Iranian Journal of Virology 2015;9(4): 29-34

Original Article

Sero-prevalence of Herpes Simplex and Epstein Barr Viruses in HIV positive patients in Tehran

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Abstract

Background and Aims: The burden of HIV infection and disease continues to be a major global public health concern all over the world. This study was conducted to measure IgG antibody against EBV viral capsid antigen (EBV-VCA IgG), Herpes Simplex Type1, and 2 to determine the seroprevalence of this infection in HIV-positive population.

Materials and Methods: A Cross-sectional study between March and August 2016 was conducted in keyvan virology laboratory enrolling 84 HIV-positive patients with different age and sexes. Enzyme-linked immunosorbent assay (ELISA) was used for determination of IgG antibody against Herpes Simplex Type1, Type 2 viruses, EBV and HIV viral load detected in plasma by Real time-PCR in obtained samples from HIV-positive patients.

Results: The overall seroprevalence was 66.7% for anti-HSV-1 IgG, 14.3% for anti-HSV-2 IgG, and 94% for anti-EBV IgG. There was no significant difference between the sex groups for HSV-1 and -2, EBV and HIV load and their IgG level. This study also showed a correlation between the age, and the antibody titers only for HSV-1 and -2 with P=0.030 and P= 0.024, respectively.

Conclusions: In our study, the seroprevalence of EBV and HSV-1 IgG were higher in HIV-positive patients. It can be derived that HSV-2 virus is not major coinfection in Iran, thus requires less attention than others, but annually monitoring needs for proper health care programs.

Keywords: HIV, EBV, HSV-1, HSV-2, Sero-prevalence

Introduction

Despite improvements in antiviral treatments and care of patients with human immunodeficiency virus, high prevalence of HIV population in the world shows a lack of success in HIV prevention approaches (1, 2). Globally, an estimated 38·8 million people have been infected with HIV/AIDS in 2015 (3). Some viral coinfections play important role in the disease progression, transmission and several associated malignancies of HIV infection (4).

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Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) are two members of the Herpesviridae family (5). Classically, HSV-1 causes orolabial or facial lesions and HSV-2 is a major cause of genital ulcers (6). HSV-1 infection is usually transmitted during childhood and often via nonsexual contact. HSV-2 is most transmitted through sexual contact (7).

In the last decades molecular and epidemiological studies show a strong relation between HSV-2 and HIV infection (8, 9). Infection with HSV-2 produces microlesions which create a gate of egress or entrance for HIV (10). The other probable mechanism is the creation of "pseudotypes", which causes change of non-permissive cells to permissive ones for HIV (8). Moreover, accumulation of some immune cells such as Dendritic cells and T cells to the local of infection , play the

[DOI: 10.21859/isv.9.4.29]

synergic role that promote HIV replication and distribution (11). Additionally, researches show HSV-2 antiviral therapy can reduce the reactivation of HSV-2 as well as HIV-1 viral loads (12).

On the other hand, Herpes simplex virus Type-1 can lead to primary genital ulcers (13). High percentage of HSV-1 genital ulcers in developed countries has might been associated with lower rates of childhood HSV-1 infections or probably a change in sexual behavior like orogenital contact (14, 15). Although the duration and severity of HSV infections is decreased by antiretroviral therapy in immunocompromised patients but subclinical shedding still remains (16).

Another member of the Herpesviridae family is Epstein-Barr virus (EBV), a high prevalent virus around the world (17). Primary infection usually occurs in childhood asymptomatically. Etiologically, it is associated with infectious mononucleosis, Burkitt's lymphoma, Hodgkin's lymphoma, nasal NK/T cell lymphoma, nasopharyngeal carcinoma and gastric carcinomas (GCs) while HIV patients often suffer more from non-Hodgkin's lymphoma, Hodgkin's disease and nasopharyngeal cancer (18-19).

So far, only a few studies were performed about seroprevalence of HSV-1, HSV-2 and EBV among HIV positive patients either in Iran or Tehran. This cross-sectional study was conducted to provide the reliable information for epidemiological and Health care strategies.

Methods

84 blood samples were collected from HIV positive patients of both sexes that were recently diagnosed positive by ELISA in Keyvan Virology Laboratory between March 10th and August 11th, 2016. These patients did not take any antiviral drugs.

