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A Randomized Controlled Study of Efficacy and Safety of Accelerated Versus Standard Hepatitis B Vaccination in Patients With Advanced CKD

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Introduction: Hepatitis B virus (HBV) vaccination is crucial for seronegative patients with advanced chronic kidney disease (CKD) for protection during dialysis while preparing for transplantation. A standard regimen for HBV vaccination requires 24 weeks to be completed. An accelerated HBV vaccination regimen completed within 8 weeks has shown early effective seroconversion in healthcare workers. However, data for patients with advanced CKD are limited.

Methods: A randomized controlled trial was conducted in patients with advanced CKD (estimated glomerular filtration rate [GFR] <30 ml/min per 1.73 m^2) and patients on dialysis. The patients were randomly assigned to either a standard HBV vaccination regimen (Engerix B; 40 μg at 0, 4, 8, and 24 weeks) or an accelerated regimen (40 μg at 0, 1, 4, and 8 weeks). The hepatitis B surface antibodies (anti-HBs) were measured at 12, 28, and 52 weeks. Seroconversion were defined as anti-HBs $\geq$10 IU/l.

Results: At 12 weeks, among the intention-to-treat (ITT) population of 133 participants (65 in the accelerated and 68 in the standard groups), the accelerated group demonstrated significantly higher rates of seroconversion (83.08% vs. 63.24%, $P = 0.01$). In the per-protocol (PP) analysis of 125 patients (62 in the standard and 63 in the accelerated groups), the accelerated group exhibited higher seroconversion rate compared with the standard group (85.71% vs. 69.35%, $P = 0.03$). At 28 and 52 weeks, the seroconversion rates were similar between the 2 groups.

Conclusion: In patients with advanced CKD, the accelerated HBV vaccination regimen demonstrated a significantly higher seroconversion rate at 12 weeks of vaccination. This finding suggests that the accelerated regimen is an effective option to achieve rapid seroconversion before initiating hemodialysis or before undergoing kidney transplantation.

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KEYWORDS: anti-HBs; chronic kidney disease; hepatitis B; hepatitis B vaccination; kidney transplantation; seroconversion

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Chronic hepatitis B infection is one of the leading causes of liver cirrhosis and hepatocellular carcinoma.[1] Despite the introduction of HBV vaccine several decades ago, the worldwide prevalence of HBV infection is still notable among the elderly.[2] According to an observational study, the global seroprevalence of hepatitis B surface antigen (HBsAg) in 2010 was approximately 3.61% of the population, which translates to about 248 million individuals, with variations across different regions.[3] HBV vaccination has been introduced in Thailand since 1988 and it has significant impact in HBV prevention. Despite the positive effect of vaccination on reducing the burden of disease, HBV remains prevalent among older individuals in several other low to middle-income countries, including Thailand.[3-5]

Patients with CKD have impairment of the immune system compared with the general population and are at high risk for infection, including HBV infection.[6] A recent large observational study revealed that the prevalence of HBV infection in patients with CKD increased as the estimated GFR (eGFR) decreased.[7] Patients with advanced CKD, who require frequent blood transfusions are at risk of acquiring transfusion-transmitted HBV infection.[8] In this regard, several studies have demonstrated an increased risk of HBV infection among individuals undergoing hemodialysis.[9-11]

According to the Kidney Disease Improving Global Outcomes guideline, all patients with G4 and G5 CKD, eGFR lower than 30 ml/min/1.73 m^2, should be informed about and considered for kidney transplantation.[12] For achieving better immune response, early HBV vaccination, before eGFR declines below 15 ml/min per 1.73 m^2, is recommended in patients with CKD who are likely to require kidney replacement therapy.[13] All anti-HBs-negative patients with CKD, especially those undergoing dialysis and awaiting kidney transplants are recommended to receive HBV vaccination.[12,14-16] In addition to protection from blood transfusion or hemodialysis-acquired HBV infection, having positive anti-HBs titers provides more opportunity for transplant recipient candidates to receive kidney allografts from HBsAg-positive or hepatitis B core antibody-positive donors.[17] However, the standard HBV vaccination program with recombinant HBV vaccine (Engerix B) for patients with CKD requires 6-month duration period, 40 μg of vaccine given at months 0, 1, 2, and 6 months (0, 4, 8, and 24 weeks), to complete.[18] An accelerated HBV vaccination schedule completed within 2 months has shown early seroconversion in healthy participants.[19] Unfortunately, there are limited data to inform the usefulness of this strategy in patients with CKD. This study aimed to investigate the efficacy of the accelerated versus standard HBV vaccination regimen among patients with advanced CKD.

