Risk Factors and Seroprevalence of Hepatitis B, C, and D Virus in Hemodialysis Patients in Istanbul

İstanbul'daki Hemodiyaliz Hastalarında Hepatit B, C ve D Virüs Seroprevalansı ve Risk Faktörleri

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ABSTRACT

Introduction: Hemodialysis units pose a risk for transmission of hepatitis viruses. In this study, we aimed to detect the prevalence of hepatitis B virus (HBV), hepatitis C virus (HCV), and hepatitis D virus (HDV) in our hospital's hemodialysis unit and to determine the risk factors for transmission of hepatitis viruses.

Materials and Methods: In Haydarpaşa Numune Training and Research Hospital Hemodialysis Unit, hepatitis B surface antigen (HBsAg), hepatitis B core IgG antibody (anti-HBcIgG), hepatitis B surface antibody (anti-HBs), antibody to hepatitis C virus (anti-HCV), and anti-delta total were studied by enzyme-linked immunosorbent assay (ELISA) method in the serum samples of 50 hemodialysis patients. Risk factors for transmission of hepatitis virus were identified in hemodialysis patients. As a control group, 50 healthy individuals were included.

Result: In hemodialysis patients, HBsAg was determined as 6% and anti-HCV as 28%, whereas anti-HDV positivity was not detected. HBsAg, anti-HBcIgG, and anti-HBs frequencies did not show statistically significant differences between the two groups, while anti-HCV frequency was found to be significantly higher in hemodialysis patients ($p=0.001$). The mean age of

HBsAg-positive hemodialysis patients was found significantly lower than that of HBsAg-negative hemodialysis patients ($p=0.045$). Similarly, anti-HCV-positive hemodialysis patients had a statistically lower mean age compared to anti-HCV-negative hemodialysis patients ($p<0.004$). Increase in hemodialysis duration and amount of blood transfusion were shown statistically to not affect anti-HBcIgG positivity. Anti-HCV positivity was found statistically significantly higher in patients undergoing hemodialysis for more than 10 years ($p=0.003$).

Conclusion: In hemodialysis patients, transmission of hepatitis viruses will decrease with promotion of the use of erythropoietin instead of blood transfusion and implementation of alternative methods of dialysis.

Key words: Hemodialysis patients, hepatitis B, hepatitis C, seroprevalence, risk factors

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ÖZET

Giriş: Hemodiyaliz üniteleri, hepatit virüslerinin geçişi için risk oluşturmaktadır. Bu çalışmada, hastanemiz hemodiyaliz ünitesinde hepatit B, C ve D prevalansının saptanması ve hepatit virüslerinin geçişi için risk faktörlerinin belirlenmesi amaçlanmıştır.

Materyal ve Metod: Haydarpaşa Numune Eğitim ve Araştırma Hastanesi Hemodiyaliz Ünitesinde hemodiyalize giren 50 kişi, kontrol grubu olarak da 50 kişinin serum örneklerinde HBsAg, anti-HBcIgG, anti-HBs, anti-HCV ve anti-delta total ELISA yöntemiyle çalışılmıştır. Hemodiyaliz hastalarında hepatit virüslerinin geçişi için risk faktörleri belirlenmiştir.

Bulgular: Hemodiyaliz hastalarında HBsAg %6 ve anti-HCV %28 olarak belirlenmiş, anti-HDV pozitifliği saptanmamıştır. Her iki grup arasında HBsAg, anti-HBcIgG, anti-HBs sıklığı istatistiksel olarak farklılık göstermezken, hemodiyaliz hastalarında anti-HCV sıklığı istatistiksel olarak anlamlı bir şekilde yüksek bulunmuştur ($p=0.001$). HBsAg pozitif hemodiyaliz hastalarının ortalama yaşı, HBsAg negatif hemodiyaliz hastalarının ortalama yaşından anlamlı bir şekilde düşük olarak bulunmuştur ($p=0.045$). Benzer şekilde anti-HCV pozitif hemodiyaliz hastalarının ortalama yaşı, anti-HCV negatif hemodiyaliz hastalarından daha düşük saptanmıştır ($p<0.004$). Hemodiyaliz süresi ve kan transfüzyonu miktarının artmasının anti-HBcIgG pozitifliğini istatistiksel olarak etkilemediği belirlenmiştir. Anti-HCV pozitifliği, 10 yılın üzerinde hemodiyalize giren hastalarda, istatistiksel olarak anlamlı bir şekilde yüksek bulunmuştur ($p=0.003$).

