



HERPES SIMPLEX INFECTION IN PATIENTS LIVING WITH HIV/AIDS

Dermatology

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ABSTRACT

BACKGROUND: Cutaneous involvement is most common in patients living with HIV/AIDS. Globally prevalence of herpes simplex infection has been increasing especially among patients with HIV. HSV-2 (herpes simplex virus-2) infection is currently the most common cause of genital ulcer disease. HSV infection may present as IRIS (Immune Reconstitution Inflammatory Syndrome) in HIV reactive patients after starting HAART (Highly Active Anti-Retroviral Therapy).

AIMS: Aim & objectives of our study were to know the prevalence and characteristics of HSV infection in patients living with HIV/AIDS and effect of anti-retroviral therapy on the course of the disease.

METHODS: After obtaining informed consent, total 200 HIV reactive patients with or without herpes simplex infection were enrolled in the study. Detail history, clinical examination, required investigations were done. Apart from anti-retroviral therapy, patients were given oral acyclovir as per NACO guidelines. Results were analyzed using excel sheet.

RESULTS: Out of 200 HIV reactive patients, 25% (50 patients) had herpes simplex infection. Majority of them were having herpes genitalis (in 88% patients out of 50). Chronic ulcerative lesion was the most common presentation. HSV infection was also seen as part of IRIS (immune reconstitution inflammatory syndrome) in some patients.

CONCLUSION: Infection by herpes simplex virus (HSV) is one of the most common opportunistic infection. Currently HSV-2 is the most common cause of genital ulcer disease. Treatment of herpes simplex infection by oral acyclovir as per NACO guidelines along with anti-retroviral therapy reduce the frequency of attacks, duration of symptoms, also reduce viral shedding from an individual.

KEYWORDS

Herpes Simplex Infection, Patients Living with HIV/AIDS

INTRODUCTION:

Cutaneous involvement is most common in patients living with HIV/AIDS. Globally prevalence of herpes simplex infection has been increasing especially among patients with HIV, and it is one of the commonest opportunistic infection in HIV-infected individuals.¹

HIV and HSV are co-transmitters of each other.² HSV-2 infection is currently the most common cause of genital ulcer disease^{3,4,5,6,7}, and it may act as a potential risk factor for the acquisition of HIV infection.^{8,9,10} Moreover herpes simplex genitalis is also a marker lesion for new HIV cases and vice versa. In HIV infection excessive viral shedding occurs from the mucosal tract even in the absence of active lesion.¹ Patient may present with typical clinical lesions in early asymptomatic stage, but atypical and chronic ulcerative lesions may occur during course of HIV infection, resulting in difficulties in diagnosis, increased drug resistance and recurrence.¹

HSV-HIV interaction may affect the outcome of HIV-1 infection and progression of AIDS, so control of HSV infection may decelerate HIV infection.¹¹ HSV infection may present as IRIS (Immune Reconstitution Inflammatory Syndrome) in HIV reactive patients after starting HAART (Highly Active Anti-Retroviral Therapy).^{12,13}

Present study is undertaken to know the prevalence of HSV infection in HIV reactive cases, characteristics of HSV infection in patients living with HIV/AIDS, and to know the effect of anti-retroviral therapy in the course of disease.

MATERIALS AND METHODS:

The study was carried out in the department of Dermatology, Venereology & Leprosy at tertiary care hospital after ethical committee approval. Our study was prospective cross-sectional type of study for one year duration. HIV reactive patients with or without herpes simplex infection attending our outpatient department were studied. Pregnant women were excluded from the study.

Confidentiality of information was maintained, and informed consent was taken from each patient. Detailed history with thorough clinical examination was carried out in each patient. Investigations like haemogram, S.VDR, CD4 count, Tzank smear, were carried out. Average duration of attack, frequency of attack, characteristics of the lesions, and effect of antiretroviral therapy were also studied. Apart from antiretroviral therapy, patients were treated with antiviral drug

acyclovir as per NACO guidelines. They were examined thoroughly on follow-up and on recurrence also, for treatment response. Data was analyzed by excel sheet.

RESULTS:

In our study we reported 200 HIV reactive patients who attended dermatology outpatient department during the study period. Among them, 25% (50 patients) had herpes simplex infection.

Out of 50 patients, 33 (66%) were males and 17 (34%) were females. Majority of males (23; that is 69%) were married, 6 (18%) were unmarried, 3 (9%) widows and 1 (3%) divorcee. Spouse of 9 males (27%) were HIV reactive, while 14 (42%) males were having HIV non-reactive spouse. Among 17 females, majority (12; that is 71%) were married, while 5 females (29%) were widow. Spouse of 10 females (6 married and 4 widows) were HIV reactive (59%), while 7 females (41%) were HIV non-reactive spouse including 1 widow. Maximum number of patients that is 54% (19 males and 8 females) was reported in the age group of 31-40 years, followed by 24% (7 males and 5 females) in 21-30 years group, and 22% (7 males and 4 females) in the age group of 41-50 years. Mean age of patients is 35.44 in our study. 82% patients gave history of unprotected multiple exposures before, while 18% patients (5 males and 4 females) had past history of blood transfusion.

