

Hepatitis B Vaccination in Chronic Kidney Disease:- Experience in A Tertiary Care Centre

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Abstract

Background: The study was conducted to examine the seroconversion rate for hepatitis B vaccination in Chronic Kidney Disease (CKD) patients and the factors which influence the sero conversion rate .

Methodology: This is a descriptive study which included 235 patients with CKD (chronic kidney disease) with eGFR < 60ml/min/m² and they were given 40microgm of Hepatitis B vaccine intramuscularly over deltoid at 0,1,2,6 months . Patient characteristics were recorded.Patient response was assessed by measuring antibodies to hepatitis b surface antigen (AntiHBs Ab) six weeks after receiving the 4th dose.

Results : 83% of the patients were seroconverted with titre $\geq 10IU/L$.The eGFR and age are found to influence the titre. Aetiology of CKD and gender has no effect on the sero conversion status.

Conclusion: HBV vaccination should be started to CKD patients at the earliest preferably in the first visit itself as the seroconversion rate declines with progression of CKD.

Keywords: chronic kidney disease, hepatitis B vaccine,seroprotection

I. Introduction

Prevention of infectious disease is an important problem worldwide .Hepatitis B may be largely preventable by vaccination.Administration of HBVvaccination leads to the development of protective antibodies in responders. Patients with CKD especilay those on dialysis are at risk of contracting HBV infection⁽¹⁾. Among HD patients susceptible to HBV infection the two year seroconversion HBV infection was 38.9% accounting for 19 seroconversions to HBsAg positivity per 100 patient years. The prevalence of HBV infection in Dialysis population in India ranges between 3.4-43% which is several folds higher than the carrier rate in general population⁽²⁾.Strict procedures controlling transmission of blood borne infections during HD (hemodialysis) sessions as well as hepatitis B vaccinations are recommended and introduced on a mandatory basis in most HD centres world wide⁽¹⁾.Although acute Hepatitis B infections tend to be mild and asymptomatic in dialysis patients ,up to two thirds may progress to chronic carriage ,with subsequent risk of chronic liver disease, cirrhosis , liver cancer and nosocomial transmission within the HD unit and among the family members⁽³⁾ .

The use of HBV vaccine and preventive measures⁽⁴⁾ have helped to reduce the annual incidence of HBV infection in patients on dialysis from 3% to 0.05% between 1971 -1997 in USA. The usual vaccination schedule of HBV in adults with normal renal function is 10-20microgm/dose in a 3 shot schedule (at 0,1, 6 months).The effectiveness of HBV vaccination in ESRD (end stage renal disease) patients was found to be lower than in subjects without CKD. These patients commonly presented with lower seroconversion rates , lower peak antibody titres and a rapid decline in antibody levels .So they are given 40 microgm / dose in 4 shots (0,1,2,6 months).Early vaccination of patients before they start dialysis has been used in order to improve the response rate⁽²⁾ .So HBV vaccination is recommended for all CKD patients and should be started in the first visit itself if possible after appropriate screening tests. Failure to complete the full course of HBV vaccination also impairs immunisation response⁽¹⁾.

II. Materials And Methods

II.1 Aims and Objectives

1. To study the proportion of seroconversion after Hepatitis B vaccination in chronic kidney disease patients.
2. To study the factors affecting seroconversion.

II.2 Study Design

The study follows a descriptive design.

II.3 Inclusion Criteria

All chronic kidney disease patients on conservative management with estimated GFR less than 60ml/min/1.73m² at the beginning of vaccination.

II.4 Exclusion Criteria

1. Patients on dialysis at the time of vaccination.
2. Patients who has not completed the required number of vaccinations or those who did not follow the recommended schedule or recommended dosage.
3. Patients on any immunosuppressive medications at the time of vaccinations.
4. Patients who did not give consent for the study.

II.5 Methodology

We collected data from 235 consecutive eligible patients who attended the outpatient department, Department of Nephrology Govt. T D Medical College Alappuzha, a tertiary care hospital in central Kerala, India during the study period from July 2015 to July 2016. The study was begun after obtaining approval from institutional research committee and ethics committee. All patients had undergone vaccination with recombinant hepatitis B vaccine 2ml (40microgram) intramuscularly in deltoid region with a total of 4 doses scheduled at 0 ,1 ,2, 6months . All patients underwent vaccination from our own hospital where potency of the vaccine is ensured before each dose. The study included patients who were vaccinated in the preceding three years. Anti HBS titre was done from a single laboratory between 6 weeks to 12 weeks after the last dose of vaccine using a sensitive assay where we used a cut off of 10 IU/L.

