DOI: https://doi.org/10.53350/pjmhs2216599

ORIGINAL ARTICLE

Immune Status of Hepatitis B Virus among Vaccinated Hemodialysis Patients

SYED ALI RAZA[1], SOHAIL HUSSAIN[2], FAIZA NAFEES KHAN[3], IMTIAZ BEGUM[4], SANTOSH KUMAR SIDHWANI[5], MADEEHA SADIQ[6]
[1]*Assistant Professor & Head of Medicine Department Consultant Physician, Dr. Ziauddin University Hospital , Karachi*
[2]*Assistant Professor / Consultant Gastroenterologist Clinical Coordinator for Postgraduate Studies , Dr. Ziauddin University Hospital, Karachi*
[3]*Assistant Professor & Consultant Nephrologist, Department of Nephrology Ziauddin University Hospital, Karachi*
[4]*Assistant Professor / Consultant Physician Dr. Ziauddin University Hospital, Karachi*
[5,6]*Assistant Professor, Department of Pathology, Ziauddin University, Karachi*
Correspondence to Dr. Syed Ali Raza, E-mail : dr.ali.raza@hotmail.com Contact : 0300-2117690

ABSTRACT

Aim: To check immune status of hemodialysis patients with vaccination history at a tertiary care hospital to Hepatitis B virus.
Methods: Study design was cross sectional study which was conducted in Department of Medicine, Ziauddin University, Karachi from May 2011 till November 2011. One hundred and three patients were included in this study who matched the inclusion criteria after taking their informed consent. Data analysis was done by SPSS version 12.
Results: The study comprised of male subjects 69(67%) and female patients were 34(33%). The mean age was 51.1 years and standard deviation age was ±14.3 years, the post vaccination duration was recorded and had a mean value of 7.6±0.9 months, mean value of anti HBs antibody level was 184.6±293.4 and the mean duration for hemodialysis was 26.4±12 months. 37(35.9%) of the patients were non-responders, while 19(18.4%) were weak responders and high responders comprised most of study sample i.e. 47(45.6%). Hemodialysis schedule of patients varied with 70(68%) had dialysis twice weekly as compared to this 33(32%) patients had hemodialysis schedule of thrice weekly.
Conclusion: this was a preliminary study which showed a very high immunization response by hepatitis-B vaccine among patients on hemodialysis that neither correlated with age, systemic inflammation nor nutritional status.
Keywords: Hepatitis B, Immunization, Hemodialysis, Immunity,

INTRODUCTION

Infection with the hepatitis B virus (HBV) and its complications, such as chronic liver disease, cirrhosis and hepatocellular carcinoma, are serious global health issues. The primary reservoir of infection is about 350 million chronic carriers worldwide[1-4].

Since the initiation of the HBV vaccination in 1982, there has been a declining incidence of Hepatitis B infection is seen, as well as the accompanying morbidity and mortality. After 6–8 weeks of receiving all three doses of the HBV vaccination, the immune response is measured by testing antibody levels. Hepatitis B surface antibody concentrations more than 10mIU/ml are thought to be protective. Patients on haemodialysis (HD) are at a significant risk of getting the hepatitis B virus (HBV). Transfusions of blood products, contamination caused by use of contaminated equipment that is used in dialysis procedure, and infections caused by other environmental sources are also potential sources of infection[5,6]. Patients who are chronically uremic, whether dialyzed or not, have a decreased immunological response to vaccination by hepatitis B vaccine. Patients with decreased kidney function and having end-stage renal disease have decreased rates of seroconversion than healthy people. While healthy subjects have a seroconversion rate of 90% to 100% after hepatitis B virus (HBV) vaccination, patients suffering from end-stage renal disease have a lower responsiveness to immunization by HBV vaccine with effective anti-hepatitis B surface (anti-HBs) antibody that ranged from 50% to 60%[6-10].

