ISSN: 2279 - 0594

Available Online at www.jbpr.in

Journal of Biomedical and Pharmaceutical Research 2 (5) 2013, 77-80

RESEARCH ARTICLE

Seroprevalence of Herpes Simplex Virus (HSV-1 and HSV-2) Infections in Sudanese Renal Transplant Recipients

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Received 16 August 2013; Revised 10 September 2013; Accepted 15 September 2013

ABSTRACT

Introduction: Viruses are among the most common causes of opportunistic infections after transplantation, because of their immunocompromised condition.

Aim: This study aimed to determine Herpes Simplex Virus-1 and Herpes Simplex Virus-2 (HSV-1 and 2) seropositivity among Sudanese kidney transplant recipients.

Material and Methods: One hundred eighty four serum samples of 92 Sudanese Kidney transplant recipients and 92 control group (blood donors) were tested serologically to detect HSV-1 and HSV-2 IgG and IgM antibodies using an enzyme-linked immunosorbent assay.

Results: The HSV1/2 IgG was positive in 99% of the renal transplant recipients, while HSV1/2 IgM was positive in 50% of renal transplant recipients. In control group, HSV1/2 IgG was positive in 90% while HSV1/2 IgM was positive in 6%. For HSV1/2 IgG and HSV1/2 IgM Seroprevalence was higher in females (100%, 53%) compared with males (94%, 25%). There was association between HSV seropositivity and age (P<0.001).

Conclusions: The Seroprevalence of HSV-1 and HSV-2 among study kidney transplant recipients was high (99%, 50% for HSV 1-2 IgG and IgM antibody respectively), so this viral infection must be remains in concern.

INTRODUCTION:

Immune suppression after transplantation renders the transplant recipient susceptible to a broad array of viral pathogens; one of these is Herpes viruses, which establishes life-long latent infection after initial infection [(1)]. Although Herpes simplex virus (HSV) infections are apart from the morbidity due to symptomatic episodes, HSV infections may have severe consequences in immunosuppressed hosts [(2)]. Herpes simplex virus type 1 (HSV-1) and Herpes Simplex Virus type 2 (HSV-2) are members of the Alphaherpesvirus subfamily of the Family Herpesviridae [(3)], glycoprotein G (gG-1 and gG-2 for HSV-1 and HSV-2, respectively) allowing for differentiation of the two virus types via the host's antigen-specific antibody response [(4)]. The incidence of HSV in renal transplant recipients is estimated to be approximately 53% [(5)]. In the majority of patients seropositive for HSV-1 or -2, virus replication occurs after transplantation, but only a minority of patients develops symptoms (~20%) [(6)]. In the absence of antiviral prophylaxis, reactivation of latent HSV infection has been reported to cause symptomatic disease in 75% of seropositive kidney recipients [(7)]. There are 3 epidemiological patterns of herpes infection, primary infection, reactivation of latent infection, and reinfection [(8)]. Most viral infections in transplant recipients are secondary infections because most individuals have had a primary infection with a herpes virus (the species of virus most responsible for infection in transplant recipients), usually in early childhood [(9)]. HSV-1 is acquired throughout life, and the prevalence increases from approximately 40% during adolescence to 80% by 60 years of age. HSV-2 is less prevalent, with rates of 30% by mid-adulthood [(10)].

Multiple factors contribute to viral activation after transplantation, including immune suppression (especially reduction of cytotoxic immunity), graft rejection therapy, inflammation (cytokines), and tissue injury. The host response is also less effective because of the mismatch in major histocompatibility antigens between the organ donor and host, which reduces the efficacy of direct pathway antiviral cellular immune responses [(11)].

HSV infection is a common early infection after organ transplantation, with secretion of virus in the throats of the majority of seropositive individuals [(1)]. Disease may be more severe, invasive, and prolonged in transplant recipients [(11)]. Mucocutaneous lesions make up the majority of HSV disease in transplant populations, and of these, orolabial lesions are the most common

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presentation – reportedly up to 85% of all HSV disease in the early post-transplant period.

