ORIGINAL ARTICLE

IMMUNE RESPONSE TO HEPATITIS B VACCINATION IN HEMODIALYSIS PATIENTS.

Kunwer Naveed Mukhtar[1*], Syed Farrukh Umair[2], Sumbal Nasir Mahmood[3]
[1,2]Department of Nephrology, Liaquat National Hospital and Medical College
[3]Department of Nephrology, Ziauddin Medical University and Hospital

ABSTRACT

Background: Hemodialysis patients are vulnerable to infections with Hepatitis B Virus and hepatitis C virus (HCV). Patients who are on maintenance hemodialysis are considered as high-risk group for acquiring hepatitis B virus, resulting in high morbidity and mortality. Therefore, to vaccinate them against the virus is mandatory. Compared to a response rate of over 90% in the normal population, only 50 to 60% of those with end-stage renal disease achieve adequate antibody levels following immunization and the objective of this study was to determine the antibody level after Hepatitis B vaccination in chronic hemodialysis patients.

Methods: 118 patients, undergoing chronic hemodialysis (HD) at the dialysis unit of Liaquat National Hospital, fulfilling the inclusion and exclusion criteria were enrolled between April 2013 and September 2013, after taking informed consent and approval from ethical review committee. AntiHbs (Hepatitis B surface antibody) titers were measured. Patients were differentiated as Immune and non immune based on antibody titers, with levels of >10IU/l being considered as immune and levels of <10IU/las non immune. AntiHbs titer was measured by ELISA (Enzyme Linked Immunosorbant Assay). Data was analyzed using SPSS version 14.0 for windows. Chi square test were used to ascertain the statistical significance. P value <0.05 was taken as statistically significant. In addition, the effect of age, gender and duration of Hemodialysis on antibody titer was also observed.

Results: Out of 118 patients enrolled, 103 (87.3%) had an adequate antibody response and were considered immune while only 15 patients (12.7%) had an inadequate antibody response rendering them non immune. AntiHbs titers showed no significant co-relation with gender and duration of Hemodialysis therapy(p>0.05), while age was found to have significant correlation as younger age group (<60years) had more immune response (p<0.001).

Conclusion: Our study showed a very good antibody response to Hepatitis B vaccination among hemodialysis patients that correlated with age with younger age group having a better response but no correlation to gender and duration of dialysis.

KEY WORDS: Hepatitis B virus, Anti-HBs antibody, Hemodialysis, Prevalence, Vaccination.

INTRODUCTION

Hepatitis B virus (HBV) infection is a common but avoidable disease. Hepatitis B virus (HBV) is a DNA virus that can be communicated via saliva, body fluids, semen, vaginal fluids, blood products, sexual contacts or prenatally influencing 350-400 million persons round the globe [1-3] . In contrast to general population, hemodialysis patients are at higher risk of acquiring Hepatitis B Virus because of direct exposure to blood products, shared hemodialysis devices, needle pricks and hemodialysis process which involve access to blood circulation. [4] Hence, hemodialysis patients are vulnerable to infections with Hepatitis B Virus and hepatitis C virus (HCV).The prevalence of Hepatitis B Virus in hemodialysis (HD) patients varies significantly between countries, ranging from minimal in developed countries to very high in some developing countries. Despite the fact that many steps have been taken for the prevention of HBV infection like mass vaccination programs, implementation of thorough blood donor screening, awareness &encouragement programs of erythropoietin use and generalize availability in hemodialysis centers, Hepatitis B Virus infection remains a major concern in Hemodialysis centers majorly in developing countries [5] . Patients who are on maintenance hemodialysis are considered as high-risk group, resulting in high incidence and mortality. Therefore, to vaccinate them against the virus is mandatory. Compared to a response rate of over 90% in the normal population, only 50 to 60% of those with end-stage renal disease achieve adequate antibody levels following immunization [6, 7] . Various tactics have been employed to overcome the low seroconversion rate like co-administering zinc, gamma-interferon, thymopentin , interleukin-2, and levamisole as immunostimulants or adjuvants as well as changing the injection mode (intradermal versus intramuscular) or doubling the vaccine dose [7, 8]

Low immune response to hepatitis B vaccination in patients on HD is noticed in several studies but has never been studied in our population. Therefore our aim is to conduct a study in our population to determine the serum Anti-Hbs levels in these patients following vaccination.