Sonuç: Hemodiyaliz hastalarında hepatit virüslerinin geçişi, kan transfüzyonu yerine eritropoetin kullanımının yaygınlaştırılması, alternatif diyaliz yöntemlerinin uygulanmasıyla azalacaktır.

Anahtar kelimeler: Hemodiyaliz hastaları, hepatit B, hepatit C, seroprevalans, risk faktörleri

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INTRODUCTION

Infections in chronic renal failure (CRF) patients are important causes of morbidity and mortality worldwide. Frequent blood transfusion due to anemia in CRF patients, need for vascular intervention in hemodialysis, exposure to infected patients, and contaminated equipment are risks for viral hepatitis agents^[1,2].

Hepatitis B, C, and D viruses (HBV-HCV-HDV), primarily transmitted parenterally, are the most common factors, that may lead to chronic liver disease in these patients. This creates difficulties in the treatment of patients with renal failure. In studies of hemodialysis patients, hepatitis B surface antigen (HBsAg) positivity has ranged between 3-42% and antibody to hepatitis C virus (anti-HCV) positivity between 5-60%, while anti-delta total positivity among HBsAg-positive patients has varied from 0-44.5% in different countries^[1,3-7].

In Turkey, HBV seroprevalence was reported as 2-8%, HCV seroprevalence as 1-1.9%, HBV seroprevalence (in the studies conducted among hemodi-

alysis patients) as 4.3-13.3%, and HCV seroprevalence as 7.6-45.7%^[8-12].

HBV, HCV and HDV infections maintain their importance despite the advances in diagnostic tests, antiviral treatments, and vaccination studies. The aim of this study was to determine the prevalence of serological indicators of HBV, HCV and HDV in CRF patients entering hemodialysis in our hospital, and to confirm the importance of hemodialysis duration and amount of blood transfusion in the transmission of these viral agents.

MATERIALS and METHODS

Study sample included, 50 patients above 18 years of age undergoing hemodialysis in Haydarpaşa Numune Training and Research Hospital from 2008-2009 and 50 healthy volunteers above 18 years of age as a control group.

Patients and the control group were questioned regarding age, gender, and history of hepatitis in the family, surgery and blood transfusion. In addition to the

causes of renal failure in hemodialysis patients, hemodialysis duration, total amount of blood transfusion (units) and erythropoietin use were determined. Our study was approved by the Ethics Committee of Haydarpasa Numune Training and Research Hospital.

Blood was sampled from all patients; sera were centrifuged at 2000 rpm and set aside. The samples were frozen at -20°C. HBsAg (Biokit, Spain), anti-HCV (Biokit, Spain) and anti-delta total (Orgenics, Israel) were studied by microenzyme immunoassay method; hepatitis B surface antibody (anti-HBs) (Abbott AxSYM) and hepatitis B core IgG antibody (anti-HBcIgG) (Abbott AxSYM) by macroenzyme immunoassay method.

The statistical analyses were performed with the use of NCSS (Number Cruncher Statistical System) 2007 and PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA). The Student's t test was used for evaluation of the parameters showing normal distribution based on the groups along with the descriptive statistical data (mean, standard deviation, median, frequency, and rate). Mann-Whitney U test was used for those showing non-normal distribution. Qualitative data were compared using Yates Continuity Correction and Fisher's exact test. A p value of < 0.05 was considered significant.

RESULTS

The mean age of 50 hemodialysis patients in the study was 45.10 ± 16.97 , and 33 (66%) were male and 17 (34%) were female (Table 1). HBsAg-positive and anti-HCV-positive patients were undergoing dialysis treatment with different dialysis machines. Table 2 shows the causes for renal failure in our hemodialysis patients. The most common cause was determined as hypertension.

In the hemodialysis patient group, HBsAg, anti-HBcIgG, and anti-HBs frequencies were 6%, 40%, and 64%, respectively. Anti-HBs was positive in 20 patients

due to vaccination, and in 12 patients due to seroconversion. In the control group, HBsAg, anti-HBcIgG, and anti-HBs frequencies were 4%, 24%, and 52%, respectively. Anti-HBs was positive in 19 patients due to vaccination, and in seven patients due to seroconversion.

