Received: 18 March 2024 | Revised: 30 April 2024 | Accepted: 11 May 2024

DOI: 10.1111/tid.14305

TRANSPLANT INFECTIOUS DISEASE

ORIGINAL ARTICLE

Hepatitis B transmission/reactivation associated with Hepatitis B core antibody and Hepatitis C nucleic acid testing positive organs: A report from the Organ Procurement and Transplantation Network Disease Transmission Advisory Committee

Helen S. Te[1] | Dong Heun Lee[2] | Ann E. Woolley[3] | Maheen Z. Abidi[4] | Cynthia Fisher[5] | Marty T. Sellers[6] | Sarah Taimur[7] | Taylor Livelli[8] | Tamika Watkins[8] | Dzhuliyana Handarova[8] | Gerald J. Berry[9] | Riki Graves[10] | Chak-Sum Ho[11] | Anna L. Hughart[12] | Michelle Kittleson[13] | Charles C. Marboe[14] | Rachel A. Miller[15] | Tanvi S. Sharma[16] | Anil J. Trindade[17] | R. Patrick Wood[18] | Lorenzo N. Zaffiri[19] | Stephanie M. Pouch[20] | Lara Danziger-Isakov[21]

Correspondence
Helen S. Te, University of Chicago Medicine, 5841 S. Maryland Ave., MC 7120, Chicago, IL 60637, USA.
Email: hte@bsd.uchicago.edu

Helen S. Te and Dong Heun Lee are the co-first authors.

Funding information
United States Department of Health and Human Services; Health Resources and Services Administration; Health Systems Bureau; Division of Transplantation, Grant/Award Number: HHSH250201900001C

Abstract

Background: Better access to direct-acting antiviral (DAA) therapy has broadened the utilization of hepatitis C virus (HCV) nucleic acid testing (NAT) positive organs with excellent outcomes. However, DAA therapy has been associated with hepatitis B virus (HBV) reactivation.

Aim: To determine the risk of HBV transmission or reactivation with utilization of HBV core antibody positive (HBcAb+) and HCV NAT positive (HCV+) organs, which presumably required DAA therapy.

Methods: The number of HBcAb+ donors with delineated HCV NAT status was obtained from the Organ Procurement and Transplantation Network (OPTN) database. The number of unexpected HBV infections from transplanted organs adjudicated as "proven" or "probable" transmission was obtained from the OPTN Ad Hoc Disease Transmission Advisory Committee database. A chart review of the donors of "proven" or "probable" cases was conducted.

Results: From January 1, 2016, to December 31, 2021, 7735 organs were procured from 3767 HBcAb+ donors and transplanted into 7469 recipients; 545 (14.5%) donors

Abbreviations: AST, American Society of Transplantation; DAA, direct-acting antiviral; DTAC, Disease Transmission Advisory Committee; HBcAb, hepatitis B core antibody; HBcAb+, hepatitis B core antibody positive; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B; HCV, hepatitis C; HCV-, hepatitis C nucleic acid testing negative; HCV+, hepatitis C nucleic acid testing positive; NAT, nucleic acid testing; OPTN, Organ Procurement and Transplantation Network.

were also HCV+. HBV transmission or reactivation occurred in seven recipients. The rate is not significantly different between recipients of HCV+ (0.18%, 2/1115) and the HCV NAT negative (HCV-) organs (0.08%, 5/6354) ($p = 0.28$) or between recipients of HCV+ and HCV- livers as well as non-liver organs. HBV transmission or reactivation occurred within a median of 319 (range, 41–1117) days post-transplant in the setting of missing, inadequate, or truncated prophylaxis.

Conclusion: HBV reactivation associated with DAA therapy for HBcAb+ HCV+ organs is less frequent than reported in the non-transplant population, possibly due to the common use of HBV prophylaxis in the at-risk transplant population.

KEYWORDS
direct-acting antiviral, donor, hepatitis B, hepatitis C, reactivation, transmission, transplant

1 | INTRODUCTION

In the previous decade, hepatitis C (HCV)-infected organs were mostly non-used or mainly utilized in HCV-infected recipients to expand the donor pool and decrease time on the transplant waitlist. When HCV-infected organs were unknowingly implanted into HCV-negative recipients, serious morbidity and mortality were reported. However, approval of the second-generation direct-acting antiviral (DAA) therapy in 2014 revolutionized HCV therapy, raising cure rates to almost 100% with manageable side effects. In turn, HCV infection as the liver transplantation indication among waitlisted individuals has progressively declined from 29.7% in 2011 to 8.3% of the liver waitlist in 2021.[1] Clinical outcomes of HCV-infected liver recipients who achieved viral eradication were also transformed, with graft survival on par with non-HCV-infected recipients.[2] These developments paved the way for the utilization of HCV-infected organs in non-HCV-infected recipients, as a means to increase access to transplantation, shorten waitlist time, and reduce waitlist mortality.[3]

