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Posttransplant HBV Vaccine Compliance, Seroprotection, and Kinetics of Hepatitis B Surface Antibody in Thoracic Organ Transplant Recipients

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ABSTRACT

Introduction: Vaccination is crucial to the thoracic solid organ transplant (SOT) population to reduce vaccine-preventable infection. However, data on posttransplant hepatitis B virus (HBV) vaccination compliance and vaccine-induced seroprotection are lacking.

Methods: We conducted a retrospective study of adult thoracic organ (heart and lung) transplant recipients at Mayo Clinic sites in Minnesota, Arizona, and Florida between January 2018 and August 2023. Recombivax HB was used before 2020, and Heplisav-B was preferred after 2020. Recipients with posttransplant hepatitis B surface antibody (HBsAb) < 10 IU/L were eligible for the HBV vaccine. HBV seroprotection was defined as an HBsAb ≥ 10 IU/L.

Results: A total of 1116 recipients were evaluated, all of whom underwent posttransplant HBsAb testing. Of these, 751 (67%) had an HBsAb level < 10 IU/L and were eligible for posttransplant HBV vaccination. Of the eligible recipients, 117 (16%) completed the HBV vaccine series during the study period. Among these 117 recipients, 40 (34%) had their HBsAb levels rechecked after completing the vaccine series, with a seroprotection rate of 37.5% (15/40). There was no statistically significant difference in the seroprotection rates between Heplisav-B and Recombivax HB vaccines (39% [13/33] vs. 29% [2/7]; $p = 0.691$). In addition, HBsAb levels were lowest at week 2 but rebounded at week 4 posttransplant and pretransplant HBsAb levels of ≥100 IU/L ensured 5-year seroprotection.

Conclusion: Suboptimal compliance with HBV vaccination and poor vaccine-induced seroprotection occur in thoracic organ transplant recipients, regardless of the vaccine used. These findings underscore the necessity of enhancing vaccination strategies for SOT recipients.

1 | Introduction

Solid organ transplant (SOT) candidates and recipients are more susceptible to infections and have an increased risk of infectious complications compared to the general population [1, 2]. Consequently, every effort should be made to ensure that SOT candidates and recipients receive recommended vaccines to mitigate these risks of vaccine-preventable disease [1, 2]. Pretransplant hepatitis B virus (HBV) vaccination is emphasized for SOT candidates as it can prevent HBV acquisition, which can have worse outcomes in immunosuppressed individuals [3]. Developing immunity to HBV may also broaden the pool of potential HBV-infected donors [3, 4]. However, a previous study from our institution noted that the completion rate of the HBV vaccine series pretransplantation was low, at 47% among thoracic organ transplant recipients [5]. The suboptimal compliance rate with the HBV vaccine series may be attributed to the urgency of thoracic organ transplantation, which can lead to an incomplete vaccination series [5].

Given that SOT candidates may either not complete the required vaccinations pretransplant or not achieve HBV seroprotection in real-world practice, studying posttransplant vaccination becomes crucial [5]. In the posttransplant period, studies have reported compliance rates and factors affecting vaccination adherence for influenza, pneumococcal, and Coronavirus Disease 2019 (COVID-19) vaccines [6, 7]. Our institution previously reported that SOT recipients residing in southeast Minnesota exhibited a compliance rate of 56% for the influenza and pneumococcal vaccines [6]. Other transplant centers have reported an 83% compliance rate for the COVID-19 vaccine (primary 3-dose series) among SOT recipients [7]. However, data regarding HBV vaccination after transplantation are scarce. This study examines the posttransplant HBV vaccine compliance rate and vaccine-induced seroprotection in thoracic organ transplant recipients. In addition, we also report a small series of early and late hepatitis B surface antibody kinetics in thoracic organ transplant recipients.

2 | Methods

2.1 | Participants and Data Collection

We conducted a retrospective study from January 1, 2018 to August 31, 2023 at Mayo Clinic sites in Arizona, Florida, and Minnesota, including all adult patients (age > 18 years) who underwent heart or lung transplantation (thoracic organ transplantation). Routine induction regimen and maintenance immunosuppression vary from organs and centers (Tables S1 and S2). During the study period, lung transplants were not performed at Mayo Clinic in Arizona. The patients were identified from a well-maintained institutional transplant database. All variables were manually extracted from the electronic medical records, including baseline demographics, HBV serology, vaccine history, and outcomes. Donors or recipients with HBV infection (i.e., hepatitis B surface antigen or hepatitis B core antibody positive) were excluded from this study. The practices of pretransplant HBV vaccination, along with factors associated with pretransplant vaccine compliance and seroprotection rate in thoracic organ transplant recipients at our institution, have been reported [5]. This study focuses on the posttransplant period using the same dataset.