There was significant difference between the mean age of HBsAg-positive and HBsAg-negative hemodialysis patients ($p = 0.045$). No significant difference was detected in terms of gender, recent operation history, and blood transfusion. A statistically significant difference was observed in familial history of jaundice ($p = 0.007$) (Table 3). Increases in the duration of hemodialysis and blood transfusion did not affect anti-HBcIgG positivity (Table 4).

The mean age of anti-HCV-positive cases was significantly lower than anti-HCV-negative dialysis patients ($p < 0.004$). Gender, family history of hepatitis, recent history of operation, and history of blood transfusion were not statistically different. Anti-HCV positivity in patients undergoing hemodialysis more than 10 years was higher than others ($p = 0.003$) (Table 5). Anti-HCV was found to be positive in 11 (28%) of 39 blood-transfused patients and in 2 (33%) out of 6 never blood-transfused but erythropoietin-applied patients.

Among hemodialysis patients, 3 (6%) cases were detected with both HBsAg and anti-HCV positivity. These three HBsAg-positive patients and two HBsAg-positive patients in the control group were examined in terms of anti-delta total, and the results were negative.

DISCUSSION

Hemodialysis treatment not only increases life expectancy in patients with CRF but also increases the likelihood of encountering parenterally infecting hepatitis viruses. In hemodialysis patients, a chronic course related to viral hepatitis is seen at a higher rate due to cellular and humoral immunodeficiency^[13]. The most

Table 1. Comparison of the hemodialysis patients with the control group

	Hemodialysis patients (n= 52)	Control group (n= 50)	p
^a Age (mean $\pm$ SD)	45.10 $\pm$ 16.97	40.38 $\pm$ 13.99	0.132
^b Male (n, %)	33 (66.0)	24 (48.0)	0.069
^c HBsAg (n, %)	3 (6.0)	2 (4.0)	1.000
^b Anti-HBs (n, %)	32 (64.0)	26 (52.0)	0.311
^b Anti-HBcIgG (n, %)	18 (36.0)	12 (24.0)	0.133
^b Anti-HCV (n, %)	14 (28.0)	0	0.001*

^a Student t test, ^b Yates Continuity Correction test, ^c Fisher's exact test.

* $p < 0.01$

Table 2. The causes of renal failure in hemodialysis patients

	n	%
Hypertension	20	40
Diabetes mellitus	12	24
Nephrolithiasis	3	6
Glomerulonephritis	2	4
Amyloidosis	1	2
Tuberculosis	1	2
Berger's disease	1	2
Non-steroidal anti-inflammatory drug	1	2
Unknown	9	18

common cause of viral hepatitis in hemodialysis patients is HCV. In addition, despite the availability of serologic tests and vaccination for HBV, it maintains its importance in hemodialysis patients^[1,2].

In the study of El-Ottol et al. with hemodialysis patients, HBV seropositivity was detected at a higher rate in male patients^[14]. The relation between the patient's age and HBV infection was found statistically

significant, with patients less than 40 years old being more sensitive to HBV. In the study of Zamani et al., anti-HCV positivity showed no difference in terms of age and gender^[15]. In our study, the difference between mean age of HBsAg-positive and -negative hemodialysis patients was statistically significant, while there was no significant difference in terms of gender. The mean age of anti-HCV-positive patients was found statistically significantly lower than that of anti-HCV-negative patients. The reason for HCV-positive patients having a lower mean age is that they started hemodialysis at earlier ages. There was no significant difference with regard to gender.

Despite the routine screening of donor blood for HBV, risk of transmission through blood transfusion is still reported as 1/205,000^[16]. Franco et al. from Italy showed a relation between HBsAg positivity and duration of hemodialysis^[17]. El-Ottol et al. determined the number of blood transfusions as a risk factor for HBV infection^[14]. In our study, we compared the duration of hemodialysis and amount of blood transfusion with anti-HBcIgG positivity, and found no statistically significant difference.