Entangled in the success of DAA therapy is a risk for hepatitis B (HBV) reactivation during or after therapy. To date, three meta-analyses have assessed HBV reactivation rates with DAA therapy in non-transplant recipients, reporting HBV reactivation in 12–24% of treated patients with chronic HBV infection (i.e., individuals with positive HBV surface antigen [HBsAg+]) and 0.4%–1.4% in those with resolved HBV infection.[4–6] Furthermore, baseline HBV surface antibody (HBsAb) titers were found to significantly correlate with the reactivation risk,[4–6] while prophylactic HBV therapy significantly reduced this risk.[4,6]

Given that HCV-infected donors may also have been exposed to HBV through a shared mode of transmission, the use of HCV-nucleic acid testing (NAT) positive organs may also potentially lead to HBV reactivation during or following DAA therapy in transplant recipients. While the American Society of Transplantation (AST) guidelines emphasize the need for HBV prophylaxis in liver transplant recipients and in susceptible non-liver organ recipients who receive HBV core antibody positive (HBcAb+) organs, this recommendation is not consistently implemented by transplant centers.[7] Thus, this study aimed to determine the risk of HBV transmission or reactivation with the use of HBcAb+ and HCV NAT-positive (HCV+) organs.

2 | METHODS

The total number of HBcAb+ donors with delineated HCV NAT status from January 1, 2016, to December 31, 2021, was obtained from the Organ Procurement Transplantation Network (OPTN) database. Donors were classified into the HCV+ group and the HCV NAT negative (HCV-) group. The use of HCV+ organs was presumed to invariably require DAA therapy early in the post-transplant course to avoid the near-universal HCV transmission observed in the past.

OPTN policy requires reporting of unexpected infections that may potentially be donor-derived, including HBV infection. Using an established algorithm,[8] cases are adjudicated by the OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC) as proven, probable, or possible transmissions, or as excluded or intervention without disease transmission cases. For this study, the number of unexpected HBV infection events from transplanted organs adjudicated as "proven" or "probable" transmission from the same time period was obtained from the OPTN DTAC database. The charts of donors previously adjudicated as "proven" or "probable" cases by DTAC were reviewed to retrieve case details and assess the status of all organs transplanted from the donor.

Using redacted aggregate data, the incidence of unexpected HBV transmission or reactivation was calculated based on the total number of "proven" and "probable" cases in relation to the number of recipients of utilized HBcAb+ organs, and the rates were compared between the HCV+ and HCV- groups. HBV transmission or reactivation in recipients of liver and non-liver organs was also compared between the two groups. Fisher's exact test was used to assess the differences in proportions, and a p-value of 0.05 was considered significant.

This study used data from the OPTN. The OPTN data system includes data on all donors, wait-listed candidates, and transplant

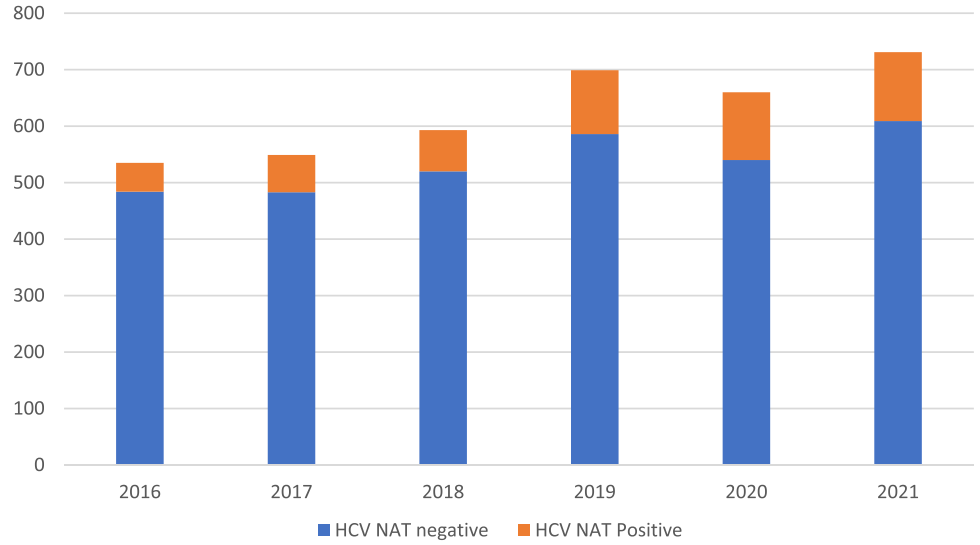

FIGURE 1 Hepatitis B core antibody positive donors by hepatitis C nucleic acid test results and year of donor recovery, 2016–2021.

recipients in the United States, submitted by the members of the OPTN. The Health Resources and Services Administration and the US Department of Health and Human Services provide oversight of the activities of the OPTN contractor.

