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Research Article

Immune Response to Hepatitis B Vaccine in Patients on Hemodialysis: Experience from Liaquat University Hospital

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Abstract: Background: Patients on hemodialysis (HD) are at risk for HBV transmission due to the frequent exchange of blood products and contact with contaminated dialysate or dialysis equipment. There is reduced immunogenic response to the standard hepatitis B vaccine often occurs.

Objective: To determine the response of hepatitis B vaccine in patients among hemodialysis dependent patient.

Materials and Methods: This is an interventional study conducted for one year duration from December 17, 2021, to December 16, 2022 at Department of Nephrology Liaquat University Hospital in Hyderabad/Jamshoro, Sindh. The study included patients on hemodialysis for at least 3 or more than 3 months, aged between 18 and 60 years, including both males and females. Four doses of the Hepatitis B vaccine were administered. The doses were given on a schedule of 0, 1, 2, and 6 months and then six-week later antibody titer levels measured against the hepatitis B surface antigen. An adequate responder to the Hepatitis B vaccine was defined as having an anti-Hepatitis B surface antigen level of 100 IU/L or higher, while an inadequate responder defined as having a level below 100 IU/L.

Result: Among the 96 patients, 64 (74%) were male, and 32 (26%) were female with a mean age of 42.92years (±9.76). Type II diabetes mellitus was observed in 42 (43.8%) patients, and hypertension was prevalent in 73 (76%) patients. Out of 96 patients, 53 (55.2%) and 43 (44.8%) had adequate and inadequate response.

Conclusion: A significant proportion of patients showed an inadequate antibody response, despite completing the full vaccination schedule, confirming reduced vaccine efficacy in this population

Keywords: Hepatitis B virus (HBV) vaccination, Chronic kidney disease, Hemodialysis (HD), End stage renal disease (ESRD).

INTRODUCTION

Hepatitis B virus (HBV) infection a significant global public health challenge [1], with approximately 296 million individuals affected worldwide. Pakistan is recognized as one of the countries where HBV is endemic, having a substantial burden of chronic viral hepatitis that shows an increasing pattern each year [2], with a carrier rate of 2.6% [3].

Kidney disease improving global outcome (KIDGO) stage-5 chronic kidney disease (CKD) patients on hemodialysis or peritoneal dialysis are at high risk for HBV infection. This risk drives from the need for blood transfusions and contact with infected dialysate or dialysis equipment [4]. Hemodialysis patients are the most affected because of prolonged and repeated exposure to the patient's blood during treatment [5].

Chances to lower infection rates start with adequate patient screening and effective vaccination programs before patients begin outpatient dialysis. A key step in the right direction is ensuring that not just susceptible patients but also dialysis staff members are vaccinated against HBV [6]. Patients receiving the HBV vaccine before the initiation of dialysis demonstrate a markedly superior immune response than those who receive the vaccine after starting the dialysis treatment. While post-dialysis initiation vaccination serves to confer some level of immunity in a much-needed way, patients who receive the vaccine after the dialysis initiation elicit inadequate response to the HBV vaccine [7, 8].

In recent years, the occurrence of hepatitis B infection has been decreasing due to the introduction of global vaccination programs, infection control measures, and comprehensive screening initiatives. Nonetheless, individuals with chronic kidney disease often show a diminished response to the vaccine because of factors like malnutrition, immune deficiencies, the impact of uremia

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and dialysis adequacy [9]. Research suggests that 20% to 40% of hemodialysis patients do not mount an immune response to HBV vaccination [10, 11]. Given the increased risk of hepatitis B infection among hemodialysis dependent patients and low immune response to vaccination, this study aims to evaluate their response to the hepatitis B vaccine in order to guide preventive strategies and enhance protection against infection.

MATERIALS AND METHODS

This is an interventional study conducted for one year duration from December 17, 2021, to December 16, 2022, at Department of Nephrology Liaquat University Hospital in Hyderabad/ Jamshoro, Sindh. After getting approval from LUMHS's Ethical Research Committee (Notification no: LUMHS/REC/-241 dated: 16-12-2021). Based on a 72% expected sero-conversion [12] with 9% margin of error and 95% confidence interval, a sample size of 96 was determined. A consecutive non probability sampling technique was employed to allow the inclusion of all eligible hemodialysis dependent patients presenting during the study period, ensuring practicality in a limited clinical population and reducing selection bias.

