

EBV Seroepidemiology in Married and Unmarried Women and Men in Iran

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Abstract

Background: Among the eight known human herpes viruses, Epstein- Barr virus (EBV) is considered to be sexually transmissible. This study was conducted to evaluate the seroepidemiology of this infection in married and unmarried Iranian couples.

Methods: In this comparative observational and cross-sectional study, 160 men and women were divided into married and unmarried groups. Serum IgG and IgM antibodies to the EBV viral capsid antigen were analyzed by Enzyme-linked Immunosorbent Assays (ELISAs).

Results: In this study 78 men and 82 women were enrolled. Ninety percent of the married and 76.2% of the unmarried women were anti-EBV IgG positive ($P = 0.08$), while 80% of the married and 94% of the unmarried men were antiEBV IgG positive ($P = 0.052$).

Conclusion: Seroepidemiology of EBV is not significantly different in married vs. unmarried women and men in Iran; therefore, sexual contact may not be the primary mechanism of EBV transmission in Iran and other developing countries. Attention to other possible routes of transmission is recommended.

Keywords: Anti-VCA, Epstein Barr Virus, Sexual contact

Introduction

Herpesviruses are a group of viruses that infect humans. A hallmark of this group of viruses is the ability to infect quite different primary and secondary cell types. The outcomes of diseases of this group of viruses are different from one type to the other (1). Epstein-Barr virus (EBV), a member of the herpesvirus group, causes infectious mononucleosis with positive heterophil antibody (2).

Of the eight known human herpesviruses, four (HSV, CMV, KSHV, and EBV) are considered to be sexually transmissible (1).

Acute EBV infection is usually subclinical, and seroconversion generally occurs without clinical

illness (3). Sometimes the infection is associated with fever, sore throat, fatigue and lymphadenopathy, but occasionally may lead to severe complications such as airway obstruction, hemolytic anemia, thrombocytopenia, myocarditis, and ophthalmologic complications, which may be fatal in some patients (4, 5).

EBV is also a tumorigenic virus associated with various malignant diseases such as Burkitt lymphoma, nasopharyngeal carcinoma, Hodgkin and non-Hodgkin lymphoma, and malignant follicular dendritic cells (6-11). In addition, association of this virus with multiple sclerosis

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Received: Nov 17, 2013; Accepted: Feb 10, 2014

(MS) has been reported (12, 13).

On the other hand, EBV is carried as a persistent infection by more than 90% of adults (14). The initial infection generally occurs early in life and is often spread within families (3). Some studies suggest that EBV is transmitted via sexual contact (14), and the most important route is said to be via saliva and oral contact, such as kissing. The virus can persist in saliva for 18 months after the initial infection and can be found intermittently in saliva for life; therefore, this infection is called the "kissing disease" (15).

In Iran, boys and girls have limited relationships before marriage; in Jahrom, a city in southern Iran, these limitations are very strict. In Jahrom boys and girls have little to no associations before marriage and in some families even betrothed couples are not allowed to associate before their weddings. The aim of our study in this region was to determine whether sexual contact is a significant route for EBV transmission. Subjects in this study were single males and females who intended to marry, and married couples who were expecting their first child.

Materials and Methods

This was a comparative, observational, cross-sectional study of 160 men and women.

The selected individuals were divided into two groups; one group was comprised of unmarried persons, and one group was comprised of married persons.

In Iran all men and women who intend to marry must visit health centers for pre-marriage lab tests. The unmarried group contained 38 males and 42 females. The married group contained 40 couples (40 men and 40 women) who visited the hospital for the delivery of their first child. The mean ages of the married and unmarried individuals were 23.3 ± 2.4

and 22.5 ± 2.8 years, respectively ($P = 0.072$). After informed consent, blood samples were obtained. The study design and informed consent documents were reviewed and approved by the research ethics committee at the Jahrom University of Medical Sciences.

The following individuals were excluded from the study:

- 1) Individuals who did not want to participate
- 2) Individuals with background diseases
- 3) In the unmarried group: previously married individuals
- 4) In the married group: spouses who previously had children.

After obtaining the blood samples, sera were isolated and stored at -20°C . IgG and IgM antibodies to the EBV viral capsid antigen in the sera were analyzed by ELISA (Diesse, Italy). Based on the manufacturer's guidelines, the test results were interpreted as either positive or negative. The data were analyzed using SPSS software, version 11.5, by the chi square test. P-values, less than 0.05 were considered to be significant.

Results

In this study 68 of 78 men (87.2%) and 68 of 82 women (82.9%) were positive for anti-EBV IgG, and 2 of 82 women (2.4%) were positive for anti-EBV IgM. None of the men were positive for anti-EBV IgM.