3 | RESULTS

From January 1, 2016, to December 31, 2021, there was a total of 107,953 deceased and living donors, of whom 3860 (3.6%) were HBcAb+ positive. Of note, the number of HBcAb+ donors as well as the prevalence of positive HCV NAT results amongst HBcAb+ donors have been increasing from 2016 to 2021 (Figure 1). Of the HBcAb+ donors, 93 had indeterminate or unreported HCV NAT results and were excluded from the analysis. From the remaining 3,767 HBcAb+ donors, 7,735 organs were recovered and transplanted into 7469 recipients.

HBcAb+ donors were then classified as HCV+ (n = 545, 14.5%) and HCV- (n = 3222, 85.5%). Demographic data of both groups are shown in Table 1. HCV+ donors were younger and more commonly of male sex and white race non-Hispanic ethnicity than HCV- donors ($p < 0.00001$). They were also more likely to have a history of intravenous drug use and identifiable risk factors for bloodborne disease transmission as defined in the OPTN policy ($p < 0.00001$).

HBV transmission was defined as a positive HBsAg or HBV DNA in the recipient who previously had a negative HBsAg or HBcAb; it was also presumed to represent a reactivation of resolved HBV infection in the HBcAb+ donor in the setting of immunosuppression, absence of recipient risk factors, and use of DAA therapy in recipients. During the same period, DTAC had adjudicated HBV transmissions or reactivations as "proven" or "probable" in seven recipients who received nine organs from seven different HBcAb+ donors, of whom two were also HCV+. None of the donors had a positive HBsAg or HBV NAT, but three had a positive HBsAb, one had a negative HBsAb, and the other three

TABLE 1 Donor characteristics for hepatitis B core antibody positive donors by hepatitis C nucleic acid test results, January 1, 2016–December 31, 2021.

Donor characteristic	HCV NAT positive ($n = 545$)	HCV NAT negative ($n = 3222$)	*p*-Value
Age <50 years	350 (64%)	1,359 (42%)	<0.00001
Male sex	373 (68%)	1,726 (54%)	<0.00001
White race, non-Hispanic ethnicity	407 (75%)	1,429 (44%)	<0.00001
History of intravenous drug use	397 (73%)	503 (16%)	<0.00001
OPTN-defined risk factors for bloodborne disease transmission	426 (78%)	853 (26%)	<0.00001
Hepatitis B surface antigen-positive	4 (0.7%)	56 (1.7%)	0.09
Hepatitis B surface antibody-positive	83 (15%)	560 (17%)	0.21
Hepatitis B NAT positive	24 (4.4%)	157 (4.9%)	0.64

