Original Article

Antibody titer after vaccination against hepatitis B virus with different schedule among patients with end-stage renal disease on maintenance hemodialysis

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ABSTRACT

Background: *Infection with the hepatitis B virus (HBV) causes high morbidity. Vaccination against HBV is very important for patients receiving hemodialysis due to end-stage renal disease (ESRD). Our study aimed to find out whether 0, 1, 2 and 6 months HBV vaccination schedule produces a better antibody response than the 0, 1, 2 months or 0,1,6 months schedule with two 20 µg [1.0 mL doses] I/M injections administered in 2 sites in each dose and to find out the overall antibody status (effectiveness) of HBV vaccine in a patient with ESRD on maintenance hemodialysis.*

Methods: *This cross-sectional study was conducted in the Department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD), Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh, from December 2020 to November 2021. All patients were collected from the Department of Hemodialysis and Nephrology diagnosed with ESRD and were on maintenance hemodialysis. Data were collected in a single sitting about their past vaccination status. An anti-HBs antibody test was sent to see the antibody status after vaccination against HBV.*

Results: *In this study, a total of 100 patients were selected, aged between 40 and 82 years, and the majority of the patients (63.0%) were male. Among them, 40 (40%) patients received 0, 1, 2 months schedule and 30 (30%) patients received 0, 1, 6 and rest of 30 (30%) patients received 0, 1, 2, 6 months schedule. We found patients who used the 0,1,2,6 months schedule, 54% of them achieved protective antibodies, and for patients who used the 0,1,2 and 0,1,6 months schedule, only 27% and 19% achieved protective antibodies, respectively. Their anti-HBs (titer) mean±SD were 293.93±122.38 (IU/L) with 0,1,2,6 months schedule and 126.14±132.90 (IU/L) and 276.66±152.07 (IU/L) with 0,1,2 months and 0,1,6 months schedule respectively. Overall we found that 37 (37.0%) of the patients had protective antibodies (>100 IU/l), 29 (29.0%) with low protective antibodies (10-100 IU/L), and the remaining 34 (34.0%) respondents we7re found to have nonprotective antibody (<10 IU/L).*

Conclusion: *Patients who received a vaccine scheduled 0,1,2,6 months achieved the highest anti-HBs titer, and the highest percentage of patients (54%) developed a protective antibody with the same schedule. So, we found that vaccine schedules (0,1,2,6 months) are preferred for better protection against HBV infection.*

Key words: *hepatitis B virus, end-stage renal disease, hemodialysis.*

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INTRODUCTION

Hepatitis B virus (HBV) infection has high morbidity. It is more likely to result in a carrier state in uraemic patients.[1-3] Vaccination against HBV is mandatory for all patients receiving renal replacement therapy or approaching end stage renal disease (ESRD).[4] Patients with chronic kidney diseases (CKD), especially those on hemodialysis, are immunocompromised and thus are less likely to achieve protective anti-HBs levels after vaccination with standard doses. [5-8] The response to hepatitis B vaccination may also be better in children. Higher seroprotection rates have been identified in patients with CKD, particularly those with mild or moderate renal failure, who were vaccinated before becoming dialysis-dependent.[9] Limited data are available on the duration of immune memory after hepatitis B vaccination in dialysis patients. No clinically significant HBV infections have been documented among immunocompromised persons who maintain protective levels of anti-HBs, and hemodialysis patients who are vaccinated against HBV have maintained anti-HBs levels>10 IU/ml; clinically significant HBV infection has not been documented.[10] For patients undergoing hemodialysis and other immunosuppressed patients, higher vaccine doses or an increased number of doses are recommended. The available hepatitis B vaccine is administered at a double standard dosage in a four-dose schedule for hemodialysis patients with two 20 ug [1.0 mL doses] administered in 2 injections.[11] Testing after vaccination is recommended to determine response. Testing should be done 1 to 2 months after the last dose of the vaccination schedule.[12-14] Anti-HBs levels of 10 IU/ml or greater are considered protective.[15]

For a patient with ESRD on maintenance hemodialysis or approaching ESRD, a recombinant Hep-8 vaccine is used at a dose of 40 μg intramuscularly in the deltoid muscle to prevent HBV infection. Three types of schedules are used in our Hemodialysis and Nephrology unit, mostly 0,1, 2, and 6 months, but some also use 0,1,2 or 0,1,6 months schedule. The aim of our study is to see the antibody status of these three different patient groups and also the overall antibody level of patients who were on maintenance hemodialysis and completed their HBV vaccination schedule and to determine which schedule produced a better antibody response.

