Preplanned Studies

Immunogenicity of Short-Course, High-Dose Hepatitis B Vaccination in Patients with Chronic Kidney Disease — Shanxi Province, China, 2019–2020

Linying Gao[1,2,3]; Xufeng Cui[1,2,3]; Xinyuan Mo[1,2,3]; Zhaoyue Men[1,2,3]; Xiuyang Xu[1,2,3]; Tian Yao[1,3,4]; Jianmin Wang[5]; Hongting Liu[6]; Hongping Guo[7]; Guowei Chai[8]; Liming Liu[5]; Fuzhen Wang[9]; Xiaofeng Liang[10,11,12,#]; Suping Wang[1,2,3]; Yongliang Feng[1,2,3,#]

Summary

What is already known about this topic?

As one of the populations at high risk of hepatitis B virus (HBV) infection, patients with chronic kidney disease (CKD) require rapid and effective development of hepatitis B surface antibodies (anti-HBs).

What is added by this report?

The short-course, high-dose regimen of hepatitis B vaccination rapidly induced comparable immunological responses to the routine regimen, achieving a seroconversion rate of 88.5%, a high-response rate of 64.1%, and anti-HBs geometric mean concentrations of 824.1 mIU/mL.

What are the implications for public health practice?

The short-course, high-dose regimen represents an effective rapid immunization strategy for CKD patients, particularly when administered prior to immunosuppressive therapy. This study provides compelling evidence for optimizing immunization protocols in the CKD population.

The hepatitis B (HepB) vaccine represents the most effective strategy for preventing hepatitis B virus (HBV) infection. However, its immunogenicity is suboptimal in chronic kidney disease (CKD) patients due to immune system impairment and frequent requirements for immunosuppressive therapy (*1*–*2*). Additionally, patient adherence to the routine vaccination schedule remains inadequate (*3*). While shortened vaccination schedules can improve completion rates and potentially stimulate earlier and more rapid hepatitis B surface antibody (anti-HBs) production, high-dose HepB vaccination is specifically recommended for CKD patients and immunocompromised individuals by both the Advisory Committee on Immunization Practices (ACIP) and the Chinese Medical Association (*4*–*5*). However, the efficacy of combining short-course vaccination with high doses to rapidly and effectively induce immune responses and improve adherence in CKD patients remains unclear. In this study, 273 CKD patients were randomized into three groups receiving HepB vaccine following either the routine regimen, a short-course regimen, or a short-course high-dose regimen. Our results suggest that the short-course high-dose regimen can serve as an effective rapid immunization protocol for CKD patients, representing significant practical importance for HepB prevention and control in this vulnerable population.

This prospective study was conducted between May 2019 and February 2020 across four hospitals in Shanxi Province, China. Sample size calculations were based on a non-inferiority design, with an expected seroconversion rate of 80% following the routine regimen based on previous studies. Using PASS15 (NCSS, Kaysville, UT, US), we calculated a required sample size of 61 subjects per group, assuming a non-inferiority margin of -10%, one-sided α =0.025, and power=0.80. Accounting for an anticipated 20% loss to follow-up, we aimed to recruit 77 subjects per group. A total of 290 subjects were enrolled, with 273 randomized into three groups according to a randomization list generated using SAS statistical software (version 9.4, NC, SAS Institute Inc., USA). Inclusion criteria comprised: 1) written informed consent; 2) CKD diagnosis and age 18–70 years; and 3) negative status for hepatitis B surface antigen (HBsAg), anti-HBs, and hepatitis B core antibody (anti-HBc). Exclusion criteria included: 1) pregnancy or severe acute/chronic diseases (liver disease, blood disease, or cancer); 2) contraindications to HepB vaccination or vaccination history within one month of enrollment; and 3) HBV-DNA positivity or HBV-related glomerulonephritis. The Ethics Committee of

