

INCIDENCE OF HSV-2 IgG ANTIBODIES IN TERM PREGNANCY

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Abstract

Background: Infection of the genital tract with HSV-1 and HSV-2 can result in genital herpes, but most cases are caused by HSV-2. HSV-2 is primarily transmitted through sexual contact and is one of the most common causes of genital ulcer disease worldwide. About 25% of first symptomatic episode of genital herpes already have antibodies to HSV-2, indicating a past asymptomatic infection. **Materials and Methods:** The present study was conducted in the outpatient department of Microbiology, SKMCH, Muzaffarpur, Bihar during July 2023 December 2023. The study group comprised of 100 asymptomatic pregnant females attending OPD of the hospital for a routine antenatal check-up. Serum specimens were screened for HSV-2 infection by detecting IgG class antibodies against HSV-2-specific glycoprotein G-2 using an ELISA kit (RADIM SpA, Italy). The serum specimen was screened for HIV-1 and HIV-2 antibodies by the ELISA technique. Statistical analysis was performed using t-test, chi-square test and Fischer test, and referenced for P-values for their significance. **Result:** Out of 100 women, 9 cases tested positive for antibodies against HSV-2 and, thus, a seroprevalence of 9% was found in our study. The frequency of asymptomatic and unrecognized infections was found to be high; only one seropositive case had a history of genital herpes. **Conclusion:** Our findings suggest that HSV-type-specific serotesting could be an efficient strategy to diagnose clinically asymptomatic HSV-2 infections and, therefore, to reduce the risk of HSV-2 and HIV sexual transmission by prophylactic counseling against unprotected intercourse.

INTRODUCTION

Schneweis in 1961 demonstrated two serotypes of herpes simplex virus (HSV); herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2).^[1] HSV-1 and HSV-2 are transmitted by different routes and involve different areas of the body, but there is considerable overlap between epidemiological and clinical manifestations of infections by these viruses. Infection of the genital tract with HSV-1 and HSV-2 can result in genital herpes, but most cases are caused by HSV-2.^[2] HSV-2 is primarily transmitted through sexual contact and is one of the most common causes of genital ulcer disease worldwide. The acquisition of HSV-2 infection may be subclinical in some patients so that they are unaware of the disease. About 25% of first symptomatic episode of genital herpes already have antibodies to HSV-2, indicating a past asymptomatic infection.^[3] In pregnancy, primary genital herpes infection manifests clinically in a manner similar to that in a non-pregnant female but with an increased risk of dissemination and mortality.^[4] Genital herpes during pregnancy is said to be associated with an

increased risk of spontaneous abortions, intrauterine growth retardation (IUGR) and premature delivery.^[5] A dreaded complication of genital herpes in pregnancy is transmission of virus to the newborn, causing neonatal herpes, a disease of high morbidity and mortality. The consequences of neonatal infection are catastrophic; death of the affected neonate or severe neurodevelopmental disability are common. Risk of transmission is 10-times higher in maternal primary infection compared with recurrent infection. Acquisition of infection with seroconversion completed before labor does not appear to affect the outcome of pregnancy, but infection acquired at the time of labor is associated with perinatal morbidity.^[5]

HSV infection has been considered to be a risk factor for subsequent or concurrent human immunodeficiency virus (HIV) infection.^[6] The increased risk may be a result of discontinuity in the genital mucosal barrier. Herpes lesions are associated with recruitment of CD4 lymphocytes, a factor responsible for increased expression of HIV on the genital mucosa, thereby increasing the viral load and consequent risk of transmission. High titers of HIV

virions are found in all genital herpes lesions, which facilitate transmission.^[7]