2.2 | Definitions

Serum samples were tested for hepatitis B surface antibody (HBsAb) using the VITROS anti-HBs quantitative assay (Ortho Clinical Diagnostics, NJ, USA), with a quantification range of 0–1,000 IU/L. According to the Centers for Disease Control and Prevention (CDC) definition, an HBsAb ≥ 10 IU/L 1–2 months after the HBV vaccine series was considered seroprotective [8]. American Society of Transplantation guidelines suggest revaccination if posttransplant HBsAb < 10 IU/L, but no specific recommendation on timing or frequency of posttransplant HBsAb evaluation is made [1]. In this study, recipients who had a posttransplant HBsAb < 10 IU/L were considered eligible for HBV vaccine series. Our study collected HBsAb data 1–6 months after posttransplant HBV vaccine completion. Obesity was defined as body mass index (BMI) ≥ 30 kg/m^2. Lymphopenia was defined as an absolute lymphocyte count < 1000 cells/μL.

2.3 | Posttransplant HBsAb Testing and HBV Vaccination

Our institution follows a posttransplant vaccination protocol that recommends initiating inactivated vaccines at least 3 to 6 months after transplantation, in alignment with the American Society of Transplantation guidelines [1]. Posttransplant HBsAb testing is ordered by our transplant providers. Subsequently, patients are referred to our institution's vaccine clinic or local providers to receive the recommended vaccines (Recombivax HB or Heplisav-B). We suggested conventional recombinant hepatitis B vaccines (Recombivax HB 40 mcg/mL, three-dose series at 0, 1, 6 months) before the year 2020 and CpG-adjuvanted recombinant hepatitis B vaccine (Heplisav-B, two-dose series at 0, 1 month) after the year 2020. Patients are encouraged to report vaccines received outside our institutions through the online patient portal. Our center's protocol for HBV management in thoracic organ transplant recipients was previously published [9].

2.4 | Outcome Measure

The primary objective was to report the posttransplant HBV vaccine compliance rate among eligible thoracic organ transplant recipients (i.e., posttransplant HBsAb < 10 IU/L) and the vaccine-induced seroprotection rate by type of vaccine given.

We aimed to examine the HBsAb trajectory of patients with HBsAb levels ≥ 10 IU/L posttransplant by completing the pretransplant HBV vaccine series. Our dataset observed that some patients underwent weekly monitoring within the first month posttransplantation (early posttransplant HBsAb kinetics) and annual monitoring for up to 5 years posttransplantation (late posttransplant HBsAb kinetics). Our secondary endpoint is to report these findings from this cohort, focusing on both early and late posttransplant HBsAb kinetics.

