International Journal of Research in Medical Sciences
Aljaafary RA et al. Int J Res Med Sci. 2026 Sep;14(9):3730-3739
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20262796

Original Research Article

Post-vaccination hepatitis B seroprotection among kidney transplant recipients in Saudi Arabia: a retrospective cohort study

Rakan A. Aljaafary*, Mohammed A. Abdulmogith, Ammar H. S. Abbas

Department of Preventive Medicine, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

Received: 15 June 2026
Revised: 29 July 2026
Accepted: 04 August 2026

***Correspondence:**
Dr. Rakan A. Aljaafary,
E-mail: Al_kasr_003@hotmail.com

ABSTRACT

Background: Evidence regarding post-vaccination hepatitis B virus (HBV) seroprotection among kidney transplant recipients in Saudi Arabia remains limited. This study estimated the prevalence of seroprotection and evaluated factors associated with vaccine nonresponse.
Methods: This single-center retrospective cohort study included adult kidney transplant recipients followed at Prince Sultan Military Medical City, Riyadh, Saudi Arabia, who had documented hepatitis B vaccination and subsequent quantitative measurement of antibodies to hepatitis B surface antigen (anti-HBs). Seroprotection was defined as an anti-HBs concentration of at least 10 mIU/ml. Participant characteristics were compared according to seroprotection status. Multivariable logistic regression was used to evaluate associations between non-seroprotection and total number of hepatitis B vaccine doses.
Results: Among 100 kidney transplant recipients, the mean (SD) age was 41.4 (15.2) years, and 66 participants (66.0%) were male. Overall, 69 recipients achieved seroprotection (69.0%; 95% CI, 59.4-77.2%), whereas 31 (31.0%) remained non-seroprotected. Vaccine dose category differed significantly by seroprotection status (p=0.014); 80.6% of non-seroprotected recipients had received only 1 to 2 doses compared with 50.7% of seroprotected recipients. In the adjusted model, no variable was independently associated with non-seroprotection. Each 10-year increase in age was associated with higher, but not statistically significant, odds of non-seroprotection (aOR, 1.44; 95% CI, 0.96-2.16; p=0.079).
Conclusions: Nearly one-third of vaccinated kidney transplant recipients lacked serological protection against HBV. Routine post-vaccination anti-HBs testing and individualized booster or revaccination strategies should be considered, particularly for older recipients and those who have received fewer vaccine doses.

Keywords: Hepatitis B vaccination, Seroprotection, Kidney transplantation, Anti-HBs antibodies, Vaccine nonresponse

INTRODUCTION

Hepatitis B virus (HBV) infection remains a major cause of preventable liver-related morbidity and mortality worldwide. The World Health Organization estimated that approximately 254 million people were living with chronic HBV infection in 2022, with about 1.2 million new infections occurring annually. Viral hepatitis caused an estimated 1.3 million deaths in 2022, most attributable to cirrhosis and hepatocellular carcinoma, and HBV accounted for the majority of this mortality burden.[1] Despite the availability of effective vaccines and antiviral treatment, progress toward the global elimination of viral hepatitis remains insufficient, particularly among populations with impaired immunity or recurrent exposure to health-care procedures.

Saudi Arabia historically had an intermediate-to-high endemicity of HBV infection. The introduction of universal infant hepatitis B vaccination in 1989–1990, together with screening of donated blood and improved infection-control practices, produced a substantial decline in HBV infection among younger generations.[2,3] Nevertheless, HBV continues to impose a clinically

important burden in the Kingdom, particularly among older adults and medically vulnerable populations who may have been born before universal vaccination or who develop inadequate immunity after vaccination.[2,3] National surveillance data from 2006 to 2021 demonstrate that acute HBV infection has not been eliminated, reinforcing the need for targeted prevention and immunity monitoring among high-risk clinical groups.[2]

Patients with advanced chronic kidney disease and kidney transplant recipients are particularly susceptible to HBV infection and its associated complications. Before transplantation, patients may experience repeated vascular access, blood-product exposure, invasive procedures, and prolonged contact with dialysis environments. Anti-HBs concentrations may decline substantially after kidney transplantation, particularly among older recipients and those receiving lymphocyte-depleting induction therapy, reinforcing the need to assess the durability of vaccine-derived immunity after transplantation.[4-6] Although HBV reactivation is relatively uncommon among non-liver solid-organ transplant recipients with resolved infection, it can lead to hepatic failure and HBV-related death; risk is higher among anti-HBs-negative recipients and those exposed to intensified immunosuppression, including rituximab or antithymocyte globulin. Recent evidence further indicates that absent anti-HBs at transplantation is associated with an increased risk of HBV reactivation among kidney transplant recipients with evidence of previous HBV exposure.[7,8]

Hepatitis B vaccination is therefore a central component of preventive care for patients with kidney disease. More than 90% of immunocompetent adults develop protective antibody concentrations after completing a standard vaccine series, whereas responses are less frequent and less durable in patients with advanced kidney disease or immunosuppression.[4,9] Uremia-associated immune dysfunction, older age, diabetes, poor nutritional status, advanced kidney failure, and immunosuppressive treatment may all contribute to reduced vaccine immunogenicity. Consequently, higher antigen doses or additional vaccine doses are commonly used in dialysis populations, and vaccination should preferably be completed before transplantation, when immune responses are generally more robust.[4,9] Nevertheless, some kidney transplant recipients either fail to achieve seroprotection or subsequently lose measurable antibodies, making reliance on vaccination documentation alone potentially insufficient.[6]

Postvaccination serological testing is important for identifying patients who remain susceptible despite completing a vaccine schedule. An antibody concentration against hepatitis B surface antigen (anti-HBs) of at least 10 mIU/ml is conventionally considered evidence of seroprotection after a documented vaccination series.[9-11] Kidney-specific guidance additionally recognizes that antibody concentrations may decline rapidly in transplant recipients and recommends consideration of booster vaccination when anti-HBs falls below protective levels.[5] However, the optimal monitoring interval, booster schedule, and target antibody concentration after kidney transplantation remain incompletely defined. Institutional data describing vaccine effectiveness under local transplant practices are therefore needed to identify nonresponders and guide practical revaccination pathways.

