

Seroconversion of Hepatitis B Vaccination among Pre-Dialysis and Dialysis Patients: A Hospital Based Observational Study

Dr. Sushama Jotkar¹, Dr. Sadhana P. Madyalkar^{2*}

¹Professor, Department of Medicine, Dr. D. Y. Patil Medical College, Kasba Bawda, Kolhapur-416006, Maharashtra-411018, India

²Post- Graduate Student, Department of Medicine, Dr. D. Y. Patil Medical College, Kasba Bawda, Kolhapur-416006, Maharashtra-411018, India

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*Corresponding author
Dr. Sadhana P. Madyalkar

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Abstract: Background: Hepatitis B infection is a constant threat despite availability of effective vaccine. Patients with Chronic Kidney Disease (CKD) have higher risk of acquiring Hepatitis B infection and further progressing to become chronic carrier. Present research aims to study seroconversion rates of Hepatitis B vaccination in pre-dialysis and dialysis patients. Also it aims to correlate seroconversion with the nutritional status of the patients. **Methods:** This is a hospital based observational study conducted in tertiary healthcare facility. Total 110 participants were enrolled for the study after obtaining written informed consent. Demographic information was captured using standardized questionnaire. Nutritional assessment was done by calculating BMI, Lean body mass and Mid Arm Circumference (MAC). Anti HBsAb estimation has been done before beginning of schedule and 1 month after last dose. Data entry and analysis done using statistical software SPSS version 20.0. **Results:** Out of total 110 patients 69 (62.7%) were males and 41 (37.3%) were females. The mean age of the patients was 46.6±11.85 years. Seroconversion rates were significantly higher (p value=0.014) in the pre-dialysis group (89.4%) than the dialysis group (69.8%). There were significant higher seroconversion rates (p value <0.05) among subjects who have better BMI, Lean Body Mass and MAC. **Conclusion:** Vaccination with HBV in early CKD gives a chance for higher seroconversion. Patients can be screened for CKD and can be immunized at the earliest for better antibody titre.

Keywords: CKD, ESRD, Hepatitis B Vaccination, Seroconversion rate, Dialysis.

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INTRODUCTION

Hepatitis B infection is a public health problem and continues to threaten even though effective vaccination is available. Chronic diseases have become a major cause of global morbidity & mortality. In India the projected number of deaths due to chronic diseases will rise from 3.78 million in 1990 (40.4% of all deaths) to an expected 7.63 million in 2020 (66.7% of all deaths)[1,2].

The increase in the prevalence of Chronic Kidney Disease (CKD) & its progression to ESRD (End Stage Renal Disease) has highlighted the importance of CKD & its risk factors in developed as well as developing countries [3]. The average incidence of ESRD in developing countries is 150 per million population which is lower than the developed countries [4]. One of the common and most serious infectious disease encountered in Chronic kidney diseases during hemodialysis is Hepatitis B Virus (HBV) [5].

Patients with CKD have higher risk of acquiring Hepatitis B infection during dialysis session & subsequently may become chronically infected to become Hepatitis B carrier [6,7]. Hepatitis B infection is difficult to treat, that is why prevention of Hepatitis B vaccine (HB vaccine) is the most efficient way to tackle the problem.

So, as a measure of prevention, Hepatitis B vaccine is recommended for all patients on maintenance hemodialysis & for all pre-end stage renal disease patients before they become dialysis dependent [8,9].

However, Patients with CKD have a reduced response to vaccination because of the general immune suppression associated with uremia and thus seroconversion to HBV is lower in patients undergoing hemodialysis than general population [10]. The present research aims to study seroconversion rates of Hepatitis B vaccination in pre-dialysis and dialysis patients. Also it aims to correlate seroconversion with the nutritional status of the patients.

METHODOLOGY

The present study is a Hospital based observational prospective study. It was carried out at tertiary care centre, Padmashree Dr. D. Y. Patil Hospital & Research Institute, Kolhapur. Ethical clearance was sought from Institutional Ethics Committee prior to the commencement of study.

