

Frequency of Occult Hepatitis B in Hemodialysis Patients

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ABSTRACT

Objective: To detect the frequency of occult hepatitis B among hemodialysis patients of Shaikh Zayed Hospital, Lahore.

Methodology: It was a cross-sectional descriptive study. Two hundred HBsAg negative hemodialysis patients were included in the study. Consecutive sampling technique was used. The blood samples of hemodialysis patients were taken from Shaikh Zayed Hospital, Lahore. Hepatitis B surface antigen (HBsAg) was performed by ELISA kit. The real-time polymerase chain reaction (PCR) was performed to detect HBV DNA in serum samples of 200 HBsAg negative hemodialysis patients. The data was analyzed by using SPSS version 21.

Results: The mean age of the study population was 47.05 ± 14.33 years. One twenty one (60.5%) patients were males and 79 (39.5%) were females. The mean duration of hemodialysis was 48.21 ± 42.21 months. In our study, 96.5% (193/200) of the patients were vaccinated and 3.5% (7/200) were unvaccinated. The frequency of occult hepatitis B was zero.

Conclusion: The frequency of occult hepatitis B was zero in hemodialysis patients. As most of the patients were vaccinated, it was concluded from our study that the prevalence of occult hepatitis B is low in vaccinated hemodialysis patients.

Keywords: Occult hepatitis B. Hemodialysis patients. HBsAg. HBV DNA.

INTRODUCTION

Occult hepatitis B (OHB) is a condition in which hepatitis B virus DNA is present in the liver and serum of hepatitis B surface antigen (HBsAg) negative individuals. The viral DNA level in the serum is low, usually less than 104 copies/ml.¹ It can be transmitted through hemodialysis, organ transplantation and blood transfusion.^{2,3} Unidentified occult hepatitis B in hemodialysis patients is a potential source of infection for other patients. These patients are highly susceptible to acquire hepatitis B especially in setups where the recommended infection control measures are not strictly followed.¹

Occult hepatitis B can develop into active hepatitis B infection by viral replication as a result of immunological disorders or immunosuppressive therapies.⁴ It can progress to cirrhosis and even hepatocellular carcinoma.^{2,3} Hepatitis B virus DNA detection in liver biopsy specimen is the most reliable method to diagnose occult hepatitis B. However, it is contraindicated in patients of hemodialysis (HD) so the diagnosis relies on HBV DNA detection in the serum sample.^{5,6}

The frequency of occult hepatitis B depends on endemicity of hepatitis B in that area and sensitivity of

the HBsAg and HBV DNA kits.⁷ The detection rate of occult hepatitis in hemodialysis patients was 3.7% in North America,⁸ 4.9% in India,⁹ 0 to 26.6% in Italy^{10,3} and 2.7% to 12.4% in Turkey.^{11,12}

Hepatitis B is common in Pakistan. There is a high risk to acquire and transmit HBV infection among HD patients by various means. The hepatitis B prevalence in hemodialysis patients was 10.2% and 12.4% according to studies conducted in Karachi and Islamabad respectively^{13,14}, whereas in normal population, HBsAg positivity was 2.5%.¹⁵ In all these studies, patients were tested for HBsAg but polymerase chain reaction (PCR) was not performed to detect HBV DNA. This study was planned to detect HBV DNA by PCR in the serum samples of hemodialysis patients who were screened negative for HBsAg. A higher frequency of occult hepatitis B was expected in these patients. These patients, as being previously undiagnosed, are a potential source of infection. Diagnosing these patients will help us in implementing better protective measures in hemodialysis patients in order to reduce its further spread.

METHODOLOGY

It was a cross-sectional descriptive study. Two hundred HBsAg negative hemodialysis patients were included in the study. Consecutive sampling technique was used. Informed consent was obtained from the patients. Personal history and other required information was documented on a Proforma sheet for each patient. The research study was approved by the Institutional Review Board (IRB) of Postgraduate Medical Institute, Shaikh Zayed Hospital, Lahore. The blood samples of hemodialysis patients were taken from Shaikh Zayed

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Hospital, Lahore. The samples were centrifuged at 5000 rpm for 5 minutes and serum was separated. HBsAg was performed by ELISA kit manufactured by CTK Biotech diagnostics. The serum samples of 200 HBsAg negative patients were included in the study. Polymerase chain reaction was performed in serum samples to diagnose occult hepatitis B by Sustaaq USA kit.

