Prevalence Of Syphilis, Neurosyphilis And Associated Factors In a Cross-Sectional Analysis Of HIV Infected Patients Attending Bugando Medical Centre Mwanza Tanzania

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SUBJECT AREAS
Epidemiology
Abstract

BACKGROUND HIV-syphilis co-infection is a combination that enhances rapid progression of early syphilis or late latent syphilis to neurosyphilis and can cause catastrophic neurological complications. In studies in Mwanza, syphilis affects ~8% of healthy outpatients, and older studies have suggested that up to 23.5% of HIV-syphilis co-infected patients also have neurosyphilis.

Background

In spite of effective preventive and treatment options syphilis is still a global health problem causing high morbidity. It is estimated that about 10 million people worldwide are infected each year with a global prevalence of about 0.5%(1). In sub-Saharan Africa the burden has dropped from 6% to around 1% in the past 50 years(1,2). In Tanzania the prevalence of syphilis ranges from 2.5% to 8% in antenatal clinics and community surveys, respectively (3,4). In sub-Saharan Africa heterosexuals are most highly affected (5).

HIV-Treponema pallidum co-infection represents an important problem with serious clinical implications. The genital ulcers caused by primary syphilis infection facilitate acquisition of HIV. The genital ulcers are usually accompanied by inflammatory cells that express HIV co-receptors, facilitating establishment of initial HIV infection in the genital mucosa(5). Additionally the presence of syphilis co-infection in HIV infected patients increases the HIV viral load (6). HIV-Treponema pallidum co-infected individuals tend to develop neurosyphilis more frequently as compared to people with T.pallidum infection alone(5). HIV infection has also been associated with syphilis treatment failure (7). The prevalence of neurosyphilis in untreated early syphilis among HIV positive patients has been reported to be as high as 23.5% in Spain (8). Likewise 24.6% of HIV positive
patients were reported to have neurosyphilis in a study done in Canada and development of neurosyphilis was significantly associated with CD4 less than 500 cells/µland uncontrolled viremia(9). Little is known about the magnitude of the problem of HIV-syphilis in Africa(10). Hence the study was designed to determine the prevalence of syphilis, neurosyphilis and associated factors among HIV positive patients at Bugando Medical Centre in Tanzania.

Methods

Sample population, Data collection, and Laboratory testing and data analysis

The study was conducted at Bugando Medical Centre’s medical department. Bugando Medical Centre is one of four zonal hospitals in Tanzania; it serves a catchment population of about 15 million people with a bed capacity of about 900. The Bugando HIV outpatient clinic was started in 2004 and at present has more than 15,000 HIV-infected patients enrolled with over 5,000 on antiretroviral therapy. The centre cares for all patients diagnosed from within the hospital and those sent from catchment facilities. All patients who are newly diagnosed with HIV are routinely screened for opportunistic infections and Hepatitis B and C. In the first three months of 2017 newly diagnosed HIV patients were screened for syphilis and 36/436(8.3%) were Venereal Disease Research Laboratory (VDRL) positive. At the time of study screening for neurosyphilis was not done routinely. This was an observational cross-sectional hospital based study. The study involved all HIV positive adult patients who were admitted to the Bugando Medical Centre; medical wards and those who were seen at CTC. All HIV positive patients 18 years and above who had tested positive for *T. pallidum* in the three months prior to study initiation or during the study period were included. We excluded all HIV negative patients.

The convenience sampling method was used and we approached all HIV-positive patients admitted to the hospital or being seen at the CTC over four months period to offer them
opportunity to participate in the study. All participants provided written consent.

A minimum sample size of 138 patients was calculated by Kish Leslie formula using a predicted prevalence of neurosyphilis among HIV positive patients of 10% \((8,9)\).

Participants were interviewed using a structured questionnaire which included age, sex marital status education and a mental status examination. Five milliliters of blood were drawn by trained personnel into Ethylene Diamine Tetra acetic Acid (EDTA) bottles and tested for *Treponema pallidum* antibodies by Treponema Pallidum Hemagglutination Assay (TPHA) as well as for CD4 count and viral load. Participants with positive results underwent a thorough neurological examination including cognitive assessment, fundoscopic examination and subjective audiometry (Weber and Rinne tests). These patients were also examined for sensory, motor, gait and balance deficits. Participants with neurologic abnormalities were offered lumbar puncture by trained personnel.

