

HERPES SIMPLEX VIRUS TYPE-2 SEROPREVALENCE AMONG ADULTS AGED 20-49 IN TRABZON

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ABSTRACT

Objective: Infections caused by Herpes simplex virus continue to be a problem in a significant part of the world. In this study we aimed to analyze the seroprevalence of Herpes simplex virus type-2 (HSV-2) and to investigate the correlation with sociodemographic characteristics in 20-49 age group in the city of Trabzon, Turkey.

Material and Method: This cross-sectional study was performed between August 2007 and August 2008 in Trabzon in an adult population between the ages of 20 and 49. The study was performed with 1983 adult subjects with an age range of 20-49 (participation rate 96.7%). HSV-2 IgG Enzyme Immunoassay (ELISA) kits were used.

Results: The mean age of participants was 33.3±8.7 with

a 1010 (50.9%) female and 973 (49.1%) male distribution. HSV-2 seroprevalence among the subjects was 7.6% (95% CI: 6.4-8.8). HSV-2 seropositivity levels by sex (7.9% in females, 7.2% in males) were similar ($p=0.541$). HSV-2 seroprevalence was lower in the 20-24 age group (3.6%) than in the other age groups ($p=0.016$), higher in widowed (18.2%) than in married (8.3%) and single (5.1%) subjects ($p=0.010$) and declined as educational level increased ($p=0.039$). The difference between HSV-2 seroprevalence levels between smokers (9.1%) and non-smokers (6.7%) was significant ($p=0.049$).

Conclusion: HSV-2 seroprevalence levels in Trabzon may be regarded as high for the Turkish population in general.

Key Words: HSV-2, seroprevalence, adult, Turkey. Nobel Med 2012; 8(2): 85-90

TRABZON İLİNDE 20-49 YAŞ ARASINDAKİ ERİŞKİNLERDE HERPES SİMPEKS VİRUS TİP 2 SEROPREVALANSI

ÖZET

Amaç: Herpes simpleks virüsünün neden olduğu enfeksiyonlar, dünyanın önemli bir kesiminde sorun olmaya devam etmektedir. Bu çalışmada Trabzon ilinde 20-49 yaş arası erişkinlerde HSV-2 seroprevalansının saptanması ve sosyodemografik özelliklerle ilişkisinin incelenmesi amaçlanmıştır.

Materyal ve Metod: Kesitsel tipteki bu çalışma Ağustos 2007- Ağustos 2008 tarihleri arasında Trabzon ilindeki 20- 49 yaş arası erişkinlerde yapılmıştır. Çalışma, 20-49 yaş arasındaki 1983 erişkinde yapılmıştır (katılım oranı %96,7). HSV-2 IgG, ELISA yöntemiyle incelenmiştir.

Bulgular: Katılımcıların 1010'u (%50,9) kadın, 973'ü (%49,1) erkek ve yaş ortalamaları 33,3±8,7 yıldır. Katılımcılarda HSV-2 seroprevalansı %7,6 (%95 GA: 6,4-8,8) olarak bulunmuştur. HSV-2 seropozitifliği cinsiyet (kadınlarda %7,9, erkeklerde %7,2) açısından benzerdir ($p=0,541$). HSV-2 seroprevalansı 20-24 yaş grubunda en düşüktür ($p=0,016$). Dullarda evlilere ve bekarlara göre ($p=0,010$); örgün eğitim almayanlarda örgün eğitim alanlara göre ($p=0,039$); sigara kullananlarda kullanmayanlara göre ($p=0,044$) yüksektir.

Sonuç: Trabzon'da HSV-2 seroprevalansını inceleyen bu ilk çalışmada bulunan değerler Türk toplumu için yüksek olarak kabul edilebilir.

Anahtar Kelimeler: HSV-2, seroprevalans, erişkin, Türkiye. Nobel Med 2012; 8(2): 85-90

INTRODUCTION

Herpes viruses are membranous icosahedral capsids with double-stranded linear DNA.¹ Mucocutaneous infections caused by Herpes Simplex Virus type 1 (HSV-1) or 2 (HSV-2) infections are continue to be a problem in a significant portion of the population and widespread across the world. One significant characteristic is that they frequently follow a subclinical course and cause latent infections.²⁻⁵ HSV infection disease spectra vary from asymptomatic infection or mild skin or mucosal lesions to fatal clinical forms such as encephalitis, or organ or systemic involvement.⁶ Symptomatic genital HSV infections resemble such clinical pictures as non-gonococcal urethritis and nonchlamydial urethritis in males and recurrent vaginitis in women.⁷⁻¹² HSV-1 infections are restricted to the oropharynx. The virus is transmitted by way of droplets or direct contact with infected saliva. HSV-2, however, is transmitted genitally or during birth to the baby by herpetic lesions in the birth canal, leading to genital or neonatal herpes infections. However, both viruses may constitute serious clinical pictures such as serious central nervous system, eye or skin infections.²⁻⁴

