



## VACCINATED HEMODIALYSIS PATIENTS; THE STATUS OF IMMUNITY AGAINST THE HEPATITIS B VIRUS, AT A TERTIARY CARE HOSPITAL

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**ABSTRACT... Objectives:** Determine the status of immunity against the hepatitis B virus among vaccinated hemodialysis patients at a tertiary care hospital. **Study Design:** Cross sectional study. **Place and Duration of Study:** All medical wards of Civil Hospital and Ojha campus, Dow University of Health Sciences, Karachi, Pakistan from May 2013 to January 2015. **Methodology:** Patients with chronic kidney disease on hemodialysis attending out-patient department were enrolled. Patients with either gender and aged 18-70 years, who give consent for participation, who are on HD for more than 9 months with a proven diagnosis of ESRD who have received a complete course of 4 doses of hepatitis B vaccination atleast 2 months back were included in this study. Non-consenting patients, present/past history of viral hepatitis, patients who were hepatitis B surface antigen (HBsAg) positive, patients on immunosuppressive agents, pregnant patients were excluded from this study. **Results:** Out of the 103 patients, 69 (67%) males and 34 (33%) females with mean age of study population was  $51.1 \pm 14.3$  years (17 to 70 years), mean duration post vaccination was  $7.6 \pm 0.9$  months (6 to 9 months), mean anti HBs antibody level was  $184.6 \pm 293.4$  (level rang 0 to 1000) and mean hemodialysis duration was  $26.4 \pm 12$  months (10 to 50 month). Out of 37 non-responders 28 (75.7%) had twice weekly schedule of hemodialysis and 09 (24.3%) had thrice weekly schedule of hemodialysis, out of 19 weak responders 13 (68.4%) had twice weekly schedule of hemodialysis and 06 (31.6%) had thrice weekly schedule of hemodialysis and out of 47 high responders 29 (61.7%) had twice weekly schedule of hemodialysis and 18 (38.3%) had thrice weekly schedule of hemodialysis ( $p=0.395$ ). **Conclusion:** Excellent response of HbsAg B vaccination for those patients, undergo dialysis procedure that is not associated with age, systemic inflammation or nutritional. Effective dialysis procedure associated with excellent response to the vaccine hepatitis B.

**Key words:** Hemodialysis, Hepatitis B, Immunity, Vaccination.

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## INTRODUCTION

Worldwide is a significant health problem occurred due to consequences of Hepatitis B virus (HBV) are chronic liver disease, cirrhosis, and hepatocellular carcinoma. Approximately 350 million chronic carriers worldwide are the main reservoir infection.<sup>1,2</sup> With accessibility of vaccine HBV since 1982, a decline was reported in the incidence of HBV infection and morbidity and mortality. The immune to HBV vaccine assessed by measuring the levels of antibodies after 6 to 8 weeks after completion of the 3 doses. Hepatitis B surface of the body is greater than 10 mIU/ml is considered to be protective.<sup>3</sup>

Patients on hemodialysis (HD) more exposure

for hepatitis B virus (HBV). Sources of HIV in the blood product transfusions, infection from the dialysis machines and other sources of environmental diseases. Patients with Chronic uremic, although dialysis or not, have a reduced immune to hepatitis B vaccine.<sup>4</sup> Although vaccination of hepatitis B virus (HBV) in healthy subjects resulted in a seroconversion rate of 90% to 100% for patients with end-stage renal disease have reduced responses to HBV vaccination with sufficient surface anti-hepatitis B (anti-HBs) unaffected by the amount of from 50% to 60%.<sup>5</sup>

Several methods have been tried to improve the immune seroconversion including adding additional capacity of inoculum injection four

lines and doubling the dose of the vaccine at / 40 mcg dose. One study reported a 80% seroconversion by this route. A. Ramezani, et al. their study found that after the initial inoculation, 87% of patients developed anti-hbs levels above 10 IU / l. 27.8% and 59.2% of them have a weak high responders respectively. 13% of patients were non-responders.<sup>6</sup>

Although infection with HBV is a matter of large health care in community and hospital settings in Pakistan, the elements to evaluate the immune system in patients undergoing hemodialysis is not available. Given the 3-4% of the general spread of the virus and of the possibility of nosocomial transmission in the case of health care is important.<sup>7</sup>

Therefore, we designed this study at a one of the largest tertiary care centers of the country to evaluate the immune response among hemodialysis patients after completion of their vaccination schedule. ESRD is a immunocompromised state and these patients have a tendency of low immunity against hepatitis B virus even on higher doses. At the end of this study we will be able to know the real scenario among the vaccinated hemodialysis patients and will be able to develop immunization protocol for Hepatitis B immunization of ESRD patients on haemodialysis.

