ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 7, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

SEROPREVALENCE OF HERPES SIMPLEX VIRUS INFECTION TYPE 1 AND 2 IN A POPULATION OF HIV-POSITIVE AND HIV-NEGATIVE INDIVIDUALS IN A TERTIARY CARE HOSPITAL

MEGHNA SHARMA[1], SAPNA SONEJA[2]*, LOVEENA OBEROI[2], ANURADHA MALHOTRA[2]

[1]Department of Microbiologist, District Hospital, Amritsar, Punjab, India. [2]Department of Government Medical College, Amritsar, Punjab, India.

***Corresponding author: Sapna Soneja; Email: drsapnabatra@gmail.com**

Received: 29 March 2024, Revised and Accepted: 13 May 2024

ABSTRACT

Objectives: The aim of this study is to determine the seroprevalence of herpes simplex virus (HSV) in a population of human immunodeficiency virus (HIV) positive and non-HIV patients and its association with CD-4 count.

Methods: 200 HIV-positive individuals attending antiretroviral treatment clinic and 100 HIV-negative individuals from the clinical departments of Government Medical College, Amritsar, were enrolled in the study. The sera were tested in parallel using anti-HSV-1 immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) (calbiotech), anti-HSV-2-IgG (calbiotech), and HSV-1/2 pool IgM ELISA (calbiotech) assays as per the manufacturer's instructions. Sysmex partec CyFlow counter IVD flow cytometer. CD4+ reagents are used for measuring absolute counts of CD4+ T lymphocytes.

Results: For anti-HSV-2 IgG, seroprevalence was positively associated with HIV-positive status. The mean CD4+ T lymphocyte counts for anti-HSV-2 IgG patients were 400.45±122.92 cells/μL in the HIV-positive group (n=163). Mean CD4+ counts in HSV-2 IgG-negative cases were 350.05±160.46 cells/μL. This association was statistically significant.

Conclusion: HSV-1 and 2 are common lifelong infections that often are asymptomatic. African studies have highlighted HSV synergism with HIV infection. Seroprevalence of this common infection and the studies covering the Northern India region are scarce. Our study has confirmed this coinfection synergism. Increasing awareness of HSV-HIV synergy can contribute to better informed decisions regarding safe sex practices.

Keywords: Herpes simplex, Acquired immunodeficiency syndrome, Human immunodeficiency virus, Sexually transmitted infections, CD4+ counts.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i7.50998. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Herpes virus, a DNA virus of the family herpesviridae, produces a recurrent lifelong infection causing a muco-ulcerative disease. It is caused either by herpes simplex virus type 1 (HSV-1) or HSV type 2 (HSV-2) and is one of the most common sexually transmitted infections throughout the world [1]. The World Health Organization (WHO) estimates that 3.7 billion people under the age of 50 which is 67% of the global population have HSV-1 infection (oral or genital). Genital herpes caused by HSV-2 affects 491 million (13%) people aged 15–49 years worldwide [2]. HSV-2 infects women almost twice as often as men because sexual transmission is more efficient from men to women. Prevalence increases with age and the highest number of new infections are in adolescents [2].

