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The Impact of Donor Viral Replication at Transplant on Recipient Infections Posttransplant: A Prospective Study

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Abstract

Background—Organ donors are often implicated as the source of posttransplant recipient infection. We prospectively studied kidney and liver donor-recipient pairs to determine if donor viral replication of cytomegalovirus (CMV), Epstein-Barr virus (EBV), and BK polyomavirus (BKV) at transplant was a risk factor for posttransplant recipient infection and disease.

Methods—Donors and recipients were studied for antibodies against CMV and EBV and for quantitative viral replication of CMV, EBV and BKV in oral washes, urine, and whole blood pretransplant. Recipient testing continued every 3 months posttransplant. Demographic and clinical data on infections and graft and subject outcomes were obtained.

Results—The 98 donor-recipient pairs included 15 liver and 83 kidney transplants (18 of whom were children). No donor had detectable CMV replication; therefore its impact on recipient CMV replication could not be analyzed. Donor EBV replication occurred in 22%, mostly in the oral wash and had no impact on posttransplant recipient EBV replication (p 0.9) or EBV viremia (p 0.6) in kidney or liver recipients. Donor BKV replication occurred in 17%, mostly in the urine and although not associated with posttransplant recipient urinary BKV replication in recipients, it was associated with BKV viremia (p 0.02), and a significantly shorter time to BKV viremia (p 0.01) in kidney recipients.

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Conclusion—Donor replication of CMV or EBV did not impact posttransplant recipient viral replication in kidney/liver transplants. Donor urinary BKV replication is associated with recipient BKV viremia in kidney transplants.

Keywords

Donor; Epstein-Barr virus; Cytomegalovirus; BK virus; Viral Replication; Solid-organ Transplant

Introduction

Viral infections cause substantial morbidity after solid organ transplantation including graft loss and death. Cytomegalovirus (CMV), Epstein-Barr virus (EBV) and BK polyomavirus (BKV) are the viruses most often implicated in posttransplant tissue-invasive disease. Even sub-clinical CMV and/or EBV infections are associated with graft dysfunction (1–3). Recipients at highest risk for CMV or EBV disease are those previously unexposed to the virus pretransplant (antibody negative = R−) who receive an organ from an antibody-positive donor (D+) (4, 5). These and other studies suggest that the donor is the source of CMV and/or EBV for many solid-organ transplant recipients (6–8). The role of the donor in the transmission of BKV is less well defined.

We conducted a 4-year prospective study that investigated whether donor viral replication of CMV, EBV or BKV in the urine, oral wash or blood at the time of transplant was a risk factor for posttransplant recipient infection and disease.

Results

We studied 98 donor-recipient pairs for 224 person years [TABLE 1]. Posttransplant follow-up ranged from 72 days to 4 years (mean 2.3 years).

Effects of Donor Viral Antibody Status and Viral Replication on Posttransplant Infection

Forty-three (44%) and 93 (95%) donors and 43 (44%) and 75 (78%) recipients were CMV and EBV antibody-positive respectively prior to transplant. When the analysis was restricted to adult recipients, the proportion of CMV and EBV antibody positivity was similar to donors. Samples for detection of CMV, EBV and BKV at the time of transplant were available for 95 donors and for all recipients.

There were 19 and 17 donor-recipient pairs that were discordantly D+ and R− for CMV and EBV respectively and all were kidney transplant pairs. D+ was associated with increased recipient replication and viremia for CMV and EBV [TABLE 2]. In fact, there was no EBV viral replication or viremia in the 3 recipients of EBV antibody-negative donors (D−).

CMV Replication in Donors and Recipients

None of the donors had detectable CMV replication at the time of transplant [TABLE 3].

Two kidney recipients (2%) had detectable CMV replication at transplant: one in oral wash (200 copies/mL) and one in whole blood (200 copies/mL). None of the liver recipients had detectable CMV replication before or posttransplant.

CMV viral replication patterns for pretransplant recipients and donors were not significantly different (p 0.6). Posttransplant, 21 (21%) kidney recipients had a positive CMV viral load. Recipient CMV viremia was significantly greater posttransplant than pretransplant (p<0.001). CMV replication was significantly higher post-kidney than post-liver transplant (p 0.02). CMV replication in urine and oral wash was rare. Since pretransplant recipient and donor CMV replication was rare, its impact on posttransplant recipient CMV replication could not be analyzed. Fifteen recipients developed CMV disease requiring active reduction of immunosuppression and antiviral therapy. Nine were D+R−, 4 D+R+ and 2 were D−R+; 8 had detectable CMV replication posttransplant (7 in blood).