Shanxi Medical University approved this study (Approval number: 2019007), and the trial was registered at ClinicalTrials.gov (CT.gov identifier: NCT03962881). Subjects received either 20 μg or 60 μg of HepB vaccine (Shenzhen Kangtai Biological Products Co., Ltd., China; Batch B201809043 and A201805008) following either a routine schedule (0-1-6 months, 20 μg) ($IM_{0\text{-}1\text{-}6*20}$ group) or rapid schedules (0-1-2 months, 20 μg or 60 μg) ($IM_{0\text{-}1\text{-}2*20}$ and $IM_{0\text{-}1\text{-}2*60}$ groups). Blood samples were collected one month after the final vaccination dose (month 7 for $IM_{0\text{-}1\text{-}6*20}$ group; month 3 for $IM_{0\text{-}1\text{-}2*20}$ and $IM_{0\text{-}1\text{-}2*60}$ groups) to measure geometric mean concentrations (GMCs) of anti-HBs. Anti-HBs levels were quantified using chemiluminescent microparticle immunoassay (ARCHITECT HBsAg/Anti-HBs Reagent Kit, Abbott Ireland Diagnostics Division, Finisklin Business Park, Sligo, Ireland). Anti-HBs concentrations <10 mIU/mL indicated non-response, while concentrations ≥10 mIU/mL and ≥100 mIU/mL defined seroconversion and high-response, respectively. CKD staging was determined by eGFR values: <15 (stage 5), 15–29 (stage 4), 30–59 (stage 3), 60–89 (stage 2), or ≥90 (stage 1).

Statistical analyses employed Pearson chi-square tests or Fisher's exact tests for categorical data and one-way analysis of variance for continuous data. Factors influencing immunogenicity were evaluated using univariate and multivariate logistic regression models. All analyses were performed using SAS (version 9.4, NC, SAS Institute Inc., USA), with statistical significance set at $P<0.05$.

A total of 273 patients with CKD were randomized into three groups, with 224 completing the study: 71 patients in the $IM_{0\text{-}1\text{-}6*20}$ group, 75 in the $IM_{0\text{-}1\text{-}2*20}$ group, and 78 in the $IM_{0\text{-}1\text{-}2*60}$ group (Supplementary Figure S1, available at https://weekly.chinacdc.cn/). Patient characteristics were comparable across all three groups (Table 1) and between those who completed the study and those lost to follow-up (Supplementary Table S1, available at https://weekly.chinacdc.cn/).

Following complete vaccination, the GMCs of anti-HBs were 1,675.2 (866.1, 2,484.4), 280.2 (170.9, 389.5), and 824.1 (86.38, 1,561.8) mIU/mL in the $IM_{0\text{-}1\text{-}6*20}$, $IM_{0\text{-}1\text{-}2*20}$, and $IM_{0\text{-}1\text{-}2*60}$ groups, respectively ($F=4.79$, $P=0.009$). Seroconversion rates were 81.7%, 77.3%, and 88.5% ($\chi^2=3.35$, $P=0.187$), while high-response rates were 69.0%, 44.0%, and 64.1% for the respective groups ($\chi^2=10.75$, $P=0.005$). Both GMCs and high-response rates were significantly higher in the $IM_{0\text{-}1\text{-}6*20}$ and $IM_{0\text{-}1\text{-}2*60}$ groups compared to the $IM_{0\text{-}1\text{-}2*20}$ group ($P<0.05$), with no significant differences between $IM_{0\text{-}1\text{-}6*20}$ and $IM_{0\text{-}1\text{-}2*60}$ groups ($P>0.05$) (Table 2). The incidence of total adverse reactions post-vaccination was comparable across groups: 8.8% (8/91), 7.7% (7/91), and 9.9% (9/91) in the $IM_{0\text{-}1\text{-}6*20}$, $IM_{0\text{-}1\text{-}2*20}$, and $IM_{0\text{-}1\text{-}2*60}$ groups, respectively ($\chi^2=0.274$, $P=0.872$). Pain and erythema were the most commonly reported adverse reactions, all of which were minor. Additionally, vaccination completion rates were numerically higher in the $IM_{0\text{-}1\text{-}2*20}$ (82.4%) and $IM_{0\text{-}1\text{-}2*60}$ (85.7%) groups compared to the $IM_{0\text{-}1\text{-}6*20}$ group (78.0%) ($\chi^2=1.84$, $P=0.398$).

After adjusting for gender, age, residence, type of chronic kidney disease, and disease duration, patients who did not receive hormones/immunosuppressants demonstrated a significantly lower non/low-response rate [adjusted odds ratio (a*OR*): 2.59; 95% confidence interval (*CI*): 1.39-4.83, $P=0.003$] (Supplementary Tables S2–S3, available at https://weekly.chinacdc.cn/). Stratification analysis by immunosuppression or hormone therapy status revealed that among patients without such therapy, the high-response rates (75.6%, 79.1%) and GMCs of anti-HBs (1,937.0, 901.4 mIU/mL) in the $IM_{0\text{-}1\text{-}6*20}$ and $IM_{0\text{-}1\text{-}2*60}$ groups were significantly higher than those in the $IM_{0\text{-}1\text{-}2*20}$ group (52.2%, 337.7 mIU/mL) ($P<0.05$). Seroconversion rates were marginally higher in the $IM_{0\text{-}1\text{-}6*20}$ and $IM_{0\text{-}1\text{-}2*60}$ groups (87.8%, 93.0%) compared to the $IM_{0\text{-}1\text{-}2*20}$ group (82.6%) ($P>0.05$). Among patients receiving immunosuppression or hormone therapy, both $IM_{0\text{-}1\text{-}6*20}$ and $IM_{0\text{-}1\text{-}2*60}$ groups showed numerically higher seroconversion rates, high-response rates, and GMCs of anti-HBs compared to the $IM_{0\text{-}1\text{-}2*20}$ group ($P>0.05$) (Table 3).