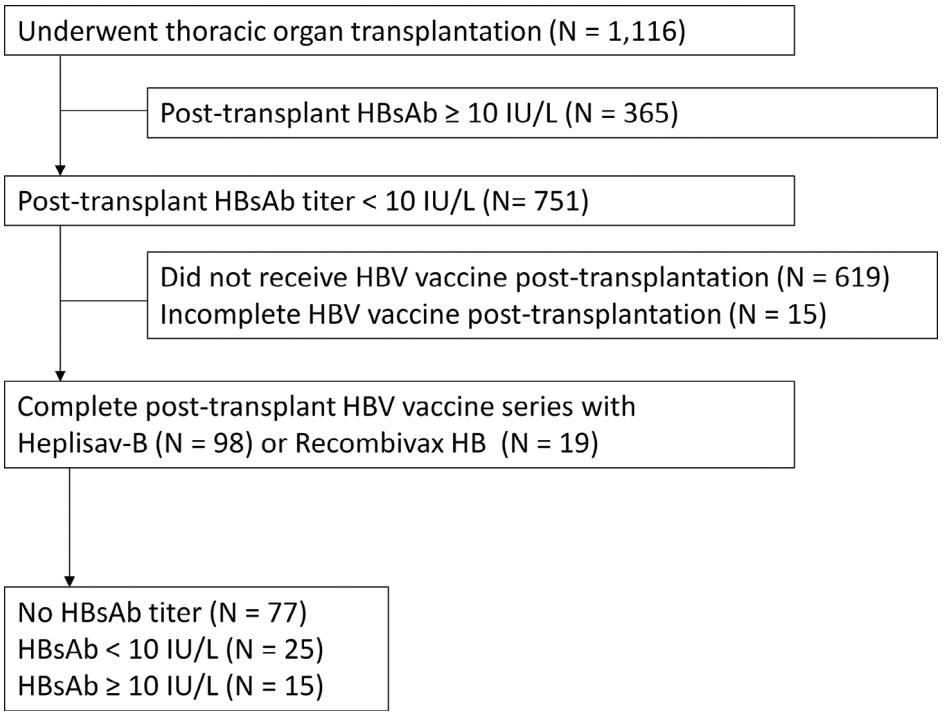

FIGURE 1 | Patient selection for this study.

Combining the insights from this study's primary and secondary outcomes will provide valuable information for developing future HBV vaccination protocols.

2.5 | Statistical Analysis

Descriptive statistics were reported as median (interquartile range [IQR]) for continuous variables and number (percentage) for categorical variables. Categorical variables were compared using Fisher's exact test, as appropriate. Continuous variables were compared using independent *t*-test or Mann–Whitney U test, as appropriate. All tests were two-sided, and $p < 0.05$ was considered statistically significant. Statistical analyses were conducted using MedCalc (version 20.027; Ostend, Belgium).

3 | Results

A total of 1116 patients underwent thoracic organ transplantation during the study period. All recipients were tested for HBsAb after transplantation. Of these, 751 recipients (67%) had HBsAb level < 10 IU/L, while 365 recipients (33%) had HBsAb level ≥ 10 IU/L (Figure 1). The median time from transplantation to the HBsAb testing was 3 months (IQR 1–6 months). The median duration of posttransplant follow-up was 40 months (IQR 24–54 months).

Among 751 recipients who had posttransplant HBsAb < 10 IU/L, most of them were male (67%), white (79%), and received heart transplantation (60%). Of these, 115 (15%) recipients completed pretransplant HBV vaccine series (73 with Heplisav-B and 42 with Recombivax HB). Seventy-five (10%) recipients had pretransplant HBsAb ≥ 10 IU/L (pretransplant HBV vaccine records were not available in 40 patients, 18 completed pretransplant Heplisav-B, and 12 completed pretransplant Recombivax HB) (Table 1). A total of 596 (79%) recipients with HbsAb < 10 IU/L posttransplant had no prior documented HBV vaccines pretransplant and expectedly had pretransplant HbsAb < 10 IU/L.

3.1 | Posttransplantation HBV Vaccine Compliance

Among the 751 recipients with a posttransplant HBsAb < 10 IU/L, 619 (82%) had no documentation of receiving any posttransplant HBV vaccine during the study period. A total of 117 (16%) recipients completed the posttransplant HBV vaccine series (Figure 1). Additional 15 (2%) recipients received only a single dose of the HBV vaccine posttransplant. Notably, of the 15 recipients who received a first dose of posttransplant Heplisav-B, none had received any pretransplant HBV vaccine, nor did they have a documented follow-up HBsAb result or a documented reason for not receiving the second dose of posttransplant Heplisav-B.

Of the 117 recipients who completed the posttransplant HBV vaccine series during the study period, 98 (84%) received Heplisav-B, and 19 (16%) received Recombivax HB (Figure 1). Among these, 34 (29%) had also completed pretransplant HBV vaccine series (Table 1). The median time from transplantation to receiving the first dose of the HBV vaccine was 11 months (IQR 4–14 months), and the median time from transplantation to completing the vaccine series was 13 months (IQR 8–18 months) (Table 1).

3.2 | HBsAb Testing After Posttransplant HBV Vaccine

Of the 117 recipients who completed the HBV vaccine series, 40 (34%) underwent HBsAb testing after series completion. Among

TABLE 1 | Demographic and clinical characteristics of thoracic organ transplant recipients with posttransplant hepatitis B surface antibody level < 10 IU/L.