Neurosyphilis was defined according to Centers For Disease Control (CDC) criteria as serum treponemal test TPHA positive plus neurological features plus CSF-VDRL positive and/or 20 WBC/microlitre or more in CSF without other clear cause\((11)\). Patients discovered to have syphilis or neurosyphilis were referred to their attending physician who provided treatment as per CDC guidelines. First line treatment of neurosyphilis was intravenous (IV) benzyl penicillin 18 to 24 MU divided in 3 to 4 MU every 4 hours for 10 to 14 days and second line was procaine penicillin G 2.4MU daily with probenecid 500mg 4hourly for 10 to 14 days. Patients were followed up for 30 days beginning on the day of treatment to assess clinical outcome after treatment\((11,12)\).

Data were collected using a coded questionnaire and entered into Microsoft Excel. Data were analyzed using STATA version 13 (College Station, Texas). All continuous variables were summarized as medians with interquartile ranges, while categorical variables were summarized as proportions or percentages using chi-squared tests. Univariable followed
by multivariable logistic regression analyses were used to determine factors associated with syphilis. Any factor with a p-value of <0.3 on univariable logistic regression analysis was included in the multivariable model. A p-value less than 0.05 was considered to be statistically significant in the final model.

Ethical clearance was obtained from the CUHAS /BMC Joint Ethics and Review Committee with certificate number CREC/242/2017. Written informed consent was obtained from each patient or patient's next of kin for those unable to consent for themselves because of illness or severe cognitive impairment. Results were communicated to the treating physician immediately and a copy of the results was placed in the patient's file.

Results

In this study a total of 1748 participants were screened for syphilis, and 167(9.6%) were found to be serum TPHA positive. More than half, 1008 (57%) of the studied participants had enrolment CD4 counts of >350 cells/uL and 1333 (76.3%) had viral loads of less than 50 copies /ml. Details of the 167 study participants who were TPHA positive are found in Table 1. Females comprised a large number with positive serum TPHA (72.5%); and the majority of those with TPHA positivity were aged 40-64 years (100/167, 59.9%). The T. pallidum seropositive group was significantly older than the TPHA negative group as shown in table 2. The TPHA positive group also had more monogamously married people and more people with only primary education. Vendors constituted the largest occupational group comprising 104 (62.3%) among those who were T. pallidum seropositive.

In 167 participants, 18 (10.8%) reported a previous history of syphilis and among them 12 (66.7%) reported prior history of treatment with penicillin injections. Of these 10 (83.3%) had 3 penicillin injection doses and 2 (16.7%) received single dose. Only 14 participants (8.4%) reported prior history of chancre while the majority reported a single genital lesion.
In nine participants (64.3%) the chancre had occurred in the past year. Only 3 (1.8%) participants had reported painless rashes on the palms or soles and none of these received treatment. All except for one participant were on ART 166(99.4%).

Details of the 141 patients who underwent neurological examination are shown in Table 3. Most of participants (138, 97.9%) had no cognitive impairment while one had mild and two had severe impairment. Only two participants (1.5%) had blurred vision, and after further examination one was found have a cataract in the left eye and the other had corneal ulcer. Both of these patients were managed by the ophthalmologist accordingly. No features of syphilis of the eye were noted. Most of patients were on ART, and the majority had been on ART for more than 2 years (111, 66.5%). A large number (130, 77.8%) of those who were seropositive for *T. pallidum* had a suppressed viral load of less than 50 copies/ml and only a small number of participants (10, 6%) had viral load of more than 1000 copies/uL. More than half of participants had CD4+T cells above 350 cells/uL (94, 56.3%).

Two patients were noted to have confusion (1.5%) of whom one had fever as well (0.7%). Both of these were bedbound and gait could not be assessed. No participant was noted to have sight loss, uveitis, or Argyll-Robertson pupils. Two of the participants were noted to have hearing loss. One had right-sided sensorineural hearing loss and all other neurological features were normal. The other had reduced cognition and thus it was difficult to assess the type of hearing loss. The bed bound patients did not have Romberg or vibration sense test done. All the other patients had negative Romberg’s test and normal vibration sense. All had normal reflexes.