To address this evidence gap, the present retrospective cohort study will evaluate adult kidney transplant recipients who completed hepatitis B vaccination and underwent post-vaccination anti-HBs testing at Prince Sultan Military Medical City. The primary objective is to estimate the prevalence of seroprotection, defined as anti-HBs of at least 10 mIU/ml. Secondary objectives are to identify demographic, clinical, transplantation-related, immunosuppressive, and vaccination-related factors associated with nonresponse. These findings may support risk-stratified antibody monitoring, booster administration, and revaccination protocols for kidney transplant recipients within the institution.

METHODS

Study design and setting

We conducted a single-center retrospective cohort study of adult kidney transplant recipients who had completed a documented hepatitis B virus vaccination schedule and subsequently underwent quantitative measurement of antibodies against hepatitis B surface antigen at Prince Sultan Military Medical City, Riyadh, Saudi Arabia from January 2015 to December 2023. Routinely collected clinical data were obtained from the preventive medicine vaccination registry, the kidney transplant clinic electronic health record, and the institutional laboratory information system. The study was reported in accordance with the strengthening the reporting of observational studies in epidemiology statement for cohort studies and the reporting of studies conducted using observational routinely collected health data extension.[12,13]

Selection criteria

The source population consisted of all adult kidney transplant recipients who received follow-up care at Prince Sultan Military Medical City during the study period. Potentially eligible recipients were identified from the kidney transplant clinic registry, and their records were linked to the institutional vaccination and laboratory databases using the unique medical record number. Patients were included if they were aged 18 years or older, had undergone kidney transplantation, received follow-up care at Prince Sultan Military Medical City, had documented completion of an eligible hepatitis B vaccination schedule, and had at least one quantitative anti-HBs measurement recorded after completion of the qualifying vaccination schedule. Patients were also required to have sufficient vaccination and laboratory

documentation to determine their post-vaccination seroprotection status.

A completed vaccination schedule was defined according to the hepatitis B vaccine product, antigen dose, and institutional vaccination protocol applicable at the time the vaccine was administered. Eligible vaccination courses included a conventional adult vaccine schedule, a higher-dose regimen used for patients with advanced kidney disease, or another approved complete schedule that could be verified in the institutional medical record. Patients were excluded if they had documented hepatitis B surface antigen positivity or known chronic HBV infection before or at cohort entry, had incomplete or unverifiable vaccination documentation, lacked an interpretable quantitative anti-HBs result after completing vaccination, or had an anti-HBs measurement recorded only before completion of the qualifying vaccine schedule. Duplicate records were reconciled before analysis, and records that could not be reliably linked or verified were excluded.

Procedure

Cohort construction and sampling

The study used non-probability consecutive sampling approach. All potentially eligible kidney transplant recipients were initially identified from the transplant clinic registry. Their records were subsequently linked to the vaccination registry and laboratory information system using their unique institutional medical record numbers. Automated electronic data extraction was supplemented by manual review when vaccination dates, transplant dates, serological findings, or immunosuppressive treatment records were incomplete, conflicting, or chronologically implausible. For recipients with more than one completed hepatitis B vaccination course, the qualifying course was defined as the most recent complete vaccine series preceding the eligible anti-HBs measurement.

Hepatitis B vaccination

The principal exposure was documented completion of a hepatitis B vaccination schedule. Extracted vaccination characteristics included vaccine product, antigen dose, administration date of each dose, total number of doses, completion date of the primary vaccination series, use of a standard-dose or higher-dose formulation, number of booster doses, and timing of vaccination relative to kidney transplantation. Immunosuppressive treatment may permit HBV reactivation in individuals with current or previous infection, necessitating risk-based screening, monitoring, and, in selected patients, antiviral prophylaxis.[14]

Outcome definition

The primary outcome was post-vaccination seroprotection, defined as an anti-HBs concentration of at least 10 mIU/ml after completion of the qualifying hepatitis B vaccination schedule. Participants with anti-HBs concentrations of at least 10 mIU/ml were classified as seroprotected, whereas those with concentrations below 10 mIU/ml were classified as non-seroprotected. An anti-HBs concentration of at least 10 mIU/ml after a documented complete vaccine series is the accepted correlate of vaccine-induced protection.[15,16] Postvaccination serological testing is generally recommended for immunocompromised individuals whose subsequent clinical management depends on confirmation of immunity. Guidance recommends measuring anti-HBs approximately 1 to 2 months after the final vaccine dose to assess the initial response.[15,16]

Anti-HBs concentration was also evaluated as a continuous variable after assessment of its distribution. Because antibody concentrations were expected to be positively skewed, logarithmic transformation was considered for analyses using the quantitative titer. In secondary analyses, antibody responses were categorised as below 10 mIU/ml, 10 to 99 mIU/ml, and at least 100 mIU/ml to distinguish non-seroprotection, conventional seroprotection, and a stronger antibody response. Laboratory values reported below or above the assay's analytical range were managed according to the lower and upper limits of quantification.

Demographic and clinical variables

Demographic characteristics included age, sex, and body mass index. Age was calculated at completion of the qualifying vaccination course. Body mass index was calculated as weight in kilograms divided by height in meters squared using the measurement recorded closest to vaccination completion or anti-HBs testing. Age and body mass index were analyzed as continuous variables in the primary models to preserve information and statistical power. Categorized values were used only for descriptive presentation or when clinically justified. Arbitrary dichotomization of continuous predictors was avoided because it can reduce statistical efficiency and obscure nonlinear associations.[23]

Study size

No formal prospective sample-size calculation was performed because the study used a census-based retrospective cohort design. All kidney transplant recipients who met the predefined eligibility criteria during the study period were included. This approach maximized the use of available institutional data and avoided additional sampling from the eligible cohort.[7,8]

Ethical considerations

The study protocol was reviewed and approved by the Prince Sultan Medical Center Research Office under approval number [IRB Approval No E- 2912 on 11 January 2026]. The requirement for individual informed consent was waived by the ethics committee because the

study involved retrospective analysis of routinely collected clinical data, required no direct patient contact, introduced no study-related intervention, and presented minimal risk to participants. Direct patient identifiers were removed from the analytic dataset and replaced with study-specific identification numbers. The study was conducted in accordance with institutional data-governance requirements and the principles of the Declaration of Helsinki.