Because HSV causes a lifelong infection with unpredictable reactivation and transmission, detecting antibodies to HSV plays an important role in identifying carriers of this infection. Type-specific tests have been developed that are based on the protein glycoprotein G from HSV-2 (gG2) or glycoprotein (gG1) from HSV 1.^[8] Because very limited sequence homology exists between gG1 and gG2, assays based on detecting these type-specific epitopes using either Western blot or enzyme-linked immunosorbent assay (ELISA) can reliably differentiate between antibodies to HSV-1 and antibodies to HSV-2. These tests can also allow in the identification of HSV-2 infection in persons with or without antibodies to HSV-1. Glycoprotein-G-based enzyme immune assays have a sensitivity of 98% and a specificity of 97%.^[9,10]

MATERIALS AND METHODS

The present study was conducted in the outpatient department of Microbiology, SKMCH, Muzaffarpur, Bihar during July 2023 December 2023. The study group comprised of 100 asymptomatic pregnant females attending OPD of the hospital for a routine antenatal check-up. Those females presenting with complaints that needed urgent or specialist attention, like hemorrhage, labor pains, severe anemia, jaundice, etc., were excluded from the study. A detailed history was obtained about the demographic details and data relevant to herpes virus infection. After an informed consent, blood samples were collected from the enrolled subjects. Serum was separated and stored at -20°C till conduction of the assay. Serum specimens were screened for HSV-2 infection by detecting IgG class antibodies against HSV-2-specific glycoprotein G-2 using an ELISA kit (RADIM SpA, Italy). The serum specimen was screened for HIV-1 and HIV-2 antibodies by the ELISA technique.

Statistical analysis was performed using t-test, chi-square test and Fischer test, and referenced for P-values for their significance.

RESULTS

Of the total 100 pregnant females enrolled for the study, 60% belonged to rural and 40% to urban areas. The age of the patients ranged from 16 to 42 years with a mean age of 22.8 ± 11.4 . The most common age groups were 21–25 years, followed by 26–30 years. Majority of the participants were illiterate. Out of 100 women, 9 cases tested positive for antibodies against HSV-2 and, thus, a seroprevalence of 9% was found in our study. The frequency of asymptomatic and unrecognized infections was found to be high; only one seropositive case had a history of genital herpes.

Evaluation of HSV-2 IgG antibodies according to age showed a statistically significant correlation with seropositivity, the risk becoming higher with increasing age. In our study, seropositivity was maximum in the age group ≥ 30 years and henceforth kept on decreasing with each descending age group. The various demographic variables studied, like place of residence, annual family income, level of education and occupation (of self and sexual partners) failed to show any significant correlation with seropositivity of HSV-2 ($P > 0.05$) [Table 1].

A statistically significant association between HSV-2 seropositivity was found with factors like increasing parity and increasing duration of marriage. No significant association of seropositivity with early age at first coitus was observed. Seropositivity was found to be highly associated with history of previous abortions. No statistically significant association of seropositivity to HSV-2 with present or past history suggestive of other sexually transmitted infections was seen. None of our cases tested positive for HIV. [Table 2]

Table 1: Correlation between HSV 2 serology and various socio-demographic characteristics of participants of the study

Patient characteristics	Total number of patients	HSV 2 serology	
		Positive	Negative
Age (years)			
<20 years	19	0	19 (100%)
20-30 years	49	2 (4.1%)	47 (95.9%)
>30 years	32	7 (21.9%)	25 (78.1%)
Place of residence			
Rural	60	3 (5%)	57 (95%)
Urban	40	6 (15%)	34 (85%)
Occupation			
Working	8	2 (25%)	6 (75%)
Housewife	92	7 (7.6%)	85 (92.4%)
Education			
Literate	58	4 (6.9%)	54 (93.1%)
Illiterate	42	5 (11.9%)	37 (88.1%)

Table 2: Correlation between HSV 2 serology and various characteristics related to sexual behaviour and gynecological history of the study participants

Patient characteristics	Total number of patients	HSV 2 serology	
		Positive	Negative

