Original Article

A cross-sectional descriptive study of clinical and serological prevalence of syphilis infection in people living with HIV and its effect on CD4+ T cells

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Abstract

Context: The natural history of syphilis could be altered in the presence of HIV. It has been documented that syphilis infection increases the risk of HIV transmission by at least 3-fold. **Aims:** The aim of the study was (1) to study clinical presentation of syphilis in HIV individuals, (2) to estimate seroprevalence of syphilis in HIV individuals, and (3) to study the effect of syphilis infection on CD4+ T cells. **Subjects and Methods:** HIV-positive patients attending sexually transmitted infection clinic for a period of 1 year from June 2017 to May 2018 in the age group of 15–70 years were included in the study. A detailed history was taken; genital and dermatological examination was done. All patients were tested with VDRL and treponema pallidum hemagglutination assay (TPHA). Pearson's Chi-square test was used to compare categorical variables and Student's *t*-test was used to compare continuous variables. **Results:** Out of ninety study population, nine (10%) had clinical manifestations of syphilis. VDRL was positive with significant titers in all cases of syphilis. TPHA was positive in 88.9% of cases with clinical syphilis and 17.3% of cases without clinical manifestations of syphilis. Mean CD4 count was low among patients having syphilis infection compared to study population. **Conclusion:** This study shows high prevalence of syphilis in HIV and highlights the importance of preventing and promptly treating syphilis in people living with HIV, as the active infection is associated with fall in CD4 count, which leads to opportunistic infections.

Key words: CD4 count, HIV, seroprevalence, syphilis

INTRODUCTION

Sexually transmitted infections (STIs), particularly genital ulcer diseases act as cofactors and facilitators for HIV transmission because of the presence of increased number of activated CD4+ T-cells.[1] The incidence of syphilis has risen in recent years mainly due to complacency regarding HIV infection, the ability to connect with sex partners online through internet sites, and the positive effects of antiretroviral therapy (ART) on quality of life.[2]

The natural history of syphilis could be altered in the presence of HIV. Syphilis not only assumes unusual clinical presentations but also exhibits an

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unusual clinical course. It has been documented that syphilis infection increases the risk of HIV transmission by at least 3-fold.[3] The present study was taken up to assess clinical presentation and seroprevalence of syphilis in people living with HIV and the effect of syphilis infection on CD4 count.

SUBJECTS AND METHODS

A cross-sectional descriptive study was conducted in the STI clinic in a tertiary care hospital, Visakhapatnam, for a period of 1 year from June 2017 to May 2018. Prior permission from the Institutional Ethics Committee was obtained. Ninety HIV-positive individuals on ART, between the age of 15 and 70 years, who gave written consent were included in the study. Detailed history and dermatological and genital examination findings were noted for each patient.

Serological tests for syphilis, VDRL, and treponema pallidum hemagglutination assay (TPHA) were done for each individual irrespective of clinical manifestations. VDRL was performed in the Department of Microbiology, whereas TPHA was performed using OSCAR TP test device, which qualitatively detects antibodies of syphilis. It has a sensitivity of 99.9% and specificity of 99.5%.

Data were entered into Microsoft Excel (2007). Pearson's Chi-square test was used to compare categorical variables and Student's *t*-test was used to compare continuous variables. Chi-square test was performed at 95% confidence interval and significant level was accepted at $P < 0.05$.

RESULTS

Out of 90 study population, 46 (51.1%) were males and 44 (48.9%) were females. Age of the study population varies from 22 to 65 years, with a mean age of 40 years. Majority (46.7%) were in the age group of 31–40 years. In study population, 61% belong to urban domicile. About two-third of study population belongs to low socioeconomic status. Most of the study population (88.9%) were heterosexual, 4.4% were homosexual, and 6.7% were bisexual. About two-third of males (76%) in study population had multiple partners, whereas 27% of females had multiple partners. CD4 count of study population varied from 20 to 1531, with mean CD4 count of 570.

Clinical manifestations of syphilis were present in 9 (10%) patients [Table 1], out of which eight were males and one was female. Three patients had chancre with inguinal lymphadenopathy [Figure 1]. Six had manifestations of secondary syphilis, out of which three had maculopapular rash [Figure 2], two had palmoplantar syphilide [Figure 3], and one had condyloma lata [Figure 4].

Table 1: Clinical manifestations of syphilis in study population

Clinical manifestations	Total syphilis cases-9		
	Males	Females	Total
Primary syphilis	3	0	3
Secondary syphilis			
Maculopapular rash	3	0	3
Palmoplantar syphilide	2	0	2
Condyloma lata	0	1	1

Syphilis and HIV co-infection was found to be more among males in the present study, with statistically significant difference ($P = 0.02$). About two-third of syphilis patients belong to low socioeconomic status. Promiscuity was observed in 88.9% of syphilis patients.