HIV the RNA virus of the retroviridae family is a major cause of mortality all over the world since its discovery in the late 1980s. The impact has been severe in the Asian and African countries. Sexual transmission and the use of common syringes for intravenous drug abuse remain the major routes of transmission along with mother-to-child transmission which remains significant. HIV affects CD-4 T cells, and hence, the patient fails to mount an effective response to infections [3]. Globally, the WHO estimates that 38.4 million people were living with HIV at the end of 2021. An estimated 0.7% (0.6–0.8%) of adults aged 15–49 years worldwide are living with HIV [4]. Studies have shown an interaction between HSV-2 and HIV-1 [5,6]. HSV-2 facilitates acquisition and transmission of HIV at least 2-fold and may accelerate the course of HIV progression [7]. HIV-positive individuals may have more frequent and more severe recurrences of genital herpes and are more likely than HIV-negative individuals to have subclinical shedding of HSV-2 [8]. The WHO in 2019 reported first global and regional estimates of HIV infections attributed to HSV-2 infection. It reported that the proportion of new sexually acquired HIV infections in the year 2016 that could be attributed to HSV-2 infection was 29.6%. It also reported that the global figure, known as the population attributable fraction (PAF), varies region wise. The African region at PAF of 37.1% reported the highest proportion of HIV infections projected to be due to HSV-2. The Americas had a projected PAF of 21.3% and in the rest of the world, the PAF ranged between 11 and 13%. The estimated PAF of HIV attributable to HSV-2 was higher among females than males (34.8% vs. 26.2%) and higher among 25–49-year olds in both genders compared with younger ages [9]. The aim of this study was to determine the seroprevalence of HSV in a population of HIV-positive and non-HIV patients and its association with CD-4 count.

METHODS

Ethics statement

The study was approved by the Institutional Ethics Committee of the Government Medical College, Amritsar, Punjab, India (Ref. No. 3352/D-26/2020). The study was carried out from February 2021 to July 2022, at the Department of Microbiology, Government Medical College, Amritsar.

Study population and subject selection

Included 200 HIV-positive individuals who attended ART after pre-test counseling at the Department of Microbiology.

Control group

Included 100 HIV-negative individuals referred from the clinical departments of Government Medical College, Amritsar, from outpatient as well as inpatient services.

Inclusion criteria

All subjects more than or equal to 18 years of age attending anti-retroviral clinic (ART) who accepted written informed consent and the standardized questionnaire were recruited.

Exclusion criteria

Minors, mentally unstable patients, non-consenting individuals, patients on corticosteroids or immunosuppressants, moribund patients, patients with a history of anti-viral treatment besides the ART were excluded.

Sample collection and testing of sera for HSV antibodies

5 mL of blood sample was drawn through venipuncture. Half blood sample was collected in a sterile plain vial and half in ethylenediaminetetraacetic acid vial for CD4+ T lymphocyte count. The sera were tested in parallel using anti-HSV-1 immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) (calbiotech), anti-HSV-2-IgG (calbiotech), and HSV-1/2 pool IgM ELISA (calbiotech) assays as per the manufacturer's instructions. The assays used, as per the kit insert, claimed to have 100% specificity and 97% sensitivity for IgG tests. For the IgM, sensitivity is 99% for HSV-1 and 2, respectively. The anti-HSV-1 and HSV-2 ELISA (IgG) assays are intended for the qualitative determination of IgG class antibodies against HSV-1-specific glycoprotein C1 and HSV-2 specific glycoprotein g2 in human serum, respectively. The cutoff value was calculated as per the manufacturer's instruction and optical density (OD) ratios were calculated by dividing the reading of each sample well by the cutoff value. Each OD ratio for the samples tested was interpreted as follows: OD ≤1.0 as negative and OD ≥1.0 as positive. All samples were tested at 1:100 serum dilutions. For those serum specimens with ambiguous test results, a repeat test was performed. For samples that were again ambiguous, the samples were considered to be negative. Sysmex partec CyFlow counter IVD flow cytometer. CD4+ reagents are used for measuring absolute counts of CD4+ T lymphocytes and help determine the percentage of CD4+ T lymphocytes in unused whole blood. A single test requires ready to use reagent tube. When whole blood is added to the reagent tube, fluorochrome-labeled antibodies in the reagent bind specifically to white blood cell surface antigens and a fluorescent nuclear dye binds to the nucleated blood cells. After a fixative solution is added, the sample is run on the instrument. During sample acquisition, the cells pass through laser light which causes the labeled cells to fluoresce. This fluorescent light is read by the instrument and counts the lymphocytes and CD4+ T lymphocytes.

