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Research Article

FREQUENCY OF HEPATITIS B IN PATIENTS OF CHRONIC KIDNEY DISEASE ON MAINTENANCE HEMODIALYSIS AND ITS RELATIONSHIP WITH NUMBER OF HEMODIALYSIS SESSIONS

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Abstract:

Introduction: Several prophylactic measures have been suggested to avoid infection by HBV and HCV in the HD patient. Strict adherence to universal precautions along with isolation of HBV and HCV infected dialysis patients might help to control disease spread in HD units.

Objectives: To determine the frequency of hepatitis B in patients of chronic kidney disease on maintenance hemodialysis and its relationship with number of hemodialysis sessions.

Materials & Methods: This descriptive cross-sectional study was conducted in Lahore General Hospital, Lahore, Pakistan started from April 2019 and completed in August 2019. A total of 270 CKD patients undergoing maintenance hemodialysis for at least 3 months, 18 to 80 years of age of both genders were included. Patients who received anti-viral therapy during last 6 months and with other known causes of raised liver enzymes were excluded. Blood samples were taken from the arterial line immediately after insertion of the needle (before dialysis was started). A real time PCR apparatus HBV RG PCR kit from QIAGEN (detection limit=100 copies/ml) was used for the detection of HBV DNA. HBV was diagnosed.

Results: In our study, frequency of patients with various number of sessions of hemodialysis in patients of CKD on maintenance hemodialysis is found as follows; <50 in 87 (32.22%), 50-100 in 100 (37.04%), 100-200 in 69 (25.56%) and >200 in 14 (5.19%) patients. Frequency of hepatitis B was found 15 (5.56%) patients of CKD on maintenance hemodialysis. Among 87 cases with dialysis <50 times, 02 patients (3.45%) were HBV DNA detected. A total of 100 patients with dialysis 50-100 times 6 patients (6.0%) were HBV DNA detected. Out of 69 patients 100-200 times dialysed patients 05 patients (7.25%) were HBV DNA detected. Similarly, out of 17 patients >200 times dialysed patients, 1 patient (5.88%) was HBV DNA detected with p-value of 0.749.

Conclusion: This study concluded that frequency of hepatitis B was found 5.56% in patients of CKD on maintenance hemodialysis with no significant difference in various number of sessions of hemodialysis.

Keywords: Chronic kidney disease, Maintenance hemodialysis, Hepatitis B.

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INTRODUCTION:

Chronic kidney disease is defined as a reduced glomerular filtration rate, increased urinary albumin excretion, or both, and is an increasing public health issue. Prevalence is estimated to be 8–16% worldwide. ¹CKD is associated with an increased risk of cardiovascular disease and chronic renal failure. Kidney disease is the ninth leading cause of death in the United States. Chronic kidney disease can be a manifestation of another chronic illness that are causing end-organ renal damage, such as diabetes mellitus or hypertension. Alternatively, chronic kidney disease can be an intrinsically renal disease, such as polycystic kidney disease. Therefore, at diagnosis of chronic kidney disease, family physicians must determine the underlying etiology so that the treatment plan can be appropriately directed.²

According to the KDIGO recommendations “patients on hemodialysis should be tested when they first start hemodialysis or when they transfer from another hemodialysis facility” while for pre-dialysis patients with chronic kidney disease the recommendation to test for hepatitis C and B is weak. Especially dialysis patients who are candidates for kidney transplantation should be screened, evaluated and if necessary treated for hepatitis C and B before entering the waiting list.^{2,3} Some factors are especially related to these high prevalence rates of HBV and HCV infections such as blood transfusions and duration of dialysis. Nosocomial routes of transmission including the use of contaminated equipment and patient-to-patient exposure are considered to be the risk factors. Several prophylactic measures have been suggested to avoid infection by HBV and HCV in the HD patient. Strict adherence to universal precautions along with isolation of HBV and HCV infected dialysis patients might help to control disease spread in Hemodialysis units.⁴

