

Original Article

Syphilis serology in HIV-positive and HIV-negative Nigerians: The public health significance

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Abstract:

Syphilis has acquired new potential for morbidity and mortality through association with increased risk for HIV infection. Case-control survey was conducted using Rapid Plasma Reagin test and confirmatory Immunochromatographic test among HIV-positive (cases) and HIV-negative (control) Nigerians. A total of 35(14.0%) of 250 HIV-positive and 5(2.0%) of 250 HIV-negative individuals studied were seropositive for syphilis, the difference was statistically significant ($P < 0.05$). The prevalence was higher among females than males of HIV-positive (15.0% versus 12.7%) and of the HIV-negative (2.1% versus 1.9%) individuals. Syphilis seroprevalence was highest among HIV-positive individuals aged 21-30 years (20.5%) and 41-50 years old HIV-negative individuals (4.5%). Sex education, promotion of safer sexual behaviour, prompt diagnosis of STDs and provision of effective, accessible treatment are recommended

Key Words: Syphilis, *Treponema pallidum*, HIV, Seroprevalence

Introduction:

Sexually transmitted diseases (STDs) are a major global cause of infertility, long-term disability and death with severe medical and psychological consequences for millions of men, women and infants.(1) Syphilis, caused by the bacterium *Treponema pallidum*, is a major STD which remains an important cause of morbidity and is associated, like other ulcerative sexually transmitted infections, with enhanced sexual transmission of human immunodeficiency virus, HIV.(2) While syphilis is largely under control in affluent part of the world, it continues to be a tragic and substantial problem in many developing countries, including Nigeria. Furthermore, through its association with increased risk for HIV infection, syphilis has acquired a new potential for morbidity and mortality.(3)

The interaction of syphilis and HIV infection is reportedly complex.(4) Isolated case reports have suggested that coexistent HIV infection may alter the natural history of syphilis and the dosage or duration of treatment required to cure syphilis.(5,6) These anecdotal reports have led to the hypothesis that in patients co-infected with HIV and *T. pallidum*, cutaneous lesions may be more severe, symptomatic neurosyphilis may be more likely to develop, the latency period before the development of meningo-vascular syphilis may be shorter, and the efficacy of standard therapy for early syphilis may be reduced.(7)

Furthermore, the genital ulcerations and inflammation caused by syphilis are implicated as cofactors making infected individuals three to five times more likely to acquire HIV if exposed to the virus through sexual contact.(8) Unless prompt diagnosis and treatment of syphilis are performed serious complications including male and female infertility may result, and in pregnancy, adverse outcomes such as stillbirth, perinatal death and serious neonatal infection may occur.(9)

There is paucity of information on syphilis serology in Nigeria as in other countries of the sub-Saharan Africa, a region where 25.4 million HIV-infected people (64% of all people with HIV) are living.(10) Available information in the region usually came from seroprevalence sentinel surveys of women attending ante-natal clinics, ANCs.(11-13) This study was therefore designed to add to the limited body of literature on syphilis serology among HIV-positive and HIV-negative individuals in the sub-Saharan Africa.

Materials and Methods: Study Area

This study was hospital-based and conducted at the Federal Medical Centre (FMC), one of the largest health institutions located in Abakaliki the capital city of Ebonyi State, South-eastern Nigeria. The FMC Abakaliki, sees an av-

erage of 3,327 out patients every month with over 30% of the patients coming from outside of the city including other neighbouring South-eastern States of Nigeria. The HIV infection prevalence of 4.6% and 1.0% for syphilis were recorded from seroprevalence survey in ANCs in the area.(12) Heterosexual intercourse is the predominant sexual behaviour in the area.(14)

Ethical Considerations

The approval of this study was obtained from Infectious Disease Research Division, Department of Medical Microbiology, Faculty of Clinical Medicine, Ebonyi State University and the Ethical Committee of the Federal Medical Centre Abakaliki.

