

# Herpes Simplex Virus Type 2 Seropositivity in a Sexually Transmitted Disease Clinic in Israel

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**Key words:** herpes simplex virus, glycoprotein, infection, sexually transmitted disease, antibody

## Abstract

**Background:** Seroepidemiologic surveys have provided valuable information on the prevalence and incidence of herpes simplex virus-2 infection in general and in selected populations.

**Objective:** To review the reliability of traditional diagnostic approaches in herpes simplex virus-2 infection.

**Methods:** In this cross-sectional study, 472 patients attending a clinic for sexually transmitted disease in 1998-1999 were evaluated for HSV-2 infection through collection of epidemiologic and clinical data. HSV-2 infection was confirmed by the presence of specific viral glycoprotein, gG-2, antibody in sera.

**Results:** The seroprevalence of HSV-2 among clinic attendees was 9.33%. Of these attendees only 22% presented with or reported a history of typical vesicular lesions in the genital area. Infection rate was higher in patients with multiple sex partners (20.8% vs. 8.7%,  $P \leq 0.0023$ ), in individuals aged 30 or older (12.6 vs. 6.4%,  $P = 0.03$ ) and in the Israeli Jewish population as compared to the Israeli Arab population (11.1% vs. 2.4%,  $P \leq 0.01$ ). Females with multiple sex partners exhibited higher rates of infection than did their male counterparts (50 vs. 16.1%,  $P \leq 0.0275$ ).

**Conclusion:** The findings support the need for HSV-2 serologic testing in patients presenting to STD clinics even when typical genital lesions are not evident but where risk factors for HSV-2 infection are identified.

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The seroprevalence of herpes simplex virus-2 is increasing worldwide [1,2]. In the United States HSV-2-related infection increased by over 30% since the late 1970s and is now detectable in roughly one in five persons over 12 years of age [2]. Risk factors for infection identified in numerous studies are sexual promiscuity, female gender, age group, non-Caucasian ethnicity, low socioeconomic status, homosexual orientation, and previous infection with human immunodeficiency or other sexually transmitted diseases [2-10].

HSV-2-related genital herpes was traditionally considered to be a typical clinical disease with vesicular lesions on an erythematous base on the glans and body of the penis and scrotum in men and similar lesions on the vulva, perineum, buttocks, vagina and cervix in women. However, based on data from 10 industrialized countries including the USA, it is estimated that only 20% of approximately 107 million people testing seropositive for HSV-2 are clinically recognized [11].

The present study identifies epidemiologic and clinical characteristics of HSV-2 infection and the importance of documented risk factors associated with infection in patient diagnosis.

## Patients and Methods

### Study population

A total of 472 patients who attended the STD clinic at Bnai Zion Medical Center in Haifa, Israel was subjected to blood testing for HSV-2 serology. HSV-2-positive patients were assessed for genital symptoms. Patients were classified as having typical symptoms if they presented with or reported a history of genital vesicles. The remaining patients were classified as having unrecognized HSV-2 infection.

### Risk factors

Epidemiologic data including gender, age, ethnicity and multiple sex partners (three different sex partners in the previous 6 months) were collected on each patient and comparisons were made. Non-Israeli patients included sailors stationed in the port of Haifa. Information was not provided for age in six patients, ethnicity in one and number of sexual partners in 22.

### HSV-2 serology

We examined serum samples for the presence of specific antibodies against HSV-2 using enzyme immunoassay (EIA-gG, Gull, USA) [12]. Positive serology for gG represents the presence of anti-HSV-2 antibody.

### Statistical analysis

Univariate analysis for testing the associations between categorical groups was performed using chi-square or Fisher-exact tests, when appropriate. A  $P$  value  $\leq 0.05$  was statistically significant. Results were expressed as numbers and percentages of patients.

## Results

Patient demographics and behavioral characteristics of the study population are presented in Table 1. Of the 472 attendees visiting the STD clinic, 50 were seropositive for HSV-2 (10.6%). Of the multiple-sex partner-patients, 20.8% (15/72) were gG-2 positive as compared to 8.7% (33/378) who were not ( $P \leq 0.0023$ ).

