Evaluation of Herpes Simplex Virus Type 1 Antibody in Dental Students of Birjand University of Medical Sciences

Parvin Parvaie  
Birjand University of Medical Sciences

Saideh EbrahimianBaghan  
Birjand University of Medical Sciences

Mahmood Zardats  
Birjand University of Medical Sciences

Gholamreza Shrifzadeh  
Birjand University of Medical Sciences

Freshteh Osmani (dr.osmani68@gmail.com)  
Birjand University of Medical Sciences  https://orcid.org/0000-0002-6112-7131

Research

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Abstract

Objective: Herpes viruses are ubiquitous human pathogens which can all be found in the oral environment. Dental practitioners have a close relationship with many patients and are at risk of cross-infection. So, HSV-1 infection as a potential occupational hazard for dental workers is important. The aim of this study was to determine the level of HSV1 antibody in dental students of Birjand in 2018-2019.

Methods: This descriptive cross-sectional study was performed on 100 dental students of Birjand University of Medical Sciences during a six-month period, who were selected by random cluster sampling. After taking written consent, demographic information and positive history of genital or oral lesions were recorded based on a researcher-made questionnaire. Then, a peripheral blood sample (5 ml) was taken from participants and an anti-virus antibody was examined using an Anti-Herpes-1 IgG kit with ELISA by a pathologist. Finally, the data were analyzed by SPSS 21.

Results: About half of the subjects (41%) had contact with HSV1 virus and were carrier of antibodies. The prevalence of HSV1 antibody in pre-clinical and clinical level was higher than in basic science, but there was no significant relationship between students' level of education and antibody prevalence (p = 0.77). Also, there was no significant difference in prevalence of HSV1 antibody by age, sex and marital status of students (p> 0.05).

Conclusion: The prevalence of HSV1 antibodies in this study is lower than that of European countries, which may be due to regional culture, which requires further study on different groups and more individuals.

Introduction

Herpes simplex virus (HSV) infections are among the most common infectious agents of humans. The natural history of HSV infection is influenced by two features of the virus (1). There are two distinct serotypes: HSV-1, which is transmitted chiefly via a non-genital route, and HSV-2, which is most often transmitted sexually or from a mother's genital infection to the newborn; and during initial (primary) infection(2). The mode of spread of each of the two virus types is reflected by its relative prevalence at different ages and by its pattern of clinical distribution within the host. Periodically, the latent virus can be reactivated to cause symptomatic or subclinical recurrent infections. Hence, HSV infections may range from subclinical to life threatening, and the specific clinical illness will be determined by the portal of virus entry, the competence of the host immune system, and whether the infection is primary or recurrent(2,4,8). Unless resulting from autoinoculation or sexual spread from the mouth to genital sites, HSV-1 infections occur most frequently during childhood and affect most often the mouth, lips, and skin sites above the waist.

An increase in infectious diseases over the past decades has attracted worldwide attention. So that many efforts and costs is spent by the government to control these diseases.
In Iran, the prevalence of HSV1 was 42.04% and HSV2 6.5% as mentioned in a meta-analysis study(4).

Mucosal covering of the mouth, nose, ears, pharynx, anus, genitals, cervix and urinary tract are areas prone to herpes virus. HSV1 usually causes ulcers in the lips and mouth areas which are usually recurrent and painful.

The average recurrence of herpes simplex infection is 2 to 3 times each year, but it is observed up to 12 times in a year. Factors such as topical skin trauma, exposure to ultraviolet radiation, hormonal and systemic changes in the body, fever, surgery, stress and immune deficiency are effective. Recurrent herpes labialis virus caused to painful mucosal lesions; as it is estimated that 30% of the population affects with this problem (5).

Cross-infections are very likely to be transmitted during dental procedures due to direct and frequent contact with blood, saliva and other body fluids, and indirect contact with contaminated surfaces, as well as airborne particles.

In the recent years, despite the diseases such as hepatitis AIDS, HSV infections, it has been focused much attention on the problem of infection transmission and the antibody level of dentists and dental students due to risk of infection transmission (7).

Also, prevalence of infections in the dental profession is high, because these people are more exposed to blood, saliva and risk of sharps (8).