DISCUSSION

This study represents the first investigation of short-course, high-dose HepB vaccination immunogenicity in CKD patients. We compared three vaccination regimens: the routine regimen (0-1-6 months, 20 μg), a short-course regimen (0-1-2 months, 20 μg), and a short-course, high-dose regimen (0-1-2 months, 60 μg). These findings demonstrate that the short-course, high-dose regimen achieved comparable immunogenicity to the routine regimen and can serve as an effective rapid immunization protocol for CKD patients. These results have important implications for optimizing HepB vaccine immunization strategies among CKD patients and advancing toward the goal

TABLE 1. Characteristics of chronic kidney disease patients who completed the full vaccination course in China from May 2019 to February 2020.

Variables	*N*	$IM_{0\text{-}1\text{-}6*20}$ (*n*=71)	$IM_{0\text{-}1\text{-}2*20}$ (*n*=75)	$IM_{0\text{-}1\text{-}2*60}$ (*n*=78)	χ^2	*P*
Gender						
Male	130 (58.0)	37 (52.1)	51 (68.0)	42 (53.9)	4.64	0.098
Female	94 (42.0)	34 (47.9)	24 (32.0)	36 (46.1)		
Age (years)						
<35	20 (8.9)	7 (9.9)	9 (12.0)	4 (5.1)	2.49	0.647
[35, 55)	122 (54.5)	37 (52.1)	40 (53.3)	45 (57.7)		
≥55	82 (36.6)	27 (38.0)	26 (34.7)	29 (37.2)		
BMI (kg/m^2)						
<18.5	2 (0.9)	0 (0.0)	2 (2.7)	0 (0.0)	5.73	0.220
[18.5, 24)	77 (34.4)	26 (36.6)	21 (28.0)	30 (38.5)		
≥24	145 (64.7)	45 (63.4)	52 (69.3)	48 (61.5)		
Area type						
Urban	58 (25.9)	21 (29.6)	15 (20.0)	22 (28.2)	2.08	0.354
Rural	166 (74.1)	50 (70.4)	60 (80.0)	56 (71.8)		
Level of education						
Primary school or lower	36 (16.1)	12 (16.9)	13 (17.3)	11 (14.1)	2.07	0.723
Junior high school	112 (50.0)	34 (47.9)	34 (45.3)	44 (56.4)		
Senior high school or higher	76 (33.9)	25 (35.2)	28 (37.4)	23 (29.5)		
Type of clinical diagnosis						
Nephrotic syndrome	129 (57.6)	40 (56.3)	49 (65.3)	40 (51.2)	4.54	0.337
Nephritic syndrome	12 (5.4)	5 (7.0)	4 (5.3)	3 (3.9)		
Others (renal tubular disorders, polycystic kidney, and unclear)	83 (37.0)	26 (36.7)	22 (29.4)	35 (44.9)		
Duration of chronic kidney disease (years)						
≤3	176 (78.6)	55 (77.5)	60 (80.0)	61 (78.2)	0.15	0.928
>3	48 (21.4)	16 (22.5)	15 (20.0)	17 (21.8)		
CKD stage						
Stage 1	84 (37.5)	34 (47.9)	26 (34.7)	24 (30.7)	9.63	0.292
Stage 2	62 (27.7)	18 (25.3)	21 (28.0)	23 (29.5)		
Stage 3	27 (12.1)	8 (11.3)	7 (9.3)	12 (15.4)		
Stage 4	44 (19.6)	8 (11.3)	18 (24.0)	18 (23.1)		
Stage 5	7 (3.1)	3 (4.2)	3 (4.0)	1 (1.3)		
History of HepB vaccine						
Yes	20 (8.9)	4 (5.6)	6 (8.0)	10 (12.8)	4.73	0.316
No	152 (67.9)	46 (64.8)	55 (73.3)	51 (63.4)		
Unknown	52 (23.2)	21 (29.6)	14 (18.7)	17 (21.8)		
Taking hormones/immunosuppressants						
Yes	94 (42.0)	30 (42.2)	29 (38.7)	35 (44.9)	0.61	0.738
No	130 (58.0)	41 (57.8)	46 (61.3)	43 (55.1)		

