

High seroprevalence of HSV-1 and HSV-2 in STD clinic attendees and non-high risk controls: A case control study at a referral hospital in south India

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ABSTRACT

Background: In Asia, HSV seroprevalence studies are sparse and they have recorded lower prevalence of HSV infection, especially HSV-2. **Aims:** To ascertain the seroprevalence of HSV-1 and HSV-2 in patients attending a STD clinic in a referral hospital in south India and to compare it with a control group. **Methods:** The study included 135 consecutive STD cases having history of ulcerative or non-ulcerative STD in the present or in the past 5 years and 135 age and sex-matched controls. Diagnostic serology was done for HSV-1 and HSV-2 using type specific IgG by indirect immunoassay using ELISA. The results were analyzed utilizing Chi-square test. **Results:** Amongst 135 STD clinic cases, 106 cases were males and 29 cases were females with male to female ratio of 3.65:1. The mean age was 32.2 years (range 16-65 years). Among study group cases, 112 (82.9%) cases were co-infected with HSV-1 and HSV-2, 11 (8.1%) cases were seropositive for HSV-1 alone and 3 (2.2%) cases were seropositive for HSV-2 alone. In the control group, 112 (82.9%) cases were co-infected with HSV-1 and 2, 12 (9.6%) for HSV-1 alone and 1(0.8%) for HSV-2 alone. Correlation of HSV-1 and HSV-2 serology with various demographic and behavioral factors was statistically insignificant. **Conclusions:** Seroprevalence of HSV-1 and HSV-2 in STD clinic cases and control group is high, similar to that recorded in sub-Saharan Africa. Thus, serological studies for HSV-1 and HSV-2 cannot be taken as a marker of sexual behavior in our set of population.

KEY WORDS: HSV 1, HSV 2, Serology in STD clinic, South India, Seroprevalence.

INTRODUCTION

Both type-specific and non-specific antibodies to herpes simplex virus (HSV) infection develop during the first several weeks following infection and persist indefinitely.^[1] Type-specific antibody-based serological tests are better than non-specific antibody-dependent

serological tests. Specific antibody-based serological tests are of two types— Western blot (which tests for a range of type-specific antigens) and glycoprotein G (gG) assays.^[2] Western blot tests are expensive, take 2–5 days to complete the screening and confirmatory steps, and require expert interpretation. Glycoprotein G assays detect antibodies to the type-specific proteins

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gG-1 and gG-2. Very little sequence homology exists between gG-1 and gG-2, allowing differentiation between established infection with HSV-1 and HSV-2 respectively. A number of gG-based tests have been commercially marketed, using a variety of test formats, most often using enzyme immunoassay (EIA) methods.^[2] These tests have mostly been used to find the seroprevalence of HSV.

The prevalence of HSV-1 infection has been found to be higher than that of HSV-2 infection in most geographic areas.^[3] In Asia, HSV seroprevalence studies are sparse and have recorded lower prevalence of HSV, especially HSV-2. The objective of our study was to ascertain the seroprevalence of HSV-1 and HSV-2 in patients attending a STD clinic in a referral hospital in south India and to compare it with a control group.

METHODS

This study was conducted between September 2001 to April 2003 in the Department of Dermatology and Sexually Transmitted Diseases, JIPMER, Pondicherry, south India. Approval of the protocol by an ethical committee of the institute was obtained. The study included 135 consecutive STD cases having history of ulcerative or non-ulcerative STD in the present or in the past 5 years. All known cases of HIV disease coming for the second visit to the hospital were excluded. One hundred and thirty-five age and sex-matched controls (having dermatological disorders other than STDs) were taken from the skin outpatient department (OPD). Patients' and controls' demographic data, age of sexual debut, lifetime number of sexual partners, type of STD, and VDRL / HIV status were studied.

Diagnosis of various STDs was made on clinical grounds with appropriate laboratory investigations (dark ground microscopy, Gram's stained smear, tissue smear, Tzanck test, biopsy from the ulcer, etc.) wherever feasible. Five ml of blood was collected from all patients and diagnostic serology was done for HSV-1 and HSV-2 using type-specific IgG by indirect immunoassay using ELISA (Using UBI-MAGIEEL™, Enzyme Immunoassay kit of herpes simplex type 1 [HSV 1 IgG] and herpes simplex type 2 [HSV 2 IgG]) after obtaining informed consent. The results were tabulated and analyzed utilizing Chi-

square test.