Posttransplant recipient CMV replication did not have a significant impact on death-censored graft survival (DCGS) (DCGS at 1 and 3 years in patients with posttransplant CMV viremia was 100% and 100% and in patients without posttransplant CMV viremia was 100% and 99% respectively; p 0.6) or recipient survival (patient survival at 1 and 3 years in patients with posttransplant CMV viremia was 94% and 83% and in patients without posttransplant CMV viremia was 97% and 96% respectively; p 0.2).

EBV Replication in Donors and Recipients

Twenty-one donors (22%) had a positive EBV viral load. Twenty had EBV in the oral wash (50–183,200 copies/mL) and 2 had viremia (1300 and 2000 copies/mL, respectively) with and without a positive viral load in the oral wash. There was no EBV DNA in donor urine samples [TABLE 3].

Of the 83 kidney and 15 liver recipients, 28 (34%) and 5 (33%) had a positive EBV viral load at the time of transplant respectively. Almost all EBV replication in these cases were detected in the oral wash, one subject had viruria and 2 subjects had isolated low grade EBV viremia.

EBV viral replication patterns for pretransplant recipients and donors were not significantly different (p 0.1).

Posttransplant, 34 (38%) recipients had a positive EBV viral load. Posttransplant EBV replication rates and patterns in kidney and liver recipients were not significantly different (p 0.13). Pre-transplant recipient EBV replication did not impact the rate of post-transplant EBV replication in oral wash (p 0.4) or viremia (p 0.4) in kidney or liver recipients. Recipient EBV viremia was significantly greater posttransplant than pretransplant (p <0.001).

Detectable *donor* EBV replication did not affect the incidence of posttransplant EBV replication in the oral wash (p 0.4) or EBV viremia (p 0.4) in kidney or liver recipients [TABLE 4] nor was the time to EBV viremia associated with donor EBV replication (p 0.5). Two subjects developed EBV disease, one of whom subsequently was diagnosed with posttransplant lymphoproliferative disorder (PTLD) and died; neither had donors with detectable EBV replication although both were D+R− for EBV.

Neither donor nor posttransplant recipient EBV replication had a significant impact on DCGS (p 0.3) or recipient survival (p 0.9). Our analysis was inadequately powered but there appeared to be no association between donor EBV replication and recipient viral disease.

BKV Replication in Donors and Recipients

Seventeen (18%) donors had BKV in the urine (800–9,056,000 copies/mL), 1 of whom also had viremia (1,300 copies/mL) [TABLE 3].

Ten (12%) kidney recipients had BKV in the urine (900–102,900 copies/mL) at transplant. Five (33%) liver recipients had detectable BKV replication at the time of transplant: 3 in the urine (300–121,100 copies/mL) and 2 in the blood (21,880–358,800). Pretransplant recipient and donor BKV replication patterns were not significantly different (p 0.2).

Posttransplant, 33 (34%) recipients had a positive BKV viral load [TABLE 2] with no significant difference between kidney and liver recipients (p 0.5). Post-kidney transplant urinary BKV replication was significantly higher than pretransplant (p 0.004) [even after excluding recipients that underwent native nephrectomy before (n=8) or at transplant (n=4) (p 0.01)], but not for liver transplants (p 0.5). Recipient BKV viremia was significantly greater posttransplant than pretransplant (p <0.001). Kidney recipients replicating BKV pretransplant were significantly more likely to have posttransplant urinary BKV replication (p 0.03) but not BKV viremia (p 0.5). Pretransplant BKV replication in liver recipients had no impact on BKV viremia or urinary replication.

