Prevalence and Risk Factors for Syphilis and Hepatitis B Co-Infection Among Newly-Diagnosed HIV-Infected Adults in Durban, South Africa

Elisabeth Brandstetter

A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Public Health

University of Washington

2017

Committee:

Paul Drain

Renee Heffron

Program Authorized to Offer Degree:

Epidemiology

University of Washington

Abstract

Prevalence and Risk Factors for Syphilis and Hepatitis B Co-Infection Among Newly-Diagnosed HIV-Infected Adults in Durban, South Africa

Elisabeth Brandstetter

Chair of the Supervisory Committee:
Paul Drain, MD, MPH, FACP
Assistant Professor, Department of Global Health

Objective

To estimate the prevalence of and risk factors for co-infection with syphilis or hepatitis B (HBV) among newly-diagnosed HIV-infected adults in an urban township of KwaZulu-Natal.

Methods

We conducted a cross-sectional study of newly-diagnosed HIV infected adults at an outpatient HIV clinic in Durban, South Africa. Baseline demographics, socio-economic indicators, behavioral factors, substance use history, mental health, and historical clinical indicators were collected prior to HIV testing. Individuals were tested for syphilis using the rapid plasma reagin and were tested for HBV using a blood antibody test. We estimated prevalence and used stepwise logistic regression to elucidate risk factors for syphilis or HBV co-infection with HIV.

Results

Among 1,900 HIV-infected adults, prevalence of syphilis and HIV co-infection was 4.0% (95% CI: 3.0%-5.3%), and prevalence of HBV co-infection was 8.8% (95% CI: 7.3%-10.6%). Syphilis co-infection was significantly associated with being <30 years old (aOR = 1.93, 95% CI: 1.03-3.60). HBV co-infection was independently associated with being male (aOR = 1.97, 95% CI: 1.29-3.01) and having a CD4 count ≤200 cells/μL (aOR = 2.29, 95% CI: 1.09-4.83) after adjusting for sex, age, and CD4 count.

Conclusions

A more universal screening program could identify many HIV-infected individuals with either syphilis or HBV co-infection at the time of HIV testing in resource-limited settings of sub-Saharan Africa.

Introduction

Among the 35 million HIV-infected people worldwide, co-infection with syphilis or hepatitis B virus (HBV) can lead to increased HIV transmission and morbidity [1]. Co-infection with syphilis is associated with an increased risk of HIV transmission and acquisition by modifying viral loads and CD4 counts [2]. Among HIV-infected individuals, syphilis infections are more virulent and more likely to be asymptomatic, which can lead to delays in treatment [3,4]. Similarly, progression of HBV infection and complications, including cirrhosis and hepatocellular carcinoma, can be accelerated in HIV-infected individuals and leads to increased morbidity and mortality [5,6]. Individuals co-infected with HIV and HBV are also more likely to develop chronic HBV in comparison to HIV-negative individuals [7–9]. There is uncertainty in the literature as to whether there is any association between HBV infection and CD4 count [10].

In the United States, the CDC recommends that certain high-risk groups— men who have sex with men, pregnant women, and immunocompromised individuals—be regularly screened for syphilis and chronic HBV [11–14]. In resource-limited settings where a more universal screening program is unrealistic, only pregnant women are routinely screened for syphilis and there is no routine screening for HBV, resulting in less than 5% of infected individuals aware of their HBV diagnosis [15,16] However still, these population groups are not always tested. For example, in South Africa, only 74.5% of prenatal care attendees were tested for syphilis at their first prenatal care visit in 2010 [17]. The implementation of a comprehensive screening program could help to better understand risk factors for syphilis and HBV infection.

Our objective was to identify the prevalence of and elucidate risk factors for co-infection with syphilis or HBV among HIV-infected adults in an urban township of Durban, South Africa. This study aims to inform resource allocation towards a more comprehensive and efficient screening program for both syphilis and HBV within HIV clinics.

Methods

Participants

We conducted a cross-sectional cohort study of HIV-infected adults in a poor urban township of KwaZulu-Natal, South Africa. The study participants were recruited in the outpatient department of iThembalabantu Clinic in Umlazi from September 2013 to February 2017. The iThembalabantu Clinic is an urban outpatient HIV clinic located in the Umlazi Township of Durban, a highly HIV-endemic area in the Province of KwaZulu-Natal. Established in 2001 by the Network of AIDS Communities in South Africa (NetComSA) and the AIDS Healthcare Foundation Global Community (AHF-GI), the clinic provides comprehensive testing, treatment, and care to HIV-infected individuals.

Adults were enrolled in the study if they were ≥ 18 years old, HIV seropositive and ART naïve, and newly diagnosed with HIV at the iThembalabantu Clinic. We excluded individuals if they were pregnant or had received anti-fungal therapy within three months of study enrollment. All participants provided written, informed consent in either English or Zulu. The study was approved by the institutional review board of the University of Washington in Seattle (IRB #49563) and the Medical Research Ethics Committee of the University of Kwa-Zulu Natal in Durban (Protocol #BF052/13).

