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Retraction

This article has been retracted due to duplicate publication.

The following article from International Journal of Community Medicine and Public Health, 'Herpes simplex virus 2 infection in HIV seropositive individuals in Tamil Nadu, India' (Int J Community Med Public Health. 2015;2(1):33-37, doi: 10.5455/2394-6040.ijcmph20150208), by Saramma Mini Jacob, Thatchinamoorthy Gopal, Sivasangeetha Kanagasabai, Anitha Durairaj, Kamala Mary Sushi, Ganesan Arumugam, was submitted 17th November 2014, accepted on 10th January 2015, and published in the Volume 2, Issue 1, February 2015. While the review was in progress, a duplicate version of the article was published online in the International Journal of Medical Science and Public Health (Int J Med Sci Public Health. 2015;4(3):404-407, doi: 10.5455/ijmsph.2015.1411201483). The authors have apologized to the Editors for this incident, which violated the policies and practices of the International Journal of Community Medicine and Public Health.

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Research Article

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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 commonest opportunistic infection in HIV seropositive patients. Studies have confirmed that genital herpes caused by HSV-2 has been associated with twofold to threefold increased risk of HIV acquisition. This study was designed to determine the seroprevalence of HSV-2 in HIV positive patients.

Methods: This was a prospective, cross sectional study conducted from July 2012 to January 2013. After obtaining written informed consent, HIV positive patients were enrolled into the study. Demographic characteristics were recorded. Serology test was performed using HSV-2 IgG ELISA test kit from Calbiotech, USA. Results were analyzed using Chi-squared test.

Results: Out of two hundred and seventy three HIV positive patients enrolled, 67% were males, 33% were females and one transgender. Average age was 38.8 years. Overall 50% of HIV positive patients had HSV-2 IgG antibodies. Seroprevalence of HSV-2 among HIV positive men and women were 47% and 57% respectively. The highest HSV-2 seropositivity was detected in the age group of 36 to 45 years. Chi-squared analysis showed a statistically significant association between HSV-2 and HIV infection ($X^2 = 55.900$, P = 0.0076). The median CD4 counts estimated in 100 patients were 563.50 cells/mm³. There was no significant difference in CD4 counts of those with or without HSV-2.

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

Keywords: HSV-2, HIV, Seroprevalence, Tamil Nadu

INTRODUCTION

Herpes Simplex Virus type II (HSV-2) is the most common cause of genital ulcer disease worldwide. ¹⁻³ The hallmarks of HSV-2 infection are periodic symptomatic reactivation and asymptomatic viral shedding. Infection with HSV-2 is a lifelong condition; 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 sero positive patients may be symptomatic or asymptomatic and is usually transmitted

through sexual contact. Seroprevalence of HSV-2 infections in general population ranges from 16.2% in USA, 5 12% in Australia, 6 24.4% in Nigeria 7 and 13.2% in China. 8 The prevalence of HSV-2 in adults in India has been reported to range from 5.2% to 14.5%. 9-11 Among the attendees in STD clinics from Pune, North India and Pondicherry from South India, the seroprevalence of HSV-2 was reported between 9.7% and 83% 10 respectively. 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 three fold increased risk of Human Immunodeficiency Virus (HIV) acquisition and up to five fold HIV transmission on a per sex act basis. A Reports from Kenya in 2011 found 81% of HIV-infected persons were co-infected with HSV-2. HSV-2 seroprevalence was 45.8% in HIV-infected patients in Croatia. High prevalence of HSV-2 seropositivity in the HIV-infected persons (49%) was reported from Andhra Pradesh, India. In Tamil Nadu, prevalence of HSV-2 IgM and IgG antibodies in HIV reactive patients were 28.6% and 60% respectively.

Limited published data exists on the prevalence of HSV-2 in HIV seropositive patients in India. Therefore this study was designed to determine the seroprevalence of HSV-2 in HIV positive patients in our setting.