To increase seroconversion antibody, many approaches have been tried, including addition of one extra dose of vaccine to a series of four-dose vaccines and doubling the vaccine dose to 40mcg/dose. This approach has been shown to result in 80% seroconversion in some investigations. In their study, A. Ramezani et al. discovered that after primary immunisation, 87% of patients obtained anti-HBs levels more than 10 IU/l. Weak responders made up 27.8% of the group, while high responders made up 59.2%. Non-responders made about 13% of the patients[7]. Despite the fact that HBV infection is a serious health concern in Pakistan's community and nosocomial settings, there is no evidence on immune response in hemodialysis patients. With a prevalence rate of 3–4% in the general community, health care environments can be potential high risk sites for nosocomial transmission.`

Received on 13-10-2021
Accepted on 23-04-2022

As a result, we conducted the current study in one of the country's biggest tertiary care hospitals to assess the immunological response of hemodialysis patients after they had completed their vaccination schedule. End stage renal disease, ESRD is an immunocompromised state, and even at larger doses, these individuals have a limited immunity to the hepatitis B virus. At the conclusion of this study, we will have a better understanding of the real situation among vaccinated patients undergoing hemodialysis and will be able to create a Hepatitis B immunization plan for ESRD patients on hemodialysis.

The goal of this study was to see the level of immunity of vaccinated patients undergoing hemodialysis at a tertiary care hospital to the hepatitis B virus.

METHODOGY

The current study was of cross sectional design conducted in Department of Medicine, Ziauddin Medical University Hospital, Karachi for a period of six months 17th May 2011 to 16th November 2011. It was a Non-probability purposive. Patients aged 18 to 70 years old, of either gender, who have hemodialysis duration exceeding 9 months, have a documented ESRD diagnosis, and have completed the course of 4 doses of hepatitis B vaccine at least 60 days prior to start of study were included. current or previous viral hepatitis, all hepatitis B surface antigen (HBsAg), patients taking medicines for immunosuppression , and pregnant females were excluded. The College of Physicians and Surgeons of Pakistan and the Hospital Ethical Review Committee gave their approval for this study.

HbsAg was defined as Hepatitis B surface antigen present at the start of infection, while Anti HBs antibody or Hepatitis B surface antibody found in serum either occurring naturally as part of achieving natural immunity or produced after vaccination. The End stage renal disease: was defined as kidney damage, as confirmed by 24hrs urinary creatinine and cockcroft gault formula as glomerular filtration rate, GFR < 60ml/min /1.73m2 for more than ≥ 3 months. Anti-HBs levels were split into three groups: non-responders (less than 10IU/l), patients showing weak response (10 to 100IU/l), and patients showing high response (equal to or greater than 100 IU/l). Patients on hemodialysis with chronic kidney disease who attended the out-patient department of the Department of Medicine, Ziauddin Medical University Hospital Karachi, were enrolled after giving informed consent.

All of the patients had dialysis twice or three times a week.

Hepatitis B surface antibody (anti HBs) testing was performed on patients who had been given recombinant hepatitis B vaccine double dose (40mcg) as intramuscular injections intramuscular at 0, 1, 2, and 6 months as part of a four-vaccine series schedule. 1–2 months following the previous injection, we used an ELISA test to determine the hepatitis B surface antibody (anti-HBs). Anti-HBs levels of patients were split into three groups: non-responders (less than 10IU/l), weak responders (10 to 100IU/l), and high responders (equal to or greater than 100 IU/l). Data was entered on the pre-designed proforma by the researcher which included age, gender, duration of hemodialysis, weekly schedule of hemodialysis, anti HBs antibody level and anti-HBs antibody status i.e. non-responders, weak responders after the 2 months of last dose of vaccination. The filled in proforma were converted into database on SPSS version 12.0 according to the objective of the study. Qualitative variable like gender, schedule/ week of hemodialysis, anti-HBs status i.e. non-responders, weak responders and high responders after 2 months of last dose of vaccination were presented as frequency and percentage. Mean±SD was computed for quantitative variables like age, duration of hemodialysis and level of anti HBs antibody after 2 months of last dose of vaccination. Grouping was done with regards to age, gender and duration of hemodialysis and weekly schedule of hemodialysis to see the effect of these on outcome.

RESULTS

One hundred and three patients fulfilling the inclusion criteria were involved in this study. There were 69(67%) males and females were 34(33%). The mean value of age of enrolled patients was 51.1 years±14.3 years standard deviation, mean post vaccination duration was 7.6±0.9 months, anti HBs mean antibody level was 184.6±293.4 and the heamodialysis mean duration was 26.4±12 months (Table I). In our study sample non responder patients were 37(35.9%), 19(18.4%) were weak responders and highest frequency was of high responders 47(45.6%). Twice weekly heamodialysis schedule was followed by 70(68%) and 33 (32%) patients had hemodialysis schedule of thrice weekly. 52.6± 14.5 years was found to be the mean age of male patients, mean post vaccination time duration was found to be 7.5 ±0.88 months for male patients, the mean value for anti HBs antibody level was 162± 260.6 for male patients, and mean time duration of hemodialysis was 28.2±13 months for male patients, whereas the mean female patients age was 48.1±13.5 years, mean time of post vaccination duration was 7.8±0.9 months for female patients, mean anti HBs antibody level was 162± 260.6 of female patients (Table II).

