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Complete List of Authors:	Eticha, Begna; Madawalabu University, Medicine Sisay, Zufan; Addis Ababa University, Aklilu Lemma Institute of Pathobiology Alemayew, Addisu; Hawasa University, Medical Laboratory Sciences Shimelis, T; Hawasa University, Medical Laboratory Sciences
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Higher sero-prevalence of syphilis among HIV infected individuals in Addis Ababa, Ethiopia: A hospital based cross-sectional study

Begna Tulu[1], Zufan Sisay[2], Addisu Alemayehu [3], and Techalew Shimelis[3]*

[1]Madawalabu University, Department of Medicine, Bale Goba, Ethiopia
[2]Addis Ababa University, Aklilu Lemma Institute of Pathobiology, Addis Ababa, Ethiopia
[3]Hawassa University, College of Medicine and Health Sciences, PO Box: 1560 Hawassa, Ethiopia

*Corresponding author: Tel: +251916828259, Email: techalew03@yahoo.com

ABSTRACT

Objective

To determine the prevalence of syphilis and its risk factors among people with human immunodeficiency virus (HIV) at a hospital in Ethiopia.

Design

A hospital based cross-sectional study

Setting

This study was conducted at one of the largest public hospitals in Addis Ababa, Ethiopia.

Participants

A consecutive 306 HIV- positive patients were recruited prospectively from January to March 2010. For comparative purposes, 224 HIV- negative consecutive attendees at the voluntary counseling and testing (VCT) center in the same period were also included. Participants under 15 years of age and treated for syphilis and with a CD4+ T cell count below 50 cells / mm^3 were excluded.

Outcome measures

Blood samples and data on socio-demographic and risk factors for syphilis were collected. All sera were screened for syphilis using Rapid Plasma Reagin (RPR) test, and those positives were re-tested using Treponema Pallidum Heamagglutination (TPHA) test.

Results

The sero-prevalence of syphilis among HIV infected individuals was 9.8% compared to 1.3% among HIV uninfected individuals (Odds ratio (OR) 8.01; 95% CI 2.4 to 26.6; p= 0.001). A comparable rate of syphilis was found among men (11%) and women (8.9%) with HIV infection. Syphilis prevalence non-significantly increased with age, with the highest rate in 40-49 years of age (16.9%).

Except a history of STIs, which associated with syphilis (OR 2.25; 95% CI 1.03 to 4.9; p= 0.042), other risk factors did not raise the odds of infection.

Conclusion

The high prevalence of syphilis among people with HIV infection highlights the need to target this population to prevent the transmission of both infections. Screening all HIV infected people for syphilis and managing those infected would have clinical and epidemiological importance.

ARTICLE SUMMARY

Article focus

- To determine the prevalence of syphilis among HIV infected people
- To compare prevalence of syphilis by HIV status
- To assess risk factors for syphilis in HIV infected people

Key Messages

- High prevalence of syphilis among HIV positive individuals was observed
- Syphilis prevalence is significantly higher among HIV positives than HIV negative people
- Syphilis prevalence is not significantly influenced by age and gender

Strength and limitation of this study

- This hospital based cross-sectional study provided preliminary data for further detailed information
- No clinical features of syphilis positive patients were assessed

INTRODUCTION

Sexually transmitted infections (STIs) are the major public health problems in most parts of the world. Based on the World Health Organization estimate, STIs and their complications are among the top five disease categories for which adults seek health care in developing countries.[1] Syphilis is one of the most important STIs, caused by the bacterium *Treponema pallidum*.[2] It has been estimated that, annually, about 12 million new infections occur worldwide; of which, almost two-thirds are in sub-Saharan Africa and south/southeast Asia.[3] Unprotected sex, blood transfusion, needle sharing, and vertical transmission from mother to the child are major mode of syphilis transmission.[2, 4]

Syphilis, as cause of ulcerative genital lesion, presents site for HIV entry and shading. Moreover, by activating immune cells and raising viral load, syphilis could facilitate HIV transmissibility.[5] On the ether hand, concurrent HIV infection may adversely affect the natural history, clinical manifestations and treatment response of syphilis.[3, 6]

In Ethiopia, studies reported syphilis prevalence ranging from 1% to 10.9% in diverse risk groups such as pregnant women, blood donors, street dwellers and elderly people.[7-10] Moreover, according to the antenatal care (ANC)-based sentinel surveillances, syphilis prevalence increased from 1.8% in the year 2003 to 2.7% in 2005, and then it stabilized at 2.3% in 2007 and 2009. The rates

of syphilis-HIV co-infection among ANC attendees had also been rising from 4.1% in the year 2003 to 4.9% in 2005 and 5.3% in 2007, but dropped to 3.9% in 2009.[11-14] However, because of the limitation that the aforementioned risk groups consist of smaller size of HIV infected individuals, and the sex and age composition of ANC attendees is limited to female gender and reproductive age group, the generated data may not reflect the true picture of syphilis among HIV infected population. Therefore, this study was conducted to determine the prevalence and risk factors of syphilis among HIV-infected clients at St. Paul's General Specialized Hospital.

METHODS AND MATERIALS

This cross-sectional study was conducted at St. Paul's General Specialized Hospital, Addis Ababa from January to March 2010. The hospital is among the largest public hospitals in Ethiopia and provides HIV voluntary counseling and testing (VCT) as a routine service. Clients who are tested HIV positive are registered at the antiretroviral therapy (ART) clinic and assessed for their disease status. Clinical and immunological assessments (CD4+ T cell count) at enrollment and at six-monthly follow-up visits help to determine patient eligibility for ART. Those receiving ART are also monitored for clinical progress on a regular basis. Services including HIV counselling and testing, clinical and immunological assessments as well as ART are provided free of charge.

Consecutive HIV-infected individuals with and without ART status, and who had immunological and biochemical testing were recruited prospectively. Clients tested HIV negative at the VCT center during the study period were also recruited for comparative

purposes. In total, 306 HIV positive and 224 HIV negative clients were considered for analysis. In both HIV sero-groups, participants under 15 years of age, and who took syphilis treatment were excluded. In HIV-positive clients, those found with a CD4+ T cell count below 50 cells / mm^3 were excluded from the study due to the unreliability of serological tests in a state of severe immunosuppression.

Counselor nurses interviewed the study participants using structured questionnaire on socio-demographic and other risk factors such as history of blood transfusion, unsafe injection, multiple sexual partner, sexual transmitted infections (STIs), and syphilis family history. Blood samples were collected and screened for syphilis using the non-treponemal serologic test, rapid plasma reagin (RPR) test (Human, Germany). Sera found to be positive by RPR tests were further tested using modified *Treponema pallidum* hemagglutination (TPHA) test (Syphicheck–WB, Qualpro Diagnostics, India). Laboratory testing was carried out according to the directions of the manufacturers and all tests were run against the positive and negative controls. Only those samples positive by both RPR and TPHA were considered to have syphilis infection.

The study was approved by the Ethics Review Committee of Aklilu Lemma Institute of Pathobiology, Addis Ababa University, and St. Paul's Hospital management body. Participation was entirely voluntary, and written consent was obtained from the study subjects. Any information obtained during the study was kept with utmost confidentiality. Syphilis screening was performed free of charge, and those tested positive were managed by physicians.

Data entry and analysis was performed using SPSS Version-16. Result was summarized using descriptive statistics including mean, range and proportions. Difference in proportions was evaluated using Pearson's Chi-square test. Binary logistic regression analysis was used to assess the effect of socio-demographic and other risk factors on syphilis sero- positivity. Odds ratio was used as a measure of the strength of association.