Table 1: Demographic Characteristics Of Patients Having Hsv Infection

Age group (in years)	Males	Females	Total	%
21-30	7	5	12	24
31-40	19	8	27	54
41-50	7	4	11	22

Out of total 50 patients having herpes simplex infection, herpes genitalis was seen in 88% patients (29 males and 15 females), and herpes labialis in 8% patients (3 males and 1 female); while 4% patients (1 male and 1 female) were having herpes genitalis and herpes labialis both. Among males, commonest site of involvement was shaft of penis (45%) followed by glans penis (27%), root of scrotum (18%), prepuce (15%) and corona of glans (9%). Among females, commonest site of involvement was vulva region (88%). Majority (80%) of the patients (24 Males and 16 Females) were having clinical features in form of superficial erosive/ulcerative lesions over genitals (which were preceded by vesicles). Rest of the patients were having typical

vesicular lesions or crusted papules. Enlargement of inguinal lymph nodes were observed in 12% patients (3 males and 3 females).

Tzanck smear was positive for multinucleated giant cells in patients presented with typical vesicular lesions. 10% patients (3 males and 2 females) had 1-2 episodes of herpes simplex infection per year; 22% (8 males and 3 females) had 3-4 episodes in a year; 30% (10 males and 5 females) patients had 5-6 recurrent attacks; 16% (5 males and 3 females) patients were having 7-8 episodes per year; while 12% (5 males and 1 female) patients had recurrent infection every month. Average duration of symptoms was 6-8 days. Oral acyclovir was administered to all patients in each episode, as all were immunocompromised. Anti-retroviral therapy was continued as it was. On follow-up of patients, frequency and duration of recurrent episodes were reduced after starting anti-retroviral therapy, along with increase in the CD4 cells count.

IRIS phenomena were noted in 44% patients (13 males and 9 females). In those, it was seen that after starting anti-retroviral therapy, within 3 months duration, patients developed episodes of herpes simplex infection (mostly herpes genitalis) with simultaneous increase in CD4 count. Infection was subsided after starting acyclovir orally and continuation of anti-retroviral therapy.

Apart from IRIS, there was no significant difference in the CD4 count of HIV reactive patients with or without HSV infection.



Herpes genitalis in male



Herpes genitalis in female

DISCUSSION:

HIV/AIDS and sexually transmitted diseases are becoming serious health problem in public. STIs (both ulcerative and non-ulcerative) increase the transmission of HIV.¹⁴ Genital ulcerative disease is a potential risk factor for acquiring HIV infection.^{6,9} Various studies have also revealed that genital herpes is currently the most common genital ulcerative disease.^{3,4,5,6,7}

The current study showed that 25% HIV reactive patients were having herpes simplex infection, which was similar (22%) to the study done by Sarna J et al.¹ Male predominance (66%) was noted in our study which was almost similar (67% males) in the study done by Jacob SM et al.¹⁵ Anuradha K et al.¹⁶ also noted the same in their study.

More than half (54%) patients were noted in the age group of 31-40 years in our study which was comparable with the study done by Anuradha K et al.¹⁶ Mean age of 35.44 was comparable with the study done by Anuradha K et al who reported mean age of 32.5 years, while the study done by Jacob SM et al reported mean age of 38.8 years.¹⁵ 90% patients (30 males and 15 females) were reported in the reproductive age group (15-45 years). This finding was similar to the study done by Sharma A et al¹⁴ who reported 84% patients in same age group.

In our study, 82% patients had heterosexual mode of transmission of HIV and HSV, and 18% patients had history of blood transfusion. While in the study done by Anuradha et al, all patients were having heterosexual mode of transmission.¹⁶

Among herpes simplex infection, most common presentation was herpes genitalis (88% out of HIV reactive patients with HSV infection). Higher rates of HSV-2 infection were also observed in other countries studies e.g. 55% in UK¹⁷, 87% in south Africa¹⁸, 86% in Uganda.¹⁹ Common site of involvement in males was shaft of penis (45%), followed by glans penis (27%), root of penis (18%), prepuce

(15%) and corona of glans (9%). Among females, vulval region was the commonest to be involved in our study (88%). The current study showed the chronic ulcerative lesion to be the most encountered presenting symptom (80%). This was also described in the study done by Strick LB et al. Whereas groups of vesicles were second most common presentation. Lymph node enlargement was noted in 12% patients in our study. Most patients presented with a recurrent infection. 30% patients had 5-6 episodes of herpes simplex infection per year, while 22% patients were having 3-4 attacks per year.

Genital ulceration related to herpes simplex virus is one of the most common presentations of immune reconstitution inflammatory syndrome^{20,21,22} which was noted in 44% patients in our study.