The data collection was done over a period of one year (July 2015–June 2016).Data were collected from the medical records of patients and hospital records .Information regarding the etiology of CKD, serum creatinine at the first dose of vaccination, anti HBs antibody titre was collected along with the baseline characteristics of the patients. Estimated GFR was calculated using the Modified Diet in Renal Disease (MDRD) formula. Data analysis was done using spss version 16. Values are expressed as mean/median plus or minus standard deviations and as percentage for categorical parameters. Differences between groups are compared with Student's t-test for parametric continuous variables. Chi-square test is applied for estimating the occurrence of categorical variables. A P value <0.05 is used as the threshold of statistical significance.

II.6 Ethical Clearance:

The ethical approval was granted from the Institutional ethical Committee . **Written** informed consent was obtained from every patient prior to the examination

III. Observations And Discussion

III. 1 Baseline Characteristics

As part of the study information from 235 patients were collected and analyzed. The mean age of the population studied was 50.5 years with a standard deviation (SD) of 14.4 years. There were 64.3% males and 35.7% females (fig.1). The native kidney disease was divided into three broad categories . Glomerular disease, chronic tubulointestinal disease and others . Majority of the glomerular disease category was constituted by diabetic nephropathy, ischemic nephropathy, lupus nephritis and primary glomerular disease like IgA nephropathy etc. Patients grouped under the tubular disease include obstructive nephropathy, ADPKD ,etc. The proportion of each subgroup in our study is depicted in fig 2.

