

Renal Data from the Arab World

Anti-HCMV IgG Positivity Rate among Renal Transplant Recipients in Baghdad

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ABSTRACT. In developing countries, the majority of infection by human cytomegalovirus (HCMV) occurs during childhood and continues as a latent infection. By adulthood, almost all the population may show anti-HCMV IgG as positive. This study was undertaken to determine the correlation between the prevalence of HCMV antibodies and HCMV infection during post transplant period among renal transplant patients in Baghdad. 43 renal transplant patients attending three renal transplantation centers, and 40 healthy individuals who served as controls were enrolled in this study. 18 (41.9%) were transplanted recently and they were under post-operative follow-up and 25 (58.1%) were transplanted more than one year ago. Detection of anti-HCMV IgG was carried out using enzyme-linked immunosorbant assay (ELISA). The results revealed that anti-HCMV IgG was significantly higher among renal transplant recipients compared to healthy controls (97.7% vs 85%, $P = 0.04$). The anti-HCMV IgG positivity rate was not affected by patients' age, sex, and duration after transplantation or immunosuppressive therapy. We conclude that the high anti-HCMV IgG positivity rate among Iraqi renal transplant recipients make them prone to considerable risk of reactivation of HCMV infection.

Introduction

Bone marrow and solid organ transplantation have evolved to become the preferred treatment options for a number of malignancies and end-stage organ dysfunction. However, despite the

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success of transplantation medicine, a problem that still continues to plague the transplantation recipient is that of infection, which remains the leading cause of death among this population.^{1,2}

Human cytomegalovirus (HCMV) is ubiquitous being endemic in all parts of the world, and presents throughout the year without seasonal variation.^{3,4} The prevalence of antibody to HCMV infection increases with the age, the highest prevalence being in developing countries and among lower socioeconomic strata of the developed nations. About 90 - 100% of general population in developing countries and those in low socioeconomic groups in developed

Table 1. Description of variables according to the age groups.

Variables	Transplanted patients (n=43)	Healthy controls (n=40)
Gender		
Male	30 (69.8%)	26 (65%)
Female	13 (30.2%)	14 (35%)
Age (years)		
< 20	1 (2.3%)	7 (17.5%)
20-39	15 (34.9%)	28 (70%)
40+	27 (62.8%)	5 (12.5%)
Duration of transplantation (years)		
<1	18 (41.9%)	
1-5	13 (30.2%)	
>5	12 (27.9%)	
Immunosuppressive therapy		
No	18 (41.9%)	
Yes	25 (58.1%)	

countries showed anti-CMV IgG antibody positive.⁵⁻⁸ Furthermore, the majority of HCMV infection in developing countries occurs during childhood, in whom the infections are almost always asymptomatic.^{9,10} The most convenient and consistent approach to the diagnosis of HCMV latent infection in normal individuals is the demonstration of HCMV specific IgG seroconversion. HCMV specific IgG antibody appears following the primary or reactivation infection and peaks about 2 - 3 months post-infection and usually persists for life.^{11,12}

Cytomegalovirus specific IgG and IgM have been investigated in renal transplant recipients by several workers which suggested that the seropositive recipients might be had a greater chance for reactivation of latent HCMV infection and probably for acute graft rejection.¹³⁻¹⁷ The documentation on HCMV infection and disease complications in Iraqi renal transplant recipients are lacking in the literature. Therefore, this study was undertaken with the objective to determine the correlation, if any, between prevalence of HCMV antibodies and HCMV infection during post transplant period among renal transplant patients in Baghdad.

Patients and Methods

A cross-sectional study was conducted from May 2007 to December 2008 in Al-Karama General Hospital, Al-Khayal private center and

the Specialist Surgical Hospital in Baghdad. The patients were referred from different Iraqi provinces for renal transplantation. 43 renal transplant patients were attending these three centers for renal transplantation. Additionally, 40 apparently healthy individuals were enrolled as control group. Ten mL of blood were collected from transplant recipients and control individuals. Furthermore, the individuals with non-functioning graft from previous transplantation, who were on scheduled pre-transplantation dialysis and those who had recent blood transfusion were excluded from the control group.

All renal transplant recipients were matched pre-operatively for human leukocyte antigens (HLA typing) and for the following viral markers; hepatitis B surface antigens (HBsAg), anti-hepatitis C virus antibody (anti-HCV antibody), anti-human immunodeficiency virus type 1 and 2 antibodies. At the time of enrollment, 25 (58.13%) patients were under immunosuppressive therapy (Azathioprine, Cyclosporine A, Prednisolone) according to specified transplantation protocol. Other 18 (41.8%) of renal transplant recipients had not started immunosuppressive therapy yet.

The sera were separated and kept at -20°C till testing. Anti-Human cytomegalovirus IgG ELISA kit (RADIM-S.R.L Pomezia RM. Italy) and the ELISA tests were used according to the procedure described by the manufacturer using microelisa washer and reader (bio-Tech, USA).

Table 2. Difference in anti-HCMV IgG positive rates among study cases and controls.

Study group	Total No.	Anti HCMV IgG	
		No.	%
Transplanted patients	43	42	97.7
Healthy group	40	34	85

The sample size was small, therefore, the P value (<0.1) level was considered statistically significant, since the chances for missing an obvious association is more than detecting a possible false one. The study was conducted in compliance with humane care standards and with ethics number AMBARUNI /07/ 021. Data were stated as mean \pm standard deviation (SD) and subjected to statistical analysis using SPSS software package (Version 11.0 windows).