RESULTS

Out of 312 HIV positive and 228 HIV negative individuals approached during the study period, 6 and 4 individuals were excluded due to refusal to participate, insufficient serum sample and incomplete questioner. Thus, 306 HIV positive and 224 HIV negative clients were considered for analysis. One hundred eighty eight (61.4%) participants with HIV were receiving ART and the rest were ART naïve (38.6%). Majority of HIV infected participants were urban dwellers (95.4%) and married (53.3%) (Table 1). HIV infected respondents had a mean age 35.8 years (SD 8.7; range 19- 73 years) compared to 28.2 years (SD 9.8; range 15- 73 years) in HIV non-infected groups. The male to female ratios in participants with and without HIV infection were 0.71:1 and 0.96:1, respectively.

Table 1. Syphilis infection in relation to socio-demography in HIV-positive and HIV- negative individuals at St. Paul Hospital, 2010

Characteristics	HIV positive			HIV negative		
	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)
Residence						

Rural	14 (4.6)	0		18(8)	0	
Urban	292(95.4)	30(10.3)	-	206(92)	3(1.5)	-
Sex						
Female	179(58.5)	16(8.9)	1	114(50.9)	1(0.9)	1
Male	127(41.5)	14(11)	1.26(0.59-2.69)	110(49.1)	2(1.8)	2.1(0.18-23.4)
Age (years)						
20	2(0.7)	0	-	52(23.2)	1(1.9)	1.84(0.11-30.1)
20-29	65(21.2)	4(6.2)	1	95(42.4)	1(1.1)	1
30-39	156(51)	13(8.3)	1.39(0.41-4.42)	47(21)	0	-
40-49	59(19.3)	10(16.9)	3.11(0.92-10.5)	19(8.5)	1(5.3)	5.2(0.31-87.4)
50	24(7.8)	3(12.5)	2.18(0.45-10.5)	11(4.9)	0	-
Marital status						
Single	60(19.6)	5(8.3)	1.41(0.39-5.1)	146(65.2)	3(2.1)	-
Married	163(53.3)	20(12.3)	2.2(0.79-6)	60(26.8)	0	
Divorced/ Widowed	83(27.1)	5(6)	1	18(8)	0	
Religion						
Orthodox	228(74.5)	24(10.5)	2.1(0.47-9.1)	170(75.9)	3(1.8)	-
Protestant	41(13.4)	4(9.8)	1.9(0.32-10.9)	25(11.2)	0	
Muslim	37(12.1)	2(5.4)	1	29(12.9)	0	
Educational status						
Illiterate	41(13.4)	9(22)	4.78(0.96-23.8)	13(5.8)	0	
Primary school	95(31)	8(8.4)	1.56(0.32-7.74)	51(22.8)	0	
Secondary school	134(43.8)	11(8.2)	1.52(0.32-7.19)	124(55.4)	2(1.6)	-
Certificate and above	36(11.8)	2(5.6)	1	36(16.1)	1(2.8)	
Occupation						
Government employee	41(13.4)	3(7.3)	1	29(12.9)	1(3.4)	1
Private employee	82(26.8)	8(9.8)	1.37(0.34-5.46)	71(31.7)	1(1.4)	0.4(0.02-6.62)

Housewife	63(20.6)	6(9.5)	1.33(0.31-5.66)	21(9.4)	0	-
Student	5(1.6)	0	-	41(18.3)	1(2.4)	0.7(0.04-11.67)
Merchant	35(11.4)	4(11.4)	1.63(0.34-7.86)	19(8.5)	0	
House maid	11(3.6)	3(27.3)	4.75(0.81-27.9)	7(3.1)	0	
No work	69(22.5)	6(8.7)	1.21(0.29-5.11)	36(16.1)	0	
Ethnicity						
Amhara	156(51)	14(9)	1	117(52.2)	2(1.7)	1
Oromo	87(28.4)	9(10.3)	1.2(0.49-2.83)	64(28.6)	1(1.6)	0.9(0.08-10.3)
Others	63(20.6)	7(11.1)	1.3(0.49-3.3)	43(19.2)	0	-

The prevalence of syphilis infection was 9.8% in HIV positive participants compared to 1.3% in HIV negative participants (Odds ratio (OR) 8.01; 95%CI 2.4 to 26.6; p= 0.001). The distribution of syphilis was similar among HIV infected clients with and without ART (11.2% versus 7.6%, respectively; p=0.31). Sera reactive by RPR test were more likely found TPHA positive among HIV positives (54.5%) than in HIV-negatives (10%) (p< 0.001) (Table 2).

Syphilis occurred exclusively among urban dwellers in either HIV sero-groups. Sero-positivity of syphilis was comparable between men (11%) and women (8.9%) with HIV infection. Syphilis prevalence seems to increase with increasing age, with the highest rate in the age range 40-49 years (16.9%), though difference was non-significant compared to age less than 30 years (OR 3.11; 95%CI 0.92 to10.5). A decreasing rate of syphilis was observed with increasing educational level, where illiterate HIV-positive participants (22%) had higher odds of infection compared to those having at least a certificate (5.6%) (OR 4.78; 95%CI 0.96 to 23.8; p= 0.056). Similarly, the association between occupation and syphilis were marginally non-significant where housemaids (27.3%) were affected compared to government employees (7.3%) (OR 4.75; 95%CI 0.81 to 27.9; p= 0.085) (Table 1).

Table 2. Syphilis serological tests in HIV positive and HIV negative individuals at Saint Paul's Hospital, 2010.

Syphilis test	Total tested	Number (%) of positive	HIV- positive						HIV- negative	
			ART Users		ART Naïve		Total			
			Tested	+Ve (%)	Tested	+Ve (%)	Tested	+Ve (%)	Tested	+Ve (%)
RPR	530	85(16)	188	36(19.1)	118	19(5.6)	306	55(18)	224	30(13.4)
TPHA	85	33(38.8)	36	21(58.3)	19	9(47.4)	55	30(54.5)	30	3(10)
Syphilis sero-positivity	530	33(6.2)	188	21(11.2)	118	9(7.6)	306	30(9.8)	224	3(1.3)

The exposure of HIV-infected and HIV-non-infected participants to different risk factors of syphilis is summarized in table 3. Except syphilis family history, which occurred in a comparable rate in either HIV sero-groups, other risk factors such as history of blood transfusion (10.5%), having multiple sexual partners (36.9%) and unsafe injection (12.7%), and a history of STIs (45.4%) were more frequently reported by HIV infected participants. However, it was only a history of STIs, which significantly associated with syphilis among HIV infected participants (OR 2.25; 95%CI 1.03 to 4.9; p= 0.042).