Data Collection

Upon enrollment and before HIV testing, a research assistant collected socio-demographic, economic and behavioral factors, HIV testing history, and their perception of acquiring HIV. Additional questions relating to depression, anxiety, and HIV stigma were administered prior to HIV testing since these responses may be significantly biased after receiving an HIV test result. Those participants who tested HIV-positive had a routine clinical assessment for signs and symptoms of disease, a clinical examination, and baseline laboratory

testing, including CD4 count. Trained nurses collected blood samples that were then sent to National Health Laboratory Service Lab at Prince Mysheni Memorial Hospital to test for CD4 count. A trained study nurse collected specimens, measured vital signs, and interviewed the patient to collect baseline clinical information.

Depression symptoms as experienced in the two weeks preceding recruitment were assessed using the 9-item Patient Health Questionnaire (PHQ-9) scale. The PHQ-9 scale has been used to measure depression among HIV-infected populations in Kenya [18], and the US [19]. Each response is scored on a 4-point Likert scale (0 for "Not at all" to 4 for "Nearly every day"), with all responses being summed into a severity score for each participant. Anxiety was measured using Generalized Anxiety Disorder scale (GAD-7), and the anxiety severity score was calculated in a manner similar to the PHQ-9 scale. The depression and anxiety scores were analyzed using severity score cut-offs described for the PHQ-9 and GAD-7 scales, respectively [20,21]. Both anxiety and depression were defined as having a severity score greater than five. HIV-related stigma was evaluated using 12 questions that explored attitudes towards people living with HIV/AIDS, fear related to HIV-acquisition in community, ideas about loss of social status, and being subjected to verbal abuse. Responses to these questions were ranked on a 3-point Likert scale. (1 for "Yes/Totally agree", 2 for "Don't know/Somewhat agree" and 3 for "No/Don't agree") and summed up for each individual to create a stigma score [22]. Higher scores for depression and anxiety indicated greater emotional distress, while higher scores for stigma indicated higher HIV-related stigma. HIV-related stigma was defined as a stigma score greater than zero.

Statistical Analyses

The primary outcomes of interest for this study were prevalence of syphilis or HBV infection at the time of HIV diagnosis. Syphilis cases were defined as individuals who tested

positive for syphilis with the rapid plasma reagin (RPR). Similarly, HBV cases were defined as individuals who were Hepatitis B surface antigen positive (HBsAg+) using a blood antibody test. Laboratory testing was performed at the National Health Laboratory Service at Prince Mysheni Hospital in Umlazi.

We calculated descriptive univariate statistics for all demographic and clinical characteristics of interest to assess distributions among the newly-diagnosed HIV-positive cohort. Age as a risk factor was evaluated as continuous rather than categorical in order to enhance statistical power. Using a bivariate logistic regression, we generated crude odds ratios, 95% confidence intervals, and likelihood ratio p-values for potential syphilis and HBV risk factors. We also conducted a stepwise multivariate logistic regression. Variables were initially included in the model if their p-value was ≤ 0.15, then subsequently removed if their p-value dropped below this threshold. We reported odds ratios with 95% confidence intervals using an alpha of <0.05 for significance. STATA (StataCorp, Version 14, College Station, TX, USA) was used to perform all statistical analyses.

Results

Demographic Characteristics

Among the 1,900 HIV-infected individuals enrolled into the study, 1,235 (65.0%) were screened for both syphilis and HBV and therefore included in these analyses. Among those screened, 711 (57.6%) were female, and the median cohort age was 31.7 years (Table 1). The majority (92.2%) of the cohort was unmarried, 82.7% had a household income of less than 2,000 South African Rand (~US $150) per month, and 74.2% had completed at least primary school. Approximately half (48.7%) of the cohort had a normal BMI (18.6-24.9 kg/m^2). Finally, of the 747 (60.5%) of participants for whom CD4 counts were measured, the median was 254 cells/μL (interquartile range 136-376 cells/μL).

Behavioral, Substance Use, and Mental Health Characteristics

Most participants (63.5%) reported having been previously tested for HIV. Of the 400 individuals assessed, 84.0% reported to always using a condom in the past three months of sexual activity. Only 24.6% of the 399 male respondents were circumcised. Among the 1,235 participants, 24.7% reported to ever smoking cigarettes, 36.8% reported to ever drinking alcohol, and 13 individuals (1.0%) reported injecting illicit drugs such as cocaine or heroin. Based on the GAD-7, 24.6% of enrollees reported any anxiety, 26.6% reported any depression based on the PHQ-9, and 42.1% reported any HIV stigma.

Prevalence of Syphilis and Hepatitis B Co-Infections with HIV

The estimated prevalence of syphilis in this cohort was 4.0% (95% CI: 3.0%-5.3%) and was not significantly higher in men than women (4.7% versus 3.5%) (Fig. 1). Prevalence did vary by age, with 5.4% prevalence among individuals <30 years old and 3.0% prevalence among individuals over 30. The estimated prevalence of HBV in this cohort was 8.8% (95% CI: 7.3%-10.6%) (Fig. 2). Co-infection was significantly increased among men compared to women (12.1% versus 6.3%). There were no trends in the distribution of age with respect to HBV co-infection. Prevalence was 8.1% among those <30 years old and 9.3% among those ≥30 years old. There were 6 individuals who had syphilis, HBV, and HIV co-infections, but there was no significant association between syphilis and HBV infection.