Out of 69 males, 42 (60.9%) had a two times a week hemodialysis schedule and 27 (39.1%) had a three times a week hemodialysis schedule, whereas out of 34 females, 28(82.4%) had a twice a week hemodialysis schedule and 6(17.6%) had a thrice a week hemodialysis schedule (p=0.028). Out of 69 males 24(34.8%) were non-responders, 11(15.9%) were weak responders and 34 (49.3%) were high responders as compared to this out of 34 females 13(38.2%) were non-responders, 8(23.5%) were weak responders and 13(38.2%) were high responders (p=0.498). Grouping of mean age, post vaccination duration, anti HBs antibody level and duration of hemodialysis among the anti HBs antibody status is described in the Table III.

Out of 37 non-responders, 28(75.7%) had two times per week hemodialysis and 9(24.3%) had three times per week hemodialysis; out of 19 patients that were weak responders, 13 (68.4%) received twice a week hemodialysis. Out of 47 patients who were high responders, 29(61.7%) had two times a week hemodialysis and 18(38.3%) had three times a week hemodialysis (p=0.395). Out of 47 high respondents, 29(61.7%) had hemodialysis twice a week and 6(31.6%) hemodialysis three times a week (p=0.395),(Fig.1).

Table I: Descriptive statistics of study sample

	Mean	Std. Deviation
Age/years	51.0971	14.28252
Post vaccination duration (months)	7.5922	.90138
Level of Anti HBs antibody	184.6369	293.35406
Hemodialysis duration (months)	26.3689	12.03507

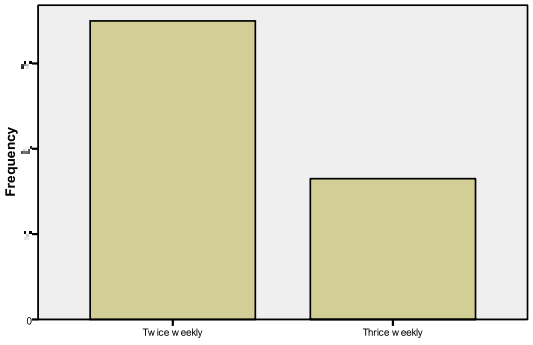
Table II: Gender differences in post vaccination duration, antibody levels and duration of heamodialysis

Gender		Age	Duration post vaccination	Anti HBs antibody level	Hemodialysis duration
Male	Mean	52.5507	7.5072	162.0377	28.1594
	Std. Deviation	14.50612	0.88489	260.62529	12.95765
Female	Mean	48.1471	7.7647	230.5000	22.7353
	Std. Deviation	13.54707	0.92307	350.41450	9.02290
P value		0.013	0.001	0.027	0.003

Table III: Gender differences in anti hbs antibody levels

Anti HBs antibody status		Age	Post vaccination Duration	Anti HBs antibody level	Duration of Heamodialysis
Non-responder	Mean	55.0000	7.4865	.0000	25.2162
	Std. Deviation	11.37981	.50671	.00000	14.32584
Weak responder	Mean	43.5789	8.2105	42.6632	26.6842
	Std. Deviation	12.85957	.91766	26.42459	11.84179
High responder	Mean	51.0638	7.4255	387.3830	27.1489
	Std. Deviation	15.83255	1.03723	335.86006	10.19586
P value		<0.05	<0.05	<0.05	<0.05

Fig. I: Frequency hemodialysis schedule of study participants



DISCUSSION

There exists a relatively elevated risk of infection by hepatitis-B virus (HBV) in hemodialysis therapy patients[1,10,11]. Infected patients' blood and other bodily fluids contain extremely high titers of HBV. Dialysis personnel can spread the virus to patients by touching contaminated surfaces or usage of contaminated equipment and supplies. In Pakistan, HBV infection is one of the major community health issue; the majority of the country's countries, including Egypt, have moderate or high HBV endemic rate. After the availability of hepatitis-B vaccine in 1982, it has been recommended for all vulnerable patients undergoing hemodialysis, however rates of seroconversion are substantially decreased in the patient population diagnosed with end-stage renal disease (ESRD)[11-13]. Three months after vaccination administration, seroconversion (anti-HBs >10 IU/1) was detected in