There were four participants who were seropositive for *T. pallidum* with neurological abnormalities who underwent lumbar puncture after counseling and consent as shown in table 5. One patient was CSF -VDRL positive and had CSF-WBC <5 cells/ uL. Three patients
had negative CSF -VDRL and CSF-WBC <5 cells/uL. In the univariable logistic regression analysis several factors were statistically significantly associated with seropositivity for *T. pallidum* including older age (Odds ratio (OR) 2.37 [95% confidence interval (CI), 1.10-5.09], p=0.027), being widowed (OR 1.88 [1.50-3.90], p=0.013) polygamy (OR 9.97, [2.15-46.16], p=0.003), prior history of genital chancre (OR 3.93, [2.07-7.44], p<0.001), and previous history of syphilis (OR 5.34 [95% CI, 2.95-9.65], P <0.001). On multivariable logistic regression analysis, only polygamy (OR 8.51 [1.71-42.37], p=0.009) and previous history of syphilis (OR 3.5[1.75-7.01], p<0.001) remained independently associated with syphilis co infection.

One patient among four had neurosyphilis confirmed with CSF- VDRL positive while CSF – WBC<5. The other three patients did not meet the criteria of neurosyphilis in HIV patients according to the CDC recommendation. Table 5 below shows the details of CSF finding after lumbar puncture in the four patients who underwent lumbar puncture.

**Discussion**

In this study of HIV positive participants (9.6%) were seropositive for *T. pallidum*. The finding was similar to a prevalence rate of 10.0% reported in a study done in Uganda (13) and another in Ethiopia where (9.8%) out of 306 HIV positive patients were found to be seropositive for *T. pallidum* (14). The Seroprevalence that we observed was lower than that found in Ghana(14.8% of 284 HIV-infected participants) and higher than a study done in Rwanda in which (4.8%) of 482 HIV-infected participants were syphilis seropositive.

People who reported being married to one person were significantly more frequently seropositive for *T. pallidum* (56.3% versus 53.5% in the TPHA negative). This finding is similar to study results from Uganda(13) and Ethiopia(14), and may be because of concurrency of partners. Specifically, Kenyon *et al* reported that male partner
concurrency in which men had an average of five concurrent partners was significantly associated with high prevalence of syphilis (15). People who were TPHA positive were significantly more likely to have only a primary education, perhaps suggesting that they may have lacked knowledge on preventive measures against sexually-transmitted infections. This finding was contrary to study done in Ethiopia in which having a secondary education was associated with TPHA positivity. Employed persons were less likely to have seropositive T.pallidum in our study. Only 10% of patients who were seropositive for T.pallidum reported previous history of syphilis. Syphilis is not screened for routinely among people living with HIV and perhaps at times not thought to be an important problem. Similarly high rates of undiagnosed syphilis have been reported from Ethiopia. For those who had syphilis, only two-thirds (66.7%) received treatment. The majority received three intramuscular penicillin doses according to CDC recommendation, as also reported by Katz and colleagues (16).