METHODS

This cross-sectional study was conducted in the Department of GHPD, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh, from December 2020 to November 2021. A total of 100 patients were selected for the study, and all patients were collected from the Department of Hemodialysis and Nephrology of BIRDEM general hospital diagnosed with ESRD and are on maintenance hemodialysis. The hepatitis B vaccine was administered with two 20 ug [1.0 mL doses] intramuscular injections in a four-dose (0,1,2,6 months) and three-dose (0,1,2 and 0,1,6 months) schedule and at least one month have passed after completion of the vaccination schedule (At least four weeks after the last dose of the schedule). Data were collected from the patient in a single setting, and an anti-HBs test was sent to assess the antibody status after vaccination against HBV. Patients with past HBV infection or carrier state, acute kidney injury (AKI) on CKD who were on hemodialysis were excluded from this study. Convenient nonprobability sampling was done. Data were stored and analyzed with standard computer software (SPSS-24). $P < 0.05$ was considered statistically significant.

An anti-HBs level (>100 IU/l) was considered well protective (10-100 IU/L), low protective, and nonprotective (<10 IU/L).[16,17]

RESULTS

In this study, we found that males were 63% and females 37%, and the male-female ratio was 1.7. All of our patients were aged between 40 and 82 years. Among the respondents, 50.0% belonged to the age group of 55-69 (Table I).

Table I. Baseline parameters of the study population (N=100)

Variables		n(%)
Years	Age Distribution	
40-54		39(39.0)
55-69		50(50.0)
70-85		11(11.0)
Mean±SD		57±9.05
Min-Max		40-82
	Sex Distribution	
Male		63(63.0)
Female		37(37.0)
	Occupation	
Farmer		5(5.0)
Business		15(15.0)
Service Holder		13(13.0)
Retired		26(26.0)
Housewife		34(34.0)
Others		7(7.0)

There anti-HBs (titer) 0,1,2 vaccine scheduled used Mean±SD were 126.14±132.90(IU/L), 0,1,2,6 vaccine scheduled used Mean±SD ware 293.93±122.38 (IU/L) and 0,1,6 vaccine scheduled used Mean±SD ware 276.66±152.07 (IU/L) respectively (Table II).

Table II. Distribution of the type of vaccine scheduled used with their anti-HBs (titer) IU/L

	Vaccine Scheduled used	
	n(%)	Anti HBs (titer)IU/L Mean±SD
0,1,2	40(40.0)	126.14±132.90
0,1,2,6	30(30.0)	293.93±122.38
0,1,6	30(30.0)	276.66±152.07

We found that 37(37.0%) patients achieved protective (>100 IU/l), 29(29.0%) had low protective (10-100 IU/L), and the remaining 34(34.0%) respondents were found to have nonprotective (<10 IU/L) antibody level (Table III).

Table III. Level of immunity against hepatitis B virus in the vaccinated patient (MHD) (N=100)

	n	%
Protective (>100 IU/L)	37	37.0
Low protective (10-100 IU/L)	29	29.0
Non-protective (<10 IU/L)	34	34.0

Protective antibody levels (>100 IU/l) were found in vaccine Scheduled (0,1,2), (0,1,2,6), and (0,1,6) months group by 27 %, 54.0 %, and 19.0 % of the responder, respectively. With Scheduled (0,1,2), (0,1,2,6), and (0,1,6), low protective antibodies (10-100 IU/L) were found in 40.0%, 20.0 %, and 40.0 % of the responder, respectively. Non-protective (<10 IU/L) antibodies were found in scheduled (0,1,2), (0,1,2,6), and (0,1,6) months group by 50.0%, 25.0%, and 25.0% of the responder, respectively (IU/L) (Table IV).

