

Herpes Simplex Virus 2 infection in HIV-seropositive individuals in Tamil Nadu, India

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Abstract

Background: Viral infection with Herpes Simplex Virus (HSV) is one of the most common opportunistic infections in seropositive patients of Human Immunodeficiency Virus (HIV). Studies have confirmed that genital herpes caused by HSV-2 has been associated with two- to threefold increased risk of HIV acquisition.

Objective: To determine the seroprevalence of HSV-2 in HIV-positive patients.

Materials and Methods: A prospective, cross-sectional study was conducted from July 2012 to January 2013 and HIV-positive patients were enrolled into the study after obtaining written informed consent. Demographic characteristics were recorded and serology test was performed using HSV-2 IgG ELISA test kit (Calbiotech, USA). Results were analyzed using χ^2 -test.

Results: Among 273 HIV-positive patients, 67% were men, 33% were women, and 1 transgender with an average age of 38.8 years. Overall, 50% of HIV-positive patients had HSV-2 IgG antibodies. Seroprevalence of HSV-2 among HIV-positive men and women was 47% and 57%, respectively. The highest HSV-2 seropositivity was detected in the age group of 36–45 years. χ^2 -Analysis showed a statistically significant association between HSV-2 and HIV infection ($\chi^2 = 55.900$, $p = 0.0076$). The median CD4 counts estimated in 100 patients were 563.50 cells/mm³. No significant difference was observed in the CD4 counts of those with or without HSV-2.

Conclusion: HSV-2 prevalence was higher in HIV-positive women than in men. The implementation of continuous interventions for sexually transmitted infections and HIV will bring down the prevalence and spread of both HSV-2 and HIV infection.

KEY WORDS: HSV-2, HIV, seroprevalence, Tamil Nadu

Introduction

Herpes Simplex Virus type 2 (HSV-2) is the most common cause of genital ulcer disease worldwide.^[1–3] Periodic symptomatic reactivation and asymptomatic viral shedding are characteristics of HSV-2 infection. HSV-2 is a long lasting infection; the virus becomes permanently latent in the nerve root ganglia corresponding to the site of inoculation (the trigeminal ganglia for orolabial infection and the sacral ganglia for genital infection).^[4] HSV-2 seropositive patients may be

symptomatic or asymptomatic and the infection is usually transmitted through sexual contact. Seroprevalence of HSV-2 infections in general population ranges from 16.2% in the USA,^[5] 12% in Australia,^[6] 24.4% in Nigeria,^[7] and 13.2% in China.^[8] In India, the prevalence of HSV-2 in adults ranges from 5.2% to 14.5%.^[9–11] Among the attendees in sexually transmitted diseases (STD) clinics from Pune (western India) and Pondicherry (south India), the seroprevalence of HSV-2 was reported to be 9.7% and 83%, respectively.^[10] HSV-2 seroprevalence was 6.7% among pregnant women from Mysore (south India).^[12] Clinical manifestations of a chronic HSV infection (HSV-1 or HSV-2) among HIV/AIDS patients have been regarded by the World Health Organization (WHO) as an important presentation defining the disease progression of HIV/AIDS.^[13]

Genital herpes is associated with two- to threefold increased risk of Human Immunodeficiency Virus (HIV) acquisition and up to fivefold HIV transmission on a per sex act basis.^[14] In 2011, in Kenya, 81% HIV-infected persons were reported to be coinfecting with HSV-2.^[15] HSV-2 seroprevalence in

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HIV-infected patients was reported to be 45.8% in Croatia^[16] and 49% in Andhra Pradesh, India.^[17] In Tamil Nadu, India, prevalence of HSV-2 IgM and IgG antibodies in HIV-positive patients was 28.6% and 60%, respectively.^[18]

In India, limited published data exist on the prevalence of HSV-2 in HIV-seropositive patients. Therefore this study was carried out to determine the seroprevalence of HSV-2 in HIV-positive patients in Indian settings.

Materials and Methods

A prospective, cross-sectional study was conducted for 6 months from July 2012 to January 2013. Blood samples were collected from HIV-positive patients (irrespective of history of genital herpes) visiting the Department of Experimental Medicine laboratory, The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India, for various investigations. Patients on Anti-Retroviral Therapy (ART) were also included. After obtaining written informed consent, HIV-positive patients were enrolled into the study. Under aseptic precautions, 2 ml whole blood was collected and serum was separated and stored at -20 °C until further testing. Demographic data, such as age, gender, and present CD4 levels, were recorded. Serology test was performed using HSV-2 IgG ELISA test kit (Calbiotech, USA) as per manufacturer's instructions. Statistical analysis of the data was carried out using χ^2 -test.

Results

A total of 273 HIV-infected patients [183 (67%) men, 89 (33%) women, and 1 transgender] were enrolled into this study aged from 18 to 76 years with an average age of 38.8 years.

Overall, 50% (137/273) of them were positive for HSV-2 IgG antibodies, with 47% (86/183, $p = 0.01$) men and 57% (51/89, $p = 0.01$) women (Figure 1). The transgender individual was HIV positive but negative for HSV-2 IgG

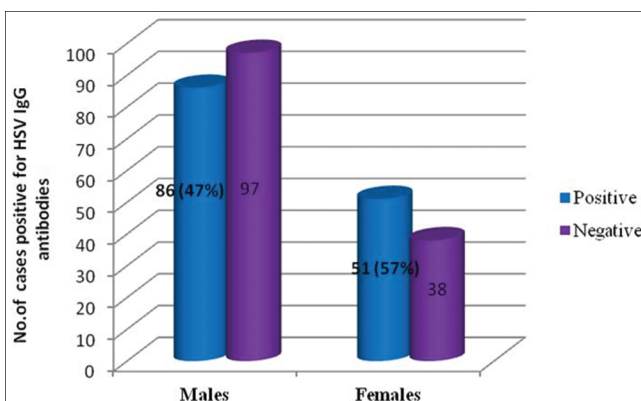


Figure 1: Seropositivity of HSV-2 IgG antibodies in HIV-positive men and women.