Most patients who were seropositive for T.pallidum had CD4+ T cells above 350 cells/uL (56.3%) and viral load levels less than 50 copies/mL (77.8%) contrary to our hypothesis that those with T.pallidum seropositivity would have low CD4+ T cell counts. We did not find an association between syphilis and CD4 counts or viral loads. This might be because most of the patients in our study were on ART and in a latent stage of syphilis. Our results contrast with the study in the US by Kate et al which reported that syphilis reduces CD4+ T cells and increases viral load (6), particularly in those with secondary syphilis on ART and those with syphilis not on ART. We also found that the majority of participants who were seropositive for T.pallidum reported no prior history of genital lesion (97.1%), possibly due to the painless lesions of syphilis that might go unnoticed in primary stages. A study in Spain similarly found that few patients who were seropositive for T.pallidum reported a past genital lesion (8).
Among the 141 participants who were serum TPHA positive and returned to the clinic for neurological assessment, 3 participants had cognitive impairment. One of those with cognitive impairment also had hearing loss. The second patient had hearing loss alone with no other symptoms. The third patient had fever, headache, and altered mental status. The patients were also assessed for any sign of meningeal irritation but no one was positive. In addition, eye examinations identified no patient with typical features of ophthalmic syphilis. Patients were also examined for gait, unilateral weakness, and sensory modalities and were all found to be normal. This is in contrast with the study done US by Katz et al which had found 12 patients with neurosyphilis, of whom had eye problems, 3 with altered mental status and five with unilateral weakness. Of note, a major difference between the Tanzania and the US study is that not all US patients were on ART, whereas all but one of the Tanzanian study patients were on ART. Among the 141 screened by examination, only 4 (2.8%) had neurological symptoms necessitating lumbar puncture to assess for neurosyphilis. This was in accordance with expert guidelines recommending lumbar punctures not in all seropositive for T. pallidum plus HIV-positive patients, but only in those with neurological abnormalities. In our study among the 4 participants with syphilis who underwent lumbar puncture one was confirmed to have neurosyphilis. That person had no prior history of syphilis and was not on ART. The CD4+ T cell count was 412 cells/μL. The patient was treated with daily intravenous ceftriaxone per the CDC guideline but died after 3 days in the ward after rapid neurologic deterioration. This patient might have suffered from the meningoencephalitic form of neurosyphilis which has fast progression with poor prognosis in HIV positive patients. This form of neurosyphilis was seen in one case study in an HIV-positive patient who presented with abnormal behavior. In HIV positive patients even those with normal CD4+ T cell counts, immune cells may have altered function increasing the risk of
syphilitic meningoencephalitis (19). Likewise a study in the US found 16 neurosyphilis patients who were identified with only CSF-VDRL positivity among 50 patient with neurosyphilis (20). By contrast, in the study done in Spain, all patients who had a diagnosis of neurosyphilis presented with mild headache, had no prior history of treatment, and improved after therapy (8). Patients, who were negative for neurosyphilis, were all on ART and reported no history of prior treatment for syphilis. This may have occurred because ART use reduces the chances of having neurosyphilis to a level comparable to that of HIV-uninfected people with syphilis (21).

In our study we found a prevalence of neurosyphilis of only 0.7% of all who were examined for neurologic features. This prevalence was surprisingly low given the findings of other studies that have suggested the prevalence could be as high as 25%. This low prevalence may be due either to ART use in most patients, or possibly to having been previously treated with antibiotics, for a different indication, that have activity against Treponema pallidum. Our findings on neurosyphilis fit with a systemic review of neurosyphilis in Africa (22), which found only two patients with meningitis (3.3%). Another study done in Brazil had shown the prevalence of neurosyphilis to be 1% among HIV positive patients with neurologic features (23). In contrast, a study by Alverez et al showed that 23.5% T. pallidum seropositive patients who were not on ART had neurosyphilis (8). Therefore, our study documents an important and encouraging finding that rates of neurosyphilis are lower in our setting than previously reported. This may be due to the expanding use of ART and also to the use of antibiotics, some of which may be excess but may serve inadvertently to treat T. pallidum seropositive patients and prevent neurosyphilis.

Our study had some limitations. It was difficult to know if patients had been previously treated for syphilis with other agents that are active against syphilis like ceftriaxone or doxycycline because of the lack of electronic data keeping. In our study we did not
perform lumbar puncture in patients without neurologic features and hence we may have missed asymptomatic neurosyphilis. We were not able to determine whether a patient may have had seroreversion of syphilis as the reagent used was only qualitative and usually stays positive for life. Risk factors for neurosyphilis could not be determined due to very small number. HIV-positive patients with neurosyphilis may die rapidly and this cross-sectional study would not have found those patients.

Conclusions

We found a high percentage of seropositivity for *T.pallidum* in HIV positive participants in which one out of ten people was affected yet a very low prevalence of neurosyphilis. This argues for the need for sexually transmitted infection (STI) screening especially syphilis with specific focus on HIV positive patients. Factors associated with syphilis were having multiple partners and having a low level of education. We also observed a high rate of untreated syphilis among HIV-positive patients. Only 10.8% of HIV-positive patients who had syphilis were aware of their diagnosis, which highlights the importance of prioritizing screening and treatment. We therefore recommend that screening for syphilis should be provided to all HIV positive individuals and that those with untreated syphilis should receive three doses of penicillin. For those with syphilis involving central nervous system manifestations urgent treatment with benzyl penicillin or ceftriaxone according to National Standard treatment guidelines or CDC recommendation is needed. Screening and treating syphilis in all HIV positive patient should be routinely done as the disease can present as fulminant meningoencephalitis and, frequently death. In HIV positive patients with neurological manifestations neurosyphilis should be considered as one of diagnosis. We recommend having further studies should be done among HIV positive patients with neurologic manifestations who are admitted to the hospital to rule out neurosyphilis.
Abbreviations

