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ORIGINAL ARTICLE

Hepatitis B Infection in Hemodialysis Patients in Tehran Province, Iran

Mirta Mahdavimazdeh [1*], Seyed Mohammadmehdi Hosseini-Moghaddam [2], Seyed Moayed Alavian [3], Hooman Yahyazadeh [4]

[1] Department of Nephrology, Tehran University of Medical Sciences, Tehran, Iran
[2] Urology and Nephrology Research Center (UNRC), Shahid Beheshti University, M.C., Iran
[3] Baqiyatallah Research Center for Gastroenterology and Liver Disease (BRCGL), Baqiyatallah University of Medical Sciences, Tehran, Iran
[4] School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Background and Aims: **Hemodialysis (HD) patients seem to be at considerable risk of acquiring HBV infection. This study was carried out to determine the seroprevalence of hepatitis B virus (HBV) infection in hemodialysis patients living in the province of Tehran and to investigate the association between viral hepatitis B and the probable risk factors for HD patients.**

Methods: **From June to August 2005, this study was done on the entire HD population of the province of Tehran (2630 patients; 1505 males and 1125 females, mean age: 53.4 years). Social and demographic data, date of onset of HD, length of time receiving HD services, history of a kidney transplant, multiple sex partners, and other probable risk factors were evaluated. Blood samples were tested for liver enzyme levels as well as human immunodeficiency virus (HIV) 1, HIV 2, hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and hepatitis C antibody (anti-HCV).**

Results: **A total of 64 patients were HBsAg positive (2.4%). The male-to-female ratio was 45/19 for HBsAg-positive patients and 1462/1104 for the remaining patients ($P = 0.03$), respectively. Except for nationality ($P < 0.001$), previous kidney transplants ($P < 0.001$), age ($P < 0.001$), and transient HD ($P < 0.001$), no association was found between HBV infection and probable risk factors.**

Conclusions: **Common erythropoietin administration, blood testing for transfusion purposes, implementation of universal precaution in dialysis units as well as the use of dedicated machines for HBV-infected patients has led to a decreasing trend of HBV infection. Periodic surveillance of HBV infection among patients undergoing hemodialysis is strongly recommended.**

Keywords: **Hepatitis B Virus, Hemodialysis, Risk Factor**

Introduction

Because hepatitis B virus (HBV) is mainly transmitted via parenteral routes, hemodialysis (HD) patients seem to be at considerable risk of acquiring HBV infection. Despite control and preventive measures, viral hepatitis B still seems to be a major concern in medical centers with HD facilities. By adherence to hemodialysis-specific infection-control practices and to hepatitis B vaccination, HBV infection has been controlled in some dialysis centers [1, 2]. On the other hand, HBV infection remains a

**** Correspondence:***
Mitra Mahdavimazdeh, M.D.
Department of Nephrology UNRC, Tehran University of Medical Sciences, No. 101, 9th Boostan St., Pasdaran Ave., Tehran, Iran.

Tel: *+98 21 2256 7222*
Fax: *+98 21 2256 7282*

E-mail: *mmahdavi@sina.tums.ac.ir*

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considerable concern in some countries [3, 4]. HBV infection outbreaks still remain a major problem; specifically, when a failure in control of nosocomial infection occurs [5, 6]. In Iranian hemodialysis patients, the prevalence of positive hepatitis B surface antigen (HBsAg) in patients on HD decreased from 3.8% in 1999 to 2.6% in 2005 [7]. More than 20 years ago, a study reported a seroprevalence rate of hepatitis B surface antibody (anti-HBsAb) in 68% of HD patients [8]. The main objectives of this study were (a) to determine the seroprevalence of HBV infections in HD patients living in the province of Tehran, and (b) to investigate the association between viral hepatitis B and probable risk factors, such as episodes of blood transfusion and time spent on HD.

Materials and Methods

In December 2005, an observational study was performed on all HD patients (2630 patients; 1505 males and 1125 females) receiving services from 56 different units in the province of Tehran, which has 13.5 million inhabitants. The age of the studied population ranged from 6 to 90 years (average 53.4 years). A standardized questionnaire was used to collect sociodemographic data, date of onset of HD, length of time receiving HD services, history of a kidney transplant, multiple sex partners, and other probable risk factors. History of vaccination against hepatitis B was determined using patients' medical records.

