



## Seroepidemiology of Herpes Simplex Virus Type 1 and 2 in Northern Iran

*S Rezaei-Chaparpordi<sup>1</sup>, \*M Assmar<sup>1</sup>, N Amirmozafari<sup>2</sup>, L Modiri<sup>1</sup>, A Massiha<sup>1</sup>, S Shokri-Fashtali<sup>3</sup>, Z Gholizadeh<sup>4</sup>, S Akbari<sup>1</sup>*

1. Dept. of Microbiology, Labijan Islamic Azad University, Labijan, Iran
2. Dept. of Microbiology, Tebran University of Medical Sciences, Tebran, Iran
3. Dept. of Mathematics, Labijan Islamic Azad University, Labijan, Iran
4. Zist Faravard Pars Company, Rasht, Iran

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### Abstract

**Background:** Herpes simplex virus (HSV) type 1 and 2 are common infectious agents worldwide. Data on prevalence of HSV-1 and HSV-2 infection are limited in Asia, especially in Iran. The aim of this study was to determine the seroprevalence of HSV type 1 and 2 based on age, gender, marital status, education, living area, job, symptoms and history of disease variables.

**Methods:** The study population included 800 randomly selected persons from laboratories in Gilan Province, Iran, from 2010 to 2011. Demographic data gathered by a well-designed questionnaire and for serological studies, blood samples were collected and centrifuged. ELISA HSV-1, 2 and HSV-2 specific ELISA kits were used to determine IgG type specific antibodies in sera samples. Person's chi-square test was applied to compare HSV-1 and HSV-2 seropositivities.

**Results:** HSV-1 and HSV-2 IgG antibodies were positive in 467 (58.4%) and 28 (3.5%) subjects, respectively. There was significant correlation between age, marital status, job, symptoms, history of disease and HSV seroprevalence ( $P < 0.05$ ).

**Conclusion:** Our findings were in agreement with prior studies in which HSV-1 infections was more prevalent than HSV-2 and seropositivity increased with age.

**Keywords:** HSV-1, HSV-2, ELISA, Prevalence, Iran

### Introduction

Herpes simplex virus (HSV) infections are caused by two types of viruses, type 1 (HSV-1) and type 2 (HSV-2), that are among the most common human viral infections worldwide (1-3). HSV-1 is transmitted by two ways: 1-casual contacts during childhood, 2-sexual contacts, but HSV-2 is a virus that is mostly transmitted sexually (4). HSV can cause severe systematic neonatal infection by transmission before or during birth (5, 6). HSV-2 is of public health importance as one of the commonest causes of genital ulceration worldwide and

implicated as an important co-factor for HIV infection" (7). HSV-1 was associated predominantly with orolabial ulceration; however, recent changes in HSV-1 and HSV-2 epidemiology have been reported, with an increase in genital and neonatal herpes particularly caused by HSV-1 (8-14). However, routine surveillance is hindered as many of those infected remain asymptomatic or fail to present to health services (15). The recent commercial development of type specific enzyme immunoassays (ELISA) that reliably distinguish be-

\*Corresponding Author: E-mail address: mehdiassmar @ yahoo.com

Available at : <http://ijph.tums.ac.ir>

tween antibodies to HSV-1 and HSV-2, enable serological studies which can measure both symptomatic and asymptomatic infection. Seropositivity is a potential indicator of infectivity and can be used to guide and reform behavioral patterns for prevention of HSV transmission (16). With several HSV candidate vaccines in clinical trial and antiviral therapy available, a clear understanding of epidemiology of HSV in different populations is required to develop the most effective and appropriate preventive and control strategies (7). The present study was the first study on determination of seroepidemiology of HSV infection in Gilan Province, northern Iran.

## Materials & Methods

Using cluster sampling method, 800 patients were selected randomly from Rasht, Anzali, Lahijan, Somea Sara and Hashtpar laboratories in Gilan Province, Iran, from 2010 to 2011.

After obtaining a verbal consent, their demographic data were recorded via a well designed questionnaire. Questionnaire included questions about age, sex, marital status, level of education, living area, job, clinical symptoms and history of disease. Having explained our goal, 5ml of peripheral venous blood was obtained, then allowed to clot and centrifuged at 1000×g for 10 minutes. Sera were collected into microtubes and transferred to the laboratory in cool box. Sera samples were frozen and stored at -20°C. Type specific serum antibodies to HSV-1 and HSV-2 were detected using HSV-1,2 and HSV-2 ELISA IgG kits (Vircell Spanish kits). ELISA tests were performed according to the manufacturer's instructions.

Person's chi-square test was applied to compare HSV-1 and HSV-2 seropositivities among different groups of randomly selected persons. Statistical significance was set at  $P < 0.05$ .

## Results

The study group comprised subjects aged from 1-85 years old. HSV infections were positive in 61.9% (495) of persons. HSV-1 and HSV-2 sero-

positivity was 58.4% (467) and 3.5% (28), respectively.

As expected, HSV-1 seroprevalence was significantly higher than that of HSV-2. Patients were classified to three age groups: 0-19, 20-39, >40 years old. The most HSV prevalence belonged to >40 (74.6%) years old persons.