ART		Antiretroviral therapy
BMC		Bugando Medical Centre
CDC		Center for Disease Control
CD4		Cluster differention
CREC	CUHAS /BMC Joint Ethics and Review Committee
CSF		Cerebrospinal fluid
CTC		Care and treatment clinics
CUHAS	Catholic University of Health and Allied Sciences
HIV		Human immunodeficiency Virus
TPHA	Treponema pallidum Haemoglutination Assay
VDRL	Venereal disease research laboratory
WBC		White blood cell

Declarations

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Ethical approval was obtained from the CUHAS /BMC Joint Ethics and Review Committee with certificate number CREC/242/201

The datasets generated and/or analyzed during the current study are available in the researchdata@springernature.com

Competing interest –Not applicable
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Authors contributions - participated from concept note to improving the proposed manuscript

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Tables

Table 1: General characteristics of the 1,748 HIV positive study participants.

| Variable | Frequency | Percent or Median (IQR) |
|----------|-----------|-------------------------|
| Gender   |           |                         |
| Male     | 496       | 28.4                    |
| Female   | 1,252     | 71.6                    |
| Age      | 1748      | 42 [34-50]              |
| Age Range | Count | Percentage |
|-----------|-------|------------|
| 18-39     | 729   | 41.7       |
| 40-64     | 966   | 55.3       |
| 65-85     | 53    | 3.0        |

| Marital status | Count | Percentage |
|----------------|-------|------------|
| Single         | 543   | 31.1       |
| Married (monogamy) | 940   | 53.8       |
| Polygamy       | 258   | 14.8       |
| Window         | 7     | 0.4        |

| Occupation | Count | Percentage |
|------------|-------|------------|
| Vendor     | 1,114 | 63.7       |
| Peasant    | 338   | 19.3       |
| Fisherman  | 10    | 0.6        |
| Employed   | 211   | 12.1       |
| Housewife  | 75    | 4.3        |

| Residence   | Count | Percentage |
|-------------|-------|------------|
| Mwanza city | 1,552 | 88.8       |
| Outside     | 196   | 11.2       |

| Education   | Count | Percentage |
|-------------|-------|------------|
| Illiterate  | 126   | 7.2        |
| Primary     | 1,170 | 66.9       |
| Secondary   | 373   | 21.3       |
| College     | 60    | 3.4        |
| University  | 19    | 1.1        |

| Reports being told to have syphilis | Count | Percentage |
|-------------------------------------|-------|------------|
| No                                  | 1,695 | 97.0       |
| Yes                                 | 53    | 3.0        |

| Reports previously being treated for syphilis | Count | Percentage |
|------------------------------------------------|-------|------------|
| No                                             | 17    | 32.1       |
| Yes                                            | 36    | 67.9       |

| Reports penicillin injection | Count | Percentage |
|-------------------------------|-------|------------|
| One                           | 4     | 11.1       |
| Three                         | 32    | 88.9       |

| History of genital lesion | Count | Percentage |
|---------------------------|-------|------------|
| No                        | 1,698 | 97.1       |
| Yes                       | 50    | 2.9        |

| Number of lesion | Count | Percentage |
|------------------|-------|------------|
|                | One | >two |
|----------------|-----|------|
|                | 15  | 35   |
|                | 30  | 70   |

**Duration of lesion**

|          | 29 | 58.0 |
|----------|----|------|
| < year   |    |      |
| 2-3 year | 11 | 22.0 |
| 4-6 year | 4  | 8.0  |
| >6 years | 6  | 12.0 |

**Rashes on palm and sole**

|         | 1,740 | 99.5 |
|---------|-------|------|
| No      |       |      |
| Yes     | 8     | 0.5  |

**Treatment for rashes**

|          | 3    | 37.5 |
|----------|------|------|
| No       |      |      |
| Yes      | 5    | 62.5 |

**ART use**

|         | 1    | 0.1  |
|---------|------|------|
| Not on ART | 1,747 | 99.9 |

**Serum TPHA**

|       | 1,581 | 90.5 |
|-------|-------|------|
| Negative |     |      |
| Positive | 167  | 9.6  |

**CD4 Cell/µl**

|          | 1,748 | 526 [362-706] |
|----------|-------|----------------|
| < 350    | 306   | 17.5           |
| >350 missing | 1,008  | 57.7           |
|          | 434   | 24.8           |