Thirty-six of 40 married women (90%) and 32 of 42 unmarried women (76.2%) were positive for anti-EBV IgG ($P = 0.08$), while 32 of 40 married men (80%) and 36 of 38 unmarried men (94.7%) were positive for anti-EBV IgG ($P = 0.052$, Table 1).

The relative risk of marriage for EBV seropositivity is estimated to be 1.18 in women and 0.84 in men.

Table 1. Serology of EBV in married and unmarried men and women.

Sex and Marriage		IgG			IgM			Total
		Positive	Negative	P value	Positive	Negative	P value	
Female	Married	36	4	0.08	2	38	0.23	40
		90%	10%		5%	95%		
	Unmarried	32	10		0	42		42
	(intend to marry)	76.2%	23.8%		0%	100%		
Male	Married	32	8	0.052	0	40	-	40
		80%	20%		0%	100%		
	Unmarried	36	2		0	38		38
	(intend to marry)	94.7%	5.3%		0%	100%		

Discussion

Sexual contact is considered to be a cause of EBV transmission. Some studies have reported EBV in male and female genital secretions (16, 17), which may be the cause of the transmission of infection in sexual contact.

In a study of 1006 new students at Edinburgh University, prevalence of EBV seropositivity was significantly greater among women than men (79.2 vs. 67.4%; $P<0.001$) and among those who had ever been sexually active than those who had not (82.7 vs. 63.7%; $P<0.001$) (14). Having multiple sex partners was a highly significant risk factor for EBV seropositivity in this study (14). A case-control analysis nested within a cohort revealed that the risk of seroconversion increased as the number of sexual partners increased: the odds ratio (OR) was 1.28 for two and 2.23 for three or more sexual partners ($P<0.05$) (18). These studies emphasize sexual contact as a cause of transmission; however, information about the transmission process via sexual contact is limited.

In our study no significant differences in frequency of EBV seropositivity were observed between women and men or married and unmarried groups.

On the basis of the culture in Jahrom, where the study was conducted, males and females do not have sex before marriage and we conclude that unmarried individuals had not had previous sexual contact. In addition having multiple partners is uncommon in this community.

In a study of Iranian and German children, 70% of Iranian and 56% of German 1-5 year-olds were EBV-positive. Unfavorable hygienic facilities and

regional overpopulation have been proposed as causes for the relatively high prevalence of EBV infection in Iran (19); however, conditions in Iran may have changed since the time of that study.

In developing countries EBV infections usually occur in early childhood and positive serology increases with age. According to Dr. Moddares's study, 70% of 14 year-olds in Tehran, Iran were EBV-positive (EBNA-IgG) and more than 85% of individuals over 40 years of age were EBV-positive (20). Similar results were reported by Hossain in a study in Saudi Arabia (21).

Infection rates are higher in low socioeconomic communities than in their more affluent counterparts (22, 23). Based on the results of this and other studies in developing countries we conclude that sexual contact is not the primary mechanism of EBV transmission in these countries and attention to other routes is recommended. Studies with larger samples and cohort designing may be preferable to evaluate sexual transmission of EBV in these communities. In addition, it should be kept in mind that marriage is not sexual contact only and with marriage a couple may live together with various close contacts; therefore, transmission may occur via other routes.

Acknowledgements

The source of this article is a medical student thesis with the title: "the comparative evaluation of infectious mononucleosis affecting rate arising from Epstein Barr Virus between single and married people based on EBV serology." We thank all the persons who help us with this work.

References

1. Pagano JS. Is Epstein-Barr virus transmitted sexually? *J Infect Dis*. 2007 Feb;195(4):469-70.
2. Cohn JI. Epstein-Barr virus Infections, including Infectious Mononucleosis. In: Braunwald E, Fauci AS, Kasper DL et al, Editors. *Harrison's Principles of Internal Medicine*. 17th Ed. New York: McGraw Hill; 2008. p. 1106-9.
3. Epstein MA, Crawford DH. Gammaherpes virus: Epstein-Barr virus. In: Mahy BWJ, Collier L, Editors. *Topley and Wilson's microbiology and microbial infections*. London: Arnold; 1998. p. 351-66.
4. Johannsen E, Kaye K. Epstein-Barr Virus (Infectious Mononucleosis, Epstein-Barr Virus-Associated Malignant Disease and other Diseases). In: Mandell GL, Editor. *Mandell, Douglas, Benett Principle and practice of Infectious Disease*. 7th Ed. Philadelphia: Churchill Livingstone; 2010. p. 1989-2005.
5. Moffat LE. Infectious mononucleosis. Primary Care Update for OB/GYNs. 2001 March-April;8(2):73-7.
6. Lindhout E, Lakeman A, Mevissen ML, de Groot C. Functionally active Epstein-Barr virus-transformed