Statistical analysis

Statistical analyses were conducted using SAS 9.4. All statistical tests were two-sided. Participant characteristics were summarized for the full cohort and according to seroprotection status. The primary seroprotection proportion was reported with an exact or Wilson 95% binomial confidence interval.[24] Standardized mean differences were calculated where appropriate to quantify the magnitude of differences independently of sample size.

For unadjusted group comparisons, categorical variables were analyzed using the Pearson χ^2 test. Fisher exact tests were used when expected cell counts were small. Continuous variables were compared using the independent-samples t-test when the distributional assumptions were adequately satisfied and the Mann–Whitney U test when distributions were markedly skewed or contained influential outliers.

Multivariable logistic regression

The primary adjusted analysis used multivariable logistic regression to identify factors associated with non-seroprotection, defined as an anti-HBs concentration <10 mIU/ml after completion of hepatitis B vaccination. Non-seroprotection was coded as the outcome (1), whereas seroprotection (anti-HBs ≥10 mIU/ml) served as the reference category (0), so that odds ratios (ORs) greater than 1 indicated higher odds of vaccine nonresponse. The multivariable model included age (per 10-year increase), sex, diabetes status (any diabetes versus no diabetes), and total number of hepatitis B vaccine doses (per additional dose). These variables were selected a priori because of their established clinical relevance and availability in the study cohort. All variables were entered simultaneously without automated variable selection.

Adjusted odds ratios were reported with 95% confidence intervals and two-sided p values. Continuous variables were retained on their original scale whenever possible. Linearity between continuous predictors and the log odds of non-seroprotection was examined using graphical assessment, Box–Tidwell terms, fractional polynomial functions, or restricted cubic splines, depending on the available sample size and software.[10] Where a nonlinear association was identified, the variable was modelled using an appropriate transformation or flexible nonlinear function. Categorization was used only when it had a clear clinical basis or when the available sample size did not permit reliable flexible modelling.

Model diagnostics and performance

The adequacy of the logistic regression model was evaluated through assessment of functional form, multicollinearity, residuals, influential observations, calibration, and discrimination. Calibration was evaluated by comparing observed and model-predicted probabilities of non-seroprotection. A calibration plot, calibration intercept, and calibration slope were reported when feasible. The Hosmer–Lemeshow test was treated as a supplementary diagnostic and was not used as the sole measure of model adequacy because of its dependence on sample size and grouping decisions.[11]

Discrimination was quantified using the area under the receiver operating characteristic curve with a 95% confidence interval. Complete or quasi-complete separation was assessed by reviewing cross-tabulations, extreme coefficient estimates, and unusually large standard errors. If separation or substantial sparse-data bias was present, Firth penalized logistic regression was applied to obtain bias-reduced estimates.[18,19] Automated stepwise selection was avoided because it can produce unstable models, biased coefficients, and overly optimistic estimates of performance.[20-22]

RESULTS

Baseline characteristics

A total of 100 kidney transplant recipients who received hepatitis B vaccination were included in the analysis, of whom 69 (69.0%; 95% CI, 59.4–77.2%) achieved seroprotection (anti-HBs ≥10 mIU/ml), while 31 (31.0%) remained non-seroprotected (Table 1 and Figure 1). The mean (SD) age of the cohort was 41.4 (15.2) years, with a median (IQR) age of 40.5 (28.0–53.0) years. Participants who achieved seroprotection tended to be younger than those who did not (mean [SD], 40.2 [14.7] versus 44.1 [16.3] years), although this difference was not statistically significant (p=0.257). Similarly, the distribution of age categories did not differ between groups (p=0.349). Overall, 66 participants (66.0%) were male and 34 (34.0%) were female. Sex distribution was comparable between seroprotected and non-seroprotected recipients, with males accounting for 63.8% and 71.0% of the two groups, respectively (p=0.649).

Diabetes mellitus was present in 29.0% of the cohort, including 18.0% with unspecified diabetes, 9.0% with type 2 diabetes, and 2.0% with type 1 diabetes. The prevalence and distribution of diabetes were similar between seroprotected and non-seroprotected recipients (p=0.627). The number of hepatitis B vaccine doses was the only baseline characteristic significantly associated with seroprotection (p=0.014). Recipients who failed to achieve seroprotection were more frequent to have received only

1–2 vaccine doses compared with seroprotected recipients (80.6% versus 50.7%), whereas completion of three doses was more frequent among seroprotected recipients (27.5% versus 6.5%). The proportion receiving four or more doses was also higher among seroprotected recipients (21.7% versus 12.9%), although this difference was less pronounced. The overall median (IQR) anti-HBs concentration was 259.0 (2.6–1000.0) mIU/ml. Seroprotected recipients demonstrated higher antibody concentrations than non-seroprotected recipients (median [IQR], 1000.0 [210.0–1000.0] versus 2.0 [2.0–2.0] mIU/ml). Among seroprotected recipients, 53.6% exhibited a very high antibody response (anti-HBs ≥1000 mIU/ml), whereas all non-seroprotected participants had anti-HBs concentrations below 10 mIU/ml by definition (Figure 2).

Factors associated with hepatitis B seroprotection

In univariable analyses, none of the evaluated baseline characteristics were significantly associated with the odds of non-seroprotection (Table 2 and Figure 4). After adjustment for age, sex, diabetes status, and the number of hepatitis B vaccine doses, no independent predictor reached statistical significance. Older age showed a trend toward lower odds of achieving seroprotection, with a 44% increase in the odds of non-seroprotection for every 10-year increase in age (adjusted OR, 1.44; 95% CI, 0.96–2.16; p=0.079). Similarly, each additional hepatitis B vaccine dose was associated with a 24% reduction in the odds of non-seroprotection, although this association did not reach statistical significance (adjusted OR, 0.76; 95% CI, 0.53–1.08; p=0.121). Sex (adjusted OR for male versus female, 1.19; 95% CI, 0.44–3.22; p=0.731) and diabetes status (adjusted OR, 0.55; 95% CI, 0.15–2.00; p=0.365) were not independently associated with seroprotection.