Risk Factors for Syphilis and HIV Co-Infection

In univariate analyses, individuals with an overweight/obese BMI (uOR = 0.48, 95% CI: 0.25-0.94 were at decreased risk for syphilis co-infection and individuals under 30 years old (uOR = 1.93, 95% CI: 1.03-3.60) were at an increased risk of co-infection. In a multivariate model adjusted for sex, age, and BMI, age under 30 was associated with a higher risk of syphilis co-infection (aOR = 1.93, 95% CI: 1.03-3.60). While BMI overall continued to be a statistically

significant predictor of co-infection, neither being underweight (aOR = 0.19, 95% CI: 0.03-1.40) or overweight/obese (aOR = 0.55, 95% CI: 0.28-1.11) were independently associated with syphilis co-infection.

Risk Factors for HBV and HIV Co-Infection

In univariate analyses, being male, smoking cigarettes, drinking alcohol, having an overweight/obese BMI, and having a CD4 count ≤200 cells/μL were significant predictors of HBV co-infection (Table 3). Males were 2.04 times more likely to have co-infection than females (95% CI: 1.35-3.09), cigarette smokers were 1.62 times more likely than non-smokers (95% CI: 1.05-2.50), alcohol drinkers were 1.66 times more likely than non-drinkers (95% CI: 1.10-2.49), individuals with an overweight/obese BMI were 0.61 times more likely (95% CI: 0.39-0.95), and individuals with a CD4 count ≤200 cells/μL were 2.48 times more likely to be co-infected in comparison to individuals with higher CD4 counts (95% CI: 1.18-5.21). When adjusting for sex, age, and CD4 count in the final multivariate model, being male was still associated with an increased risk of co-infection (aOR = 1.97, 95% CI: 1.29-3.01) and having a CD4 count ≤200 cells/μL (aOR = 2.29, 95% CI: 1.09-4.83). Of the eight individuals with a history of injection drug use who were evaluated for HBV, only one tested positive.

Discussion

In a poor, urban township of South Africa, the prevalence of both syphilis and HBV was moderate at the time of HIV diagnosis. Syphilis co-infection was associated with decreased age and normal BMI, but had no significant difference between males and females. Co-infection with HBV was associated with being male and having a CD4 count less than 200 cells/μL, but was not associated with age. HBV was not associated with injection drug use, a practice that was very low in this setting. A more universal screening program could identify many HIV-infected

individuals with either syphilis or HBV co-infection at the time of HIV testing in resource-limited settings of sub-Saharan Africa.

Few studies have investigated risk factors for syphilis and HIV co-infection in a low-resource setting (20, 21). To our knowledge, none of these studies have examined syphilis or HBV at HIV diagnosis, as most are retrospective in nature. Studies conducted in Nigeria and Ethiopia, respectively, found a syphilis co-infection prevalence of 2.1%-7.3%, but these studies were conducted among hospitalized patients (22, 23). An evaluation of syphilis co-infection among fishing communities in Uganda found a prevalence of 4.3% among 1,618 people tested. Similar to our study, they found that younger age was independently associated with higher risk of co-infection, and there was no significant difference in prevalence between men and women [24]. To our knowledge, no other studies have found an association between overweight/obese BMI and syphilis/HIV co-infection.

We found that the prevalence of HBV and HIV co-infection was consistent with findings from similar epidemiologic studies in South Africa and elsewhere on the continent, though prevalence varied by geographical location. A study of women recruited from antenatal and pediatric clinics in Durban and Kimberley, South Africa, found the prevalence of co-infection to be 9.7% among 507 people [27]. However, their study targeted high-risk individuals and may not represent a general population presenting for HIV testing. Similar to our study, they found a weak association between HBV/HIV co-infection and lowered CD4 count [27]. Another study conducted in a government HIV clinic in Johannesburg found the HBV/HIV co-infection prevalence to be approximately 4.8%, with prevalence slightly more elevated in men compared to women, consistent with our findings [28].

In South Africa, there is no routine screening program for syphilis and HBV for adult males. Our study showed that men were at a slightly higher risk of co-infection, particularly HIV/HBV co-infection. In addition to a routine screening of women and children at high risk for vertical transmission, early detection and subsequent treatment of co-infection among men could largely alleviate population-level morbidity associated with these infections. Specifically, screening males for syphilis could reduce syphilis transmission to women, particularly those who are pregnant. Stabinski et al. examined the impact that a more universal HBV screening program could have on the burden of HIV/HBV morbidity, but acknowledged that more data was needed to demonstrate the cost-effectiveness of such a program [29]. Further, while individuals should receive the same treatment for HIV regardless of syphilis infection status, HIV co-infection with HBV requires special clinical management, and treatment may be further hampered by resistance to lamivudine [30–32].

Screening coverage rates in low-resource settings are particularly low due to access and affordability barriers for diagnostic testing. Coverage rates could be improved by utilizing point-of-care (POC) diagnostic tests, many of which are available for both syphilis and HBV. This would minimize the time between when an individual is tested and when results are received, thus allowing clinicians to make more prompt and accurate clinical decisions [33]. However, since test efficacy is dependent on the prevalence of infection, further research needs to be conducted to ensure that the benefits of improved clinical outcomes outweigh operational costs needed to administer the POC test.