All syphilis patients had positive VDRL with significant titers (titre >1:8). In our study population, 22 (24.4%) were TPHA positive [Table 2], of which eight had clinical manifestations of syphilis, whereas 14 had no manifestations of syphilis at the time of examination.

Mean CD4 count of syphilis patients was 478, which is low when compared to the mean CD4 count of study population.

DISCUSSION

Syphilis facilitates both HIV transmission and HIV acquisition through various mechanisms:

a. Chancres cause epithelial and mucosal breaches, facilitating the transmission of HIV virions
b. Expression of CCR5 (the major co-receptor for HIV entry) on human monocytes within chancre is induced, thereby enhancing the susceptibility of these cells to HIV infection
c. *Treponema pallidum* induces immune activation, measured by the increased percentage of activated CD4 cells which enhance transmission of HIV
d. Syphilis can increase HIV viral load and viral shedding.

Because of immune suppression and immune dysregulation, the presence of HIV modifies the features of syphilis:

a. Increased susceptibility and frequency of all STIs including syphilis
b. Altered natural history and atypical clinical presentation is more common
c. Resistance to treatment and frequent recurrences.

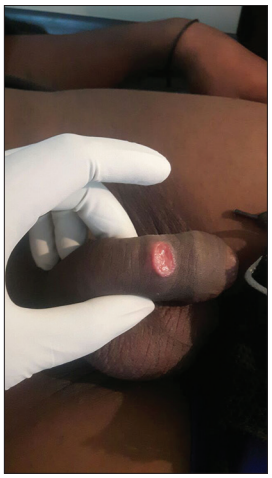

Figure 1: Chancre over the shaft of penis

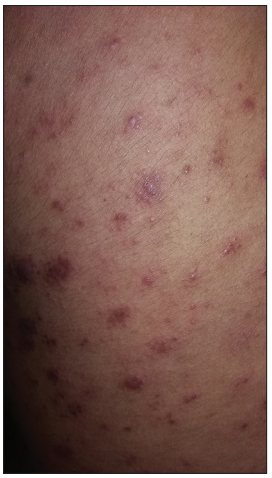

Figure 2: Papular rash over the trunk

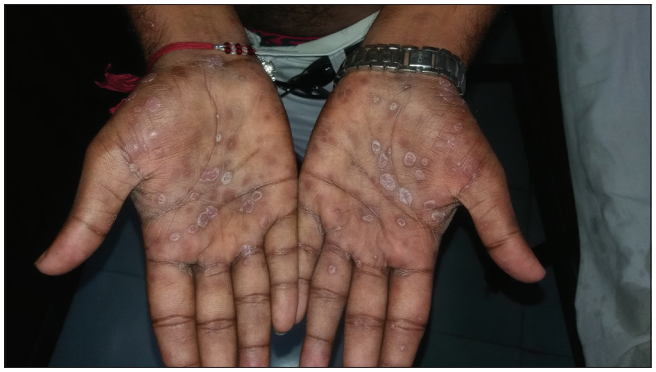

Figure 3: Palmar syphilide

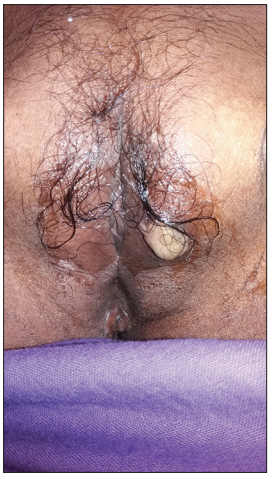

Figure 4: Condyloma lata

As HIV infection modifies the features of genital ulcer diseases, estimates based on case reports alone will vastly underestimate the prevalence of infection. Instead, true prevalence for these infections is based on prevalence surveys, which measure the presence of antibodies to infectious agent, irrespective of clinical manifestations.

Serological testing is the primary tool for diagnosing syphilis in HIV-infected patients, especially those who are not significantly immune compromised. However, unusual serologic responses, such as higher than expected titers, false negative results or delayed sero-reactivity and biological false-positive results may occur. When clinical findings are suggestive of syphilis, but serological tests are nonreactive or their interpretation is unclear, alternative tests such as biopsy of the lesion, dark field examination, and polymerase chain reaction of lesion material might be useful for diagnosis.

Syphilis and HIV co-infection in the present study was 10%. The syphilis and HIV co-infection in the present study is comparable to study conducted by Agmon-Levin *et al.*[4] [Table 3]. This difference in prevalence among various studies might be due to study design, study population, and diagnostic tests used or potentially temporal factors.