Table 3 syphilis infection in relation to syphilis risk factors in HIV-positive and HIV- negative individuals at St. Paul Hospital, 2010

Characteristics	HIV positive	HIV negative

	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)
Blood transfusion						
No	274(89.5)	28(10.2)	1	216(96.4)	3(1.4)	-
Yes	32(10.5)	2(6.2)	0.59 (0.13-2.58)	8(3.6)	0	
Multiple sexual partner						
No	193(63.1)	19(9.8)	1	195(87.1)	2(1)	1
Yes	113(36.9)	11(9.7)	0.99(0.45-2.16)	29(12.9)	1(3.4)	3.45(0.3-39.2)
Unsafe injection						
No	267(87.3)	27(10.1)	1	219(97.8)	3(1.4)	-
Yes	39(12.7)	3(7.7)	0.71(0.21-2.57)	5(2.2)	0	
Syphilis family history						
No	281(91.8)	26(9.3)	1	200(89.3)	2(1)	1
Yes	25(8.2)	4(16)	1.87(0.60-5.86)	24(10.7)	1(4.2)	4.3(0.38-49)
STI						
No	167(54.6)	11(6.6)	1	182(81.2)	2(1.1)	1
Yes	139(45.4)	19(13.7)	2.25(1.03-4.9)	42(18.8)	1(2.4)	(0.19-24.8)

DISCUSSION

This study showed that the prevalence of syphilis among HIV positives was 9.8%, with no significant difference between those receiving ART (11.2%) and ART naives (7.6%). The finding appears to be compatible with rates of HIV-syphilis co-infection among street dwellers (7.9%)[8] and elderly people (6%)[9] in northwest Ethiopia (Gondar) and in Nigeria (14%).[15] However, contrasting our result, the co-infection rate was lower among ANC-attendees in Ethiopia (3.9%)[14] and higher among STD clinic attendees in

Argentina (59.7%).[16] The observed inconsistencies may be because of the composition of the investigated sub-population, where ANC attendees, for instance, have apparently lower risk of syphilis compared to STD clinic attendees. In view of the adverse impact syphilis has to facilitate the transmission of coexisting HIV, intervention measures targeting this particular risk group has greater importance to prevent both infections.

In the present study, syphilis was significantly associated with HIV infection, where HIV infected individuals had about eight-fold higher risk of syphilis compared to HIV non-infected people. This result was in line with findings that revealed the existence of association between HIV and syphilis in different localities and sub- populations. A consistent two-fold increase in syphilis-HIV co-infection rates among ANC attendees[11-14] and four-fold among street dwellers in Ethiopia,[10] as well as eight-fold in HIV infected population in Nigeria[15] may be because of the fact that HIV and syphilis shares routes of transmission. These reports also indicated the varying strength of association between HIV and syphilis in diverse risk groups. However, none of these studies pointed out whether syphilis and HIV were contracted concurrently or one infection preceded another to explain the causal nature of such epidemiologic synergy between HIV and syphilis.

The sero-prevalence of syphilis was not significantly affected by gender in either HIV sero-groups, similar to findings elsewhere.[10, 15] However, Griemberg *et al*. reported men had excess risk of HIV, syphilis and syphilis-HIV co-infection compared to women.[16] This report is also in contrast to the established higher rate of HIV among women in our region,[17] which may be due to difference in risk behavior by gender in various geographical regions. We also found increasing syphilis prevalence with age among HIV infected

individuals, with the highest rate reported in the age group 40-49 years (16.9%), followed by age group above 50 years (12.5%), though the difference was non-significant. A raising syphilis prevalence with age was consistently reported by others,[8, 10, 14, 15] which might be due to the increased risk of exposure to syphilis with time. Moreover, our data showed that illiterate and housemaid HIV infected participants were disproportionately affected by syphilis, which point the significance of education to prevent syphilis transmission.

In Ethiopia, where HIV and syphilis has strong association, and transmission of the former is primarily through heterosexual exposure,[17] people with multiple sexual partners would obviously be at higher risk of contracting syphilis as well. Of course, the significance of such a risk behavior to influence syphilis prevalence in our context was documented, where having more than two sexual partners increased odds of syphilis infection six-fold compared to those with no sexual partner.[10] However, the lack of association between a history of multiple sexual partner and syphilis in our study deserves further investigation for possible explanation. Syphilis prevalence was about two-fold higher among HIV infected participants who reported a history of STIs compared with those with no history of STIs.

In conclusion, this study showed high prevalence of syphilis among HIV infected people compared to HIV non-infected people. Thus, intervention measures targeting HIV infected individuals would have paramount importance to prevent transmission of syphilis as well as HIV. As part of this effort, screening all HIV infected people for syphilis and managing those infected is critically needed. Further studies using a longitudinal design would reliably investigate the possible interaction between HIV and syphilis.

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Authors' contributions

BT was the principal investigator for the study; BT, AA and ZS contributed to the design of the study; BT carried out the laboratory work; ZS and AA supervised data collection; BT and TS performed the statistical analyses; BT, ZS and TS interpreted the result; all authors contributed to the write up and approved the final manuscript.

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Begna Tulu[1], Zufan Sisay[2], Addisu Alemayehu [3], and Techalew Shimelis[3]*

[1]Madawalabu University, Department of Medicine, Bale Goba, Ethiopia
[2]Addis Ababa University, Aklilu Lemma Institute of Pathobiology, Addis Ababa, Ethiopia
[3]Hawassa University, College of Medicine and Health Sciences, PO Box: 1560 Hawassa, Ethiopia

*Corresponding author: Tel: +251916828259, Email: techalew03@yahoo.com

ABSTRACT

Objective

To determine the prevalence of syphilis and its risk factors among people with human immunodeficiency virus (HIV) at a hospital in Ethiopia.

Design

A hospital based cross-sectional study

Setting

This study was conducted at one of the largest public hospitals in Addis Ababa, Ethiopia.

Participants

A consecutive 306 HIV- positive patients were recruited prospectively from January to March 2010. For comparative purposes, 224 HIV- negative consecutive attendees at the voluntary counseling and testing (VCT) center in the same period were also included. Participants under 15 years of age and treated for syphilis and with a CD4+ T cell count below 50 cells / mm^3 were excluded.

Outcome measures

Blood samples and data on socio-demographic and risk factors for syphilis were collected. All sera were screened for syphilis using rapid plasma reagin (RPR) test, and those positives were re-tested using *Treponema pallidum* haemagglutination assay (TPHA) test.

Results

The sero-prevalence of syphilis among HIV infected individuals was 9.8% compared to 1.3% among HIV uninfected individuals odds ratio (OR)=8.01 (95% confidence interval (CI)=2.4 to 26.6; p= 0.001). A comparable rate of syphilis was found among men (11%) and women (8.9%) with HIV infection. Syphilis prevalence non-significantly increased with age, with the highest rate in 40-49 years of age (16.9%). Except a history of STIs, which associated with syphilis OR= 2.25 (95% CI=1.03 to 4.9; p= 0.042), other risk factors did not raise the odds of infection.

Conclusion

The high prevalence of syphilis among people with HIV infection highlights the need to target this population to prevent the transmission of both infections. Screening all HIV infected people for syphilis and managing those infected would have clinical and epidemiological importance.

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Key Messages

- High prevalence of syphilis among HIV positive individuals was observed
- Syphilis prevalence is significantly higher among HIV positives than HIV negative people
- Syphilis prevalence is not significantly influenced by age and gender

Strength and limitation of this study

- This hospital based cross-sectional study provided preliminary data that would inform future research.
- The study did not use stronger statistical power to detect the differences in risk factors by syphilis status
- No clinical features of syphilis positive patients were assessed

INTRODUCTION

Sexually transmitted infections (STIs) are the major public health problems in most parts of the world. Based on the World Health Organization estimate, STIs and their complications are among the top five disease categories for which adults seek health care in developing countries.[1] Syphilis is one of the most important STIs, caused by the bacterium *Treponema pallidum*.[2] It has been estimated that, annually, about 12 million new infections occur worldwide; of which, almost two-thirds are in sub-Saharan Africa and south/southeast Asia.[3] Unprotected sex, blood transfusion, needle sharing, and vertical transmission from mother to the child are major mode of syphilis transmission.[2, 4]

Syphilis, as cause of ulcerative genital lesion, presents site for HIV entry and shading. Moreover, by activating immune cells and raising viral load, syphilis could facilitate HIV transmissibility.[5] On the ether hand, concurrent HIV infection may adversely affect the natural history, clinical manifestations and treatment response of syphilis.[3, 6]

In Ethiopia, studies reported syphilis prevalence ranging from 1% to 10.9% in diverse risk groups such as pregnant women, blood donors, street dwellers and elderly people.[7-10] Moreover, according to the antenatal care (ANC)-based sentinel surveillances, syphilis prevalence increased from 1.8% in the year 2003 to 2.7% in 2005, and then it stabilized at 2.3% in 2007 and 2009. The rates of syphilis-HIV co-infection among ANC attendees had also been rising from 4.1% in the year 2003 to 4.9% in 2005 and 5.3% in 2007, but dropped to 3.9% in 2009.[11-14] However, because of the limitation that the aforementioned risk groups consist of smaller size of HIV infected individuals, and the sex and age composition of ANC attendees is limited to female gender and reproductive age group, the generated data may not reflect the true picture of syphilis among HIV infected population. Therefore, this study was conducted to determine the prevalence and risk factors of syphilis among HIV-infected clients at St. Paul's General Specialized Hospital.