Patients were dialyzed with two different types of dialyzers: cuprophane membrane and polysulfone membrane. Reprocessing of hemodialyzers for reuse is not practiced in Iran at all. Although use of dedicated HD machines is not routine for HD patients with hepatitis C, all HBsAg positive patients were put on separate machines [9]. Using personal protective equipment like gloves, masks, aprons, and protective glasses were mandatory for staff. According to the manufacturers' instructions, HD machines were bleached and rinsed between dialysis sessions. Subjects had specific dialysis stations assigned to them, but chairs and beds were still cleaned after each use. After identifying HBsAg positive patients prior to HD, each patient was assigned to his or her own machine to decrease the risk of spreading the infection.

Monthly blood samples were taken from all HD patients for assessment of serum levels of different elements in the blood prior to the HD session. All samples were tested for alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels by a colorimetric method. The patients were also screened for human immunodeficiency virus (HIV) 1 & 2, HBsAg, anti-HBsAb, and hepatitis C antibody (anti-HCV) by enzyme-linked immunosorbent assays (ELISA, Abbott Laboratories, US) every three months. ELISA generation III is the assay that is usually used to check for HCV antibody. For statistical analysis, prevalence rates and 95% confidence intervals (CI 95%) were calculated. Chi-square tests or Fisher's exact tests were performed to evaluate the distribution of variables and characteristics associated with hepatitis B infection. Statistical significance was assessed at the 0.05 probability level in all analyses.

Results

The mean age of patients in this study was 53.4 ± 17.06 years. Patients were on maintenance HD for 49.0 ± 17.9 months. A total of 2,376 patients (90.3%) received three dialysis sessions per week, while 236 (9%) received two sessions per week. Ninety-seven patients (3.7%) were of a nationality other than Iranian (mainly from Afghanistan). A total of 744 patients (28.3%) were illiterate. Three patients (0.1%) were HIV-infected. Sixty-four patients (2.4%) were HBsAg positive, and a protective level of anti-HBsAb (more than 10 mIU/ml) was present in 1,831 patients (69.6%). Eight HBsAg-positive patients (12.5%) were foreigners. In this study, 55% of patients were vaccinated against hepatitis B. Thirty percent of patients refused this treatment. The mean time on dialysis was 47.14± 45.37 months and 51.61 ± 59.15 months in HBsAg-positive and HBsAg-negative patients, respectively. Table 1 shows the characteristics of patients with hepatitis B.

Discussion

HD patients are vulnerable to infection with HBV and HCV because of a history of blood transfusion, frequent injections, partial immunosuppression, and history of a kidney transplant. Duration of HD treatment seems to be a considerable variable in controlling HBV infection in medical centers with HD facilities. This variable has been reported to be strictly correlated with seroprevalence of hepatitis B, demonstrating the significant risk of HBV nosocomial transmission [4, 10-12]. In addition, Ferriera *et al.* found that subjects on HD maintenance for more than 3 years had a 2.6-times-higher risk (95% CI: 1.7-4.0) of acquiring HBV infection compared to patients

Table 1. Characteristics of HBsAg-positive vs. HBsAg-negative patients.

Variables	HBsAg positive (n=64)	HBsAg negative (n=2566)	P value
Age (year, mean ± SD)	48.7 ± 15.8	53.5 ± 16.5	<0.001
Sex (M/F)	45/19	1441/1081	0.03
Marriage situation (single/married)	11/53	311/2255	0.2
Nationality (Iranian/foreigners)	56/8	2436/86	<0.001
Education (literate/illiterate)	41/23	1846/720	0.2
History of previous renal transplant (+/-)	7/57	919/1647	<0.001
Transient hemodialysis	4/60	30/2536	<0.001
Anti-HIV(+/-)	0/64	3/2563	0.7
Anti-HCV(+/-)	1/63	226/2340	0.4
Serum cholesterol level (mg/dl)	159.7 ± 45.8	161.6 ± 44.1	0.8
Serum triglyceride level (mg/dl)	158.7 (50-487)	170.1 (31-980)	0.5
History of cadaver/live donor for renal transplant	0/7	71/848	0.5
Age of patient at initiation of hemodialysis (years)	44.7 ± 17.1	49.1 ± 17.9	0.06
History of CAPD (+/-)	1/63	50/2516	0.8
Mean duration on hemodialysis (months)	47.14	51.6	0.5

who had undergone HD for less than 12 months [13]. Similarly, Hosseini-Moghaddam *et al.* have reported a significant association between duration of being on HD and HCV infection [14]. This association was not found to be significant for HBV infection in our study. Instead, infection was mainly due to implementation of special strategies (*e.g.,* universal vaccination of all neonates against HBV since 1993), which helps to control transmission according to the Iranian national guidelines for the prevention and control of viral hepatitis. The serologic status should be determined prior to dialysis for all patients who appear to require HD. In Iran, implementation of universal precautionary measures is mandatory in medical centers with HD facilities as a cornerstone for prevention of viral hepatitis B; moreover, machine dedication is a rule [7, 9]. Farzadegan *et al.* reported the prevalence of HBsAg and anti-HBsAb among high-risk groups in Iran in 1979. They found that anti-HBsAb was present in 68% of HD patients [8]. One year later in a study on hepatitis B among blood donors, Farzadegan *et al.* reported an incidence rate of 3.5% [15]. With these methods the prevalence of HBsAg positivity in HD patients decreased from 3.8% in 1999 to 2.6% in 2005 in the whole country [7].