This study had many strengths. To the best of our knowledge, this is the first study conducted in a low-resource setting that evaluated risk factors for syphilis and HBV at HIV-diagnosis. Additionally, we were able to collect robust data on a large sample size, particularly

on co-infected males, for which data is lacking in low-resource settings. Our study also had several limitations. First, because this was a cross-sectional study conducted at a single study clinic, the results are not generalizable outside of this clinic. Secondly, we had limited information on sexual behaviors, including a lack of data on the frequency of multiple sex partners, transactional sex, sex under the use of drugs and alcohol, age at sexual debut, type of sex partner and sexual activity, and number of recent sex partners. At the beginning of the study, participants were not asked any questions about their condom use habits. Several individuals who tested positive for HIV were not subsequently screened for syphilis or HBV, resulting in a potential underestimate of the prevalence of each of these infections. This may be the result of biases specific to this clinic in administering these tests, or patient stigma surrounding sexually transmitted infections. Finally, it is possible that there may have been a discrepancy between the prevalence of active versus latent syphilis co-infection or acute versus chronic HBV co-infection, but this information was not readily available for this study. While our study found an association between HBV infection and decreased CD4 count, we were not able to establish temporality in our study and cannot draw direct conclusions about this finding. HBV infection could further decrease CD4 count, but the association between lower CD4 count and co-infection could also be explained by an increased risk of HBV acquisition among HIV-infected individuals.

In conclusion, our study showed that decreased age and BMI were associated with increased risk of syphilis/HIV co-infection. Being male and having a CD4 count <200 cells/μL were both independently associated with HBV/HIV co-infection. We recommend that a more comprehensive screening of sexually transmitted infections, especially syphilis and HBV, be considered at HIV diagnosis in low-resource settings. Implementing such a screening program

could help to reduce comorbidities associated with these co-infections, especially by preventing the transmission of disease from undiagnosed males to females.

Funding

This work was supported by the Harvard Global Health Institute (PKD); the Fogarty International Clinical Research Scholars and Fellows Program at Vanderbilt University [R24 TW007988] (PKD); the Infectious Disease Society of America Education & Research Foundation and National Foundation for Infectious Diseases (PKD); Massachusetts General Hospital Executive Committee on Research (PKD); the Program in AIDS Clinical Research Training Grant [T32 AI007433] (PKD); the Harvard University Center for AIDS Research [P30 AI060354] (PKD); the National Institute of Allergy and Infectious Diseases [K23 AII08293] (PKD). The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health or other funding agencies.

Acknowledgments

We thank the women and men who participated in this study, the clinical sites for sharing their space, and the research staff and nurses who conducted the study.

Conflict of Interest Statement

We declare that we have no conflicts of interest.

References

1 Kourtis AP, Bulterys M, Hu DJ, *et al.* HIV-HBV Coinfection - A Global Challenge. *N Engl J Med* 2012;**366**:1749–52.

2 Buchacz K, Patel P, Taylor M, *et al.* Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections. *AIDS* 2004;**18**:2075–9. doi:10.1097/00002030-200410210-00012

3 Mandel G, Bennet J, Dolin R. Treponema pallidum (Syphilis). In: *Principles and Practice of Infectious Diseases*. 2005.

4 Karumudi U, Augenbraun M. Syphilis and HIV: a dangerous duo. *Expert Rev Anti Infect Ther* 2005;**3**:825–31.

5 Olawumi HO, Olanrewaju DO, Shittu AO, *et al.* Effect of hepatitis-B virus co-infection on CD4 cell count and liver function of HIV infected patients. *Ghana Med J* 2014;**48**:96–100.

6 Konopnicki D, Mocroft A, de Wit S, *et al.* Hepatitis B and HIV: prevalence, AIDS progression, response to highly active antiretroviral therapy and increased mortality in the EuroSIDA cohort. *AIDS* 2005;**19**:593–601. doi:10.1097/01.aids.0000163936.99401.fe

7 Hadler S, FN J, PM O, *et al.* Outcome of hepatitis B virus infection in homosexual men and its relation to prior human immunodeficiency virus infection. *J Infect Dis* 1991;**163**:454–9.

8 Bodsworth N, Cooper D, Donovan B. The influence of human immunodeficiency virus type 1 infection on the development of the hepatitis B virus carrier state. *J Infect Dis* 1991;**163**:1138–40.

9 Gatanaga H, Yasuoka A, Kikuchi Y, *et al.* Influence of prior HIV-1 infection on the development of chronic hepatitis B infection. *Eur J Clin Microbiol Infect Dis* 2000;**19**:237–9.

10 Matthews P, Geretti A, Goulder P, *et al.* Epidemiolgoy and impact of HIV coinfection with hepatitis B and hepatitis C viruses in Sub-Saharan Africa. *J Clin Virol* 2014;**66**:20–33.

11 Weinbaum CM, Williams I, Mast EE, *et al.* Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection. 2008.

12 CDC. Sexually Transmitted Diseases Treatment Guidelines. 2015.

13 Mendelson M, Kew M, Maartens G, *et al.* Management of HIV-Hepatitis B Co-Infection. *South Afr J HIV Med* 2011;:27–33.