Statistical analysis

Data were entered into MS Excel and data analysis was done using the Statistical Package for the Social Sciences. Normally distributed data were expressed as mean (standard deviation). Categorical data were presented as percentages and the Pearson Chi-square test was used to test the level of significance. p-value (calculated probability) <0.05 was considered significant. Prevalence was expressed in percentage. Wherever Chi-square was not applicable, an unpaired t-test was used and p-value was calculated.

RESULTS

The key determinants of HSV seropositivity are shown in Table 1. The p-value for anti-HSV 1 and 2 IgM reactivity in HIV-positive and HIV-negative groups was 0.257. The difference was not statistically significant. In HSV-1 IgG ELISA in HIV-positive group and HIV-negative group, the p-value was calculated to be 0.158. The difference was not statistically significant. For anti-HSV-2 IgG ELISA in HIV-positive group and HIV-negative group, the p-value was 0.000. The difference was statistically significant. In HSV-1 and 2 IgG ELISA in HIV-positive group and HIV-negative group, the p-value was calculated to be 0.000. The difference was statistically significant. This is shown in Table 2. The mean age in IgM, IgG HSV-1, IgG HSV-2, and IgG HSV-1 and 2 in HIV-positive and negative groups had statistically significant differences with p<0.001 for each category. This is shown in Table 3.

The mean CD4+ T lymphocyte counts for anti-HSV 1 and 2 IgM patients were 384.26±148.54 cells/μL in HIV-positive group (n=34). Mean CD4+ counts in HSV-1 and 2 IgM-negative cases were 392.53±128.42cells/μL. The p-value was calculated (0.740) and the difference was not statistically significant. The mean CD4+ T lymphocyte counts for anti-HSV-1 IgG patients were 397.12±132.83 cells/μL in HIV-positive group (n=176). Mean CD4+ T cell counts in HSV-1 IgG-negative cases were 347.17±116.26 cells/μL. The p-value was calculated (0.081) and the difference was not statistically significant. The mean CD4+ T lymphocyte counts for anti-HSV-2 IgG patients were 400.45±122.92 cells/μL in HIV-positive group (n=163). Mean CD4+ counts in HSV-2 IgG negative cases were 350.05±160.46 cells/μL. The p-value was calculated (0.035) and the difference was statistically significant. Mean CD4+ T-cell count in HSV1 and 2 IgG dual positive in HIV positive was 404.78±122.85 cells/μL, whereas the mean CD4+ T cell count in dual negative in HIV-positive patients was 353.26±148.26 cells/μL. The p-value was calculated (0.014) and the difference was statistically significant. This is shown in Table 4.

DISCUSSION

In this study, we worked on determining the seroprevalence of HSV type 1 and type 2 in HIV-positive and negative patients reporting to a tertiary care center in North India and also determined its association with various risk factors. It has been established that HSV shares a synergistic relationship with HIV infections and there is a need to formulate consolidated programs to control co-transmission of HSV and HIV infections [10].

In the present study, the prevalence of HSV-1 and 2 IgM in HIV-positive and HIV-negative cases was 17.00% and 12%, respectively. The difference was statistically insignificant. The prevalence of HSV-1 IgG in HIV-positive and HIV-negative cases was 88.00% and 82.00%, respectively. The difference was statistically insignificant. The prevalence of HSV-2 IgG in HIV-positive and HIV-negative cases was 81.50% and 31.00%, respectively. The difference was statistically significant. In HIV-positive group, 147 patients (73.50%) tested positive for both anti-HSV-1 and anti-HSV-2. In HIV-negative group, 29 patients (29%) tested positive for both anti-HSV-1 and anti-HSV-2. The difference is statistically significant indicating a strong correlation between HSV-2 and HIV. Nag *et al*., in eastern India, found that the overall seroprevalence of HSV-2 IgG was 42.3%. It was 59.79% in the HIV-positive group and 17.78% in the HIV-negative group. Our study also showed a higher prevalence in HIV-positive and negative patients.

