

Overview of blood-borne viral infections in hemodialysis patients: hepatitis B, hepatitis C, human immunodeficiency virus infections

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ABSTRACT

Aim: This study aimed to examine the blood-borne viral infections such as hepatitis B, hepatitis C and human immunodeficiency virus (HIV) and to determine the risk factors in hemodialysis patients.

Material and Method: The datas of patients who underwent hemodialysis in the hemodialysis unit of our hospital between March 1, 2020 and March 1, 2021 were reviewed retrospectively. Their sociodemographic characteristics, habits, underlying diseases and virological indicators related to hepatitis B, hepatitis C and HIV were obtained from patient files and hospital data processing system.

Results: A total of 96 patients were included in the study. Of them, 43.8% (n=42) were female and 56.2% (n=54) were male. Their mean age was 62.61±18.11 years, ranging from 17 to 92. The duration of dialysis was less than 3 months for 46.9% (n=45) of the patients, between 3 months and 3 years for 19.8% (n=19), and 3 years and above for 33.3% (n=32). Thirty patients (31.3%) had diabetes mellitus. In addition, 1% (n=1) of the patients had HBsAg positivity, 3.1% (n=3) had anti-HCV positivity, 59.4% (n=57) had Anti- HBs positivity and 2.1% (n=2) had anti-HIV positivity. No statistically significant difference was found between the patients' HBsAg, anti-HCV and anti-HIV positivity according to gender, duration of dialysis, dialysis application site, alcohol use, surgical intervention and blood transfusion history (p>0.05).

Conclusion: Hemodialysis patients may be at risk for hepatitis B, hepatitis C and HIV infection if infection control guidelines are not followed strictly. In addition to complying with these guidelines, both health workers and patients should be trained constantly, patients' virological indicators should be tested regularly and hepatitis B vaccine should be administered to hemodialysis patients without seroconversion.

Keywords: Hemodialysis, HBV, HCV, HIV, seroprevalance

INTRODUCTION

Hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) are pathogens that can be transmitted by blood and blood products, causing significant public health issues across the world. Hemodialysis patients with end-stage renal disease are at risk due to transmission routes of these infections.

Turkey is a medium endemic region in terms of HBV infection with an estimated HBsAg positivity of 4% (1). Studies of hemodialysis patients have reported different rates of HBsAg positivity reaching at 8.7% (2). While anti-HCV positivity is estimated to be 1% in the population, studies report this rate up to 16%

in hemodialysis patients (3, 4). According to the latest data, there are a total of 25,809 HIV-infected individuals across Turkey and HIV positivity is below 0.5% in hemodialysis patients (5,6).

An evaluation of HBsAg, anti-HCV and anti-HIV positivity and Hepatitis B vaccine responses of the patients followed up in the hemodialysis unit of our hospital will guide us in following up our patients, determining relevant risk factors and developing proper prevention strategies, and also contribute to the literature on the seroprevalence of hemodialysis patients in İstanbul, Turkey.

MATERIAL AND METHOD

Patients followed in the hemodialysis unit of our hospital between March 1, 2020 and March 1, 2021 were included in the study. The study was approved by the Medeniyet University Göztepe Training and Research Hospital Ethics Committee (Date: 02.09.2020, Decision No: 2020/0551). The study was conducted in accordance with the Declaration of Helsinki rules. Their sociodemographic data, histories of blood transfusion and surgical intervention, vaccination status, alcohol and intravenous drug use, presence of fistula or catheter, duration of hemodialysis, and virological indicators (HBsAg, anti-HBs, anti-HBc total, anti-HCV, anti-HIV) were obtained retrospectively from patient files or hospital data processing system. Their HBsAg, anti-Delta, anti-HBs, anti-HBc total, anti-HCV and anti-HIV serology were tested using the enzyme linked immunosorbent assay (ELISA) method. Anti-HBs titer of 10 mIU/mL and above was accepted as protective antibody titer for hepatitis B. HBsAg, anti-HCV, anti-HIV positive patients were tested using HBV DNA, HCV RNA, HIV RNA test PCR (Polymerase Chain Reaction) method (Qiagen, Hilden, Germany) respectively.