Parity			
0	21	0	21 (100%)
1	36	0	36 (100%)
2	20	2 (10%)	18 (90%)
>2	23	7 (30.4%)	16 (69.6%)
Duration of marriage			
<5 years	24	0	24 (100%)
5-10 years	64	1 (1.6%)	63 (98.4%)
>10 years	12	8 (66.7%)	4 (33.3%)
History of abortion			
Yes	31	6 (19.4%)	25 (80.6%)
No	69	3 (43.5%)	66 (56.5%)
History suggestive of STI			
Yes	22	5 (22.7%)	17 (77.3%)
No	78	4 (5.1%)	74 (94.9%)

DISCUSSION

Epidemiology of genital herpes varies between different countries and between groups of individuals depending on the demographic and clinical characteristics of the population. The seroprevalence of HSV-2 antibodies is an accurate method of determining the epidemiology of this infection. Serological assay utilizing type-specific glycoprotein gG1 and gG2 is more accurate in differentiating between antibodies directed against HSV-1 and HSV-2.

The prevalence of genital herpes has increased markedly in the past few decades. In the present study, a seroprevalence of 9% was found among pregnant females. In contrast to our study, a much higher HSV-2 seroprevalence has been reported from various rural and urban populations from Africa (60–90% and South and North America (30–70%).^[11,12] This could be because of a higher prevalence of promiscuous sexual behavior, large number of sexual partners and high prevalence of other sexually transmitted infections in these communities. Nizami et al,^[13] reported a seroprevalence of 63.1% in pregnant women whereas Tideman et al. reported a seroprevalence of 11.3%,^[14] and Dan et al. reported a seroprevalence of 13.3%.^[15] Prevalence in the general population in developing Asian countries appears to be lower (10–30%).^[16] Maitra and Gupta,^[17] found a seroprevalence of 23.3% in a general gynecology clinic and Chawla et al,^[18] reported a seroprevalence of 7% and 8.6% in two urban communities in Delhi.

In our study, the HSV-2 seroprevalence rose steadily with age. These findings are comparable to the previous studies.^[13,14] No statistically significant correlation was observed with other demographic variables in our study, such as place of residence, whether rural or urban, education, annual family income, occupation and socioeconomic status. Similar findings were reported by Fleming et al.^[12] However, some studies have found a significant association between HSV-2 seropositivity and sociodemographic factors while assessing the risk factors for HSV-2 infection in women.^[14,18]

In our study, we also assessed the role of various sexual behavioral markers in the seropositivity to HSV-2 and a significant correlation was observed

with increasing number of previous pregnancies, and duration of sexual activity or marriage. Breinig et al,^[19] and Tideman et al,^[14] reported a significant association between seropositivity and increasing parity. The effect of increasing number of previous pregnancies on seropositivity may not be direct but may be a reflection of increased duration of sexual activity, which itself is a risk factor for HSV seropositivity. No statistically significant association of seropositivity to HSV-2 with respect to history suggestive of other sexually transmitted infections and HIV serology was seen in our study. Similar findings have been reported by Chawla et al.^[18]

A high frequency of unrecognized and asymptomatic HSV-2 infections was observed in our study; only one out of 9 seropositive cases reported a history of genital herpes, although 57% of these cases complained of vague symptoms like itching discharge, dysuria, discomfort, etc. The increasing prevalence of genital herpes, high frequency of asymptomatic and unrecognized infections, high rate of recurrence, potential for transmission to neonate and lack of a definitive cure have made this disease of great concern. Another aspect of genital herpes is that transmission can occur in long-standing monogamous relationships, a low-risk group for sexually transmitted infections, as the virus may be transmitted to susceptible partner after a long time of sexual contact because infection due to unrecognized reactivation in the infected partner is intermittent.

CONCLUSION

Our findings suggest that HSV-type-specific serotesting could be an efficient strategy to diagnose clinically asymptomatic HSV-2 infections and, therefore, to reduce the risk of HSV-2 and HIV sexual transmission by prophylactic counseling against unprotected intercourse. It may also be a useful adjunct in detecting cases who present with symptoms not directly suggestive of genital herpes. Type-specific serological screening has been recommended to identify women at risk of acquiring genital HSV-2 infection close to term when there is a high (30–50%) risk of neonatal herpes.

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