The inflicted individuals have to undergo maintenance peritoneal dialysis, hemodialysis, or renal transplantation. All these are associated with risks of blood-borne infections being transmitted, among other complications. Being on dialysis means repetitive exposure to potentially infected instruments and hence increased risk of infections.⁵

In a study, 10.2% (124 out of 1220) patients were HBV DNA detected.⁶ Another study reported that the overall prevalence of hepatitis B virus was found to be 3.8 % (33 cases).⁷ One local study was done on 60 cases only in which they compared HBV positivity according to no

of hemodialysis session. They reported that among 28 cases with dialysis <50 times, 2 patients (7.14%) were HBV DNA detected and 26 patients (92.85%) were HBV DNA not detected. A total of 22 patients with dialysis 50-100 times 4 patients (18.18%) were HBV DNA detected and 18 patients (81.81%) were HBV DNA not detected. Out of 6 patients 100-200 times dialyzed patients no patient (0%) was HBV DNA detected so 6 patients (100%) were HBV DNA not detected. Similarly, out of 4 patients >200 times dialyzed patients, 1 patient (25%) was HBV DNA detected and 3 patients(75%) were HBV DNA not detected.⁸

MATERIALS & METHODS:

This descriptive cross-sectional study was conducted in Lahore General Hospital, Lahore, Pakistan started from April 2019 and completed in August 2019. Sample size of 270 cases is estimated using percentage of >200 times dialyzed patients as 6.6%.⁸ The sample size is calculated using 95% confidence level and 3% margin of error.

SAMPLE SELECTION:**a. Inclusion Criteria:**

1. Age 18-80 years
2. Either gender
3. CKD patients undergoing maintenance hemodialysis for at least 3 months (as per-operational definition).

b. Exclusion Criteria:

1. Patients who received anti-viral therapy during last 6 month
2. Patients with other known causes of raised liver enzymes including
 - Alcohol,
 - Autoimmune hepatitis,
 - hemochromatosis, primary biliary cirrhosis, primary sclerosing cholangitis,
 - Usage of drugs (pyrazinamide, rifampicin, paracetamol,
 - Nonalcoholicsteato-hepatitis (NASH),
 - Wilson's disease,
 - Alpha I antitrypsin deficiency, celiac disease,
 - Recent surgery of hepatobiliary tract, and obstructed biliary tract.

DATA COLLECTION PROCEDURE:

The study was started after taking approval of synopsis from CPSP, prior informed consent was taken from 270 cases meeting inclusion criteria before starting the study. All cases were taken from department of medicine LGH. All patients were asked about their basic demographic information like age, gender and contact details. All cases were asked about their number of hemodialysis and recorded as per-

operational definition. Blood samples were taken from the arterial line immediately after insertion of the needle (before dialysis was started). A real time PCR apparatus HBV RG PCR kit from QIAGEN (detection limit=100 copies/ml) was used for the detection of HBV DNA. HBV was diagnosed as per operational definition. All data was collected by researcher himself on attached perform.

STATISTICAL ANALYSIS:

All data was entered and analyzed using SPSS version 22. Mean \pm S.D were applied for quantitative data like age, duration of hemodialysis and number of hemodialysis. Frequency and percentage were applied for categorical data like gender, number of hemodialysis sessions and HBV. HBV (yes or no) was compared in various number of hemodialysis session (< 50 , 50-100, 100-200 and > 200) using chi-square test. By keeping in mind different effect modifiers like age, gender, socioeconomic status and duration of dialysis data was stratified for these confounders. Post stratified chi-square test was applied taking p-value ≤ 0.05 significant.

RESULTS

Age range in this study was from 18 to 80 years with mean age of 47.66 ± 10.52 years. Majority of the patients 189 (70.0%) were between 18 to 50 years of age as shown in Table I.