Table IV. Level of antibody against hepatitis B virus in vaccinated patients used different vaccine scheduled (MHD) (N=100)

	0,1,2(%)	0,1,2,6(%)	0,1,6(%)	p-value
Protective (>100 IU/L)	27.0%	54.0%	19.0%	0.621
Low protective (10-100 IU/L)	40.0%	20.0%	40.0%	
Non-protective (<10 IU/L)	50.0%	25.0%	25.0%	

DISCUSSION

Bangladesh has an intermediate hepatitis B virus infection prevalence with a 4% HBsAg positive population.[19] In a previous study 3.5% prevalence rate of hepatitis B virus infection in pregnant women of Bangladesh was seen.[20] It was observed in the present study that among the respondents (50.0%) who belonged to the age group of 55-69 majority of the patients (63.0%) were male. Furthermore, we selected patients from two hemodialysis units where HBsAg positive patients were not accepted for hemodialysis to minimize the risk of spreading HBV infection. [21-23]

There anti-HBs (titer) level in 0,1,2 vaccine scheduled group Mean±SD were 126.14±132.90(IU/L), 0,1,2,6 vaccine scheduled used group Mean±SD 293.93±122.38 (IU/L) and 0,1,6 vaccine scheduled group Mean±SD ware 276.66±152.07(IU/L) respectively. 40.0% of the patients used (0,1,2) months, 30.0% used (0,1,2,6) months, and the rest of the 30.0% used (0,1,6) months schdeul.[24,25] In our study, we found that protective (>100 IU/l) antibody levels were achieved by the patient who used (0,1,2), (0,1,2,6), and (0,1,6) scheduled by 27 %, 54.0 %, and 19.0 % respectively and 40.0 %, 20.0 %, and 40.0 % achieved low protective (10-100 IU/L) antibody by (0,1,2), (0,1,2,6), and (0,1,6) months scheduled. Non-protective (<10-3IU/L) antibodies were achieved by 50.0 %, 25.0 %, and 25.0 % of participant who used vaccines Scheduled (0,1,2), (0,1,2,6), and (0,1,6), respectively.

Our analysis found that only 37% have protective immunity, 29% have low protective immunity, and 34% have nonprotective immunity, indicating that approximately one-third of the dialysis patients had no protection despite vaccination, probably due to

immunosuppression. [26] In the present study, there is a significant difference seen in the proportion of the patients with protective and nonprotective titers among the scheduled vaccinated (0,1,2,6 months) and non-Scheduled (0,1,2 or 0,1,6 months) vaccinated subjects. The vaccination schedule used (0,1,2) doses by 40%, (0,1,2,6) doses by 30%, and (0,1,6) doses by 30% of the population. The highest antibody level Mean±SD (293.93±122.38 IU/L) was achieved by vaccine Scheduled used 0,1,2,6 months, and the highest percentage of patients, 54%, achieved protective antibody with 0.1,2,6 months scheduled compared to only 27% and 19% with 0,1,2 and 0,1,6 months schedule respectively. It has been suggested that advanced age reduces the response to the HBV vaccine in hemodialysis patients. This relatively low response may be due to higher age, the presence of diabetes, and lower doses of vaccination schedule as the majority (79%) took a three-dose regimen. Some studies showed that vaccine response is 64% with three doses, whereas 86% with four doses.[27]

Observational studies were included, and the results of these studies may not be as robust as randomized clinical trials. The matched comparison groups and objective outcome measures (i.e., anti-HBs levels) strengthen the data quality.

We can conclude that there is a significant difference in the proportion of patients with protective and nonprotective titers among the scheduled vaccinated and non-Scheduled vaccinated subjects. So we recommend that a four-dose vaccination schedule (0,1,2,6 months) should be preferred for better protection against HBV infection. Due to the overall poor immune response in ESRD patients, it is also recommended that antibodies should be checked at least one month after the last vaccine dose to check for adequate immune response.

Author's contributions: All authors discussed the results and commented on the manuscript. Sajjad SM, Mahfuz EK, Bhuiyan TM, Azam G, Datta IK, Mamoon MAA, Ahmed S, and Mahmud A contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript. The decision to submit the article for publication is carried out by Sajjad SM.

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