Table 2: Serological tests for syphilis in the study population

Serological test	Male	Female	Total (%)
VDRL			
1:8 or more	8	1	9 (10)
<1:8	3	1	4
TPHA	13	9	22 (24.4)

TPHA: Treponema pallidum hemagglutination assay

A treponemal test like TPHA was used to know the seroprevalence of syphilis irrespective of clinical manifestations, because nontreponemal test like VDRL or RPR is useful only to know the incidence of syphilis, to monitor the treatment response, but it becomes negative after around 6 months to 1 year after treatment. Treponemal test can detect present infection as well as past treated and

Table 3: Prevalence of syphilis and HIV co-infection in various studies

Authors	Prevalence (%)
Present study	10
Agmon-Levin *et al.*[4]	14.1
Shrivastava and Bobhate[5]	2.7
Signorini DJ *et al.*[6]	2.7
Callegari *et al.*[6]	5.3
Adolf *et al.*[7]	20.5

untreated cases; hence, it is useful to estimate the true seroprevalence of syphilis.

In the study population, 22 (24.4%) were TPHA positive, of which eight had clinical manifestations of syphilis and 14 were clinically asymptomatic. TPHA positives include patients who had previously treated for syphilis, who had contracted syphilis long ago and were not treated, and who had recently acquired syphilis. The evidence of previous infection and treatment were obtained by careful genital examination for healed scar of primary chancre and by asking the patient about deep intramuscular injection into two buttocks, following intradermal test to check for penicillin sensitivity, as injection benzathine penicillin 2.4 MU which will be given deep intramuscular is the treatment of choice for syphilis. TPHA becomes positive later in the course of early syphilis and like nontreponemal tests; it becomes negative after treatment, only if the treatment was initiated in early syphilis. However, once it reaches the stage of secondary syphilis, it is likely to remain positive for the rest of the patient's life, irrespective of treatment, because once the antitreponemal antibody appears, it usually persists for life.[8]

Patients usually do not seek medical treatment in the early syphilis, because of painless nature of chancre and occurrence of chancre in hidden places. Hence, there is high chance of progression to secondary syphilis, which results in persistent positive TPHA even after treatment. The American CDC guidelines recommend screening sexually active individuals with HIV infection for syphilis at least once annually and every 3–6 months for those with multiple sex partners.[9]

In the present study, 18.6% with single partner and 29.8% with multiple partners were TPHA positive. The TPHA seroprevalence was found to be high among people with multiple sex partners because of increased risk of exposure. Treatment optimism is responsible for increase in the unprotected sex. The success of ART in reducing plasma HIV viral load has led to an unfounded loss of fear of transmitting or being infected with HIV. Hence, effort must be made to educate and counsel regarding the promotion of safe sex practices.

The CD4+ T cell count has been shown to be influenced by sex, age, race, time of specimen collection (diurnal rhythms), physical and psychological stress, pregnancy, drug administration (cancer chemotherapy, nicotine, and steroids), tuberculosis, viral infections, and procedures such as splenectomy.[10,11] Females tend to have higher CD4 counts than males; on the contrary, males have higher CD8+ T-cells than females.[10,11] Although age does not have significant influence on CD4 cell counts, decrease may be observed in geriatric population.

The mean CD4 count of TPHA-reactive males was 417 and TPHA-reactive females was 774. TPHA-reactive males had mean CD4 count less than that of total TPHA-reactive population because out of 13 TPHA-reactive males, 7 had active syphilis, which causes decline in CD4 count. Whereas, TPHA-reactive females had mean CD4 count more than that of TPHA-reactive males, because out of 9 TPHA-positive females, only one had active syphilis. CD4 count tends to fall during active infection but rises after treating infection.

In a study conducted by Cassim *et al.*,[12] there was statistically significant difference in mean CD4 count between syphilitic participants and nonsyphilitic participants. There was statistically significant difference in mean CD4 count between male and female participants also in their study, which is comparable to our study.

Lower CD4 count in HIV patients with syphilis compared to HIV patients without syphilis indicate rapid progression to AIDS, a morbidity that will leave many of them suffering from constant opportunistic infections which will increase the mortality.

CONCLUSION

In the present study, we have not observed any unusual clinical presentations of syphilis in HIV. We observed fall in CD4 count during active syphilis infection, which returns to normal after treating the infection. Treating syphilis among people with HIV increases CD4 cell counts as well as decreases plasma viral loads. Integration of syphilis testing with HIV testing provides an opportunity to quantify sexually transmitted infection risk in HIV-infected individuals and in women, a potential opportunity for preventing HIV vertical transmission and congenital syphilis.

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Conflicts of interest
There are no conflicts of interest.

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