## SUBJECTS AND METHODS

This study was conducted in different medical wards of Civil Hospital and Ojha campus, Dow University of Health Sciences, Karachi, Pakistan from May 2013 to January 2015. Patients with chronic kidney disease on hemodialysis attending out-patient department were enrolled. Patients who received a double dose (40 mcg) a recombinant hepatitis B vaccine immunization four rows of the program as intramuscular injections in the deltoid muscle at 0, 1, 2 and 6 months were selected for hepatitis B antibodies (anti HBS) tests. Measurement of hepatitis B surface of the body of the patient (anti-HBs) by ELISA after 1-2 months after the last injection. Subjects were divided into three groups according

to the level of anti-HBs: Non-Responders (<10 IU / l), responding patients (10 to <100 IU / l) and high responders (equal to or more than 100 IU / l). Patients with either gender and aged 18-70 years, who give consent for participation, who are on HD for more than 9 months with a proven diagnosis of ESRD who have received a complete course of 4 doses of hepatitis B vaccination atleast 2 months back were included in this study. Non-consenting patients, present/past history of viral hepatitis, patients who were hepatitis B surface antigen (HBsAg) positive, patients on immunosuppressive agents, pregnant patients were excluded from this study.

## RESULTS

Out of the 103 patients, 69 (67%) males and 34 (33%) females with mean age of study population was  $51.1 \pm 14.3$  years (17 to 70 years), mean duration post vaccination was  $7.6 \pm 0.9$  months (6 to 9 months), mean anti HBs antibody level was  $184.6 \pm 293.4$  (level rang 0 to 1000) and mean hemodialysis duration was  $26.4 \pm 12$  months (10 to 50 month). Out of 69 males 42 (60.9%) had twice weekly schedule of hemodialysis and 27 (39.1%) had thrice weekly schedule of hemodialysis as compared to this out of 34 females 28 (82.4%) had twice weekly schedule of hemodialysis and 06 (17.6%) had thrice weekly schedule of hemodialysis. Analysis of anti HBS antibody status 37 (35.9%) patients were non-responders, 19 (18.4%) were weak responders and 47 (45.6%) were high responders.

On analysis of descriptive statistics among the gender it was observed that mean age of male patients was  $52.6 \pm 14.5$  years, mean duration post vaccination of male patients was  $7.5 \pm 0.88$  months, mean anti HBs antibody level of male patients was  $162 \pm 260.6$  and mean hemodialysis duration of male patients was  $28.2 \pm 13$  months as compared to these the mean age of female patients was  $48.1 \pm 13.5$  years, mean duration post vaccination of female patients was  $7.8 \pm 0.9$  months, mean anti HBs antibody level of female patients was  $230.5 \pm 350.4$  and mean hemodialysis duration of female patients was  $22.7 \pm 9$  months (Table-I).

Gender	Age Mean (years)	Duration post vaccination (months)	Anti HBs antibody level	Hemodialysis Duration (months)
Male	52.55+14.5	7.50+0.88	162+260.6	28.15+12.9
Female	48.14+13.54	7.76+0.92	230+350.4	22.73+9.0
P value	0.013	0.001	0.027	0.003

Table-I. Analysis of Descriptive Statistics among the Gender

Out of 37 non-responders 28 (75.7%) had twice weekly schedule of hemodialysis and 09 (24.3%) had thrice weekly schedule of hemodialysis, out of 19 weak responders 13 (68.4%) had twice weekly schedule of hemodialysis and 06 (31.6%) had thrice weekly schedule of hemodialysis and out of 47 high responders 29 (61.7%) had twice weekly schedule of hemodialysis and 18 (38.3%) had thrice weekly schedule of hemodialysis (p=0.395) (Figure-1).

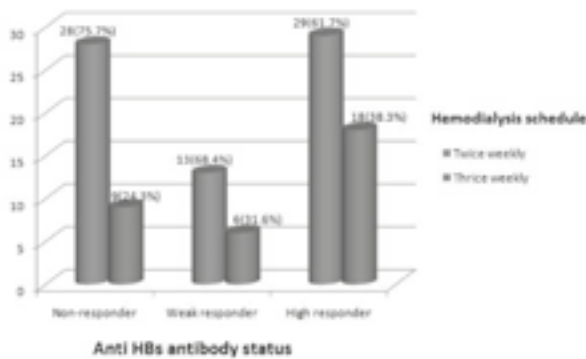


Figure-1. Analysis of Anti HBs Antibody Status among the Hemodialysis Schedule

**DISCUSSION**

Contact with Hepatitis B virus (HBV) is considered to be fairly high-risk among patients receiving treatment through dialysis. HBV in infected patients measures in at astonishingly elevated levels through blood and other contaminated bodily fluids. Handling of infected equipment and body surfaces of HBV patients assists in the transmission of HBV by dialysis technicians and healthcare professionals. In Pakistan, HBV is an escalating concern gaining serious attention regarding public health safety, while in numerous other countries of intermediate endemicity or high infection of HBV.<sup>8</sup>