METHODS AND MATERIALS

This cross-sectional study was conducted at St. Paul's General Specialized Hospital, Addis Ababa from January to March 2010. The hospital is among the largest public hospitals in Ethiopia and provides HIV voluntary counseling and testing (VCT) as a routine service. Clients who are tested HIV positive are registered at the antiretroviral therapy (ART) clinic and assessed for their disease status. Clinical and immunological assessments (CD4+ T cell count) at enrollment and at six-monthly follow-up visits help to determine patient eligibility for ART. Those receiving ART are also monitored for clinical progress on a regular basis. Services including HIV counselling and testing, clinical and immunological assessments as well as ART

are provided free of charge. HIV infected patients are not routinely screened for syphilis and only those with clinical indications are tested.

Consecutive HIV-infected individuals with and without ART status, and who had immunological and biochemical testing were recruited prospectively. Clients tested HIV negative at the VCT center during the study period were also recruited for comparative purposes. In total, 306 HIV positive and 224 HIV negative clients were considered for analysis. In either HIV sero-group, participants less than 15 years of age, and who took syphilis treatment were excluded, as reactive non-treponemal test result may not remain after treatment. In HIV-positive clients, those found with a CD4+ T cell count below 50 cells / mm^3 were excluded from the study due to the unreliability of serological tests in a state of severe immunosuppression.

Counselor nurses interviewed the study participants using structured questionnaire on socio-demographic and other risk factors such as history of blood transfusion, unsafe injection, multiple sexual partner, STIs, and syphilis family history. Blood samples were collected and screened for syphilis using the non-treponemal serologic test, rapid plasma reagin (RPR) test (Human, Germany). Sera found to be positive by RPR tests were further tested using treponemal test, modified *Treponema pallidum* haemagglutination assay (TPHA) (Syphicheck–WB, Qualpro Diagnostics, India). Laboratory testing was carried out according to the directions of the manufacturers and all tests were run against the positive and negative controls. Only those samples positive by both RPR and TPHA were considered to have syphilis infection.

The study was approved by the Ethics Review Committee of Aklilu Lemma Institute of Pathobiology, Addis Ababa University, and St. Paul's Hospital management body. Participation was entirely voluntary, and written consent was obtained from the study subjects. Any

information obtained during the study was kept with utmost confidentiality. Syphilis screening was performed free of charge, and those tested positive were managed by physicians.

Data entry and analysis was performed using SPSS Version-16. Results were summarized using descriptive statistics.. Pearson's Chi-square (X^2) test was used to evaluate differences between proportions; X^2 for linear trend was also calculated using Epi Info Version -7. Binary logistic regression analysis was used to assess the effect of socio-demographic and other risk factors on syphilis sero- positivity. The odds ratio (OR) was used as a measure of association.

RESULTS

Out of 312 HIV positive and 228 HIV negative individuals approached during the study period, 6 and 4 individuals were excluded due to refusal to participate, insufficient serum sample and incomplete questionnaire. Thus, 306 HIV positive and 224 HIV negative clients were considered for analysis. One hundred eighty eight (61.4%) participants with HIV were receiving ART and the rest were ART naïve (38.6%). Majority of HIV infected participants were urban dwellers (95.4%) and married (53.3%) (Table 1). HIV infected respondents had a mean age 35.8 years (standard deviation (SD)= 8.7; range=19-73 years) compared to 28.2 years (SD=9.8; range= 15-73 years) in HIV non-infected groups. The male to female ratios in participants with and without HIV infection were 0.71:1 and 0.96:1, respectively.

The prevalence of syphilis infection was 9.8% in HIV positive participants compared to 1.3% in HIV negative participants; OR=8.01 (95% confidence interval (CI)=2.4 to 26.6; p= 0.001). The distribution of syphilis was similar among HIV infected clients with and without ART (11.2% versus 7.6%, respectively; p=0.31). Sera reactive by RPR test were more likely found TPHA positive among HIV positives (54.5%) than in HIV-negatives (10%) (p< 0.001) (Table 2).

Syphilis occurred exclusively among urban dwellers in either HIV sero-groups. Sero-positivity of syphilis was comparable between men (11%) and women (8.9%) with HIV infection. Syphilis prevalence seems to increase with increasing age, with the highest rate in the age range 40-49 years (16.9%), though X^2 for linear trend analysis showed no statistical significance (X^2=2.46; p = 0.117). A decreasing rate of syphilis was observed with increasing educational level, where illiterate HIV-positive participants (22%) had higher odds of infection compared to those having at least a certificate (5.6%); OR= 4.78 (95% CI=0.96 to 23.8; p= 0.056). Similarly, the association between occupation and syphilis were marginally non-significant where housemaids (27.3%) were affected compared to government employees (7.3%); OR= 4.75 (95% CI=0.81 to 27.9; p= 0.085) (Table 1).

RPR, rapid plasma reagin; TPHA, *Treponema pallidum* haemagglutination; ART, antiretroviral therapy; +ve, positive

The exposure of HIV-infected and HIV-non-infected participants to various risk factors of syphilis is summarized in table 3. Except syphilis family history, which occurred in a comparable rate in either HIV sero-groups, other risk factors such as history of blood transfusion (10.5%), having multiple sexual partners (36.9%) and unsafe injection (12.7%), and a history of STIs (45.4%) were more frequently reported by HIV infected participants. However, it was only a history of STIs, which significantly associated with syphilis among HIV infected participants; OR=2.25 (95% CI=1.03 to 4.9; p= 0.042).

DISCUSSION

This study showed that the prevalence of syphilis among HIV positives was 9.8%, with no significant difference between those receiving ART (11.2%) and ART naives (7.6%). The finding appears to be compatible with rates of HIV-syphilis co-infection among street dwellers (7.9%)[8] and elderly people (6%)[9] in northwest Ethiopia (Gondar) and in Nigeria (14%).[15] However, contrasting our result, the co-infection rate was lower among ANC-attendees in Ethiopia (3.9%)[14] and higher among STD clinic attendees in Argentina (59.7%).[16] The observed inconsistencies may be because of the composition of the investigated sub-population, where ANC attendees, for instance, have apparently lower risk of syphilis compared to STD clinic attendees. In view of the adverse impact syphilis has to facilitate the transmission of coexisting HIV, intervention measures targeting this particular risk group has greater importance to prevent both infections.