Figure1

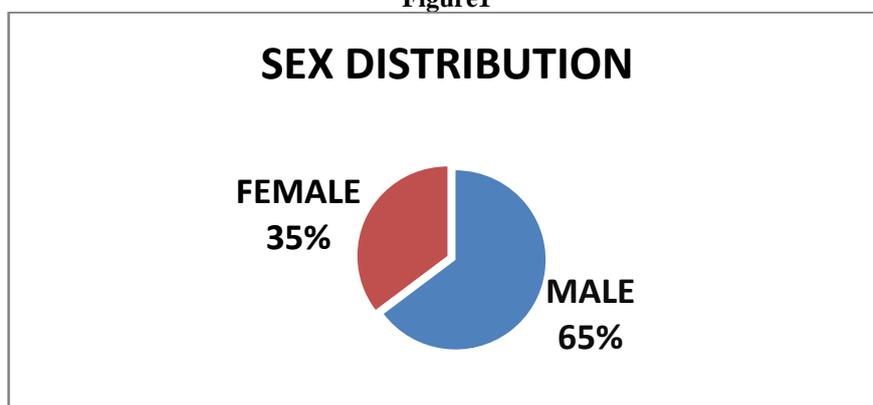
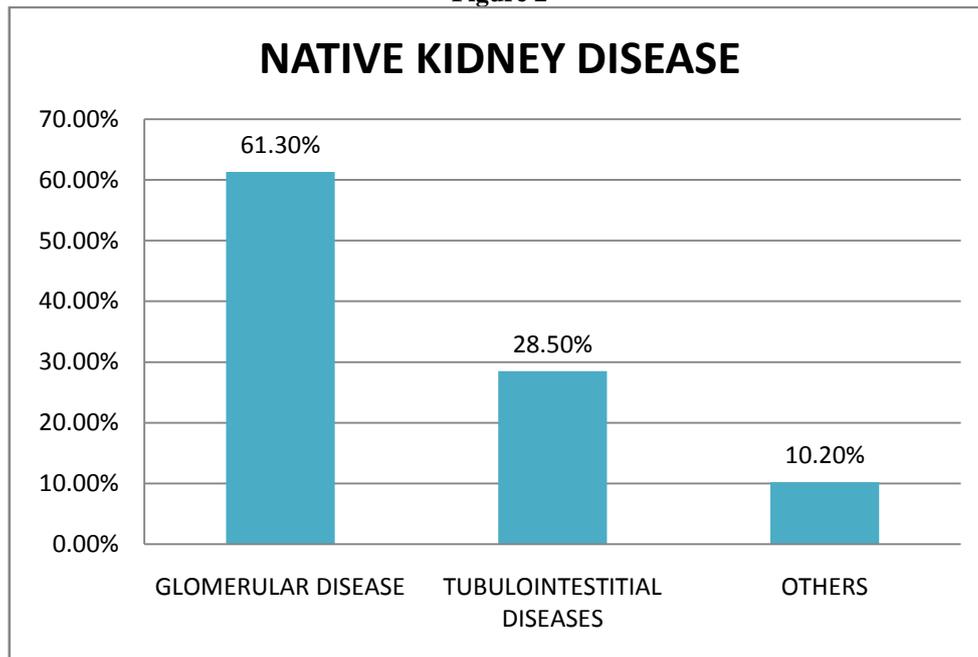
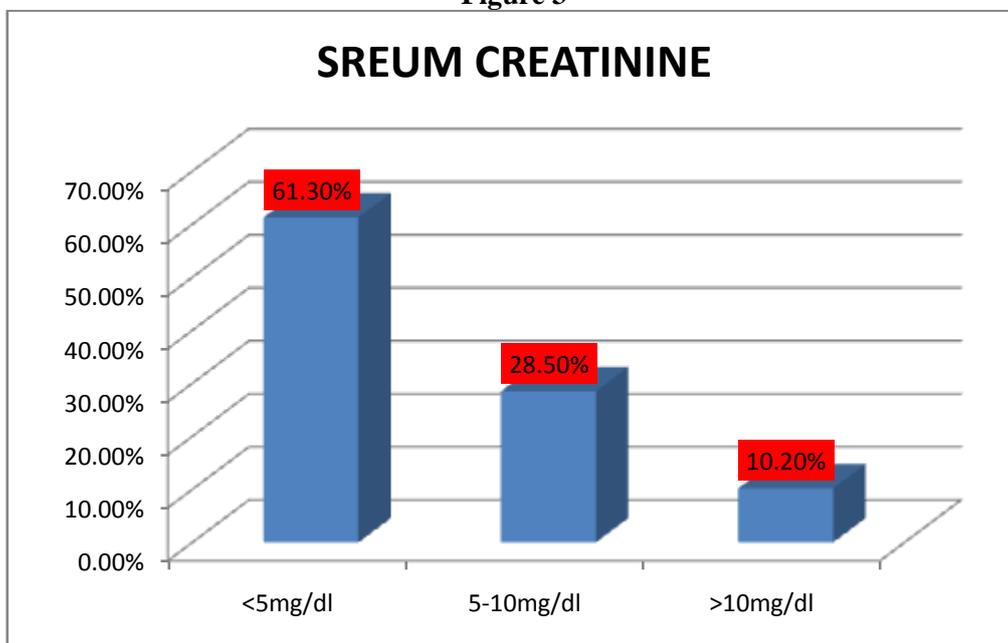


Figure 2



Unfortunately Hepatitis B vaccination of CKD patients is not routinely practiced in the periphery. So many patients reach our hospital unvaccinated even in end stage renal disease. In our cohort of patients also vaccination was carried out at different stages of CKD. 61.3% had their vaccination initiated when the serum creatinine was below 5 mg/dl but not less than 10% of subjects began their vaccination when the creatinine was well above 10mg/dl. This shown in fig 3.

Figure 3



The mean serum creatinine at the initiation of vaccination is 4.69mg/dl (SD 3.3mg/dl) . Creatinine value ranged from 1-19mg/dl. Estimated GFR was calculated using the MDRD(Modified Diet in Renal Disease) formula. Patients were categorised into 4 based on the eGFR.(44-60, 30-44,15-29,<15ml/min/1.73m²). eGFR ranged from 3 -60 with a mean of 26.29 ml/min/1.73m² (SD-16.5).(fig 4)

