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Prevalence and determinants of genital shedding of herpes simplex virus among women attending Italian colposcopy clinics

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Abstract

Objectives: To determine the prevalence of herpes simplex virus (HSV) shedding among women attending Italian colposcopy clinics and describe their lifestyle, demographic characteristics, genital symptoms and signs. *Study design:* A cross-sectional study was performed to assess shedding of HSV among 4565 women requiring a gynecological consultation. An amplified enzyme immunoassay that detects an HSV type-common glycoprotein D was used to reveal HSV shedding in cervical specimens. Statistical analysis was performed using Chi-square test and Student's *t* test. *Results:* A prevalence of 7.8% was found among colposcopy clinic patients. No significant differences regarding patients' average age, age at first sexual intercourse, contraceptive method used, and number of sexual partners in the previous year were found between subjects with and without viral shedding ($P > 0.05$). The detection of a concomitant genital infection with *Trichomonas vaginalis* as well as the report of previous episodes of genital herpes (GH) were significantly higher in the positive group ($P < 0.01$). Only 2.8% of the patients shedding HSV presented with vesicles and ulcers, with the majority of them being asymptomatic. *Conclusion:* This is the first Italian survey on genital herpes conducted among colposcopy clinic patients. Our data show that the prevalence of HSV shedding in this study population is high and confirms that the disease is often asymptomatic. The demographics and behavioural variables of women shedding HSV seem to differ from the ones assessed in high risk patients.

Keywords: Genital herpes; Viral shedding; Enzyme immunoassay; Colposcopy clinics

1. Introduction

Genital herpes (GH) is one of the most commonly diagnosed sexually transmitted diseases (STDs) in industrialized countries. It is classically caused by herpes simplex virus type 2 (HSV 2) infection, although in recent years an increasing number of cases has been reported to be due to HSV type 1 (HSV 1) [1]. While the majority of patients are completely asymptomatic [2–4], GH can show a wide variety of clinical presentations ranging from severe genital disease with or without systemic complications, to asymptomatic local infection [5].

The seroprevalence of HSV 2 type-specific antibodies has been considered an effective indicator of GH prevalence, since serologic assays can allow even asymptomatic carriers to be identified, and HSV 2 is responsible for the majority of GH cases [6,7].

The seroprevalence of HSV 2 has been shown to be higher among at risk subjects, such as STD clinic patients and commercial sex workers, ranging from 20 to 90% [8–11]. Two recent studies performed among attendees of two Italian STD clinics revealed HSV 2 seroprevalence to be 29.5 and 24.6%, respectively, without significant differences between males and females [12,13]. The prevalence of HSV 2 antibodies was, in fact, much higher than the 5.5% reported among low-risk Italian populations [14].

Different HSV type-specific serological assays have become commercially available. These can ascertain if a subject has been previously infected by HSV but, unless detecting seroconversion to anti-HSV reactivity, they do not reveal the frequency of viral shedding, which represents the primary source of infection. In other words, serological tests only detect the potential sources of GH in a specific population, not the current ones.

In the current survey, we analysed the prevalence of genital herpes from the gynecologist's point of view, as the study population consisted in women attending 16 Italian colposcopy clinics. The aim of this study was to ascertain the

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effective sources of infection. The prevalence of HSV shedding was determined by Wellcozyme HSV®, an enzyme immunoassay detecting an HSV type common antigen. We also described the lifestyle, demographic characteristics, symptoms and signs of the women with genital shedding of HSV.

2. Materials and methods

2.1. Study population

We conducted a multicentral cross-sectional study to evaluate the prevalence of genital HSV shedding on cervical specimens, from January 1993 to March 1997. The study population consisted in 4565 women attending Modena Policlinico and 15 other Italian colposcopy clinics.

In Italy, women with symptoms consistent with lower genital tract infections or STDs are referred to either STD clinics or colposcopy clinics. Clinics for sexually transmitted diseases are run by dermatologists, whereas colposcopy clinics are run by gynecologists. However, for female patients, both diagnostic and therapeutic procedures on the lower genital tract, included STD management, are currently performed in colposcopy clinics.

2.2. Study protocol

Consent to participate in the study was obtained from women referred to colposcopy clinics for specific diagnostic examinations or for outpatient surgical treatments. Before the procedures were performed, a cervical specimen was collected from each woman enrolled in the survey to determine the presence of HSV shedding. Cultures were performed in association with cervical sampling, to assess the presence of *Chlamydia trachomatis*, *T. vaginalis*, *Naisseria gonorrheae*, non-specific bacterial infections and *Candida* species. In addition sera were collected from each subject and tested for syphilis (RPR* and, in case of positive results, TPHA** was performed). Patients were also examined with colposcopy and vulvoscopy to detect vulvar, vaginal or cervical condilomata. We questioned the study population on demographics and behavioural variables. Information was collected on the age at first sexual intercourse, number of sexual partners in the previous year, contraceptive method used, smoking habits, complaints of symptoms consistent with lower genital tract infections and any previous oral or genital herpetic infections.

Women were classified as ''smokers'' if they reported such a habit when enrolled in the study and/or they had smoked for at least 2 years. Inquiries on contraception considered the contraceptive method that each subject used in the year preceding enrolment in the survey. When women reported more than one method, the method used most frequently was considered:

- RPR*: Rapid Plasma Reagent;
- TPHA**: Treponema Pallidum Hemo Agglutination.

2.3. Laboratory methods

Wellcozyme HSV® (Glaxo Wellcome, Verona, Italy) was used to diagnose HSV shedding in cervical specimens. This test is an amplified enzyme immunoassay that relies upon the use of two murine antibodies against HSV type-common glycoprotein D.

According to the manufacturer's protocol, cervical specimens were collected using sterile swabs that were put in tubes containing 2 ml of transport medium, and then extracted. The test was performed within 2 days after sampling, storing the receptacle at 4 °C before processing.

Slomka et al. tested specimens taken from patients presenting with genital ulcerations or symptoms suggestive of genital herpes using Wellcozyme HSV®, viral culture and HSV Polymerase Chain Reaction (PCR). In comparison to PCR and cell culture, Wellcozyme HSV® presented a sensitivity of 80.9 and 65.2%, with a specificity of 100 and 98.7%, respectively. When compared to viral culture, Wellcozyme HSV® presented a sensitivity of 80.7% which fell within the broad sensitivity range described for commercial HSV enzyme immunoassays [15].

All specimens were processed in the laboratory of the Department of Gynecology, University of Modena and Reggio Emilia.

2.4. Statistical analysis

Statistical analysis was performed using Chi-square test and Student's *t*-test by SPSS version 6.1 (SPSS Inc., Milan, Italy, 1993). Chi-square test was employed to investigate the correlations between Wellcozyme HSV® responses and the anamnestic report of previous herpetic oral/genital infections, contraception, smoking, concomitant genital infections at enrolment, symptoms/signs at enrolment and number of sexual partners in the previous year. To assess possible correlations between Wellcozyme HSV® results and the patients' age at enrolment as well as the age at first sexual intercourse, Students' *t*-test was used. $P < 0.05$ was considered statistically significant.

3. Results

The presence of the HSV antigen was detected in 357 out of the 4565 collected cervical specimens, 7.8% being the overall prevalence of viral shedding.

No significant difference concerning patients' age was found between the HSV-positive and the HSV-negative group, the average ages being 39.6 ± 12.3 and 39.2 ± 10.9 years, respectively ($P > 0.05$) (Table 1). Previous herpetic infections were more common among subjects with