The study population included 306 (60.8%) males and 494 (62.6%) females (Table 1). Seropositivity in persons who were married (71.3%) and lived in villages (70.6%) was more than single (33.7%) persons that lived in city (60.5%).

**Table 1:** Prevalence of HSV antibodies in the sample studied by age, sex, marital status, living area and education level

Variables	Positive n (%)	Negative n (%)
<b>Age</b> ( $P=0$ )		
0-19	42(28.6)	105(71.4)
20-39	180(62.7)	107(37.3)
>40	273(74.6)	93(25.4)
<b>Sex</b> ( $P=0.653$ )		
Males	186(60.8)	120(39.2)
Females	309(62.6)	185(37.4)
<b>Marital status</b> ( $P=0$ )		
Single	67(33.7)	132(67.3)
Married	428(71.2)	173(28.8)
<b>Living area</b> ( $P=0.064$ )		
City	418(60.5)	273(39.5)
Village	77(70.6)	32(29.4)
<b>Education level</b> ( $P=0.271$ )		
University degree	83(53)	60(42)
High school degree	164(62.4)	99(37.6)
Guidance school degree	70(61.4)	44(38.6)
Elementary school degree	80(70.2)	34(29.8)
Illiterate	98(59)	68(41)

According to education level, we classified patients to 5 groups. Results showed high prevalence rate in elementary educated persons (Table1). There were patients with different kinds of jobs but seropositivity was high among the barbers and beauticians (100%).

Some of the subjects had symptoms that were classified into 4 groups as follows: 1- general

symptoms (69.8%) including fatigue, backache, headache, influenza like symptoms 2- sore and eczema, 3-pain during urination, 4- Alzheimer's disease. Seroprevalence was 87.8% in persons with Alzheimer's disease. Persons who had history of genital, skin and oral diseases were more seropositive (73.9%) than others (Table 2). According to chi-square test there was significant correlation between age, marital status, job, symptoms and history of disease with seropositivity ( $P < 0.05$ ).

**Table 2:** Prevalence of HSV antibodies in the sample studied by job, clinical symptoms and history of disease

Variables	Positive n(%)	Negative n(%)
<b>Job</b> ( $P= 0$ )	5(62.5)	3(37.5)
Physician and other related job		
Barber	2(100)	0(0)
Farmer	16(88.9)	1(11.1)
Employee	42(70)	18(30)
Teacher	15(75)	5(25)
Worker	9(90)	1(10)
Free job	64(65.3)	34(34.7)
Other	341(58.6)	241(41.4)
<b>Clinical symptoms</b> ( $P= 0.001$ )		
General symptoms	199(69.8)	86(30.2)
Eczema & sore	34(82.9)	7(17.1)
Pain during urinate	43(76.8)	13(23.2)
Alzheimer disease	36(87.8)	5(12.2)
Without clinical symptoms	258(55.5)	207(44.5)
<b>History of disease</b> ( $P=0$ )		
With history	289(73.9)	102(26.1)
Without history	206(50.4)	203(49.6)

## Discussion

Although the incidence and prevalence of herpes simplex infection is growing, there is little information about HSV prevalence for Iranian population that shows the necessity of more studies on this subject to be done.

This paper is the first to our knowledge to present the comparative seroepidemiology of HSV-1 and HSV-2 in Gilan Province. The seroprevalence of HSV-1 and HSV-2 IgG antibody was 58.4% and 3.5%, respectively. Like other studies, we found

that HSV-1 is more prevalent than HSV-2 and seroprevalence of HSV infection increased with age. The most prevalence rate was found in old and married persons ( $>40$ ) probably because they have more time for contact to receive the virus.

Barbers are always in contact with skin and customer's saliva so we expected to have high prevalence in this group of people.

The seroprevalence was high in persons with Alzheimer's disease and history of oral, skin, genital diseases.

"Up to 70% of genital HSV infections are unrecognized, hence seroepidemiological studies are critical for understanding the pattern and distribution of infection within populations" (17). According to Looker and Xu studies in United states, Europe and some developed countries, HSV-1 is the main causative agent of genital herpes (18,19). In a study in Europe, HSV-1 was 52% (Finland), 57% (Netherlands), 67% (Belgium), 81% (Czech republic), 84% (Bulgaria) and HSV-2 seroprevalence was 24% (Bulgaria), 14% (Germany), 13% (Finland), 11% (Belgium), 9% (Netherlands), 6% (Czech republic), and 4% (England and Wales) (7). In Brazil, HSV-1 and HSV-2 seroprevalence was 67.2% and 11.3%, respectively. In this study, seroprevalence increased with age and past history of STD was a major risk factor for HSV-2 infection (20).

There is a correlation between educational level and HSV seroprevalence. HSV-1 and HSV-2 seroprevalence rate was 80% and 19.3% (21).

Another study in USA showed declines in HSV-1 (57.7%) and HSV-2 (17%) seroprevalence rate during 1999-2004 (19). The seroprevalence of HSV-1 and HSV-2 in our study was lower than some African countries where its HSV-1 and HSV-2 seroprevalence rate has been reported 90% and 82%, respectively (22).

This study highlights the frequency of HSV infection in Gilan province, Iran. Reducing risk factors and awareness of the population are among the helpful health policies against this infection.

## Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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