Genital herpes is a frequently seen disease generally transmitted sexually.¹³ Transmission taking place in the subclinical period, the ability to remain latent, the development of recurrent attacks, the disease leading to atypical pictures, society being ignorant of the risks posed by these infections, their being co-carcinogenic for cervical cancer, and the serious risk of transmission to the baby during pregnancy and birth all further increase the significance of HSV-2 infections.

Studies have reported the following risk factors for HSV-2; female gender, aged 20-30, low income, low educational level, a high number of sexual partners, black or Hispanic race, homosexual activity and Human Immunodeficiency Virus (HIV) infections.¹⁴

There is a wide variation in prevalence levels in studies of HSV-2 seroprevalence. HSV-2 infection is more widespread in Sub-Saharan Africa and the Far East, where 78.2% of women and 45.5% of men are infected. The level for women in America is 20%-40%, and 10%-15% for men. Levels in the general population in Asia are 30%-60% for women and 12%-48% for men. In addition to HSV-2 seroprevalence being globally higher in women than in men, it also increases with age, being highest in the 35-39 age group in particular.^{15,16}

HSV-2 is not a mandatory to report disease in Turkey, despite being a sexual transmitted disease (STD), regular records are not maintained. Seroprevalence studies are

few and generally concentrate on high-risk groups such as infertile women applying to polyclinics, pregnant women, blood donors, sex workers, patients with genital warts and hotel staff. HSV-2 prevalences of between 4.8% and 60.0% have been reported in such studies.^{13,17-19}

Limited data on type specific HSV-2 seroprevalence in Turkey are available. There have been only a few hospital-based studies on this subject in the country. This study is the first survey of the sexually active general population in Trabzon. The aim was to determine HSV-2 seroprevalence in sexually active adults aged 20-49 in the Turkish province of Trabzon and to investigate the correlation with sociodemographic characteristics.

MATERIAL and METHOD

Study populations

This sectional study was carried out between August 2007 and August 2008 among adults aged 20-49 in the Trabzon provincial center and nine outlying districts. The Trabzon province central district and other districts have a total population of 734,810, of whom 332,410 are aged between 20 and 49.²⁰ Taking the highest HSV-2 prevalence value of 45% from the studies performed, with a 99% degree of certainty and 3% deviation, a smallest sample size of 1825 was found at using the formula $n = Z^2_{1-\alpha/2} / [p(1-p)/d^2]$.²¹ The size of the sample was increased by 10% considering the likelihood of refusal to participate, subsequent failure to attend to give blood despite the survey having been performed or missing data from the questionnaire. As a result, a total of 1983 people living in the Trabzon provincial center and nine outlying districts were enrolled.

Screening phases

A multi-stage simple sampling procedure was employed. In the first stage, nine of the 17 districts affiliated to the province of Trabzon were selected on the basis of the province's geographical characteristics. In the second phase, adults aged between 20 and 49 were classified on the basis of settlement location, age group and gender. In the third stage, the records of primary health care centers were referred to. The sample number to be taken from each health clinic area was calculated on the basis of age groups and gender. In the final stage, we sought to establish a target group on the basis of health clinic records.

Measurement and Questionnaire Form

The study was explained to the individuals determined →

in the sampling. When these agreed to participate the informed consent form was read, explained and signed, following which the questionnaire was administered using the face-to-face interview technique. If participants included in the sampling were not at their address, two further visits were made. A new subject was selected from the same region to replace a participant who refused to participate or who was not available despite 3 visits being made. A questionnaire developed by the authors was used in order to obtain data from all the individuals enrolled in the study. The questionnaire elicited information such as age, gender, marital status, education, profession, monthly income, social security, presence of chronic disease, life style and cigarette and alcohol use, and was completed during face-to-face interviews with one of 10 medical faculty students who had received training in questionnaire procedures, and height and weight measurement. Subjects administered the questionnaire were invited to the health clinic the next day; 7-8 ml venous blood samples were taken from the brachial veins using special needles and placed in vacutainers with no anti-coagulant in such a way as to avoid exposure to the air. Serum samples were obtained by centrifuging the specimens for 8 min at 3000 rpm. Serums were forwarded to the Karadeniz Technical University Medical Faculty Hospital Microbiology Research Laboratory within 1 h at most. HSV-2 IgG Enzyme Immunoassay (ELISA) [DIA.PRO, Milan] kits were used. Specific IgG antibodies forming against HSV-2 in human serum are determined using the assay in line with the manufacturer's instructions. Test sensitivity and specificity are >98%.²²

The study was reviewed and approved by the Karadeniz Technical University Research Ethics Board (meeting no: 05.07.2007/ 13, decision no:08).