Figure 4

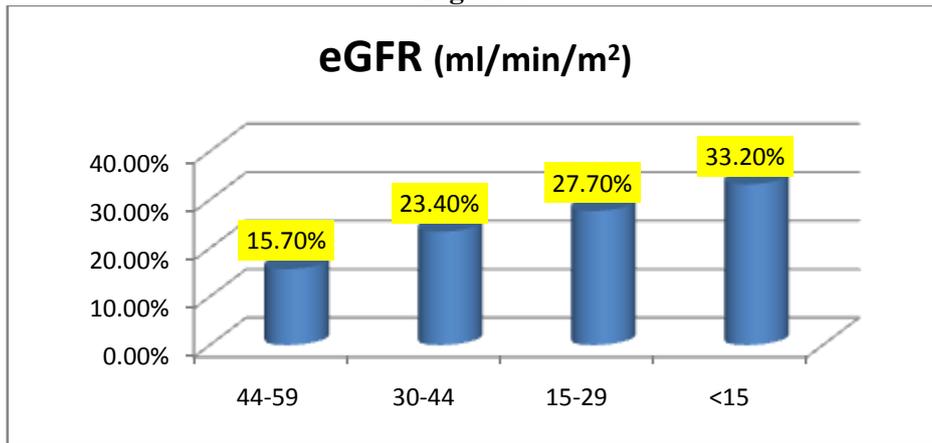


Figure 5

Anti HBS titre estimation is done 6 weeks after the last dose of vaccine. Out of the 235 patients 194 had titre more than 10 IU/L. Maximum titre reported in our laboratory is 1000 IU /L and test has to be repeated after further dilution to know the exact titre above 1000 IU which is not done as it is laborious and do not seem to have any clinical relevance. 17.4% were reported to have inadequate titre (below 10 IU). These patients were initiated on repeat vaccination schedule. The titre did not follow normal distribution ,still the mean titre was 297 IU. The curve has a positive skewing and around 55% patients had their titre less than 200 IU/ml. 12% subjects had strongly positive titres well above 1000 IU/ml which is clustered around the upper limit in the histogram given below (fig 6).

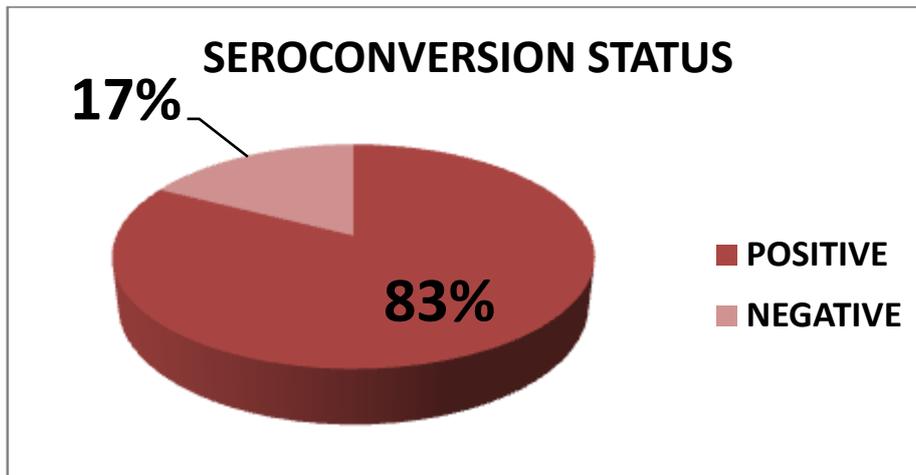
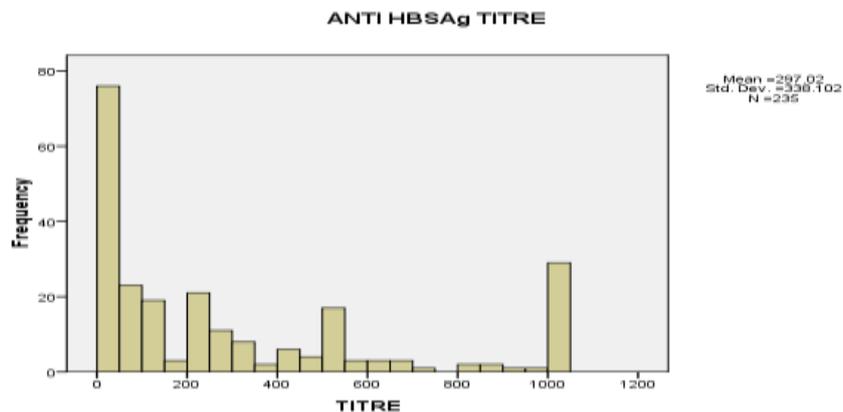


Figure 6



We have analyzed the factors that could affect the response to vaccination in CKD patients.