Note: Chronic kidney disease staging was defined by estimated eGFR as follows: Stage 5: <15 mL/min; Stage 4: 15–29 mL/min; Stage 3: 30–59 mL/min; Stage 2: 60–89 mL/min; Stage 1: ≥90 mL/min.
Abbreviation: BMI=body mass index; CKD=chronic kidney disease; HepB=hepatitis B; eGFR=estimated glomerular filtration rate.

TABLE 2. Immune responses to different hepatitis B vaccination regimens in chronic kidney disease patients in China from May 2019 to February 2020.

Response	$IM_{0\text{-}1\text{-}6*20}$ (*n*=71)	$IM_{0\text{-}1\text{-}2*20}$ (*n*=75)	$IM_{0\text{-}1\text{-}2*60}$ (*n*=78)
GMC, mIU/mL (95% *CI*)	1,675.2 (866.1, 2,484.4)*	280.2 (170.9, 389.5)†	824.1 (86.38, 1,561.8)*
Seroconversion rate, % (95% *CI*)	81.7 (71.2, 89.0)	77.3 (66.7, 85.3)	88.5 (79.5, 93.8)
High-response rate, % (95% *CI*)	69.0 (57.5, 78.6)*	44.0 (33.3, 55.3)†	64.1 (53.0, 73.9)*

Note: group with * or † indicates no significant differences between two groups (*P*>0.05); group with † and * indicates significant differences between two groups (*P*<0.05).
Abbreviation: CKD=chronic kidney disease; GMC=geometric mean concentration; *CI*=confidence interval.

TABLE 3. Vaccination responses in chronic kidney disease patients stratified by immunosuppressive or hormone therapy status in China from May 2019 to February 2020.

Response	Taking hormones/immunosuppressants	
	Yes	No
GMC, mIU/mL (95% *CI*)		
$IM_{0\text{-}1\text{-}6*20}$	1,317.5 (441.2, 2,193.7)	1,937.0 (663.0, 3,211.0)*
$IM_{0\text{-}1\text{-}2*20}$	189.0 (1.91, 379.8)	337.7 (203.0, 472.4)†
$IM_{0\text{-}1\text{-}2*60}$	729.0 (154.9, 1,613.0)	901.4 (260.4, 2,603.3)†
P	0.119	0.016
Seroconversion rate, % (95% *CI*)		
$IM_{0\text{-}1\text{-}6*20}$	73.3 (55.6, 85.8)	87.8 (74.4, 94.7)
$IM_{0\text{-}1\text{-}2*20}$	68.9 (50.8, 82.7)	82.6 (69.3, 90.9)
$IM_{0\text{-}1\text{-}2*60}$	82.9 (67.3, 91.9)	93.0 (81.4, 97.6)
P	0.413	0.327
High-response, % (95% *CI*)		
$IM_{0\text{-}1\text{-}6*20}$	60.0 (42.3, 75.4)	75.6 (60.7, 86.2)*
$IM_{0\text{-}1\text{-}2*20}$	31.0 (17.3, 49.2)	52.2 (38.1, 65.9)†
$IM_{0\text{-}1\text{-}2*60}$	45.7 (30.5, 61.8)	79.1 (64.8, 88.6)*
P	0.083	0.012

Note: group with * or † indicates no significant differences between two groups (*P*>0.05); group with † and * indicates significant differences between two groups (*P*<0.05).
Abbreviation: CKD=chronic kidney disease; GMC=geometric mean concentration; *CI*=confidence interval.

of HepB elimination by 2030.

Previous research has demonstrated that short-course immunization (0-1-2 months) with 10 μg recombinant HepB vaccine induces comparable immune responses to routine immunization in healthy populations, achieving seroconversion rates of 84.6%–89.4% (*6*–*7*). In high-risk populations such as drug users, short-course regimens (0-1-2 months, 20 μg) produced seroconversion rates (65%) similar to routine regimens (62%) (*8*). In this CKD patient cohort, the short-course regimen yielded a 77.3% seroconversion rate, marginally lower than the routine regimen's 81.7%. The variation in seroconversion rates across studies can be attributed to population differences and vaccination dosages. These findings suggest that while short-course immunization can effectively provide rapid protection, it demonstrates slightly reduced GMC and high-response rates compared to routine regimens in CKD patients.