Data Analysis

Data obtained by measurement are expressed as mean plus standard deviation, and data obtained mathematically as number and percentage. Prevalence values are given with a 95% degree of confidence. The chi-square test was used to compare HSV-2 seropositive and non-seropositive groups. $P < 0.05$ was regarded as significant.

RESULTS

This study involved 1983 sexually active adults aged 20-49; 1010 (50.9%) of these were women and 973 (49.1%) men, with a mean age of 33.3 ± 8.7 years.

HSV-2 seroprevalence among the subjects was 7.6% (95% CI:6.4-8.8). Between women and men were

Table 1: HSV-2 seroprevalence distribution by subjects' sociodemographic characteristics

Sociodemographic characteristics	n	HSV-2 seroprevalence		Confidence interval	p
		No.	%		
Sex	1983				0.541
Female	1010	80	7.9	6.2-9.6	
Male	973	70	7.2	5.6-8.8	
Age Group	1983				0.016
20-24	419	15	3.6	1.8-5.4	
25-29	369	28	7.6	4.9-10.3	
30-34	327	30	9.2	6.1-12.3	
35-39	293	26	8.9	5.6-12.2	
40-44	312	31	9.9	6.6-13.2	
45-49	263	20	7.6	4.4-10.8	
Educational level	1982				0.039
No formal education	60	5	8.3	1.3-15.3	
Primary	880	83	9.4	7.5-11.3	
High school	725	44	6.1	4.4-7.8	
University	317	18	5.7	3.1-8.3	
Marital status	1981				0.010
Single	530	27	5.1	3.2-7.0	
Married	1429	118	8.3	6.9-9.7	
Widowed	22	4	18.2	2.1-34.3	
Monthly income *	1849				0.583
Below 500 TL	167	10	6.0	2.4-9.6	
500- 999 TL	775	63	8.1	6.2-10.0	
1000- 1499 TL	486	32	6.6	4.4-8.8	
Above 1500 TL	421	35	8.3	5.7-10.9	
Residence	1983				0.089
Urban	1277	87	6.8	5.4-8.2	
Rural	706	63	8.9	6.8-11.0	
Cigarettes	1980				0.049
Smokers	762	69	9.1	7.1-11.1	
Non-smokers	1218	81	6.7	5.3-8.1	
Alcohol	1980				0.440
Users	205	18	8.8	4.9-12.7	
Non-users	1775	132	7.4	6.2-8.6	

*1 Turkish Lira (TL) is worth approximately \$0.67.

no significant difference ($p=0.541$). Participants' sociodemographic variables and seroprevalence values are given in Table 1, and age-adjusted prevalence values in Table 2.

HSV-2 seroprevalence was 3.6% in ages 20-24, 7.6% in ages 25-29, 9.2% in ages 30-34, 8.9% in ages 35-39, 9.9 in ages 40-44, 7.6% in ages 45-49 ($p=0.016$). HSV-2 seroprevalence was lower in the 20-24 age group than in the other age groups ($p=0.016$). In this study, HSV-2 seroprevalence was higher in the widowed (18.2%) than in married (8.3%) and single (5.1%) subjects ($p=0.010$). HSV-2 seroprevalence declined as educational level increased ($p=0.039$). The difference between HSV-2 seroprevalence levels between smokers (9.1%) and non-smokers (6.7%) was significant ($p=0.049$). HSV-2 seroprevalence levels according to men and women's demographic →

Table 2: Participants' crude and age-adjusted HSV-2 seroprevalences

Age group	Crude prevalence		Age-adjusted prevalence	
	%	95% CI	%	95% CI
20-24	3.6	1.8-5.4	3.0	2.3-4.9
25-29	7.6	4.9-10.3	6.0	5.7-9.5
30-34	9.2	6.1-12.3	7.0	7.1-11.3
35-39	8.9	5.6-12.2	6.4	6.7-11.1
40-44	9.9	6.6-13.2	6.5	7.5-12.3
45-49	7.6	4.4-10.8	4.6	5.4-9.8
All ages	7.6	6.4-8.8	33.1	31.8-34.4

Table 3: HSV-2 seroprevalence distribution by sociodemographic characteristics in men and women

