

Seroepidemiological Study of Herpes Simplex Virus Type 2 (HSV-2) Antibody in Shiraz, Iran

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ABSTRACT

Background: Herpes Simplex Virus (HSV) Type 2 is a widespread human infectious agent responsible for persistent and latent infections. **Objectives:** To estimate the regional seroprevalence of anti HSV-2 antibody in Shiraz, Iran and to investigate the possible correlation of seropositivity with malignant changes in subjects' Papanicolaou (Pap) tests. **Methods:** Data were collected in a cross-sectional study. A randomly selected population of 915 women, from nine primary health care centers according to regional population size, was recruited in this study. HSV type specific serum IgG was determined by an Enzyme Linked Immunosorbent assay. **Results:** The overall seroprevalence of HSV-2 antibody was 258/915 (28.19%). Most of the seropositive cases (87.6%) were categorized in the group of less educated women. None of the individuals with positive serum antibody had malignant change in the uterine cells obtained with the help of Pap smear. **Conclusion:** HSV-2 infection is relatively common and largely unrecognized among our study participants. The HSV-2 antibody was more prevalent in the studied population in comparison with European and American women, and less prevalent than African women. Although HSV-2 is reported to be in correlation with cervical cancer, none of our studied subjects had any malignant change in cervical cells.

Key words: Cervical Cancer, Genital Herpes, HSV Type 2, Pap Smear, Seroprevalence

INTRODUCTION

Herpes genitalis is one of the most common sexually transmitted diseases (STD) worldwide (1). Infection with HSV type 2, an almost always sexually transmitted virus, is the leading cause of genital ulcer disease (GUD), in both developed and developing countries (2). The accumulating data indicate that HSV-2 seroprevalence is on the rise and HSV-induced genital ulcerative disease facilitates both transmission and acquisition of human immunodeficiency virus (HIV) infection, particularly in developing countries (3,4). Therefore, the genital herpes is a persistent health care

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problem and needs continuous public awareness to optimize control strategies. In addition, as serious morbidity and mortality are caused by HSV-2, effective programs are required to halt the spread of HSV-2 infection (3,4).

HSV-2 is usually more prevalent in women than men, blacks than in non blacks and in population with higher risk sexual behavior (1-6). Previous studies have demonstrated the statistically significant increase in the overall frequency of viral infection among individuals with 30 years of age or older, multiple sexual partners and in whom beginning sexual activity before 21 years of age, have less education, low socioeconomic status (SES) and history of spontaneous abortion (1,2,5-7).

Furthermore, women with cervical cancer have shown a higher rate of seropositivity against HSV-2 infection than that of women from general population (6).

The seroprevalence of HSV-2 antibodies substantially varies among different countries, regions within countries, and population subgroups (4). For instance, in the U.S. general population, HSV-2 antibody prevalence has been reported to be 21.7%, whereas rates in the United Kingdom general population have been cited to be 3 to 5% (1). HSV-2 prevalence, in general, is highest in Africa and America, lower in Western and Southern Europe than in Northern Europe and North America, and lowest in Asia (4). Since only about 20% of patients with genital herpes are diagnosed, and many infections are neither recognized nor diagnosed by patients or clinicians, transmission of HSV-2 by asymptomatic seropositive subjects is considered to be a relevant mode of infection (1,2,8). Patients shed the virus and transmit it even in the absence of clinical signs. Although the efficacy of transmission is more remarkable at the time of lesions, but most of the transmissions have been shown to occur during periods of asymptomatic viral shedding (2).

Despite the above, data on herpes simplex virus type 2 among women in the general population of developing countries is very limited (9). To our best knowledge, there has been no regionally accurate statistical study in terms of HSV-2 antibody prevalence in Iran. To plan a management strategy for the prevention and treatment of genital herpes, we need to assess the prevalence thereof in different geographic localities.

The objectives of the present study were to determine the seroprevalence of Herpes Simplex Type 2 Immunoglobulin G antibody amongst randomly selected women referring to primary health care centers and its correlation with their Pap smear.

MATERIALS AND METHODS

Using cluster sampling method, 915 consecutive patients attending health care clinics affiliated to Shiraz University of Medical Sciences were enrolled in this cross-sectional study, over a one-year period from 2003 to 2004. Considering population distribution, the nine centers in different regions of Shiraz city and women under their coverage were randomly chosen as study population according to random table of numbers. Our sample consisted of individuals not at high risk for STDs, who had been seeking health care, because these cases may not reflect a random sample of general population, and our sample may have been overrepresented.

After obtaining a verbal consent, data were collected via direct interview by center

physicians and information on age, level of education, and any positive history of genital and/or oral herpetic lesion were recorded according to structured questionnaire. Five ml peripheral blood specimen of participants was drawn. The presence of anti Herpes Simplex Virus Type 2 antibody was tested using a commercial enzyme-linked immunosorbent assay (ELISA) that detected type-specific IgG to HSV-2, at the Shiraz Institute for Cancer Research. Pap smears were studied for the individuals who had positive serum IgG antibody. Samples were then definitely investigated for malignant cells by the pathologist and all the findings were analyzed by χ^2 test using EPI-info 2002 software.

RESULTS

The study group comprised of 915 women aged from 20 to 55 years old.

Nuptial status of studied persons revealed that all these women had only one sexual partner. Of the cases, 90 (9.83%) had university education and the rest; 825 (90.17%) were educated up to high school degree. No information on age, sexual practice, and SES of patients was available.