Results

A total of 43 renal transplant patients were attending the centers for renal transplantation, 30 (69.7%) males and 13 (30.3%) females. 40 healthy individuals, 26 (65%) males and 14 (35%) females served as control group. The mean age of renal transplant patients was 42 ± 12.8 years. Among these patients, 1 (2.3%) was less than 20 years, 15 (34.9%) were 20 - 39 years and 27 (62.8%) were more than 40 years of age. The results of pre-transplantation testing for anti-HIV, anti-HCV antibodies and HBsAg were negative for all patients. In the control group, the mean age was 29 ± 10.5 years. The highest proportion (70%) were young (20 - 40) years of age, while 17.5% of them were less than 20 years, and 12.5% were more than 40 years of age. The results of anti-HIV, HBsAg

and anti-HCV antibody in the control group were also negative for all (Table 1).

At the time of the study in 18 (41.9%) patients post-transplantation period was less than one year, while in 25 (58.1%) it was more than one year. Of the latter, 13 (30.2%) were between 1 - 5 years and 12 (27.9%) were above five years of duration. Twenty five (58.1%) of transplanted patients were under immunosuppressive therapy (Cyclosporin A, Azathioprin and Prednisolone), while 18 (41.9%) patients didn't receive any immunosuppressive drugs (Table 1). The prevalence of anti-HCMV IgG antibody in the transplanted patients was significantly higher than that in the control group, 97.7% vs 85% ($P < 0.04$) (Table 2). Table 3 shows that neither age nor gender of healthy controls correlated with anti-HCMV IgG antibody positivity. The prevalence of anti-HCMV IgG antibody was higher among renal transplant recipients with longer duration after transplantation (more than one year). Recipients more than 20 years old, females and individuals under immunosuppressive therapy showed insignificant results (Table 4).

Discussion

In renal allograft recipients, the HCMV infection has been associated with acute and chronic

Table 3. Anti-HCMV IgG positivity rates by age and gender among healthy controls.

Variables	No.	Anti-HCMV IgG positive	
Gender			
Female	14	11	78.6
Male	26	23	88.5
P value		0.35 (NS)	
Age in years			
<20	7	6	85.7
20-39	28	24	85.7
40 +	5	4	80
P value		0.95 (NS)	

NS: not significant

Table 4. Anti-HCMV IgG positivity rate by age, gender, duration of transplantation and type of immunosuppressive therapy in patient groups.

Variables	No.	Anti-HCMV IgG	
		No.	%
Gender			
Female	13	13	100
Male	30	29	96.7
<i>P</i> value		0.35 (NS)	
Age (years)			
<20	1	1	100
20-39	15	15	100
40 +	27	26	96.3
<i>P</i> value		0.62 (NS)	
Duration of transplantation			
<1	18	17	94.4
1-5	13	13	100
>5	12	12	100
<i>P</i> value		0.41 (NS)	
Immunosuppressive therapy			
No	18	17	94.4
Yes	25	25	100
<i>P</i> value		0.42 (NS)	

NS: not significant

graft rejection. Acute allograft rejection remains an important cause of morbidity after kidney transplantation, and has been shown to be a crucial determinant of long-term graft function. The introduction of new potent antiviral agents offers a wider choice of drugs for viral prophylaxis and treatment.¹⁷⁻¹⁹

The results of this study showed significant higher prevalence of anti-HCMV IgG positivity among renal transplant recipients compared to healthy control group. Such studies on HCMV infection and its complications in Iraqi renal transplant recipients are lacking in the literature. In most places, like the area of this study, the screening tests of blood units before transfusion include only anti-HIV 1 & 2, anti-HCV antibody and HBsAg, but unfortunately does not include anti-HCMV antibody test. Basically, these patients were frequently hospitalized for renal dialysis and received blood transfusions before the decision of renal transplantation. Therefore, pre-transplantation dialysis and blood transfusion may explain the significantly higher rates of anti-HCMV IgG among these patients. This result is consistent

with what previous works have documented. Renal transplantation always remains as an option for patients with end-stage renal disease.²⁰⁻²² The transmission of HCMV infection from seropositive donor to seronegative recipient through the transplanted kidney constitutes an important route that was usually associated with unfavorable consequences.^{1,13,23}

The result of this study shows insignificant effect of age and gender on the prevalence of anti-HCMV IgG in the healthy controls. This result was also consistent with what have been documented in previous studies from other developing countries, where most of infections with HCMV occurred during childhood with no significant difference between males and females. The virus then remains in a dormant stage for the rest of the life and.⁵

The results in present study also showed that the prevalence of anti-HCMV IgG among renal transplanted recipients was higher in the cases with longer post transplant duration and in those who were under immunosuppressive therapy. These results, however, are not surprising, since immunosuppressed renal transplant reci-

patients are at a higher risk of acquiring HCMV infection, and longer the duration of post transplant period, higher would be the influence of immunosuppressive drugs and the risk HCMV infection.^{16,24,25} In another study on 20 renal transplant cases, were asymptomatic in first six months and later on, all patients were tested positive for anti-HCMV IgG.²⁶

It has been reported that the critical exogenous factor influencing the HCMV reactivation following transplantation was dependant on the type and intensity of immunosuppressive therapy, and also the level of immunosuppression in any given patient, determined by the dose and the duration. These compounds not only diminished the capacity of level of immune surveillance of the host, but also increased reactivation of latent HCMV from infected cells.^{16,17,24} For instance, high cyclosporine levels in blood have been associated with an increased risk of developing HCMV infection.²⁷ Steroids appeared to have minimal effects on reactivation of latent HCMV, however, the addition of high doses of corticosteroid to anti-lymphocyte therapy has been associated with a higher incidence and increased severity of CMV infection.²⁸ We conclude that the high anti-HCMV IgG positivity rate among Iraqi renal transplant recipients make them prone to considerable risk for reactivation of HCMV infection.

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