Patients attending OPD & IPD in the institute diagnosed as Chronic kidney disease (CKD) from e-GFR during the period September 2016 to August 2018 were included only after obtaining written informed consent from them. The subjects with age 18 years or more with Laboratory confirmed negative serology result to HbsAg and those on renal dialysis or a pre-dialysis patients with e-GFR less than 60 ml/min for more than 3 months were included in the study. Stages of CKD were categorized from stage 0 to 5 according to Cockcroft - Gault formula [$e\text{-GFR} = \frac{(140 - \text{age}) \times \text{weight}}{72} \times \text{serum creatinine} \times 0.85$ (if female)]. The subjects with previous hepatitis B infection, HBV vaccination, immuno-compromised patients, those on systemic immune-modulatory medications, haemoglobin <7 g/dl were excluded from the study.

Total 110 patients including 69 male and 41 females were part of the study. Demographic information was captured using standardized questionnaire. Nutritional assessment was done by calculating BMI, Lean body mass and Mid Arm Circumference (MAC) with standardized formula and procedure. All patients received vaccination according to vaccination protocol for CKD in Indian Journal Nephrology, 2016 guidelines with Energix at interval of 0, 1, 2 and 6 months. Anti HBsAb estimation has been done before beginning of schedule and 1 month after last dose. Anti-HBs titre >10 mIU/ml were defined as good responders while Antibody titre <10 mIU/ml were considered as poor responders.

Data entry and analysis was done using statistical software SPSS 20.0. Demographic and clinical profile of the participants is represented as frequency and percentage. Chi square test was applied to study correlation between Hepatitis B vaccination seroconversion rates among pre-dialysis and dialysis patients and also correlation of seroconversion rates with the nutritional status of the subjects. P value of statistical tests less than 0.05 was considered to be significant.

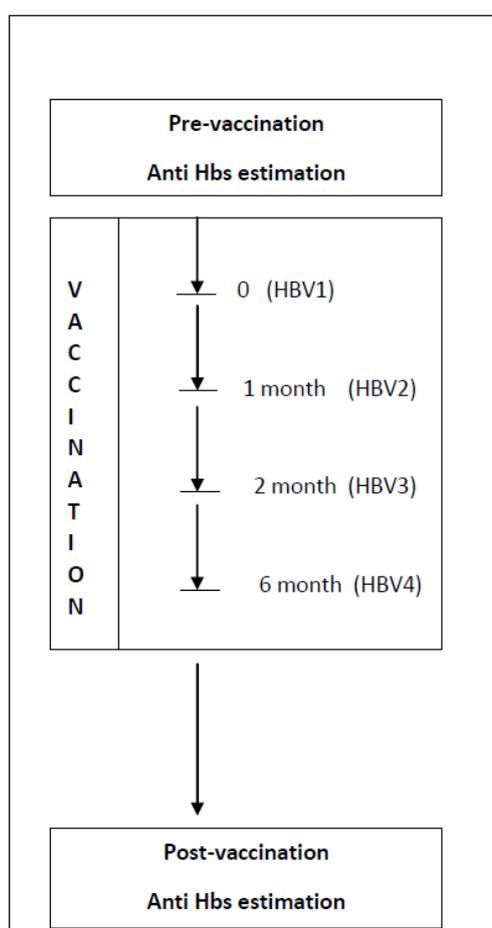


Fig-1: Sequence of events in the present research

RESULTS

Out of total 110 patients 69 (62.7%) were males and 41 (37.3%) were females. The mean age of the patients was 46.6 ± 11.85 years. As per Cockcroft - Gault formula, 10.1% belonged to CKD stage 1, 15.4% belonged to CKD stage 2, 16.3% belonged to CKD stage 3, 22.7% belonged to stage 4 and rest 34.5% belonged to CKD stage 5. Majority of the patients presented with breathlessness (69%) followed by generalised weakness (63.6%), oedema (59%), anorexia (56.3%), decreased urine output (39%), abdominal pain