HSV is the most common form of encephalitis in transplant recipients. Diffuse interstitial pneumonitis may complicate disseminated disease [12]; also, fulminans hepatic failure from primary and reactivated infections following deceased donor transplantation has been reported [13]. Moreover, multi-visceral involvement with HSV infection is often fatal [11]. As neurotropic and neuro-invasive viruses, HSV-1 and -2 persist in the body by becoming latent and hiding from the immune system in the cell bodies of neurons. After the initial or primary infection, some infected people experience sporadic episodes of viral reactivation or outbreaks. In an outbreak, the virus in a nerve cell becomes active and is transported via the neuron's axon to the skin, where virus replication and shedding occur and cause new sores [14]. Furthermore, genital ulcer disease due to HSV is a risk factor for sexual acquisition and transmission of HIV infection [15].

MATERIALS AND METHODS:

One hundred eighty four blood samples were collected in period from November 2012 to March 2013, 92 samples from renal transplant patients attend to Renal Transplant Recipients society. All of the participants provided informed consent. Data were collected regarding these variables: age, and gender. 92 blood samples were also collected from blood donor as control group.

In all of the patients and control group, ELISA for detection of human antibodies (IgG and IgM) was performed for HSV-1 and HSV-2 using SERION ELISA classic Herpes Simplex Virus IgG/IgM. The IgM tests systems have sensitivity of 98.0% and specificity of 98.0%. The HSV1+2 IgG test system was used for the determination of the immune status and this system have sensitivity >99.0 and specificity >99.0%. The method was conducted according to manufacturer instruction, cutoff value were calculated and specimen were considered positive or negative as the manufacturer instructed. A statistical analysis was performed with SPSS.

RESULTS

The main age of the study population was range from 51 years old to 65 years old and 85% were men. Overall, 91 renal transplant recipients (99%), and 84 donor of control group (91%) were seropositive for HSV1/2 IgG, as demonstrated in table (1) which show HSV1/2 IgG was significantly higher in renal transplant recipients than in donor control group (P = 0.017). In addition, Seroprevalence of HSV1/2 IgM was significantly higher in renal transplant recipients (50%) than in donors control group (6%) (P =0.00) as demonstrated in figure (1).

There was a statistical significant with age group and prevalence of HSV 1/2 infections. High prevalent of HSV1/2 IgG and IgM show in age from 51 to 80 years, as seen in table (2) and figure (2) respectively. According to gender, seroprevalence of HSV 1/2 IgG and HSV 1/2 IgM was significantly higher in females (100%, 53% respectively) than in males (94%, 25% respectively) as show in table (3) and table (4).

Table 1: Results of ELISA for HSV1/2 IgG among renal transplant and control group. (P value 0.017)

	ELISA IgG result		
Study Group	Positive	Negative	**Total**
Renal transplant	**91** (98.91%)	**01** (1.09%)	**92**
Control group	**84** (91.30%)	**08** (8.7%)	**92**
Total	**175**	**09**	**184**

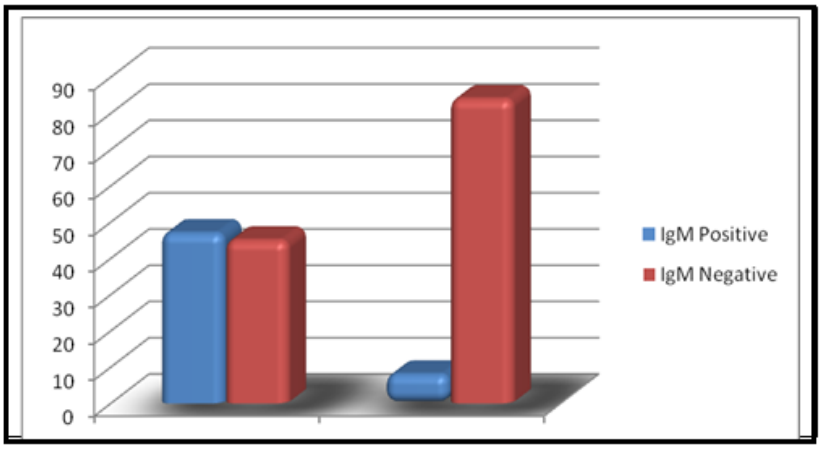

Figure 1: Results of ELISA for HSV1/2 IgM among renal transplant and control group. (P 0.00).

