

## SHORT COMMUNICATION

# Detection of Cytomegalovirus Antibodies in the Serum of Hemodialysis Patients

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### SUMMARY

**Background:** The infection with Cytomegalovirus (CMV) is one of the main causes of morbidity and mortality in hemodialysis patients.

**Objectives:** This study aims to investigate CMV serostatus in renal failure patients undergoing hemodialysis.

**Methods:** The study included a total of 134 cases (55 females and 79 males) with an age range of 35 - 68 years (mean age  $37.43 \pm 13.42$  years). HCMV-IgG and IgM were determined in subjects' sera.

**Results:** Eighty-seven out of 134 (65%) were undergoing hemodialysis, while 47 (35%) had normal kidney functions without HCV infection. Sixty-eight (78.2%) and 31 (35.6%) cases out of 87 hemodialysis patients were positive for CMV-IgG and IgM antibodies, respectively. No significant differences were noted between females and males in terms of seroprevalence rates. High rate of positive CMV-IgG was observed among hemodialysis patients who were 48 - 64 years old.

**Conclusions:** Our data suggest that seroprevalence of CMV antibodies among hemodialysis cases is high and causes complications for these patients.

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### KEY WORDS

CMV-IgG, CMV- IgM, hemodialysis, renal failure

### INTRODUCTION

Cytomegalovirus (CMV) is a worldwide virus which can cause severe morbidity and mortality in immunocompromised patients, such as AIDS patients, allograft recipients, and patients with renal failure [1]. HCMV (HHV-5) is the prototype of subfamily *betaherpesvirinae*. Like all herpes viruses, latency and persistence are life-long in individuals [2,5]. For the most part CMV infection is asymptomatic or followed only by specific mild symptoms [3]. The reactivation of the virus occurs in immunosuppressed patients such as the HIV cases, elderly patients, hemodialysis patients and subjects submitted to chemotherapy and ionized radiation treatment

and pregnant women, due to immaturity of the immunological system [1,4].

There are three different subtypes of HCMV infection. Primary infection (first time) occurs in an individual with no immunity against cytomegalovirus. Afterwards, the second type of infection establishes latency from which it may reactivate [6,8]. The third type of infection is called reinfection when contact with an infectious individual who has already been infected occurs despite their possession of natural immunity [7,11].

The transmission of the human cytomegalovirus in renal failure patients may occur through transplantation or through hemodialysis [5,9]. Among the hemodialysis patients the probability of direct contact with the human cytomegalovirus is high [10].

Reactivation of the latent virus in the renal failure patients undergoing hemodialysis can result in a severe systemic disease, with high fever, multiple organ dysfunctions with leukopenia, and CMV in the blood [12, 14].

Many procedures for CMV detection are available, including serology techniques, conventional virus culture, shell-vial, and molecular techniques [13]. Among the highly sensitive and specific immunological techniques used for the detection of specific human anti-cytomegalovirus antibodies (IgM and IgG) is the microparticle enzyme-linked immunosorbent assay (ELISA) [15]. This study was proposed to evaluate the prevalence of CMV antibodies (IgM and IgG) by serological tests such as ELISA in renal failure patients undergoing hemodialysis.

## MATERIALS AND METHODS

### Ethical approval

This research was approved by the Review Board of Ain Shams University.

### Study population

One hundred and thirty-four cases were enrolled in this study. The 134 cases included 55 females and 79 males, with an age range of 35 - 68 and mean of  $37.43 \pm 13.42$  years. All blood samples were collected from different hospitals (Waddi El-Nile, Dar El-Fouaad, General Daqahlyia, and Qena hospitals). Cases were divided into two types; hemodialysis cases who were suffering from failure and undergoing hemodialysis (n = 87) and control cases (n = 47) who had normal kidney functions and were negative for HCV antibodies. The infected cases (n = 87) were selected from patients under treatment at Nephrology Departments of the previous hospitals. Consent forms that include (name, age, gender, history of blood transfusion) were obtained from each subject before sampling. All sera samples were separated after centrifugation at 1,000 rpm for 10 minutes. Antibodies against HCMV (IgG, IgM) were assessed and recorded for all samples.

### Serological analysis of HCMV

HCMV-IgM and HCMV-IgG antibodies were determined by the enzyme-linked immunosorbent assay (ELISA) technique using commercially available CMV-IgM and IgG Kits (BioCheck, Foster City, CA, USA). Tests were done according to the manufacturer's instructions, and results of HCMV IgM and IgG were expressed as optical density (OD) units.

### Statistical analysis

SPSS software package version 23.0 (IBM SPSS Statistics for Windows; IBM Corp., Armonk, NY, USA) was used for data management and data analysis. The statistical significance of difference was considered when  $p \leq 0.05$ .