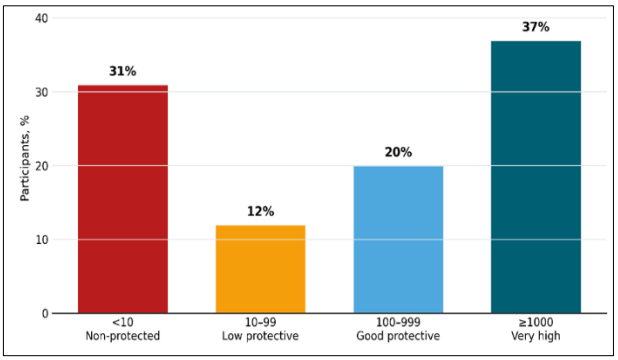

Figure 2: Distribution of post-vaccination anti-HBs response categories and the overall seroprotection prevalence.

Bars show the proportion of kidney transplant recipients in each postvaccination anti-HBs response category. Anti-HBs concentrations were classified as less than 10 mIU/ml (non-protected), 10–99 mIU/ml (low protective response), 100–999 mIU/ml (good protective response), and at least 1000 mIU/ml (very high response). Percentages were calculated using the total analytic cohort as the denominator (N=100). Anti-HBs indicates antibody to hepatitis B surface antigen

Table 1: Characteristics of kidney transplant recipients overall and by hepatitis B seroprotection status.

Characteristic	Overall (n=100), N (%)	Seroprotected (n=69), N (%)	Not seroprotected (n=31), N (%)	P value
Age, years, mean±SD	41.4±15.2	40.2±14.7	44.1±16.3	0.257
Age, years, median (IQR)	40.5 (28.0–53.0)	38.0 (28.0–51.0)	46.0 (29.0–58.0)	
Age category, years				0.349
<30	27 (27.0)	19 (27.5)	8 (25.8)	
30–44	30 (30.0)	24 (34.8)	6 (19.4)	
45–59	29 (29.0)	18 (26.1)	11 (35.5)	
≥60	14 (14.0)	8 (11.6)	6 (19.4)	
Sex				0.649
Female	34 (34.0)	25 (36.2)	9 (29.0)	
Male	66 (66.0)	44 (63.8)	22 (71.0)	
BMI, kg/m², n available	40	29	11	
BMI, mean±SD	26.7±4.4	26.4±4.3	27.2±4.7	0.624
BMI, median (IQR)	27.0 (23.0–29.7)	26.0 (23.1–30.0)	27.0 (23.8–29.3)	
BMI category				0.338
Underweight (<18.5)	1/40 (2.5)	1/29 (3.4)	0/11 (0.0)	
Normal (18.5–24.9)	11/40 (27.5)	8/29 (27.6)	3/11 (27.3)	
Overweight (25.0–29.9)	18/40 (45.0)	12/29 (41.4)	6/11 (54.5)	
Obesity class I (30.0–34.9)	9/40 (22.5)	8/29 (27.6)	1/11 (9.1)	
Obesity class II/III (≥35)	1/40 (2.5)	0/29 (0.0)	1/11 (9.1)	
Diabetes status				0.627
No diabetes	71 (71.0)	49 (71.0)	22 (71.0)	
Diabetes, unspecified	18 (18.0)	13 (18.8)	5 (16.1)	
Type 1 diabetes	2 (2.0)	2 (2.9)	0 (0.0)	

Continued.

Characteristic	Overall (n=100), N (%)	Seroprotected (n=69), N (%)	Not seroprotected (n=31), N (%)	P value
Type 2 diabetes	9 (9.0)	5 (7.2)	4 (12.9)	
Vaccine doses				0.014
1–2	60 (60.0)	35 (50.7)	25 (80.6)	
3	21 (21.0)	19 (27.5)	2 (6.5)	
≥4	19 (19.0)	15 (21.7)	4 (12.9)	
Anti-HBs titre, mIU/ml, mean±SD	462.2±458.1	668.7±407.2	2.4±1.0	—
Anti-HBs titre, median (IQR)	259.0 (2.6–1000.0)	1000.0 (210.0–1000.0)	2.0 (2.0–2.0)	—
Anti-HBs category				—
<10 mIU/ml (non-protected)	31 (31.0)	0 (0.0)	31 (100.0)	
10–99 mIU/ml (low protective)	12 (12.0)	12 (17.4)	0 (0.0)	
100–999 mIU/ml (good protective)	20 (20.0)	20 (29.0)	0 (0.0)	
≥1000 mIU/ml (very high response)	37 (37.0)	37 (53.6)	0 (0.0)	
Seroprotected (anti-HBs ≥10 mIU/ml)	69 (69.0)	69 (100.0)	0 (0.0)	—
Seroprotection prevalence, 95% CI	69.0% (59.4–77.2)			

Data are n (%), mean±SD, or median (IQR), unless otherwise indicated. Percentages for BMI categories use participants with available BMI as the denominator (overall n=40; seroprotected n=29; not seroprotected n=11). BMI was missing for 60 participants (60.0%) and was not imputed. Seroprotection was defined as an anti-HBs concentration of at least 10 mIU/ml. Anti-HBs categories were defined as <10 mIU/ml (non-protected), 10–99 mIU/ml (low protective response), 100–999 mIU/ml (good protective response), and ≥1000 mIU/ml (very high response). P values compare seroprotected and non-seroprotected participants. Welch's t test was used for continuous variables; Fisher's exact test was used for sex; and Pearson χ^2 tests were used for multicategory variables. Anti-HBs titre, anti-HBs category, and seroprotection were not tested because they define the outcome. he 95% CI for seroprotection was calculated using the Wilson method. Values may not total 100% because of rounding. Anti-HBs=antibody to hepatitis B surface antigen; BMI=body-mass index; CI=confidence interval; IQR=interquartile range; SD=standard deviation