The study included patients on hemodialysis for more than 3 months, aged between 18 and 60 years, including both males and females. Patients with a prior diagnosis of hepatitis B virus infection, those already vaccinated against hepatitis B, and individuals with HIV-positive status were excluded.

After obtaining written consent from the participants, a detailed history was recorded. Four doses of the Hepatitis B vaccine (40 mcg, double dose) were administered intramuscularly in the deltoid region at the vaccination clinic of Liaquat University Hospital. The doses were given on a schedule of 0, 1, 2, and 6 months. Six weeks after the final dose, 2 ml of blood was collected and sent to the LUMHS Diagnostic and Research Laboratory in Hyderabad to measure the antibody titre levels against the hepatitis B surface antigen. An adequate responder to the Hepatitis B vaccine was defined as having an anti-Hepatitis B surface antigen level of 100 IU/L or higher, while an inadequate responder was defined as having a level below 100 IU/L.

STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) version 22 was used to conduct the statistical analysis. Categorical variables are displayed as frequencies and percentages, and numeric variables are represented as means and standard deviations. Post stratification Chi square test was applied and a p-value equal to or less than 0.05 was deemed significant.

RESULT

Among the 96 patients, 64 (74%) were male, and 32 (26%) were female. Minimum age of participants was 21 years and maximum of 60 years, with a mean age of 42.92years (±9.76). The mean duration of hemodialysis was 5.61 months (±4.08), and the mean body mass index (BMI) was 25.38 kg/m² (±4.31). The frequency distribution of the duration of hemodialysis revealed that 62 (64.6%) patients had been on hemodialysis for ≤6 months, whereas 34 (35.4%) patients had been on hemodialysis for more than six months. Regarding the number of hemodialysis sessions per week, 76 (79.2%) patients underwent hemodialysis ≤3 times per week, while 20 patients (20.8%) had sessions more than three times per week. Regarding comorbid conditions, type II diabetes mellitus was observed in 42 (43.8%) patients, and hypertension was prevalent in 73 (76%) patients. Out of 96 patients, 53 (55.2%) and 43 (44.8%) had adequate and inadequate response.

Table **1** summarizes the response to the Hepatitis B vaccination in relation to various clinical variables, including the duration and frequency of hemodialysis, as well as the presence of type 2 diabetes mellitus and hypertension. However, the frequency of hemodialysis sessions per week and the presence of type 2 diabetes mellitus demonstrated a statistically significant association with the vaccination response.

Table 1. Hepatitis B Vaccine Response according to Clinical Variables (n=96).

Variables	Adequate Response	Inadequate Response	P Value*
Duration of Hemodialysis			
≤ 6 Months (62)	38 (61.3%)	24 (38.7%)	0.106
> 6 Months (34)	15 (44.1%)	19 (55.9%)	
Hemodialysis Per Week			
≤ 3 (76)	37 (48.7%)	39 (51.3%)	
> 3 (20)	16 (80%)	04 (20%)	0.012
Type-2 Diabetes Mellitus			
Yes (42)	17 (40.5%)	25 (59.5%)	0.01
No (44)	36 (66.7%)	18 (33.3%)	
Hypertension			
Yes (73)	37 (50.7%)	36 (49.3%)	0.112
No (23)	16 (69.6%)	07 (30.4%)	

* The chi-squire test was applied.

DISCUSSION

Kidney dysfunction is closely associated with an elevated risk of chronic hepatitis B virus (HBV) infection [13]. Vaccination significantly reduces the chances of hepatitis B infection in individuals with ESRD [14]. Nevertheless, the risk remains for those who do not respond well to the vaccine, putting them at a higher risk of infection [15, 16].