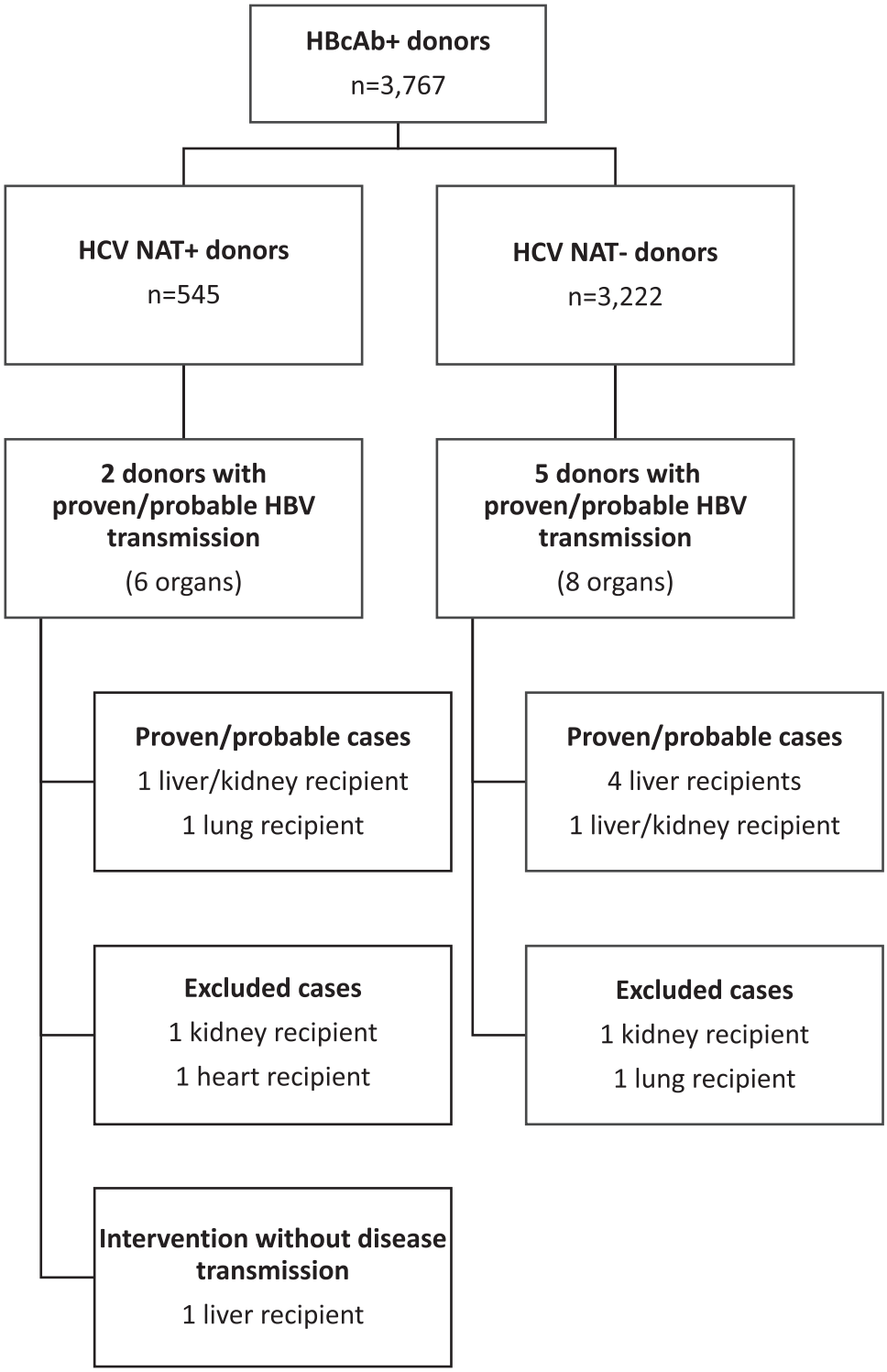

FIGURE 2 Flowchart of donors and recipients.

did not have the result reported. Further investigation into the seven donor cases revealed a total of 14 organs were recovered and transplanted into 12 recipients, of whom seven recipient cases (nine organs) were adjudicated as "proven" or ''probable, four as "excluded" and one adjudicated as "intervention without disease transmission" due to use of HBV prophylaxis (Figure 2). Five of the seven donors had a history of intravenous drug use and OPTN-defined risk factors for blood-borne disease transmission.

Of the seven recipients with "proven" or "probable" transmission or reactivations, four received a liver, two received a liver and kidney simultaneously, and one received a double lung transplant (Figure 2). Pretransplant serologies showed all recipients were HBsAg negative

TABLE 2 Hepatitis B transmission or reactivation rates per recipient according to donor hepatitis C virus (HCV) nucleic acid testing (NAT) status in hepatitis B core antibody positive donors, January 1, 2016–December 31, 2021.

	HCV NAT positive	HCV NAT negative	*p*-Value
Total recipients	2/1115 (0.18%)	5/6354 (0.08%)	0.28
Livers	1/392 (0.26%)	5/2046 (0.24%)	1
Non-liver organs	1/723 (0.13%)	0/4308 (0%)	0.14

Abbreviations: HCV, hepatitis C virus; NAT, nucleic acid testing.

and five were HBcAb negative, but HBcAb was not reported in the other two. One simultaneous liver-kidney recipient had detectable HBsAb, but five recipients had no HBsAb titers detected, and it was not reported in one. One recipient was HCV+ and received an HCV+ organ, two were HCV- and the rest had no reported HCV NAT status.

There were 1115 recipients of HCV+ organs and 6354 recipients of HCV- organs. The transmission or reactivation rate was not significantly different in the recipients of HCV+ (0.18%, 2/1115) than in the HCV- organs (0.08%, 5/6354) ($p = 0.28$). There was also no significant difference in the HBV transmission or reactivation rate with HCV+ (0.26%, 1/392) versus HCV- livers (0.24%, 5/2,046) ($p = 1$). There was only one case of HBV transmission or reactivation through an HCV+ non-liver (double lung) organ (0.13%, 1/723) and no transmission occurred through an HCV- nonliver organ (0%, 0/4308) ($p = 0.14$) (Table 2).