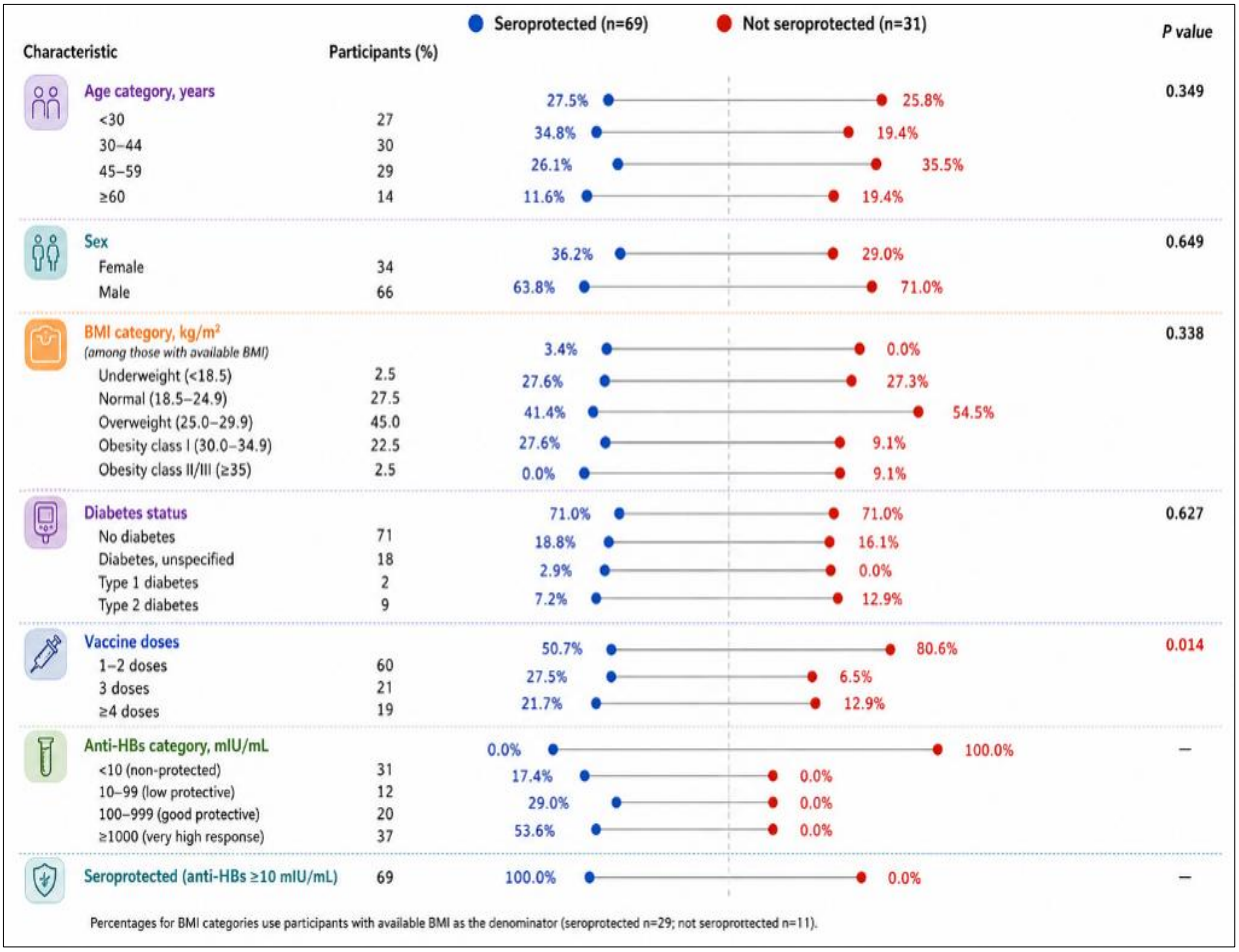

Figure 1: Characteristics of kidney transplant recipients overall and by hepatitis B seroprotection status.

Table 2: Univariable and multivariable logistic regression for non-seroprotection.

Predictor	Crude OR	95% CI	P value	Adjusted OR	95% CI	P value
Age, per 10-year increase	1.23	0.92–1.65	0.167	1.44	0.96–2.16	0.079
Male versus female	1.50	0.58–3.88	0.403	1.19	0.44–3.22	0.731
Any diabetes versus no diabetes	1.03	0.40–2.63	0.953	0.55	0.15–2.00	0.365
HBV vaccine doses, per additional dose	0.77	0.55–1.08	0.129	0.76	0.53–1.08	0.121

Data are odds ratios (ORs) with 95% confidence intervals. The outcome was non-seroprotection, defined as anti-HBs <10 mIU/ml. Adjusted ORs were mutually adjusted for all variables shown. BMI was not included in the primary model because it was missing for 60 of 100 participants. No automated variable selection was used