(7.2%) & altered sensorium (2.7%). Hypertension & Diabetes Mellitus were the most prevalent co-morbidities present in 81.1% & 56.3% patients respectively while 37.2% patients had associated cardiovascular diseases & 11.8% had renal disease. Nutritional assessment was done using BMI, Lean Body Mass and Mid Arm Circumference values. The Mean Mid Arm Circumference, Lean Body Mass & BMI values of patients were 21.62 ± 2.19 cm, 38.07 ± 2.23 kg & 22.64 ± 1.91 kg/m² respectively.

Table-1: Demographic and clinical profile of the study participants

1. Age (years)	Categorization	N	Percent
	21-30	12	10.9%
	31-40	25	22.7%
	41-50	38	34.5%
	51-60	17	15.4%
	>60	18	16.3%
2. Sex	Male	69	62.7%
	Female	41	37.3%
3. Symptoms	Breathlessness	76	69%
	Generalised weakness	70	63.6%
	Oedema	65	59%
	Anorexia	62	56.3%
	Decreased urine output	43	39%
	Abdominal pain	8	7.2%
	Altered sensorium	3	2.7%
4. Stages of CKD	CKD1	12	10.9%
	CKD2	17	15.5%
	CKD3	18	16.4%
	CKD4	25	22.7%
	CKD5	38	34.5%
Associated Co-morbidities	Hypertension	90	81.1%
	Diabetes Mellitus	62	56.3%
	Cardiovascular disease	41	37.2%
Addiction	Smoking/tobacco chewers	42	38%
	Alcohol	27	24.5%

Mean HbsAb titre for CKD stage I, stage II, stage III, stage IV and stage V were observed to be 30.58 ± 2.58 , 25.26 ± 2.18 , 19.26 ± 2.56 , 15.35 ± 2.46 , 11.29 ± 1.45 among good responders. Among the poor responders antibody titre in stage II, stage III, stage IV,

stage V were 8.62 ± 1.03 , 6.26 ± 2.23 , 8.75 ± 1.23 , 5.62 ± 1.36 . Pre-dialysis patients i.e. Stage I, II and III of CKD and dialysis patients i.e. Stage IV and V of CKD are plotted against their mean HBsAb titre as shown in the figure no.1 and fig no.2

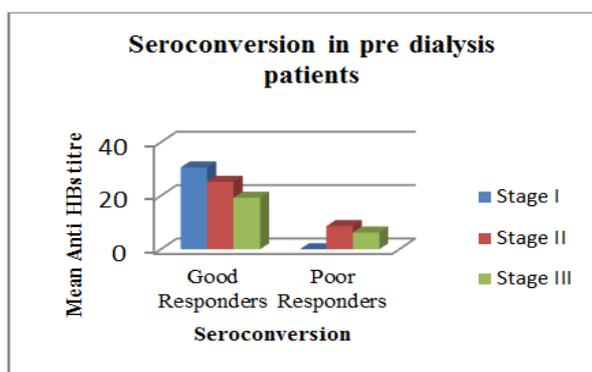


Fig-2: Anti HBsAb titre in pre-dialysis patients

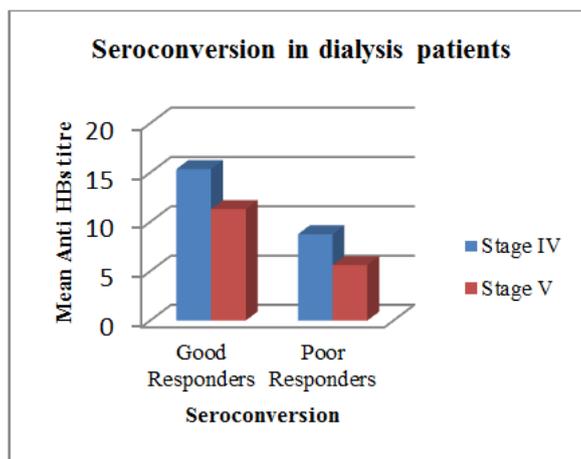


Fig-3: Anti HBsAb titre in dialysis patients

Seroconversion rates of pre-dialysis patients were compared with that of dialysis patients. It was observed that seroconversion rates were significantly higher (p value=0.014) in the pre-dialysis group

(89.4%) than the dialysis group (69.8%) implicating role of early vaccination. The same is represented in tabular form in table no.2.

