydia in 19 (4%), syphilis in 11 (3%)

and gonorrhoea in seven (2%). One or more of these four STIs was diagnosed in 98 (22%) of the 450 women.

Risk assessment

Women with STIs were younger (24 versus 25 years, $P = 0.02$), had higher CD4 counts (521 versus 460 cells/ μL , $P = 0.03$) and tended to have more lifetime sexual partners (3.7 versus 3.3, $P = 0.08$) compared with women without any STIs. Compared with women without STIs, more women with STIs were younger than 21 (21% versus 11%, $P = 0.01$), had only a primary school education (70% versus 57%, $P = 0.03$) and had a history of a previous STI (20% versus 13%, $P = 0.05$) (see Table 1). No significant difference between the two groups was detected by the symptom frequency of vaginal discharge. On physical exam, no significant difference was found between the two groups in the prevalence of abnormal vaginal discharge, genital warts or genital ulcers.

When compared with women without BV, women with BV had higher CD4 counts (493 versus 454 cells/ μL , $P < 0.01$) and had more abnormal vaginal discharge on exam (57% versus 47%, $P = 0.05$) but did not differ significantly by symptoms of vaginal discharge or vulvitis.

For women with one or more STIs, self-reported symptoms of vaginal discharge and vulvitis had PPVs of less than 50% (25% and 40%, respectively) while the specificities of both were greater than 90% (94% and 98%, respectively) (see Table 2). Abnormal vaginal discharge on exam had a PPV of 25% and a specificity of 51%. The sociodemographic factors that were significantly associated with the presence of STIs were age < 21 , a history of STI and lack of advanced education. Each of these risk factors had a PPV of less than 40%. The presence of all three sociodemographic factors showed a PPV of 78% with a specificity of 99% and a sensitivity of 7%. The presence of abnormal vaginal discharge on exam and one or more of the risk factors had a PPV of 29% and a specificity of 70%.

Vaginal discharge on exam demonstrated a PPV of 42% for a diagnosis of BV with a sensitivity and specificity of just over 50% (57% and 53%, respectively). Symptomatic vaginal discharge had a PPV of 26%, sensitivity of 4% and specificity of 92% for diagnosis of BV.

DISCUSSION

Among this cohort of 'low-risk' pregnant, HIV-infected women in Nairobi, Kenya, one or more STIs was found in more than one in five women. STIs and BV prevalence rates found in this study were consistent with other published data from sub-Saharan Africa.^{9–12} As in other studies of this region, the presence of STIs was found to be significantly associated with young age and lack of secondary education.^{13,14} Women in our cohort were also more likely to have an STI if they had a history of an STI and a higher CD4 count. Abnormal vaginal discharge on exam was significantly associated with the presence of BV but not STIs.

The use of syndromic diagnostic algorithms using these risk factors performed poorly at detection and prediction of STIs and BV. The syndromic diagnosis algorithms advocated by the WHO for vaginal infections including BV and STIs often begin with a patient's complaint of vaginal discharge. Such algorithms were demonstrated to be of limited value among our study cohort, as very few women complained of vaginal discharge when asked (6.3%), despite high prevalence rates of BV (37%) and trichomoniasis (16%). Syndromic algorithms may have higher validity in other populations such as family planning and women clinics where patients present specifically due to reproductive health symptoms such

as vaginal discharge. Given that most STIs, including syphilis, chlamydia and gonorrhoea, do not typically present with abnormal vaginal discharge, syndromic algorithms based on this presenting symptom are more likely to miss these more consequential STIs than BV and trichomoniasis. Our study demonstrated the inadequacy of risk assessment for STIs; even with algorithms based on significant risk factors of STIs among our study cohort, we would at best have missed 25% of all cases of STIs.

A potential limitation of this study is that STI histories and self-reported risk behaviours may have been under-reported due to social acceptability bias in interviews with health-care workers. Sociodemographic and behavioural characteristics of the cohort may differ from the wider population, thus reducing the generalizability of the study. In sub-Saharan Africa, it has been frequently found that it is the behaviour of the male partner which places a woman at risk for STI acquisition.¹⁵ Risk assessment based on male characteristics would have been interesting; however, we were unable to do so based on high rates of missing partner data.

In HIV-infected individuals, untreated STIs have been shown to increase risk for MTCT of HIV and also to increase horizontal HIV transmission by augmenting HIV-1 viral shedding in the genital tract.^{16,17} Treatment of STIs has been demonstrated to reduce HIV shedding by at least two-fold,¹⁸ suggesting that effective treatment of STIs may reduce HIV transmission risk; however, treatment of HSV-2 with acyclovir surprisingly does not appear to reduce HIV transmission despite a reduction in ulceration and HIV viral load.¹⁹ However, it seems logical that targeting HIV-infected, pregnant women with current STIs, who are at high risk for both vertical and horizontal HIV transmission, may represent an opportunity for an efficient public health intervention.

