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Do we need to screen our patients for EBV IgG antibody before kidney transplantation?

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ABSTRACT

Background: Epstein-Barr virus (EBV) can cause serious complications in kidney transplant patients. Current guidelines are recommended that both recipients and donors, be routinely tested for EBV IgG antibody before kidney transplantation.
Objectives: The aim of the study was to evaluate the value of this recommendation.
Patients and Methods: In a cross sectional study from February 2009 to March 2010, we evaluated donors and recipients who referred to our kidney transplant center. Routine pretransplante laboratory testes including EBV IgG and IgM antibody were performed.
Results: A total of 112 people, 52 donors (29 male and 23 Female) and 60 recipients (38 male and 22 female) were included in the study. Mean age of donors and recipients were 31.3 ± 6.7 years and 42.1 ± 12.57 years, respectively. Marker of HBV and HCV infections were positive in only 1 and 2 recipients and negative in all of donors. EBV IgG antibody was positive in 70 percent of recipients (n = 42) and 52 percent of donors (n = 27) but there was no statistically significant difference between them (p = 0 .053) and between males and females (p = 0.94). EBV IgM antibody was negative in 97 percent of recipients (n = 57) and 100 percent of donors (n = 67).
Conclusion: The seroprevalence of EBV infection among candidate for kidney transplantation in khuzestan is not very high compared to other provinces in Iran, although we should perform screening for EBV to avoid kidney donation from seropositive donor to seronegative recipient.

Implication for health policy/practice/research/medical education:
Performing paraclinical screening in patients before renal transplantation has considerable importance from the point of prevention from infection diseases. Reading this article is suggested for clinicians especially in the field of nephrology and infectious disease who are authorized for patient's treatment.

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Background

Epstein-Barr virus (EBV), or human herpesvirus 4, is one of the most common viruses in human. Yvonne Barr and Anthony Epstein together with Bert Achong discovered the viruses in 1964 and EBV is named after that (1). The host range of the virus is restricted to humans and certain primates including cotton top marmosets and squirrel monkeys (2). EBV is spread by intimate contact between susceptible persons and asymptomatic EBV shedders. It also can be transmitted from the donors to the recipients by the transplanted kidney. The most common manifestation of primary infection with EBV is infectious mononucleosis, a self-limited clinical syndrome. However, it can cause serious complications in immunocompromised hosts and therefore its one of the most important infection in renal transplant recipients (3-6). To prevention of these complications, both the recipient and the donor are routinely tested for EBV IgG and IgM antibodies before transplantation.

Objectives

Aims of the study were to assess the value of this approach and to determine the seroprevalence of EBV antibody in the donors and recipients candidate for renal transplantation in our transplant center in Ahvaz city, Iran.

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Material and Methods

From February 2009 to March 2010, in an epidemiologic study, we investigated renal allograft recipients and living donors candidate for kidney transplantation who referred to our kidney transplant center before transplantation. We used a standardized questionnaire for collection of demographic data (for both donors and recipients) and etiology of chronic kidney disease, date of onset of renal replacement therapy (RRT), kind of RRT [hemodialysis (HD) or peritoneal dialysis (PD)], length of time receiving RRT services and history of a kidney transplant (for recipients). Before transplantation, IgG and IgM anti-EBV anti¬bodies levels were determined by using commercially available sensitive enzyme-linked immunosorbent assay (ELISA) method. Screening for human immunodeficiency virus (HIV), HBsAg, and hepatitis C antibody (anti-HCV) were also performed in both groups (donors and recipients) by ELISA method.

Statistics

The statistical package for social sciences (SPSS) version 15.0 software was used for data 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 EBV infection. Statistical significance was assessed at the 0.05 probability level in all analyses.

Results

In overall, 112 people, 52 donors (50 male and 29 Female) and 60 recipients (46 male and 23 female), referred to our kidney transplant center were enrolled for the study. Mean age of donors was 31.3 ± 6.7 years (range: 20-68 yrs), and recipients was 42.1 ± 12.6 years (range: 19-48 yrs). The age distribution of donors and recipients were shown in *Figures 1 and 2*. To evaluate the association between prevalence of EBV infection among different age of recipients, they were divided into four groups: group 1; less than 30 year (n = 9), group 2; 30-39 year (n = 13), group 3; 40-49 year (n = 11) and group 4; 50 and more than 50 year (n = 20). The etiologies of end stage renal disease (ESRD) in our patients were included hypertension in 15, unknown causes in 13, diabetes mellitus in 12, glomerulopathy in 8, obstructive uropathy in 7 and polycystic kidney disease (PKD) in 5 patients. *Table 1* shows the Causes of ESRD of recipients. In overall, the prevalence of EBV IgG antibody in all people (donors and all groups of recipients) was 62 percent (n = 69) with no association between males and females (p = 0.94). Although it was higher in recipients (n = 42; 70 percent) to donors (n = 27; 52 percent), there was not a statistically significant difference between them (p = 0.053). In recipients, the prevalence of EBV IgG antibody in groups 1, 2, 3 and 4 were (78%; n = 7), (62%; n = 8), (73%; n = 8) and (75%; n = 15) respectively and there were no association between four groups (p = 0.45). EBV IgM antibody was negative in 100% of donors (n = 52) and 97% of recipients (n = 58). Although the percent of negative EBV IgM antibody people was higher in recipients, there was no significant difference between them (p = 0 .59). Serologic marker of HBV and HCV infection (HBsAg and HCV Ab) were positive in only 1 and 2 recipients and they were negative in all donors. HIV antibody was also negative in all recipients and donors.