They found a high overall prevalence of anti-HSV-1 IgG (92.3%). The prevalence was similar in both HIV-positive and HIV-negative groups. In the present study, we also observed a high prevalence of anti-HSV-1 IgG. Nag *et al*. found higher anti-HSV-2 IgM in HIV-positive group than HIV-negative group (34.6% vs. 2.2%). This is higher than the values in our study. This may be due to differences in the at-risk groups [11].

In the study by Munawwar et al. done at All India Institute of Medical Sciences New Delhi, male only cohort, the prevalence of IgG antibodies against HSV-1, regardless of HIV status, was 75.21%. The prevalence was 77.25% in HIV-infected and 71.18% in HIV-negative groups. They found this difference to be statistically insignificant. The prevalence of IgG antibodies against HSV-2 was 28.20%. In HIV-positive group, this prevalence was 39.91% and in HIV-negative individuals, it was 5.08%. They found only 3.0% of subjects with HSV-1/2 IgM. Our study showed a higher prevalence of anti-HSV-1 IgG and anti-HSV-2 IgG in both groups [12]. In the study, the mean CD4+ T lymphocyte counts for anti-HSV-2 IgG patients was 400.45±122.92 cells/μL in HIV-positive group (n=163). This was significantly different from the HSV-1 IgG- negative group (p=0.035). Mean CD4+ T cell count in HSV-1 and 2 IgG dual positive in HIV positive was 404.78±122.85 cells/μL. This was significantly different from HSV-1 and 2 IgG-negative group (p=0.014). There was no association between HSV IgM and HSV-1 IgG seropositivity with CD4+ counts. Overall, in our study, there is no association of CD4+ T cell count to anti-HSV-positivity.

Table 1: Determinants of HSV seropositivity in HIV-positive and HIV-negative cases

	HSV seropositivity (HIV positive) cases (n=200)				HSV seropositivity (HIV negative) cases (n=100)			
Characteristic	**HSV-1 and 2 IgM, n (%)**	**HSV-1 IgG, n (%)**	**HSV-2 IgG, n (%)**	**HSV-1 and 2 IgG, n (%)**	**HSV-1 and 2 IgM, n (%)**	**HSV-1 IgG, n (%)**	**HSV-2 IgG, n (%)**	**HSV-1 and 2 IgG, n (%)**
Age(in years)								
18–30	31 (15.5)	34 (17)	38 (19)	24 (12)	9 (9)	23 (23)	1 (1)	24 (24)
31–40	3 (1.5)	58 (29)	43 (21.5)	41 (20.5)	3 (3)	15 (15)	7 (7)	41 (41)
41–50	0	48 (24)	48 (24)	48 (24)	0	20 (20)	8 (8)	48 (48)
51–60	0	25 (12.5)	24 (12)	24 (12)	0	15 (15)	7 (7)	24 (24)
>60	0	11 (6.5)	10 (5)	10 (5)	0	11 (11)	8 (8)	10 (10)
Mean age	38.99±11.88 years				39.86±13.06 years			
Male	24 (12)	115 (57.5)	106 (53)	97 (48.5)	8 (8)	58 (58)	19 (19)	18 (18)
Female	10 (05)	61 (30.5)	57 (28.5)	50 (25)	4 (4)	24 (24)	12 (12)	11 (11)
HIV-positive	34 (17)	176 (88)	163 (81.5)	147 (73.5)	12 (12)	82 (82)	31 (31)	29 (29)
Married	14 (7)	149 (74.5)	130 (65)	126 (63)	5 (05)	70 (70)	29 (29)	27 (27)
Unmarried	20 (10)	27 (13.5)	33 (16.5)	21 (10.5)	7 (07)	12 (12)	2 (02)	2 (02)
Literate	23 (12.5)	130 (65)	123 (1.5)	110 (55)	11 (11)	75 (75)	29 (29)	27 (27)
Illiterate	11 (6.5)	46 (23)	40 (20)	37 (18.5)	01 (01)	7 (07)	2 (02)	2 (02)
Employed	11 (6.5)	74 (37)	66 (33)	63 (31.5)	2 (02)	39 (39)	16 (16)	17 (17)
Unemployed	23 (11.5)	102 (51)	97 (48.5)	84 (42)	10 (10)	43 (43)	15 (15)	12 (12)
Urban	22 (11)	119 (59.5)	112 (66)	102 (51)	8 (08)	59 (59)	23 (23)	21 (21)
Rural	12 (06)	57 (28.5)	57 (28.5)	45 (22.5)	4 (04)	23 (23)	8 (08)	8 (08)
Intravenous drug abuse								
Yes	10 (05)	52 (36)	45 (22.5)	41 (20.5)	00	00	00	00
No	24 (12)	124 (67)	118 (59)	106 (53)	12 (12)	82 (82)	31 (31)	29 (29)
Medical comorbidities								
Yes	5 (2.5)	41 (20.5)	37 (18.5)	34 (17)	01 (01)	27 (27)	16 (16)	15 (15)
No	29 (14.5)	135 (67.5)	126 (63)	113 (56.5)	11 (11)	55 (55)	15 (15)	14 (14)
High-risk sexual behavior								
Yes	3 (1.5)	15 (7.5)	16 (08)	15 (7.5)	01 (01)	02 (02)	0	00
No	31 (16.5)	161 (80.5)	147 (73.5)	132 (66)	11 (11)	80 (80)	31 (31)	29 (29)
Mean CD4+ (cells/μL)	384±148	397±132.83	400.45±122.92	404±122.85	-	-	-	-
Clinical features								
Genital ulcers	2 (01)	12 (06)	13 (6.5)	00	01 (01)	02 (02)	00	00
Orofacial ulcers	2 (01)	14 (07)	13 (6.5)	00	01 (01)	03 (03)	02 (02)	00
Skin ulcers	7 (3.5)	18 (9)	19 (9.5)	00	01 (01)	02 (02)	00	00
Paresthesias	4 (02)	25 (12.5)	23 (12.5)	00	00	00	00	00