In the present study, syphilis was significantly associated with HIV infection, where HIV infected individuals had about eight-fold higher risk of syphilis compared to HIV non-infected people. This result was in line with findings that revealed the existence of association between HIV and syphilis in different localities and sub- populations. A consistent two-fold increase in syphilis-HIV co-infection rates among ANC attendees[11-14] and four-fold among street dwellers in Ethiopia,[10] as well as eight-fold in HIV infected population in Nigeria[15] may be because of the fact that HIV and syphilis shares routes of transmission. These reports also indicated the varying strength of association between HIV and syphilis in diverse risk groups. However, none of these studies pointed out whether syphilis and HIV were contracted

concurrently or one infection preceded another to explain the causal nature of such epidemiologic synergy between HIV and syphilis.

The sero-prevalence of syphilis was not significantly affected by gender in either HIV sero-groups, similar to findings elsewhere.[10, 15] However, Griemberg *et al*. reported men had excess risk of HIV, syphilis and syphilis-HIV co-infection compared to women.[16] This report is also in contrast to the established higher rate of HIV among women in our region,[17] which may be due to difference in risk behavior by gender in various geographical regions. We also found increasing syphilis prevalence with age among HIV infected individuals, with the highest rate reported in the age group 40-49 years (16.9%), followed by age group above 50 years (12.5%), though no statistically significant linear trend was observed. A raising syphilis prevalence with age was consistently reported by others,[8, 10, 14, 15] which might be due to the increased risk of exposure to syphilis with time. Moreover, our data showed that illiterate and housemaid HIV infected participants were disproportionately affected by syphilis, which point the significance of education to prevent syphilis transmission.

In Ethiopia, where HIV and syphilis has strong association, and transmission of the former is primarily through heterosexual exposure,[17] people with multiple sexual partners would obviously be at higher risk of contracting syphilis as well. Of course, the significance of such a risk behavior to influence syphilis prevalence was documented in our context, where having more than two sexual partners increased odds of syphilis infection six-fold compared to those with no sexual partner.[10] However, the lack of association between a history of multiple sexual partner and syphilis in our study deserves further investigation for possible explanation. Syphilis

prevalence was about two-fold higher among HIV infected participants who reported a history of STIs compared with those with no history of STIs.

Findings in this study need to be interpreted in light of its methodological limitations. First, absence of association between various risk factors and syphilis might be due to the fact that the study did not use stronger statistical power to detect the differences. Second, the reduced sensitivity of non-treponemal tests in primary as well as late latent syphilis and the potential for false-negative results due to prozone reactions might lead to misinterpretation of non-reactive RPR test result as absence of the infection. Moreover, the limitation of possible false-positive reaction with non-treponemal and treponemal tests needs to be given attention, as positive results may not necessarily indicate disease activity. Last, this study overlooked the importance of including clinical data, which would have been a good opportunity to describe the clinical presentation of syphilis among HIV infected patients.

In conclusion, this study showed high prevalence of syphilis among HIV infected people compared to HIV non-infected people. Thus, intervention measures targeting HIV infected individuals would have paramount importance to prevent transmission of syphilis as well as HIV. As part of this effort, screening all HIV infected people for syphilis and managing those infected is critically needed. Further studies using a longitudinal design with stronger power would reliably investigate the possible interaction between HIV and syphilis.

Acknowledgment

We would like to thank the physicians, counselor nurses and laboratory staff of St. Paul's Hospital for their kind assistance during data collection. Our appreciation also goes to the study subjects who volunteered to participate in the study. We acknowledge the Aklilu Lemma Institute of Pathobiology, Addis Ababa University, for financial and logistic support.

Authors' contributions

BT was the principal investigator for the study; BT, AA and ZS contributed to the design of the study; BT carried out the laboratory work; ZS and AA supervised data collection; BT and TS

performed the statistical analyses; BT, ZS and TS interpreted the result; all authors contributed to the write up and approved the final manuscript.

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Competing Interest: None declared.

Data Sharing

We have no additional unpublished data from the study

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Table 1. Syphilis infection in relation to socio-demography in HIV-positive and HIV- negative individuals at St. Paul Hospital, 2010

Characteristics	HIV positive			HIV negative		
	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)
Residence						
Rural	14 (4.6)	0		18(8)	0	
Urban	292(95.4)	30(10.3)	-	206(92)	3(1.5)	-
Sex						
Female	179(58.5)	16(8.9)	1	114(50.9)	1(0.9)	1
Male	127(41.5)	14(11)	1.26(0.59-2.69)	110(49.1)	2(1.8)	2.1(0.18-23.4)
Age (years)						
<19	2(0.7)	0	-	52(23.2)	1(1.9)	1.84(0.11-30.1)
20-29	65(21.2)	4(6.2)	1	95(42.4)	1(1.1)	1
30-39	156(51)	13(8.3)	1.39(0.41-4.42)	47(21)	0	-
40-49	59(19.3)	10(16.9)	3.11(0.92-10.5)	19(8.5)	1(5.3)	5.2(0.31-87.4)
>50	24(7.8)	3(12.5)	2.18(0.45-10.5)	11(4.9)	0	-
Marital status						
Single	60(19.6)	5(8.3)	1.41(0.39-5.1)	146(65.2)	3(2.1)	-
Married	163(53.3)	20(12.3)	2.2(0.79-6)	60(26.8)	0	
Divorced/ Widowed	83(27.1)	5(6)	1	18(8)	0	
Religion						
Orthodox	228(74.5)	24(10.5)	2.1(0.47-9.1)	170(75.9)	3(1.8)	-
Protestant	41(13.4)	4(9.8)	1.9(0.32-10.9)	25(11.2)	0	
Muslim	37(12.1)	2(5.4)	1	29(12.9)	0	
Educational status						
Illiterate	41(13.4)	9(22)	4.78(0.96-23.8)	13(5.8)	0	
Primary school	95(31)	8(8.4)	1.56(0.32-7.74)	51(22.8)	0	

Secondary school	134(43.8)	11(8.2)	1.52(0.32-7.19)	124(55.4)	2(1.6)	-
Certificate and above	36(11.8)	2(5.6)	1	36(16.1)	1(2.8)	
Occupation						
Government employee	41(13.4)	3(7.3)	1	29(12.9)	1(3.4)	1
Private employee	82(26.8)	8(9.8)	1.37(0.34-5.46)	71(31.7)	1(1.4)	0.4(0.02-6.62)
Housewife	63(20.6)	6(9.5)	1.33(0.31-5.66)	21(9.4)	0	-
Student	5(1.6)	0	-	41(18.3)	1(2.4)	0.7(0.04-11.67)
Merchant	35(11.4)	4(11.4)	1.63(0.34-7.86)	19(8.5)	0	
House maid	11(3.6)	3(27.3)	4.75(0.81-27.9)	7(3.1)	0	
No work	69(22.5)	6(8.7)	1.21(0.29-5.11)	36(16.1)	0	
Ethnicity						
Amhara	156(51)	14(9)	1	117(52.2)	2(1.7)	1
Oromo	87(28.4)	9(10.3)	1.2(0.49-2.83)	64(28.6)	1(1.6)	0.9(0.08-10.3)
Others	63(20.6)	7(11.1)	1.3(0.49-3.3)	43(19.2)	0	-

Table 2. Syphilis serological tests in HIV positive and HIV negative individuals at Saint Paul's Hospital, 2010.

