

Renal Data from Asia - Africa

Prevalence and Risk Factors of Hepatitis B Infection among Hemodialysis Patients in Tabriz: A Multicenter Report

Jalal Etemadi¹, Mohammad Hossein Somi², Mohammad Reza Ardalan¹, Seyed Sadradin Rasi Hashemi¹, Gilda Ghazi Soltani³, Mohammadali Mohajel Shoja⁴

¹Department of Nephrology, Dialysis and Transplantation, ²Liver and Gastrointestinal Disease Research Center, ³Faculty of Medicine, ⁴Tuberculosis and Lung Disease Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

ABSTRACT. Hepatitis B virus (HBV) infection is an important issue in hemodialysis. Risk factors and local prevalence varies between different regions. The current study was undertaken to determine the prevalence of HBV infection and its associated risk factors among hemodialysis patients from five hemodialysis centers in Tabriz, a Northwestern Iranian city. Hepatitis B serologic markers were evaluated in chronic hemodialysis patients. Patients ($n = 412$) were divided into two groups: Group 1 – patients with positive hepatitis B surface antigen (HBsAg) and Group 2 – patients with negative HBsAg. The median age was 54.9 years (range, 13–90 years). Thirteen patients (3.2%) were found to be positive for HBsAg. Among the studied factors, the history of war injury was significantly associated with the risk of HBV infection ($P = 0.023$). In conclusion, our study shows that the risk of HBV infection among Tabrizian hemodialysis patients is a factor of dialysis-independent parameters.

Introduction

Hepatitis B virus (HBV) infection is a major problem in hemodialysis patients,^{1,2} but the prevalence varies between countries and between dialysis units within one country.² Previous studies have shown that factors such as number of blood transfusion,² dialysis duration more than two years,^{3,4} gender, blood transfu-

Correspondence:

Dr. Jalal Etemadi,
Department of Nephrology, Dialysis and
Transplantation, Tabriz University of
Medical Sciences, Tabriz, Iran
E-mail: jalaletemadi@yahoo.com

sion before 1993,⁵ age, history of renal transplantation, transient hemodialysis and nationality⁶ were linked with the rate of HBV infection among hemodialysis patients.

As distribution of the above-mentioned risk factors varies between different regions, it is important to determine the local prevalence and risk factors associated with HBV infection among hemodialysis patients in a given region. This information may be of particular importance in the local preventive planning.

Our study aimed to determine the prevalence of HBV infection and its associated risk factors among hemodialysis patients from five hemodialysis centers.

Table 1. Characteristics of Tabrizian hemodialysis patients according to hepatitis B surface antigen (HBsAg) status.

	Total		HBsAg(+)		HBsAg(-)	
	Frequency	N	Frequency	N	Frequency	N
Sex (F/M)	148/264	412	5/8	13	143/256	399
Marital state (married)	367	412	12	13	355	399
Family history of HBV infection	3	412	0	13	3	399
History of transfusion	296	412	9	13	287	399
Intravenous illicit drug use	1	412	0	13	1	399
Tattooing	12	412	0	13	12	399
History of surgery	219	412	9	13	210	399
History of war injury	8	412	2	13	6	399
HCV infection	58	411	0	13	58	398
History of suspicious sexual contact	1	411	0	13	1	399
History of DM	127	412	3	13	124	399
History of vaccination	268	412	7	13	261	399
History of renal transplantation	47	412	0	13	47	399
Vaccine response	81	200	0	7	81	193

Patients and Methods

In a cross-sectional study, hepatitis B serologic markers including hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs) and antibody to hepatitis B core antigen (anti-HBc IgG antibody) were evaluated in chronic hemodialysis patients from five dialysis units (Madani, Twenty-Nine Bahman, Artesh, Amir al-Momenin and Kodakan hospitals) in Tabriz, a Northwestern Iranian city. Patients older than 12 years who were on hemodialysis for more than 90 days were included. The patients were divided into two groups: Group 1 – patients with positive HBsAg ($n = 13$) and Group 2 – patients with negative HBsAg ($n = 399$).