14 Jooste P, van Zyl A, Adland E, *et al.* Screening, characterisation and prevention of Hepatitis B virus (HBV) co-infection in HIV-positive children in South Africa. *J Clin Virol* 2016;**85**:71–4. doi:10.1016/j.jcv.2016.10.017

15 WHO. Guidelines on Hepatitis B and C Testing. 2017.

16 Kuznik A, Lamorde M, Nyabigambo A, *et al.* Antenatal Syphilis Screening Using Point-of-Care Testing in Sub-Saharan African Countries : A Cost-Effectiveness Analysis. *PLOS Med* 2013;**10**. doi:10.1371/journal.pmed.1001545

17 WHO. Sexually Transmitted Infections. 2010.http://gamapserver.who.int/gho/interactive_charts/sti/anc_syphilis_test/atlas.html

18 Monahan PO, Shacham E, Reece M, *et al.* Validity / Reliability of PHQ-9 and PHQ-2 Depression Scales Among Adults Living with HIV / AIDS in Western Kenya. *J Gen Intern Med* 2009;**24**:189–97. doi:10.1007/s11606-008-0846-z

19 Crane P, Gibbons L, Willig J, *et al.* Measuring depression levels in HIV-infected patients

as part of routine clinical care using the nine-item Patient Health Questionnaire (PHQ-9). *AIDS Care* 2010;**22**:874–85. doi:10.1080/09540120903483034
20 Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. *J Gen Intern Med* 2001;**16**:606–13.
21 Spitzer RL, Kroenke K, Williams JBW, *et al.* A Brief Measure for Assessing Generalized Anxiety Disorder. *Arch Intern Med* 2006;**166**:1092–7.
22 Macpherson P, Webb EL, Choko AT, *et al.* Stigmatising Attitudes among People Offered Home- Based HIV Testing and Counselling in Blantyre , Malawi : Construction and Analysis of a Stigma Scale. *PLoS One* 2011;**6**. doi:10.1371/journal.pone.0026814
23 Todd J, Munguti K, Grosskurth H, *et al.* Risk factors for active syphilis and TPHA seroconversion in a rural African population. *Sex Transm Infect* 2001;**77**:37–45. doi:10.1136/sti.77.1.37
24 Asiki G, Mpendo J, Abaasa A, *et al.* HIV and syphilis prevalence and associated risk factors among fishing communities of Lake Victoria, Uganda. *Sex Transm Infect* 2011;**87**:511–5. doi:10.1136/sti.2010.046805
25 Nnoruka E, J EA. Evaluation of syphilis in patients with HIV infection in Nigeria. *Trop Med Int Heal* 2005;**10**:58–64.
26 Shimelis T, Lemma K, Ambachew H, *et al.* Syphilis among people with HIV infection in southern Ethiopia : sero-prevalence and risk factors. *BMC Infect Dis* 2015;**15**:1–7. doi:10.1186/s12879-015-0919-7
27 Matthews PC, Beloukas A, Malik A, *et al.* Prevalence and characteristics of hepatitis B virus coinfection among HIV-Positive women in South Africa and Botswana. *PLoS One* 2015;**10**:1–11. doi:10.1371/journal.pone.0134037
28 Firnhaber C, Reyneke A, Schulze D, *et al.* The prevalence of hepatitis B co-infection in a South African urban government HIV clinic. *South African Med J* 2010;**98**:541–4.
29 Stabinski L, Connor SO, Barnhart M, *et al.* Prevalence of HIV and hepatitis B virus co-infection in Sub-Saharan Africa and the potential impact and program feasibility of hepatitis B surface antigen screening in resource-limited settings. *J Acquir Immune Defic Syndr* 2015;**68**.
30 Karp G, Schlaeffer F, Jotkowitz A, *et al.* Syphilis and HIV co-infection. *Eur J Intern Med* 2009;**20**:9–13. doi:10.1016/j.ejim.2008.04.002
31 Luetkemeyer A. Hepatitis B and HIV Coinfection. HIV InSite Knowl. Base Chapter. 2010.http://hivinsite.ucsf.edu/InSite?page=kb-05-03-04#S6.2.2X
32 Bisceglie AM Di, Maskew M, Schulze D, *et al.* HIV-HBV coinfection among South African patients receiving antiretroviral therapy. *Antivir Ther* 2010;**15**:499–503. doi:10.3851/IMP1494.HIV
33 Drain PK, Hyle EP, Noubary F, *et al.* Diagnostic point-of-care tests in resource-limited settings. *Lancet Infect Dis* 2014;**14**:239–49. doi:10.1016/S1473-3099(13)70250-0

Table 1: Demographic and clinical characteristics of clinic attendees during enrollment period at an urban HIV clinic in Durban, South Africa (N=1,235).

Demographic & Clinical Characteristics	n (%)
Demographics	
Sex	
Female	711 (57.6)
Male	524 (42.4)
Age (years)	
< 30	502 (40.7)
≥ 30	733 (59.3)
Number of Children	
0	224 (18.2)
1+	1,009 (81.8)
Marital Status	
Married or Widowed/Divorced	96 (7.8)
Never Married	1,139 (92.2)
Distance from Nearest Health Clinic	
< 5 km	1,095 (88.8)
> 5 km	138 (11.2)
Socio-Economic	
Employed?	
No	705 (57.1)
Yes	530 (42.9)
Income (ZAR/month)	
< 2,000	1,006 (82.7)
≥ 2,000	210 (17.3)
Education	
None	319 (25.8)
Any	916 (74.2)
Behavioral Factors	
Times Previously Tested for HIV	
None	451 (36.5)
1-3	491 (39.8)
> 3	292 (23.7)
Partner tested for HIV	
No or Unknown Status	704 (57.2)
Yes, HIV negative	173 (14.1)
Yes, HIV positive	353 (28.7)
Frequency of Condom Use in Past 3 Months	