Syphilis test	Total tested	Number (%) of positive	HIV- positive						HIV- negative	
			ART Users		ART Naïve		Total			
			Tested	+Ve (%)	Tested	+Ve (%)	Tested	+Ve (%)	Tested	+Ve (%)

RPR	530	85(16)	188	36(19.1)	118	19(5.6)	306	55(18)	224	30(13.4)
TPHA	85	33(38.8)	36	21(58.3)	19	9(47.4)	55	30(54.5)	30	3(10)
Syphilis sero-positivity	530	33(6.2)	188	21(11.2)	118	9(7.6)	306	30(9.8)	224	3(1.3)

RPR, rapid plasma reagin; TPHA, *Treponema pallidum* haemagglutination; ART, antiretroviral therapy; +ve, positive

Table 3 syphilis infection in relation to syphilis risk factors in HIV-positive and HIV- negative individuals at St. Paul Hospital, 2010

Characteristics	HIV positive			HIV negative		
	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)
Blood transfusion						
No	274(89.5)	28(10.2)	1	216(96.4)	3(1.4)	-
Yes	32(10.5)	2(6.2)	0.59 (0.13-2.58)	8(3.6)	0	
Multiple sexual partner						
No	193(63.1)	19(9.8)	1	195(87.1)	2(1)	1
Yes	113(36.9)	11(9.7)	0.99(0.45-2.16)	29(12.9)	1(3.4)	3.45(0.3-39.2)
Unsafe injection						
No	267(87.3)	27(10.1)	1	219(97.8)	3(1.4)	-
Yes	39(12.7)	3(7.7)	0.71(0.21-2.57)	5(2.2)	0	
Syphilis family history						
No	281(91.8)	26(9.3)	1	200(89.3)	2(1)	1
Yes	25(8.2)	4(16)	1.87(0.60-5.86)	24(10.7)	1(4.2)	4.3(0.38-49)
STIs						
No	167(54.6)	11(6.6)	1	182(81.2)	2(1.1)	1
Yes	139(45.4)	19(13.7)	2.25(1.03-4.9)	42(18.8)	1(2.4)	(0.19-24.8)

STIs, sexually transmitted infection

~~Higher s~~Sero-prevalence of syphilis among HIV infected individuals in Addis Ababa, Ethiopia: A hospital based cross-sectional study

Begna Tulu[1], Zufan Sisay[2], Addisu Alemayehu [3], and Techalew Shimelis[3]*

[1]Madawalabu University, Department of Medicine, Bale Goba, Ethiopia
[2]Addis Ababa University, Aklilu Lemma Institute of Pathobiology, Addis Ababa, Ethiopia
[3]Hawassa University, College of Medicine and Health Sciences, PO Box: 1560 Hawassa, Ethiopia

*Corresponding author: Tel: +251916828259, Email: techalew03@yahoo.com

ABSTRACT

Objective

To determine the prevalence of syphilis and its risk factors among people with human immunodeficiency virus (HIV) at a hospital in Ethiopia.

Design

A hospital based cross-sectional study

Setting

This study was conducted at one of the largest public hospitals in Addis Ababa, Ethiopia.

Participants

A consecutive 306 HIV- positive patients were recruited prospectively from January to March 2010. For comparative purposes, 224 HIV- negative consecutive attendees at the voluntary counseling and testing (VCT) center in the same period were also included. Participants under 15 years of age and treated for syphilis and with a CD4+ T cell count below 50 cells / mm^3 were excluded.

Outcome measures

Blood samples and data on socio-demographic and risk factors for syphilis were collected. All sera were screened for syphilis using rRapid Pplasma rReagin (RPR) test, and those positives were re-tested using *Treponema pPallidum* hHeaacmagglutination assay (TPHA) test.

Results

The sero-prevalence of syphilis among HIV infected individuals was 9.8% compared to 1.3% among HIV uninfected individuals (Oodds ratio (OR)= 8.01; (95% confidence interval (CI)= 2.4 to 26.6; p= 0.001). A comparable rate of syphilis was found among men (11%) and women (8.9%) with HIV infection. Syphilis prevalence non-significantly increased with age, with the highest rate in 40-49

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years of age (16.9%). Except a history of STIs, which associated with syphilis (OR= 2.25; (95% CI=1.03 to 4.9; p= 0.042), other risk factors did not raise the odds of infection.

Conclusion

The high prevalence of syphilis among people with HIV infection highlights the need to target this population to prevent the transmission of both infections. Screening all HIV infected people for syphilis and managing those infected would have clinical and epidemiological importance.

ARTICLE SUMMARY

Article focus

- To determine the prevalence of syphilis among HIV infected people
- To compare prevalence of syphilis by HIV status
- To assess risk factors for syphilis in HIV infected people

Key Messages

- High prevalence of syphilis among HIV positive individuals was observed
- Syphilis prevalence is significantly higher among HIV positives than HIV negative people
- Syphilis prevalence is not significantly influenced by age and gender

Strength and limitation of this study

- This hospital based cross-sectional study provided preliminary data that would inform future ~~for further detailed information~~ research.
- The study did not use stronger statistical power to detect the differences in risk factors by syphilis status
- No clinical features of syphilis positive patients were assessed

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INTRODUCTION

Sexually transmitted infections (STIs) are the major public health problems in most parts of the world. Based on the World Health Organization estimate, STIs and their complications are among the top five disease categories for which adults seek health care in developing countries.[1] Syphilis is one of the most important STIs, caused by the bacterium *Treponema pallidum*.[2] It has been estimated that, annually, about 12 million new infections occur worldwide; of which, almost two-thirds are in sub-Saharan Africa and south/southeast Asia.[3] Unprotected sex, blood transfusion, needle sharing, and vertical transmission from mother to the child are major mode of syphilis transmission.[2, 4]

Syphilis, as cause of ulcerative genital lesion, presents site for HIV entry and shading. Moreover, by activating immune cells and raising viral load, syphilis could facilitate HIV transmissibility.[5] On the ether hand, concurrent HIV infection may adversely affect the natural history, clinical manifestations and treatment response of syphilis.[3, 6]

In Ethiopia, studies reported syphilis prevalence ranging from 1% to 10.9% in diverse risk groups such as pregnant women, blood donors, street dwellers and elderly people.[7-10] Moreover, according to the antenatal care (ANC)-based sentinel surveillances, syphilis prevalence increased from 1.8% in the year 2003 to 2.7% in 2005, and then it stabilized at 2.3% in 2007 and 2009. The rates of syphilis-HIV co-infection among ANC attendees had also been rising from 4.1% in the year 2003 to 4.9% in 2005 and 5.3% in 2007, but dropped to 3.9% in 2009.[11-14]~~[11-14]~~ However, because of the limitation that the aforementioned risk groups consist of smaller size of HIV infected individuals, and the sex and age composition of ANC attendees is limited to female gender and reproductive age group, the generated data may not reflect the true picture of syphilis among HIV infected population. Therefore, this study was conducted to determine the prevalence and risk factors of syphilis among HIV-infected clients at St. Paul's General Specialized Hospital.

METHODS AND MATERIALS

This cross-sectional study was conducted at St. Paul's General Specialized Hospital, Addis Ababa from January to March 2010. The hospital is among the largest public hospitals in Ethiopia and provides HIV voluntary counseling and testing (VCT) as a routine service. Clients who are tested HIV positive are registered at the antiretroviral therapy (ART) clinic and assessed for their disease status. Clinical and immunological assessments (CD4+ T cell count) at enrollment and at six-monthly follow-up visits help to determine patient eligibility for ART. Those receiving ART are also monitored for clinical progress on a regular basis. Services

including HIV counselling and testing, clinical and immunological assessments as well as ART are provided free of charge. HIV infected patients are not routinely screened for syphilis and only those with clinical indications are tested.

Consecutive HIV-infected individuals with and without ART status, and who had immunological and biochemical testing were recruited prospectively. Clients tested HIV negative at the VCT center during the study period were also recruited for comparative purposes. In total, 306 HIV positive and 224 HIV negative clients were considered for analysis. In ~~both~~ either HIV sero-group~~s~~, participants ~~under~~less than 15 years of age, and who took syphilis treatment were ~~excluded~~excluded, as reactive non-treponemal test result may not remain after treatment. In HIV-positive clients, those found with a CD4+ T cell count below 50 cells / mm^3 were excluded from the study due to the unreliability of serological tests in a state of severe immunosuppression.