METHODS

After taking informed consent and approval from ethical review committee, 118 patients undergoing HD in Liaquat

Corresponding Author: Kunwer Naveed Mukhtar *

National Hospital were screened for anti-HBs between April 2013 and September 2013. Sample size was calculated after literature search that showed seroconversion rate of 40%- 70 % of hepatitis B antibody after vaccination in this group of patients. Therefore, taking minimum frequency as 50% with a bound on error of 0.09(9%),with a power of 0.8 and an alpha significance level of 0.05, sample size for 95% Confidence level came out to be 118 which were enrolled in the study. A questionnaire was used to collect the demographic data and duration of HD. All patients were included in HD unit who underwent primary vaccination within last one year (four doses: recombinant HB vaccine; 40ug , intramuscularly, at 0, 1, 2 and 6 months) [20] . Exclusion criteria included patients on immunosuppressive drugs, malignancy or HIV positive patients. Enzyme linked immunosorbent assay (ELISA, Biokit, Spain) was used to measure Anti-HBs antibodies titers. The data was analyzed by SPSS ® for windows® (version 14.0 Chicago, IL, USA). A p value <0.05 was considered statistically significant.

RESULTS

We enrolled total of 118 patients on Hemodialysis who were recently vaccinated. Demographics are shown in Figure 1.Patient's age ranged from 20-71 years. 46.6 %(N=55) were Male with mean age 53.2 ±10.02 yrs and 53.1 %(N=63) were Females with mean Age of 51.59 ±10.63 yrs. Results are shown in table (1). Age was found to have significant impact on Hepatitis B surface antibody titer with patients <60 years of age being more immune (p<0.05).Correlation between gender and anti-HBs antibody titer was not statistically significant (p>0.05).Out of 118 patients, 15 (12.7%) were found to have Inadequate response or Non-immune, whereas, 104 (87.3%) had an Adequate response and responded well to the immunization. Duration on Hemodialysis ranges from 1-4 yr with mean duration of 1.97±0.77 years, most of the patients had less than 3 years of Hemodialysis 97.5% (N=115/118) and only 3 patients (2.5%) were in year 4. Duration of Hemodialysis failed to show any significant impact on Hepatitis B vaccination response rate (p>0.05).

Table -1

AGE, GENDER AND DURATION OF HEMODIALYSIS IMPACT ON HEP B ANTIBODY LEVEL

		Hepatitis B s Antibody Level			P-value
		Inadequate	Adequate	Total	
Age	<60 yrs	5	82	87	0.001
	<60 yrs	10	21	31	
	Total	15	103	118	
Gender	Male	8	47	55	0.59
	Female	70	56	63	
	Total	15	103	118	
Duration on Hemodialysis	<1 yr	1	33	34	0.128
	1-2 yr	9	47	56	
	2-3 yr	4	21	25	
	3-4 yr	1	2	3	
	Total	15	103	118	