	Posttransplant HBsAb ≤ 10 IU/L	Posttransplant HBV vaccine completion	Posttransplant HBV vaccine completion with HBsAb testing			
	Total *N* = 751	Total *N* = 117	Total *N* = 40	HBsAb < 10 IU/L *N* = 25	HBs Ab ≥ 10 IU/L *N* = 15	*p* value[a]
Characteristic						
Age, median year (IQR)	56 (50–65)	59 (51–66)	56 (50–66)	58 (49–66)	61 (57–67)	0.409
Male	503 (67)	79 (68)	26 (65)	15 (58)	11 (42)	0.502
Race						0.648
White	593 (79)	94 (80)	30 (75)	19 (63)	11 (37)	
African American or Black	113 (15)	15 (13)	9 (23)	6 (67)	3 (33)	
Others	45 (6)	8 (7)	1 (2)	0 (0)	1 (100)	
Organ of transplantation						1.000
Heart	450 (60)	71 (61)	26 (65)	16 (62)	10 (38)	
Lung	301 (40)	46 (39)	14 (35)	9 (64)	5 (36)	
BMI ≥ 30 kg/m^2	225 (30)	34 (29)	13 (33)	9 (69)	4 (31)	0.730
Pre-transplant HBV vaccine completion[b,c]	115 (15)	34 (29)	12 (30)	10 (83)	2 (17)	0.152
Pre-transplant HBsAb ≥ 10 IU/L	75 (10)[d]	17 (15)[e]	8 (20)	7 (88)	1 (12)	0.219
HBV vaccine after transplantation						0.691
Heplisav-B	N/A	98 (84)	33 (83)	20 (61)	13 (39)	
Recombivax HB	N/A	19 (16)	7 (17)	5 (71)	2 (29)	
From transplantation to HBsAb level testing, median months (IQR)	N/A	3 (1–6)	3 (1–6)	3 (1–6)	3 (1–7)	0.713
From transplantation to receiving the first dose HBV vaccine, median months (IQR)	N/A	11 (4–14)	10 (5–14)	11 (6–13)	8 (4–15)	0.556
First dose of HBV vaccine administration (posttransplant)						0.273
3—6 months posttransplant	N/A	36 (31)	11 (27.5)	5 (45)	6 (55)	
> 6 months posttransplant	N/A	81 (69)	29 (72.5)	20 (69)	9 (31)	
From transplantation to the completion of HBV vaccine series, median months (IQR)	N/A	13 (8–18)	12 (7–16)	12 (9–17)	9 (7–16)	0.263

(Continues)

TABLE 1 | (Continued)

	Posttransplant HBsAb ≤ 10 IU/L	Posttransplant HBV vaccine completion	Posttransplant HBV vaccine completion with HBsAb testing			
	Total *N* = 751	Total *N* = 117	Total *N* = 40	HBsAb < 10 IU/L *N* = 25	HBs Ab ≥ 10 IU/L *N* = 15	*p* value[a]
From vaccine completion to HBsAb level testing, median month (IQR)	N/A	N/A	2 (1–5)	2 (1–6)	2 (1–4)	0.819
Lymphopenia						
Lymphopenia at first dose of HBV vaccine	N/A	51 (44)	19 (48)	11 (44)	8 (53)	0.745
Lymphopenia at second dose of HBV vaccine	N/A	55 (47)	18 (45)	9 (36)	9 (60)	0.194
Lymphopenia at third dose of HBV vaccine	N/A	31 (32)[f]	11 (33)[g]	8 (40)[h]	3 (23)[i]	0.456
Induction regimen						0.233
Anti-thymocyte globulin	376 (50)	57 (49)	21 (53)	15 (71)	6 (29)	
Basiliximab	240 (32)	42 (36)	15 (38)	9 (60)	6 (40)	
Methylprednisolone	113 (15)	13 (11)	4 (10)	1 (25)	3 (75)	
Alemtuzumab	22 (3)	5 (4)	0 (0)	0 (0)	0 (0)	
Other immunosuppression						
Rituximab	10 (1)	8 (7)	3 (8)	3 (100)	0 (0)	0.279
Eculizumab	6 (0.7)	4 (3)	0 (0)	0 (0)	0 (0)	N/A
Daratumumab	5 (0.6)	3 (3)	0 (0)	0 (0)	0 (0)	N/A
Belatacept	2 (0.2)	0 (0)	0 (0)	0 (0)	0 (0)	N/A
Posttransplant complication						
Acute rejection	188 (25)	32 (27)	9 (23)	7 (78)	2 (22)	0.440
CMV viremia	278 (37)	42 (36)	16 (40)	10 (63)	6 (37)	1.000
Dialysis	195 (26)	27 (23)	11 (28)	8 (73)	3 (27)	0.486