Sociodemographic characteristics	Women				Men			
	n	%	95% CI	p	n	%	95% CI	p
Marital status				0.036				0.289
Single	10	4.7	1.9-7.5		17	5.4	2.9-7.9	
Married	67	8.6	6.6-10.6		51	7.8	5.7-9.9	
Widowed	3	20.0	0.0-40.2		1	14.3	0-40.2	
Age groups				0.138				0.203
20-24	9	4.2	1.5-6.9		6	2.9	0.6-5.2	
25-29	13	6.8	3.2-10.4		15	8.4	4.3-12.5	
30-34	16	9.5	5.1-13.9		14	8.8	4.4-13.2	
35-39	15	9.9	5.1-14.7		11	7.7	3.3-12.1	
40-44	18	11.3	6.4-16.2		13	8.6	4.1-13.1	
45-49	9	7.1	2.6-11.6		11	8.0	3.5-12.5	
Monthly income*				0.271				0.290
Below 500 TL	6	6.7	1.5-11.9		4	5.1	0.2-10.0	
500-999 TL	30	7.1	4.6-9.6		33	9.3	6.3-12.3	
1000-1499 TL	16	6.9	3.6-10.2		16	6.3	3.3-9.3	
Above 1500 TL	21	11.4	6.8-16.0		14	5.9	2.9-8.9	
Educational level				0.180				0.273
No formal education	5	8.9	1.4-16.4		0	0.0		
Primary	49	9.6	7.0-12.2		34	9.2	6.3-12.1	
High school	20	6.4	3.7-9.1		24	5.8	3.5-8.1	
University	6	4.7	1.0-8.4		12	6.3	2.8-9.8	
Residence				0.119				0.410
Urban	45	6.9	5.5-8.3		42	6.7	5.3-8.1	
Rural	35	9.7	7.5-11.9		28	8.1	6.1-10.1	
Family structure				0.325				0.096
Nuclear family	61	8.4	6.4-10.4		56	8.1	6.1-10.1	
Extended family	19	6.6	3.7-9.5		14	5.0	2.4-7.6	
Cigarettes				0.008				0.526
Smokers	29	12.0	10.7-13.2		40	7.7	6.7-8.7	
Non-smokers	51	6.7	5.7-7.6		30	6.0	5.7-7.6	
Alcohol				0.147				0.298
Users	3	17.6	16.2-19.1		15	8.0	6.9-9.0	
Non-users	77	7.8	6.7-8.8		55	7.0	6.0-8.0	

*1 Turkish Lira is worth approximately \$0.67.

characteristics are given in Table 3. HSV-2 prevalence was low in single and non-smoking women (p=0.036, p=0.008, respectively). No significant difference between HSV-2 seroprevalence and sociodemographic variables was determined in men.

DISCUSSION

Sexually transmitted diseases (STDs) are a significant public health problem since they can lead to serious complications, sequels, death and economic losses. Due to cultural and religious beliefs, different sociocultural groups in Turkey (male/female, urban/rural, age, educational level) are known to exhibit different characteristics in terms of sexual attitudes and behavior; no sex before marriage and monogamy are emphasized. It was thought that these help to remain STDs under control in society.^{2,6}

Many people regard open discussion of sexual matters as taboo, and women used to be prohibited from engaging in sexual relations outside marriage.⁹ Indeed, sexuality with different partners is forbidden to women yet permitted, and even regarded as an expected activity for men.²³ However this situation has changed in favor of women nowadays. For example, the levels of people with sexual experience before marriage are reported as 70% in men and 16.6% in women.²⁴ While 83.9% of young people disapprove of premarital sex for women, the level is only 56.8% for men.²⁵ This variation may alter according to STDs patterns.

Men may still engage in extramarital relations, even though sexuality is regarded as a taboo subject in Turkey and monogamy is widespread. It is common for men not to apply to health institutions with health problems they encounter following such relations, and even if they do, to refrain from mentioning or conceal such relations. In addition, as a result of difficulties in asking about STDs on the part of the physician examining the individual and a failure to keep proper records, only the tip of the STDs iceberg is visible in Turkey and has now come to pose a severe danger.²⁴⁻²⁷ Despite investigating HSV-2, as an STDs, the difficulty of asking about sexual matters during a field study in Turkish society represented the greatest limitation in this study. Unfortunately, no questions regarding sexuality were included in the questionnaire in this study and no analysis or evaluation regarding sexuality was performed.