Serum separated from blood samples, and then each serum sample was divided into two micro tubes and stored at -80°C until ELISA assay. Unfrozen serum was tested to determine HIV viral load by COBAS®AmpliPrep/COBAS® TaqMan® HIV-1 Test, v2.0 (ROCHE, Heidelberg, Germany). Serum IgG titers against HSV-1 and HSV-2 were done collectively for all the samples by (The EUROIMMUN Anti-HSV-1 (gC1) ELISA (IgG), Anti-HSV-2 (gG-2) ELISA (IgG) and Anti-EBV-CA ELISA (IgG) respectively.

Before enrolling in this study, all patients gave a written informed consent. The study was approved by the Ethics Committee of Iran University of Medical Sciences, Tehran, Iran.

Data were entered into Microsoft Excel (2013) and further statistical analysis such as Pearson's chi-square, Mann-Whitney, Kruskal Wallis, ANOVA tests were performed at 95% confidence interval and significant level was accepted at $p < 0.05$ by using Statistical Package for Social Sciences (SPSS version 22.0, Chicago, Inc).

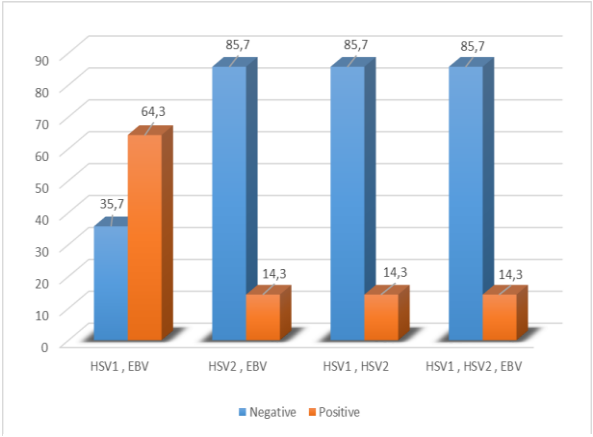

Fig. 1. Combinations of the three viral coinfections among HIV positive patients in Tehran.

Results

A total of 84 patients were participated in this study, 64 (76.19%) were males and 20 (23.81%) were females. The mean age was 36.45 years (range, 2–63). The overall, fifty six of 84 samples (66.7%) were positive for HSV-l IgG antibody, twelve of 84 (14.3%) were positive for HSV-2 IgG antibody and seventy nine of 84 (94.0%) were positive for EBV IgG antibody.

Present study only showed significant increase between HSV-1, HSV-2 IgG titers and age with P-value being 0.30 for HSV-1 and P= 0.24 for HSV-2. Analysis of the results showed

[DOI: 10.21859/isv.9.4.29]

Table 1: HIV load in subjects who recently diagnosed positive, by sex, age, Epstein-Barr virus, Herpes simplex virus Type 1 and 2 serostatus.

Variable	No.	HIV load, mean log10 copies/mL	SD	P Value
Age, years				
1-15	8	3.79	0.87	
16-29	11	3.96	1.44	0.590
30-39	27	4.14	1.04	
40-49	26	4.06	1.40	
50-63	12	4.61	1.14	
Sex				
Male	64	4.19	1.25	0.405
Female	20	3.93	3.93	
EBV				
Seronegative	5	4.37	0.89	0.645
Seropositive	79	4.11	1.23	
HSV-1				
Seronegative	28	4.29	1	0.387
Seropositive	56	4.04	1.31	
HSV-2				
Seronegative	74	4.12	1.21	0.966
Seropositive	12	4.14	1.30	

no association between EBV, HSV-1, HSV-2 IgG titers in the two sex groups. Fifty two (64.3%) HIV positive patients were with HSV-1-EBV and twelve (14.3%) were infected with HSV-1-HSV-2, EBV-HSV-2 (Fig. 1). Table 1 shows no significant correlation with HIV viral load and the other parameters.

Discussion

HIV infected individuals often suffer from opportunistic infections (OIs). These agents play critical role on their morbidity and mortality. With regard to common route of HIV transmission with HSV and their health problems or EBV-associated malignancies both proper management of OIs and antiretroviral therapy (ART) are important in preventing of these life-threatening viral illnesses among HIV-infected persons (7, 20, 21).