Always	336 (27.2)
Sometimes	56 (4.5)
Never	8 (0.7)
Missing	*385 (67.6)*
Substance Use	
Cigarette Smoking Status	
Never Used	929 (75.3)
Ever Used	304 (24.7)
Alcohol Consumption	
Never Used	779 (63.2)
Ever Used	453 (36.8)
Injection drug use (cocaine, heroin)	
Never Used	1,220 (99.0)
Ever Used	13 (1.0)
Mental Health	
Anxiety (GAD-7)	
None (< 5)	922 (75.4)
Any (≥ 5)	301 (24.6)
Depression (PHQ-9)	
None (< 5)	896 (73.4)
Any (≥ 5)	324 (26.6)
HIV stigma	
None	715 (57.9)
Any (> 0)	520 (42.1)
Historical Clinical Indicators	
Male Circumcision (n=526)	
No	301 (57.2)
Yes	98 (18.6)
Missing (for males)	127 (24.1)
Ever Tested Positive for TB?	
No	1,150 (93.1)
Yes	85 (6.9)
BMI (kg/m^2)	
Underweight (≤ 18.5)	92 (7.5)
Normal Weight (18.6-24.9)	601 (48.7)
Overweight/Obese (≥ 25.0)	541 (43.8)
Laboratory Testing	
CD4 Count at Baseline	
> 350 cells/μL	220 (17.8)
201-350 cells/μL	246 (19.9)

≤ 200 cells/μL	281 (22.8)
Missing	*488 (39.5)*
Syphilis Status	
Positive	44 (4.0)
Negative	1,058 (96.0)
Hepatitis B Status	
Positive	102 (8.8)
Negative	1,057 (91.2)

Figure 1: Prevalence of syphilis and HIV co-infection stratified by age group and sex (N=1,102).

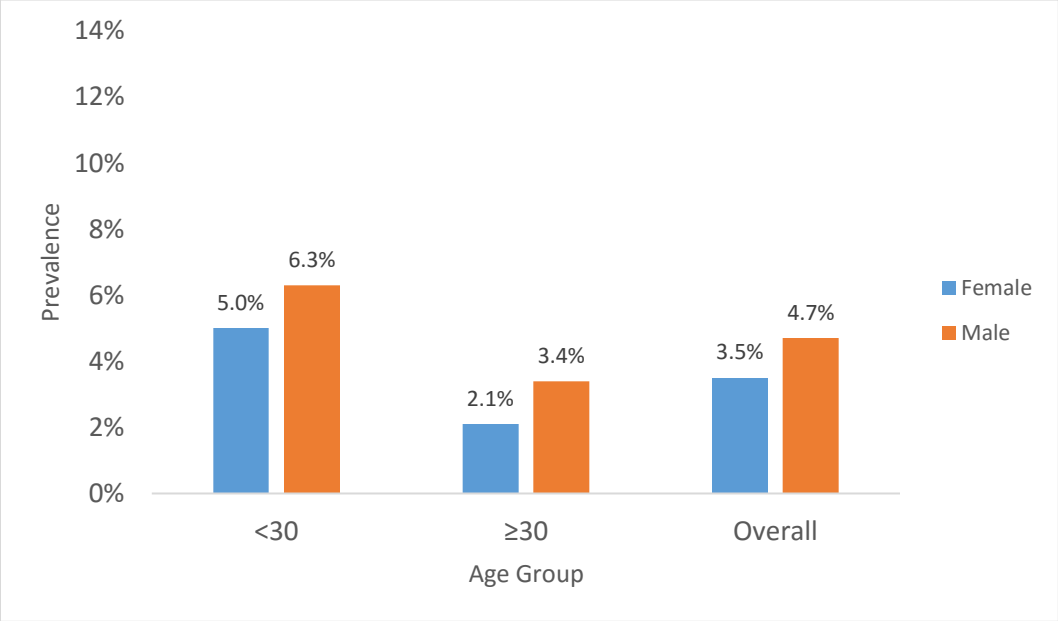

Figure 2: Prevalence of hepatitis B and HIV co-infection stratified by age group and sex (N=1,159).