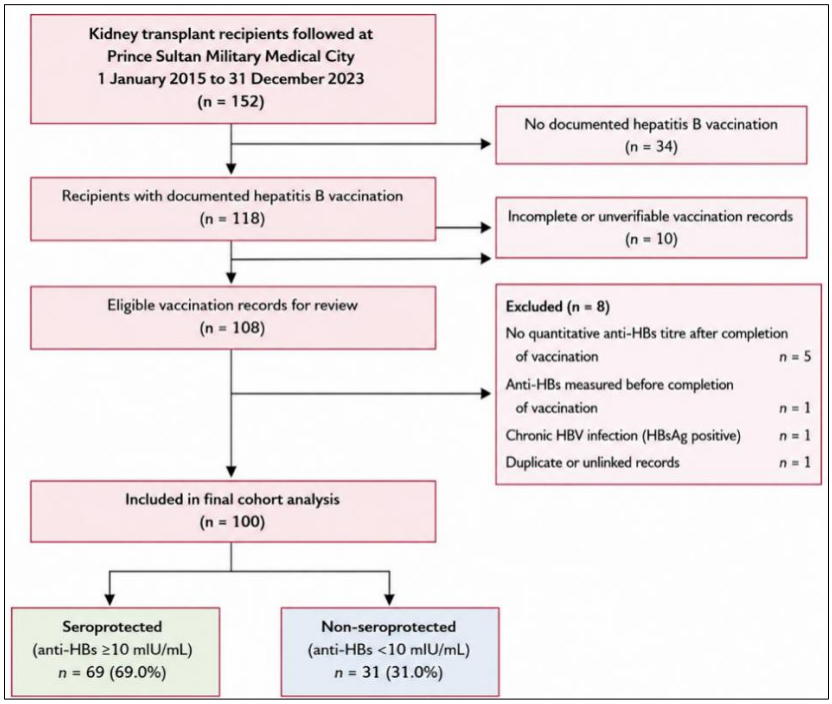

Figure 3: Cohort identification, eligibility assessment, and hepatitis B seroprotection status among kidney transplant recipients.

Model diagnostics

The multivariable logistic regression model converged successfully, with no evidence of complete or quasi-complete separation. Model discrimination was modest, with an area under the receiver operating characteristic curve of 0.655 (95% bootstrap CI, 0.527–0.773). Overall prediction error was acceptable, with a Brier score of 0.198. The Hosmer–Lemeshow test showed no evidence of gross lack of fit (χ^2=4.29; df=8; p=0.830), although this test was interpreted as a supplementary diagnostic. Multicollinearity was low, with a maximum variance inflation factor of 1.77. Box–Tidwell tests provided no evidence of nonlinearity in the logit for age or number of vaccine doses (both p>0.30). Four observations had Cook distances greater than conventional 4/N threshold; however, the maximum Cook distance was 0.106, and no observation demonstrated extreme leverage (Figures 5 and 6).

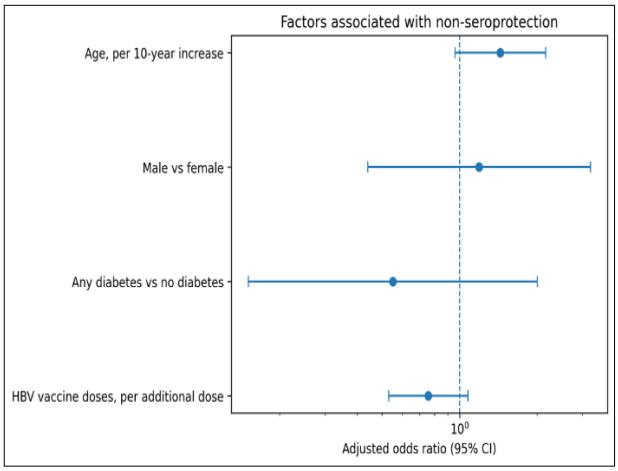

Figure 4: Adjusted associations with non-seroprotection.
Error bars indicate 95% confidence intervals.

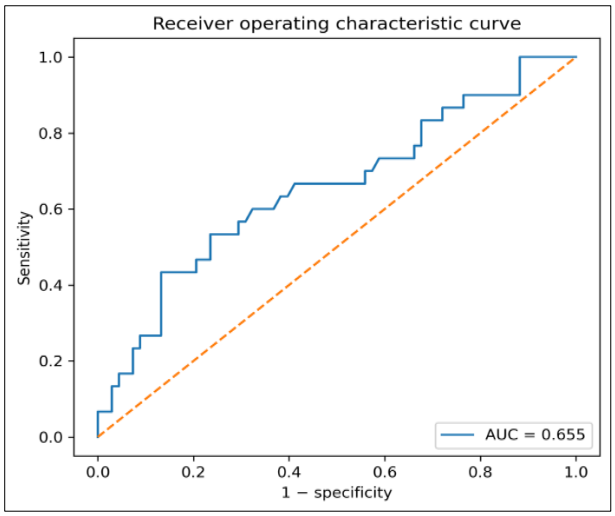

Figure 5: Receiver operating characteristic curve for the primary logistic regression model.

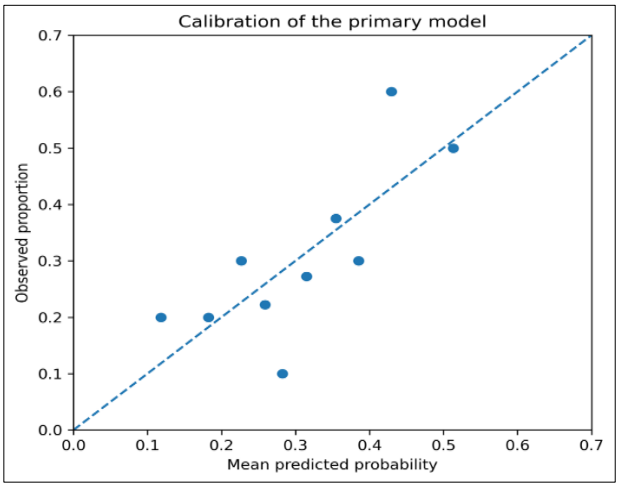

Figure 6: Observed and predicted non-seroprotection probabilities by tenths of predicted risk.

DISCUSSION

In this retrospective cohort of kidney transplant recipients, 69% achieved seroprotection after hepatitis B vaccination, while 31% remained susceptible despite documented vaccination. No variable was independently associated with seroprotection after multivariable adjustment, although a greater number of vaccine doses and younger age each showed a clinically meaningful trend toward higher seroprotection. These findings indicate that a substantial minority of kidney transplant recipients remain inadequately protected after vaccination and argue against inferring immunity from vaccination history alone.

The observed seroprotection rate is well below the 90% to 95% typically achieved in immunocompetent adults and is consistent with contemporary evidence identifying patients with advanced kidney disease and transplant recipients as poorly responsive populations. The reduced response is biologically plausible given the effects of chronic kidney disease and post-transplant immunosuppression on antigen presentation, T-cell activation, B-cell function, and immune memory.[23] A recent scoping review across chronic kidney disease, dialysis, and transplant populations similarly concluded that conventional vaccination schedules are frequently insufficient and that evidence specifically addressing optimal vaccination strategies in kidney transplant recipients remains limited.[23,26] Together, these observations support routine measurement of anti-HBs after vaccination rather than assuming protection from completion of a standard vaccine series.