Out of 270 patients, 150 (55.56%) were male and 120 (44.44%) were females with male to

female ratio 1.25:1 as shown in Figure V. Distribution of patients according to socioeconomic status is shown in Figure VI. Mean duration of hemodialysis in our study was 5.45 ± 2.16 years as shown in Table II.

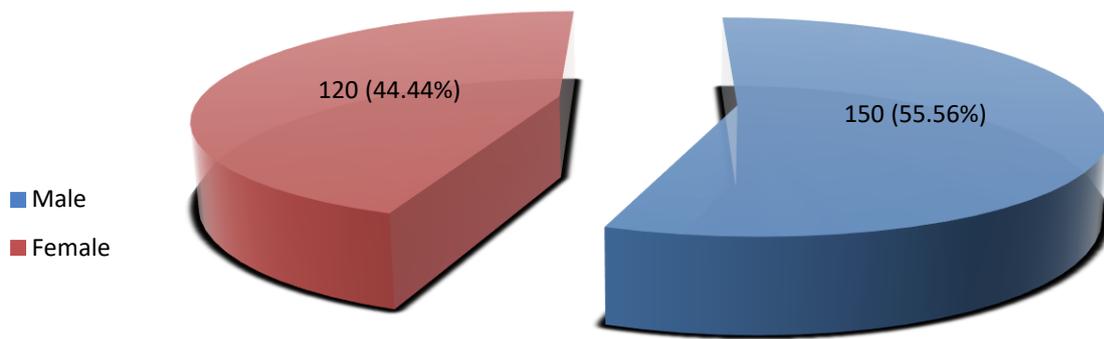
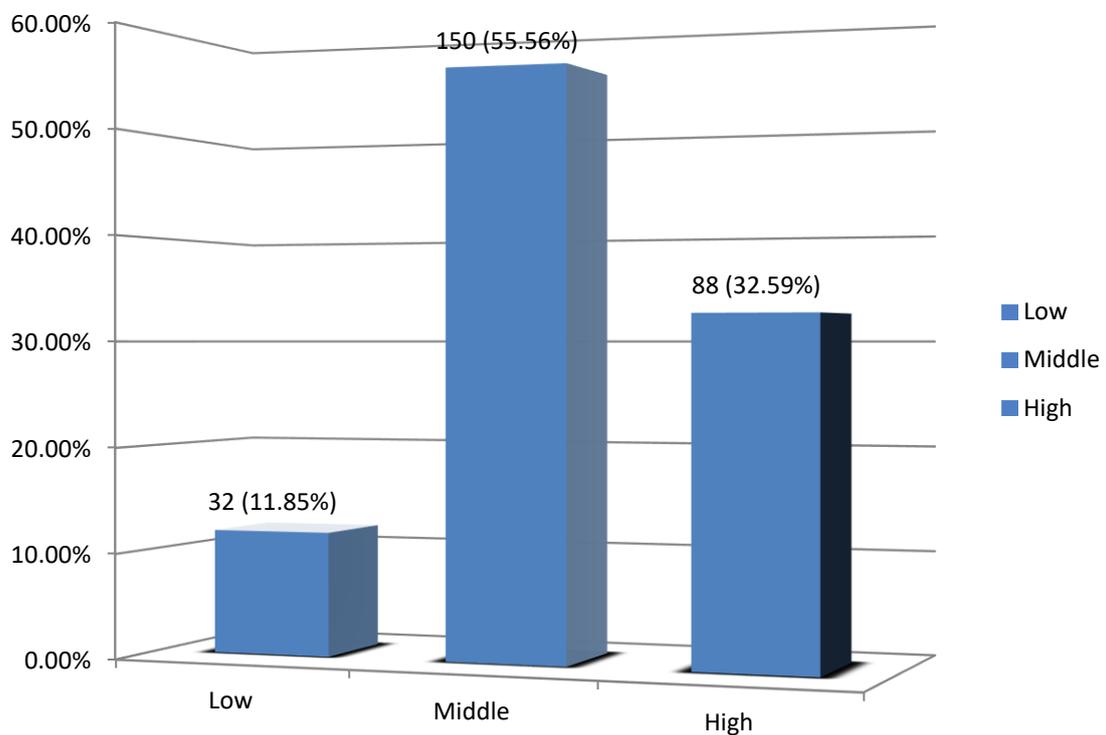
In our study, frequency of patients with various number of sessions of hemodialysis in patients of CKD on maintenance hemodialysis is found as follows; <50 in 87 (32.22%), 50-100 in 100 (37.04%), 100-200 in 69 (25.56%) and >200 in 14 (5.19%) patients (Table III). Mean number of sessions of hemodialysis in patients of CKD on maintenance hemodialysis 82.66 ± 50.12 . Frequency of hepatitis B was found 15 (5.56%) patients of CKD on maintenance hemodialysis (Figure VII). Among 87 cases with dialysis <50 times, 02 patients (3.45%) were HBV DNA detected. A total of 100 patients with dialysis 50-100 times 6 patients (6.0%) were HBV DNA detected. Out of 69 patients 100-200 times dialyzed patients 05 patients (7.25%) were HBV DNA detected. Similarly, out of 17 patients >200 times dialyzed patients, 1 patient (5.88%) was HBV DNA detected as shown in Table IV with p-value of 0.749