METHODS

Study Design and Oversight

We conducted a randomized clinical trial at 3 tertiary care hospitals including King Chulalongkorn Memorial Hospital, Benchakitti Park Hospital, and Bhumirajanagarindra Kidney Institute Hospital, Bangkok, Thailand from August 2021 through December 2022. The trial protocol was approved by the ethical committee (IRB 795/2563). All participants signed informed consents before any trial-specific procedure commenced. The safety of the participants was monitored by nurses and investigators after receiving vaccination and telephone interview. The analyses were conducted by statisticians of Chulalongkorn University. The clinical trial was registered at the Thai Clinical Trials Registry number (TCTR20210327001). The trial was sponsored by Ratchadapisek Sompoch Endowment Fund, Chulalongkorn University.

Participants

Patients aged above 18 years with advanced stage CKD, defined as an eGFR below 30 ml/min per 1.73 m^2 and had seronegative test for anti-HBs, a level below 10 IU/l, were eligible for enrollment in the study. Exclusion criteria comprised patients with a history of HBV infection, positivity for HBsAg, positivity for hepatitis B core antibodies, HIV infection, recent receipt of immunosuppressive drugs or tetanus-diphtheria vaccine, history of allergic adverse effects to other vaccines, and/or acute febrile illness.

Randomization and Vaccination

After enrollment, history of vaccination was obtained from each participant by questionnaire or medical record. Participants were randomized to receive either an accelerated hepatitis B vaccination regimen or a standard regimen, using block randomization with a block size of 4. The randomization process was stratified by participants' history of HBV vaccination.

After randomization, participants in the accelerated group received HBV vaccination with 4 double doses of Engerix B 20 μg (each dose injected to each arm) at 0, 1, 4, and 8 weeks, whereas those in the standard group obtained the 4 double dose of 20 μg at 0, 4, 8, and 24 weeks (Figure 1). At each follow-up visit, anti-HBs levels, adverse events, and adherence to the trial regimen were recorded. Participants who underwent transplantation during the study period were excluded from the analysis.

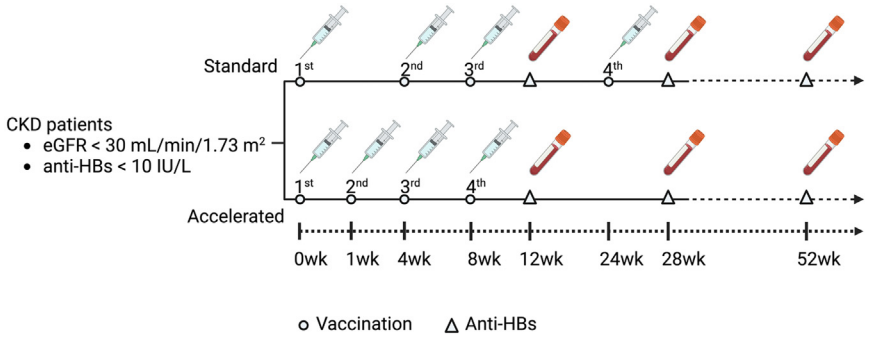


Figure 1. Study design.

Outcomes

The primary outcome of the study was the seroconversion rate at 12 weeks after the first dose of vaccination. The secondary outcomes included the seroconversion rates at 28 and 52 weeks, as well as the rates of anti-HBs ≥100 IU/l at 12, 28, and 52 weeks, which correlate with longer protection. In addition, the anti-HBs levels were evaluated at 12, 28, and 52 weeks. Any adverse events that occurred were carefully monitored throughout the study. Seroconversion was defined as achieving anti-HBs titers equal to or higher than 10 IU/l. The levels of HBsAg, anti-HBs antibodies, and hepatitis B core antibodies were assessed using the Roche Elecsys HBsAg II (cut off: 0.1 IU/ml), Roche Elecsys Anti-HBs II (ranges 2–1000 IU/l), and Roche Elecsys Anti-HBc II assays (detection limit: ≤0.8 IU/ml, respectively, by the electrochemiluminescence immunoassay with the Cobas analyzer. Adverse events were documented through multiple methods, including observation after vaccination, telephone interview 1 week after the vaccination, and self-reporting throughout the study period.

Statistical Analysis

Sample size calculations were based on a study by Elhanan *et al.*,[20] who showed that in dialysis patients given 3 doses of Engerix B - HBV vaccine, the seroconversion rate was 22%, and after the fourth dose at 6 months, the seroconversion rate at 7 months was 48% among patients with no previous vaccination history. For patients who had formerly been vaccinated but failed to seroconvert, the seroconversion rate was approximately 81%. We conservatively estimated that after 4 vaccine doses in the accelerated vaccination arm, the seroconversion rate at 3 months would be 48% compared to 22% in the standard vaccine arm.[20] This equates to an absolute difference in seroconversion rates of 26%.

Under these assumptions, enrolling 60 patients per group would provide 80% power to accurately identify a difference in seroconversion rates of 22% or more, with a 2-sided significance level of 5%. We inflated sample size by 10% in the event of dropouts, resulting in a sample size of 66 participants for each randomized arm.