HBV transmission or reactivation occurred within a median of 319 (range, 41–1117) days post-transplant, all in the setting of missing ($n = 4$, 3 liver recipients and 1 lung recipient), inadequate ($n = 1$ liver/kidney recipient who received only one dose of HBV vaccine prior to transplant), or truncated ($n = 2$, 1 liver recipient and 1 liver/kidney recipient who received only 40 days and 167 days, respectively) HBV prophylaxis with a nucleoside or nucleotide analog. In the two recipients of HCV+ organs, HBV transmission or reactivation occurred in the midst of DAA therapy with either ledipasvir-sofosbuvir or velpatasvir-sofosbuvir. HBV transmission or reactivation was treated with entecavir in four recipients, with tenofovir in two, and with an unspecified drug in one. There were no graft failures or deaths resulting from HBV infection.

4 | DISCUSSION

The United States Food and Drug Administration approved the second-generation DAA for the treatment of HCV in non-transplant populations in 2014, and subsequently, there was a rapid off-label adoption of the drugs to treat HCV in transplant recipients. The new regimen was not only highly effective in the transplant population, but it was also devoid of the significant adverse effects of prior interferon-based therapy that included a risk of graft rejection in non-liver transplant recipients. This ground-breaking success in HCV cure led to the concept of utilizing HCV-infected donors for uninfected candidates on the transplant waitlist to expand the donor pool and decrease the time from listing to transplantation. This hypothesis was first formally investigated in kidney transplant recipients, where a 100% cure rate was observed with DAA therapy started early in the post-transplant period[9] and DAA prophylaxis started prior to transplantation was successful in preventing HCV transmission.[10] With extrapolated data from these pilot studies, the practice gained traction in other solid organ transplantations as well.[7,11] Today, HCV infection in donors, with the exception of the presence of advanced fibrosis in livers, is no longer believed to affect the quality of the transplanted organ. Given the near-universal cure rates of the DAA therapy, HCV transmission through transplanted organs is not expected to impact the post-transplant clinical outcome as well.

In 2016, case reports and case series of HBV reactivation during DAA therapy emerged in the literature,[12,13] initially creating controversy on the cause and effect. HBV reactivation is now a recognized complication of DAA therapy that may occur during or after the completion of therapy. The mechanism of HBV reactivation in the setting of HCV eradication is not clear, but a common hypothesis is that HBV replication is suppressed by HCV co-infection. In a humanized mouse model, HCV clearance by DAA therapy was accompanied by a downregulation of the RIG-I-like helicase system, which in turn reduced hepatic interferon response and subsequently allowed HBV replication.[14]

Practice guidelines of the American Association for the Study of Liver Diseases, the European Association for the Study of the Liver, and the Asian Pacific Association for the Study of the Liver recommend routine screening for hepatitis B exposure prior to DAA therapy and monitoring for reactivation in at-risk individuals.[15–17] The risk of HBV reactivation during DAA therapy has been quantified by three meta-analyses to be substantial at 12%–24% of treated patients with active HBV infection, although this is lower at 0.4%–1.4% in those with resolved HBV infection.[4–6] In the current study, the HBV transmission or reactivation rate per recipient in the setting of DAA therapy was similar to those without DAA therapy, even when the liver is the organ transplanted. It is also lower than that observed with DAA therapy in the non-transplant population, and this may be due to the use of appropriate HBV prophylaxis in the transplant recipients when the donor serologies indicated the intervention. In a randomized-controlled trial, HBV prophylaxis with entecavir was shown to be effective in preventing HBV reactivation during DAA therapy of HBV and HCV co-infected individuals.[18] Other studies have also demonstrated that the risk for and timing of occurrence of HBV reactivation in the setting of DAA therapy is inversely correlated with the HBsAb titer levels.[4–6,19] Thus, prophylaxis with a nucleotide or nucleoside analog and/or effective immunization against HBV can provide protection against HBV transmission or reactivation in transplant recipients.