RESULTS

The correlation of HSV-1 and HSV-2 serology with various demographic, behavioral factors, clinical features and investigations is given in Table 1. Seventy-two cases were diagnosed to have STDs, others were following up for an STD in the past. Out of the 72 STD cases, 53 (73.6%; 33 male, 20 female) were in the ulcerative STD group (genital herpes-37 cases, primary syphilis-12 cases, donovanosis-2 cases, lymphogranuloma venereum and chancroid-1 case each); the remaining 19 cases (26.3%; male 17 cases, female 2 cases) were in the non-ulcerative group (condyloma acuminata-10 cases, gonorrhoea-8 cases, and non-gonococcal urethritis- 1 case).

None of the cases was found to be seropositive for HIV antibodies. Out of the 135 study group cases, 123 (91.5%) were seropositive for HSV-1, 115 (85.1%) were seropositive for HSV-2, 112 (82.9%) were co-infected with HSV-1 and HSV-2, 11 (8.1%) were seropositive for HSV-1 alone and 3 (2.2%) were seropositive for HSV-2 alone. In the control group of 135 cases (having almost similar demographic and behavioral characteristics as the study group with a promiscuity level of 28.2%), 124 (91.8%) were seropositive for HSV-1, 113 (83.7%) were seropositive for HSV-2, 112 (82.9%) were co-infected with HSV-1 and 2, 12 (9.6%) for HSV-1 alone and 1(0.8%) for HSV-2 alone.

Amongst the 53 cases (73.6%) of ulcerative STDs, 37 cases (63%) were clinically diagnosed as having genital herpes, of which 9 cases (24.3%) were of first episode genital herpes and 28 cases (75.6%) were of recurrent genital herpes. In the first episode genital herpes group, 6 cases (66.6%) each were positive for HSV-1 and HSV-2, and 5 cases (55.5%) were co-infected with HSV-1 and 2. In the recurrent genital herpes group, 27 cases (96.4%) each were positive for HSV-1, HSV-2 and both HSV-1 and 2. None of these above correlations reached the level of significance.

DISCUSSION

Serological tests may be used to detect antibodies to

Table 1: Distribution of HSV-1 and HSV-2 serostatus by demographic and behavioral characteristics in study group

Variable (No. of cases)	Seronegative (No. of cases)	HSV-1 only (No. of cases)	HSV-2 only (No. of cases)	Coinfected (No. of cases)
STD clinic cases (135)	9	11	3	112
Control group (135)	10	12	1	112
Age				
<40 years (111)	8	9	3	91
≥40 years (24)	1	2	0	21
Sex				
Male (106)	7	9	2	88
Female (29)	2	2	1	24
Sexual debut				
<20 years (18)	1	1	0	16
20-25 years (99)	6	9	3	81
>25 years (18)	2	1	0	15
Marital status				
Married (99)	5	8	2	84
Unmarried (36)	4	3	1	28
Sexual practice				
Heterosexuals (133)	9	11	3	110
Bisexual (1)	0	0	0	1
Homosexual (1)	0	0	0	1
Male Condom users				
Never used (98)	5	8	2	83
Occasionally (8)	2	1	0	5
Partners in last 12 months				
< 5 (64)	5	5	1	53
≥ 5 (71)	4	6	2	59
Life time number of partners				
< 10 (57)	3	5	1	48
≥ 10 (78)	6	6	2	64
Contact history				
Known person (32)	2	2	1	27
CSWs (56)	4	6	1	45
Both (47)	3	3	1	40
Type of sex				
Genital (129)	9	11	2	107
Oral (3)	0	0	1	2
Anal (3)	0	0	0	3
Occupation				
Manual laborer (92)	5	8	3	76
Housewife (25)	1	1	0	23
Skilled laborer (9)	1	1	0	7
Student (7)	2	1	0	4
Professional (2)	0	0	0	2
Other risk factors				
Smokers (38)	2	2	0	34
Alcoholic (11)	1	1	1	8
Both (5)	0	0	1	4
None (81)	6	8	1	66
Symptomatic STD cases				
Ulcerative (53)	3	2	1	47
Non-ulcerative (19)	1	2	1	15
Asymptomatic STD cases (63)	5	7	1	50
Genital herpes				
First episode (9)	2	1	1	5
Recurrent (28)	1	0	0	27
<5 episodes/yr (14)	0	0	0	14
≥5 episodes/yr (14)	1	0	0	13
VDRL test				
Reactive (12)	0	1	0	11
Non-reactive (123)	9	10	3	101