Counselor nurses interviewed the study participants using structured questionnaire on socio-demographic and other risk factors such as history of blood transfusion, unsafe injection, multiple sexual partner, ~~sexual transmitted infections (~~STIs~~)~~, and syphilis family history. Blood samples were collected and screened for syphilis using the non-treponemal serologic test, rapid plasma reagin (RPR) test (Human, Germany). Sera found to be positive by RPR tests were further tested using treponemal test, modified *Treponema pallidum* haemagglutination assay (TPHA) ~~test~~ (Syphicheck–WB, Qualpro Diagnostics, India). Laboratory testing was carried out according to the directions of the manufacturers and all tests were run against the positive and negative controls. Only those samples positive by both RPR and TPHA were considered to have syphilis infection.

The study was approved by the Ethics Review Committee of Aklilu Lemma Institute of Pathobiology, Addis Ababa University, and St. Paul's Hospital management body. Participation was entirely voluntary, and written consent was obtained from the study subjects. Any information obtained during the study was kept with utmost confidentiality. Syphilis screening was performed free of charge, and those tested positive were managed by physicians.

Data entry and analysis was performed using SPSS Version-16. Results ~~was~~ were summarized using descriptive statistics~~, including mean, range and proportions.~~ . Pearson's Chi-square (X^2) test was used to evaluate ~~D~~differences ~~in~~ between proportions; X^2 ~~was evaluated using Pearson's Chi-square test~~for linear trend was also calculated using Epi Info Version -7. Binary logistic regression analysis was used to assess the effect of socio-demographic and other risk factors on syphilis sero- positivity. The ~~O~~odds ratio (OR) was used as a measure of ~~the strength of~~ association.

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RESULTS

Out of 312 HIV positive and 228 HIV negative individuals approached during the study period, 6 and 4 individuals were excluded due to refusal to participate, insufficient serum sample and incomplete ~~questioner~~questionnaire. Thus, 306 HIV positive and 224 HIV negative clients were considered for analysis. One hundred eighty eight (61.4%) participants with HIV were receiving ART and the rest were ART naïve (38.6%). Majority of HIV infected participants were urban dwellers (95.4%) and married (53.3%) (Table 1). HIV infected respondents had a mean age 35.8 years ~~(~~(standard deviation (SD)~~=~~ 8.7; range~~=~~ 19-~~-~~73 years) compared to 28.2 years (SD~~=~~

9.8; range= 15- 73 years) in HIV non-infected groups. The male to female ratios in participants with and without HIV infection were 0.71:1 and 0.96:1, respectively.

Table 1. Syphilis infection in relation to socio-demography in HIV-positive and HIV- negative individuals at St. Paul Hospital, 2010

Characteristics	HIV positive			HIV negative		
	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)
Residence						
Rural	14 (4.6)	0		18(8)	0	
Urban	292(95.4)	30(10.3)	-	206(92)	3(1.5)	-
Sex						
Female	179(58.5)	16(8.9)	1	114(50.9)	1(0.9)	1
Male	127(41.5)	14(11)	1.26(0.59-2.69)	110(49.1)	2(1.8)	2.1(0.18-23.4)
Age (years)						
<1920	2(0.7)	0	-	52(23.2)	1(1.9)	1.84(0.11-30.1)
20-29	65(21.2)	4(6.2)	1	95(42.4)	1(1.1)	1
30-39	156(51)	13(8.3)	1.39(0.41-4.42)	47(21)	0	-
40-49	59(19.3)	10(16.9)	3.11(0.92-10.5)	19(8.5)	1(5.3)	5.2(0.31-87.4)
≥50	24(7.8)	3(12.5)	2.18(0.45-10.5)	11(4.9)	0	-
Marital status						
Single	60(19.6)	5(8.3)	1.41(0.39-5.1)	146(65.2)	3(2.1)	-
Married	163(53.3)	20(12.3)	2.2(0.79-6)	60(26.8)	0	
Divorced/ Widowed	83(27.1)	5(6)	1	18(8)	0	
Religion						
Orthodox	228(74.5)	24(10.5)	2.1(0.47-9.1)	170(75.9)	3(1.8)	-
Protestant	41(13.4)	4(9.8)	1.9(0.32-10.9)	25(11.2)	0	

Muslim	37(12.1)	2(5.4)	1	29(12.9)	0	
Educational status						
Illiterate	41(13.4)	9(22)	4.78(0.96-23.8)	13(5.8)	0	
Primary school	95(31)	8(8.4)	1.56(0.32-7.74)	51(22.8)	0	
Secondary school	134(43.8)	11(8.2)	1.52(0.32-7.19)	124(55.4)	2(1.6)	-
Certificate and above	36(11.8)	2(5.6)	1	36(16.1)	1(2.8)	
Occupation						
Government employee	41(13.4)	3(7.3)	1	29(12.9)	1(3.4)	1
Private employee	82(26.8)	8(9.8)	1.37(0.34-5.46)	71(31.7)	1(1.4)	0.4(0.02-6.62)
Housewife	63(20.6)	6(9.5)	1.33(0.31-5.66)	21(9.4)	0	-
Student	5(1.6)	0	-	41(18.3)	1(2.4)	0.7(0.04-11.67)
Merchant	35(11.4)	4(11.4)	1.63(0.34-7.86)	19(8.5)	0	
House maid	11(3.6)	3(27.3)	4.75(0.81-27.9)	7(3.1)	0	
No work	69(22.5)	6(8.7)	1.21(0.29-5.11)	36(16.1)	0	
Ethnicity						
Amhara	156(51)	14(9)	1	117(52.2)	2(1.7)	1
Oromo	87(28.4)	9(10.3)	1.2(0.49-2.83)	64(28.6)	1(1.6)	0.9(0.08-10.3)
Others	63(20.6)	7(11.1)	1.3(0.49-3.3)	43(19.2)	0	-

The prevalence of syphilis infection was 9.8% in HIV positive participants compared to 1.3% in HIV negative participants; ~~(Odds ratio (~~OR~~)=~~ 8.01~~;~~ (95% confidence interval (C~~C~~I)=~~ 2.4 to 26.6; p= 0.001). The distribution of syphilis was similar among HIV infected clients with and without ART (11.2% versus 7.6%, respectively; p=0.31). Sera reactive by RPR test were more likely found TPHA positive among HIV positives (54.5%) than in HIV-negatives (10%) (p< 0.001) (Table 2).

Syphilis occurred exclusively among urban dwellers in either HIV sero-groups. Sero-positivity of syphilis was comparable between men (11%) and women (8.9%) with HIV infection. Syphilis prevalence seems to increase with increasing age, with the highest rate in the age range 40-49 years (16.9%), though X^2 for linear trend analysis showed no ~~difference was~~ statistical ~~non~~ significance~~t compared to age less than 30 years (OR 3.11; 95%CI 0.92 to10.5)~~(X^2=2.46; p = 0.117). A decreasing rate of syphilis was observed with increasing educational level, where illiterate HIV-positive participants (22%) had higher odds of infection compared to those having at least a certificate (5.6%); ~~(~~OR= 4.78~~;~~ (95% CI= ~~-~~0.96 to 23.8; p= 0.056). Similarly, the association between occupation and syphilis were marginally non-significant where housemaids (27.3%) were affected compared to government employees (7.3%); ~~(~~OR= 4.75 (~~;~~ 95% CI= ~~-~~0.81 to 27.9; p= 0.085) ~~-~~(Table 1).

