



RESEARCH ARTICLE

PREVALENCE OF HERPES SIMPLEX VIRUS 1/2 AND HUMAN CYTOMEGALOVIRUS IN  
SUDANESE SCHIZOPHRENIC PATIENTS

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ABSTRACT

**Background:** Cognitive impairment in the form of decreased working memory and executive functions has been recognized as a key deficit in schizophrenia. Neurotropic viruses such as Herpes virus and human cytomegalovirus have been associated with focal gray matter deficits in patients with schizophrenia.

**Aim:** The study was carried out to detect the prevalence and relationship of herpes simplex virus (HSV 1/2) and human cytomegalovirus (HCMV) among Sudanese schizophrenia patients.

**Methods:** A total number of 60 plasma samples were collected randomly from schizophrenia patients at Kubar hospital in Khartoum, Sudan. On the other hand, 30 samples were collected from healthy individuals were served as controls. The detection of HSV1/2 and HCMV IgG antibodies were performed by using an Enzyme-linked immunosorbent assay (ELISA).

**The results:** HSV1/2 IgG antibodies were detected in 95% schizophrenic patients and 93.3% control (0.75 *P* value), while IgG antibodies to HCMV were detected in 96.7% schizophrenic patients and (90.0%) control (*P* value 0.19).

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INTRODUCTION

Schizophrenia was first coined by Eugen Bleuler in 1907, he described the separation of function between personality, thinking, memory and perception<sup>(1)</sup>. Virus factors had been implicated in the pathogenesis of schizophrenia, evidenced for an infectious includes the 5 - 8% increased risk among those born in the winter-spring months, when infectious diseases are more prevalent and at times when other infections show increased activity<sup>(2)</sup>. Herpes viruses are capable of infecting human and many other animal species and it can establish latent infections<sup>(3)</sup>. The integrated herpes virus DNA can become reactivated after a number of stimuli, with the resulting production of virus particles and the subsequent infection of additional cells<sup>(4)</sup>. This process can lead to the establishment of a lifelong cycle of recurrent infections and development of persistent IgG class antibodies<sup>(5,6)</sup>. Many herpes viruses are capable of infecting cells within the human central nervous system. Human herpes viruses with neurotropic potential include herpes simplex viruses 1 (HSV-1) and 2 (HSV-2), cytomegalovirus (CMV), Epstein-Barr virus (EBV), Varicella-zoster virus (VZV), and human herpes virus 6 (HHV-6)<sup>(7)</sup>. For some of these viruses, such as CMV, VZV, and EBV, infection of the central nervous system is rare and occurs primarily in individuals whose immune system is compromised due to congenital or acquired immunodeficiency states<sup>(8)</sup>. Herpesvirus infections of the central nervous system can result in varying degrees of encephalitis, which can be associated with a high degree of morbidity and mortality in the absence of antiviral therapy<sup>(9)</sup>. Herpes viruses can also cause self-limiting infections of the central nervous system that can be difficult to detect during the acute phase of infection<sup>(10)</sup>. A viral hypothesis for the pathogenesis of schizophrenia has been under serious consideration for more than 70 years.

Several lines of evidences suggest that HSV1/2 and HCMV may play an etiological role in schizophrenia<sup>(11)</sup>. Epidemiologically, both have a worldwide distribution and an increased prevalence in lower socioeconomic groups. Studies have reported that some patients experiencing initial episodes of schizophrenia have increased levels of IgG antibodies against HSV1/2 and HCMV but not other herpes virus's family in their sera<sup>(12)</sup>. The current study aimed to determine the prevalence of herpes simplex virus (HSV1/2) and human cytomegalovirus (HCMV) antibodies among Sudanese schizophrenia patients.

METHODS

Study design and population

This is a case control study performed between August 2012 and January 2013. Sixty of schizophrenic patients without any admission of antiviral therapy during the study at Kubar Hospital and 30 matched healthy control volunteers were recruited in this study. This study was approved by Al-Neelain University ethical committee board and an informed consent was obtained from each patient or their relatives before collecting the demographic and clinical data.