The number of vaccine doses showed the strongest, although not statistically independent, association with seroprotection in our cohort. This is consistent with evidence that enhanced, adjuvanted, or repeated vaccination schedules may improve responses in immunocompromised populations, although the benefit appears to vary according to vaccine formulation, timing, and the degree of established nonresponse.[23,26] In thoracic transplant candidates, a CpG-adjuvanted vaccine was associated with higher series completion and seroprotection than a conventional recombinant vaccine.[24] However, evidence from kidney transplant recipients demonstrates that once nonresponse is established, additional conventional doses may have limited effectiveness. In the study by Iwata et al, only 5 of 26 kidney transplant recipients who had failed an initial 3-dose series achieved seroconversion after booster vaccination, and switching to a different vaccine product did not clearly outperform administration of the same product.[28] These findings suggest that simply administering additional doses may not be sufficient for all nonresponders and that future studies should assess more immunogenic formulations, optimized timing, and tailored revaccination strategies.

The distribution of antibody titers among responders provides additional clinical context. More than half of seroprotected recipients had anti-HBs concentrations above 100 mIU/ml, and more than one-third exceeded 1000 mIU/ml, indicating that vaccination can produce a robust antibody response in a substantial subset of kidney transplant recipients. Nevertheless, the conventional threshold of 10 mIU/ml may not adequately reflect durability of protection in immunosuppressed recipients. Previous transplant studies have found that patients with intermediate pretransplant titers of 10 to 100 mIU/ml are particularly vulnerable to subsequent loss of seroprotection.[25] In a 3-year kidney transplant study, recipients with anti-HBs below 100 IU/l were given a booster, after which 86% and 93% achieved concentrations of at least 100 IU/l at 1 and 3 months, respectively.[29] These findings support the clinical relevance of a higher antibody target and suggest that recipients with titers between 10 and 100 mIU/ml should not necessarily be regarded as durably protected.

The importance of maintaining measurable immunity extends beyond prevention of community-acquired infection. Contemporary transplantation practice increasingly considers kidneys from donors with evidence of current or previous HBV infection. A recent meta-analysis of kidneys from donors with active HBV reported a pooled transmission rate of 4.0%, but the rate was lower in cohorts in which recipients had positive surface antibodies.[27] Similarly, a meta-analysis of 2,516 recipients of kidneys from anti-HBc-positive donors found an overall de novo HBV infection rate of only 0.36%, with comparable graft and patient survival to recipients of anti-HBc-negative kidneys.[30] Identifying and correcting inadequate immunity may not only protect recipients from infection but may also facilitate the safe use of selected HBV-positive donor kidneys when accompanied by appropriate antiviral prophylaxis and virological monitoring.[27,30,31]

These findings are particularly relevant to Saudi Arabia, where universal infant vaccination has substantially reduced population-level HBV transmission, but many older transplant recipients may have been born before implementation of universal vaccination or may have experienced waning immunity after the onset of chronic kidney disease and immunosuppression. Given the country's substantial kidney transplant activity and the scarcity of local data on post-vaccination seroprotection, our findings support incorporating routine anti-HBs testing into transplant care. Patients with concentrations below 10 mIU/ml should be considered non-seroprotected, while those with intermediate concentrations of 10 to 100 mIU/ml may warrant closer monitoring or booster vaccination because minimal seroprotection may not be durable.[25,26,29] Adjuvanted or enhanced-immunogenicity vaccines may be considered where available, although their effectiveness specifically among kidney transplant recipients requires further evaluation.[24,26,28]

Limitations

This study has several limitations. The retrospective, single-center design limits causal inference and generalizability. The modest sample size reduced statistical power for multivariable analysis and increased the risk of type II error, particularly for clinically plausible associations involving age and vaccine dose number. Important clinical information, including time since transplantation, immunosuppressive regimen, graft function, donor characteristics, lymphocyte counts, and vaccine timing relative to transplantation, was unavailable. Consequently, residual confounding cannot be excluded, and the independent contribution of these established determinants of vaccine responsiveness could not be evaluated. Antibody durability and responses to booster vaccination were also not assessed; therefore, the persistence of long-term protection and the effectiveness of booster doses in restoring seroprotection could not be determined. In addition, vaccination history did not fully capture vaccine formulation, dose strength, or whether vaccination occurred before or after transplantation, factors that may influence immunogenicity. Nevertheless, the study provides clinically relevant local evidence showing that documented vaccination does not reliably indicate serological protection among kidney transplant recipients.

CONCLUSION

Approximately one-third of kidney transplant recipients remained unprotected against HBV despite vaccination, underscoring the need for routine post-vaccination antibody testing in this vulnerable population. Although independent predictors were not identified, the observed associations with vaccine dose number and increasing age support optimization of vaccination strategies and continued serological surveillance. Larger prospective multicenter studies from Saudi Arabia are warranted to identify determinants of vaccine responsiveness and to refine evidence-based revaccination and booster protocols for kidney transplant recipients.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organization. Global hepatitis report 2024: action for access in low- and middle-income countries. 2024. Available at: https://www.who.int/publications/i/item/9789240091672. Accessed on 15 May 2026.
2. Alghamdi IG, Alghamdi RM, Alghamdi MS, Alghamdi AM, Alghamdi MI, Alghamdi ZI, et al. Epidemiology of hepatitis B in Saudi Arabia from 2006 to 2021. Hepat Med. 2023;15:233-47.
3. Abdo AA, Sanai FM, Al-Faleh FZ. Epidemiology of viral hepatitis in Saudi Arabia: are we off the hook? Saudi J Gastroenterol. 2012;18:349-57.
4. Chancharoenthana W, Traitanon O, Leelahavanichkul A, Ronco C. Optimizing hepatitis B vaccination in chronic kidney disease: a comprehensive scoping review of strategies across CKD stages, dialysis, and transplant populations. Ren Fail. 2025;47:2541873.
5. Kidney Disease: Improving Global Outcomes Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant 2009;9(3):S1-155.
6. Dadhania DM, Cravedi P, Blumberg E, Stryniak G, Montez-Rath ME, Maltzman JS. Age-related decline in anti-HBV antibodies in vaccinated kidney transplant recipients. Transpl Infect Dis. 2023;25:e14090.
7. Yin S, Zhang F, Wu J, Lin T, Wang X. Incidence, risk factors, and clinical outcomes of HBV reactivation in non-liver solid organ transplant recipients with resolved HBV infection: a systematic review and meta-analysis. PLoS Med. 2023;20:e1004196.