Higher vaccine doses consistently produce elevated GMCs of anti-HBs and enhanced immune responses. Previous research in HIV patients demonstrated that a higher dose (40 μg) short-course regimen significantly increased GMCs (398.0 IU/L *vs.* 158.5 IU/L) and high-response rates (80.6% *vs.* 50.0%) compared to standard-dose (20 μg) short-course vaccination (*9*). This study is the first to examine whether higher doses in short-course regimens can rapidly and effectively induce enhanced immune responses in CKD patients. We found that the short-course, high-dose regimen achieved immunogenicity comparable to routine vaccination, producing GMCs of 824.1 mIU/mL and a high-response rate of 64.1%. This regimen demonstrated significantly superior immunogenicity

compared to the standard-dose short-course regimen. Furthermore, extensive research and clinical experience have established the safety profile of HepB vaccines. This study corroborated these findings, with no serious adverse events reported following short-course, high-dose vaccination. Therefore, to rapidly and effectively generate protective anti-HBs, we recommend short-course, high-dose HepB vaccination for CKD patients.

Chronic kidney disease patients frequently require immunosuppressive or hormone therapy, which can significantly attenuate protective immunity (*4*). Feng et al. (*10*) identified immunosuppression or hormone therapy as an independent risk factor affecting HepB vaccine immunogenicity. Consistent with these findings, this study demonstrated that CKD patients receiving hormones/immunosuppressants exhibited higher rates of non/low-response status and diminished overall immunogenicity. However, this pattern was not observed in patients who did not receive such therapy. Further stratification analysis revealed that among patients not taking hormones/immunosuppressants, both the short-course, high-dose and routine regimens induced comparable seroconversion and high-response rates, which exceeded those of the short-course regimen. The short-course, high-dose regimen generated GMCs of 901.4 mIU/mL. Although this was lower than the routine regime group, the short-course vaccination offered key advantages of earlier protection and improved vaccination completion rates. Therefore, to achieve optimal seroconversion, CKD patients should receive short-course, high-dose HepB vaccination prior to initiating immunosuppressive therapy.

This study had several limitations. First, while immune response was assessed one month post-vaccination, the duration of protective effect could not be fully evaluated due to the limited follow-up period. Extended follow-up studies are needed to determine the longevity of anti-HBs maintenance. Second, patient attrition during follow-up resulted in reduced sample sizes for analysis as the study progressed.

In conclusion, short-course, high-dose HepB vaccination demonstrated immunogenicity comparable to routine regimens in CKD patients. This short-course, high-dose protocol can be recommended as a rapid immunization strategy for CKD patients, particularly when administered before immunosuppressive therapy.

Conflicts of interest: The authors declare that there is no potential conflict of interest.

Funding: Supported by the National Science and Technology Major Project of the Ministry of Science and Technology of the People's Republic of China under Grant [2018ZX10721202], the Key Research and Development Program of Lvliang under Grant [2020SHFZ52], and the Key Research and Development Program of Science and Technology of Linfen under Grant [2136].

doi: 10.46234/ccdcw2024.264

[#] Corresponding authors: Yongliang Feng, yongliang.feng@sxmu.edu.cn; Xiaofeng Liang, liangxf@Jnu.edu.cn.

[1] School of Public Health, Shanxi Medical University, Taiyuan City, Shanxi Province, China; [2] Key Laboratory of Coal Environmental Pathogenicity and Prevention (Shanxi Medical University), Ministry of Education, Taiyuan City, Shanxi Province, China; [3] Center of Clinical Epidemiology and Evidence Based Medicine, Shanxi Medical University, Taiyuan City, Shanxi Province, China; [4] First Hospital/First Clinical Medical College of Shanxi Medical University, Taiyuan City, Shanxi Province, China; [5] Department of Nephrology, Linfen Central Hospital, Linfen City, Shanxi Province, China; [6] Department of Nephrology, Yuncheng Central Hospital, Yuncheng City, Shanxi Province, China; [7] Department of Nephrology, Linfen People's Hospital, Linfen City, Shanxi Province, China; [8] Department of Nephrology, Houma People's Hospital, Houma City, Shanxi Province, China; [9] National Immunization Program, Chinese Center for Disease Control and Prevention, Beijing, China; [10] Institute of Vaccine Industry, Jinan University, Guangzhou City, Guangdong Province, China; [11] Institute of Disease Control and Prevention, Jinan University, Guangzhou City, Guangdong Province, China; [12] Chinese Preventive Medicine Association, Beijing, China.