**Viral load (copies/µL)**

|          | 1748 | 19 [19-20] |
|----------|------|------------|
| < 50     | 1,333 | 76.3       |
| 50-999   | 78   | 4.5        |
| >1000    | 84   | 4.8        |
| Missing  | 253  | 14.5       |

**Table 2:** Socio-demographic and reported clinical characteristics of 167 HIV-positive
individuals who were serum *T. pallidum* seropositive compared to 1581 *T. pallidum* seronegative Participants

| Variable                        | TPHA Positive | \( \chi^2 \) |
|--------------------------------|---------------|--------------|
|                                | YES N(%)      | NO N(%)      |                |
| **Gender**                     |               |              |                |
| Male                           | 46 (27.5)     | 450 (28.5)   | 0.063          |
| Female                         | 121 (72.5)    | 1131 (71.5)  |                |
| **Age**                        |               |              |                |
| 18-39                          | 58 (34.7)     | 671 (42.4)   | 6.349          |
| 40-64                          | 100 (59.9)    | 866 (54.8)   |                |
| 65-84                          | 9 (5.4)       | 44 (2.8)     |                |
| **Marital status**             |               |              |                |
| Single                         | 38 (22.8)     | 505 (31.9)   | 15.73          |
| Married (monogamy)             | 94 (56.3)     | 846 (53.3)   |                |
| Widow                          | 32 (19.2)     | 226 (14.3)   |                |
| Polygamy                       | 3 (1.8)       | 4 (0.25)     |                |
| **Education**                  |               |              |                |
| Illiterate                     | 29 (17.4)     | 97 (6.1)     |                |
| Primary                        | 112 (67.1)    | 1058 (66.9)  |                |
| Secondary                      | 21 (12.5)     | 352 (22.3)   | 34.53          |
| College                        | 3 (1.8)       | 57 (3.6)     |                |
| University                     | 2 (1.2)       | 17 (1.1)     |                |
| **Residence**                  |               |              |                |
| Mwanza city                    | 148 (88.6)    | 1404 (97)    | 0.005          |
| Outside Mwanza city            | 19 (11.4)     | 177 (11)     |                |
| **Occupation**                 |               |              |                |
| Vendor                         | 104 (62.3)    | 1010 (63.9)  |                |
| Peasant                        | 44 (26.4)     | 294 (18.6)   |                |
| Fisherman                      | 2 (1.2)       | 8 (0.5)      | 19.28          |
| Employed                       | 6 (4.0)       | 205 (13.0)   |                |
| House wife                     | 11 (6.6)      | 64 (4.1)     |                |
| **Reports previous history of syphilis** |           |              |                |
| No                             |               |              |                |
| Yes                            | 149 (89.2)    | 1546 (97.8)  | 37.68          |
|                                | 18 (10.8)     | 35 (2.2)     |                |
| Reported previous treated syphilis | No | Yes |
|-----------------------------------|----|-----|
|                                   | 6(33.3) | 12(66.7) | 11(0.7) | 24(1.5) | 0.02 |
| Reports penicillin injection       | One | 2(16.6) | 2(8.30) | 0.563 |
|                                   | Three | 10(83.3) | 22(91.7) |  |
| History of genital lesion          | No | 153(91.6) | 1545(97.7) | 20.27 |
|                                   | Yes | 14(8.4) | 36(2.3) |  |
| Number of lesion                   | One | 10(71.4) | 5(13.9) | 15.89 |
|                                   | Two or more | 4(28.6) | 31(89.1) |  |
| Duration of lesion                 | Less than a year | 9(64.3) | 20(55.6) | 0.536 |
|                                   | Two to three year | 3(21.5) | 8(22.2) |  |
|                                   | 4 to six year | 1(7.1) | 3(8.3) |  |
|                                   | More than six year | 1(7.1) | 5(13.9) |  |
| Rashes on palms and soles         | No | 164(98.2) | 1576(99.6) | 7.264 |
|                                   | Yes | 3(1.8) | 5(0.3) |  |
| Treatment for rashes               | No | 3(100.0) | 0(0) | 8 |
|                                   | Yes | 0(0.0) | 5(100) |  |
| ART use                            | No | 1(0.6) | 0(0) | 9.473 |
|                                   | Yes | 166(99.4) | 1681(100) |  |
| Duration of ART use                | Less 6 month | 3(1.8) | 0 | 1400 |
|                                   | 6 month to 2 years | 25(15.0) | 0 |  |
|                                   | Above 2 yrs | 111(66.5) | 0 |  |
|                                   | Missing | 28(16.8) | 1681 |  |
| Viral load (copies/ml) | Less than 50 | 50-999 | 1000 or more | Missed viral load |
|-----------------------|--------------|--------|--------------|------------------|
|                       | 130 (77.8)   | 7 (4.2)| 10 (6.0)     | 20 (12.0)        |
|                       | 1203 (79.1)  | 71 (4.5)| 74 (4.7)     | 233 (14.7)       |