Abbreviations: CMV, cytomegalovirus; HBsAb, hepatitis B surface antibody; HBV, hepatitis B virus; IQR, interquartile range; N/A, not applicable.

[a]*p* value compared HBsAb < 10 IU/L group and HBsAb ≥ 10 IU/L group.

[b]Completed two-dose Heplisav-B series or three-dose Recombivax HB.

[c]Completed HBV vaccine series pre-transplant did not guarantee pretransplant HBsAb ≥ 10 IU/L.

[d]A total of 75 patients with pretransplant HBsAb levels ≥ 10 IU/L had decreased levels < 10 IU/L posttransplant, making them eligible for posttransplant HBV vaccination. A total of 40 patients did not have documentation of the HBV vaccine received pretransplant, 18 completed pretransplant Heplisav-B, and 12 completed pretransplant Recombivax HB.

[e]None of these 17 patients had documentation of the HBV vaccine received pretransplant.

[f]A total of 98 patients received Heplisav-B.

[g]A total of 33 patients received Heplisav-B.

[h]A total of 20 patients received Heplisav-B.

[i]A total of 13 patients received Heplisav-B.

these, 25 recipients (62.5%) had HBsAb level < 10 IU/L (i.e., lack of seroprotection), while 15 recipients (37.5%) had HBsAb level ≥ 10 IU/L (i.e., achieved seroprotection) (Figure 1). The median time from the completion of the HBV vaccine to the subsequent HBsAb testing was 2 months (IQR 1–5 months). Subgroup analysis showed no statistically significant difference in the seroprotection rate (39% [13/33] vs. 29% [2/7], $p = 0.691$) or in the median HBsAb level (0 IU/L [IQR 0–5.5] vs. 0 IU/L [IQR 0–22]) between Heplisav-B and Recombivax HB. (Table 1).

Furthermore, analysis of recipient characteristics such as age, gender, race, transplanted organ type, obesity, pretransplant HBV vaccination, pretransplant HBV seroprotection, received the first dose of HBV vaccine within 3–6 months versus > 6 months posttransplant, lymphopenia at the time of vaccination, induction regimen, exposure to rituximab, and posttransplant complications (including acute rejection, CMV infection, and the need for dialysis) revealed no significant differences between the group with HBsAb level < 10 IU/L and the group with HBsAb level ≥ 10 IU/L (Table 1).

In a subgroup analysis of 28 recipients who exclusively received the HBV vaccine posttransplant (i.e., without pretransplant HBV vaccines or pretransplant HBsAb levels ≥ 10 IU/L), no statistically significant difference was observed in the seroprotection rates between Heplisav-B and Recombivax HB (52% [11/21] vs. 29% [2/7], $p = 0.396$).

3.3 | Early and Late HBsAb Kinetics Posttransplantation

A total of 365 recipients (33%) had HBsAb level ≥ 10 IU/L by completing the pretransplant HBV vaccine series (Figure 1). Four recipients with pretransplant HBsAb < 100 IU/L (Case 1—Case 4) had weekly HBsAb levels for 4 weeks posttransplantation (Figure 2A). The nadir of HBsAb occurred in the second week posttransplantation, and all cases had HBsAb rebound afterward. In two cases (Case 3 and Case 4), the fourth week HBsAb was higher than pretransplant HBsAb.

Seven recipients (Case 5—Case 11) had annual HBsAb levels for 5 years posttransplantation (Figure 2B). Two cases (Case 5 and Case6) with pretransplant HBSAb > 1000 IU/L maintained HBsAb > 1000 IU/L throughout follow-up. In two cases (Case 7 and Case 8) with pretransplantation HBsAb 100–1000 IU/L, HBsAb continued to decline over time but remained ≥ 100 IU/L at 5 years posttransplantation. Three cases (Case 9—Case 11) with pretransplantation HBsAb 10–100 IU/L lost seroprotection at 5 years posttransplantation. The characteristics of these patients are in Table S3.