Table 1. Cause of ESRD in recipients

Causes of ESRD	Patients Number
Hypertension	15
Unknown	13
Diabetes mellitus	12
Glomerulopathy	8
Obstructive uropathy	7
PKD	5

Discussion

Although the majority of primary EBV infections are asymptomatic and in apparent, however, this virus is also known as a human tumor virus, and is the first virus associated with human malignancy. It is associated with lymphoproliferative disorders, especially in weakened immune systems in organ transplant recipients (4-6). In addition there is an increased risk of posttransplant lymphoproliferative disorders (PTLD) among organ recipients with negative EBV serologic markers from EBV positive donors (7, 8). These patients, who had no preoperative immunity to EBV, usually acquired the infection posttransplant from the donor. As an example, risk factors for the development of PTLD were assessed in a series of 274 pediatric renal transplant recipients receiving calcineurin inhibitor, sirolimus, basiliximab and steroids (9). The prevalence of PTLD was 6.9% and the relative hazard for PTLD was 4.7-fold higher in EBV-negative versus EBV-positive children (p = 0.02). Among EBV-negative recipients with EBV-positive donors, the relative hazard increased by 6.1-fold (p = 0.0001). Similar observations have reported within renal and non renal transplant recipients in other studies (10-12). For example, in a single-center, matched case-control study among adult kidney transplant patients has showed that EBV-negative recipients have a strong risk for development of PTLD. In this study, PTLD diagnosed in twenty cases, 3-168 month after transplantation with median time of 55 month and the incidence rate of PTLD was 2.4% (10). In the lung transplant recipients have also demonstrated that EBV-negative patients are much more likely to develop PTLD compared those EBV-positive recipients (11).

According to important role of the virus, current guidelines are recommended that both the recipient and the donor candidate for kidney transplantation should be routinely tested for EBV IgG and IgM antibodies before transplantation to avoid kidney donation from seropositive donor to seronegative recipient (13). This approach is very important especially in pediatric end stage renal disease patients, who frequently are EBV –seronegative and hence more likely to be EBV infected from an EBV- seropositive organ donor (14, 15). However, there are some debates for this recommendation in the adult patients live in Iran. For example saghafi *et al.* reported that the prevalence of EBV IgG antibody is 100% among adult potential donors and recipients in Qom province. Then, they concluded that we should consider all of candidate for transplantation, positive for the virus and therefore it does not need to routinely screen all of adult donors and recipients prior to transplantation (16). The results of our study are different and its prevalence among general population in khuzestan province by the time they reach adulthood is not very high compared to some other provinces in Iran and only about half of all the healthy people (donors) and

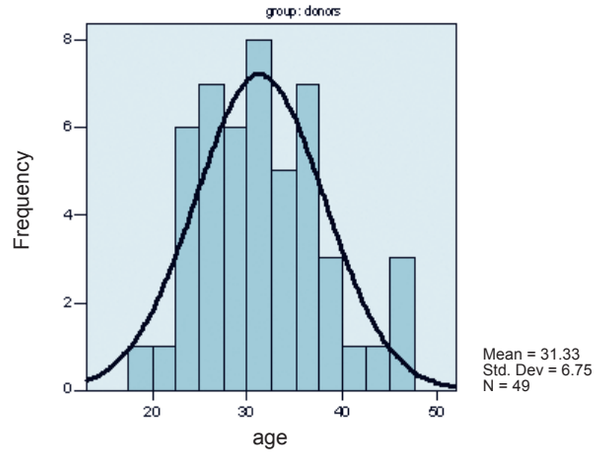

Figure 1. Age distribution of donors

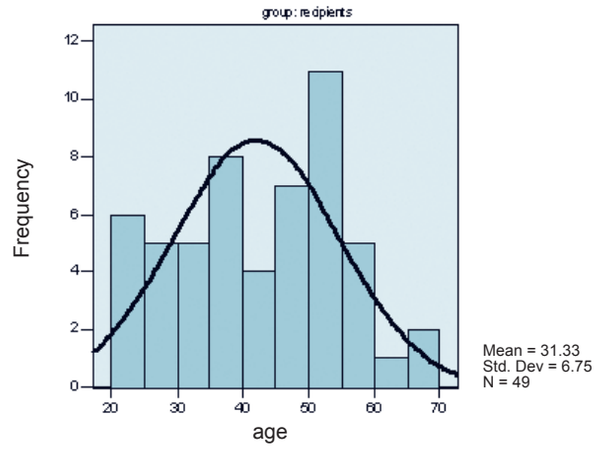

Figure 2. Age distribution of recipients

two-thirds of recipients have IgG anti-EBV antibodies in the plasma and therefore if we don't perform above screening method, some of EBV-negative recipients may be EBV infected from an EBV- positive organ donor. The prevalence of EBV infection in our province is also lower than other countries. As an example, John L Sullivan *et al.* are reported that "Antibodies to EBV have been demonstrated in all population groups with a worldwide distribution; approximately 90 to 95 percent of adults are EBV-seropositive" (17). Jeffrey I Cohen is also reported that "by adulthood, more than 90% of individuals have been infected and have antibodies to the virus" (18). Eric C. Johannsen *et al.* is also reported that " Antibodies to EBV are acquired earlier in life in developing countries than in industrialized countries, but by adulthood, more than 90% to 95% of most populations have demonstrable EBV antibodies" (19). The seroprevalence of EBV infection among donors and recipients candidate for kidney transplantation is not same in different countries and also among different provinces in Iran. As an example, in Khuzestan province only about half of donors and two-thirds of recipients have EBV IgG antibody. According to increment risk of posttransplant lymphoproliferative disorders (PTLD) among organ recipients with negative EBV serologic markers from EBV positive donors, we suggest that both the recipient and the donor candidate for kidney transplantation should be routinely tested for EBV IgG and IgM antibodies before transplantation to avoid kidney donation from seropositive donor to seronegative recipient.

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Conflict of interest

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