Serological analysis

Specific enzyme based immunoassays (Virion/Serion, ELISA Kits, Würzburg, Germany) for IgG antibodies to HSV1/2 and HCMV were performed on serum samples from all cases and controls as previously described. An individual was considered to have been exposed to an infectious agent if his or her serum had a level of reactivity which was greater than that of predetermined standards defined for each infectious agent.

Data Analysis

Statistical analyses were conducted using SPSS.

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## RESULTS

Of the 60 schizophrenic patients, 47 (78.3%) were males and 13 (21.7%) were females. While the 30 healthy participants control included 19 (63.3%) males and 11 (36.7%) were females. The age range between 19 and 68 and median age is 35.8 years.. All patients and controls blood samples were tested by ELISA for detection of HSV1/2 IgG antibodies, 57 (95.0%) of those patients were positive while 28 (93.3%) of the control were positive for the HSV1/2 IgG antibodies, (*P values* 0.75). Furthermore the ELISA positive results for HCMV IgG Antibodies were showed that 58 (96.7%) of the patients were positive, while 27 (90.0%) of the control were positive for the HCMV IgG antibodies (*P values* 0.19).

Patients, gender, age, HSV1/2 IgG and CMV IgG

Characteristic	Patients	Control	Total	<i>P. value</i>
Study group	60 (66.7%)	30 (33.3%)	90 (100.0%)	
Gender				
Male	47 (78.3%)	19 (63.3%)	66 (73.3%)	
Female	13 (21.7%)	11 (36.7%)	24 (26.7%)	0.13
Age, years				
< 30	17 (28.3%)	06 (20.0%)	23 (25.6%)	
30 – 50	41 (68.4%)	16 (53.3%)	57 (63.3%)	0.004
> 50	02 (03.3%)	08 (26.7%)	10 (11.1%)	
HSV1/2 IgG				
Positive	57 (95.0%)	28 (93.3%)	85 (94.4%)	
Negative	03 (05.0%)	02 (06.7%)	05 (05.6%)	0.75
HCMV IgG				
Positive	58 (96.7%)	27 (90.0%)	85 (94.4%)	
Negative	02 (03.3%)	03 (10.0%)	05 (05.6%)	0.19

## DISCUSSION

Schizophrenia is a common, debilitating disorder characterized by disturbances in thought, perception, and affect that lead to significant deterioration in function. Cognitive impairment on a broad range of tasks is known to be an important component of schizophrenia<sup>(11)</sup>. The present study focused on the serologic detection of HSV1/2 and HCMV IgG antibodies, in 60 samples collected from schizophrenic patients, and 30 samples collected from healthy participants as a control. The presence of these antibodies indicates that the individual has been exposed to the target virus at some point in life and that the viral DNA has been integrated into the host genome. However the presence of antibody is not necessarily indicator of active infection. HSV1/2 IgG antibodies were detected in 95% schizophrenic patients, compared to 93.3% in the control (*P value* 0.75). In the other hand HCMV IgG antibodies were detected in 96.7% in schizophrenic patients compared to 90.0% in the control (*P value* 0.19). These results showed that there is no statistical significant relationship between these viruses and schizophrenia. In this study the prevalence of these viruses was too high compared with a study done in 2006 by Dickerson, F. *et. al.*, 2006<sup>(12)</sup> who found that the prevalence of HSV1/2 and CMV were 35.3% and 52.3% respectively, but the two studies agreed that there is no significant statistical association between serologic evidence of these viruses and schizophrenia. Thus, this finding supports Duggal, S. *et. al.*, 2008<sup>(13)</sup> ideas that various mechanisms are involved in pathogenesis of schizophrenia including genetic susceptibility and environmental factors. Although various studies document an increased risk of schizophrenia with viral infection, no particular virus has been unequivocally established as a

causative agent. In other hand, Dickerson, *et. al.*, 2003<sup>(14)</sup> found that the prevalence of HSV1/2 and CMV were 45.5% and 35.9% respectively, but they found that there is a significant association between serologic evidence of these viruses and schizophrenia.

## Conclusion

The prevalence of Herpes simplex virus 1/2 (HSV1/2) and human cytomegalovirus (HCMV) is high among both schizophrenic patients and control group and no significant statistical association was found between these viruses and schizophrenia.

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