We summarized differences in seroconversion proportions as percentage differences (95% confidence interval [CI]) in the accelerated versus the standard group as a reference; formal comparisons between randomized arms were made using Fisher exact test. Geometric mean concentrations (GMCs) were summarized by randomized arm, and a linear regression model with the log-transformed titers was used to calculate the difference between groups (95% CI). These estimates were exponentiated to give GMC ratios for the accelerated versus the standard group as a reference. Concentrations above the limit of quantification were imputed as the upper limit of quantification. A *post hoc* subgroup analysis of seroconversion rates at 12 weeks was performed using a test for interaction between the subgroup and the treatment arm. The subgroups of interest were age ≥60 or <60 years, diabetic status, dialysis status, hemoglobin ≥10 or <10 g/dl and white blood cell count ≥6000 or <6000 cells/μl. Adverse event rates were compared by arm using Fisher exact test. The primary end point was assessed in all randomly allocated participants in the vaccination group they were assigned (ITT) population. In addition, the PP population, which excluded participants who were lost or who missed their scheduled vaccination date by more than 7 days were also analyzed. Participants lost before 12 weeks were imputed as nonseroconverters in the ITT analysis of the primary outcome. All other analyses were based on the PP population.

Safety outcomes were reported as frequency (%) of all adverse events occurring after receiving the first vaccine dose until 7 days after last dose; formal comparisons between groups were determined by Fisher exact test. All analyses were performed using Stata 18 (StataCorp LLC, College Station, TX).

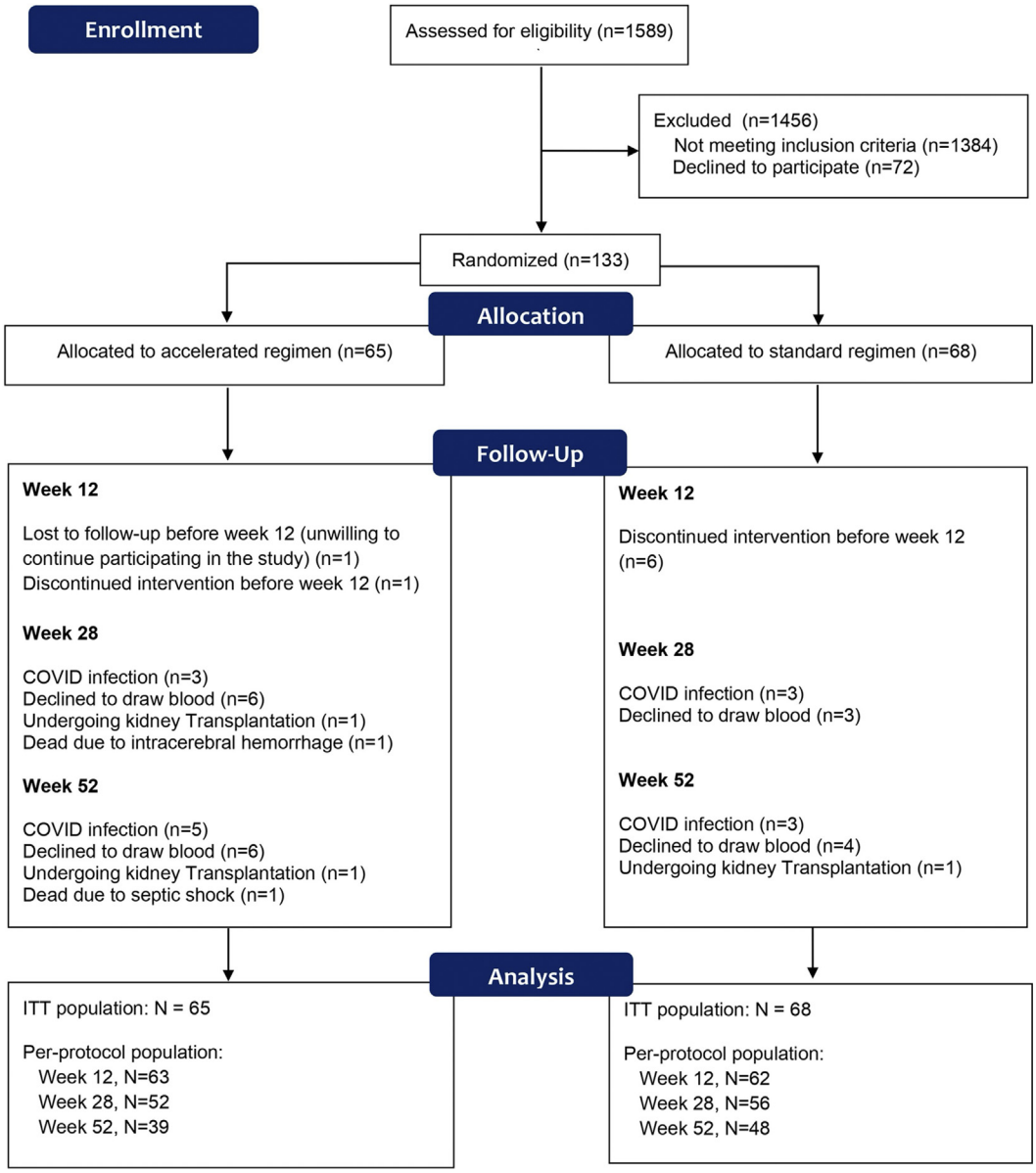


Figure 2. Flow of participants in study.