The results showed that 15 (1.63%) of cases had only genital herpetic lesions, 560 (61.2%) had only oral herpetic lesions and 340 (37.15%) had never experienced any oral or genital lesions. Eight (0.87%) of subjects had positive history of both oral and genital herpetic lesions. Three cases with only genital lesion had university degree and 12 cases were educated lower than high school.

On the basis of serological results, 258 (28.19%) of clinic attendees had positive anti HSV-2 antibody while the rest; 657 (71.81%), were negative for anti HSV-2 antibody (Fig. 1). Of the subjects with positive serologic results, 226 (87.6%) were educated up to high school.

Of 258 cases with positive anti HSV-2 antibody, 200 women accepted Pap smear sampling. The pathological results indicated that none of these individuals had any pathological change in favor of cervical cancer.

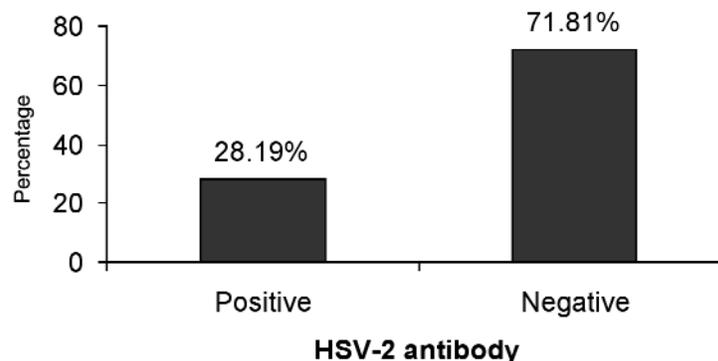


Figure 1. Seroprevalence of anti HSV-2 antibody in studied participants

DISCUSSION

Population based data on HSV-2 will be useful for designing potential HSV-2 vaccination strategies and for focusing on the other prevention efforts used for HSV-2 infection (1). It is also important in view of the fact that HSV-2 prevalence among HIV-infected persons is higher than 90%, in some developing societies (4).

Of interest, it is reported that 17.3% of pregnant women have anti HSV-2 antibody in their serum, so they can easily pass on the virus to their newborns. This finding bears an idea that the knowledge of HSV-2 serostatus in pregnant women can fairly be useful in implementation of specific programs to prevent transmission to the fetus or newborn (1).

This study describes the seroprevalence of HSV-2 antibody in a selected population of Shiraz, Iran. Our data was generated from nine various health care centers and convenient samples were studied; and therefore can not be strictly representative of the general population. However, it does provide useful insight into the extent of infection and would provide a useful benchmark for sample size estimates for more definitive epidemiological or interventional studies.

Data regarding medical history of participants reveals that the prevalence of herpetical lesions is quite high; however, a few number of cases, i.e. 1.63%, have been afflicted by genital herpes. Considering these findings and the rate of anti HSV-2 seropositivity, i.e. 28.19%, it is logical to assume that not only the serologic evidence of HSV-2 infection is common in our society but also most of infected persons are not aware of their infection with HSV-2.

Comparing our study outcome with other studies indicates that HSV-2 antibody in our area is more prevalent than western developed countries; Canada (9.1%), Germany (12.8%), Switzerland (14.6%), UK (20%), Netherlands (22%), Italy (24.6%), Spain (25%), less prevalent than Mexico (29.3%) and significantly less common than Tanzania (79.7%), Cameroon (70%) and Brazil (42%) (1-3,6,8,10-14). While the increasing prevalence has been observed in both developed and developing countries, there are some investigations supporting the conclusion that HSV-2 infection is becoming less common in the course of past years (15).

Level of education has relation to and can act as a predictive factor in HSV-2 outbreak (5). In this case, 12 (80%) of cases who reported only genital herpetical lesion did not have university education. This finding, in accord with other investigations, states that the more women are educated the less they become infected by HSV-2.

Some studies have mentioned that having multiple sex partners raises the chance of HSV-2 infection (9). In the present study, since none of the cases had history of second marriage or more than a sex partner this issue could not be addressed.

The role of HSV-2 in predisposition to cervical cancer is still a controversial issue. According to some studies, *in vitro* infusion of the HSV-2 genome into normal cells starts malignant changes in these cells (16,17). In contrast, others indicated that HSV-2 can not be certainly a co-factor in initiating the cervical carcinoma (15,16). Accordingly, our findings are on the side of latter point of view as all of the 200 taken Pap smears from subjects with anti HSV-2 antibody did not show any changes towards cervical malignancy. However, to expand this issue, it is now quite believed

that the generally accepted and highly successful screening regime of repeated cytological smears of the cervix has a considerable rate of false negatives, hence it is inappropriate to implement in developing countries (18). To improve the efficiency and sensitivity in routine cervical disease screening programs, human papillomavirus (HPV) DNA testing by means of polymerase chain reaction (PCR) test; an adjunct to the Papanicolaou (Pap) cytology test, is on the way to become a common strategy in cervical cancer prevention programs (18). A combination of HPV DNA and Pap testing is reported to have almost 100% sensitivity and negative predictive value with a slightly lower specificity than the Papanicolaou test (18).

To draw a conclusion, preventive measures are not currently perfect and a relatively high proportion of our population is infected with HSV-2 virus. Reducing risk factors and awareness of the population are among the helpful health policies against this infection.

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