| CD4 cell/μL           | Less than 350 | 350 and above | Missing |
|-----------------------|---------------|----------------|---------|
|                       | 35 (21.0)     | 94 (56.3)      | 38 (22.7)|
|                       | 271 (17.1)    | 914 (57.8)     | 396 (25.15)|

| CSF WBC/UL            | Less than or equal 5 | Greater 5 |
|-----------------------|-----------------------|-----------|
|                       | 4 (100.0)             | 0 (0.0)   |

| CSF Treponema antibody | Negative | Positive |
|------------------------|----------|----------|
|                        | 3 (75.0) | 1 (25.0) |

Table 3: Clinical findings among 141 HIV positive patients who were seropositive for *T. pallidum* and returned for further evaluation Mwanza Tanzania
| Variable                                      | Frequency | Percent |
|----------------------------------------------|-----------|---------|
| MMS                                          | 138       | 97.9    |
| Neck pain noted on examination                |           |         |
| Yes                                          | 0         | 0       |
| No                                           | 141       | 100     |
| Noted reduced vision                         | 2         | 1.5     |
| Yes                                          | 1         | 99.3    |
| No                                           | 142       | 0.7     |
| Seen with confusion                          | 2         | 1.5     |
| Yes                                          | 139       | 98.5    |
| No                                           |           |         |
| Had noted with fever                         | 1         | 99.3    |
| Yes                                          | 142       | 0.7     |
| No                                           |           |         |
| Gait                                          |           |         |
| Normal                                       | 139       | 98.5    |
| Abnormal                                     | 0         | -       |
| Bedbound                                     | 2         | 1.5     |
| Sight loss right                             |           |         |
| Absent                                       | 141       | 100.0   |
| Present                                      | 0         | -       |
| sight loss left                              |           |         |
| Absent                                       | 141       | 100.0   |
| Present                                      | 0         | -       |
| Uveitis                                      |           |         |
| Absent                                       | 141       | 100.0   |
| Present                                      | 0         | -       |
| Argyll-Robertson pupil                       |           |         |
| Absent                                       | 141       | 100.0   |
| Present                                      | 0         | -       |
| Hearing loss right                           |           |         |
| Absent                                       | 140       | 99.3    |
| Present                                      | 1         | 0.7     |
| Hearing loss left                            |           |         |
| Absent                                       | 140       | 99.3    |
| Present                                      | 1         | 0.7     |
| Type of hearing loss                         |           |         |
| No deficit                                   | 140       | 99.3    |
| Sensorineural                                | 1         | 0.7     |
| Conductive                                   | 0         | -       |
| Romberg's sign                               |           |         |
| Negative                                     | 141       | 100.0   |
| Positive                                     | 0         | -       |
| Position sense                               |           |         |
| Normal                                       | 141       | 100.0   |
| Abnormal                                     | 0         | -       |
| Vibration sense                              |           |         |
| Normal                                       | 141       | 100.0   |
| Abnormal                                     | 0         | -       |
| Reflexes                                     |           |         |
| Normal                                       | 141       | 100.0   |
| Reduced                                      | 0         | -       |
| Exaggerated                                  | 0         | -       |