Since its development in 1982, the Hepatitis-B

vaccine is strongly recommended for all at risk patients undergoing dialysis treatment, however the seroconversion rates are rather decreased in the end-stage renal disease (ESRD) patient population.<sup>9,10</sup> Between 73-76.7% of hemodialysis patients, seroconversion (anti-HBs > 10 IU/l) occurred after three months of vaccine therapy, while an appropriate response (anti-HBs >100 IU/l) was noted in only 53.5% in one series. Further decreased response rates ranging between 47-58% to HBV vaccine have been observed after the fourth injection.<sup>11</sup>

Apart from the lower response rates, immunogenicity of the hepatitis-B vaccine is frequently short-lived, therefore requiring booster shots to receive continued protection against HBV.<sup>12</sup> One study found that 41% of responders had no measurable levels of anti-HBs in the serum throughout a three-year follow-up. Factors such as malnutrition, uremia, old age are correlated to poorer responses, along with an immunocompromised level of patients with chronic kidney disease.<sup>13</sup>

Elements linked with higher response rates to HBV vaccine include being below 40 years of age, well-nourished, and maintain tolerability to dialysis treatment. However, components such as the length of time of dialysis treatment, hemoglobin and parathyroid hormone level, along with the Hep C virus (HCV) infection didn't considerably impact antibody response to vaccine for hepatitis-B. Recent study demonstrated an elevated response to hepatitis-B vaccination among hemodialysis patient population. After full administration of the vaccination, 45.6% of patients revealed high antibody response (>100 IU/L). Past research studies have noted fluctuating hepatitis-B vaccination response rates that ranged between 47-73% in hemodialysis

patient populations. In comparison, satisfactory responses to the hepatitis-B vaccine among dialysis patients have also been monitored in regions with endemicity (prevalence 2-8%) of HBV, an example includes Brazil, which came within reach of 89.5% in a study.<sup>13</sup>

Numerous research have shown when the hepatitis-B vaccine is administered, even in high doses, it don't stimulate as notable a response in chronic renal failure patients as it does in non-hemodialysis patient population. There are various reasons behind the poor response of vaccination among hemodialysis patients. For example, uremia inhibits activation of and antigen-presentation to T-cells, and following antibody production.<sup>14</sup>

Fernandez et al<sup>15</sup>. Conducted a study which showed that malnutrition in the side of the target response to HBV in dialysis patients. 3-3.5 g/dl albumin levels of 87.5% patients were non-responders than when compared with 18.8% in group having serum albumin level between 4.5-5 g/dl. Another research study done by Kara et al<sup>16</sup>. noted that patients with serum albumin levels greater than 3.5 g/dl had too great an antibody response to the hepatitis-B vaccine. 17 clinical trials demonstrated less response to the hepatitis-B vaccination among elderly dialysis patients, which could be linked to the age-related variations in the immune system.

Physiological manifestations such as immune dysfunction, monocyte activation, and overproduction of pro-inflammatory cytokines are related with ESRD. Little previous research is available regarding the linked with chronic inflammation and immune response to the objectives of dialysis. This study was conducted and found no significant difference statistically in the CRP levels among responders as compared to non-responders.<sup>17</sup>

This result may be supported by the inconstant counter-production of interleukin-10 (IL-10), subsequently resulting in adequate B-cell function in uremic patients. In patients generating greater

levels of IL-10, reduction in uremia is noted, as well as dialysis-induced chronic inflammation, along with improvements outcomes after vaccine application.<sup>18</sup> Previous literature has mentioned the positive effect of effective dialysis on vaccination response to HBV in hemodialysis patients. One study conducted on patient's peritoneal dialysis immunize with the hepatitis-B vaccine, the initial weekly Kt/V was 2.37 in responders, as compared to the 2.01 in the non-responders group. Since dialysis assists to replace impaired B7-2 (CD-86) expression on monocytes in hemodialysis patients, effective dialysis may lead to a greater response. However, many other researchers have yet to confirm the advantageous effect of efficient dialysis on immune function.<sup>19</sup> The entire patient population in this research study was reported to be positive for the anti-HCV antibody viral marker.<sup>20</sup>

## CONCLUSION

Very good response hepatitis B vaccination for patients undergoing dialysis that is not correlated with age, systemic inflammation, or the state of nutrition. Dialysis succeeded associated with good response to the goal hepatitis B. Future research to determine the most efficient format of vaccination in dialysis patients in our region.

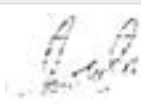

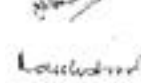
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### AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Dr. Fawed Qureshi	Data Collection	
3	Dr. Muhammad Umar Khan	Drafting of the article	
4	Dr. Rakhshinda Jabeen	Data Collection	