HSV: Herpes simplex virus, HIV: Human immunodeficiency virus, IgM: Immunoglobulin M, IgG: Immunoglobulin G

Table 2: Comparison of HSV seropositivity in HIV-positive and HIV-negative groups

Seropositivity	p-value	Significance
Anti HSV-1 and 2 IgM	0.257*	No
Anti HSV-1 IgG	0.158*	No
Anti HSV-2 IgG	0.000*	Yes
Anti HSV-1 and 2 IgG	0.000*	Yes

Significant (p<0.05). HSV: Herpes simplex virus, HIV: Human immunodeficiency virus, IgM: immunoglobulin M, IgG: Immunoglobulin G

In the study by Sufiawati *et al*., no significant correlation between HSV-1 and HSV-2 seropositivity and CD4+ counts (p more than 0.05) was reported [13]. In HIV-positive patients, a history of genital ulcers was present in 15 (7.5%) patients. Matthew *et al*., in their study, reported the prevalence of genital ulcerative disease to be 18.2% in HIV-positive patients which was higher than our study [14]. Schaftenaar *et al*., in HSV-1 seropositive cases, reported a history of cold sores and oral lesions in 15% and 14% of individuals [15]. HSV-1 and 2 IgM were positive in 02 (13.33%) HIV-positive patients who had genital ulcers. HSV-1 IgG was positive in 12 (80%) HIV-positive patients who had genital ulcers. HSV-2 IgG was positive in 13 (86.66%) HIV-positive patients who had genital ulcers. Matthew *et al*. reported that the prevalence of genital ulcer disease was 61.9% in anti-HSV IgG-positive cases and 33.6% in those without genital ulcer disease [14]. The mean age of HSV IgM seropositive patients in HIV-positive group was 24.80±4.49 years, 41.19±11.76 for HSV-1 IgG, 42.24±11.95 years for HSV-2 IgG, and 43.69±11.17 years for both HSV-1 and 2 IgG. Mean age reported by Ramchandani *et al*., in their research to study HSV shedding in tears, oral and nasal mucosa, reported mean age of the study cohort to be 37 (range 24–43). This is similar to the findings of our study [16]. In the current study, no statistically significant gender bias in the seroprevalence of herpes virus was observed. Nag *et al*., in a study on seroprevalence of HIV and herpes simplex coinfection in Eastern India, reported 57.7% males and 42.3% females in HIV and HSV blister group and 55.56% males and 44.44% females in non-HIV non-HSV blister group [11]. In literate HIV-positive cases, HSV IgM, HSV-1 IgG, HSV-2 IgG, and HSV IgG-1 and 2 prevalence was 23 (67.65%), 130 (73.86%), 123 (75.46%), and 110 (74.83%), respectively. Munawwar *et al*. reported 54.02% seropositivity of HSV-1 and 2 in the educated group and 45.98% in the uneducated group [12]. In HIV-positive employed cases, HSV IgM, HSV-1 IgG, HSV-2 IgG, and HSV-1 and 2 IgG prevalence were 11 (32.35%), 74 (42.05%), 66 (40.49%), and 63 (42.86%), respectively. Munawwar *et al*. reported HIV-1 and 2 seropositivity of 78.16% in the employed and 21.84% in the unemployed group [13]. In HIV-positive intravenous drug abuser cases, HSV IgM, HSV-1 IgG, HSV-2 IgG, and HSV-1 and 2 IgG prevalence was 10 (29.41%), 52 (29.55%), 45 (27.61%), and 41 (27.89%), respectively. In HIV-negative subjects, no history of intravenous drug abuse was reported. Munawwar *et al*. reported 89.65% HSV-1 and 2 seropositivity in alcohol abusers versus 10.34% in the sober group [13]. In HIV-positive urban cases, HSV IgM, HSV-1 IgG, HSV-2 IgG, and HSV-1 and 2 IgG prevalence was 22 (64.71%), 119 (67.61%), 112 (68.71%), and 102 (69.39%), respectively. Schneider *et al*. reported 3.8% seropositivity of HSV-2 in rural population and 7.8% seropositivity in urban population of men in the age group of 15–49 years [17]. Ren *et al*. analyzed the correlation of human herpesvirus (HHV) infection and its predictive factors in an HIV seropositive population of a town in China. They confirmed that older age, being married, higher HIV-1 plasma viral load, and use of antiviral medicine PIs were correlated independently with increased

Table 3: Mean age according to seropositivity

HSV seropositive cases	Mean±SD		Unpaired t-test	p
	HIV-positive	HIV-negative		
IgM	24.80±4.49	41.90±11.38	10.04	<0.001*
HSV 1 (IgG)	41.19±11.76	27.52±8.21	7.244	<0.001*
HSV 2 (IgG)	42.242±11.951	33.849±10.978	5.981	<0.001*
HSV 1 and 2 (IgG)	43.699±11.177	33±10.992	8.22	<0.001*

*Significant (p<0.05). HSV: Herpes simplex virus, HIV: Human immunodeficiency virus, SD: Standard deviation, IgM: immunoglobulin M

Table 4: Mean CD4+counts (cell/µL) in herpes simplex virus co-positive with HIV-positive status

IgM status	Mean CD4+count±SD (cells/µL), mean±SD
Positive	384.26±148.54
Negative	392.53±128.42
HSV 1 (IgG) status	
Positive	397.12±132.83
Negative	347.17±116.26
HSV 2 (IgG) status	
Positive	400.45±122.92
Negative	350.05±160.46
IgG1+G2 status	
Positive	404.78±122.85
Negative	353.26±148.36

SD: Standard deviation, HSV 1: Herpes simplex virus, HIV: Human immunodeficiency virus, IgM: Immunoglobulin M

frequency of HHVs, but CD4 count, the WHO HIV clinical stage and HIV infection duration were not associated with HHVs. A high prevalence of HHVs (89.3%) was observed in individuals with HIV infections, with HSV-2 (65.3%) and HSV-1 (59.5%) being the most common. Coinfection with more than two different HHVs was more common in patients with HIV infections receiving antiretroviral therapy (72.7%) than in healthy controls. This is in sync with the trends observed in our study [18].