Donor BKV replication was not associated with posttransplant recipient urinary BKV replication in kidney (p 0.12) or liver recipients (p 0.55), but was associated with increased posttransplant BKV viremia in kidney recipients (p 0.02) [TABLE 4]. We were unable to discern whether the BK viruria was from the native kidneys or the donor kidney. Of the 12 recipients that had native nephrectomies before or at transplant, 5 recipients had post-transplant BKV urinary replication (2 had donors with a positive BK viral load) and 3 had viremia post-kidney transplant (2 had donors with a positive BK viral load). Time to BKV viremia in the kidney recipients was significantly shorter if their donors had detectable BKV replication (p 0.01) [FIGURE 1] with 6 month BKV viremia free survival of 71% vs. 95% in recipients of donors with and without detectable BKV replication. Eleven subjects were clinically diagnosed with BKV-related disease but there were no biopsy-proven cases of BKV nephropathy. None of the 11 required immunosuppression reduction and only 3 had donors that were replicating virus at transplant.

Neither donor nor posttransplant recipient BKV replication had a significant impact on death-censored graft survival or recipient survival.

Co-infection in Donors and Recipients

EBV antibody-positive recipients were significantly more likely to be CMV antibody-positive than EBV antibody-negative recipients even when the analysis was restricted to pediatric recipients (p 0.01). Eight (8%) of 98 recipients were replicating EBV and CMV posttransplant: one died suddenly 3 months posttransplant (40,000 copies of CMV/mL

whole blood and 5,000 copies of EBV/mL whole blood). The cause of death was not apparent at autopsy.

Donor replication of EBV and BKV was almost mutually exclusive: donors that had detectable EBV replication rarely had positive BKV replication (1/21) and donors that had detectable BKV rarely had positive EBV replication (1/17) (p=0.07). But the converse was true of post-transplant recipients in whom detectable BKV replication occurred in recipients with EBV replication (20/37=54%) more often than in those without EBV replication (13/61=21%) (p=0.001).

Detectable BKV replication posttransplant occurred in recipients with CMV replication (3/21=14%) less often than without (30/77=39%) (p=0.03). One patient with CMV disease had a simultaneous diagnosis of BKV nephropathy.

Discussion

While donor replication of CMV or EBV at transplant did not increase the risk of posttransplant infection or disease, finding BKV in donor urine at transplant was associated with an increased incidence of BKV viremia (p 0.02), and a shorter time to BKV viremia (p 0.01).

The occurrence of BKV nephropathy in kidney but not liver recipients suggests that BKV infection originates in the donor organ though this is not well defined (9, 10). In an immunocompetent person, BKV is thought to colonize the urinary tract and establishes latency (11). We provide evidence that the transplanted kidney and ureter are likely the source of posttransplant recipient BKV infection supported by the fact that BKV viruria/ viremia was not observed in liver recipients posttransplant whose donors were replicating BKV. In keeping with our finding, Barzon *etal.* showed that the cumulative proportion of subjects BKV viremia free in the first year posttransplant was significantly decreased if the pre-implantation graft biopsy, preservation and washing solutions contained BKV DNA (12). High BKV-specific antibody titers in donors (possibly representing recent BKV exposure / higher graft load) and detection of BKV infection within 5 days of transplantation are risk factors for BKV nephropathy in kidney recipients (13). Therefore, the association of donor BKV replication and posttransplant recipient BKV viremia is likely due to tropism of BKV for the kidney and the high BKV antibody prevalence in healthy adult (14, 15) kidney donors. While the lack of BKV antibody data in our study is unfortunate, BKV antibody testing is not routinely done at most centers including ours.

The increased viremia associated with donor BKV viruria was not associated with increased BKV-related disease. Because our numbers were small, a larger study is necessary to truly assess the impact of kidney donor BKV replication on BKV disease posttransplant. Pretransplant kidney recipient BK viruria was independently and significantly associated with posttransplant recipient BKV viruria (p 0.03) but not viremia. We acknowledge that our study does not allow identification of the source of BKV in recipients posttransplant – native kidneys vs. donor kidney particularly since the number of patients that had native nephrectomies at or pretransplant was small. BKV viruria in the absence of BK viremia is

not usually associated with an increased risk for BKV disease (16). Therefore, we conclude that despite the association of recipient BK viruria pre- and posttransplant, there is probably no benefit to screening recipients pretransplant for urinary BKV.