RESULTS

Participants and Follow-Up

Between August 2021 and April 2022, a total of 1589 participants were screened for eligibility, 133 participants of whom were randomized. The remaining 1456 participants were deemed ineligible (Figure 2). Among the randomized participants, 65 were assigned to the accelerated vaccination group, and 68 were assigned to the standard vaccination group. The mean age of the participants was 58.3 years (SD: 15.7), with 71 (53.4%) being male. Seventeen participants (12.9%) had a history of previous HBV vaccination. Eight patients, 2 from the accelerated group and 6 from the standard group, were lost to follow-up before the assessment of the primary outcome (Table 1).

Primary Outcome

After randomization, in the ITT population, the seroconversion rates at 12 weeks were 54 of 65 (83.08%) and 43 of 68 (63.24%) in the accelerated and standard groups, respectively. In the PP analysis population, the seroconversion rates were 85.71% in the accelerated and 69.35% in the standard groups. The accelerated group revealed a significantly higher seroconversion rate at 12 weeks compared with the standard group, as observed in both ITT (mean difference = 19.84; 95% CI: 5.14–34.54; $P = 0.01$) and PP population (mean difference = 16.36; 95% CI: 1.94–30.78; $P = 0.03$). These findings were consistent with the higher rate of anti-HBs $\geq$ 100 IU/l observed in both ITT and PP populations (Figure 3).

Table 1. Participant characteristics at baseline by randomized group

Characteristics[a]	Total (N = 133)	Standard group (n = 68)	Accelerated group (n = 65)	P
Age, yr, mean (±SD)	58.3 (±15.7)	59.3 (±17.8)	57.3 (±13.3)	0.48
Male, *n* (%)	71 (53.4%)	35 (51.5%)	36 (55.4%)	0.65
Body surface area, kg/m^2, mean (±SD)	24.2 (±5.3)	23.5 (±4.6)	25.0 (±5.8)	0.11
Diabetes mellitus, *n* (%)	55 (41.4%)	30 (44.2%)	25 (38.5%)	0.60
History of cancer, *n* (%)	15 (11.3%)	10 (14.7%)	5 (7.7%)	0.28
Previous HBV vaccination, *n* (%)	17 (12.9%)	9 (13.4%)	8 (12.3%)	1.00
History of smoking, *n* (%)	5 (4.2%)	2 (3.2%)	3 (5.5%)	0.66
History of HCV infection, *n* (%)	2 (1.5%)	1 (1.5%)	1 (1.5%)	1.00
Hemoglobin, g/dl, mean (±SD)	11.0 (±2.1)	11.1 (±2.2)	10.9 (±2.0)	0.50
WBC, cells/ul, median (IQR)	6.4 (5.5 - 8.0)	6.3 (5.2 - 7.4)	6.6 (5.5 - 8.3)	0.09
Dialysis status, *n* (%)				
Nondialysis	40 (30.1%)	21 (30.9%)	19 (29.2%)	0.83
Hemodialysis	79 (59.4%)	38 (55.9%)	41 (63.1%)	0.39
Peritoneal dialysis	14 (10.5%)	9 (13.2%)	5 (7.7%)	0.30
Etiology of CKD, *n* (%)				
Diabetic nephropathy	50 (37.6%)	26 (38.2%)	24 (36.9%)	1.00
Hypertensive nephropathy	26 (19.5%)	13 (19.1%)	13 (20.0%)	1.00
Chronic glomerulonephritis	10 (7.5%)	5 (7.4%)	5 (7.7%)	1.0
IgA nephropathy	9 (6.8%)	6 (8.8%)	3 (4.6%)	0.49
Cardiorenal syndrome	8 (6.0%)	5 (7.4%)	3 (4.6%)	0.72
Drug/Herbal use/toxin	8 (6.4%)	5 (8.1%)	3 (4.8%)	0.49
Obstructive uropathy	5 (3.8%)	1 (1.5%)	4 (6.2%)	0.20
Lupus nephritis	4 (3.0%)	1 (1.5%)	3 (4.6%)	0.36
Focal segmental glomerulosclerosis	3 (2.3%)	0 (0.0%)	3 (4.6%)	0.11
Infectious glomerulonephritis	1 (0.8%)	1 (1.5%)	0 (0.0%)	1.00
Thrombotic microangiopathy	1 (0.8%)	1 (1.5%)	0 (0.0%)	1.00
Cryoglobulinemic glomerulonephritis	1 (0.8%)	1 (1.5%)	0 (0.0%)	1.0
Myeloma cast nephropathy	1 (0.8%)	1 (1.5%)	0 (0.0%)	1.0
Polycystic kidney disease	1 (0.8%)	0 (0.0%)	1 (1.5%)	0.49
Undefined etiology	7 (5.3%)	4 (5.9%)	3 (4.6%)	1.0