Study Population/Sampling Technique:

The study was a case-control investigation conducted from January 2004 to April 2005. During the study period, 1,672 patients who visited the FMC Abakaliki, comprising of individuals with symptoms suggestive of retroviral infection, referred to the laboratory unit by their physicians for HIV antibody testing, and others who had tested HIV positive by enzyme-linked immunosorbent assay (ELISA) elsewhere and were referred to the hospital for confirmatory test, were considered for the study. Also considered for the study were 937 individuals who visited the hospital for various reasons, such as premarital screening tests, antenatal tests, paediatrics care tests, and pre-employment/admission tests of which HIV antibody testing was among the tests required. The sex of each patient was recorded while age was obtained by interview. About 4mls of blood sample was obtained by venepuncture from each patient and serum was separated and stored at -20°C until serological analysis (HIV antibody and syphilis testing) was performed. After the HIV antibody testing of all subjects, the HIV serostatus of

483 patients was confirmed positive, 32 were indeterminate while the rest were HIV-negative. Serum samples from the first confirmed 250 HIV-positive and 250 HIV-seronegative individuals were selected and thereafter subjected to syphilis serology. Individuals whose HIV serostatus was indeterminate by immunoblot analysis were excluded from the syphilis serology. Only a total of 500 samples were screened due to financial constraints and the number of available syphilis tests. The syphilis serology was conducted as an anonymous and unlinked survey.

HIV and Syphilis Serology

The HIV Tri Line Test kits, commercially available (Biosystem INC., Austria) were first used to detect antibodies to HIV-1 and HIV-2 in the serum samples. Thereafter the HIV-seropositive samples were confirmed by immunoblot analysis using the BIORAD New Lav Blot kits, commercially available (Bio-Rad Novapath Diagnostic Group US.). The first 250 serum samples, confirmed HIV-positive (cases) and the first 250 serum samples, confirmed HIV-seronegative (control) were further screened for syphilis using the Rapid Plasma Reagin (RPR) Test and reactive samples were confirmed using immunochromatographic (IC) rapid syphilis test kits, commercially available (Cal-Tech Diagnostic INC.).

Statistical Analysis:

Differences in proportion were evaluated using the chi-square test. Statistical significant was achieved if $P < 0.05$.

Results:

A total of 35(14.0%, 95% CI., 9.7-18.3%) of the cases (250 HIV-positive)and 5(2.0%, 95%CI., 0.3-3.7%) of the control (250 HIV-negative) individuals were seropositive for syphilis (Odd ratio=7.98, 95% CI., 5.6-10.4), indicating *T. pallidum* infection (Table 1), and the difference was statistically significant ($\chi^2=34.5$, $df=1$, $P<0.05$).

Table 1: Summary of prevalence of *T. pallidum* infection among HIV-positive and HIV-negative individuals in Abakaliki, South-eastern Nigeria.

HIV-serostatus	Male		Female		Overall total		95% Confidence interval
	Number examined	Number (%) infected	Number examined	Number (%) infected	Number examined	Number (%) infected	
HIV-positive	110	14(12.7)	140	21(15.0)	250	35(14.0)	9.7-18.3
HIV-negative	106	2(1.9)	144	3(2.1)	250	5(2.0)	0.3-3.7
Total	216	16(7.4)	284	24(8.5)	500	40(8.0)	5.6-10.4

Among the HIV-positive individuals (110 males and 140 females), the prevalence of *T. pallidum* infection was higher in the females (15.0%, 95% CI., 9.1-20.9%) than in the males (12.7%, 95% CI., 6.5-18.9%), but there was no significant difference statistically ($\chi^2=0.27$, $df=1$, $P>0.05$). Individuals of the 21-30 and 31-40 years age groups had the highest prevalence of 20.5% (95% CI., 11.2-29.8%) and 20.0% (95% CI; 9.4-30.6%) respectively (Table 2). This was followed by those aged 11-20 years (10.0%, 95% CI; 0.7-19.3%). *T. pallidum* infection was not observed among individuals less than 10 years old. Males and the females had almost equal prevalence of *T. pallidum* infection in the age category 21–30 and 31-40 years while females were more infected in the age category 11-20 than the males (13.3% vs. 8.0%), the reverse was the case among the 41-50 years age group (7.4% vs 8.0%) (Table 2). Statistical analysis showed no significant difference in the trend ($\chi^2 = 9.51$, $df = 5$, $P > 0.05$)

Table 2: Age-related prevalence of *T. pallidum* infection among HIV-positive individuals in Abakaliki, South-eastern Nigeria.