To reduce maternal and child morbidity and mortality, a consistent and effective approach is needed to diagnose and treat STI and BV in the developing world during the vulnerable antenatal period. This study demonstrated the limited usefulness of syndromic diagnosis in a population of HIV-infected pregnant women in Nairobi. More accessible, simple and cost-effective STI diagnostic tests must be developed and utilized in resource-poor settings. This study supports that pregnant HIV-infected women, a population with high rates of STI and high risk of HIV transmission, represent a key group that should be prioritized for diagnostic STI testing.

Acknowledgments

NIH/NICHD HD34123 provided funding for the parent study. Support for G Marx and funding for the present study was provided by the NIH TL1 Multidisciplinary Predoctoral Clinical Research Training Program. Overseas support was provided by the Fogarty International Center through the University of Washington AITRP (D43 TW000007). This research was supported by the University of Washington Center for AIDS Research (CFAR), an NIH funded programme (P30 AI027757), which is supported by the following NIH institutes and centres (NIAID, NCI, NIMH, NIDA, NICHD, NHLBI, NCCAM).

References

1. World Health Organization. Sexually transmitted and other reproductive tract infections. 2005;1:11–21.
2. Moodley P, Sturm A. Sexually transmitted infections, adverse pregnancy outcome and neonatal infection. *Sem Neonat* 2000;5:255–69.
3. Wabire-Mangen F, Gray R, Mmiro F, et al. Placental membrane inflammation and risks of maternal-to-infant transmission of HIV-1 in Uganda. *J Acquir Immune Defic Syndr* 1999;22:379–85. [PubMed: 10634200]
4. Fawzi W, Msamanga G, Renjifo B, et al. Predictors of intrauterine and intrapartum transmission of HIV-1 among Tanzanian women. *AIDS* 2001;15:1157–65. [PubMed: 11416718]

5. Drake A, John-Stewart G, Wald A, et al. Herpes simplex virus type 2 and risk of intrapartum human immunodeficiency virus transmission. *J Obstet Gynaecol* 2007;109:403–9.
6. Mwapasa V, Rogerson S, Kwiek J, et al. Maternal syphilis infection is associated with increased risk of mother-to-child transmission of HIV in Malawi. *AIDS* 2006;20:1869–77. [PubMed: 16954728]
7. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines. *MMWR* 2006;55:6–8.
8. U. S. Preventive Services Task Force. Screening for bacterial vaginosis in pregnancy to prevent preterm delivery: U.S. preventive services task force recommendation statement. *Ann Intern Med* 2008;148:214–19. [PubMed: 18252683]
9. Tann C, Mpairwe H, Morison L, et al. Lack of effectiveness of syndromic management in targeting vaginal infections in pregnancy in Entebbe, Uganda. *Sex Transm Infect* 2006;82:285–9. [PubMed: 16877576]
10. Thomas T, Choudhri S, Kariuki C, Moses S. Identifying cervical infection among pregnant women in Nairobi, Kenya: limitations of risk assessment and symptom-based approaches. *Genitourin Med* 1996;72:334–8. [PubMed: 8976848]
11. Gerbase A, Rowley J, Heymann D, Berkley S, Piot P. Global prevalence and incidence estimates of selected curable STDs. *Sex Transm Infect* 1998;74:S12–16. [PubMed: 10023347]
12. Mayaud P, Uledi E, Cornelissen J, et al. Risk scores to detect cervical infections in urban antenatal clinic attenders. *Sex Transm Infect* 1998;74:S139–46. [PubMed: 10023365]
13. Aboyeji A, Nwabuisi C. Prevalence of sexually transmitted diseases among pregnant women in Ilorin, Nigeria. *J Obstet Gynaecol* 2003;23:237–639.
14. Rassjo E, Mirembe F, Darj E. Vulnerability and risk factors for sexually transmitted infections and HIV among adolescents in Kampala, Uganda. *AIDS Care* 2006;18:710–16. [PubMed: 16971279]
15. Chersich M, Rees H. Vulnerability of women in southern Africa to infection with HIV: biological determinants and priority health sector interventions. *AIDS* 2008;22:S27–40. [PubMed: 19033753]
16. Ghys P, Fransen K, Diallo M, et al. The associations between cervicovaginal HIV shedding, sexually transmitted diseases and immunosuppression in female sex workers in Abidjan, Cote d'Ivoire. *AIDS* 1997;11:F85–93. [PubMed: 9342059]
17. Wright T, Subbarao S, Ellerbrock T, et al. Human immunodeficiency virus 1 expression in the female genital tract in association with cervical inflammation and ulceration. *Am J Obstet Gynecol* 2001;184:279–85. [PubMed: 11228474]
18. McClelland R, Wang C, Mandaliya K, et al. Treatment of cervicitis is associated with decreased cervical shedding of HIV-1. *AIDS* 2001;15:105–10. [PubMed: 11192850]
19. Celum C, Wald A, Lingappa J, et al. Acyclovir and transmission of HIV-1 from persons infected with HIV-1 and HSV-2. *N Engl J Med* 2010;362:427–39. [PubMed: 20089951]