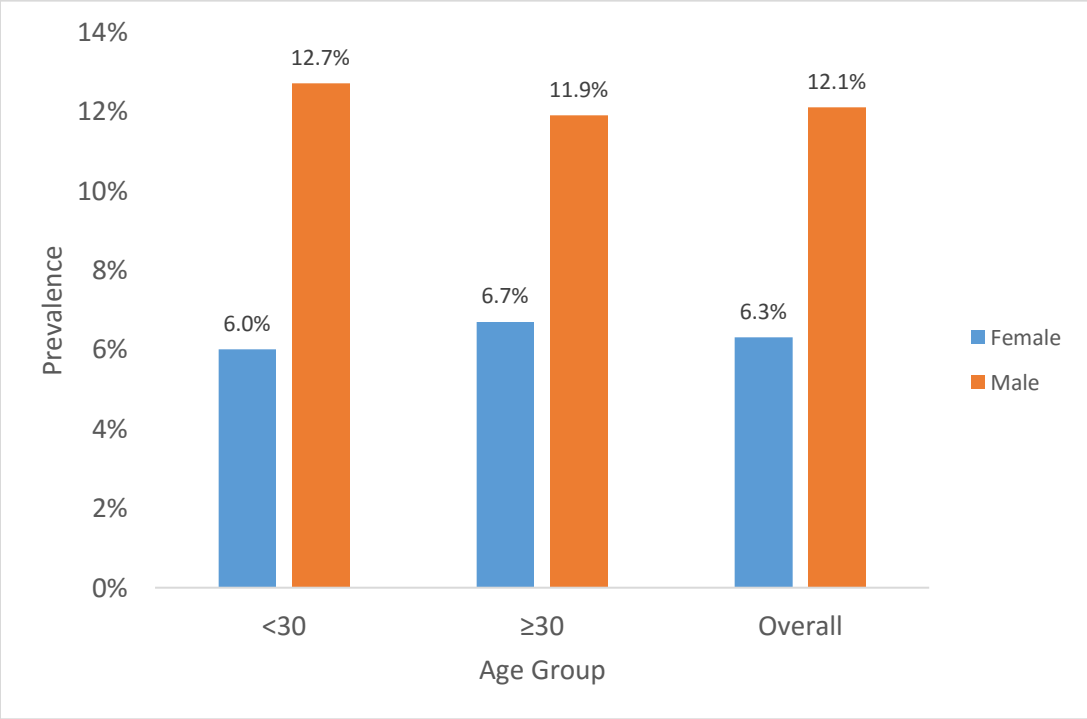

Table 2: Unadjusted and adjusted odds ratios of risk factors for prevalent syphilis at time of enrollment as diagnosed by rapid plasma reagin (N=1,102).

Covariates	# Positive/ Total at Risk (Prevalence)*	uOR (95% CI)	P-value	aOR (95% CI)	P-value
Demographics					
Sex			0.323		0.315
Female	22/631 (3.5)	Reference		Reference	
Male	22/471 (4.7)	1.36 (0.74-2.48)		1.39 (0.73-2.66)	
Age (years)			0.049		0.039
< 30	24/442 (5.4)	1.84 (1.00-3.37)		1.93 (1.03-3.60)	
≥ 30	20/660 (3.0)	Reference		Reference	
Number of Children			0.431		
0	10/204 (4.9)	Reference			
1+	33/896 (3.7)	0.74 (0.36-1.53)			
Marital Status			0.365		
Married or Widowed/Divorced	2/87 (2.3)	Reference			
Never Married	42/1,015 (4.1)	1.83 (0.44-7.71)			
Distance from Nearest Clinic			0.709		
< 5 km	38/970 (3.9)	Reference			
> 5 km	6/130 (4.6)	1.19 (0.49-2.86)			
Socio-Economic					
Employed?			0.473		
No	23/634 (3.6)	Reference			
Yes	21/468 (4.5)	1.25 (0.68-2.28)			
Education			0.457		
None	14/296 (4.7)	Reference			
Any	30/806 (3.7)	0.78 (0.41-1.49)			
Behavioral Factors					
Times Previously Tested for HIV			0.657		
None	16/404 (4.0)	Reference			

1-3	20/442 (4.5)	1.15 (0.59-2.25)	
> 3	8/255 (3.1)	0.79 (0.33-1.86)	
Partner Tested for HIV			0.110
No or Unknown Status	28/630 (4.4)	Reference	
Yes, HIV negative	2/154 (1.3)	0.28 (0.07-1.20)	
Yes, HIV positive	14/314 (4.5)	1.00 (0.52-1.93)	
Condom use in previous 3 months			0.396
Always	10/318 (3.1)	Reference	
Sometimes	1/54 (1.9)	0.58 (0.07-4.63)	
Never	1/7 (14.3)	5.13 (0.56-46.70)	
Missing	*32/723 (4.4)*	*1.43 (0.69-2.94)*	
Substance Use			
Cigarettes			0.334
Never Used	30/820 (3.7)	Reference	
Ever Used	14/280 (5.0)	1.39 (0.72-2.65)	
Alcohol			0.572
Never Used	26/694 (3.8)	Reference	
Ever Used	18/405 (4.4)	1.19 (0.65-2.21)	
Injection drug use (cocaine, heroin)			--
Never Used	44/1,088 (4.0)	Reference	
Ever Used	0/12 (0.0)	--	
Mental Health			
Anxiety (GAD-7)			0.094
None (< 5)	37/804 (4.6)	Reference	
Any (≥ 5)	7/286 (2.5)	0.52 (0.23-1.18)	
Depression (PHQ-9)			0.854
None (< 5)	32/778 (4.1)	Reference	
Any (≥ 5)	12/310 (3.9)	0.94 (0.48-1.85)	
HIV Stigma			0.236
None	28/606 (4.6)	Reference	
Any (> 0)	16/496 (3.2)	0.69 (0.37-1.29)	
Historical Clinical Indicators			
Male Circumcision (n = 473)			0.355

No	15/270 (5.6)	Reference			
Yes	4/81 (4.9)	0.88 (0.28-2.74)			
Missing (for males)	*3/122 (2.5)*	*0.42 (0.12-1.51)*			
Previously Tested TB+?			0.464		
No	42/1,023 (4.1)	Reference			
Yes	2/79 (2.5)	0.61 (0.14-2.55)			
BMI (kg/m^2)			0.022		0.041
Underweight (≤ 18.5)	1/86 (1.2)	0.20 (0.03-1.49)		0.19 (0.03-1.40)	
Normal Weight (18.6-24.9)	30/542 (5.5)	Reference		Reference	
Overweight/Obese (≥ 25.0)	13/473 (2.8)	0.48 (0.25-0.94)		0.55 (0.28-1.11)	
Lab Testing					
CD4 Count at Baseline (cells/μL)			0.654		
> 350	9/201 (4.5)	Reference			
201-350	7/236 (3.0)	0.65 (0.24-1.78)			
≤ 200	9/264 (3.4)	0.75 (0.29-1.93)			
Missing	*19/401 (4.7)*	*1.06 (0.47-2.39)*			

* May not sum to N=1,102 due to missing data.