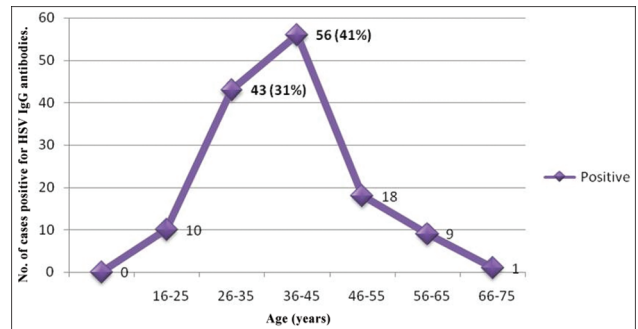


Figure 2: Age-wise prevalence of HSV-2 IgG antibodies in HIV-positive patients.

antibodies. The prevalence of HSV-2 IgG antibodies was highest (41%) among the age group of 36–45 years followed by 31% in the age group of 26–35 years (Figure 2). χ^2 -Analysis showed statistically significant association between HSV-2 and HIV infection ($\chi^2 = 55.900$, $p = 0.0076$). CD4 counts were available for 100 HIV-infected patients who were ART naive. The median CD4 counts were 563.50 cells/mm³. No significant difference was found in the CD4 counts of those with or without HSV-2.

Discussion

In this study, of 273 HIV-infected patients, 50% were positive for HSV-2 and 41% of them were in the age group of 36–45 years. The study further proved that HSV-2 seropositivity was higher in women than in men.

A study recorded seropositivity of HSV-2 in HIV-infected patients to be 47% in Kolkata,^[19] 49% in Andhra Pradesh,^[17] and 48.4% in Delhi^[20], which were similar to our observations. However higher rates were observed in other countries, for example, 55% in the UK,^[21] 87% in South Africa,^[22] and 86% in Uganda.^[23] These results confirm the strong association of HSV-2 infection with HIV. HSV-2 is the most common cause of genital ulcers and it can result in increased transmission of HIV to sexual partners.^[24] However HSV-2 infected patients are mostly asymptomatic or have mild symptoms. The majority of sexual HSV transmission occurs during asymptomatic periods because the patients are unaware of asymptomatic virus shedding.^[25] Multiple studies have shown that frequent genital herpes recurrences increase the amount of HIV in the blood and the genital tract. The HIV virus is also discharged from genital herpes ulcers and persons with such ulcers can transmit HIV to others more efficiently.^[26] The prevalence of HSV-2 shedding is four to five times greater in HIV-positive individuals than in HIV-negative individuals, likely increasing HSV transmission.^[27]

In this study, HSV-2 seropositivity was higher in women than in men confirming the fact that acquisition of HIV and HSV is more in women than men. Our findings were consistent with other studies from India,^[17] the UK,^[28] and Kenya.^[29]

A study was conducted in the USA to assess the impact of HIV on both HSV-2 prevalence and viral shedding at delivery. The study indicated viral shedding at delivery was more than three times higher among those with HIV.^[30] Studies have found that women are more susceptible to HSV-2 infection biologically.^[31,32] Transmission of the virus from male to female is more common than from female to male. Moreover, the female genitalia have plenty of soft tissue that is exposed for skin contact, which is presumably more receptive to any virus or STD.

In this study, the highest numbers of HSV-2 seropositive patients were in 36–45 age group, which gradually increased in the 18–35 years age group, peaked at 36–45 years, and then decreased with further increase in age. Similar observations were also reported from the WHO.^[33] Young middle-aged patients between 36 and 45 years are vulnerable and sexually active.

HSV-2 is one of the most common opportunistic infections among HIV-seropositive patients. It has been confirmed that genital herpes caused by HSV-2 has been associated with two- to threefold increased risk of HIV acquisition. HSV-2 seroprevalence rates are higher in HIV-positive patients than in HIV-negative patients.^[7] Discontinuity of the genital mucosal barrier enhances HIV entry in HIV-negative patients and the associated inflammation increases the recruitment of CD4 lymphocytes that are the target cells for HIV. Reactivation of HSV-2 may promote HIV shedding in the genital tract, thus increasing the HIV viral load. Thus, HSV-2 infection alters the course of HIV disease. It is known that acute or reactivated HSV-2 infection may stimulate HIV replication leading to the progression of HIV disease. However, like other studies,^[34,35] this study also did not find any difference in the CD4 counts of patients with or without HSV-2.

Studies have shown that initiation of HSV-2 suppressive therapy in patients coinfecting with HIV 1 and HSV-2 would benefit by reducing herpes transmission and herpes reactivation and also through salutary effects on HIV.^[36] Initiation of such therapy in Indian settings will further reduce the silent spread of HIV infection.

One of the limitations of the study is that it is a cross-sectional study and is based on HIV-positive patients visiting our laboratory for various tests. This might not be a representation of the population of Tamil Nadu. Another limitation is that the clinical spectrum of HSV-2 has not been analyzed. These factors may limit the generalizability of the estimates of HSV-2 infection rates.

Conclusion

HSV-2 prevalence was significantly higher in HIV-positive women than in men. This suggests a higher risk of acquisition of HSV-2 infection among women. These findings have relevant public health implications. The implementation of continuous interventions for sexually transmitted infections and HIV will decrease the prevalence and spread of both

HSV-2 and HIV. Offering serological HSV-2 testing routinely to HIV-infected persons will identify asymptomatic or unrecognized HSV-2 infection.

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