8. Chen J, Wu B, Chen J, Chu Q. Incidence and risk factors for hepatitis B virus reactivation in kidney transplant recipients: a systematic review and meta-analysis. BMC Nephrol. 2026;27:325.
9. Schillie S, Vellozzi C, Reingold A, Harris AM, Haber P, Ward JW, et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep. 2018;67:1-31.
10. World Health Organization. Consolidated guidelines on hepatitis B and C prevention, testing, treatment, service delivery and monitoring: an implementation handbook for a public health approach. 2026. Available at: https://www.who.int/publications/i/item/9789240119529. Accessed on 15 May 2026.
11. Al Saran K, Sabry A, Al Halawany Z, Ismail M. Factors affecting response to hepatitis B vaccine among hemodialysis patients in a large Saudi hemodialysis center. Saudi J Kidney Dis Transpl. 2014;25:185-91.
12. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology statement: guidelines for reporting observational studies. Lancet. 2007;370:1453-7.
13. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, et al. The REporting of studies Conducted using Observational Routinely-collected health Data statement. PLoS Med. 2015;12:e1001885.
14. Lau G, Yu ML, Wong G, Thompson A, Ghazinian H, Hou JL, et al. APASL clinical practice guideline on hepatitis B reactivation related to the use of immunosuppressive therapy. Hepatol Int. 2021;15:1031-48.
15. Weng MK, Doshani M, Khan MA, Frey S, Ault K, Moore KL, et al. Universal hepatitis B vaccination in adults aged 19-59 years: updated recommendations of the Advisory Committee on Immunization Practices—United States, 2022. MMWR Morb Mortal Wkly Rep. 2022;71:477-83.
16. Conners EE, Panagiotakopoulos L, Hofmeister MG, Spradling PR, Hagan LM, Harris AM, et al. Screening and testing for hepatitis B virus infection: CDC recommendations—United States, 2023. MMWR Recomm Rep. 2023;72:1-25.
17. Altman DG, Royston P. The cost of dichotomising continuous variables. BMJ. 2006;332:1080.
18. Firth D. Bias reduction of maximum likelihood estimates. Biometrika. 1993;80:27-38.
19. Heinze G, Schemper M. A solution to the problem of separation in logistic regression. Stat Med. 2002;21:2409-19.
20. Brown LD, Cai TT, DasGupta A. Interval estimation for a binomial proportion. Stat Sci. 2001;16:101-33.
21. Harrell FE Jr. Regression modeling strategies: with applications to linear models, logistic regression, and survival analysis. New York, NY: Springer; 2001.
22. Christodoulou E, Ma J, Collins GS, Steyerberg EW, Verbakel JY, Van Calster B. A systematic review shows no performance benefit of machine learning over logistic regression for clinical prediction models. J Clin Epidemiol. 2019;110:12-22.
23. Jain SR, Kumar D. Vaccination for the post-kidney transplant population. Curr Opin Nephrol Hypertens. 2019;28:581-6.
24. Chiu CY, Sampathkumar P, Brumble LM, Vikram HR, Watt KD, Beam E. Optimizing hepatitis B virus seroprotection in thoracic organ transplantation: the role of the HepB-CpG vaccination schedule. Vaccine. 2025;47:126705.
25. Chiu CY, Sampathkumar P, Brumble LM, Vikram HR, Watt KD, Beam E. Hepatitis B vaccine compliance, serologic response, and durability in adult thoracic organ transplant recipients. Clin Transplant. 2024;38:e15464.
26. Velikova T, Gerasoudis S, Batselova H. Vaccination for solid organ transplanted patients: recommendations, efficacy, and safety. World J Transplant. 2024;14:92172.
27. Waller KMJ, De La Mata N, Hedley JA, Sharma T, Davies R, Garrett E, et al. Transmission risk of intentional transplantation of kidneys from donors with active hepatitis B to recipients without active hepatitis B: a systematic review and meta-analysis. Transplantation. 2026;110:e912-22.
28. Iwata K, Ikegaki S, Hyodo Y, Miyake H. Hepatitis B boosters using a different product versus the same product for kidney transplant recipients: a retrospective study with Bayesian inference. Clin Transplant. 2025;39:e70307.
29. Chancharoenthana W, Leelahavanichkul A, Udomkarnjananun S, Wattanatorn S, Avihingsanon Y, Praditpornsilpa K, et al. Durability of antibody response against the hepatitis B virus in kidney transplant recipients: a proposed immunization guideline from a 3-year follow-up clinical study. Open Forum Infect Dis. 2019;6:ofy342.
30. Yin S, Chen X, Li X, Zhang F, Wu J, Lin T. Was antiviral prophylaxis necessary after kidney transplantation utilizing anti-HBc-positive donors? A systematic review and meta-analysis. Transplant Rev (Orlando). 2024;38:100840.
31. Paschereit A, Greese V, Sakurayama K, Duerr M, Halleck F, Liefeldt L, et al. Impact of hepatitis B infection on patient and graft survival after kidney transplantation. J Clin Med. 2025;14:2124.

Cite this article as: Aljaafary RA, Abdulmogith MA, Abbas AHS. Post-vaccination hepatitis B seroprotection among kidney transplant recipients in Saudi Arabia: a retrospective cohort study. Int J Res Med Sci 2026;14:3730-39.