The incidence of donor-derived HBV transmission in solid organ transplant recipients, in general, is quite rare, but transmissions do still occur despite routine HBV screening of donors and guidelines recommendations for HBV prophylaxis in at-risk individuals.[20] The 2020 OPTN DTAC report noted that 52% of HBV transmissions occurred

from donors who had negative HBV serologies, which makes it difficult to administer prophylactic measures. In organs from donors who were HBcAb positive, the risk was highest with livers and transmission occurred mostly in the absence of HBV prophylaxis.[7] In this study, the liver was also the most commonly involved organ and all HBV transmissions or reactivations occurred in the setting of missing, inadequate, or truncated prophylaxis. In addition, only one recipient had evidence of HBV immunity prior to transplant. Both scenarios reflect missed opportunities for potential prevention of HBV transmission or reactivation, despite guidelines and policies that recommend both prophylaxis and vaccination.[20,21] The AST guidelines on viral hepatitis recommend long-term nucleos/tide analog prophylaxis for non-HBV-infected recipients of livers from HBcAb+ donors. Prophylaxis is typically administered indefinitely, although a recent study suggested that it can be safely withdrawn in specific patients who are more than a year from liver transplantation and have developed sustained HBsAb titers of at least 100 IU/L.[22] Similarly, prophylaxis for up to 1 year post-transplant is recommended for non-HBV-immune recipients of non-liver organs from HBcAb+ donors.[20] However, it is noteworthy that HBV transmission has been low at 0.3% in kidney recipients of HBcAb+ organs,[23,24] even in the absence of HBV prophylaxis and with only 40% of the recipients having detectable HbsAb[24]. Nonetheless, OPTN policy 15.2 requires the transplant candidates' HBV vaccination status to be reported and suggests HBV vaccination to be initiated or completed for susceptible candidates prior to transplantation if feasible,[25] a strategy that is also recommended by the AST guidelines.[20]

In the 2020 OPTN DTAC report, HBV transmission or reactivation occurred at a median of 362 days from transplant, with 32% occurring beyond 3–6 months.[7] This focused study had a few overlapping cases with the 2020 OPTN DTAC report, where a similarly long interval from transplant to detection of infection was observed as well, with diagnosis occurring at a median of 319 days. The delayed diagnosis may potentially be due to a small amount of viral inoculation at the time of transplant which may take time to become clinically evident, truncation of HBV prophylaxis after which transmission occurs, or the short time interval prescribed for screening in the past that may have allowed transmission to go undetected until it becomes symptomatic. Due to the identified lag time in prior studies, the Center for Disease Control and Prevention recommended testing for HBV infection up to 1 year after transplant, even if previous tests were negative.[26] This recommendation has been adopted for liver recipients in the OPTN policy in 2021.[21]

This study is limited by several factors, the most prominent one being the inherent deficiencies that come with the use of a redacted database where relevant details are not consistently available and the need to present aggregate data only. Secondly, the incidence of HBV reactivation or transmission in the setting of DAA therapy was based on the number of unexpected HBV transmissions reported to DTAC. While reporting of suspected donor-derived disease is mandated by OPTN policy, this may not necessarily be recognized and strictly followed by transplant centers, leading to a potential underestimation. Publication of DTAC reports, such as this, can potentially raise awareness and promote better compliance. Thirdly, recipients themselves may have had occult HBV infection that escaped detection by routine pretransplant serologies or they may have had contracted HBV infection after transplantation, although risk factors for such are taken into consideration by DTAC during adjudication. To decrease the likelihood of false positives, cases that were adjudicated as "possible" transmissions were not included in the analysis. Finally, utilization of HBV prophylaxis, as would be indicated by the implantation of an organ from an HBcAb+ donor into an at-risk recipient, can prevent HBV transmission. This appropriate intervention can result in an underestimation of the true risk of HBV reactivation with DAA therapy in this population, as HBV prophylaxis is not routinely utilized with DAA therapy in the non-transplant population.

In conclusion, HBV transmission or reactivation associated with DAA therapy of HBcAb+ and HCV+ organs is infrequent in transplant recipients, likely due to the common use of HBV prophylaxis in the at-risk transplant population. However, there remains room to improve the use of HBV vaccination in all transplant candidates and/or adequate HBV prophylaxis in at-risk recipients, measures that are key to preventing HBV transmission or reactivation.

AFFILIATIONS

[1]Center for Liver Diseases, Chicago, Illinois, USA

[2]Division of Infectious Diseases, University of California San Francisco Medical Center, San Francisco, California, USA

[3]Division of Infectious Diseases, Boston, Massachusetts, USA

[4]Division of Infectious Diseases, Denver, Colorado, USA

[5]Division of Allergy & Infectious Diseases, Seattle, Washington, USA

[6]Tennessee Donor Services, Nashville, Tennessee, USA

[7]Division of Infectious Diseases, Mt. Sinai Medical Center, New York, New York, USA

[8]United Network for Organ Sharing, Richmond, Virginia, USA

[9]Department of Pathology, Stanford University Medical Center, Stanford, California, USA

[10]Sherrie and Alan Conover Center for Liver Disease & Transplantation, Houston Methodist Hospital, Houston, Texas, USA