Table 2: ELISA of HSV1/2 IgG among age groups (P 0.045)

Age Group (years)	**ELISA IgG result**		**Total**
	Positive	Negative	
20 - 35	**74** (90.34%)	08 (9.76%)	**82** (100%)
36 - 50	**28** (96.55%)	01 (3.45%)	**29** (100%)
51 - 65	**45** (100%)	0 (0.0%)	**45** (100%)
66 - 80	**28** (100%)	0 (0.0%)	**28** (100%)
Total	**175**	**09**	**184**

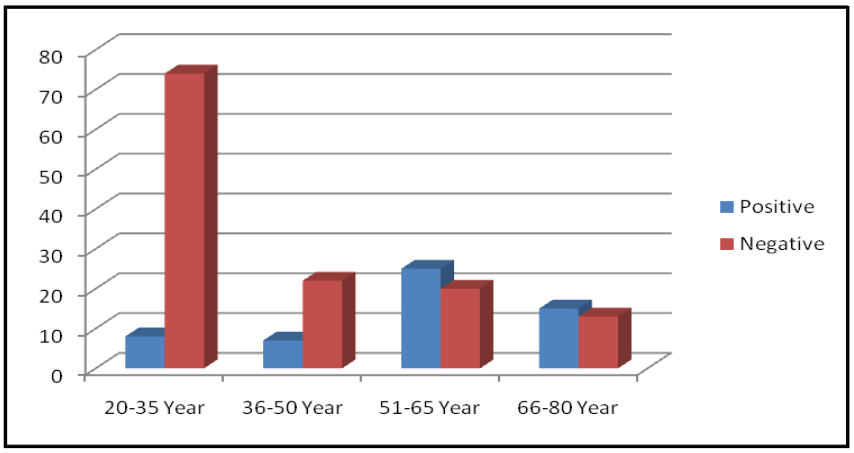

Figure 2: show result of ELISA for HSV1/2 IgM among age groups. (P value 0.00).

Table 3: show ELISA of HSV1/2 IgG among male and female (P value 0.212)

Gender	**ELISA IgG result**		**Total**
	Positive	Negative	
Male	**149** (94.30%)	**09** (5.7%)	**158** (100%)
Female	**26** (100%)	**0** (0.0%)	**26** (100%)
Total	**175**	**9**	**184**

Table 4: show ELISA of HSV1/2 IgM among male and female (P value 0.001)

Study Group	**ELISA IgM result**		**Total**
	Positive	Negative	
Male	**40** (25.32%)	**118** (74.68%)	**158** (100%)
Female	**15** (57.69%)	**11** (42.31)	**26** (100%)
Total	**55**	**129**	**184**

DISCUSSION:

The objective of this study is to determine the prevalence of HSV1 and 2 IgG and IgM among renal transplant and control group (Blood donors), in this study we found high prevalence of HSV infections in Sudanese renal transplant recipients (99%, 50% for HSV 1-2 IgG and IgM antibody respectively) compared to control group (91%, and 6% for HSV 1-2 IgG and IgM antibody respectively), presence of HSV IgG indicate past infection and HSV IgM indicate current infection, recent infection or persistent low titre from past infection, the high prevalence of HSV IgM among renal transplant due they are more probable to reactivation of HSV infection, this result in agree previous data the incidence of HSV in renal transplant recipients is estimated to be approximately 53% [5, 17].

In a previous study done in Iran demonstrated a serologic frequency of HSV-2 to be 5.4% in renal transplant recipients [18]. This result is disagree with our result, in fact, HSV-2 prevalence is highest in Africa and the Americas lower in western and southern Europe than in northern Europe and North America, and lowest in Asia [19]. Moreover, HSV seroprevalence was mentioned to be

associated with increasing age [18], in our study there was a significant association between HSV seropositivity and elder patients (P=0.045). HSV-1 and HSV-2 seroprevalence appears significantly higher in female than in male. This similar to several studies that mentioned HSV-2 infection is more prevalent in women than in men [19, 20]. To our best knowledge, there have been no studies addressing the post-transplant incidence of HSV infection or its seroprevalence so far.

CONCLUSION:

The Seroprevalence of HSV-1 and HSV-2 among study kidney transplant recipients was high (99%, 50% for HSV 1-2 IgG and IgM antibody respectively), so this viral infection must be remains in concern.

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