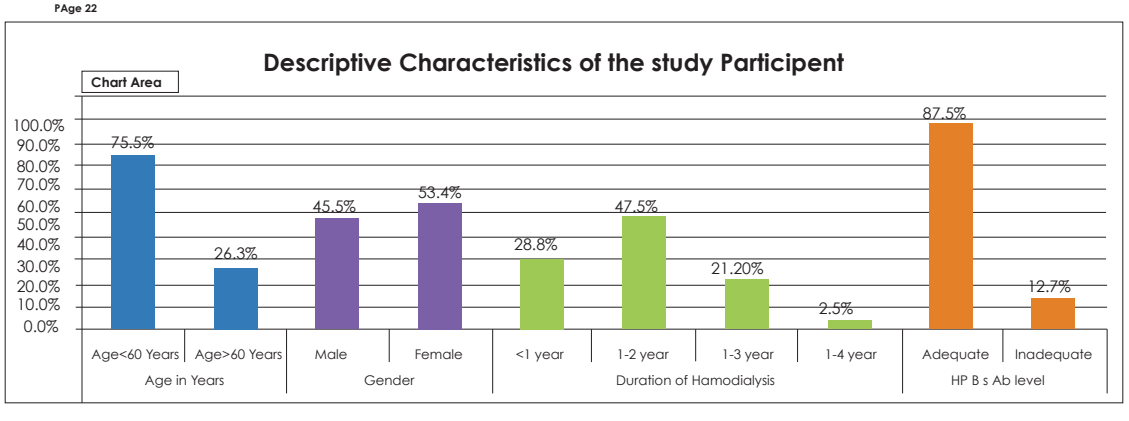

Figure 1 : Descriptive characteristics of the study paticipants

DISCUSSION

An increased risk of exposure to HBV infection is observed in patients on maintenance hemodialysis [9] It has been observed that after vaccination for Hepatitis B, hemodialysis patients develop lower antibody titers compared to healthy individuals, and even if they are immunized, their antibody titers fallsshortly within a year [10] .

The present study showed a very high response to hepatitis-B vaccination among hemodialysis patients. One hundred and four (87.6%) patients showed good antibody response after vaccination. Our results are similar to results published by Nahar et al [23] which showed 80% response to vaccine and by Al Saran et al [24] that showed 89% response after complete immunization. Previous studies in hemodialysis patients have shown a variable hepatitis-B vaccination response rate, ranging from 47%-73%. [11-13] .Comparable good results to hepatitis-B vaccination in hemodialysis patients had also been observed in areas with intermediate endemicity (2-8%) prevalence of Hepatitis B Virus ,such as in Brazil , which approached 89.5% in one study. [14]

A recent meta-analysis of 17 clinical trials showed decreased response to hepatitis-B vaccination among older dialysis patients[15] which might be attributed to age associated changes to immune status, where "older" was defined at age 50 yrs. Our patients mean age were 52.3±10.04 yrs correlating with Meta analysis age group, and our results are similar with older patients having less immune response. [11, 16, 17]

In the present study, gender and duration of hemodialysis therapy did not have any correlation to hepatitis-B vaccination. These results are in agreement with those reported by Peces et al [18] Dacko et al [16] and Tele et al[14] .Similarly, Roozbeh et al[19] also confirmed the same results and showed that gender did not differ between responders (immune) and non-responders (non-immune) to hepatitis-B vaccination. A recent review by Alicia E. Grzegorzewska [22] also stressed the need for vaccination not only in patients on dialysis but patients who have chronic kidney disease. Another review by Gasim GI et al. emphasized on genetitic investigations to make a break through concerning HBV vaccination to improve response rate [25].

Our study has limitation that it's a short study with a small sample size. In addition we only observed whether patients were immune or non-immune and did not considered if immune patients had significant high titers (> 100 i.u/L). Further studies, in our population are needed to see whether patients who are immune lose their immunity after certain period of time and require re-vaccination or booster. This has been recently shown in a study by Ayub et al [21], in which patients lose their antibody titers over time.

CONCLUSION

We report a very good response to hepatitis-B vaccination among hemodialysis patients that is neither co-relating with gender or duration of hemodialysis. This was a preliminary study in our population which only estimated the response rate against vaccination. Future studies are needed to determine the impact of nutritional status and adequacy of hemodialysis on the response rate of vaccination as previous studies has shown their influences over titer levels.