HSV-2 is widespread in sexually active populations worldwide. Indeed, there is no population in the world in which HSV-2 antibodies have not been found. Studies show that HSV-2 seroprevalence varies from country to country values ranging from 3.6% to 26%.^{6,28-38} The reasons for this variation are given as racial, socioeconomic, geographical differences, or genetic-biological differences in the host. Studies have been conducted in Turkey on HSV-2 seroprevalences among sex workers and hotel staff and people applying to maternity, though there have been no studies in →

society in general. Only Dolar et al. investigated the above groups in a study performed in 2006; HSV-2 seroprevalences were also investigated among 725 sexually active adults, and prevalence of 4.8% was reported.¹³ Ours was a sectional study performed in a sexually active group in Turkey aged 20-49, with an HSV-2 seroprevalence of 7.6%. Bearing in mind that HSV-2 is an STDs, this level may be regarded as quite high for Turkey.

Gender is a significant and controversial variable for HSV-2 infection. It has been suggested that there is a greater predisposition toward HSV-2 infection in women. Transmission of HSV-2 infections is higher from men to women than from women to men.³⁹ The female genital mucosa and skin are said to be more sensitive to HSV-2 compared to the keratinized epithelium of the penis. In addition, men and women may exhibit different sexual behavior. Study concluded that women's sexual partners might be older than them and more experienced, and that there was therefore a greater likelihood of young women encountering the virus because of their sexual partners.⁴⁰ It has been reported that HSV-2 seroprevalence is higher among women in all regions apart from South and East Asia; and some studies have even emphasized that the differences are significant, although other studies have determined no difference in terms of gender.^{6,13,16,28,30,32,33,36-38,41} No statistical difference in seroprevalence was determined between men and women in this study.

Age is another important variable. HSV-2 begins to be seen with postpubertal sexual activity, and the risk of HSV-2 acquisition rises as the sexually active period grows. Therefore, HSV-2 seroprevalence increases with age.^{33,36,38,41} Seroprevalence in this study was low in the 20-24 age group compared with subsequently increased seroprevalence values.

HSV-2 seroprevalence among subjects with a high educational level in Switzerland was reported as 26%, compared to 17.2% in those with a low level of education.³⁷ In contrast, a higher HSV-2 seroprevalence has been determined in those with a low level of education in other studies.^{34,35} HSV-2 seroprevalence in our study was higher in subjects with a low level of education, though the difference was not statistically significant. When the sexes were considered separately, HSV-2 seroprevalence was slightly higher in subjects with low educational levels in both men and women, and we think this may be due to men in this group paying for sexual relations and then transmitting the disease to their wives.

Another variable correlated to HSV-2 is marital status.

Study conducted in Switzerland among adults aged 25-74 reported a higher HSV-2 seroprevalence in widowed subjects than in married ones.³⁷ In a study conducted in France, Malkin et al. investigated marital status by gender and reported that HSV-2 seroprevalence was higher in single and widowed/separated subjects of both sexes compared with married subjects.³⁰ In our study, too, HSV-2 seroprevalence was higher in married and single individuals in both the total study group and in women. Perceptions of honor in Turkey are totally built around virginity being the norm. Honor is perceived as a prohibition on pre-marital sex and sexual relations outside marriage, and is a taboo subject for both men and women.⁴²

Could urban or rural residence have an effect on HSV-2 seroprevalence? One study conducted in Poland compared four geographical regions, the highest seroprevalence (12.6%) being observed in the Zachodnio-Pomorskie region, 70% of whose population lives in towns.⁶ In a study carried out in Mexico HSV-2 seroprevalence varied between 21.2% and 33.7% in the southern part of the country compared to 8.8% and 17.1% in the north and central parts.³⁴

In a study conducted in Australia Cunningham et al. determined a seroprevalence of 9% in rural dwellers compared to 13% among town dwellers.³¹ Rural and urban seroprevalence values were similar in our study, being very slightly higher in rural areas.

HSV-2 seroprevalence was higher among smokers both in total and among women. In a cohort study from Japan Doi et al. reported that current smokers had a higher risk of HSV-2 infection than those who had never smoked among both men and women.³²

This association could be compounded by sexual behavior, immune suppression similar to that observed in HIV-positive individuals and smoking increasing susceptibility to HSV-2 infection by damaging the cervical epithelium through DNA modification may play an important role. In addition, regrettably, women in Turkey who smoke are those with a better education and higher status. This, together with the changing role of women in social life, leads to a freer life style, and the consequence may emerge in the form of elimination of sexual taboos.

This seroprevalence level in Turkey appears to be similar to those in other "low" HSV-2 prevalence areas in European countries. However, the seroprevalence levels in this socially-based study of HSV-2, as a STDs, may be regarded as high for Turkish populations. These results reveal the necessity for social and medical precautions on the subject of STDs in Turkey.



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