Table 1

Cohort characteristics of women who were not diagnosed with STI compared with women who were diagnosed with one or more STIs

Characteristic (N = 450)	No STIs* [n, (%)]	STIs [n, (%)]	OR	95% CI	P
Age < 21	39 (11.1)	21 (21.4)	2.19	1.22–3.93	0.01
Current relationship >1 year [†]	270 (81.1)	74 (77.1)	0.79	0.45–1.36	0.39
Primary education only [‡]	198 (57.2)	67 (69.8)	1.73	1.06–1.81	0.03
Regular employment	103 (29.3)	21 (21.4)	0.66	0.39–1.13	0.12
History of accepting material goods for sex	4 (1.1)	3 (3.1)	2.73	0.60–12.42	0.18
Prior use of condoms in lifetime	17 (4.8)	3 (3.1)	0.62	0.18–2.17	0.45
Single relationship status	19 (5.4)	3 (3.1)	0.55	0.16–1.91	0.34
History of STIs in lifetime	44 (12.5)	20 (20.4)	1.80	1.00–3.22	0.05
Abnormal vaginal discharge on exam [§]	167 (48.5)	56 (57.7)	1.45	0.92–2.28	0.11
Genital warts seen on exam [§]	24 (7.0)	4 (4.1)	0.57	0.19–1.69	0.31
Complaint of vaginal discharge**	15 (6.1)	5 (6.8)	1.14	0.40–3.24	0.81
Complaint of vulvitis [§]	6 (1.7)	4 (4.1)	2.42	0.67–8.77	0.16

STI = sexually transmitted infections; CI = confidence interval; OR = odds ratio

* STIs is defined as one or more of trichomoniasis, gonorrhoea, chlamydia or syphilis on diagnostic testing

[†] n = 429

[‡] n = 442

[§] n = 441

** n = 320

Table 2

Performance estimates of syndromic diagnosis algorithms for women with STIs

Symptom	Women with STIs* [n (%)]	N = 98	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Symptom						
Complaint of vaginal discharge	5 (6.8)		6.8 (2.5–15.9)	93.9 (90.0–96.4)	25.0 (9.6–49.4)	77.3 (72.1–81.9)
Complaint of vulvitis	4 (4.1)		4.1 (1.3–10.8)	98.3 (96.1–99.3)	40.0 (13.7–72.6)	78.4 (74.2–82.2)
Clinical sign						
Abnormal vaginal discharge on exam	56 (57.7)		57.7 (47.3–67.6)	51.5 (46.0–56.8)	25.1 (19.7–31.4)	81.2 (75.2–86.0)
Cervical ulcer seen on exam	4 (4.1)		4.1 (1.3–10.8)	99.1 (97.3–99.8)	57.1 (20.3–88.2)	78.6 (74.3–82.3)
Risk factor						
Age < 21	21 (21.4)		21.4 (14.0–31.1)	88.9 (85.1–91.9)	35.0 (23.4–48.5)	80.3 (75.9–84.0)
History of STIs in lifetime	20 (20.4)		20.4 (13.2–30.0)	87.5 (83.5–90.7)	31.3 (20.6–44.2)	79.8 (75.4–83.6)
Primary education only	67 (69.8)		69.8 (59.4–78.5)	42.8 (37.5–48.2)	25.3 (20.3–31.0)	83.6 (77.1–88.6)
Syndromic algorithm						
All three above risk factors	7 (7.1)		7.1 (3.2–14.7)	99.4 (97.7–99.9)	77.8 (40.2–96.1)	79.4 (75.2–83.0)
Any one of above three risk factors	73 (74.5)		74.5 (64.5–82.5)	35.5 (30.6–40.8)	24.3 (19.7–29.7)	83.3 (76.2–88.7)
Complaint of vaginal discharge + any one of above risk factors	4 (4.1)		4.1 (1.3–10.7)	97.7 (95.4–98.9)	33.3 (11.3–64.6)	78.5 (74.3–82.2)
Abnormal vaginal discharge on exam + any one of above risk factors	44 (44.9)		44.9 (34.9–55.3)	69.9 (64.8–74.6)	29.3 (22.3–37.4)	82.0 (77.1–86.1)

STI = sexually transmitted infections; CI = confidence interval; NPV = negative predictive value; PPV = positive predictive value

* STIs (sexually transmitted infections) is defined as one or more of trichomoniasis, gonorrhoea, chlamydia or syphilis on diagnostic testing