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Seroprevalence of Cytomegalovirus Antibody in Renal Transplant Recipients and Donors in Khuzestan Province, Iran.

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Abstract:

Objective: Cytomegalovirus (CMV) has been recognized as one of the most important opportunistic pathogens in kidney transplant patients.
The aim of this study was to determine the prevalence of CMV antibody in donors and recipients before transplantation.
Material and Methods: In a cross sectional study from March 2008 to August 2009 we prospectively studied donors and recipients who referred to our kidney transplant center.
All of routine pretransplante laboratory studies including liver function tests and CMV IgG and IgM antibody were performed for them.
Results: A total of 148 patients (79 donors and 69 recipients) were included in the study. Mean age of donors and recipients were 30 ± 8 years and 40 ± 18 years respectively.
Liver Function tests (SGOT and SGPT) were at normal range and marker of HBV infection was negative in both groups but HCV antibody was positive in 2.89 percent of recipients (n=2) and negative in all of donors.
CMV IgG antibody was positive in 100 percent of recipients and 98.73 percent of donors (n=78).
CMV IgM antibody was negative in 98.55 percent of recipients (n=68) and 100 percent of donors (n=79).
Conclusion: CVM infection is very common in donors and recipients candidate for kidney transplantation in Khuzestan province and almost all of them in this study have CMV IgG antibody.

Keywords: Renal Transplantation, CMV IgG Antibody, CMV IgM Antibody.

Introduction:

Cytomegalovirus (CMV) is a member of the genus Herpesvirus and belongs to the family Herpesviridae.[1]

Cytomegalovirus is present in body fluids and transmission can occur horizontally (by direct contact, person to person with virus containing secretions such as saliva, urine, cervical secretions or semen) and vertically (mother to newborn) before, during or after birth.[1] It also can be transmitted from the donors to the recipients either by blood transfusion or by infected organs in the transplantation.

In transplant patients, the concurrent administration of immunosuppressive drugs to prevent rejection further increases the risk of clinically relevant CMV disease.[2, 3, 4, 5] Thus, both the recipient and the donor are routinely tested for anti-CMV antibodies prior to transplantation.[3, 5, 6]

Although, many studies about the prevalence of CMV infection in general population or transplant candidate were done in developed countries, but there are a few studies in developing countries. Therefore, in this prospective study, we investigated the prevalence of CMV infection in the donors and recipients candidate for kidney transplantation in Ahvaz city, Iran.

Material and Methods:

In a cross sectional study, we prospectively studied all candidate for renal allograft recipients and living donors who referred to our kidney transplant center before transplantation from March 2008 to August 2009.

A standardized questionnaire was used to collect sociodemographic data (for donors and recipients) and cause of ESRD, date of onset of HD, length of time receiving HD services and history of a kidney transplant (for recipients).

Blood samples were taken from recipients and donors for check of IgG and IgM anti-CMV antibodies. The levels of antibodies were determined using commercially available sensitive enzyme-linked immunosorbent assay (ELISA) method.

To evaluate the association between CMV Infection and the age of Patients, they were divided into three groups: group 1; 20-29 year, group 2; 30-39 year and group 3; more than 40 year The patients and donors were also screened for human immunodeficiency virus (HIV), HBsAg, and hepatitis C antibody (anti-HCV) by ELISA method.

All samples were also tested for liver function tests including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels by a colorimetric method.

Statistical analysis:

For statistical analysis, prevalence rates and 95% confidence intervals (CI 95%) were calculated. Chisquare tests or Fisher's exact tests were performed to evaluate the distribution of variables and characteristics associated with CMV infection.

Statistical significance was assessed at the 0.05 probability level in all analyses.

Results:

A total of 148 patients, 79 donors (50 male and 29 Female) and 69 recipients (46 male and 23 female), referred to kidney transplant center of Ahvaz city were enrolled for the study.

Mean age of donors and recipients were 30 ± 8 years and 40 ± 18 years respectively.

Causes of ESRD of recipients included high blood pressure in 19 patients (27.53%), diabetes mellitus in 18 patients (26.08%), unknown in 12 patients (17.39%), glomerolonephritis in 9 patients (13.04%), polycystic kidney disease (PKD) in 6 patients (8. 69%) and obstructive uropathy in 5 patients (7.24%). Table 1 shows the Causes of ESRD in the recipients.

Causes of ESRD	Patients Number	Patients Percent
Hypertension	19	27.53
Diabetes mellitus	18	26.08
Unknown	12	17.39
Glomerulopathy	9	13.04
PKD	6	8.69
Obstructive uropathy	5	7.24

Table 1. Cause of ESRD in the recipients

In overall, IgG anti-CMV antibody was detected in 99.32 percent (n=147) of all subjects enrolled in the study.

It was positive in 100 percent of recipients (n=69) and 98.73 percent of donors (n=78). Although the prevalence of CMV infection was higher in recipients, but there were no statistically significant difference between them (p =0 .592).