STATISTICAL ANALYSIS

The data was analyzed by using the statistical package of social sciences (SPSS) version 21. Age and duration of hemodialysis were described by using mean \pm SD. Gender, cause of ESRD, vaccination status of patients and PCR results were presented by using frequency and percentages. A p-value < 0.05 was considered as statistically significant.

RESULTS

The mean age of hemodialysis patients was 47.05 ± 14.33 years. One twenty one (60.5%) patients were males and 79 (39.5%) were females. The age distribution of the patients is shown in figure 1.

The mean duration of hemodialysis was 48.21 ± 42.21 months. The minimum duration of hemodialysis was 3 months and the maximum duration was 264 months (22 years). The common causes of the end-stage renal disease was hypertension (HTN) accounting for 42% of the cases followed by both HTN and diabetes mellitus (DM) in 27% of the patients. Diabetes mellitus alone was the cause of ESRD in 6.5% cases. Other causes are glomerulonephritis, nephrolithiasis/obstructive nephropathy, nephritic syndrome, hydronephrosis, polycystic kidney disease and congenital one kidney. The cause was unknown in about 11.5% of the patients. In our study, 96.5% (193/200) of the patients were

vaccinated and 3.5% (7/200) were unvaccinated. The frequency of occult hepatitis B was zero. The 4 quantitative standards, negative template control, a known hepatitis B positive serum sample and 200 study samples were run on the Rotor-Gene instrument. HBV DNA was not detected in any study sample.

DISCUSSION

The frequency of occult hepatitis B ranges from 0 to 58% worldwide depending on the endemicity of hepatitis B in that region.¹⁶ It not only differs from country to country but also among different regions of the same country. In a study conducted in Italy, the prevalence of occult hepatitis B was 26.6% whereas in another study the prevalence of occult hepatitis B was 0 in Italy. It may be attributed to the difference in prevalence of hepatitis B in these areas.^{10,3}

Our results showed that the frequency of occult hepatitis B was zero in hemodialysis patients. Similar results were found in other studies. The prevalence of occult hepatitis B in hemodialysis patients was 1.25% in Turkey (Ankara). Eighty hemodialysis patients with negative HBsAg were enrolled. The serum sample of only 1 patient was positive for HBV DNA.¹⁶ In another study carried out in Turkey (Diyarbakir), the prevalence of occult hepatitis B was 0. Out of 50 HBsAg negative hemodialysis patients, HBV DNA was not detected in any patient.¹⁷ In contrast to our study, the prevalence of occult hepatitis B was high in hemodialysis patients in other studies. The prevalence of occult hepatitis B was 58% in Spain and 20.4% in another study in Greece.⁸

Occult hepatitis B is much more common in unvaccinated hemodialysis patients.⁵ In our study, 96.5% (193/200) of the patients were vaccinated and 3.5% (7/200) were unvaccinated. In a study by Ersoy in Turkey, 73.75% (59/80) patients were vaccinated and