REFERENCES

1. Lee WM. Hepatitis B virus infection. N Engl J Med. 1997 ; 337(24):1733-45.
2. Lok AS, Heathcote EJ, Hoofnagle JH. Management of hepatitis B: summary of a workshop. Gastroenterology. 2001; 120(7):1828-53.
3.Ganem D, Prince AM. Hepatitis B virus infection--natural history and clinical consequences. N Engl J Med. 2004 ; 350(11):1118-29.
4. Edey M, Barraclough K, Johnson DW. Review article: Hepatitis B and dialysis. Nephrology (Carlton). 2010 ; 15(2):137-45.
5. Alavian SM, Bagheri-Lankarani K, Mahdavi-Mazdeh M, Nourozi S. Hepatitis B and C in dialysis units in Iran: changing the epidemiology. Hemodial Int. 2008 ; 12(3):378-82.
6.Fabrizi F, Dixit V, Bunnapradist S, Martin P. Meta-analysis: the dialysis mode and immunological response to hepatitis B virus vaccine in dialysis population. Aliment Pharmacol Ther. 2006 ; 23(8):1105-12.
7.Sali S, Alavian SM, Hajarizadeh B. Effect of levamisole supplementation on hepatitis B virus vaccination response in hemodialysis patients. Nephrology (Carlton). 2008; 13(5):376-9.
8.Fabrizi F, Dixit V, Magnini M, Elli A, Martin P. Meta-analysis: intradermal vs. intramuscular vaccination against hepatitis B virus in patients with chronic kidney disease. Aliment Pharmacol Ther. 2006; 24(3):497-506.
9.Santos M DR, Que E, Balmaceda R, Padilla B. Prevalence of hepatitis B and hepatitis C in haemodialysis patients. Nephrology. 1998; 4(12):101-4.
10.Rodby R TG. Vaccination of the dialysis patient. Seminars in Dialysis. 1991; 4(2):102-5.
11.Navarro JF, Teruel JL, Mateos ML, Marcen R, Ortuno J. Antibody level after hepatitis B vaccination in hemodialysis patients: influence of hepatitis C virus infection. Am J Nephrol. 1996; 16(2):95-7.
12.Buti M, Viladomiu L, Jardi R, Olmos A, Rodriguez JA, Bartolome J, et al. Long-term immunogenicity and efficacy of hepatitis B vaccine in hemodialysis patients. Am J Nephrol. 1992; 12(3):144-7.
13.Pasko MT, Bartholomew WR, Beam TR, Jr., Amsterdam D, Cunningham EE. Long-term evaluation of the hepatitis B vaccine (Heptavax-B) in hemodialysis patients. Am J Kidney Dis. 1988 ; 11(4):326-31.
14.Tele SA, Martins RM, Lopes CL, dos Santos Carneiro MA, Souza KP, Yoshida CF.Immunogenicity of a recombinant hepatitis B vaccine (Euvax-B) in haemodialysis patients and staff. Eur J Epidemiol. 2001; 17(2):145-9.
15.Fabrizi F, Martin P, Dixit V, Bunnapradist S, Dulai G. Meta-analysis: the effect of age on immunological response to hepatitis B vaccine in end-stage renal disease. Aliment Pharmacol Ther. 2004 ; 20(10):1053-62.
16.Dacko C, Holley JL. The influence of nutritional status, dialysis adequacy, and residual renal function on the response to hepatitis B vaccination in peritoneal dialysis patients. Adv Perit Dial. 1996; 12:315-7.
17.Elwell RJ, Neumann M, Bailie GR. Factors associated with long-term antibody production induced by hepatitis B vaccine in patients undergoing hemodialysis: a retrospective cohort study. Pharmacotherapy. 2003 ; 23(12):1558-63.
18.Peces R, de la Torre M, Alcazar R, Urra JM. Prospective analysis of the factors influencing the antibody response to hepatitis B vaccine in hemodialysis patients. Am J Kidney Dis. 1997 ; 29(2):239-45.
19.Roozbeh J, Moini M, Lankarani KB, Sagheb MM, Shahpoori S, Bastani B. Low dose intradermal versus high dose intramuscular hepatitis B vaccination in patients on

chronic hemodialysis. ASAIO J. 2005 ; 51(3):242-5.
20. Centers for Disease Control and Prevention (CDC). Outbreaks of hepatitis B virus infection among hemodialysis patients- California, Nebraska and Texas. 1994 MMWR Morb Mortal Wkly Rep. 1996;45(14): 285-289.
21. Ayub MA, Bacci MR, Fonseca FLA, Chehter EZ. Hemodialysis and hepatitis B vaccination: a challenge to physicians. IntJ of General Med 2014:7 109-114.
22. Grzegorzewska AE. Hepatitis B vaccination in chronic kidney disease: Review of evidence in non-dialyzed patients. Hepat Mon. 2012;12(11):e7359.
23.Nahar K, Jahan M, NessaA,Tabassum S. Antibody response after hepatitis B vaccination among maintenance hemodialysis patients.Bangladesh Med Res Counc Bull 2011; 37:88-91.
24. 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(1):185-91.
25. Gasim GI, Bella A, Adam I. Immune response to hepatitis B vaccine among patients on hemodialysis. World J Hepatol. 2015; 7(2):270-5.