CKD, chronic kidney disease; HBV, hepatitis B virus; HCV, hepatitis C virus; IQR, interquartile range; WBC, white blood cell count.
[a]Data are presented as mean (SD) or frequency (%) unless otherwise indicated.

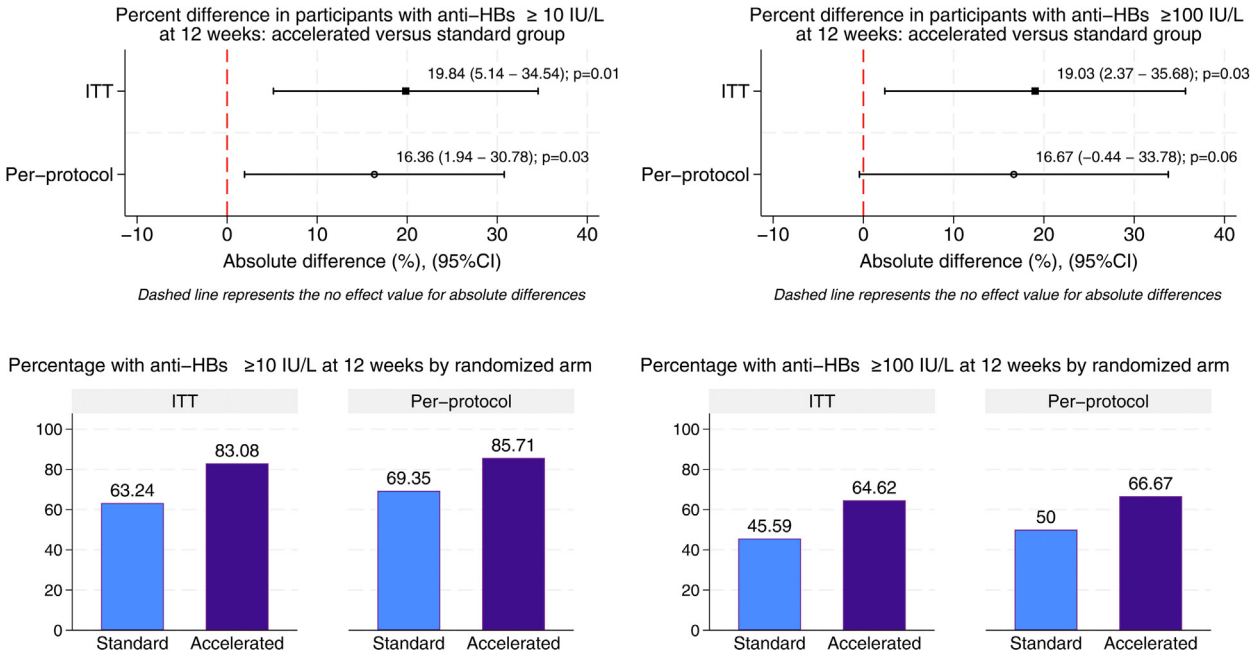
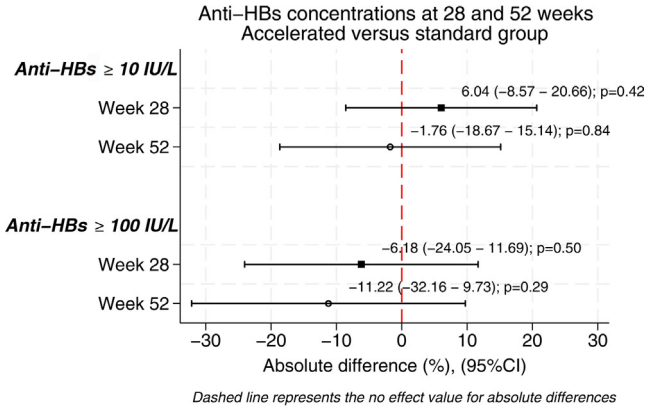
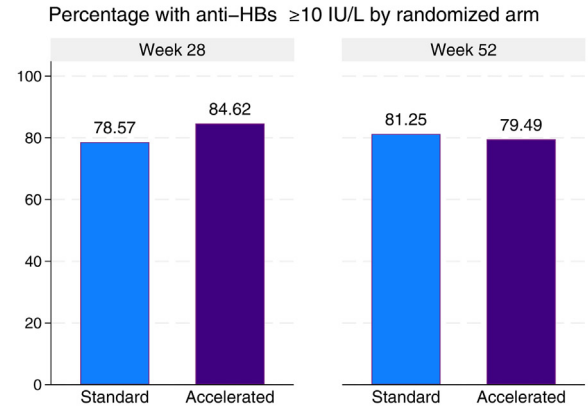


Figure 3. Seroconversion rate (anti-HBs ≥10 IU/l) and rate of anti-HBs ≥100 IU/l at 12 weeks.