## RESULTS

### Total HCMV-IgG antibodies responses

Sixty-eight out of 87 patient cases (78.2%) were positive for HCMV-IgG antibodies, while 19 (21.8%) were negative for HCMV-IgG. Among Control Cases, 24 out of 47 (51%) had detectable HCMV-IgG antibodies, while 23 (49%) cases were negative for HCMV-IgG (Table 1).

### Total HCMV-IgM antibodies responses

Among hemodialysis cases, 31 out of 87 patient cases (35.6%) were positive for HCMV-IgM antibodies, while 56 (64.4%) were negative for HCMV-IgG. Ten out of 47 control cases (21.3%) had detectable HCMV-IgM antibodies, while 37 (78.7%) cases were negative for HCMV-IgM (Table 2).

## DISCUSSION

Human Herpes Virus-5 (HHV-5, also known HCMV) is one of the  $\beta$ -herpes viruses which cause infection for 75 - 90% of the world population. HCMV infections are regulated by the effective immune system, but without the virus' ultimate clearance [15,20].

During periods of down-regulation of the immune system such as treatment with pharmaceutical products and stress associated with illness, or viral co-infection, CMV can be reactivated [16].

CMV was first identified as cause of mortality in elderly, organ allograft recipients, and hemodialysis patients [17]. Another study shows the presence of the infection due to activated HCMV in population which presents alterations of the immune system [18,25].

In this study, we investigated the seroprevalence of HCMV in Egyptian renal failure patients undergoing hemodialysis. The results showed that the percentage of seropositive CMV-IgG was significantly higher ( $p < 0.01$ ) in hemodialysis cases than those in control cases (normal kidney function without HCV infection). Also, CMV-IgM was detected in 35.6% of hemodialysis pa-

**Table 1. HCMV-IgG rates in Hemodialysis and Control cases.**

	Total no. of cases	HCMV-IgG				p-value
		Positive		Negative		
		No.	%	No.	%	
Hemodialysis cases	87	68	78.2%	19	21.8%	< 0.001
Control cases	47	24	51%	23	49%	> 0.5

**Table 2. HCMV-IgM antibodies rates in Hemodialysis and Control cases.**

	Total no. of cases	HCMV-IgM				p-value
		Positive		Negative		
		No.	%	No.	%	
Hemodialysis cases	87	31	35.6%	56	64.4%	< 0.01
Control cases	47	10	21.3%	37	78.7%	< 0.02

tients (69% of them had positive IgG antibodies) compared with 12% of control group with negative CMV-IgG. The results of this study showed the seropositivity of CMV-IgG and IgM was higher in elderly hemodialysis patients. Our data were in agreement with other studies and confirmed the correlation between CMV seropositivity and prevalent frailty in older people [19]. Other studies illustrated that the source of infection in the majority of allograft recipients (60 - 75%) during kidney transplantation is a kidney from a seropositive donor [22]. The remaining infections (25 - 40%) are due to transfusion of leukocyte-containing blood products from CMV-positive donors [18,26]. CMV infection is a frequent complication and the main cause of death in end-stage renal failure disease [23,27]. Acquired immunity is suppressed in uremic cases [24,25]. Other studies suggested that the number of circulating T-cells was reduced and suppressor cells increased, where hemodialysis could not recover the weakness of the immune response in renal failure patients [18,26]. These factors contribute to the suppression of the adaptive immune response and increase the incidence of CMV infection among hemodialysis patients [14,27]. Also, our data showed insignificant variation between male and female hemodialysis patients with positive HCMV antibodies. These results are similar to other studies which concluded that there is no significant difference in CMV seroprevalence by gender [21]. Sagedal et al. [15] reported a highly significant prevalence of CMV antibodies in chronic hemodialysis patients compared to healthy individuals. In our findings, the percentage of hemodialysis patients positive for anti-CMV IgG was found to be significantly higher than in the healthy volunteers. CMV infection

risk increases with the increasing the time of dialysis treatment.

**CONCLUSION**

Based on our results, 78.2% of seropositivity was found for HCMV-IgG and 35.6% for HCMV-IgM in hemodialysis patients, showing high morbidity rate by cytomegalovirus in these individuals. Therefore, it is important to estimate the route of transmission of CMV and verify the risk of the transmission through hemodialysis to seropositive and seronegative cases and define strategies of selection. So, we recommended that patients with renal failure undergoing hemodialysis should be screened for HCMV before dialysis and viral survey must be performed periodically to avoid transmission of viral infection through dialysis procedure.

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**Consent to Participate:**

All patients were recruited after a written informed consent. The study protocol was approved by the ethics review committee Ain Shams University, Cairo, Egypt.

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**Declaration of Interest:**

The authors declare no competing of interest.

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