[11]Gift of Hope Organ & Tissue Donor Network, Itasca, Illinois, USA

[12]William J. von Liebig Center for Transplantation and Clinical Regeneration, Mayo Clinic, Minnesota, Minnesota, USA

[13]Cardiology Department, Cedars Sinai Medical Center, Los Angeles, California, USA

[14]Department of Pathology and Cell Biology, New York Presbyterian Hospital/Columbia University Medical Center, New York, New York, USA

[15]Division of Infectious Diseases, Duke University School of Medicine, Durham, North Carolina, USA

[16]Division of Infectious Diseases, Boston Children's Hospital, Boston, Massachusetts, USA

[17]Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA

[18]LifeGift Organ Donation Center, Houston, Texas, USA

[19]Division of Pulmonary and Critical Care Medicine, Cedars-Sinai Medical Center, Los Angeles, California, USA

[20]Division of Infectious Diseases, Emory University School of Medicine, Atlanta, Georgia, USA

[21]Division of Infectious Diseases, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

ACKNOWLEDGMENTS

This work was funded by the US Department of Health and Human Services, Health Resources and Services Administration (HRSA), Health Systems Bureau, Division of Transplantation under contract number HHSH250201900001C, and was conducted under the auspices of the United Network for Organ Sharing (UNOS), the contractor for the Organ Procurement and Transplantation Network (OPTN). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the OPTN or the US Government.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Helen S. Te https://orcid.org/0000-0002-3172-6184
Maheen Z. Abidi https://orcid.org/0000-0002-0783-6535
Sarah Taimur https://orcid.org/0000-0002-1776-7510
Gerald J. Berry https://orcid.org/0000-0002-6176-2629
Anil J. Trindade https://orcid.org/0000-0003-1399-7228
Stephanie M. Pouch https://orcid.org/0000-0002-5628-2444
Lara Danziger-Isakov https://orcid.org/0000-0002-5691-5221