Table-2: Seroconversion rates in pre-dialysis and dialysis patients

	Good Responders	Poor Responders	Total
Pre-dialysis	42 (89.4%)	5 (10.6%)	47 (100%)
Dialysis	44 (69.8%)	19 (30.2%)	63 (100%)
P value	0.014		

Nutritional status of the subjects was done using the anthropometric parameters i.e. Body Mass Index (BMI), Lean Body Mass and Mid-Arm Circumference (MAC). There were significant higher

seroconversion rates among subjects who have better BMI, Lean Body Mass and MAC i.e. higher the anthropometric parameters better is the seroconversion (Table no.3).

Table-3: Anthropometric parameters according to CKD stages & its correlation with seroconversion

Anthropometric parameters	CKD Stages	Good Responders	Poor Responders	p value
BMI (kg/m ²)	I	25.6±1.4	-	-
	II	24.2±2.0	23.2±2.0	<0.01
	III	22.1±2.4	21.5±3.1	<0.01
	IV	20.2±1.5	19.2±1.7	<0.01
	V	18.1±2.0	16.9±1.9	<0.01
Lean Body Mass (kg)	I	40.0±3.8	-	-
	II	39.1±1.9	38.2±2.0	<0.01
	III	36.0±2.3	34.1±3.0	<0.01
	IV	35.0±1.6	32.9±2.7	<0.01
	V	33.9±1.6	31.0±1.9	<0.01
MAC (cm)	I	26.6±2.7	-	-
	II	25.9±1.9	24.1±2.0	<0.01
	III	23.9±2.3	21.2±2.0	<0.01
	IV	21.5±1.6	20.0±2.6	<0.01
	V	20.6±1.4	18.9±1.9	<0.01

DISCUSSION

A hospital based observational, prospective study was conducted with 110 patients to study the pattern of seroconversion of Hepatitis B vaccination in CKD patients.

The seroconversion rates reported in various studies ranges from 78% to 83%. Gomthy S *et al.* reported 82.6% was the overall seroconversion rate and the rest 17.4% with low antibody titre had to re-vaccinated [11]. Hashemi B *et al.* reported 78% as overall seroconversion rate to HBV vaccination [8]. In present study, we found overall seroconversion rate to be 78.18% which is consistent with above studies.

With regard to seroconversion rates among different stages of CKD there are variation in different studies. In one of study by Ghadiani MH *et al.* [12] study comparing the response rate to HB vaccine observed CKD stages 3-4 patients had higher response rate than dialysis patients ($P < 0.001$). In another study by Hashemi *et al.* there was no statistically significant difference in seroconversion rates among different stages of CKD. In present study, we found seroconversion rates were significantly higher (p -value=0.014) in the pre-dialysis group (89.4%) than the dialysis group (69.8%).

There is a significant correlation between BMI ($p < 0.01$), lean body mass ($p < 0.01$) & MAC ($p < 0.01$) with seroconversion. Similar observations were noted in the studies of Vanitha-Rani N *et al.* [13], Pearson *et al.* [14] and Yigit IP *et al.* [15].

CONCLUSION

Immunization in early stages of CKD has a good chance for higher seroconversion i.e. if patients are vaccinated early, pre-dialysis HBV infection may be avoided. Nutritional status also has an impact on seroconversion of Hepatitis B vaccine, better the nutritional status better is the seroconversion.

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