In keeping with our current understanding of CMV and EBV risk factors (4, 5), the highest risk group for post-transplant viral replication of CMV and/or EBV was D+ for the respective viruses regardless of the type of organ transplanted (17). Viral replication patterns for CMV, EBV and BKV were not significantly different for donor and recipients pretransplant suggesting that chronic kidney/liver disease did not promote active viral replication. CMV replication was not detected in any donor and rarely in recipients pretransplant. EBV replication was observed in donors (22%) and recipients (33%) pretransplant mostly in the oral wash. Oropharyngeal epithelial cells are permissive for EBV replication (18, 19), which could account for this observation. BKV has been identified in the urine of immunocompetent subjects (20), which is consistent with our observation of almost exclusive BKV replication in the urine of healthy donors (18%) and recipients (12%) pretransplant.

Donor replication of BKV and EBV was almost mutually exclusive. In a study of 30 EBV antibody-positive healthy adults with documented EBV oral replication, blood, urine and oral wash samples tested every 2 months for 14 months were negative for BKV replication (21). The significance and mechanism responsible is unclear particularly since we did not make this observation in the recipients pretransplant. Could there be a mechanism whereby EBV replication protects healthy adults from BKV replication and vice versa? CMV viremia was associated with a decreased incidence of BKV reactivation in kidney transplant recipients in a recent study and while the authors proposed it could be due to reduction in immunosuppression (22); this could have been due to an ongoing protective CD8+ lymphocyte response activated by the preceding CMV (23). Perhaps a similar mechanism could explain our findings.

Posttransplant, recipients with EBV replication were more likely to replicate BKV than recipients without EBV replication (p 0.001) and recipients with posttransplant CMV replication were also more likely to have a positive BKV viral load (p 0.03). The increased likelihood of co-infection could merely represent the overall state of immunosuppression of the recipient or may be the result of the immunosuppressive effects of CMV and EBV (24–26). Or it could mean that some individuals have certain Class-1 HLA-antigens responsible for presenting virus to CD8+ lymphocytes that are less effective in presenting some viral antigens than others. We were unable in our small cohort to identify a predominant cluster/cross-reacting group of Class I HLA antigens that appeared in those with any of the viremias to suggest a defect in presentation in those individuals.

Immunosuppression had the obvious effect and viremia was significantly greater posttransplant for all 3 viruses ($p < 0.001$) as was BK viruria in kidney recipients (p 0.004). Posttransplant CMV replication was greater in kidney than liver recipients (p 0.02) likely representing the increased immunosuppression utilized in kidney recipients. However for EBV and BKV, posttransplant replication was not significantly different for liver and kidney transplant.

As stated above, donor replication of CMV or EBV at transplant did not increase the risk of posttransplant infection or disease. Since EBV is known to establish latency in B cells, it seems reasonable that the mode of donor-recipient transmission of virus in organ transplantation is via circulating blood cells within the transplanted organ. The prevalence of EBV DNA in the preservation and washing solutions has been shown to be similar to the blood in healthy blood donors (12) and since the blood and oral compartments are separate, donor oral EBV replication (a known aspect of latent EBV infection in healthy adults (27)) may not cause transmission of infection to the recipient. However, recipients of the 2 donors who were replicating EBV in their blood at the time of transplant did not have EBV DNA in their blood, urine or oral wash at any time posttransplant. This does not rule out the transmission of EBV via the infected blood within the organ since the virus could be latent within the transplanted organ without overt recipient viral replication.

Replication of CMV, EBV and/or BKV in recipients posttransplant had no significant impact on death-censored graft survival, patient survival or viral disease free survival. Our findings are contrary to previous publications that suggest a negative impact of these viruses on graft and patient outcome (1, 2). However, the number of subjects with viral disease in our cohort was small and our analysis was inadequately powered to be definitive. In addition, it is important to recognize that the difference in susceptibility to viral replication alone vs. virus organ penetration and infection may be due to the net level of immunosuppression or genetic susceptibility and could account for the differences in the negative impact these viruses have on outcomes.

In conclusion, testing living donors for EBV or CMV viral replication at transplant did not predict posttransplant viral transmission. However, it may be worthwhile to monitor urinary BKV replication in kidney transplant donors with increased vigilance posttransplant for BKV viremia in the recipients of donors replicating BKV. This will allow early identification of BKV infection and stepwise reduction of immunosuppression which has been shown to effectively curtail BKV viremia and replication in the kidney allograft (28, 29).