In this study, it was found a high seroprevalence of anti-EBV IgG (94%) and anti-HSV-1 IgG (66.7%). approximately, these findings are close to seroprevalence of EBV in Abdollahie et al's study (90.4%)(19), and Na He et al'study amongest Chinese patients (96.6%)(4).

With regard to the absence of data about prevalence of HSV-1 in the Iranian HIV positive patients, studies on non-infected HIV cases in Gorgan (22), northern Iran (23) and Anzali city (24)were Surprisingly similar to our finding (44.3%,58.4%,65.5%) respectively. Although prevalence of the EBV and HSV-1 are high in other studies like in Africa Report 2014, seroprevalence of EBV (100%) and HSV-1 (98%)(25), the Chinese survey HSV-1 (91.5%)(4),and in Tan et al'study HSV-1(73.8%)(26) but these high rates of prevalence are significantly reported higher than EBV and especially HSV-1 prevalence in Iran.

[DOI: 10.21859/isv.9.4.29]

This study showed seroprevalence of HSV-2 infection was not high (14.3%). This finding was confirmed by Janbakhash et al'study in Kermanshah (6.5%) (27). In addition, other studies in non–HIV-infected Iranian patients also reported low prevalence of HSV-2, for instance it was reported (3.5%) in Rezaei-Chaparpordi et al'study (23), (5.3%) in Sabouri Ghannad et al'study (28).

On the other hand most studies were performed in other countries showed higher seroprevalence of HSV-2 than our report, and also the others in Iran such as Chakraborty et al's study in India was reported (47%) (29), Na He et al's study in China (34.1%) (4), Tan et al's study in Canada (56.4%) (26), Erik Schafenaar et al's study in Africa (87%) (25).

The analysis of the correlation of gender and the serum IgG titers or seropositivly revealed no significant association for any of the viruses. As our study, Abdollahie et al found the same result but Patekar et al. showed a significant increase in the antibody titer against EBV in the patients (19, 30). The study in Africa again reported no correlation with the viruses (25).

Age was also found to be dependently associated with HSV-1 and 2 serum IgG titers or seropositivly as same as the other study like Mofidi et al's study(HSV-1) (22)or Na Ha et al's study (HSV-2)(4), SM Jacob's study in India (HSV-2)(31), KE Iche's study(HSV-1 and 2)(32).

This study also showed that prevalence of EBV-HSV-1 coinfections were higher than the other combinations of the viruses among HIV-infected patients (64.3%). The study was confirmed by chinese survey (4). It seems likely because of the high prevalence of both viruses in the general population of the world.

Lingappa and Celum demonstrated in their studies that taking antiretroviral therapy like acyclovir could reduce plasma HIV-1 levels (12, 33). Furthermore some evidence showed active herpes simplex virus infection was able to promote HIV-1 plasma RNA levels (34).

Despite what has been stated, we did not identify any significant associations with HIV viral load (table1). Besides our findings showed the mean of HIV viral load in male cases (mean, 4.19 log10 copies/mL) were higher than females cases (mean, 3.93 log10 copies/mL), RH Gray et al's study confirmed our finding (35).

Over all, the differences between this investigation and the others might be explained by various years of studying, population study, sampling strategies, various lifestyle, social, cultural, religion, multiple sexual partnership, sexual practice, and different HIV prevalence rates in our country and the other countries.

Conclusions

In this study it was shown that there was a lower prevalence of HSV-2 infection in HIV infected patients. However, awareness, and prevention training programs should not always be excluded. This is contrary to the studies in other countries which reported high rate of super infection of HSV-2 in HIV positive patients.

This research showed infections of EBV and HSV-1 were high in HIV-positive people that should be more considered during their clinical examinations. With regard to lack of evidence of sexually transmitted HSV-1 in Iran, Further studies in this field can be useful to make prevention, training and treatment decisions.

Acknowledgments

The authors thank the Keyvan Virology Laboratory for their assistance. This work was supported by the virology department of Iran University of Medical Sciences.

Funding/support

This study has been funded by the research deputy of Iran University of Medical Sciences (IUMS) with Grant no.

Conflict of Interests

The authors declare that they have no conflict of interests regarding the publication of this paper.

[DOI: 10.21859/isv.9.4.29]

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[DOI: 10.21859/isv.9.4.29]

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[DOI: 10.21859/isv.9.4.29]