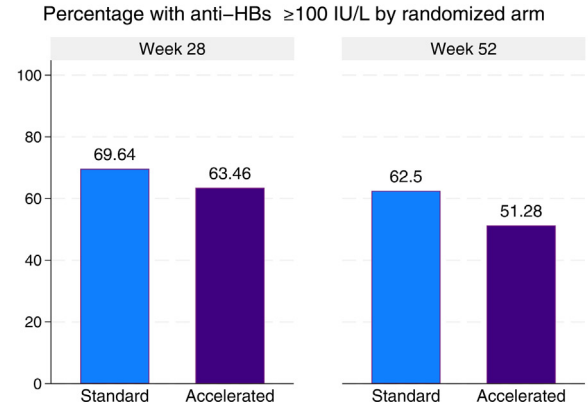


Figure 4. Seroconversion rate (anti-HBs ≥10 IU/l) and rate of anti-HBs ≥100 IU/l at 28 and 52 weeks.

Secondary Outcomes

At 28 weeks, the seroconversion rates were comparable between the 2 groups with 44 of 52 participants (84.62%) in the accelerated group, and 44 of 56 participants (78.57%) in the standard group (mean difference = 6.04 [95% CI: −8.57 to 20.66]; $P = 0.42$) (Figure 4). Among these participants, the rate of anti-HBs ≥100 IU/l was 63.46% in the accelerated group, and 69.64% in the standard group (mean difference = −6.18 [95% CI −24.05 to 11.69]; $P = 0.50$). At 52 weeks, the seroconversion rate in the accelerated groups was 79.49% (31 of 39 participants) which is comparable to 81.25% (39 of 48 participants) in the standard group (mean difference = −1.76 (95% CI: −18.677 to 15.14}; $P = 0.8$). The anti-HBs ≥100 IU/l at 52 weeks was observed in 51.28% of participants in the accelerated group and 62.50% in the standard group (mean difference = −11.22 (95% CI: −32.16 to 9.73]; $P = 0.29$) (Figure 4).

At 12 weeks, the anti-HBs GMC in the accelerated group were 178.7 IU/l (95% CI: 104.6–305.4) which was higher than 70.5 IU/l (95% CI: 36.3–137.0) of the standard group (Table 2). The anti-HBs GMC ratio between the accelerated and standard group was 2.53 (95% CI: 1.09–5.89; $P = 0.03$). At 28 weeks, the anti-HBs GMC were 146.5 IU/l (95% CI: 80.6–266.1) in the accelerated groups and 179.8 IU/l (95% CI: 91.8–352.5) in the standard group, resulting in a GMC ratio of 0.81 (95% CI: 0.33–1.99; $P = 0.65$). At 52 weeks, the anti-HBs GMC of the accelerated and standard groups were comparable, 81.6 IU/l (95% CI: 39.6–167.8) and 137.6 IU/L (95% CI: 67.4 – 281.2) respectively, yielding a GMC ratio of 0.59 (95% CI 0.22–1.63; $P = 0.31$). Despite the lack of statistical significance, it should be noted that the titers were approximately 2-folder higher in the standard group.

Subgroup Analysis

Our *post hoc* subgroup analysis revealed no significant differences in the seroconversion at 12 weeks between both groups in patients with diabetes (nondiabetic, $n = 72$; and diabetic, $n = 53$), by dialysis status (non-dialysis, $n = 36$; and dialysis, $n = 89$), hemoglobin level dichotomized at 10 g/dl (hemoglobin <10 g/dl, $n = 41$; and hemoglobin ≥10 g/dL, $n = 84$), or white blood cell count dichotomized at 6000 cells/μl (white blood cell count <6000/μl, $n = 46$; and white blood cell count ≥6000/μl, $n = 79$). However, there was a significant interaction between vaccination group and age (<60 years, $n = 59$; or ≥60 years, $n = 66$), indicating

Table 2. Anti-HBs geometric mean concentrations and geometric mean concentration ratios in the accelerated versus the standard arm as a reference, at study weeks 12, 28 and 52

	Geometric mean concentration (95% CI)			
Visit	Standard group	Accelerated group	GMCR (95% CI)	*P* value
12 weeks	70.5 (36.3–137.0)	178.7 (104.6–305.4)	2.53 (1.09–5.89)	0.03
28 weeks	179.8 (91.8–352.5)	146.5 (80.6–266.1)	0.81 (0.33–1.99)	0.65
52 weeks	137.6 (67.4–281.2)	81.6 (39.6–167.8)	0.59 (0.22–1.63)	0.31

anti-HBs, hepatitis B surface antibodies; CI, confidence interval; GMCR, geometric mean concentration ratio.