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Table 2. Syphilis serological tests in HIV positive and HIV negative individuals at Saint Paul's Hospital, 2010.

Syphilis test	Total tested	Number (%) of positive	HIV- positive						HIV- negative	
			ART Users		ART Naïve		Total			
			Tested	+Ve (%)	Tested	+Ve (%)	Tested	+Ve (%)	Tested	+Ve (%)
RPR	530	85(16)	188	36(19.1)	118	19(5.6)	306	55(18)	224	30(13.4)
TPHA	85	33(38.8)	36	21(58.3)	19	9(47.4)	55	30(54.5)	30	3(10)
Syphilis	530	33(6.2)	188	21(11.2)	118	9(7.6)	306	30(9.8)	224	3(1.3)

sero-positivity

RPR, rapid plasma reagin; TPHA, *Treponema pallidum* haemagglutination; ART, antiretroviral therapy; +ve, positive

The exposure of HIV-infected and HIV-non-infected participants to ~~different~~ various risk factors of syphilis is summarized in table 3. Except syphilis family history, which occurred in a comparable rate in either HIV sero-groups, other risk factors such as history of blood transfusion (10.5%), having multiple sexual partners (36.9%) and unsafe injection (12.7%), and a history of STIs (45.4%) were more frequently reported by HIV infected participants. However, it was only a history of STIs, which significantly associated with syphilis among HIV infected participants; ~~(~~OR=2.25~~;~~ (95% CI=1.03 to 4.9; p= 0.042).

Table 3 syphilis infection in relation to syphilis risk factors in HIV-positive and HIV- negative individuals at St. Paul Hospital, 2010

Characteristics	HIV positive			HIV negative		
	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)	Number(%) tested	Number(%) positive for syphilis	Crude odds ratio(95% CI)
Blood transfusion						
No	274(89.5)	28(10.2)	1	216(96.4)	3(1.4)	-
Yes	32(10.5)	2(6.2)	0.59 (0.13-2.58)	8(3.6)	0	
Multiple sexual partner						
No	193(63.1)	19(9.8)	1	195(87.1)	2(1)	1
Yes	113(36.9)	11(9.7)	0.99(0.45-2.16)	29(12.9)	1(3.4)	3.45(0.3-39.2)
Unsafe injection						

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No	267(87.3)	27(10.1)	1	219(97.8)	3(1.4)	-
Yes	39(12.7)	3(7.7)	0.71(0.21-2.57)	5(2.2)	0	
Syphilis family history						
No	281(91.8)	26(9.3)	1	200(89.3)	2(1)	1
Yes	25(8.2)	4(16)	1.87(0.60-5.86)	24(10.7)	1(4.2)	4.3(0.38-49)
STIs						
No	167(54.6)	11(6.6)	1	182(81.2)	2(1.1)	1
Yes	139(45.4)	19(13.7)	2.25(1.03-4.9)	42(18.8)	1(2.4)	(0.19-24.8)

STIs, sexually transmitted infection

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DISCUSSION

This study showed that the prevalence of syphilis among HIV positives was 9.8%, with no significant difference between those receiving ART (11.2%) and ART naives (7.6%). The finding appears to be compatible with rates of HIV-syphilis co-infection among street dwellers (7.9%)[8] and elderly people (6%)[9] in northwest Ethiopia (Gondar) and in Nigeria (14%).[15] However, contrasting our result, the co-infection rate was lower among ANC-attendees in Ethiopia (3.9%)[14] and higher among STD clinic attendees in Argentina (59.7%).[16] The observed inconsistencies may be because of the composition of the investigated sub-population, where ANC attendees, for instance, have apparently lower risk of syphilis compared to STD clinic attendees. In view of the adverse impact syphilis has to facilitate the transmission of coexisting HIV, intervention measures targeting this particular risk group has greater importance to prevent both infections.

In the present study, syphilis was significantly associated with HIV infection, where HIV infected individuals had about eight-fold higher risk of syphilis compared to HIV non-infected people. This result was in line with findings that revealed the existence of association between HIV and syphilis in different localities and sub- populations. A consistent two-fold increase in syphilis-HIV co-infection rates among ANC attendees[11-14] and four-fold among street dwellers in Ethiopia,[10] as well as eight-fold in HIV infected population in Nigeria[15] may be because of the fact that HIV and syphilis shares routes of transmission. These reports also indicated the varying strength of association between HIV and syphilis in diverse risk groups. However, none of these studies pointed out whether syphilis and HIV were contracted concurrently or one infection preceded another to explain the causal nature of such epidemiologic synergy between HIV and syphilis.

The sero-prevalence of syphilis was not significantly affected by gender in either HIV sero-groups, similar to findings elsewhere.[10, 15] However, Griemberg *et al*. reported men had excess risk of HIV, syphilis and syphilis-HIV co-infection compared to women.[16] This report is also in contrast to the established higher rate of HIV among women in our region,[17] which may be due to difference in risk behavior by gender in various geographical regions. We also found increasing syphilis prevalence with age among HIV infected individuals, with the highest rate reported in the age group 40-49 years (16.9%), followed by age group above 50 years (12.5%), though no statistically significant linear trend was observed.~~the difference was non-significant.~~ A raising syphilis prevalence with age was consistently reported by others,[8, 10, 14, 15] which might be due to the increased risk of exposure to syphilis with time.

Moreover, our data showed that illiterate and housemaid HIV infected participants were disproportionately affected by syphilis, which point the significance of education to prevent syphilis transmission.

In Ethiopia, where HIV and syphilis has strong association, and transmission of the former is primarily through heterosexual exposure,[17] people with multiple sexual partners would obviously be at higher risk of contracting syphilis as well. Of course, the significance of such a risk behavior to influence syphilis prevalence was documented in our context ~~was documented~~, where having more than two sexual partners increased odds of syphilis infection six-fold compared to those with no sexual partner.[10] However, the lack of association between a history of multiple sexual partner and syphilis in our study deserves further investigation for possible explanation. Syphilis prevalence was about two-fold higher among HIV infected participants who reported a history of STIs compared with those with no history of STIs.

Findings in this study need to be interpreted in light of its methodological limitations. First, absence of association between various risk factors and syphilis might be due to the fact that the study did not use stronger statistical power to detect the differences. Second, the reduced sensitivity of non-treponemal tests in primary as well as late latent syphilis and the potential for false-negative results due to prozone reactions might lead to misinterpretation of non-reactive RPR test result as absence of the infection. Moreover, the limitation of possible false-positive reaction with non-treponemal and treponemal tests needs to be given attention, as positive results may not necessarily indicate disease activity. Last, this study overlooked the importance of including clinical data, which would have been a good opportunity to describe the clinical presentation of syphilis among HIV infected patients.

In conclusion, this study showed high prevalence of syphilis among HIV infected people compared to HIV non-infected people. Thus, intervention measures targeting HIV infected individuals would have paramount importance to prevent transmission of syphilis as

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well as HIV. As part of this effort, screening all HIV infected people for syphilis and managing those infected is critically needed. Further studies using a longitudinal design with stronger power would reliably investigate the possible interaction between HIV and syphilis.

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Authors' contributions

BT was the principal investigator for the study; BT, AA and ZS contributed to the design of the study; BT carried out the laboratory work; ZS and AA supervised data collection; BT and TS performed the statistical analyses; BT, ZS and TS interpreted the result; all authors contributed to the write up and approved the final manuscript.

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Competing Interest: None declared.

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