Table 4: Univariable and multivariable analysis for factors associated with syphilis co-infection
|                | Male       | Female     |
|----------------|------------|------------|
| **Sex**        | 1          | 1.04 (0.73-1.50) | 0.802 |
| **Age**        |            |            |
| 18 - 39        | 1          | 1.34 (0.95-1.87) | 0.094 |
| 40-64          |            | 1.13 (0.78-1.63) | 1.13 |
| 65-85          | 2.37 (1.10-5.09) | 0.027 | 1.34 (0.57-3.13) |
| **Marital status** |            |            |
| Single         |            |            |
| Married        | 1.48 (1.00-2.29) | 0.052 | 1.42 (0.94-2.14) |
| Widow          | 1.88 (1.50-3.90) | 0.012 | 1.47 (0.86-2.52) |
| Polygamy       | 9.97 (2.15-46.16) | 0.003 | 8.51 (1.71-42.37) |
| **Education**  |            |            |
| Illiterate     |            |            |
| Primary        | 0.35 (0.22-0.56) | < 0.001 | 0.38 (0.23-0.61) |
| Secondary      | 0.2 (0.19-0.36) | < 0.001 | 0.26 (0.14-0.50) |
| College        | 0.18 (0.05-0.60) | 0.006 | 0.29 (0.08-1.06) |
| University     | 0.39 (0.86-1.80) | 0.230 | 0.77 (0.16-3.67) |
| **Occupation** |            |            |
| Vendor         |            |            |
| Peasant        | 1.45 (1.00-2.17) | 0.051 | 1.15 (0.77-1.72) |
| Fisherman      | 2.43 (0.51-11.58) | 0.226 | 1.76 (0.29-10.54) |
| Employed       | 0.28 (0.12-0.66) | 0.003 | 0.33 (0.14-0.78) |
| House wife     | 1.16 (0.85-3.26) | 0.134 | 1.57 (0.79-3.13) |
| **Chancre**    |            |            |
| No             |            |            |
| Yes            | 3.93 (2.07-7.44) | <0.001 | 2.1 (0.96-4.58) |
| **Rashes**     |            |            |
| No             |            |            |
| Yes            | 5.76 (1.37-24.34) | 0.017 | 2.02 (0.41-9.92) |
| **Told syphilis** |            |            |
| No             |            |            |
| Yes            | 5.34 (2.95-9.65) | <0.001 | 3.5 (1.75-7.01) |
| **Previously treated syphilis** |            |            |
| No             |            |            |
| Yes            | 0.92 (0.27-3.08) | 0.888 |
| **Viral load (copies/uL)** |            |            |
| < 50           |            |            |
| 50-999         | 0.91 (0.41-2.02) | 0.822 |
| 1000 or more   | 1.25 (0.63-2.48) | 0.522 |
| Not tested     | 0.79 (0.49-1.30) | 0.358 |
Table 5: Clinical Descriptions of Four seropositive for *T. pallidum* patients who had neurologic abnormalities and underwent lumbar puncture.

| Patient number | 1         | 2         | 3         | 4         |
|----------------|-----------|-----------|-----------|-----------|
| Gender         | Male      | Female    | Female    | Female    |
| Age in (years) | 50        | 65        | 57        | 30        |
| ART use        | Not on ART| yes       | yes       | yes       |
| Duration of ART| -         | 4 months  | 2 years   | 7 y       |
| Neurologic features | Headache | Confusion | Disturbed memory | Confusion |
|                 | Confusion | fever     | -         | Hearing loss left |
|                 |           |           |          | Disturbed memory and cognition |
|                 |           |           |          | Hearing loss |
|                 |           |           |          | Low |
| CD4+/uL        | 412       | -         | 219       | 270       |
| Viral load (copies/UL) | Not tested | Not tested | 19        | 19        |
| CSF finding    | -Positive VDRL | -WBC <5/uL | Negative VDRL | -Ne |
|                 | WBC <5/uL | Normal glucose | WBC <5 cell/uL | WB |
|                 | Normal protein | Normal protein | Normal glucose | Nor |
|                 | Cryptococcal antigen negative(CRAG) | Negative CRAG | Negative culture | Ne |
|                 | Clear fluid with negative gram stain and culture | Negative culture | Negative CRAG | |
| Diagnosis      | Neurosyphilis with meningoencephalitis | Presumed HIV Encephalopathy | Presumed HIV Encephalopathy | HIV | Hyp |
| Outcome        | Admitted to the ward and started on Ceftriaxone 2g IV BD. Died after three days in the course of treatment in the ward. | Alive, cognition deficit improving on ART. | Discharged home alive but later died at home. | Alive | im |
Prevalence of syphilis among 1748 study participants
Figure 2

Prevalence of Neurosyphilis among 141 HIV-positive patients in Mwanza Tanzania