The patients were routinely dialyzed with polysulfone hollow-fiber dialyzers two or three times each week in 4-h sessions using acetate or bicarbonate containing dialysate; dialyzers were not reused. According to manufacturers' instruction, hemodialysis machines were bleached and rinsed between dialysis sessions. HBsAg-positive patients were dialyzed in a separate, isolated room. Per routine plan, serum samples were collected every three to six months from our patients and tested for HBsAg, anti-HBs, anti-HBc and anti-hepatitis C virus. Isolated anti-HBc-positive patients tested for qualitative HBV DNA,

and if positive it would be tested for quantitative HBV DNA by polymerase chain reaction.

The following information was collected: age, sex, marital status, family history of HBV infection, history of previous transfusion, number of blood transfusion, duration of dialysis, intravenous illicit drug use, tattooing history, history of previous surgery, history of war injury, previous suspicious sexual contact, history of renal transplantation, etiology of renal failure, history of diabetes mellitus, history of vaccination against HBV, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, prothrombin time, albumin and total and direct bilirubin.

Statistical Analysis

Data are presented as means \pm SD or percentages. Statistical analysis was performed using SPSS version 13 using Fisher's exact test and Man-Whitney U test. P -values less than 0.05 were considered as statistically significant.

Results

A total of 412 patients (264 men and 148 women) from five hemodialysis centers were included in the study. The characteristics of patients are shown in Tables 1 and 2.

Thirteen (3.2%) patients were found to be po-

Table 2. Characteristics of Tabrizian hemodialysis patients according to hepatitis B surface antigen (HBsAg) status.

	Total		HBsAg(+)		HBsAg(-)	
	Mean \pm SD	N	Mean \pm SD	N	Mean \pm SD	N
Age	54.9 \pm 15.85	412	51.9 \pm 12.90	13	55.0 \pm 16.0	399
Number of blood transfusions	2.75 \pm 3.53	412	5.23 \pm 8.80	13	2.67 \pm 3.21	399
Duration of dialysis (months)	53.5 \pm 46.3	411	44.7 \pm 33.8	13	46.4 \pm 54.0	398
Aspartate aminotransferase	18.1 \pm 9.44	315	17.6 \pm 4.86	8	18.2 \pm 9.53	307
Alanine aminotransferase	18.7 \pm 12.94	315	18.4 \pm 7.11	8	18.7 \pm 13.1	307
Alkaline phosphatase	419 \pm 391	293	312 \pm 331	7	423 \pm 393	286
Prothrombin time	13.1 \pm 1.26	287	13.0 \pm 0.48	7	13.1 \pm 1.27	280
Albumin	4.11 \pm 0.60	288	4.58 \pm 0.45	7	4.10 \pm 0.60	281
Bilirubin total	0.71 \pm 0.78	284	0.76 \pm 0.33	7	0.71 \pm 0.79	277
Bilirubin direct	0.18 \pm 0.12	284	0.16 \pm 0.09	7	0.18 \pm 0.13	277

sitive for HBsAg (Table 3). The median age was 54.9 years (range, 13–90 years). The primary causes of ESRD were diabetic nephropathy in 115 (28.1%) patients, hypertension in 140 (34.2%), glomerulonephritis in 15 (3.7%), tubulointerstitial nephritis in 10 (2.4%), polycystic kidney disease in 33 (8.1%), hereditary nephritis in five (1.2%), urologic disorders in 21 (5.1%) and unknown etiology in 70 (17.1%). Fourteen (4.6%) patients had isolated anti-HBc antibody; HBV DNA was not detected in these patients.