Patient on HD have recommended schedule for vaccination is 40 mcg intramuscularly (IM) at 0, 1, 2, and 6 months [17]. Our study reported an adequate response of 55.2% in patient who follow this regimen contrast to a study by Szer *et al.* who reported that 80% seroconversion rate [18]. This finding indicating individuals with ESRD often exhibit reduced vaccine responsiveness due to compromised immune function [19].

Response to vaccination is affected by several factors including dialysis frequency per week [20]. Those who are one >3 session of hemodialysis per week have reduced response due to continuous inflammatory process activation and physiological stress [21]. In our study, the patients who were receiving ≤3 sessions of dialysis each week had the poorest response to the hepatitis B vaccine. The patients who were receiving >3 sessions of dialysis each week had a much better response to the vaccine in contrast to Yongliang F. *et al* reported that higher dialysis frequency were independent risk factors of hypo-response to hepatitis B vaccine [22].

Diabetes further impairs this response, as studies indicate lower rates of seroconversion among diabetic patients undergoing hemodialysis [23]. Fabrizio F, *et al.* demonstrated a clear association between diabetes mellitus and reduced rates of seroconversion in this population, suggesting that diabetes contributes to immune dysfunction in these patients [24]. Similarly, our study observed a comparable trend, highlighting that diabetic patients on hemodialysis are less likely to achieve adequate seroconversion following HBV vaccination.

Hypertension has been considered as a potential influencer of vaccine immunogenicity due to its link with systemic inflammation and immune system dysregulation. Our study, consistent with the findings of Johannes L, *et al.* failed to find a statistically significant association between hypertension and the immune response to hepatitis B vaccination [25]. These results indicate that while hypertension may have some effect on immune competence, it does not seem to impair the specific antibody response we measure after hepatitis B vaccination.

LIMITATION

The study is limited by the relatively small sample size, it may have limited the statistical power for detecting associations, potentially decreasing the ability to identify associations between clinical variables and vaccine response. Another constraint is the failure to consider genetic, immunological, or socioeconomic factors that could influence vaccine effectiveness. Future research must certainly address these limitations if we are to obtain a more comprehensive understanding of the many factors that affect the efficacy of the Hepatitis B vaccination in this susceptible population.

CONCLUSION

This study evaluated the efficacy of Hepatitis B vaccination for the patients on hemodialysis and found that less than two-thirds developed an adequate immune response. The results of this study indicate that other factors, such as the number of hemodialysis sessions per week, may play an important role in influencing the vaccine's ability to protect these patients. Future research should focus on identifying these determinants of poor response and exploring strategies to improve seroconversion rates. Studies could explore whether higher vaccine doses, additional booster shots, or newer vaccine formulations could make a difference. Personalizing vaccination strategies based on individual patient factors might also help ensure better immunity. These efforts could play a vital role in keeping patient's safe and reducing the risk of hepatitis B transmission within dialysis units.

LIST OF ABBREVIATIONS

CKD: Chronic Kidney Disease.

ESRD: End Stage Renal Disease.

HBV: Hepatitis B Virus.

HD: Hemodialysis.

WHO: World Health Organization.

AUTHORS' CONTRIBUTION

Mukesh Kumar: Conceptualization, Study Design, Methodology, Data analysis and interpretation, Writing draft, Critical review, & revision the manuscript and final approval.

Pooran Mal: Conceptualization, Writing draft, Critical review and revision the manuscript and final approval.

Abdul Ghani Rahimon and **Kaneez Zahera**: Writing draft, Critical review and revision the manuscript and final approval.

Rekha Vankwani and **Vershia Kanwal**: Study Design, Methodology, Data analysis and interpretation and final approval.

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DECLARATIONS

Data Availability

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

Ethical Approval

Ethical approval taken from LUMHS's Ethical Research Committee (Notification no: LUMHS/REC/-241 dated: 16-12-2021).

Consent to Participate

Written informed consent was obtained from all individual participants included in the study.

Consent for Publication

Consent for publication was obtained from all participants whose data are included in this manuscript.

Conflict of Interest

Declared none.

Competing Interest/Funding

Declared none.

Use of AI-Assisted Technologies

The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were utilized in the writing of this manuscript, in the creation of images/graphics/tables/captions, or in any other aspect of its preparation.

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