4 | Discussion

To our knowledge, this study is the first to report compliance rates with the posttransplant HBV vaccine and seroprotection rate among thoracic organ transplant recipients. We found that both the completion rate (16%) of the HBV vaccine series and the seroprotection rate (37.5%) in the posttransplant period are lower than those reported in the pretransplant period, where both rates are approximately 50% according to reference studies [3, 5, 10]. Although Heplisav-B is more effective than the recombinant HBV vaccine in healthy individuals and people living with human immunodeficiency virus [11, 12], our preliminary findings were not powered to detect a significant difference in the seroprotection rate between Heplisav-B series and Recombivax HB series (39% [13/33] vs. 29% [2/7], $p = 0.691$) in thoracic organ transplant recipients who completed HBV vaccine posttransplant.

SOT recipients require several post-transplant vaccines [1], which can be categorized into three groups in clinical practice: (i) vaccines that need to be repeated periodically, such as tetanus/diphtheria/pertussis vaccine every 10 years or the influenza vaccine annually; (ii) vaccines that require only the primary series without subsequent monitoring of immune response, like the shingles vaccine; and (iii) vaccines that required both the primary series and ongoing immune response monitoring, such as the HBV vaccine, which is more labor-intensive than (i) and (ii). Other factors also lead to low uptake of the posttransplant HBV vaccine. First, the availability of various HBV vaccines and lack of clear guidance on the most cost-effective option for SOT recipients [1, 8]. Second, while SOT recipients are more susceptible to infectious conditions, the incidence of HBV acquisition is relatively low compared to the risks of other vaccine-preventable illnesses [2, 13, 14]. Third, recipients may be receiving a variety of antirejection immunosuppressive therapies that are not suitable for vaccination. Fourth, the COVID-19 pandemic has disrupted HBV immunization [15]. Consequently, this poses a challenge for clinicians in determining the priority of HBV vaccination and may be perceived as a low priority in the posttransplant setting.

A previous study reported that the pre-transplant HBV vaccine completion rate is approximately 50% [5, 10]. In contrast, our study found that the posttransplant HBV vaccine completion rate is even lower, at only 16%. Among thoracic organ transplant candidates during the pretransplant period, the vaccine-induced seroprotection rate was approximately 50% with the conventional HBV vaccine and 75% with Heplisav-B [3, 5, 16, 17]. In our study, the posttransplant vaccine-induced seroprotection rates were 39% (13/33) for the Heplisav-B group and 29% (2/7) for the Recombivax HB group. Therefore, compliance rates with HBV vaccination seroprotection appear better during pretransplant than posttransplant. However, completing the HBV vaccine series prior to transplantation presents practical challenges, including the urgency of transplantation in critically ill patients, the waitlist duration at transplant centers, and vaccine hesitancy (either delay in acceptance or refusal of vaccines) [18]. Heplisav-B, requiring only two doses one month apart, demonstrates improved compliance in thoracic organ transplant candidates compared to the three-dose Recombivax HB, as shown by our center's experience with pretransplant HBV vaccine compliance [5], warranting further stewardship on its potential advantages in posttransplant populations.

Vaccine-induced immune responses in SOT recipients are suboptimal compared to healthy individuals, and the optimal timing for posttransplant vaccination remains to be determined [1]. Most transplant centers initiate vaccination approximately 3–6 months posttransplant when steady immunosuppression levels