73-76.7% of hemodialysis patients, while an acceptable response (anti-HBs >100 IU/1) was only reported in 53.5% in one series. Others have reported lower HBV vaccination response rates, ranging from 47 to 58% one month following the fourth shot[13,14]. In one trial, after three years of follow-up, 41% of responders had no detectable anti-HBs levels in the serum[1]. Malnourishment, uremia, advanced age, and immunocompromised status of individuals with chronic renal disease are all factors that contribute to a poor response.

Young age (under 40 years), decent nutritional health, and enough dialysis have all been linked to a positive response to HBV immunization[7-10]. Dialysis length, haemoglobin and parathyroid hormone levels, and hepatitis-C virus (HCV) infection, on the other hand, had no effect on antibody responses to hepatitis-B vaccine.

The current study found that hemodialysis patients had a very high response to hepatitis-B immunisation. After the full vaccination, 47(45.6%) of the participants had a high antibody response (>100 IU/L). Hepatitis-B vaccination response rates in hemodialysis patients have ranged from 47 to 73% in previous studies[16-18]. Geographical areas with intermediate levels of endemic HBV, prevalence between 2-8% showed comparable, good responses to hepatitis-B immunization in patients undergoing hemodialysis such as in Brazil, in one study the level approached 89.5% [7].

Several studies on the contrary have demonstrated low response to Hep B vaccination in patients with Chronic renal disease , even when used at high dose, as compared to its use in normal population.[15-19] There are several explanations for hemodialysis patients' poor vaccine response. Presentation of antigens to T lymphocytes and activation of T cells, as well as ensuing antibody generation, are all hampered by uremia.

Monocyte activation, proinflammatory cytokines overproduction, and immunological dysfunction are all linked to ESRD. In the dialysis population, there is little data on the link between chronic inflammation and antibody response to vaccines. The difference in means was not statistically significant in CRP levels between the responders and the nonresponders in the current study.

This observation could be explained by the varied response of anti-inflammatory cytokines such interleukin-10 (IL-10) as a response in uremic patients, resulting in improved B-cell activity. Patients who produce more IL-10 have less uremia and chronic inflammation caused by dialysis, and they respond better to vaccinations.

In hemodialysis patients, a beneficial effect of effective dialysis on HBV vaccine response has previously been described. Similarly, the initial weekly Kt/V in responders and nonresponders in a study of peritoneal dialysis patients inoculated with the hepatitis-B vaccine was 2.37 and 2.01, respectively, in responders and nonresponders.[13-15] Since dialysis has an effective role in restoring defective B7-2 (CD 86) expression on dialysis patients' monocytes, efficient dialysis may lead to an increased response. Other researchers, on the other hand, have not verified the beneficial effect of effective dialysis on immunological function.

HCV antibody seroprevalence was found to be high (49.1%) among patients diagnosed with end stage renal disease in Egypt, and it was found to be substantially linked with blood transfusion 20. All of the patients in this research had anti-HCV antibodies.

CONCLUSION

This study reports a significant response to immunization by hepatitis-B vaccine in patients undergoing hemodialysis that did not correlate with age, nutritional or septic profile of patients. Hemodialysis efficiency was associated with better response to hepatitis-B vaccine. There is a need of future studies for determination of the most cost-effective vaccination regimen that may be recommended for patients undergoing hemodialysis in ethnic communities residing in our region.