The frequency of HSV-2 seropositivity in the female population (14.8%, 17/115) was greater than in the male population (9.2%, 33/357). This difference was not statistically significant. When

HSV = herpes simplex virus  
STD = sexually transmitted disease

**Table I.** Patient demographics and behavioral characteristics

<b>Gender</b>	
Male	357
Female	115
<b>Sexual activity</b>	
Non-multi-partner	378
Multi-partner	72
<b>Ethnicity</b>	
Israeli	418
Non-Israeli	53
Jews	333
Arabs	85
<b>Age</b>	
<30	277
≥30	189

comparing populations with multiple sex partners on the basis of gender, females had a significantly higher prevalence of HSV-2 seropositivity than males – 50% (5/10) vs. 16.1% (9/62),  $P \leq 0.0275$ . HSV-2 seropositivity was significantly greater in patients over 30 years of age – 35/277 (12.6%) vs. 12/189 (6.4%),  $P \leq 0.03$ .

Of the three ethnic groups evaluated, the non-Israeli group had the greatest prevalence of HSV-2 seropositivity, 18.9% (10/53). The seroprevalence of the Israeli population attending the STD clinic was 9.33%. Israeli Jews exhibited a significantly higher incidence of HSV-2 seropositivity than did Israeli Arabs – 37/333 (11.1%) vs. 2/85 (2.4%),  $P \leq 0.01$ .

Of a total 50 seropositive patients, 11 (22%) presented with or reported a history of vesicular lesions in the genital area. Of the remaining 39 HSV-2-seropositive patients, 31 (62%) presented with or reported a history of dysuria, urinary frequency, perineal pain, meatitis, urethral discharge, vaginal discharge, genital tenderness or itching.

## Discussion

In a 1988–1994 study of a population aged 15–74 in the U.S., the serologic frequency of HSV-2 was 21.9% [2]. In recent years, STD clinics in Spain, England, The Netherlands, and Japan have reported seropositivities ranging from 10.4 to 25% [3,5,7,13]. The prevalence among Israelis in our sample population fell slightly below this range.

A study by Nahmias et al. [4] in 40,000 patients with anti-HSV-2 antibodies established that the risk of infection increases with increasing numbers of sex partners. In our population, patients with multiple sex partners had a significantly greater prevalence of HSV-2 seropositivity.

Differences in HSV-2 seropositivity have been shown to exist between patient groups of different gender. In the U.S., 65% of African American woman are seropositive compared with 45% of males, while among Caucasian women 15% are seropositive compared with 12% of men [6]. In our sample the prevalence of HSV-2 seropositivity was slightly greater among females, although the difference was not statistically significant. When males and females were stratified for level of sexual activity, females were found to have a significantly greater prevalence than males.

Several studies established a relationship between patient age and infection rates. In the NHANES III study the overall seroprevalence rose rapidly in the younger age groups, peaking in the 30–39 year old age group at 27.8% and then leveling off [2]. Our study revealed a significantly greater prevalence of HSV-2 seropositivity in patients over 30 years of age.

Ethnic origin has been identified as a risk factor for HSV-2 infection. The NHANES III study found differences between African Americans, Hispanics, and Caucasians in infection rates for HSV-2 [2]. In our study the Israeli Jewish population had a higher frequency of HSV-2 seropositivity than the Israeli non-Jewish population. This difference corresponds to different predisposition for multiple sex partners.

The majority of patients with serologic evidence of HSV-2 infection has no history of genital herpes [2,11,14,15]. In one study, as few as 10% of HSV-2-seropositive patients reported typical symptoms of genital herpes [2]. Our HSV-2-seropositive population also exhibited a low percentage of typical HSV-2 presentation. The different presentations described in the remaining HSV-2-seropositive patients cannot be clearly associated with HSV-2 due to other STD organisms isolated in two-thirds of these patients (data not shown).

In summary, as in general populations, HSV-2 seropositivity among the Israeli population is significant and presents in a majority of cases without typical symptoms of HSV-2 infection. Therefore, when risk factors, particularly multiple sex partners, are identified, the possibility of HSV-2 infection should be thoroughly investigated.

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