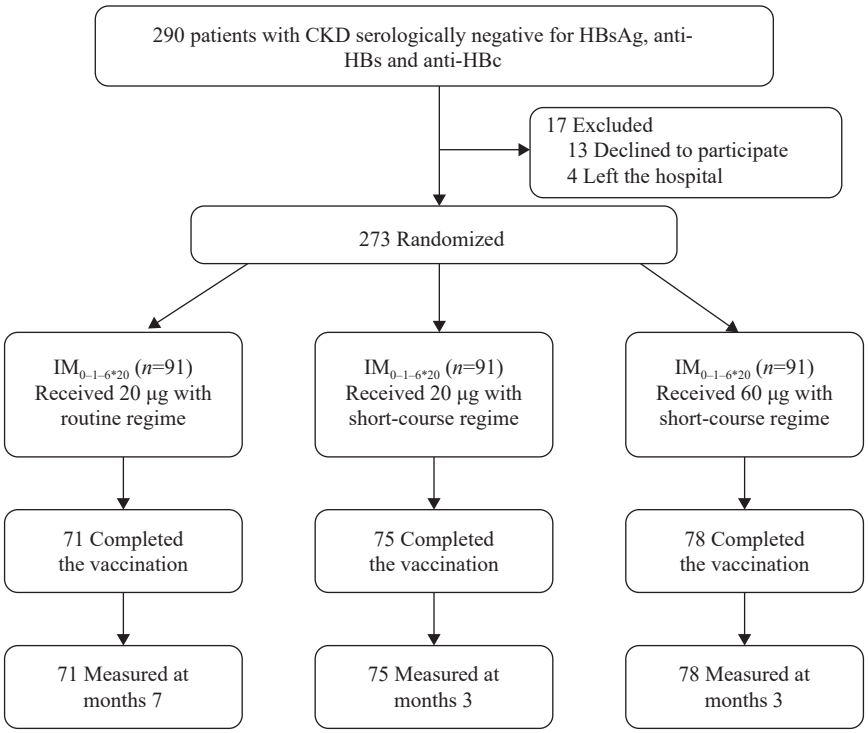
Submitted: April 18, 2024
Accepted: December 06, 2024
Issued: December 13, 2024

REFERENCES

1. Windpessl M, Heine GH, Becker SL, Scheuer AL, Sester M, Kronbichler A. The impact of immunosuppression and chronic kidney disease on immunogenicity of COVID-19 vaccines. Dtsch Med Wochenschr 2021;146(19):1277 – 82. https://doi.org/10.1055/A-1550-7288.
2. Papp KA, Haraoui B, Kumar D, Marshall JK, Bissonnette R, Bitton A, et al. Vaccination guidelines for patients with immune-mediated disorders taking immunosuppressive therapies: executive summary. J Rheumatol 2019;46(7):751 – 4. https://doi.org/10.3899/jrheum.180784.
3. Habib MB, Ali K, Rahhal A, Obeidat I, Altermanini M, Sawaf B, et al. Determinants of vaccine adherence among non-dialysis chronic kidney disease patients in Qatar. Qatar Med J 2024;2023(4):33. https://doi.org/10.5339/qmj.2023.33.
4. Krueger KM, Ison MG, Ghossein C. Practical guide to vaccination in all stages of CKD, including patients treated by dialysis or kidney transplantation. Am J Kidney Dis 2020;75(3):417 – 25. https://doi.org/10.1053/j.ajkd.2019.06.014.
5. Chinese Society of Hepatology, Chinese Medical Association, Chinese Society of Infectious Diseases, Chinese Medical Association. Guidelines for the prevention and treatment of chronic hepatitis B (version 2022). Chin J Clin Infect Dis 2022;15(6):401 – 27. https://doi.org/10.3760/cma.j.issn.1674-2397.2022.06.001.
6. Zhang X, Wang J, Chen X, Yu ML, Yu SB, Sun YY, et al. Short-term immunogenicity of standard and accelerated hepatitis B virus vaccination schedules in healthy adults: a comparative field study in China. Biosci Rep 2018;38(5):BSR20180846. https://doi.org/10.1042/