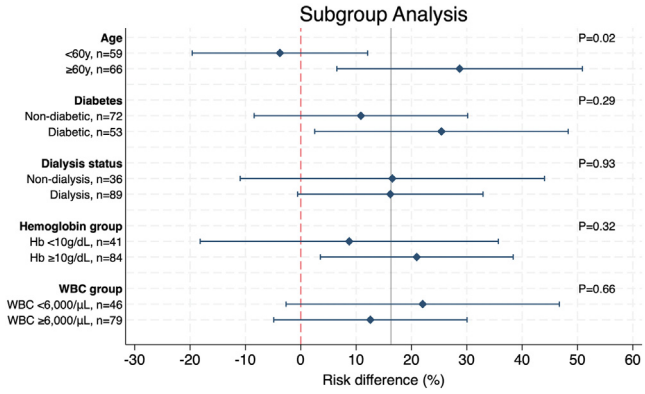


Figure 5. Primary outcome subgroup analysis.

that participants in the older age group achieved significantly higher levels of seroconversion in the accelerated group compared with the standard group ($P = 0.02$, Figure 5). Fifteen participants (8 in the accelerated group and 7 in the standard group) had received prior vaccination against HBV. We did not perform a subgroup analysis due to the low numbers. However, at 12 weeks, 8 of 8 participants (100%) with a prior HBV vaccination in the accelerated group and 5 of 7 participants (71.43%) in the standard group achieved seroconversion. At 28 weeks, all 7 previously vaccinated participants in the standard arm had seroconverted.

Adverse Events

The incidence of adverse events was comparable between the 2 groups. The most frequently reported side effect was mild injection-site pain (11.2%), which was effectively managed with acetaminophen. The duration of pain was less than 24 hours after injection. No serious adverse events were observed in either groups during the follow-up period (Table 3).

DISCUSSION

Our study demonstrated that patients with advanced CKD randomized to an accelerated HBV vaccination regimen achieved significantly higher seroconversion (anti-HBs ≥10 IU/l) and anti-HBs ≥100 IU/l rates at 12 weeks, without any serious adverse events, compared with those who obtained the standard regimen. The PP analysis suggested that for every 100 accelerated vaccinations, we would expect an additional 16 seroconversions and anti-HBs ≥100 IU/l responder than if participants received the standard vaccination schedule. At 28 and 52 weeks, seroconversion and anti-HBs ≥100 IU/l rates were comparable between the 2 groups indicating the durability of response in the accelerated arm. The accelerated group completed the vaccination in 8 weeks whereas the standard group required 24 weeks. These findings suggest that the accelerated HBV vaccination regimen is a safe and effective approach for achieving seroconversion in advanced patients with CKD.

Current guidelines recommend that all patients with advanced CKD and those undergoing dialysis who are negative for HBsAg should receive hepatitis B vaccination at double standard dosage (total of 40 μg of Engerix B), administered at 0, 1, 2, and 6 months.[21] Seroconversion of anti-HBs in response to the vaccination can protect patients from HBV infection during dialysis and enable them to receive a kidney from an HBsAg-positive donor.[17] Kidney transplantation from an HBV-positive donor can reduce the risk of dialysis complications such as cardiovascular or cerebrovascular events, vascular access problems, and volume overload.[17] By shortening the time of vaccination, the risk of HBV infection is decreased, and the donor pool for candidate recipients is increased.

A previous meta-analysis demonstrated that older age was associated with poor seroconversion to HBV vaccine.[22] Although, the mechanism of immunesenescence was still unestablished, it is believed that an imbalance of Th1/Th2 cytokines and impaired memory CD4 T cells contribute an important role to the lower seroconversion rate.[23,24] However, our *post hoc* subgroup analysis found that patients 60 years or older had a more pronounced response to the accelerated vaccination schedule than those under 60. This suggests that poorer serological responses in older patients could at least be partially overcome by a rapid double-dose vaccination schedule.