- follicular dendritic cell-like cell lines. *J Exp Med.* 1994 Apr;179(4):1173-84.
7. Morshed K, Polz-Dacewicz M, Szymanski M, Ziaja M, Golabek W. Epstein-Barr virus antibodies in blood serum of patients with laryngeal cancer. *Otolaryngol Pol.* 2002;56(1):45-8.
8. Pickard A, Chen CJ, Diehl SR, Liu MY, Cheng YJ, Hsu WL, et al. Epstein-Barr virus seroreactivity among unaffected individuals within high-risk nasopharyngeal carcinoma families in Taiwan. *Int J Cancer.* 2004 Aug;111(1):117-23.
9. Vasef MA, Ubaidat MA, Khalidi HS, Almasri NM, Al-Abbadi M, Annab HZ. Association between Epstein-Barr virus and classic Hodgkin lymphoma in Jordan: a comparative study with Epstein-Barr virus-associated Hodgkin lymphoma in North America. *South Med J.* 2004 Mar;97(3):273-7.
10. Sandlund JT, Gorban ZI, Berard CW, Sixbey J, Razzouk B, Talalayev AG, et al. Large proportion of Epstein-Barr virus-associated small noncleaved cell lymphomas among children with non-Hodgkin's lymphoma at a single institution in Moscow, Russia. *Am J Clin Oncol.* 1999 Oct;22(5):523-5.
11. Henry JB. Clinical diagnosis and management by laboratory methods. 20th Ed. New York W.B. Saunders Co; 2001.
12. Myhr KM, Riise T, Barrett-Connor E, Myrnes H, Vedeler C, Gronning M, et al. Altered antibody pattern to Epstein-Barr virus but not to other herpesviruses in multiple sclerosis: a population based case-control study from western Norway. *J Neurol Neurosurg Psychiatry.* 1998 Apr;64(4):539-42.
13. Ascherio A, Munger KL, Lennette ET, Spiegelman D, Hernan MA, Olek MJ, et al. Epstein-Barr virus antibodies and risk of multiple sclerosis: a prospective study. *Jama.* 2001 Dec;286(24):3083-8.
14. Crawford DH, Swerdlow AJ, Higgins C, McAulay K, Harrison N, Williams H, et al. Sexual history and Epstein-Barr virus infection. *J Infect Dis.* 2002 Sep;186(6):731-6.
15. Crawford DH, Macsween KF, Higgins CD, Thomas R, McAulay K, Williams H, et al. A cohort study among university students: identification of risk factors for Epstein-Barr virus seroconversion and infectious mononucleosis. *Clin Infect Dis.* 2006 Aug;43(3):276-82.
16. Sixbey JW, Lemon SM, Pagano JS. A second site for Epstein-Barr virus shedding: the uterine cervix. *Lancet.* 1986 Nov;2(8516):1122-4.
17. Israele V, Shirley P, Sixbey JW. Excretion of the Epstein-Barr virus from the genital tract of men. *J Infect Dis.* 1991 Jun;163(6):1341-3.
18. Woodman CB, Collins SI, Vavrusova N, Rao A, Middeldorp JM, Kolar Z, et al. Role of sexual behavior in the acquisition of asymptomatic Epstein-Barr virus infection: a longitudinal study. *Pediatr Infect Dis J.* 2005 Jun;24(6):498-502.
19. Alebouyeh M, Peller P, Goetz O, Ameri MA. Comparative study of the prevalence of Epstein-Barr virus infections in Iran and Germany. *Monatsschr Kinderheilkd.* 1984 Nov;132(11):850-1.
20. Noorbakhsh S, Siadati A, Ashtiani F, Mamishi S, Kooh Paiezadeh S. Comparative study of specific ebv antibodies between children manifest classic triad of mononucleosis with unaffected children in hazrat rasool akram hospital (1998-2000). *Iran J Allergy Asthma Immunol.* 2003 Jun;2(2):81-8.
21. Hossain A. Infectious mononucleosis and mononucleosis-like illnesses in children and adults in Saudi Arabia. *J Trop Pediatr.* 1989 Jun;35(3):121-5.
22. Ozkan A, Kilic SS, Kalkan A, Ozden M, Demirdag K, Ozdarendeli A. Seropositivity of Epstein-Barr virus in Eastern Anatolian Region of Turkey. *Asian Pac J Allergy Immunol.* 2003 Mar;21(1):49-53.
23. Figueira-Silva CM, E. PF. Prevalence of Epstein-Barr virus antibodies in healthy children and adolescents in Vitoria, State of Espirito Santo, Brazil. *Rev Soc Bras Med Trop* 2004 Sep-Oct;37(5):409-12.