There are only a few reports of HSV cross-infection in the dental practice. The frequency of herpetic whitlow was observed to be higher among practicing dentists compared to the normal population (9). However, reports confirming the transmission of infection from the patient to the dental team infection are available in the literature (8). Also the cross-infection of HSV from dental team to patients has been shown. A dental hygienist with a herpetic whitlow, who did not use gloves routinely, infected 20 out of 46 patients (10).

A large portion of the adult population is infected with HSV-1 and reactivations resulting in subclinical or symptomatic infection are frequent. However, few researches are published on the cross-transmission and infection of HSV-1 through the dental practice.

Adherence to safety principles is essential during dental treatment for health of the dentist, patient and clinic staff and their families. Since dental students are in close contact with patients during their education and are exposed to cross-infection, so, if the infection control principles are not adhered, the probability of transmission of HSV1 virus to them increase through the saliva and mucus secretions of patients.

Therefore, the aim of present study was to investigate the rate of HSV1 antibody titer in dental studentsof Birjand University of Medical Sciences in 2018–2019.
Materials And Methods

In this descriptive cross-sectional study, dental students of Birjand University of Medical Sciences were selected using cluster sampling method over a six-month period 2018–2019. The sample size was estimated according to the following formula, in which the prevalence of HSV1 was considered equal to 42%

\[ n = \frac{Z^2 p(1 - p)}{d^2} \]

Where \( Z^2 \) is constant, \( p \) is the prevalence and \( d \) is the estimated error risk. As result, 100 individuals, according to the student's level, from 3 different levels (basic sciences, pre-clinical, clinical) the subjects were randomly selected as the study sample on the basis of random number stable. After explaining about research project, each student completed an informed consent form. The risk factors and epidemiological characteristics were based on a review of the literature, information such as age, sex, marital status, educational level, history of genital or oral lesions and use of any antiviral or immunosuppressive drugs were recorded based on a researcher-made questionnaire.

Peripheral blood samples (5 ml) were taken from participants. The specimens were placed in sterile-covered storage tubes. After serum separation, the samples were kept at -28 °C until collection of all the samples. Then, the presence of anti-virus antibody was then evaluated by a pathologist using a dedicated Anti-Herpes-1 IgG kit and by an Enzyme-Linked Immunosorbent Assay (ELISA) method. Experienced technicians performed the blood sampling, data gathering, and questionnaire administration above criteria was determined.

Statistical Analysis:

This study was approved by the ethics and scientific committee of Birjand University of Medical Sciences, Iran (approval code: bums.1394.11). The quantitative and qualitative data were analyzed using SPSS, ver. 21 (Chicago, IL, U.S.). For qualitative data, the normal distribution was assessed using the K-S test. For data with a normal distribution, the means ± standard deviation (SD) were computed, and independent T-tests and the Mann-Whitney test were performed. Qualitative data were described and analyzed using frequencies and prevalence, in addition to the chi-squared and fisher exact tests test. A p-value less than 0.05 was considered statistically significant.

Results

A total of 100 dental students (43 males and 57 females) participated in the study as shown in Table 1 with mean age of 22.8 ± 3.9 years. Their age ranged from 19 to 46 years. Demographic characteristics of the studied students are presented in Table 1.
### Table 1
Frequency distribution of demographic Characteristics in the Study Participants

| Variable                  | Frequency | percentage |
|---------------------------|-----------|------------|
| Sex                       |           |            |
| male                      | 43        | 43         |
| female                    | 57        | 57         |
| marital status            |           |            |
| single                    | 87        | 87         |
| married                   | 13        | 13         |
| Educational level         |           |            |
| Basic Sciences            | 33        | 33         |
| Pre-clinic                | 31        | 31         |
| Clinical                  | 36        | 36         |
| History of herpes         |           |            |
| Yes                       | 31        | 31         |
| No                        | 69        | 69         |
| History of antiviral drugs|           |            |
| Yes                       | 1         | 1          |
| No                        | 99        | 99         |
| Antibody titer status     |           |            |
| Negative                  | 59        | 59         |
| Positive                  | 41        | 41         |

According to the results of Table 1, 31% of the studied students had a history of herpes and 1% had a history of taking antiviral drugs.