III.1 Age at the time of vaccination

It is obvious that the rate of seroconversion declines as the age advances. Among our patients the mean age of patients with titre more than 10 IU was 48.2 and that of patients with titre less than 10 IU was 61.43 years. The difference is statistically significant (p=0.046).

III. 2 Gender

We could not find any significant difference in seroconversion between male and female patients. (p=0.89) contrary to the earlier studies where male sex negatively correlated with seroconversion.

III. 3. Native Kidney Disease

No statistically significant difference could be found among the three groups.

III.4 . Estimated glomerular filtration rate

The difference among the eGFR subgroups were found to be statistically significant. (p<0.005). The titre positive group had a mean GFR of 27.47 ml/min/m² against 19.83ml/min/m² in the titre negative patients.

We also did correlation analysis and found that there is positive correlation between GFR and anti HBStitre and negative correlation between age Vs GFR and serum creatinine Vs anti HBS titre.

IV .Conclusions

Hepatitis B vaccination in CKD patients with GFR less than 60ml/min/m² has a failure rate of 17%. Our study also shows that the anti HBS titre decreases as the age of the patient at the time of vaccination increases. Similarly antiHBS titre is low when the eGFR is low at the time of vaccination. The etiology of kidney disease or gender has no effect on the response to vaccination contrary to the literature which shows that male gender has impaired seroconversion.

Hepatitis B virus (HBV) infection is a serious global health problem. The prevalence of viral hepatitis B is higher in dialysis patients than in the general population because of the opportunity for exposure during the dialysis procedure. Immunization is the most effective way to prevent transmission of hepatitis B virus (HBV) and hence the development of acute or chronic hepatitis B. It is well established that patients with end-stage renal disease including dialysis-dependent patients, have an impaired immune response to hepatitis B vaccine. End stage renal diseases (ESRD) patients have lower seroconversion rates compared with the subjects with intact renal function. Moreover, even after the completion of vaccination schedule anti-hepatitis B (anti-HBs) titers of responder dialysis patients are low and decline logarithmically with time. The impaired efficacy of HBV vaccine in patients with ESRD has been attributed to numerous factors such as immune compromise because of uremia and some other factors.

Less severe immune abnormalities in early CKD stages give a chance for higher seroconversion rates, If patients are vaccinated early, pre-dialysis HBV infection may be avoided,

A response to booster doses in patients responding for the primary vaccination in early CKD stages is usually maintained during RRT. Hence it is highly essential to screen the vaccinated individuals periodically for the presence of optimal antiHBS titre and if shows decline in its level, may be given booster doses.

V. Suggestions

The study undoubtedly shows that the response to vaccination and titre is low in advanced CKD patients. We could also demonstrate the habit of delayed initiation of vaccination in the CKD patients. The result gives a strong evidence to recommend initiation of vaccination at the earliest in CKD patients. Even though we don't have direct evidence, it is advisable to vaccinate patients who are at risk of developing CKD as theoretically immune response to vaccination fades with establishment of chronic kidney disease. CKD is asymptomatic especially in its early phase and at which time these patients are taken care of by the primary care physicians especially in developing countries because of the dearth of renal care physicians. So patients at risk of developing CKD (those Diabetes Mellitus, Hypertension, urolithiasis, various systemic diseases, family history of CKD, Chronic NSAID ingestion etc) should be screened and if features of CKD are evident should be given the Hepatitis B vaccination at the earliest after appropriate screening tests. So it is highly essential to create an awareness among primary care physicians in this regard especially in developing countries.

VI .Limitatins

1. The study lacks a control group to compare the response to vaccination. It would have been ideal to have another cohort without CKD or CKD with GFR >60ml/min/m² for comparison as that would have provided more useful information and eliminated the role of any possible confounding factors in the study although ample data are available in the literature for comparison.
2. The study considered the aetiology of renal failure as broad categories and hence the effect of each etiology on vaccination could not be inferred.
4. There are many issues unaddressed in this study like effect of dialysis, fate of non responders to repeat vaccination, need for routine booster dosing etc. A long term follow up study with serial measurement of titre is needed to solve these unresolved queries.

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