HSV in blood. However, they are generally indicative of past infection.^[2] Although the utility of type-specific serology for HSV in epidemiological studies is

undisputed, the use of these tests for diagnostic purposes remains contentious. Though the epidemiological gold standard is Western blot analysis,

it is available in few research centers and is expensive. The gold standard for diagnosing HSV infection being viral culture has severely underestimated the number of individuals affected. Recently developed type-specific IgG ELISA has shown promise, being less expensive, has no cross-reactivity and found to be effective in detecting HSV antibodies.^[4] Possible uses of type-specific serology for HSV include assessment of asymptomatic sexual partners of patients with genital herpes, diagnosis of genital ulcers where viral culture repeatedly gives negative results, exclusion of herpes in pregnancy, and routine testing as part of a screen for sexually transmitted diseases.^[5] There are several limitations: the test usually does not give positive results until about six weeks after exposure; a positive test result indicates previous exposure but does not prove that particular clinical signs or symptoms are due to herpes; and the sensitivity and specificity of the tests range from 95% to 99%.^[5] Reliable data on the prevalence of HSV-1 and HSV-2 serum antibodies provide an epidemiological measure of population burden of these infections.^[3]

Smith and Robinson^[3] have done a global review of type-specific HSV prevalence in different geographic areas. According to them, HSV-2 prevalence is highly variable and depends on many factors including country and region of residence, population subgroup, sex and age. HSV-2 prevalence is in general higher among higher risk sexual behavior groups and in women than men. Its seroprevalence is strongly associated with age, increasing from negligible levels in children younger than 12 years to as high as 80% among high-risk population. In a given population and age group, HSV-1 prevalence is almost always greater than HSV-2 prevalence.^[3] Almost similar observations were made in our study.

It has been stated that the prevalence of HSV-1 infection is high in most geographic areas worldwide and is more prevalent than HSV-2 infection in all non high-risk populations studied.^[3] Exceptions to this are groups with HIV seropositive persons, and commercial sex workers (CSW) where HSV-2 prevalence is > 65%. Among adolescents and adults > 15 years of age, HSV-1 seroprevalence is high (>91%) in Central Africa, Eritrea and Uganda.^[3] In Asia, the prevalence of HSV-1 among

STD clinic attendees of Osaka, Japan was found to be 73%.^[6] In our study, prevalence of HSV-1 among STD clinic cases was 91.5% and among controls (those attending skin OPD) was 91.8%. There was no difference in HSV-1 prevalence among high-risk population versus non-high risk population.

HSV-2 seroprevalence is in general highest in areas of Africa and in parts of America, is modest in western and southern Europe, usually lower than northern Europe and North America and in Asia lower than all other geographic areas.^[3] In Asia, seroprevalence of HSV 2 among STD clinic attendees of Dhaka, Bangladesh was 63%,^[7] and that in STD clinic attendees of Japan has been found to be 23%.^[8] HSV-2 seroprevalence in sub-Saharan Africa is among the highest in the world, sometimes reaching 80% in women and men of 35 years.^[3] In populations with evidence of higher risk sexual behavior and in STD clinic attendees, the prevalence of HSV-2 infection is consistently higher than in non-high-risk populations. Seroprevalence of HSV-2 among STD clinic cases was 85.1% and among controls was 82.9% in our study. Though HSV-2 prevalence was slightly higher amongst the high-risk population as compared to the non-risk population, the difference was not statistically significant. The seroprevalence of HSV-1 and HSV-2 in STD clinic cases and control group was high in our study, similar to that recorded in sub-Saharan Africa.^[3]

A higher seroprevalence of HSV-2 among females as compared to males has been recorded in the literature.^[9,10] A 3-fold higher seroprevalence among younger women of 15-19 years compared to men of a similar age group was observed in Tanzania.^[10] Others have found an equal prevalence of HSV-2 among men and women in Japan and Germany.^[6,11] In our study, the prevalence of HSV-1 among males was 91.5%, which was more compared to females (89.6%), but the prevalence of HSV-2 among females (86.2%) was more than males (85%). These differences were statistically insignificant.

Our study showed 100% prevalence for HSV-1 and 91.8% for HSV-2 among those who were positive for VDRL. Suligoj et al^[12] in their study found that 62% patients showed a positive serology among those who were

TPHA positive. Shaw et al^[13] found that among those who had positive serology for syphilis, 32% were positive for HSV-2.

Among those who had clinical evidence of genital herpes, 94.2% were positive for both HSV-1 and HSV-2. In the cases of first episode herpes genitals, 6 of 9 cases (66%) were positive for HSV-1 and HSV-2, whereas in recurrent herpes genitals, 27 of 28 cases (96.4%) were positive for HSV-1 and HSV-2. Evans et al^[14] found 55.2% prevalence of HSV-2 among those who had current episode of genital herpes and 94.4% in those who had past history of genital herpes.