The history of war injury was significantly associated with the risk of HBV infection among the patients ($P = 0.023$). No significant difference was detected between HBsAg-positive and HBsAg-negative patients in terms of age, sex, marital status, positive family history of HBV infection, history of previous transfusion, number of blood transfusion, duration of dialysis, intravenous illicit drug use, history of tattooing, previous surgery, previous suspicious sexual contact, renal transplantation, etiology of renal failure, diabetes mellitus and hepatitis B vaccination. There was a significant difference in the median levels of albumin between the two subgroups (4.7 versus 4.2 g/L, $P = 0.036$). The HBV seroconver-

sion rate after vaccination was 40.5%. There were no new cases of seroconversion to HBsAg positivity during hemodialysis among our patients.

Discussion

It is estimated that there are more than 350 million HBV carriers in the world.⁷ The prevalence of HBV carriers in the general population varies from less than 2% in low-prevalence areas to 8% in high-prevalence areas.⁸ The prevalence of positive HBsAg in Iran is 3.5%.⁹ The lack of significant association between the studied risk factors and HBV infection in our study except the risk of war injury (dialysis-independent risk factor) and absence of new seroconversion case to HBsAg positivity during hemodialysis as well as concordance of observed prevalence of HBV infection with the general population led us to propose that the risk of HBV infection among Tabrizian hemodialysis patients is a factor of dialysis-independent parameters.

In the present study, 14 (4.6%) of the patients were found to have isolated anti-HBc antibody. Yildirim et al recently investigated the rate of HBV-DNA positivity among 45 pa-

Table 3. Hepatitis B serology among Tabrizian hemodialysis patients according to hepatitis B surface antigen (HBsAg) status.

	Total (n = 412)		HBsAg(+) (n = 13)		HBsAg(-) (n = 399)	
	Frequency	N	Frequency	N	Frequency	N
Anti-HBs	109	308	0	13	109	295
Anti-HBc	68	401	10	13	58	388
Isolated anti-HBc	14	303	0	13	14	290

tients with only anti-HBc-positive tests and found that 24.4% of them had positive HBV-DNA titers.¹⁰ In another study, over 395 high-risk patients, including 289 on HD and 106 HIV-infected, HBV-DNA was detected in 12 of 40 patients who had isolated anti-HBc antibody.¹¹ Even though HBV DNA was not detected among Tabrizian hemodialysis patients who had isolated anti-HBc antibody, this may not diminish the significance of anti-HBc as the sole marker of HBV infection in hemodialysis patients. It may be prudent to employ more sensitive assays in isolated anti-HBc antibody-positive hemodialysis patients for reducing the potential risk of HBV transmission.

The response rate to HBV vaccine in hemodialysis patients ranges from 50% to 80% in the different studies.¹²⁻¹⁴ The response rate after vaccination in the present study was 40.5%. Factors such as older age at the time of vaccination,¹⁵ poor nutrition,¹⁶ infection with hepatitis C virus,¹⁷ presence of certain HLA haplotypes,^{18,19} diabetes mellitus, lower urea clearance by dialysis (KT/V) and lower ratio of lean to total body mass²⁰ are associated with a low vaccine response rate among hemodialysis patients. The lower response rate in our study may mandate need for use of different vaccination protocol or adjuvant therapy.

There was significant difference in the median levels of albumin between the two subgroups (4.7 versus 4.2 g/L, $P = 0.036$) in our study, but this finding may not have a clinical significance.

In conclusion, our study shows that the risk of HBV infection among Tabrizian hemodialysis patients is a factor of dialysis-independent parameters.