Table 3. Features of HBsAg positive and HBsAg negative hemodialysis patients

	HBsAg positive n (%)	HBsAg negative n (%)	p
Number of cases	3 (6)	47 (94)	
Male ^a	3 (100)	30 (63.8)	0.542
Age ^b	28 (21-29)	48 (18-77)	0.045
Family history of jaundice ^a	2 (66.6)	1 (2.1)	0.007
Recent history of operation ^a	2 (66.6)	22 (46.8)	0.602
History of transfusion ^a	2 (66.6)	37 (78.7)	0.534

^a Fisher's exact test, ^b Mann-Whitney U test.

Table 4. The relation of anti-HBcIgG positivity with hemodialysis duration and blood transfusion

	Anti-HBcIgG positive	Anti-HBcIgG negative	p
Amount of transfusion	n= 14	n= 25	
1-5 units ^a	9 (33.3%)	18 (66.6%)	0.723
5-10 units ^a	1 (33.3%)	2 (66.6%)	1.000
> 10 units ^a	4 (44.4%)	5 (55.5%)	0.696
Dialysis duration	n= 20	n = 30	
< 5 years ^b	8 (32%)	17 (68%)	0.386
5-10 years ^b	7 (46.6%)	8 (53.3%)	0.753
> 10 years ^a	5 (50%)	5 (50%)	0.494

^a Fisher's exact test, ^b Yates Continuity Correction test.

Table 5. Features of anti-HCV positive and anti-HCV negative dialysis patients

	Anti-HCV positive n (%)	Anti-HCV negative n (%)	p
Number of cases	14 (28%)	36 (72%)	
Male ^a	10 (71.4%)	23 (63.8%)	0.746
Age ^b	31 (18-55)	50 (18-77)	0.004
History of hepatitis ^a	2 (14.2%)	1 (2.7%)	0.186
Recent history of operation ^c	6 (42.8%)	18 (50%)	0.890
History of transfusion ^a	11 (78.5%)	28 (77.7%)	1.000
Amount of transfusion	n= 11	n= 28	
1-5 units ^a	5 (45.5%)	22 (78.6%)	0.061
5-10 units ^a	1 (9.1%)	2 (7.1%)	1.000
> 10 units ^a	5 (45.5%)	5 (17.9%)	0.109
Duration of dialysis	n= 14	n= 36	
< 5 years ^c	3 (21.4%)	22 (61.1%)	0.027
5-10 years ^a	4 (28.5%)	11 (30.6%)	1.000
> 10 years ^a	7 (50%)	3 (8.3%)	0.003

^a Fisher's exact test, ^b Mann-Whitney U test, ^c Yates Continuity Correction test.

HBV infections become chronic in hemodialysis patients at a rate of 30-60%^[18]. The importance of HBV vaccination increases in this patient group that progresses to chronic disease. In our study, we found the anti-HBs rate of hemodialysis patients as 64%. Immunization to HBV in patients with CRF before starting dialysis treatment, if possible, will ensure protection against HBV and its complications.

In dialysis patients, the frequency of blood transfusion and duration of hemodialysis are risk factors for HCV infection, and HCV seroprevalence is higher with respect to the general population^[14,15,19]. In the study of Hardy et al., anti-HCV positivity was 15% for patients undergoing less than two years of hemodialysis and 59% for patients undergoing two or more years of dialysis^[20]. In the study of Kashem et al. from Iran, 34 (80%) of 42 HCV-positive patients had a history of blood transfusion, and it was determined that HCV positivity increased in conjunction with an increase in the number of blood transfusions^[21]. In our study, we determined that the duration of hemodialysis showed a parallel increase with HCV prevalence.

Although anti-HBcIgG and anti-HCV positivity increased as the amount of blood transfusion rose, it was not statistically significant in this study. The incompatibility of our results with those in the literature can be attributed to the limited number of our cases.

Although it is controversial in hemodialysis units to separate the machines of HCV-infected patients, in our hospital's hemodialysis unit, HCV-infected patients undergo treatment with different hemodialysis machines. Although there are studies showing that the separation of machines for anti-HCV-positive patients reduces the transmission of HCV, placement of sero-positive patients on separate dialysis machines is not recommended by the Centers for Disease Control and Prevention (CDC)^[22-24].

Transmission of hepatitis virus among CRF patients will decrease with full implementation of infection control measures, observance of HBV vaccination, reduction in the number of blood transfusions, increase in the use of erythropoietin, and implementation of alternative dialysis methods.

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