CMV IgM antibody was negative in 100 percent of donors (n=79) and 98.55 percent of recipients (n=68) and there also were no significant difference (p =0 .624).

Mean of AST and ALT levels in both groups were at normal range. It was in donors 28±8 and 26±9and in recipients 27±5 and 24±6 respectively. There was no significant difference between donors and recipients in AST (P= 0.03) and ALT (P= 0.02) levels.

Marker of HBV and HIV infection were negative in all of patients, but HCV antibody was positive in 2.89 percent of recipients (n=2) and negative in all of donors.

Discussion:

The spectrum of human illness caused by cytomegalovirus (CMV) is diverse and mostly dependent on the host. CMV infections in the immunocompetent host is generally asymptomatic or may present as a mononucleosis syndrome. However, it can cause serious complications and substantial morbidity and mortality in persons with weakened immune systems, especially among transplant recipients and those infected with the human immunodeficiency virus (HIV). Therefore, its one of the most important and also one of the most common infection in renal transplant recipients.[4, 5, 7]

Exposure to the virus, as indicated by the presence of detectable IgG anti-CMV antibodies in the plasma varies throughout the world and between and within developed and developing countries, with seroprevalence rates ranging between 40 to 100 percent of the adult population.[8]

The prevalence of CMV-specific antibody also increases with age in the general

population .As an example, in a study from Finland, the seroprevalence rate was 47 percent in 10 to 12 year olds. However it increased to 68 percent in 15 to 35 year olds, and 81 percent in 36 to 60 year olds.[9]

Age-related increases in the seroprevalence of CMV antibody have also been shown in the United States. In a US-based study, the prevalence of CMV infection increased from 36 percent in 6 to 11 year olds to 91 percent among those aged >80 years.[10]

It is therefore common for the adult recipient and/or donor to be CMV-specific antibody positive at the time of transplantation. It is also estimated that more than two-thirds of Americans donors and recipients carry cytomegalovirus prior to transplantation.[2]

Seroprevalence generally correlates inversely with a country's socioeconomic development, with highest rates observed in developing countries throughout Africa and Asia.[11]

In the US-based study,seroprevalence of CMV also varied by race and ethnicity as follows: 82 percent in Mexican Americans, 76 percent in non-Hispanic black persons and 51 percent in non-Hispanic white persons. Racial and/or ethnic differences in cytomegalovirus seropositivity persisted when controlling for household income level, marital status, area of residence, census region, family size, education, country of birth, and type of medical insurance.[10]

According to the present study, the prevalence of CMV infection and exposure to the virus in adult general population candidate for kidney transplantation in Khuzestan province, Iran, is very high and almost all of recipients and donors (99.32 percent) have IgG anti-CMV antibodies in the plasma. On the basis of these results, we estimate that the prevalence of CMV infection in adult person ,older than 20 years, in our province is near to 100 percent unreceptive to sex and health difference.

Although socioeconomic status was once a major factor affecting the frequency of CMV infection in the general population in other studies [11], we couldn't show this association in our study because almost all of donors were in low socioeconomic status. It does not seem that socioeconomic difference is a major factor affecting the frequency of this virus in our recipients because all of them in the study were CMV positive and they were in different socioeconomic status.

Thus, although in developed countries, both the recipient and the donor are routinely tested for anti-CMV antibodies prior to transplantation [12]; it appears likely that in our province and other province and countries like us, we don't need to routinely test this antibody prior to transplantation. However, we should assume that our recipients and donors have CMV infection and we strongly recommend performing measures for prophylactic prevention of CMV reactivation in recipients.[13, 14, 15]

It must be emphasized that these measures are very important because reactivation of infection with the cytomegalovirus (CMV) in organ transplant recipients may cause significant morbidity and mortality.[16, 17, 18, 19]

Previously, treatment was only administered once CMV disease occurred and it was not routine to perform prophylactic

treatment for organ transplant patients with risk of CMV reactivation and CMV disease. This approach resulted occurrence of clinically relevant CMV disease in approximately half of recipients. Subsequently, some preventive strategies have been developed and recommended by different organ transplant centers throughout the world that have significantly lowered the incidence of CMV disease, which is approximately five percent with modern approaches.

In practice, there are two principal and important strategies for prevention of CMV disease in end stage renal disease patients undergoing kidney transplantation: Universal prophylaxis and preemptive therapy.[14, 20]

1- Universal prophylaxis involves the administration of antiviral agents to all at-risk patients immediately after transplant for a defined duration.

2- Preemptive therapy, sometimes referred to as "targeted or guided prophylaxis", involves periodic monitoring patients for early evidence of CMV viremia, principally using polymerase chain reaction (PCR), to permit prompt treatment after the detection of very early systemic infection.[20, 21, 22]

Conclusion:

In conclusion, results of our study suggest that the prevalence of CMV infection in Khuzestan province is very high. Thus, we don't need to routinely check CMV antibody before organ transplantation, but we should assume that all of donors and recipients are CMV antibody positive. In addition all of our recipients need to receive prophylactic measures for prevention of CMV reactivation according to current protocols.

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