LETTER TO THE EDITORS

The incidence of hepatitis B coinfection after deceased-donor kidney transplantation from hepatitis C infected donors to hepatitis C negative recipients

Makoto Tsujita[1,2,3], Ambreen Azhar[1,2], Kiran Joglekar[4], Manish Talwar[1,2], Vasanthi Balaraman[1,2], Anshul Bhalla[1,2], James D. Eason[1,2] & Miklos Z. Molnar[5]

1 James D. Eason Transplant Institute, Methodist University Hospital, Memphis, TN, USA
2 Division of Transplant Surgery, Department of Surgery, University of Tennessee Health Science Center, Memphis, TN, USA
3 Department of Kidney Transplantation, Masuko Memorial Hospital, Aichi, Japan
4 Division of Gastroenterology, Department of Medicine, University of Tennessee Health Science Center, Memphis, TN, USA
5 Division of Nephrology & Hypertension, Department of Medicine, University of Utah, Salt Lake City, Utah, USA
E-mail: miklos.molnar@hsc.utah.edu

Dear Editors,

The incidence of kidney transplant from hepatitis C virus-infected (HCV+) donors to HCV negative (HCV-) recipients is rising due to the availability of highly effective direct-acting antiviral agents (DAA) with high cure rates above 95% [1, 2]. Kidney transplants from HCV infected donors have similar outcomes than noninfected organs [3] hence use of these organs should be optimized to minimize the current organ shortage [4]. These donors might be at high risk for hepatitis B virus (HBV) coinfection. To prevent this transmission, 2020 Public Health Service guideline (PHS) recommends testing for HBV using nucleic acid test (NAT) 4–6 weeks post-transplantation [5]. However, the risk of HBV co-transmission after transplantation of kidneys from HCV infected donors remains unknown. The most recent US PHS Guideline identified this knowledge gap and called for data regarding HBV co-transmission in recipients who received HCV-infected kidneys [5].

From March 2018 to May 2020, a total of 100 kidney transplants from HCV infected donors to HCV negative recipients were performed James D. Eason Transplant Institute, Methodist University Hospital, Memphis, TN. Among 100 recipients, 77 were hepatitis B surface antibody (HBsAb) positive, 7 were anti-Hepatitis B core (HBc) antibody-positive and all recipients were hepatitis B surface antigen (HBsAg) negative at the time of pre-transplant evaluation. Ninety-nine patients with detectable HCV RNA were started on a DAA regimen (glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, or sofosbuvir/ledipasvir). All patients had negative HCV ribonucleic acid levels at 12 weeks after completion of DAA therapy and achieved sustained virologic response [3, 6]. Table 1 summarizes the HBV laboratory markers before and after kidney transplantation. HBV coinfection was defined as newly developed HBsAg or HBV deoxyribonucleic acid (DNA) or anti-HBc positivity after transplantation. None of the recipients from donors (n = 5) who were anti-HBc positive and HBs antigen negative donors, developed new HBV infection. From the 95 recipients, whose donors were received anti-HBc and HBs antigen negative, one recipient, with HBsAb level >100 IU/L before transplantation, became temporarily anti-HBc positive but remained HBV DNA negative. This recipient was receiving intravenous immunoglobulin (IVIG) treatment for de-novo donor-specific antibody at the time of detection of anti-HBc positivity. IVIG preparations are screened for transmissible infectious agents, including HBV, but passive transmission of antibody was reported. Lu et al. reported, in 870 cancer patients who received IVIG, the predicted probability of anti-HB positivity is 34% within the first week after IVIG administration and only 4% at three months [7]. In our patient, the anti-HBc became negative after completion of IVIG treatment and thought to be attributed to passive transfer of anti-HBc antibody. HBV DNA was not detected in any recipient.

Transplantation of kidneys from HCV infected donors to HCV negative recipients is safe and has very low risk of HBV coinfection. Protective HBsAb level before transplantation and strict follow-up after

doi:10.1111/tri.13877

Table 1. Hepatitis B laboratory markers in kidney transplant recipients before and after kidney transplantation

	Anti-HBc negative and HBs antigen negative donors (n = 95)		Anti-HBc positive and HBs antigen negative donors (n = 5)	
	Before Tx	After Tx	Before Tx	After Tx
Anti-HBc positive, *N* (%)	6 (6)	7 (8)[‡]	1 (20)	1 (33)[‡]
HBs antigen positive, *N* (%)	0 (0)	0 (0)[§]	0 (0)	0 (0)
HBs antibody titer, median (IQR), IU/l	53 (12 - 303)*	N/A	38 (27 - 329)	N/A
HBs antibody >10 IU/l, *N* (%)	72 (76)[†]	N/A	5 (100)	N/A
HBV DNA positive, *N* (%)	No data	0 (0)[¶]	No data	No data
Received HBV prophylaxis, *N* (%)	N/A	1 (17)**	N/A	1 (100)*[*]
Newly developed HBs antigen/HBV DNA/anti-HBc positivity	N/A	1 (1)	N/A	0 (0)

Data were presented as *N* (%) for categorical variables and median and interquartile range (IQR) for continuous variables.

*Data regarding the number of HBs antibody measurement, *N* = 94.

[†]Data regarding the number of HBs antibody measurement, *N* = 94.

[‡]Data regarding the number of anti-HBc measurement, *N* = 84.

[§]Data regarding the number of HBs antigen measurement, *N* = 92.

[¶]Data regarding the number of HBV DNA measurement, *N* = 7.

**Data regarding the number of HBV DNA measurement, *N* = 6.

[††]Data regarding the number of HBV DNA measurement, *N* = 3.

[‡‡]Data regarding the number of HBV DNA measurement, *N* = 1.

transplantation is needed to reduce the risk of HBV transmission.

Funding

The authors have declared no funding.

Conflicts of interest

Dr. Molnar has received grant/research support from Viracor, CareDx and served as advisor for Merck, CareDx and AbbVie. The rest of the authors have no conflicts of interest or disclosures.

REFERENCES

1. Afdhal N, Zeuzem S, Kwo P, *et al.* Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. *N Engl J Med* 2014; **370**: 1889.
2. Foster GR, Afdhal N, Roberts SK, *et al.* Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. *N Engl J Med* 2015; **373**: 2608.
3. Molnar MZ, Azhar A, Tsujita M, *et al.* Transplantation of kidneys from hepatitis C Virus-Infected donors to hepatitis C virus-negative recipients: one-year kidney allograft outcomes. *Am J Kidney Dis* 2020. https://doi.org/10.1053/j.ajkd.2020.10.017
4. Durand CM, Bowring MG, Thomas AG, *et al.* The drug overdose epidemic and deceased-donor transplantation in the United States: a national registry study. *Ann Int Med* 2018; **168**: 702.
5. Jones JM, Kracalik I, Levi ME, *et al.* Assessing solid organ donors and monitoring transplant recipients for human immunodeficiency virus, hepatitis B virus, and hepatitis C virus infection—US Public Health Service Guideline, 2020. *MMWR Recommendations Rep* 2020; **69**: 1.
6. Molnar MZ, Nair S, Cseprekal O, *et al.* Transplantation of kidneys from hepatitis C–infected donors to hepatitis C–negative recipients: Single center experience. *Am J Transplantat* 2019; **19**: 3046.
7. Lu H, Lok AS, Warneke CL, *et al.* Passive transfer of hepatitis B core antibody after intravenous immunoglobulin administration in patients with cancer: retrospective chart review. *Lancet Haematol* 2018; **5**: e474.