BSR20180846.
7. Wang J, Liu CH, Ma YJ, Zhu X, Luo LR, Ji YL, et al. Two-year immune effect differences between the 0-1-2-month and 0-1-6-month HBV vaccination schedule in adults. BMC Infect Dis 2022;22(1):159. https://doi.org/10.1186/s12879-022-07151-6.
8. Hwang LY, Grimes CZ, Tran TQ, Clark A, Xia P, Lai DJ, et al. Accelerated hepatitis B vaccination schedule among drug users: a randomized controlled trial. J Infect Dis 2010;202(10):1500 – 9. https://doi.org/10.1086/656776.
9. Vargas JI, Jensen D, Martínez F, Sarmiento V, Peirano F, Acuña P, et al. Comparative efficacy of a high-dose vs standard-dose hepatitis B revaccination schedule among patients with HIV: a randomized clinical trial. JAMA Netw Open 2021;4(8):e2120929. https://doi.org/10.1001/jamanetworkopen.2021.20929.
10. Feng YL, Han YJ, Yao T, Wang JM, Liu HT, Guo HP, et al. Immunogenicity and influencing factors of hepatitis B vaccination based on different vaccination schedules among chronic kidney disease patients. Chin J Epidemiol 2022;43(2):241 – 7. https://doi.org/10.3760/cma.j.cn112338-20210807-00618.

SUPPLEMENTARY MATERIALS



SUPPLEMENTARY FIGURE S1. Study flow diagram, China, May 2019 to February 2020.

SUPPLEMENTARY TABLE S1. Characteristics of chronic kidney disease patients who completed follow-up compared to those lost to follow-up in China from May 2019 to February 2020.

Variables	*N* (%)	Patients completed follow-up (*N*=224) *n* (%)	Patients lost to follow-up (*N*=49) *n* (%)	χ^2	*P*
Gender					
Male	161 (59.0)	130 (58.0)	31 (63.3)	0.45	0.500
Female	112 (41.0)	94 (42.0)	18 (36.7)		
Age (years)					
<35	30 (11.0)	20 (8.9)	10 (20.4)	5.56	0.062
[35, 55)	144 (52.8)	122 (54.5)	22 (44.9)		
≥55	99 (36.2)	82 (36.6)	17 (34.7)		
BMI (kg/m^2)					
<18.5	2 (0.7)	2 (0.9)	0 (0.0)	0.44	0.802
[18.5, 24)	94 (34.4)	77 (34.4)	17 (34.7)		
≥24	177 (64.9)	145 (64.7)	32 (65.3)		
Residence					
Urban	70 (25.6)	58 (25.9)	12 (24.5)	0.04	0.839
Rural	203 (74.4)	166 (74.1)	37 (75.5)		
Level of education					
Primary school or lower	47 (17.2)	36 (16.1)	11 (22.5)	2.82	0.244
Junior High School	139 (50.9)	112 (50.0)	27 (55.0)		
Senior high school or higher	87 (31.9)	76 (33.9)	11 (22.5)		
Type of clinical diagnosis					
Nephrotic syndrome	157 (57.5)	129 (57.6)	28 (57.1)	0.16	0.923
Nephritic syndrome	14 (5.1)	12 (5.4)	2 (4.1)		
Others(renal tubular disorders, polycystic kidney, and unclear)	102 (37.4)	83 (37.0)	19 (38.8)		
Duration of chronic kidney disease (years)					
≤3	214 (78.4)	176 (78.6)	38 (77.5)	0.02	0.875
>3	59 (21.6)	48 (21.4)	11 (22.5)		
CKD stage					
Stage 1	99 (36.3)	84 (37.5)	15 (30.6)	7.48	0.112
Stage 2	82 (30.0)	62 (27.7)	20 (40.8)		
Stage 3	32 (11.7)	27 (12.1)	5 (10.2)		
Stage 4	49 (18.0)	44 (19.6)	5 (10.2)		
Stage 5	11 (4.0)	7 (3.1)	4 (8.2)		
History of HepB vaccine					
Yes	23 (8.4)	20 (8.9)	3 (6.1)	2.08	0.354
No	182 (66.7)	152 (67.9)	30 (61.2)		
Unknown	68 (24.9)	52 (23.2)	16 (32.7)		
Taking hormones/immunosuppressants					
Yes	116 (42.5)	94 (42.0)	22 (44.9)	0.14	0.707
No	157 (57.5)	130 (58.0)	27 (55.1)		
Vaccination schedule					
$IM_{0\text{-}1\text{-}6*20}$	91 (33.3)	71 (31.7)	20 (40.8)	1.84	0.398
$IM_{0\text{-}1\text{-}2*20}$	91 (33.3)	75 (33.5)	16 (32.7)		
$IM_{0\text{-}1\text{-}2*60}$	91 (33.4)	78 (34.8)	13 (26.5)		

Note: Chronic kidney disease staging was defined by estimated eGFR as follows: Stage 5: <15 mL/min; Stage 4: 15–29 mL/min; Stage 3: 30–59 mL/min; Stage 2: 60–89 mL/min; Stage 1: ≥90 mL/min.
Abbreviation: CKD=chronic kidney disease; HepB=hepatitis B; eGFR=estimated glomerular filtration rate.