Conflict of interest: Nil

REFERENCES

1. Rasoul A, El Bahnasy , Michael AA, Hendy OM, Ahmed AR. Hepatitis B viral markers and vaccination status among health care providers in menoufia governorate. Egyp J Occupational Med 2010;34(2):267-9.
2. Yacoub R, Ali R, Moukeh G, Lahdo A, Mouhammed Y, Nasser M. Hepatitis B vaccination status and needle stick injuries among Health Care workers in Syria. J Global Inf Disea. 2010;2(1):28-34.
3. Somi MH, Hajipour B. Improving Hepatitis B Vaccine Efficacy in End-Stage Renal Diseases Patients and Role of Adjuvants. ISRN Gastroenterol. 2012;10-15.
4. 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.
5. Fabrizi F, Dixit V, Martin P, Messa P. Hepatitis C virus and the immunological response to hepatitis B virus vaccine in dialysis patients: Meta-analysis of clinical studies. J ViralHepat.2011;18:871–6.
6. EdeyM, BarracloughK, Johnson DW. Review article: Hepatitis Banddialysis. Nephrology (Carlton) 2010;15(2):137–45.
7. Moreira RC, Deguti MM, Lemos MF, Saraceni CP, Oba IT, Spina AM, Nascimento-Lima AS, Fares J, Azevedo RS, Gomes-Gouvêa MS,Carrilho FJ, Pinho JR. HBV markers in haemodialysis Brazilian patients: a prospective 12-month follow-up. Mem Inst Oswaldo Cruz. 2010;105(1):107–8.
8. Naha RK,J ahan M, Nessa A, Tabassum S. Antibody responses after hepatitis B vaccination among maintenance haemodialysis patients. Bangladesh Med ResCouncBull2011;37:88-91.
9. SitD, Esen B, Atay AE, Kayabaş H. Is hemodialysis a reason for unresponsiveness to hepatitis B vaccine? Hepatitis B virus and dialysis therapy. World J Hepatol. 2015 Apr18;7(5):761–768.
10. Mayhall CG. Hospital epidemiology and infection control. Philadelphia: Lippincott Williams & Wilkins; 2012.
11. Pérez ER. Catheter-Related Blood stream Infections in Critical Care. INTECH Open Access Publisher; 2012.
12. Mashragi F, Bernstein RS, Al-Mazroa M, Al-Tawfiq JA, Filemban S, Assiri A et al. HIV transmission at a Saudi Arabia hemodialysis unit. Clin Infect Dis. 2014;59(6):897–902.doi:10.1093/cid/ciu373.
13. Su Y, Yan R, Duan Z, Norris JL, Wang L, Jiang Y, et al. Prevalence and risk factors of hepatitis C and B virus infections in hemodialysis patients and their spouses: amulticenter study in Beijing, China.JMedVirol.2013;85(3):425–32.doi:10.1002/jmv.23486.
14. Dervisoglu E, Simsek M, Yilmaz A. Antibody response following hepatitis B vaccination in peritoneal dialysis patients: does normalized urea clearance matter?.*Clinics(SaoPaulo)*.2011;66(9):1559–1562. doi:10.1590/s1807-59322011000900009
15. Mohammed AA, Enan KA, Khair OM, Hussien MO, El Hussein ARM, Elkhidir IM. Prevalence of occult hepatitis B virus (HBV) infections in haemodialysis patients in Khartoum State, Sudan from2012 to2014. JMed Lab Diagn. 2015;6(4):22–6.
16. Zahedi MJ, Darvish Moghaddam S, Alavian SM, Dalili M. Seroprevalence of Hepatitis Viruses B, C, D and HIV Infection Among Hemodialysis Patients in Kerman Province, South-EastIran. HepatMon.2012;12(5):339–43. doi:10.5812/hepatmon.5969.
17. Aghasadeghi MR, Mohraz M, Bahramali G, Aghakhani A, Banifazl M, Foroughi M et al. Frequency and Genotype of Hepatitis D Virus Infection in Patients Infected with HIVandThoseUndergoingHemodialysis.HepatMon.2013;13(5):e32971. doi:10.5812/hepatmon.7481.
18. CentersforDiseaseControl.EpidemiologyandPreventionofVaccine-PreventableDiseases. The Pink Book: Course Textbook -12th ed, Second Printing. USA: Centers for Disease Controland Prevention;2012.
19. Lioussfi Z, Errami Z, Radoui A, Rhou H, Ezzaitouni F, Ouzeddoun N, Bayahia R, Benamar L. Viral hepatitis C and B among dialysis patients at the Rabat University Hospital: prevalence and risk factors. Saudi J Kidney DisTranspl.2014;25:672–679.
20. El-Shishtawy S, Sherif N, Abdallh E, Kamel L,Shemis M, Saleem AA, Abdalla H, El Din HG. Occult Hepatitis C Virus Infection in Hemodialysis Patients; Single Center Study. *Electron Physician*. 2015 Dec 20;7(8):1619-25. doi:10.19082/1619.PMID:26816589;PMCID:PMC4725416