Omori *et al*. studied HIV/HSV-2 biological interaction. They reported a crude odds ratio between 1.38 and 9.93, with a mean of 6.45. However, due to sexual behavior confounding the HIV and HSV acquisition, they pointed out that the observed HIV and HSV-2 association may just be because of two infections sharing the same mode of transmission [19].

CONCLUSION

HSV-1 and 2 are common lifelong infections that often are symptomatic. Seroprevalence of this common infection and the studies covering Northern India, especially the Punjab region, is scarce. The detection of IgG antibodies against HSV may help seropositive people identify symptoms and protect their partners from acquiring HIV or vice versa and protect HIV patients from acquiring HSV. Increasing awareness of HSV-HIV synergy can contribute to better informed decisions regarding safe sex practices. This study was conducted to estimate the seroprevalence of HSV infection in HIV-positive patients and to identify patient-related risk factors.

AUTHOR'S CONTRIBUTION

Concept and design: Dr. Meghna Sharma, Dr. Sapna Soneja, Dr. Loveena Oberoi, Dr. Anuradha Malhotra. Data compilation: Dr. Meghna Sharma, Dr. Sapna Soneja. Editing and statistical analysis: Dr. Meghna Sharma, Dr. Sapna Soneja, Dr. Loveena Oberoi, Dr. Anuradha Malhotra.

CONFLICTS OF INTEREST

Nil.

FUNDING

Nil.