Treatment of herpes simplex infection by oral acyclovir as per NACO guidelines along with anti-retroviral therapy reduce the frequency of attacks, duration of symptoms, also reduce viral shedding from an individual.^{15,23} Apart from IRIS, no significant difference in CD4 counts was found in patients infected with or without HSV-2. This finding was similar to the study done by Saramma MJ et al. HIV infected group had significantly more male patients. These patients were also younger, had increased hypertrophic type symptoms, longer duration of symptoms, an increased complication rate and higher likelihood of recurrence. So apart from treating ulcers, due attention should be given to suppressive therapy to reduce recurrence and prevent transmission.

CONCLUSION:

Herpes simplex infection is one of the most common coinfections among HIV reactive patients globally. HSV-2 is the most common cause of genital ulcer disease currently. Treatment of herpes simplex infection by oral acyclovir as per NACO guidelines along with anti-retroviral therapy reduce the frequency of attacks, duration of symptoms, also reduce viral shedding from an individual. So screening for that should be done in all HIV-infected patients as early as possible.

REFERENCES:

- Sarna J, S. A. (2008). Protean manifestations of herpes infection in AIDS cases. *Indian J Sex Transm Dis*, 29: 26-8.
- Wald A, L. K. (2002). Risk of human immunodeficiency virus infection in herpes simplex virus type 2-seropositive persons: A meta-analysis. *J Infect Dis*, 185:45-52.
- Haliona B, M. J.E. (1999). Epidemiology of genital herpes: Recent advances. *Eur J Dermatol*, 9:177-84.
- Kumar B, G. S. (2001). Epidemiology of genital herpes: Current concepts. *Indian J Sex Transm Dis*, 22:2-4.
- O' Farrell N. (2001). Targeted interventions required against genital ulcers in African countries worst affected by HIV infection. *Bull World Health Organ*, 79:569-77.
- Chen CY, B. RC. (2000). Human immunodeficiency virus infection and genital ulcer disease in South Africa: The herpetic connection. *Sex Transm Dis*, 27:21-9.
- Gresenguet G, W. HA. (2005). Aetiology of genital ulcer disease among women in Ghana and Central African Republic: randomised trial of acyclovir treatment in addition to syndromic management (ANSR 1212 study) [abstract M0-605]. In: Program and abstracts of the 16th biennial meeting of the International Society for Sexually Transmitted Diseases Research (Amsterdam, The Netherlands)
- Sayal SK, G. CM. (1999). HIV infection in patients of sexually transmitted disease. *Indian J Dermatol Venereol Leprol*. 65:131-3.
- Stamm WE, H. HH. (1988). The association between genital ulcer disease and acquisition of HIV infection in homosexual men. *JAMA*, 260:1429-33.
- Severson LL, T. SK. (1999). Relation between herpes simplex viruses and Human immunodeficiency virus infection. *Arch Dermatol*, 135:1393-7.
- Palu G, B. L. (2001). Molecular basis of interactions between herpes simplex viruses and HIV-1. *Herpes*. 8:50-5.
- Reyes M, S. N. (2003). Acyclovir-resistant genital herpes among persons attending sexually transmitted diseases and immune-deficiency virus clinics. *Arch Intern Med*, 163:76-80.
- Price P, M. N. (2001). Immune dysfunction and immune restoration disease in HIV patients given highly active antiretroviral therapy. *J Clin Virol*, 22:279-87.
- Sharma A, M. YS. (2009). Reproductive tract infections in HIV positive women: A case control study. *Indian J Sex Transm Dis*, 30:16-8.
- Saramma MJ, T. G. (2015). Herpes simplex virus 2 infection in HIV seropositive individuals in Tamil nadu, India. *Int J Community Med Public Health*, 2(1): 33-37.
- Anuradha K, H. M. (2008). Herpes simplex virus 2 infection: A risk factor for HIV infection in heterosexuals. *Indian J Dermatol Venereol Leprol*, 74(3):230-3.
- Hill C, M. E. (2009). Epidemiology of Herpes simplex virus types-2 and 1 amongst men who have sex with men attending sexual health clinics in England and Wales: implications for HIV prevention and management. *Euro Surveill*, 14:34-9.
- Schaftenaar E, V. G. (2014). High Seroprevalence of human herpes viruses in HIV infected patients attending primary healthcare facilities in rural South Africa. *PLoS One*, 9(6): e99243.
- Nakubulwa S, M. FM. (2009). Association between HSV 2 and HIV serostatus in pregnant women of known HIV serostatus attending Mulago hospital antenatal clinic, Kampala, Uganda. *J Infect Dev Ctries*. 3(10):803-6.
- Sharma S, S. M. (2011). HIV and immune reconstitution inflammatory syndrome (IRIS). *Indian J Med Res*, 134(6):866-877.
- Ratnam I, C. C. (2006). Incidence and risk factors for immune reconstitution inflammatory syndrome in an ethnically diverse HIV type-1 infected cohort. *Clin Infect Dis*, 42: 418-27.
- Bosamiya S. (2011). The immune reconstitution inflammatory syndrome. *Indian J Dermatol*, 56(5):476-479.
- Posavad CM, Wald A. (2004). Frequent Reactivation of Herpes Simplex Virus among HIV-1 Infected Patients Treated with Highly Active Antiretroviral Therapy. *J Inf Dis*, 190:690-96.