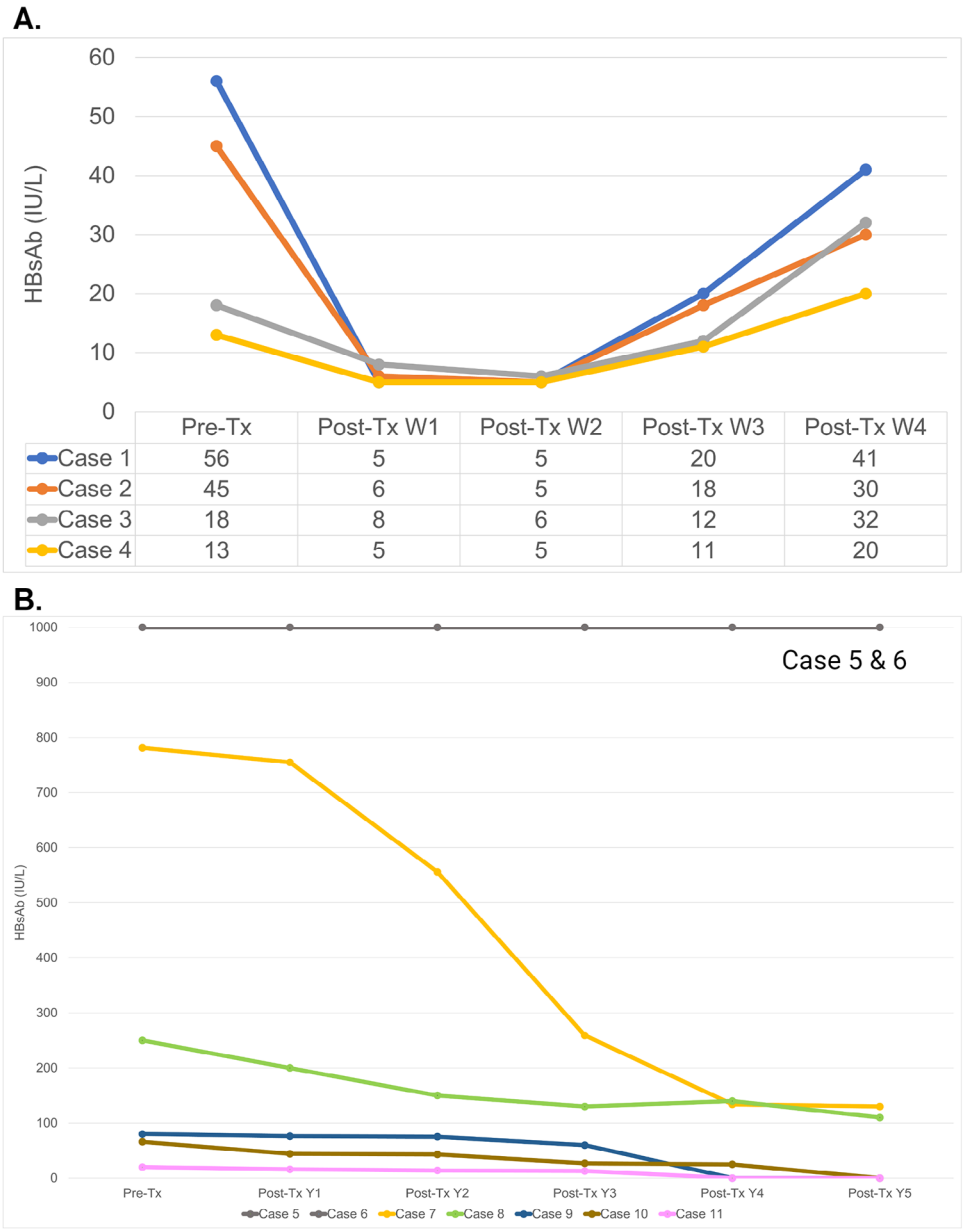

FIGURE 2 | (A) Weekly HBsAb follow-up posttransplantation for 4 weeks. (B) Annual HBsAb follow-up for 5 years posttransplantation.

are attained [1]. In our study, there was no statistically significant difference in seroprotection rates when the first dose of the HBV vaccine was administered within 3–6 months versus > 6 months posttransplantation. On the other hand, there is considerable variability in the timing from transplantation to HBsAb testing (IQR 1–6 months) and from transplantation to the administration of the first dose HBV vaccine (IQR 4–14 months) in this study, highlighting the current variation in the timing of vaccination in clinical practice.

HBsAb levels decrease over time, and the disappearance of HBsAb does not necessarily imply a loss of HBV immunity in fully vaccinated individuals [19]. Studying the efficacy of post-transplant HBV vaccination may not be feasible, as the incidence of HBV infection is rare [2]. In our study, among the recipients eligible for the posttransplant HBV vaccine, only 15% had completed the pretransplant HBV vaccine series. Additionally, 10% had pretransplant HBsAb levels ≥ 10 IU/L, yet most (40/75, 53%) had no vaccination records. This highlights the current era's practical difficulties in obtaining lifelong vaccine records for SOT candidates. A practical approach might involve simply obtaining HBsAb and recommending HBV vaccination based solely on these results when vaccine records are not readily available, as additional immunization poses no risk [20]. Currently, the CDC recommends annual HBsAb surveillance and HBV vaccine booster if HBsAb levels < 10 IU/L in patients on hemodialysis, but routine HbsAb monitoring recommendations have not been established in other immunocompromised populations and depend on anticipated HBV exposure risk [20].