METHODS

This was a prospective, cross sectional study conducted for six months from July 2012 to January 2013. Blood was collected from HIV positive patients (irrespective of history of genital herpes) attending the department of medicine experimental laboratory for investigations. Patients on Antiretroviral Therapy (ART) were also included. After obtaining written informed consent, HIV positive patients were enrolled into the study. Two ml of whole blood was collected under aseptic precautions and sera was separated and stored at -20°C until further testing. Demographic data such as age, gender and present CD4 levels, when available were recorded. Serology test was performed using HSV-2 IgG ELISA test kit from Calbiotech, USA as manufacturer's instructions. Statistical analysis of the data was done using Chi-squared test.

RESULTS

Two hundred and seventy three HIV infected patients were enrolled into this study. Their age ranged from 18 to 76 years with an average age of 38.8 years. There were 183 (67%) males, 89 (33%) females and one transgender.

Overall 50% (137/273) of them were positive for HSV-2 IgG antibodies. Forty seven percent (86/183, P=0.01) of HIV positive males and fifty seven percent (51/89, P=0.01) of HIV infected females were positive for HSV-2 IgG antibodies (Figure 1). The transgender individual was HIV positive but negative for HSV-2 IgG antibodies. The prevalence of HSV-2 IgG antibodies was highest (41%) among the age group of 36 to 45 years followed by 31% in the 26-35 age group (Figure 2). Chi-squared analysis showed that there is a statistically significant association between HSV-2 and HIV infection ($X^2=55.900$, 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. There was no significant difference in the CD4 counts of those with or without HSV-2.

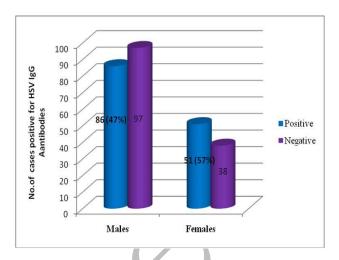


Figure 1: Seropositivity of HSV-2 IgG antibodies in HIV positive males and females.

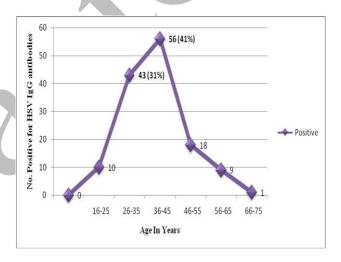


Figure 2: Age wise prevalence of HSV-2 IgG antibodies in HIV reactive patients.

DISCUSSION

In this study, out of 273 HIV infected patients, 50% were positive for HSV-2 and 41% of them were in the 36-45 age group. The study further showed that HSV-2 seropositivity was higher in females than in males.

A study from Kolkata recorded 47% seropositivity of HSV-2 in HIV infected patients, 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 e.g. 55% in 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 this can results in increased transmission of HIV to sexual partners. ²⁴ However most of the time HSV-2 infected patients are

asymptomatic or have mild symptoms. The majority of sexual HSV transmission occurs during asymptomatic periods because the patients are unaware of asymptomatic virus shedding. 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 shed from genital herpes ulcers and persons with such ulcers can transmit HIV to others more efficiently. The prevalence of HSV-2 shedding is 4-5 times greater in HIV positive individuals than in HIV negative individuals, likely increasing HSV transmission. HSV

In this study, HSV-2 seropositivity was higher in females than in males 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 UK²⁸ and Kenya.²⁹ A study was done in US 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 likely than 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.

The highest numbers of HSV-2 seropositives in our study were in 36-45 age group. There was a gradual increase in the seropositivity from 18 years to 35 years, peaked at 36 to 45 years and then there was decrease in the seropositivity with increase in age. Similar observations were also reported from WHO.³³ Young middle age patients in 36 to 45 years category are vulnerable and sexually active.

HSV-2 is one of the commonest opportunistic infection in HIV seropositive patients. It has been confirmed that genital herpes caused by HSV-2 has been associated with twofold to threefold increased risk of HIV acquisition. HSV-2 seroprevalence rates are higher in HIV positives than in HIV negative patients. 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, similar to other studies, 34,35 this study also did not find any difference in the CD4 counts of patients infected with or without HSV-2.

Studies have shown that initiation of HSV-2 suppressive therapy in patients co-infected 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's cross sectional 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.

CONCLUSIONS

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 STIs and HIV will bring down 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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institutional ethics committee

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