Blood transfusion is another significant risk factor for hepatitis B in HD patients [4, 12]. Ferriera *et al.* pointed out that patients who received a blood transfusion before 1993 had a 2.3-times-greater risk (95% CI: 1.6.-3.3) of HBV positivity compared to those who were transfused later [13]. Screening of blood products for HBsAg and anti-HBc in Iranian blood banks since 1993 has been another successful strategy to reduce this risk. Additionally, the widespread use of recombinant erythropoietin for anemia treatment has decreased blood transfusion in HD patients drastically [7]. Although marital status was once a major factor affecting the frequency of hepatitis B infection in the general population in Islamic countries [16], our findings showed that this factor did not play a significant role in HBV infection among HD patients, possibly due to the high prevalence of sexual dysfunction attributable to the effects of uremia, neuropathy, depression and so forth. Moreover, Ghanaat *et al.* have reported a low level of HBV infection (approximately 14%) in Iran, even in cases with sexually transmitted diseases (STDs) [17]. Similarly, our study demonstrated that HCV as well as HIV infection were not contributing factors for the acquisition of HBV infection in HD cases living in Iran. A low frequency of HIV

infection in Iran may partly explain this finding, but a low level of association between HBV and HCV infection in these subjects seems to require further investigation. Our report demonstrated that physicians should not merely rely on AST or ALT levels to uncover viral hepatitis in cases receiving HD services. Kurcer *et al.* [18] have demonstrated a significant risk factor for HBV infection among illiterate subjects (OR: 2.1, 95% CI: 1.180-3.326). Ali *et al.* [16] reported that HBV infection as well as other STDs were more common among patients who were illiterate or only had a preparatory-school education than patients who had a high–school, university, or post-graduate education. Our findings demonstrated that illiteracy did not play a major role in acquiring HBV infection in patients on HD. It seems that in HD units there are some unavoidable policies regarding vaccination that could be missed by illiterate patients, but this did not seem to have a significant effect on infection.

Hung *et al.* showed that the acquisition of HBV infection by continuous ambulatory peritoneal dialysis (CAPD) patients is low and HBV infection in these subjects usually occurs before initiation of chronic peritoneal dialysis therapy in a region hyperendemic to HBV [19]. In our report, no association was found between the acquisition of HBV infection and CAPD. This might be due to the low level of risk in peritoneal dialysis compared to HD and the low numbers of peritoneal dialysis patients versus HD patients. Considering the pathogenicity of hepatitis D virus (HDV) in HBsAg-positive patients, one may assume that the disease burden of viral hepatitis B in HD cases may be partly attributed to HDV. Rezvan *et al.* [20] studied the seroprevalence of hepatitis D in HD patients in Iran from 1986 to 1988 [21]. Their report demonstrated that 2.0% of 50 anti-HBsAb-positive dialysis patients tested positive for HDV antibody (anti-HDV) (1 of 50), whereas the rate of anti-HDV positivity was 44.5% in HD patients positive for HBsAg (16 of 36). Our report did not focus on HDV in HBsAg-positive cases, but because of a lack of information on the frequency of HDV infection in HD cases with HBV infection living in Iran in recent years, further studies in this regard seem necessary.

Blood testing for transfusion purposes reduces the risk of HBV infection. In addition, common erythropoietin administration provided a considerable reduction of the number of transfusions necessary for treatment. All of the factors mentioned above seem to improve the health level in medical centers with HD facilities so that generally nowadays no significant increase is seen in the incidence of HBV infection with a longer duration of HD treatment. We strongly recommend a periodic surveillance of HBV infection among patients receiving medical services from centers with hemodialysis facilities.

Conclusions

Prevention and control of hepatitis B is quite important in hemodialysis units. It seems that vaccination should not be optional in dialysis centers and perhaps should be encouraged in the pre-end stage of renal disease. Given their considerable roles in limiting HBV transmission in HD units, an isolation policy for HBV-positive patients and universal precautionary measures in dialysis units should be under constant and close supervision.

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