Our study showed that 72.6% (98 of 135 STD clinic cases) of patients who did not give history suggestive of genital herpes were positive for HSV-2 serology. Similarly, Varela et al^[15] found that 70% of their patients did not have history of genital herpes but were positive for HSV-2 serology. Rosa-Santos et al^[16] found that only 10% of those who were positive for HSV-2 revealed previous history of genital herpes.

Since HSV-1 and HSV-2 prevalence in the STD clinic cases and control group was very high, HSV serology cannot be used in this set of population to distinguish genital herpes caused by HSV-2 from genital herpes caused by HSV-1. Serology will also not be helpful in the identification of cases where genital lesions did not show multinucleate giant cells on Tzanck smear and viral culture studies were negative. The high seroprevalence of HSV-1 and HSV-2 in STD clinic cases and control group is similar to that recorded in sub-Saharan Africa. Thus, serological studies for HSV-1 and HSV-2 cannot be taken as a marker of sexual behavior in our set of population.

REFERENCES

1. Center For Disease Control. Sexually transmitted diseases: Treatment guidelines 2002. MMWR Morbidity Mortality Weekly Report 2002;51:11-50.
2. Scoular A. Using the evidence base on genital herpes: optimising the use of diagnostic tests and information provision. *Sex Transm Infect* 2002;78:160-5.
3. Smith JS, Robinson NJ. Age specific prevalence of infection with herpes simplex virus types 2 and 1. A global review. *J Infect Dis* 2002;186:S23-8.
4. Goldman BD. Herpes serology for dermatologists. *Arch Dermatol* 2000;136:1158-61.
5. Gilson RJ, Mindel A. Recent advances-Sexually transmitted infections. *BMJ* 2001;322:1160-4.
6. Hashido M, Lee FK, Nahmias AJ, Tsugami H, Isomura S, Nagata Y, et al. An epidemiologic study of herpes simplex type 1 and 2 infection in Japan based type specific serological assays. *Epidemiol Infect* 1998;120:179-86.
7. Rahman M, Alam A, Nessa K, Hossain A, Nahar S, Datta D, et al. Etiology of sexually transmitted infections among street based female sex workers in Dhaka, Bangladesh. *J Clin Microbiol* 2000;38:1244-6.
8. Hashido M, Kawana T, Matsunaga Y, Inouye S. Changes in prevalence of herpes simplex virus 1 and 2 antibodies from 1973 to 1993 in the rural districts of Japan. *Microbiol Immunol* 1999;43:177-80.
9. Fleming DT, McQuillan GM, Johnson RE, Nahmias AJ, Aral SO, Lee FK, et al. Herpes simplex virus type-2 in the United States, 1976 to 1994. *N Engl J Med* 1997;337:1105-11.
10. Obasi A, Mosha F, Quigley M, Sekirassa Z, Gibbs T, Munguti K, et al. Antibody to herpes simplex type-2 as a marker of sexual risk behaviour in rural Tanzania. *J Infect Dis* 1999;179:16-24.
11. Wutzler P, Doerr HW, Farber I, Eichhorn U, Helbig B, Sauerbrei A, et al. Seroprevalence of herpes simplex type 1 and 2 in selected German populations-relevance for the incidence of genital herpes. *J Med Virol* 2000;61:201-7.
12. Suligoi B, Tchamgmena O, Sarmati L, Bugarini R, Toma L, Bakary DK, et al. Prevalence and risk factors for herpes simplex type 2 infections among adolescents and adults in northern Cameroon. *Sex Transm Dis* 2001;28:690-3.
13. Shaw M, Van der Sande M, West B, Paine K, Ceesay S, Bailey R, et al. Prevalence of herpes simplex type-2 and syphilis serology among young adults in rural Gambian community. *Sex Transm Infect* 2001;77:358-65.
14. Evans BA, Kell PD, Bond RA, MacRae KD, Slomka MJ, Brown DW. Predictors of seropositivity to herpes simplex virus type 2 in women. *Int J STD AIDS* 2003;14:30-6.
15. Varela JA, Garcia-Corbeira P, Aguanell MV, Boceta R, Ballesteros J, Aguilar L, et al. Herpes simplex virus type 2 seroepidemiology in Spain: prevalence and seroconversion rate among sexually transmitted disease clinic attendees. *Sex Transm Dis* 2001;28:47-50.
16. Da Rosa-Santos OL, Goncalves Da Silva A, Pereira AC Jr. Herpes simplex virus type 2 in Brazil: Seropidemiologic survey. *Int J Dermatol* 1996;35:794-6.