Materials and Methods

Study Design

All subjects receiving their first kidney or liver from a living donor were consecutively enrolled pretransplant and followed for as long as 4 years from December 1st, 2008 to December 1st, 2011. Donors and recipients were studied at transplant for the presence of IgG antibodies against CMV and EBV, and for quantitative viral replication of CMV, EBV and BKV in oral washes, urine, and ethylenediamine tetraacetic acid (EDTA) anti-coagulated whole blood. Viral load samples were collected from recipients approximately every 3 months posttransplantation for upto 49 months posttransplant. All recipients received antiviral prophylaxis with valganciclovir (450mg daily if creatinine clearance was 40–60mL/min; 900mg daily if clearance was >60mL/min; or 15mg/kg in children with maximum dose of 900mg daily depending on creatinine clearance) for at least 3 months. CMV antibody negative, or EBV antibody negative pediatric recipients of EBV antibody

positive organ donors received 12 months of prophylaxis. CMV or EBV antibody negative adult recipients of antibody positive organ donors received 6 months of prophylaxis.

Demographic and clinical data on infections, graft and subject outcomes were obtained from the database of prospectively recorded demographics and outcomes data for all kidney and liver transplants performed at the University of Minnesota. Induction and maintenance immunosuppression was almost identical in all the patients. Kidney transplant recipients received Thymoglobulin induction and an anti-metabolite (azathioprine or mycophenolate), a calcineurin inhibitor (tacrolimus or cyclosporine) and steroids if under 5 years of age and steroid avoidance (6 days) if over 5 years of age while liver transplant recipients received Basilimab induction with mycophenolate, steroid avoidance (5 days to 1 month) and tacrolimus. This study was approved by the Research Subjects Protection Program of the University of Minnesota (IRB # 0804M31463) and informed consent was obtained from donors and their recipients before participation.

Quantitative viral DNA assays

Viral DNA was extracted from the samples using the QIAamp® DNA minikit (QIAGEN, Inc, Valencia, CA). CMV, EBV, and BKV viral loads were measured by real-time quantitative TaqMan PCR assays, all of which were developed and validated by our research and diagnostic virology laboratories.

Viral antibody tests

CMV IgG and EBV VCA IgG antibodies were measured by semiquantitative enzyme immunoassays (EIAs) performed with the manual method according to the manufacturer's (Diamedix Corporation, Miami, FL) instructions. Specimens, calibrators and controls tested for EBV VCA IgG antibodies were pre-diluted 1:21; those for CMV IgG and were pre-diluted 1:101 prior to placing them in the test wells.

Data gathering, data coordination, and statistics

The following data were evaluated:

1. Donor and recipient baseline CMV and EBV antibody status at transplant.
2. Recipient serial measurements of CMV, EBV, and BKV viral loads treated as categorical variables. A positive viral load was defined as: CMV, ≥100 copies/mL of sample; EBV, ≥200 copies/mL of sample; and BKV, ≥500 copies/mL of sample.
3. All physician-initiated treatment of viral disease was recorded. Viral replication was considered positive if there was a viral load in urine, oral wash or blood. CMV disease was defined as CMV DNA in the blood (viremia) on ≥2 occasions plus clinical and pathological confirmation of CMV end-organ disease. EBV disease was defined as EBV viremia plus evidence of EBV in a tissue biopsy or radiologic demonstration of mass lesion(s) consistent with EBV disease. BKV disease was a pathologic diagnosis of BKV nephropathy from a kidney biopsy.

Donor and recipient demographics (age, race and gender) and virology data were analyzed. Pearsons χ^2 test of association was used to assess the association between donors who were

actively replicating CMV, EBV or BKV at the time of transplant and posttransplant recipient viral replication of the respective virus. Actuarial viremia-free survival rates were computed by the Kaplan-Meier method. Viremia-free survival was compared between recipients with and without donors who were actively replicating virus at transplant using log-rank analysis. Statistical significance was set at a p value <0.05, two sided. All statistical analyses were performed using STATA 11.0 software (STATA Corporation, College Station, TX, USA).