Age (years)	Male		Female		Overall total		95% Confidence interval
	Number examined	Number (%) infected	Number examined	Number (%) infected	Number examined	Number (%) infected	
≤ 10	4	0 (0.0)	6	0(0.0)	10	0(0.0)	-
11-20	25	2 (8.0)	15	2(13.3)	40	4(10.0)	0.7-19.3
21--30	29	6 (20.7)	44	9(20.5)	73	15(20.5)	11.2 –29.8
31-40	20	4(20.0)	35	7(20.0)	55	11(20.0)	9.4 –30.6
41-50	25	2 (8.0)	27	2(7.4)	52	4(7.7)	0.5- 14 .9
>50	7	0 (0.0)	13	1(0.9)	20	1 (5.0)	4.6 –14.6
Total	110	14(12.7)	140	21(15.0)	250	35(14.0)	9.7-18.3

Among the HIV-negative individuals (106 males and 144 females), two males (1.9%, 95% CI., 0.7-4.5%) and three females (2.1%, 95% CI., 0.2–4.4%) were seropositive for syphilis. Chi-square test showed no significant difference in the trend ($\chi^2=0.01$, $df=1$, $P>0.05$) (Table 3). The HIV-negative individuals aged 41-50 years old had the highest *T. pallidum* prevalence of 4.5% (95% CI., 4.2-13.2%) followed by individuals 21-30 years old (3.7%, 95% CI; 0.4-7.8%). *T. pallidum* infection was not observed among those less than 10 years old (Table 3). No statistical significant difference was observed in the trend ($\chi^2= 3.85$, $df = 5$, $P > 0.05$).

Table 3: Age-related prevalence of *T. pallidum* infection among HIV-negative individuals in Abakaliki, South-eastern Nigeria.

Age (years)	Male		Female		Overall total		95% Confidence interval
	Number examined	Number (%) infected	Number examined	Number (%) infected	Number examined	Number (%) infected	
< 10	7	0 (0.0)	5	0(0.0)	12	0(0.0)	-
11-20	30	1 (3.3)	35	0(0.0)	65	1(1.5)	1.5-4.5
21--30	35	1(2.9)	46	2(4.3)	81	3(3.7)	0.4-7.8
31-40	15	0(0.0)	30	0(0.0)	45	0(0.0)	-
41-50	10	0(0.0)	12	1(8.3)	22	1(4.5)	4.2-13.2
>50	9	0(0.0)	16	0(0.0)	25	0(0.0)	-
Total	106	2(1.9)	144	3(2.1)	250	5(2.0)	0.3-3.7

Discussion:

One of the principal problems confronting syphilis research in most developing tropical countries is the inability to reproducibly culture *T. pallidum* in the routine laboratory.(15) Serological tests are currently the mainstay for syphilis diagnosis and management and the nontreponemal tests are useful in screening patients for the presence of nonspecific reagin antibodies that appear and rise in titer following infection.(16,17) The choice of the rapid plasma reagin (RPR) test, a non-treponemal serological test for syphilis, in this study, were because it is widely used as a screening test in the developing world, easy to perform, does not need advanced equipment, and is inexpensive.(18,19)

In this study, it was established that the seroprevalence of *T pallidum* infection was significantly higher among the HIV-positive than HIV-negative individuals (14.0% vs 2.0%) ($P<0.05$). This is consistent with the findings in a similar study in Cuba.(20) A plausible explanation is that the impairment of both cell-mediated and humoral immunity by HIV (21), could limit the host's defenses against *T. pallidum*, thereby enhancing susceptibility to syphilis and also altering the clinical manifestations or natural course of the infection.(7) In addition it is well established that the prevalence of infections transmitted sexually is usually higher in HIV- positive than HIV-negative individuals (22,23), presumably because sexual behaviors that increase the risk for ac-

quiring HIV also increase the risk for acquiring other STIs including syphilis.(1) These may have accounted for the higher prevalence of *T. pallidum* infection among the HIV infected individuals in the study area.