Previous studies investigating accelerated HBV vaccination have used various regimen schedules.[19,25] Asli *et al.*[19] reported that the accelerated HBV vaccination regimen consisting of a 20 μg dose administered at 0, 1, 4, and 8 weeks resulted in significantly higher seroconversion rates since 4 weeks after the first dose of vaccination in healthy prisoners compared with standard vaccination regimen. Our HBV vaccination schedule was similar to the accelerated regimen used in the aforementioned study. As stated earlier, we used a

Table 3. Frequency of adverse events reported after Hepatitis B vaccination in patients with advanced CKD

Reported event	Standard group ($n = 62$)	Accelerated group ($n = 63$)	*P* value
Number (%)			
Injection- site pain	9 (14.52%)	5 (7.94%)	0.27
Fever	2 (3.23%)	1 (1.59%)	0.62
Fatigue	1 (1.61%)	0 (0)	0.50
Cough	1 (1.61%)	0 (0)	0.50
Coryza	0 (0)	1 (1.59%)	1.0
Alopecia	1 (1.61%)	0 (0)	0.50

CKD, chronic kidney disease.

double-dose vaccination in the present study due to the impaired immune function observed in patients with CKD.

Previous studies reported seroconversion in patients with advanced CKD ranging from 44.3% to 64% after completion of the standard vaccination schedules.[26,27] In the present study, the seroconversion rates after completion of the vaccination using the accelerated regimen were 85.71% compared with 78.57% for the standard regimen. The difference of seroconversion rates of the studies can be explained by various factors, including eGFR level, underlying kidney disease, stage of CKD, mode of dialysis, and the different type of adjuvant.[25,27,28]

The benefits of the accelerated regimen does not only provide the earlier seroconversion, but also yield improved adherence and vaccination completion rates.[29] A retrospective study assessing compliance and completion of multidose hepatitis A and hepatitis B vaccinations demonstrated that the accelerated regimen had higher compliance and completion rates compared with the standard regimen.[30]

There is no clear evidence of durability of HBV vaccination and the importance of booster doses in patients with advanced CKD.[22,27] To ensure anti-HBs remains above 100 IU/l, some studies suggested giving a booster doses every year in patients with anti-HBs between 10 to 100 IU/l and every 5 years in those with anti-HBs >100 IU/l.[31-33] At 12 weeks, the anti-HBs GMC in our accelerated group were significantly higher than those in the standard group. Although the titers in the accelerated group were comparable to the standard group at 28 and 52 weeks, they had begun to wane, and continued to decrease by 52 weeks. This could be explained by the longer duration since the last vaccination dose in the accelerated group compared to the standard group (44 weeks vs. 28 weeks). We recommend conducting anti-HBs titer measurements for patients in the accelerated HBV vaccination group at 28 weeks. Those with anti-HBs titers below 100 IU/l should be considered as candidates for a booster HBV vaccination after 28 weeks.

Alternative hepatitis B vaccines, such as Sci-B-Vac and HEPLISAV-B, demonstrated comparable seroconversion rates at 28 weeks, when compared to Engerix-B. However, the antibody titers for Sci-B-Vac and HEPLISAV-B were significantly higher than those for Engerix-B.[20,32] Girndt *et al*. reported that Fendrix exhibited immunogenicity similar to Engerix-B 4 weeks after the initial vaccination. Notably, Fendrix displayed significantly fewer local reactions compared to both Engerix-B and HEPLISAV-B.[33]

In the present study, there were no serious adverse events such as anaphylaxis. The most common adverse event was mild pain at the injection-site, which could be relieved with acetaminophen. Cough, coryza, and alopecia reported by some participants were thought to be unrelated to the vaccine.

This study is the first randomized controlled trial to assess the efficacy and safety of an accelerated HBV vaccination program in patients with advanced CKD. In addition, we demonstrated the durability of the HBV vaccine in both the accelerated and standard HBV vaccination regimens among patients with advanced CKD. Shortening the duration for completion of HBV vaccination, the accelerated HBV vaccination regimen would be the preferable option for patients with advanced CKD, particularly those waiting for kidney transplantation. By rapidly achieving protection against HBV infection, this approach offers the potential to reduce waiting time by expanding the pool of possible donors and improve patient survival after kidney transplantation.[34]

Admittedly, our study had some limitations. First, we did not demonstrate the long-term durability of the vaccine and the potential booster effect in patients with advanced CKD. Second, the anti-HBs titers in this study may have been underestimated because the upper limit was truncated at 1000 IU/l. Third, a number of study participants who had seroconverted at 12 weeks did not have subsequent blood tests for anti-HBs due to reasons such as undergoing kidney transplantation or limitations imposed by the COVID-19 pandemic. During certain periods, there was limited availability of COVID-19 vaccines in Thailand, and some participants developed COVID-19 or were unwilling to attend follow-up visits. This reduction in sample size increases the width of the 95% CI and the range of plausible data consistency. Future studies with larger sample sizes will provide more precise estimates of the impact of the accelerated vaccine schedule. Longitudinal studies are crucially needed to further investigate the durability and longevity of the vaccine response.

Conclusion

The accelerated HBV vaccination regimen demonstrated significantly higher seroconversion rates at 12 weeks compared with standard HBV vaccination regimen among patients with advanced CKD. This approach can be considered as an effective option for achieving rapid seroconversion, particularly before hemodialysis initiation and in preparation for kidney transplantation.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

CONSORT checklist

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