Stratification of hepatitis B with respect to age groups and gender is shown in Table V & VI respectively. Table VII & VIII have shown the stratification of hepatitis B with respect to duration of hemodialysis and socioeconomic status respectively.

Table-I: Distribution of patients according to Age (n=270).

Age (in years)	No. of Patients	%age
18-50	189	70.0
51-80	81	30.0
Total	270	100.0

➤ Mean \pm SD = 47.66 ± 10.52 years

Figure 1: Distribution of patients according to gender (n=270).**Figure II: Distribution of patients according to socioeconomic status (n=270)****Table-II: Distribution of patients according to duration of hemodialysis (n=270).**

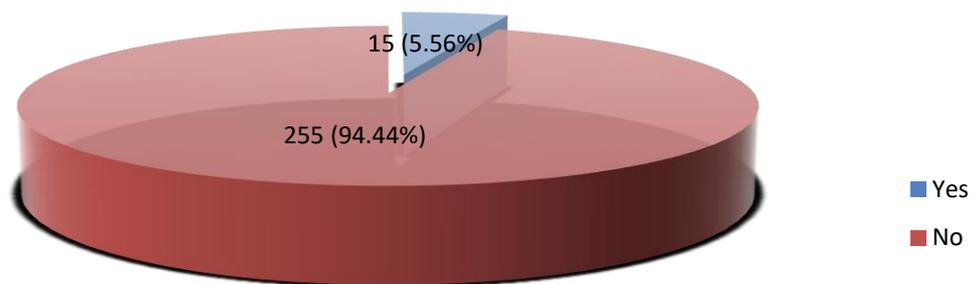
Duration of hemodialysis (in years)	No. of Patients	% age
<5 years	180	66.67
>5 years	90	33.33

➤ Mean \pm SD = 5.45 \pm 2.16 years

Table-III: Distribution of patients according to various number of sessions of hemodialysis (n=72).

Number of sessions of hemodialysis	No. of Patients	%age
<50	87	32.22
50-100	100	37.04
100-200	69	25.56
>200	14	5.19

- Mean \pm SD = 82.66 \pm 50.12

Figure III: Frequency of hepatitis B in patients of CKD on maintenance hemodialysis (n=270).**Table IV: Stratification of hepatitis B with respect to various number of sessions of hemodialysis.**

Number of sessions	Hepatitis B		p-value
	Yes	No	
<50	03	84	0.749
50-100	06	94	
100-200	05	64	
>200	01	13	

Table V: Stratification of hepatitis B with respect to age groups.