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List of Abbreviations

BKV	BK polyomavirus
CMV	Cytomegalovirus
EBV	Epstein Barr virus
EDTA	Ethylenediamine tetraacetic acid
EIAs	Enzyme immunoassays
PTLD	Posttransplant lymphoproliferative disorder

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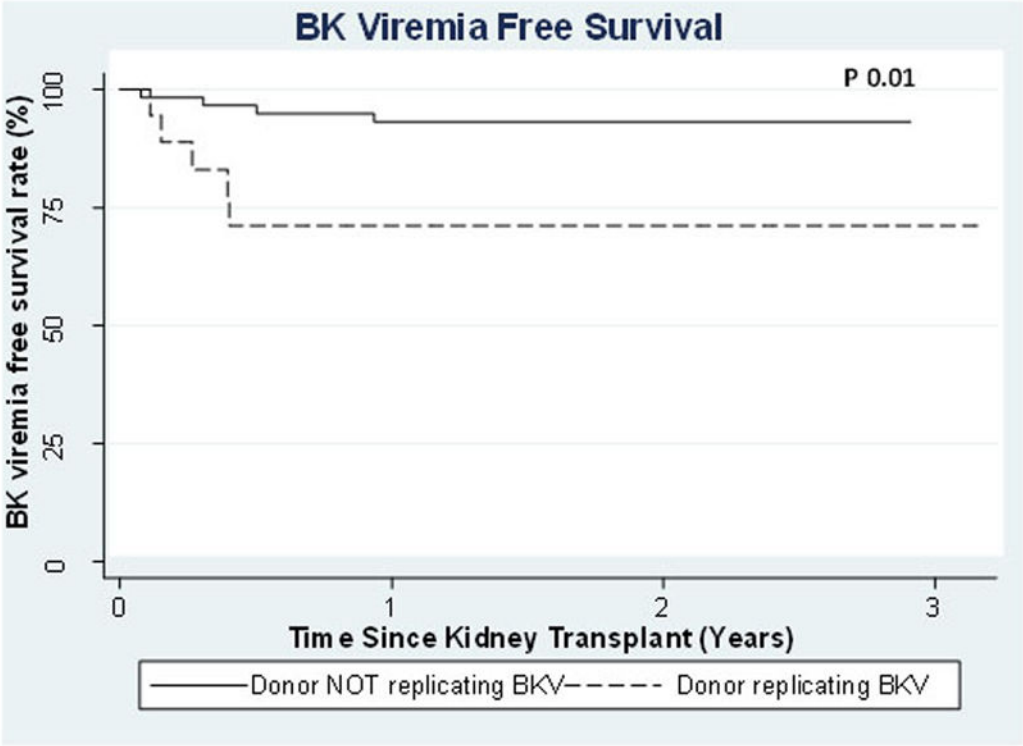

Figure 1.

TABLE 1

Demographics of 98 Living Donor/Recipient Pairs Studied

Characteristic	Number of Subjects or Mean Value
Type of transplant	
Kidney	83
Liver	15
Pediatric transplants (all kidney)	18
Donors	
Living Related	52
Living Unrelated	46
Recipient Characteristics	
Mean age in years (range)	42.8 (1.2–73.3)
Females	23
Ethnicity:	
Caucasian	87
African American	7
Asian	3
American Indian	1
Donor Characteristics	
Mean age in years (range)	40.8 (15.8–65.1)
Females	60
Ethnicity:	
Caucasian	91
African American	5
Asian	2
Donor Recipient Pretransplant Antibody Status for CMV	
D+R+	26
D+R−	17
D−R+	17
D−R−	38
Donor Recipient Pretransplant Antibody Status for EBV	
D+R+	74
D+R−	19
D−R+	2
D−R−	3
Total number of donor samples tested	957
Total number of recipient samples tested	4390

Characteristic	Number of Subjects or Mean Value
Mean number of samples tested/donor (range)	10±3.3 (0–12)
Mean number of samples tested/recipient (range)	45±20.4 (10–84)
Mean follow up time in days/recipient (range)	835±380 (72–1485)

TABLE 2

Posttransplant Recipient CMV and EBV Replication Stratified by Pretransplant Donor-Recipient Antibody Status for the Corresponding Virus