The mean of IgG titer in the studied students was $16.1 \pm 17.2$ with a median of 3.35, ranged from 0.8 to 45.9 and 59% of the studied students had negative antibody titer [Table 2].
Table 2
Comparison of frequency distribution of antibody titer status according to the demographic variables of the studied students

| Antibody titer status | Negative | Positive | Chi Square's test |
|-----------------------|----------|----------|------------------|
| **Variable**          |          |          |                  |
| fSex                  |          |          |                  |
| male                  | 22(51.2) | 21(48.8) | $\chi^2 = 1.92, \text{ df} = 1$ |
| female                | 37(64.9) | 20(35.1) | $P = 0.17$       |
| Age                   |          |          |                  |
| < 21                  | 27(60)   | 18(40)   | $\chi^2 = 0.17, \text{ df} = 2$ |
| 22–24                 | 21(60)   | 14(40)   | $P = 0.92$       |
| > 25                  | 11(55)   | 9(45)    |                  |
| Marital status        |          |          |                  |
| single                | 51(58.6) | 36(41.4) | $\chi^2 = 0.04, \text{ df} = 1$ |
| married               | 8(61.5)  | 5(38.5)  | $P = 0.84$       |
| Educational level     |          |          |                  |
| Basic Sciences        | 21(61.6) | 12(36.4) | $\chi^2 = 0.52,$ |
| Pre-clinic            | 17(54.8) | 14(45.2) | $\text{ df} = 2$ |
| Clinical              | 21(58.3) | 15(41.7) | $P = 0.77$       |
| History of herpes     |          |          |                  |
| Yes                   | 4(12.9)  | 27(87.1) | $\chi^2 = 39.5, \text{ df} = 1$ |
| No                    | 55(79.7) | 14(20.3) | $P < 0.001$      |

There was observed no statistically significant difference in antibody titer status by sex and age in the studied students ($p > 0.05$)[Table 2].

There was no statistically significant difference in the status of antibody titer according to marital status and educational level ($p > 0.05$). However, it was significantly lower in subjects with a history of herpes than in students without this history (20.3% vs 87.1%) ($p < 0.001$) [Table 2].

According to Table 3, no statistically significant difference was observed in the mean IgG titer in terms of gender, marital status, educational level and age in the studied students ($p > 0.05$), but IgG antibody titer in students with a history of herpes was significantly higher than students without a history ($p < 0.001$).
Table 3. Comparison of IgG antibody titer mean by demographic variables in students

| Antibody titer status | Mean±SD | Mann-Whitney or Kruskal–Wallistest |
|-----------------------|---------|----------------------------------|
| **Sex**               |         |                                  |
| male                  | 17.97±2.94 | Z=67                             |
| female                | 16.37±2.17 | P=0.51                           |
| **Age**               |         |                                  |
| <21                   | 16.1±17.42 | λ²=0.53, df=2                    |
| 22-24                 | 15.1±16.73 | P=0.77                           |
| >25                   | 17.77±18.2 |                                  |
| **Marital status**    |         |                                  |
| single                | 16.16±17.22 | Z=0.08                           |
| married               | 15.5±17.67 | P=0.94                           |
| **Educational level** |         |                                  |
| Basic Sciences        | 14.59±16.77 | λ²=0.09, df=2                    |
| Pre-clinic            | 17.63±17.58 | P=0.95                           |
| Clinical              | 16.1±17.6  |                                  |
| **History of herpes** |         |                                  |
| Yes                   | 38.8±12.69 | Z=5.91                           |
| No                    | 33.2±13.1  | P<0.001                          |

**Discussion**

Infectious diseases are serious health challenges worldwide. Due to the frequent contact of dental workers with factors such as blood and saliva of patients and because most human pathogens can be transmitted through blood and saliva, therefore, the risk of infectious diseases among dental personnel is higher than other people in the community and the prevention of contagion and transmission of infections from patients to the dental team and vice versa are important.

Researches show that the dentist and his assistant are able to inhale 0.014 microliters of the patient's salivary glands within 15 minutes of exposure to oral aerosols, so adhering to the principles of safety during dental treatment for the health of the dentist and patient, clinic workers and their families are needed.