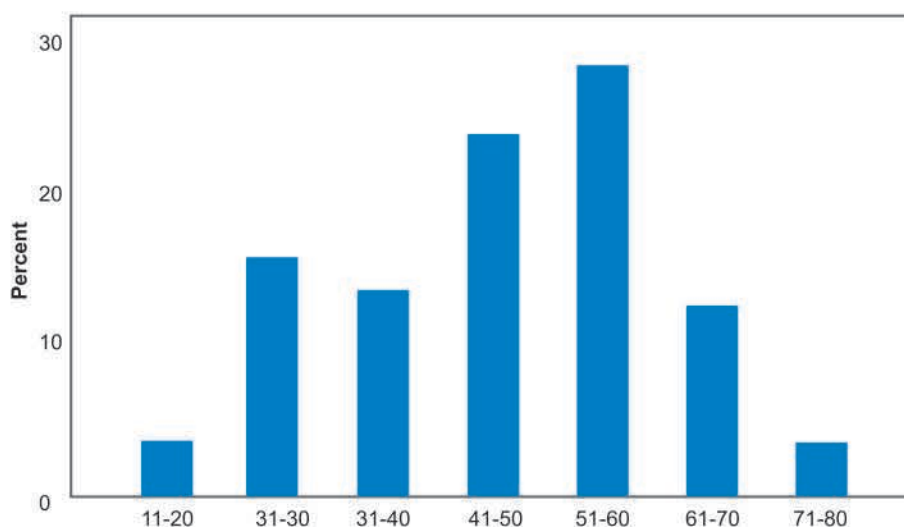


Figure 1: Age distribution of the study subjects.

26.25% (21/80) were unvaccinated.¹⁶ According to a study in Spain, the prevalence of OHD was found to be 58%. In this study, 33 HD patients and 24 dialysis staff members were included. All of the study participants were HBsAg negative. Only 3 HD patients and 16 staff members were vaccinated whereas 8 staff members had a history of previous HBV infection. HBV DNA was present in 19 (58%) HD patients and 8 staff members (who had past HBV infection). The reason behind this higher prevalence of occult hepatitis B may rely on the enrollment of high risk participants in the study (those with a history of previous hepatitis B or who were anti-HBc positive). Secondly, vaccination decreases the rate of transmission of occult hepatitis B. In this study, only 3 HD patients were vaccinated.⁸

The type of sample used for PCR also affects the detection of occult hepatitis B. The detection rate is greater in peripheral blood mononuclear cells (PBMCs) as compared to the serum sample. In our study, serum samples were used for detection of HBV DNA. In a study by Oesterreicher et al. PCR was performed in both the serum and PBMCs of 67 HBsAg hemodialysis patients. Six patients (8.9%) had HBV DNA in their PMBCs whereas none of them had detectable HBV DNA in their serum.⁵

The level of viremia varies in occult hepatitis B and can be a factor altering the frequency of occult hepatitis B. According to a study in Austria, PCR was done on 82 serum samples and 16 liver specimens. These patients were negative for HBsAg and had chronic hepatitis C. Hepatitis B virus DNA was present in 22% serum samples and 19% liver specimens. The serum samples were again collected from these patients and HBV DNA was analyzed. The results found were inconsistent. The previously positive HBV DNA samples showed negative results and vice versa. These results suggest that the level of viremia fluctuates during the disease.⁵

The rate of HBV DNA detection is also affected by the sensitivity of the assays used. In a study carried out in Korea, 98 HD patients were included. Four (4.1%) patients had positive HBsAg and they were excluded. The HBsAg negative patients were tested for HBV DNA by using two different techniques of PCR. HBV DNA was detected in 3 (3.2%) patients by Cobas Amplicor HBV monitor test and 1 (1.1%) patient by Taqman real-time PCR kit.¹⁸

CONCLUSION

The frequency of occult hepatitis B was zero in hemodialysis patients. As most of the patients were vaccinated, it was concluded from our study that the prevalence of occult hepatitis B is low in vaccinated hemodialysis patients. Occult hepatitis B is transmissible among HD patients but we do not

recommend routine screening of HD patients for HBV DNA.

LIMITATIONS OF THE STUDY

- Our study population included patients from a single hemodialysis unit of Shaikh Zayed Hospital. So, our results cannot predict the frequency of occult hepatitis B in other hemodialysis units of the country.

- HBV DNA testing was done on serum samples in contrast to peripheral blood mononuclear cells and liver. This may have underestimated the true frequency of occult hepatitis B.

RECOMMENDATIONS

- The study participants should be enrolled from multiple hemodialysis units.

- The peripheral blood mononuclear cells and liver specimens (if possible) should be analyzed for detecting HBV DNA along with the serum samples.

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