References

1. Cendoroglo Neto M, Draibe SA, et al. Incidence of and risk factors for hepatitis B virus and hepatitis C virus infection among haemodialysis and CAPD patients: evidence for environmental transmission. *Nephrol Dial Transplant* 1995;10:240-6.
2. Cao YL, Wang SX, Zhu ZM. Hepatitis B viral infection in maintenance hemodialysis patients: A three year follow-up. *World J Gastroenterol* 2007;13(45):6037-40.
3. Munther AH, Yousef AA. Hepatitis B infection among patients receiving chronic hemodialysis at the Royal Medical Services in Jordan. *Saudi J Kidney Dis Transpl* 2008;19(2):260-7.
4. Albertoni F, Battilomo A, DiNardo V, et al. Evaluation of a region-wide hepatitis B vaccination program in dialysis patients: Experience in an Italian region. *Nephron* 1991;58:180-3.
5. Ferreira RC, Teles SA, Dias MA, et al. Hepatitis B virus infection profile in hemodialysis patients in central Brazil: prevalence, risk factors, and genotypes. *Mem Inst Oswaldo Cruz, Rio de Janeiro* 2006;101(6):689-92.
6. Mahdavi-mazdeh M, Hosseini-Moghaddam SM, Alavian SM, Yahyazadeh H. Hepatitis B Infection in hemodialysis patients in Tehran province, Iran. *Hepatitis Monthly* 2009;9(3):206-10.
7. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepa* 2004;11:97-107.
8. Lok AS, McMahon BJ. Chronic hepatitis B. *Hepatology* 2007;45:507-39.
9. Farzadegan H, Shamszad M, Noori-Arya K. Epidemiology of viral hepatitis among Iranian population-a viral marker study. *Ann Acad Med Singapore* 1980;9(2):144-8.
10. Yildirim M, Yavuz MT, Ozdemir D, Behçet M, Sencan I. High rate of hepatitis B virus DNA positivity in anti-HBc only-positive patients. *Mikrobiyol Bul* 2008;42(3):535-6. [Turkish]
11. Ramezani A, Mohraz M, Banifazl M, Eslamifard A, Aghakhani A. Significance of hepatitis B core antibody as the only marker of hepatitis B virus infection in high risk patients. *Iranian Journal of Pathology* 2009;4(2):80-4.
12. Seaworth B, Drucker J, Starling J, Drucker R, Stevens C, Hamilton J. Hepatitis B vaccines in patients with chronic renal failure before dialysis. *J Infect Dis* 1988;157(2):332-7.
13. Stevens CE, Alter HJ, Taylor PE, Zang EA, Harley EJ, Szmuness W. Hepatitis B vaccine in patients receiving hemodialysis: Immunogenicity and efficacy. *N Engl J Med* 1984;311(8):496-501.
14. Bel'eed K, Wright M, Eadington D, Farr M, Sellars L. Vaccination against hepatitis B infection in patients with end stage renal disease. *Postgrad Med J* 2002;78(923):538-40.

15. Jadoul M, Goubau P. Is anti-hepatitis B virus (HBV) immunization successful in elderly hemodialysis (HD) patients? *Clin Nephrol* 2002;58(4):301-4.
16. Fernandez E, Betriu MA, Gomez R, Montoliu J. Response to the hepatitis B virus vaccine in haemodialysis patients: Influence of malnutrition and its importance as a risk factor for morbidity and mortality. *Nephrol Dial Transplant* 1996;11(8):1559-63.
17. Navarro JF, Teruel JL, Mateos M, Ortuno J. Hepatitis C virus infection decreases the effective antibody response to hepatitis B vaccine in hemodialysis patients. *Clin Nephrol* 1994;41(2):113-6.
18. McDermott AB, Zuckerman JN, Sabin CA, Marsh SG, Madrigal JA. Contribution of human leukocyte antigens to the antibody response to hepatitis B vaccination. *Tissue Antigens* 1997;50(1):8-14.
19. Caillat-Zucman S, Gimenez JJ, Albouze G, et al. HLA genetic heterogeneity of hepatitis B vaccine response in hemodialyzed patients. *Kidney Int Suppl* 1993;41:S157-60.
20. Chin AI. Hepatitis B virus vaccine response in hemodialysis: baseline patient characteristics. *Hemodial Int* 2003;7(4):296-303.