REFERENCES

1. Freeman EE, Weiss HA, Glynn JR, Cross PL, Whitworth JA, Hayes RJ. Herpes simplex virus 2 infection increases HIV acquisition in men and women: Systematic review and meta-analysis of longitudinal studies. AIDS. 2006 Jan 2;20(1):73-83. doi: 10.1097/01.aids.0000198081.09337.a7, PMID: 16327322
2. World Health Organization. Herpes Simplex Virus; 2017. Available from: https://www.who.int/mediacentre/factsheets/fs400/en/#hsv1 [Last accessed on 2023 Feb 08].
3. Longo DL, Fauci AS, Kasper DL, Hause SL, Jameson JL, Loscalzo J. Harrison's Internal Medicine. 18th ed. The United States of America: McGraw Hill; 2012.
4. WHO. Summary of Global HIV Epidemic; 2021. Available from: https://www.who.int/data/gho/data/themes/hiv-aids [Last accessed on 2023 Feb 08].
5. Looker KJ, Elmes JA, Gottlieb SL, Schiffer JT, Vickerman P, Turner KM, *et al*. Effect of HSV-2 infection on subsequent HIV acquisition: An updated systematic review and meta-analysis. Lancet Infect Dis. 2017 Dec;17(12):1303-16. doi: 10.1016/S1473-3099(17)30405-X, PMID: 28843576; PMCID: PMC5700807
6. Nowak RG, Liska TA, Bentzen SM, Kim E, Chipato T, Salata RA, *et al*. Brief report: Herpes simplex virus type-2 shedding and genital ulcers during early HIV in Zimbabwean women. J Acquir Immune Defic Syndr. 2021 Jun 1;87(2):789-93. doi: 10.1097/QAI.0000000000002641, PMID: 33587502; PMCID: PMC8131209
7. Yi TJ, Walmsley S, Szadkowski L, Raboud J, Rajwans N, Shannon B, *et al*. A randomized controlled pilot trial of valacyclovir for attenuating inflammation and immune activation in HIV/herpes simplex virus 2-coinfected adults on suppressive antiretroviral therapy. Clin Infect Dis. 2013;57(9):1331-8. PMID: 23946220
8. Shi M, Zhang X, Chen M. Prevalence of herpes simplex virus 2 among MSM in Mainland China: A systematic review and meta-synthesis. AIDS Res Ther. 2022 Oct 1;19(1):46. doi: 10.1186/s12981-022-00469-w, PMID: 36182910; PMCID: PMC9526959
9. WHO. First Global and Regional Estimates of HIV Infections Attributable to HSV-2 Infection. Available from: https://www.who.int/news/item/19-11-2019-first-global-and-regional-estimates-of-hiv-infections-attributable-to-hsv-2-infection
10. Akinyi B, Odhiambo C, Otieno F, Inzaule S, Oswago S, Kerubo E, *et al*. Prevalence, incidence and correlates of HSV-2 infection in an HIV incidence adolescent and adult cohort study in Western Kenya. PLoS One. 2017 Jun 6;12(6):e0178907. doi: 10.1371/journal.pone.0178907, PMID: 28586396
11. Nag S, Sarkar S, Chattopadhyay D, Bhattacharya S, Biswas R, SenGupta M. Seroprevalence of herpes simplex virus infection in HIV coinfected individuals in Eastern India with risk factor analysis. Adv Virol. 2015 Oct 19;2015:537939. doi: 10.1155/2015/537939
12. Munawwar A, Gupta S, Sharma SK, Singh S. Seroprevalence of HSV-1 and 2 in HIV-infected males with and without GUD: Study from a tertiary care setting of India. J Lab Physicians. 2018;10:326-31.
13. Sufiawati I, Widyaputra S, Djajakusumah TS. Seroprevalence of herpes simplex virus types 1 and 2 and their association with CD4 count among HIV-positive patients. Dent J (Majalah Kedokt Gigi). 2012;45:114-20. doi: 10.20473/j.djmkg.v45.i2
14. Matthew O, Ndomb T, Onakewhor J, Matawal B, Osagie E, Abimiku A, *et al*. Multi-center study on the prevalence of human immunodeficiency virus/herpes simplex virus type-2 co-infection among pregnant women in Nigeria. Int J Virol AIDS. 2019;6:052. doi: 10.23937/2469-567X/1510052
15. Schaftenaar E, Verjans GM, Getu S, McIntyre JA, Struthers HE, Osterhaus AD, *et al*. High seroprevalence of human herpesviruses in HIV-infected individuals attending primary healthcare facilities in rural South Africa. PLoS One. 2014 Jun 10;9(6):e99243. doi: 10.1371/

journal.pone.0099243, PMID: 24914671

16. Ramchandani M, Kong M, Tronstein E, Selke S, Mikhaylova A, Magaret A, *et al*. Herpes simplex virus type 1 shedding in tears and nasal and oral mucosa of healthy adults. Sex Transm Dis. 2016 Dec;43(12):756-60. doi: 10.1097/OLQ.0000000000000522, PMID: 27835628
17. Schneider JA, Lakshmi V, Dandona R, Kumar GA, Sudha T, Dandona L. Population-based seroprevalence of HSV-2 and syphilis in Andhra Pradesh state of India. BMC Infect Dis. 2010 Mar 9;10:59. doi: 10.1186/1471-2334-10-59, PMID: 20214795; PMCID: PMC2848152
18. Ren L, Wang B, Miao Z, Liu P, Zhou S, Feng Y, *et al*. A correlation analysis of HHV infection and its predictive factors in an HIV-seropositive population in Yunnan, China. J Med Virol. 2020 Mar;92(3):295-301. doi: 10.1002/jmv.25609. PMID: 31621089
19. Omori R, Nagelkerke N, Abu-Raddad LJ. HIV and herpes simplex virus type 2 epidemiological synergy: Misguided observational evidence? A modelling study. Sex Transm Infect. 2018 Aug;94(5):372-6. doi: 10.1136/sextrans-2017-053336, PMID: 29203577; PMCID: PMC6204970