REFERENCES

1. Kwong AJ, Ebel NH, Kim WR, et al. OPTN/SRTR 2021 annual data report: liver. *Am J Transplant*. 2023;23(2 Suppl 1):S178-S263. doi:10.1016/j.ajt.2023.02.006
2. Cotter TG, Paul S, Sandikci B, et al. Improved graft survival after liver transplantation for recipients with hepatitis C virus in the direct-acting antiviral era. *Liver Transpl*. 2019;25(4):598-609. doi:10.1002/lt.25424
3. Wang JH, Gustafson SK, Skeans MA, et al. OPTN/SRTR 2018 annual data report: hepatitis C. *Am J Transplant*. 2020;20(Suppl s1):542-568. doi:10.1111/ajt.15679
4. Jiang XW, Ye JZ, Li YT, Li LJ. Hepatitis B reactivation in patients receiving direct-acting antiviral therapy or interferon-based therapy for hepatitis C: A systematic review and meta-analysis. *World J Gastroenterol*. 2018;24(28):3181-3191. doi:10.3748/wjg.v24.i28.3181
5. Mucke MM, Backus LI, Mucke VT, et al. Hepatitis B virus reactivation during direct-acting antiviral therapy for hepatitis C: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. 2018;3(3):172-180. doi:10.1016/S2468-1253(18)30002-5
6. Oh JH, Park DA, Ko MJ, et al. Direct-acting antivirals and the risk of hepatitis B reactivation in hepatitis B and C co-infected patients: a systematic review and meta-analysis. *J Pers Med*. 2022;12(12):1957. doi:10.3390/jpm12121957
7. Woolley AE, Singh SK, Goldberg HJ, et al. Heart and lung transplants from HCV-infected donors to uninfected recipients. *N Engl J Med*. 2019;380(17):1606-1617. doi:10.1056/NEJMoa1812406
8. Theodoropoulos NM, La Hoz RM, Wolfe C, et al. Donor derived hepatitis B virus infection: analysis of the Organ Procurement & Transplantation Network/United Network for Organ Sharing Ad hoc Disease Transmission Advisory Committee. *Transpl Infect Dis*. 2021;23(1):e13458. doi:10.1111/tid.13458
9. Reese PP, Abt PL, Blumberg EA, et al. Twelve-month outcomes after transplant of hepatitis C-infected kidneys into uninfected recipients: a single-group trial. *Ann Intern Med*. 2018;169(5):273-281. doi:10.7326/M18-0749
10. Durand CM, Bowring MG, Brown DM, et al. Direct-acting antiviral prophylaxis in kidney transplantation from hepatitis c virus-infected donors to noninfected recipients: an open-label nonrandomized trial. *Ann Intern Med*. 2018;168(8):533-540. doi:10.7326/M17-2871
11. Cotter TG, Paul S, Sandikci B, et al. Increasing utilization and excellent initial outcomes following liver transplant of hepatitis C virus (HCV)-viremic donors into HCV-negative recipients: outcomes following liver transplant of HCV-viremic donors. *Hepatology*. 2019;69(6):2381-2395. doi:10.1002/hep.30540
12. Aggeletopoulou I, Konstantakis C, Manolakopoulos S, Triantos C. Risk of hepatitis B reactivation in patients treated with direct-acting antivirals for hepatitis C. *World J Gastroenterol*. 2017;23(24):4317-4323. doi:10.3748/wjg.v23.i24.4317
13. Lieber SR, Fried MW. Controversies in hepatitis C therapy: Reactivation of hepatitis B virus. *Clin Liver Dis*. 2017;10(4):87-92. doi:10.1002/cld.665
14. Murai K, Hikita H, Kai Y, et al. Hepatitis C virus infection suppresses hepatitis B virus replication via the RIG-I-like helicase pathway. *Sci Rep*. 2020;10(1):941. doi:10.1038/s41598-020-57603-9
15. Bhattacharya D, Aronsohn A, Price J, Lo Re V, Panel A-IHG. Hepatitis C guidance 2023 Update: AASLD-IDSA recommendations for testing, managing, and treating hepatitis C virus infection. *Clin Infect Dis*. 2023. doi:10.1093/cid/ciad319
16. European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C: final update of the series☆. *J Hepatol*. 2020;73(5):1170-1218. doi:10.1016/j.jhep.2020.08.018
17. Kanda T, Lau GKK, Wei L, et al. APASL HCV guidelines of virus-eradicated patients by DAA on how to monitor HCC occurrence and HBV reactivation. *Hepatol Int*. 2019;13(6):649-661. doi:10.1007/s12072-019-09988-7
18. Cheng PN, Liu CJ, Chen CY, et al. Entecavir prevents HBV reactivation during direct acting antivirals for HCV/HBV dual infection: a randomized trial. *Clin Gastroenterol Hepatol*. 2022;20(12):2800-2808. doi:10.1016/j.cgh.2021.11.032
19. Poola S, Sanaka S, Sewell K, Tillmann HL. Hepatitis B surface antibody titres and hepatitis B reactivation with direct-acting antiviral therapy for hepatitis C. *J Viral Hepat*. 2021;28(2):373-382. doi:10.1111/jvh.13421
20. Te H, Doucette K. Viral hepatitis: guidelines by the American Society of Transplantation Infectious Disease Community of Practice. *Clin Transplant*. 2019;33(9):e13514. doi:10.1111/ctr.13514
21. Organ Procurement and Transplant Network. OPTN policies, Policy 15.3.C. 2024. Accessed January 21, 2024. Available from: https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf
22. Busebee B, Myhre L, Mara K, Aqel B, Taner T, Watt KD. De novo hepatitis B infection following liver transplantation with core antibody positive grafts: the role of surface antibody status in guiding long-term prophylaxis. *Clin Transplant*. 2024;38(2):e15263. doi:10.1111/ctr.15263
23. Mahboobi N, Tabatabaei SV, Blum HE, Alavian SM. Renal grafts from anti-hepatitis B core-positive donors: a quantitative review of the literature. *Transpl Infect Dis*. 2012;14(5):445-451. doi:10.1111/j.1399-3062.2012.00782.x

24. Wang XD, Liu JP, Song TR, et al. Kidney transplantation from hepatitis B surface antigen (HBsAg)-positive living donors to HBsAg-negative recipients: clinical outcomes at a high-volume center in China. *Clin Infect Dis*. 2021;72(6):1016-1023. doi:10.1093/cid/ciaa178
25. Organ Procurement and Transplant Network. OPTN Policies, Policy 15.2. 2024. Accessed January 21, 2024. Available from: https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf
26. Bixler D, Annambhotla P, Montgomery MP, et al. Unexpected hepatitis B virus infection after liver transplantation—United States, 2014–2019. *MMWR Morb Mortal Wkly Rep*. 2021;70(27):961-966. doi:10.15585/mmwr.mm7027a1

How to cite this article: Te HS, Lee DH, Woolley AE, et al. Hepatitis B transmission/reactivation associated with Hepatitis B core antibody and Hepatitis C nucleic acid testing positive organs: A report from the Organ Procurement and Transplantation Network Disease Transmission Advisory Committee. *Transpl Infect Dis*. 2024;e14305. https://doi.org/10.1111/tid.14305