Age (years)	Hepatitis B		p-value
	Yes	No	
18-50	13	176	0.147
51-80	02	79	

Table VI: Stratification of hepatitis B with respect to gender.

Gender	Hepatitis B		p-value
	Yes	No	
Male	07	143	0.476
Female	08	112	

Table VII: Stratification of hepatitis B with respect to duration of hemodialysis.

Duration (years)	Hepatitis B		p-value
	Yes	No	
<5 years	09	171	0.573
>5 years	06	84	

Table VIII: Stratification of hepatitis B with respect to socioeconomic status.

Socioeconomic status	Hepatitis B		p-value
	Yes	No	
Low	02	30	0.977
Middle	08	142	
High	05	83	

DISCUSSION:

Hemodialysis is routinely used as renal replacement therapy for end stage renal disease (ESRD) patients.⁹ In 2012, 2.1 million patients worldwide were estimated to require hemodialysis and this number is expected to increase by 7% annually.¹⁰ Chronic hemodialysis patients are at increased risk for both HCV and HBV infections associated with contaminated blood and blood product transfusion and exposure to contaminated hemodialysis equipment during treatment.¹¹⁻¹⁴ Like the community, chronic hemodialysis patients may also acquire HBV and HCV through other at-risk activities, such as unprotected sexual contact and injecting drug use.¹⁵⁻¹⁶ Several infection prevention strategies that are effective in reducing the acquisition of blood borne virus by patients in high resourced healthcare settings includes erythropoiesis-stimulating agents which has reduced the need of blood transfusion, HBV vaccination and the adherence by hemodialysis services to specific hemodialysis infection control guidelines.¹⁷

I have conducted this study to

determine the frequency of hepatitis B in patients of chronic kidney disease on maintenance hemodialysis and its relationship with number of hemodialysis sessions. Age range in this study was from 18 to 80 years with mean age of 47.66 ± 10.52 years. Majority of the patients 189 (70.0%) were between 18 to 50 years of age. Out of 270 patients, 150 (55.56%) were male and 120 (44.44%) were females with male to female ratio 1.25:1. In our study, frequency of patients with various number of sessions of hemodialysis in patients of CKD on maintenance hemodialysis is found as follows; <50 in 87 (32.22%), 50-100 in 100 (37.04%), 100-200 in 69 (25.56%) and >200 in 14 (5.19%) patients. Mean number of sessions of hemodialysis in patients of CKD on maintenance hemodialysis 82.66 ± 50.12 . Frequency of hepatitis B was found 15 (5.56%) patients of CKD on maintenance hemodialysis. Among 87 cases with dialysis <50 times, 02 patients (3.45%) were HbsAg positive. A total of 100 patients with dialysis 50-100 times 6 patients (6.0%) were HBV DNA detected. Out of 69 patients 100-200 times dialysed patients

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In a study, 10.2% (124 out of 1220) patients were HBV DNA detected.⁶ Another study reported that the overall prevalence of hepatitis B virus was found to be 3.8 % (33 cases).⁷ One local study was done on 60 cases only in which they compared HBV positivity according to no of hemodialysis session. They reported that among 28 cases with dialysis <50 times, 2 patients (7.14%) were HBV DNA detected and 26 patients (92.85%) were HBV DNA not detected. A total of 22 patients with dialysis 50-100 times 4 patients (18.18%) were HBV DNA detected and 18 patients (81.81%) were HBV DNA not detected. Out of 6 patients 100-200 times dialysed patients no patient (0%) was HBV DNA detected so 6 patients (100%) were HBV DNA not detected. Similarly, out of 4 patients >200 times dialysed patients, 1 patient (25%) was HBV DNA detected and 3 patients(75%) were HBV DNA not detected.¹⁸