In our study, 10 patients completed the HBV vaccine series both pre and posttransplant but did not achieve HBV seroprotection (Table 1). Although HBsAb is one of the simplest endpoints for assessing HBV vaccine efficacy, the definition, associated

factors, and management of HBV vaccine nonresponders in the SOT population are not well-established and remain poorly studied. It is worth noting that the disappearance of HBsAb does not necessarily indicate a loss of HBV immunity in fully vaccinated, immunocompetent individuals. This is due to the preservation of vaccine-induced HBV immune memory through the selective expansion and differentiation of antigen-specific B and T lymphocyte clones [19].

In our small series of patients with frequent measure HBsAb, we found (1) HBsAb levels were lowest at week 2 but rebounded at week 4 posttransplant (Figure 2A); (2) Pretransplant HBsAb levels of ≥100 IU/L ensured 5-year seroprotection (Figure 2B), whereas HbsAb < 100 IU/mL should be considered for closer monitoring of HbsAb levels 3–5 years posttransplant and booster dosing if seroprotection is lost. Due to the limited sample size, a thorough analysis of how immunosuppression affects the loss of HBV seroprotection wasn't feasible. While identifying the specific effects of immunosuppression on long-term seroprotection may be of limited clinical significance, monitoring HBsAb levels provides a direct and practical approach for clinicians to determine the need for an HBV vaccine booster for those with ongoing perceived risk of HBV infection. Subsequent studies should focus on delineating the trajectory of HBsAb levels across a broader cohort, while the current study suggests > 100 IU/L is a reasonable target for pretransplantation seroprotection without evidence of seroprotection loss after transplant [5].

There are several limitations in this study. First, we could not thoroughly examine the predictors (such as maintenance immunosuppression and different lymphocyte thresholds) of vaccine-induced seroprotection in the posttransplant period due to the small sample size of patients with available post-vaccine HBsAb. More extensive trials are needed to directly compare the efficacy between Heplisav-B and Recombivax HB in the posttransplant population. Second, other factors that may influence HBV serology results include intravenous immunoglobulin, which can cause false positive results [21], and plasmapheresis, which can remove HBsAb. Therefore, HBsAb levels should be interpreted cautiously in this context. Third, there is a possibility that some patients who received the recommended vaccines from local providers did not report these vaccinations to us, which could lead to an underestimation of the vaccine compliance rate. Fourth, our study included all thoracic organ transplant recipients with HbsAb < 10 IU/L in posttransplant settings regardless of pretransplant HBV vaccine receipt or HbsAb measurements. However, we did not see any interaction with pretransplant HBV vaccine receipt or pretransplant HbsAb > 10 IU/L with posttransplant HBV seroprotection after receipt of posttransplant HBV vaccine.

In conclusion, regardless of the vaccine used, we observed suboptimal posttransplant HBV vaccine compliance and poor vaccine-induced seroprotection in thoracic organ transplant recipients. This study's findings emphasize the need to explore alternative posttransplant HBV vaccination strategies to improve compliance and seroprotection offered with current vaccine guidance. Based on the findings of our prior study combined with this study [5], we recommend completing a full HBV vaccine series before transplantation in the thoracic organ transplant population.

Author Contributions

Chia-Yu Chiu: conceptualization, methodology, software, data curation, investigation, formal analysis, writing – original draft. **Priya Sampathkumar:** writing – review & editing. **Lisa M Brumble:** writing – review and editing. **Holenarasipur R. Vikram:** writing – review and editing. **Kymberly D. Watt:** writing – review and editing, supervision. **Elena Beam:** supervision, writing – review and editing, conceptualization.

Ethics Statement

The journal's ethical policies, as noted on the journal's author guidelines page, have been adhered to. The Mayo Clinic Institutional Review Board reviewed the study protocol and granted it an exempt status (study number 23–009119).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

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

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.