Since dental students are future dentists of community, awareness of HSV1 antibody levels in students may lead to the need to provide more effective solutions to adhering to the principles of infection control for dental students. The results of this study showed that 59% of students had negative antibody titer and 41% had positive antibody titer. Study of Sorbzadeh et al., has been found 49% in blood transfusion subjects with 15–45 years old, which illustrates same result in contrast to this study (11). In Mofidi’s study, HSV1 antibody was reported 44.3% (12). In study conducted by Tayebi et al., who examined HSV1 and HSV2 antibody titers in the university students, the rate of HSV1 antibody was 79.2% (13).
Various studies conducted in industrialized countries have reported different results, for example Suligoi (14), reported 51.6% on Italian people; Smith reported 90.4% on 15–65 years old people in carodina and Michelle Howard reported 51.1% HSV1 antibody level in Canadian adults aged 15–44 years old which all of these is higher than the present study. The difference in antibody titer may be due to social situation and age groups in different parts of these surveys (16).

According to the results of the present study, the mean of HSV1 antibody titer in different age groups increased with age and increased from 16.1 in <21-year-old group to 17.77 in the <25-year-old group, but this increasing trend didn't show asignificant difference between groups. Other researchers, in different countries, such as Sweden, Italy, Germany and Swiss have been reported age as an effective factor in increasing rates of HSV1 antibody titers, which is similar to the results of this study.

Another finding of this study showed that, 35.1% of women and 48.8% of men were positive for IgG antibody. Although men accounted for a higher percentage than women, but there was no significant relationship between gender and HSV1 antibody titers. In the study of Auslander et al. [8], the prevalence of antibody was 53.1% in men and 46.9% in women, which, as the present study, it was higher in men than women.

In the study of Michael Howard et al, prevalence of antibodies was 57.7% and 42.3% in women and men respectively [16]. Also, Theng and Rabenau studies reported higher prevalence of antibodies in women than men, which is not consistent with the results of this study. In the studies [11, 15, 17], there was no significant difference between gender and frequency of HSV1 antibody, which is consistent with the results of this study.

According to the results of this study, prevalence of antibody in pre-clinical and clinical students was higher than those in basic sciences, but there was no significant relationship between antibody prevalence and educational level. In the Herbert's study, that examined the sero-epidemiology of herpesvirus among dental workers and students, there was no significant difference between HSV1 antibody and educational level, but antibody level in clinical students was higher than pre-clinical level. The reason is probably due to more contacts of these students' with patients[22].

The results showed no significant difference between prevalence of HSV1 and marital status, so that the result of mofidi's study is similar to the present study.

Rezai et al. who investigated the sero-epidemiology of HSV1 and HSV2, reported marital status as an effective factor on HSV1 antibody levels[23], which is inconsistent with the results of this study. In the present study, 20.3% of people who did not have herpes had positive antibody titer. Because who with anti-HSV antibody may have received oral HSV infection during childhood, but they did not recur and therefore did not report a history of herpes.

**Conclusions**
The results of this study should alert all dentists of future dental care providers to consider how their students are educated about providing care for patients with HSV infections and, more importantly, patients with infectious and communicable diseases in general. Specifically, this study showed that about half of the subjects have contact with HSV1 virus and carry the antibody. There was no significant difference between the prevalence of HSV1 antibody in terms of age, sex and marital status of students. In summary, addressing students’ apprehensions might be a crucial moderator that will determine whether they will provide the best possible care for these patients in their future professional lives.

It is recommended to design studies to increase students' awareness of the principles of infection control when dealing with people with herpes simplex. It also recommended that studies be designed wider and with more samples.

Declarations

Ethics approval and consent to participate

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Birjand University of Medical Sciences ethics board committee, reference number: IR.BUMS.REC.1398.324. Written informed consent was obtained from all participants and questionnaires were anonymous and encoded. For the participants, all processes were free of charge.

Consent for publication

All authors read the content of this study and approved for publication

Availability of data and materials

It will be available to the corresponding author upon reasonable request

Competing interests

None

Funding

None

Authors' contribution
Dr. Parvayi and Dr. Zardast designed and performed the research study analyzed the data and wrote the paper. Dr. Parvayi designed the research study; Dr. Ebrahimian analyzed the data and wrote the paper. Dr. Osmani, designed the research study and analyzed the data and wrote the paper. S. Ebrahimian contributed to the data collection and wrote the paper. All authors critically reviewed the manuscript and authorized the final version of the paper.

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