Approximately 2 billion people worldwide have evidence of past or present infection with HBV, and it is estimated that 248 million individuals are chronic carriers [i.e., positive for hepatitis B surface antigen (HBsAg)].¹⁹ Prevalence of HBsAg is reported to be 3.6%; however, it varies depending upon the geographic area. Roughly 600,000 die annually from HBV-related liver disease.²⁰ HBsAg positivity rates in dialysis patients, although significantly decreased over the several years, correlate with endemicity in the general population with 1% in US²¹ through 1.3–14.6% in Asian Pacific countries.²²

In 2017, Malyszko J et al conducted a study on 300 potential kidney transplant recipients from 26 dialysis centers in Poland, representing 9.7% of all dialysis patients in these units.²³ The author found that hepatitis B virus (HBV) and HCV taken together were more prevalent in patients on the inactive waiting list compared to those on the active list (3.0 vs. 1.5%, $p < 0.05$). The author also looked at the prevalence of HBV and HCV, as well as that of anti-HBc antibodies, in patients from Fresenius Medical Care dialysis units (n = 5890, representing 1/3 of the whole hemodialysis population in Poland). The author then compared the results with similar data from 2007 and with data from the transplantation waiting list in 2017. On the waiting list, HBs+/HBV–DNA+ were found in 0.5%, HBs+/HBV–DNA– in 0.5%, anti-HCV–/HCV–RNA+ in 0.2%, and anti-HBc in

21.1% of the patients. In 2007, anti-HBc was not tested. According to the results, the prevalence of HCV in Polish dialysis and waitlisted populations is comparable to that in the general population worldwide and much lower than that in the US.²⁴ This could be due to the very strict infection control policy in our dialysis units, including the use of separate machines and rooms for HBV and HCV positive patients, as well for patients with anti-HBc antibodies. It also appears that, thanks to vaccination, the prevalence of HBV has declined. In our population, prevalence of HBV infection was similar to that of US²⁵, Malaysia and Japan, but much lower than in China, Thailand and Korea.²⁶

In Arab countries, the prevalence of chronic HBV among Hemodialysis patients ranged from 2.0 % in Morocco to 11.8 % in Bahrain.²⁷⁻²⁹ Moreover, the prevalence of HCV antibodies among HD patients has been reported to range from 27 % in Lebanon to 48.9 % in Syria.³⁰ In Jordan, the prevalence of HBV in seven hospitals of the Royal Medical Services was found to be 5.9 % out of the 427 studied subjects.³¹ In Casablanca, Morocco a high HCV prevalence (76 %; N = 186) was reported compared to relatively small HBV prevalence (2 %; N = 186) among chronic hemodialysis patients in the university hospital.³² In Egypt however, a cross-sectional study was conducted on 2977 individuals. The study determined the prevalence of anti-HCV and HBV surface antigen seropositivity in Damietta Governorate, Egypt. Only 1.1 % were infected with HBV and 9.3 % with HCV.³³ Regarding other parts of the world, in India for example, the prevalence of HBV and HCV were found to be 5.5 and 10.9 %, respectively after starting the HD.³⁴ Moreover, in spite of the reduction in HBV spread within dialysis centers, some isolated outbreaks of HBV infection continue to be reported among HD patients in developed countries.³⁵

Literature review from different articles showed some relation in HBV infection and variables such as frequency of dialysis in week, total number of dialysis and type of dialysis (HD/ PD). Although these variables are contributing factors toward HBV infection, but our study shows there is no significant association between HCV/HBV infection and our variables. Prophylactic vaccine against HBV has already been developed which can decrease its incidence. Comparatively, low rate of HBsAg positivity is evidence for effectiveness of HBV vaccine. Although, HBV infection is a very serious public health problem

with an estimated 2 billion individuals infected worldwide and 350 million with chronic HBV infection.³⁶

CONCLUSION:

This study concluded that frequency of hepatitis B was found 5.56% in patients of CKD on maintenance hemodialysis with no significant difference in various number of sessions of hemodialysis. So, we recommend that of strict infection prevention measures should be implemented in these particular patients in order to reduce the morbidity of these particular patients.

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