SUPPLEMENTARY TABLE S2. Univariate analysis of factors affecting high anti-HBs response rates after hepatitis B vaccination in chronic kidney disease patients in China from May 2019 to February 2020.

Variables	Non/Low-response, *n* (%)	High-response, *n* (%)	χ^2	*P*
Gender				
Male	61 (46.9)	69 (53.1)	4.38	0.036
Female	31 (33.0)	63 (67.0)		
Age (years)				
<35	5 (25.0)	15 (75.0)	2.42	0.297
[35, 55)	53 (43.4)	69 (56.6)		
≥55	34 (41.5)	48 (58.5)		
BMI (kg/m^2)				
<18.5	0 (0.0)	2 (100.0)	1.50	0.471
[18.5, 24)	33 (42.9)	44 (57.1)		
≥24	59 (40.7)	86 (59.3)		
Residence				
Urban	17 (29.3)	41 (70.7)	4.47	0.034
Rural	75 (45.2)	91 (54.8)		
Level of education				
Primary school or lower	14 (38.9)	22 (61.1)	1.96	0.376
Junior High School	51 (45.5)	61 (54.5)		
Senior high school or higher	27 (35.5)	49 (64.5)		
CKD stage				
Stage 1	38 (45.2)	46 (54.8)	3.01	0.557
Stage 2	24 (38.7)	38 (61.3)		
Stage 3	8 (29.6)	19 (79.4)		
Stage 4	20 (45.5)	24 (54.5)		
Stage 5	2 (28.6)	5 (71.4)		
Type of clinical diagnosis				
Nephrotic syndrome	60 (46.5)	69 (53.5)	5.36	0.069
Nephritic syndrome	2 (16.7)	10 (83.3)		
Others (renal tubular disorders, polycystic kidney, and unclear)	30 (36.1)	53 (63.9)		
Duration of chronic kidney disease (years)				
≤3	78 (44.3)	98 (55.7)	3.58	0.059
>3	14 (29.2)	34 (70.8)		
History of HepB vaccine				
Yes	7 (33.3)	13 (65.0)	0.38	0.826
No	64 (42.1)	88 (57.9)		
Unknown	21 (40.4)	31 (59.6)		
Taking hormones/immunosuppressants				
Yes	51 (54.3)	43 (45.7)	11.63	<0.001
No	41 (31.5)	89 (68.5)		
Vaccination schedule				
$IM_{0\text{-}1\text{-}6*20}$	22 (31.0)	49 (69.0)	9.27	0.002
$IM_{0\text{-}1\text{-}2*20}$	42 (56.0)	33 (44.0)		
$IM_{0\text{-}1\text{-}2*60}$	28 (35.9)	50 (64.1)		

Note: Chronic kidney disease staging was defined by estimated eGFR as follows: Stage 5: <15 mL/min; Stage 4: 15–29 mL/min; Stage 3: 30–59 mL/min; Stage 2: 60–89 mL/min; Stage 1: ≥90 mL/min.
Abbreviation: CKD=chronic kidney disease; HepB=hepatitis B; eGFR=estimated glomerular filtration rate.

SUPPLEMENTARY TABLE S3. Multifactorial analysis of factors affecting high anti-HBs response rates after hepatitis B vaccination in chronic kidney disease patients in China from May 2019 to February 2020.

Variables		*β*	*S.E.*	*Wald* χ^2	*P*	*OR* (95% *CI*)	a*OR* (95% *CI*)*
b		1.71	0.43	15.77	<0.001		
Taking hormones/ immunosuppressants	Yes					1.00	1.00
	No	0.48	0.16	8.96	0.003	2.54 (1.47, 4.39)	2.59 (1.39, 4.83)
Vaccination Schedule	$IM_{0\text{-}1\text{-}6*20}$					1.00	1.00
	$IM_{0\text{-}1\text{-}2*20}$	−1.11	0.38	8.66	0.003	−0.36 (0.19, 0.71)	0.33 (0.15, 0.69)
	$IM_{0\text{-}1\text{-}2*60}$	−0.11	0.37	0.09	0.871	0.82 (0.42, 1.62)	0.89 (0.43, 1.86)

Abbreviation: CKD=chronic kidney disease; *CI*=confidence interval; *OR*=odds ratio; a*OR*=adjusted odds ratio.
* Adjusted for gender, age, residence, type of chronic kidney disease, and disease duration.