It is worth noting that infection with HIV may not only alter the clinical presentation of syphilis, but also the performance of syphilis serologic tests. Thus the diagnosis of syphilis may be more complicated in HIV-infected patients because of false-negative and false-positive serologic results for *T. pallidum*.(7,24) Co-infection with HIV and syphilis however, does not generally impair the sensitivity of syphilis testing, although there are sporadic reports of absent or delayed response to nontreponemal tests.(25) In contrast, HIV infection may reduce the specificity of syphilis testing.(24,25) Although, serologic tests appear to be accurate and reliable for the diagnosis of syphilis and the evaluation of treatment response in the majority of HIV-infected patients (7), the interpretation of non-treponemal specific serological tests in a population where syphilis and HIV are endemic such as the sub-Saharan Africa may be encountered with difficulty due to lack of confirmatory tests and experienced personnel.(26,27) In many of such communities, the prevalence of reactive serology did not accurately reflect infectious syphilis largely because of unavailability of confirmatory tests.(28)This problem was however surmounted in this study by the use of

immunochromatographic (IC) rapid syphilis test kits (Cal-Tech Diagnostic INC.), that served as confirmatory test and substantiated the findings.

Females generally had higher rates of infection with *T. pallidum* than the males in this study. Although no statistical significant difference was observed, this was in conformity with the findings of Hwang et al.(29) who reported that women had up to 4.5% higher prevalence of *T. pallidum* infection than men. This was also consistent with the findings of Todd et al. (30) who also reported higher prevalence of *T. pallidum* infection in women (9.1%) than in men (7.5%) in a rural African population. On the contrary, a higher prevalence of *T. pallidum* infection was observed in males (27.5%) than in females (12.4%) in United State.(31) It is well established that syphilis in the females is less likely to be symptomatic; hence the prevalence of antibodies is usually higher among them compared to the males.(4,19) Secondly, there is generally a diminished access to health services by the females in the sub-Saharan Africa including Nigeria as in other developing countries.(32,33) These may explain the higher prevalence of syphilis among the females.

Individuals in their third decade of life in this study were found to have relatively high rate of *T. pallidum* infection. This was more obvious in the HIV infected population and was not unexpected. In Nigeria individuals in their third decade of life are known to have the highest rate of infections associated with sexual activities because the group is the most sexually active age category.(14) This was supported by the findings from a similar study in Ethiopia where it was indicated that *T. pallidum* infection was more pronounced among the young age group of 15-24 years.(13)

It is important to state that this study was not without a few limitations. In this investigation, we have not been able to demonstrate that the presence

of syphilis actually facilitated HIV infection because we were unable to establish whether syphilis infections pre-dated the HIV infections or vice versa. A more complex study to achieve this goal using immunological and molecular biologic tools is advocated. Our inability to report the different stages of syphilis among those infected, obtain sufficient socio-demographic data from subjects, and the rather limited study population size, were draw backs to the study. Further studies incorporating period of syphilis infection and detailed socio-demographic parameters as well as larger population size are advocated.

In conclusion, this study has provided additional insights on the burden of *T. pallidum* infection in Nigeria. As a public health measure, the need to intensify efforts on the promotion of safer sexual behaviour particularly among adolescents and provision of effective, accessible treatment for STDs in developing countries can not be overstated. Transforming such measures into public health policy is indispensable to the success of HIV/STD interventional programmes.

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