Table 3: Unadjusted and adjusted odds ratios of risk factors for prevalent HBV at time of enrollment as diagnosed by a blood antibody test (N=1,159).

Covariates	# Positive/ Total at Risk (Prevalence)†	uOR (95% CI)	P-value	aOR (95% CI)	P-value
Demographics					
Sex			< 0.001		0.001
Female	42/664 (6.3)	Reference		Reference	
Male	60/495 (12.1)	2.04 (1.35-3.09)		1.97 (1.29-3.01)	
Age (years)			0.499		0.915
< 30	38/468 (8.1)	0.87 (0.57-1.32)		0.98 (0.63-1.51)	
≥ 30	64/691 (9.3)	Reference		Reference	
Number of Children			0.698		
0	17/209 (8.1)	Reference			
1+	85/948 (9.0)	1.11 (0.65-1.92)			
Marital Status			0.092		
Married or Widowed/Divorced	4/91 (4.4)	Reference			
Never Married	98/1,068 (9.2)	2.20 (0.79-6.12)			
Distance from Nearest Health Clinic			0.752		
< 5 km	92/1,033 (8.9)	Reference			
> 5 km	10/124 (8.1)	0.90 (0.45-1.77)			
Socio-Economic					
Employed?			0.130		
No	51/662 (7.7)	Reference			
Yes	51/497 (10.3)	1.37 (0.91-2.06)			
Income (ZAR/month)			0.124		
< 2,000	78/947 (8.2)	Reference			
≥ 2,000	23/195 (11.8)	1.49 (0.91-2.44)			
Education			0.770		
None	25/298 (8.4)	Reference			
Any	77/861 (8.9)	1.07 (0.67-1.72)			
Behavioral Factors					

Times Previously Tested for HIV			0.548
None	38/433 (8.8)	Reference	
1-3	44/453 (9.7)	1.12 (0.71-1.76)	
> 3	20/272 (7.4)	0.82 (0.47-1.45)	
Partner Tested for HIV			0.519
No or Unknown Status	54/665 (8.1)	Reference	
Yes, HIV Negative	14/161 (8.7)	1.08 (0.58-1.99)	
Yes, HIV Positive	34/329 (10.3)	1.30 (0.83-2.05)	
Condom Use in Previous 3 Months			0.265
Always	19/308 (6.2)	Reference	
Sometimes	5/55 (9.1)	1.52 (0.54-4.26)	
Never	1/8 (12.5)	2.17 (0.25-18.58)	
Missing	*77/788 (9.8)*	*1.65 (0.98-2.77)*	
Substance Use			
Cigarettes			0.034
Never Used	68/875 (7.8)	Reference	
Ever Used	34/283 (12.0)	1.62 (1.05-2.50)	
Alcohol			0.016
Never Used	53/730 (7.3)	Reference	
Ever Used	49/427 (11.5)	1.66 (1.10-2.49)	
Injection drug use (cocaine, heroin)			0.953
Never Used	101/1,146 (8.8)	Reference	
Ever Used	1/12 (8.3)	0.94 (0.12-7.36)	
Mental Health			
Anxiety (GAD-7)			0.507
None (< 5)	80/879 (9.1)	Reference	
Any (≥ 5)	21/269 (7.8)	0.85 (0.51-1.40)	
Depression (PHQ-12)			0.789
None (< 5)	74/860 (8.6)	Reference	
Any (≥ 5)	26/285 (9.1)	1.07 (0.67-1.70)	
HIV Stigma			0.957
None	61/696 (8.8)	Reference	
Any (> 0)	41/463 (8.9)	1.01 (0.67-1.53)	

Historical Clinical Indicators					
Male Circumcision (n = 497)			0.676		
No	35/290 (12.1)	Reference			
Yes	10/96 (10.4)	0.85 (0.40-1.78)			
Missing (for males)	*16/111 (14.4)*	*1.23 (0.65-2.32)*			
Previously Tested TB+			0.592		
No	94/1,083 (8.7)	Reference			
Yes	8/76 (10.5)	1.24 (0.58-2.65)			
BMI (kg/m^2)			0.079		
Underweight (≤ 18.5)	8/84 (9.5)	0.89 (0.41-1.94)			
Normal Weight (18.6-24.9)	60/568 (10.6)	Reference			
Overweight/Obese (≥ 25.0)	34/506 (6.7)	0.61 (0.39-0.95)			
Lab Testing					
CD4 Count at Baseline (cells/μL)			0.019		0.032
> 350	10/203 (4.9)	Reference		Reference	
201-350	14/227 (6.2)	1.27 (0.55-2.92)		1.23 (0.53-2.84)	
≤ 200	30/263 (11.4)	2.48 (1.18-5.21)		2.29 (1.09-4.83)	
Missing	*48/466 (10.3)*	*2.22 (1.10-4.47)*		2.16 (1.07-4.37)	

† May not sum to N=1,159 due to missing data.