Donor Recipient Serology	KIDNEY (n=83)				LIVER (N=15)			
	EBV viral replication in urine/oral wash post-tx (p 0.8)	EBV viremia post-tx (p 0.09)	CMV viral replication in urine/oral wash post-tx (p 0.2)	CMV viremia post-tx (p 0.02)	EBV viral replication in urine/oral wash post-tx (p 0.8)	EBV viremia post-tx (p 0.8)	CMV viral replication in urine/oral wash post-tx	CMV viremia post-tx
D+R−	5/19 (32%)	8/19 (42%)	1/17 (12%)	6/17 (35%)	0	0	0	0
D+R+	16/61 (33%)	10/61 (16%)	1/23 (9%)	8/23 (35%)	2/13 (15%)	2/13 (15%)	0/3 (0%)	0/3 (0%)
D−R+	0/1 (0%)	0/1 (0%)	2/13 (8%)	3/13 (23%)	0/1 (0%)	0/1 (0%)	0/4 (0%)	0/4 (20%)
D−R−	0/2 (0%)	0/2 (0%)	0/30 (0%)	1/30 (3%)	0/1 (0%)	0/1 (0%)	0/8 (0%)	0/8 (25%)

TABLE 3

Quantitative Viral Replication in Urine, Oral Wash, and Blood at Transplant and Posttransplant among 98 Donor and Recipient Pairs

VIRUS	Donors at Transplant (Samples available in 95/98)	KIDNEY (N=83)		LIVER (N=15)	
		Recipients at Transplant	Recipients Posttransplant	Recipients at Transplant	Recipients Posttransplant
	Number (quantitative range in copies/mL)				
EBV					
- Any site	21 (22%)	28 (34%)	34 (41%)	5 (33%)	3 (20%)
- Oral wash	21 (50–183,200)	26 (100–6,115,000)	26 (200–1,844,700)	5 (200–125,700)	2 (1,700–13,600)
- Urine	0	1 (11,900)	1 (800)	0	0
- Whole blood	2 (1300–2000)	2 (200)	18 (200–52,800)	0	2 (300–46,300)
CMV					
- Any site	0	2 (2%)	21 (25%)	0 (0%)	0
- Oral wash	0	1 (200)	5 (200–300)		0
- Urine	0	1 (200)	0		0
- Whole blood	0	0	18 (100–388,600)		0
BKV					
- Any site	17 (17%)	10 (12%)	29 (35%)	1 (7%)	4 (27%)
- Oral wash	0	0	0	0	0
- Urine	17 (800–9,056,000)	10 (900–102,900)	25 (400–≥10,000,000)	1 (102,900)	2 (300–121,100)
- Whole blood	1 (1300)	0	12 (300–1,575,000)	0	2 (21,880–358,800)

TABLE 4

Quantitative Viral Replication in Urine, Oral Wash, and Blood in Donors at Transplant and Recipients Posttransplant among 98 Donor and Recipient Pairs [*], [**]

AT TRANSPLANT	POST-TRANSPLANT			
KIDNEY (N=83)				
Donor EBV replication in Blood/Urine/Oral Wash	*Recipient EBV Replication in Urine/Oral Wash*		*Recipient EBV viremia*	
Positive (n=21)	4 (19%)	p 0.45	6 (29%)	p 0.38
Negative (n=62)	17 (27%)		12 (19%)	
Donor BKV replication in Blood/Urine/Oral Wash	*Recipient BKV Replication in Urine/Oral Wash*		*Recipient BKV viremia*	
Positive (n=15)	7 (47%)	p 0.12	5 (33%)	p 0.02[***]
Negative (n=68)	18 (26%)		7 (10%)	
LIVER (N=15)				
Donor EBV replication in Blood/Urine/Oral Wash	*Recipient EBV Replication in Urine/Oral Wash*		*Recipient EBV viremia*	
Positive (n=1)	0	p 0.69	0	p 0.69
Negative (n=14)	2 (14%)		2 (14%)	
Donor BKV replication in Blood/Urine/Oral Wash	*Recipient BKV Replication in Urine/Oral Wash*		*Recipient BKV viremia*	
Positive (n=2)	0	p 0.55	0	p 0.55
Negative (n=13)	2 (15%)		2 (15%)	

[*] There was no donor replication of CMV and therefore its impact on recipient CMV viral replication/viremia could not be demonstrated

[**] Only 2 donors had EBV viremia and 1 donor had BKV viremia. Therefore the impact of donor EBV and BKV viremia on recipient viral replication is not shown separately. The kidney recipients of the donor that had isolated EBV viremia as well as of the donor that had isolated BKV viremia at the time of transplant did not have posttransplant BKV replication in urine/oral wash or blood.

[***] $p<0.05$ is considered significant