Statistical Analysis

The Number Cruncher Statistical System (NCSS) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used to evaluate the data. Shapiro-Wilk test and graphical examinations were used to test the conformity of quantitative data to normal distribution. Mann-Whitney U test was used for comparisons between two groups of quantitative variables without normal distribution. Pearson chi-square test, Fisher's exact test and Fisher-Freeman-Halton test were used to compare qualitative data. Statistical significance was accepted as $p < 0.05$.

RESULTS

A total of 96 patients were included in the study. Their mean age was 62.61 ± 18.11 years, ranging from 17 to 92. Of the patients, 43.8% ($n=42$) were female, 56.2% ($n=54$) were male, and 77.6% were married. The duration of dialysis was less than 3 months for 46.9% ($n=45$) of the patients, between 3 months and 3 years for 19.8% ($n=19$), and 3 years and above for 33.3% ($n=32$). Thirty patients (31.3%) had diabetes mellitus and five patients (5.2%) had hypertension. In addition, there were history of malignancy in 9 patients (9.3%) and polycystic kidney disease in 4 patients (4.2%).

Of the patients, 1% ($n=1$) had HBsAg positivity, 3.1% ($n=3$) had anti-HCV positivity and 2.1% ($n=2$) had anti-HIV positivity. The HBsAg positive patient had negative delta antibody. HBsAg, Anti-HCV, Anti-HIV positivities were all detected before starting the dialysis program. Anti-HBs positivity was observed in 59.4% ($n=57$) of the patients, and six (6) of them were naturally immunized. No isolated anti-HBc total positivity was observed. Anti-HBs values of six (6.3%) patients who received Hepatitis B vaccine and developed protective antibody levels were found to be negative in the following examinations.

In addition, 46.9% ($n=45$) of the patients were on dialysis via fistula and 53.1% ($n=51$) were on dialysis via catheter. Only 2.1% ($n=2$) of them were social drinkers, there were no patients with intravenous drug use. While 54.2% ($n=52$) had a history of blood transfusion, and 76% ($n=73$) had a history of surgical intervention.

No statistically significant difference was found between the patients' HBsAg, anti-HCV and anti-HIV positivity according to gender, duration of dialysis, dialysis application site, alcohol use, surgical intervention and blood transfusion history, and no additional risk factor was detected ($p > 0.05$). **Tables 1, 2 and 3** show the patients' HbsAg, anti-HCV and anti-HIV status and their demographic characteristics.

Table 1. Comparison of patients' HBsAg status according to their demographic characteristics

	HBsAg		P
	Negative (n=95)	Positive (n=1)	
Age			
Mean±Sd	62.62±18.21	62	
Median (Min-Max)	64 (17-92)	62 (62-62)	
Gender			^a 1.000
Male	53 (55.8)	1 (100.0)	
Female	42 (44.2)	0 (0)	
Duration of dialysis			^d 0.523
≤3 months	45 (47.4)	0 (0)	
3 months - 3 years	19 (20.0)	0 (0)	
≥3 years	31 (32.6)	1 (100.0)	
Dialysis application site			^a 0.469
Fistula	44 (46.3)	1 (100.0)	
Catheter	51 (53.7)	0 (0)	
Alcohol use	2 (2.1)	0 (0)	^a 1.000
Surgical intervention			^a 1.000
No	23 (24.2)	0 (0)	
Yes	72 (75.8)	1 (100.0)	
Blood transfusion			^a 0.458
No	43 (45.3)	1 (100.0)	
Yes	52 (54.7)	0 (0)	

^aFisher's Exact Test, ^dFisher Freeman Halton Test

Table 2. Comparison of patients' anti-HCV status according to their demographic characteristics

	Anti-HCV		P
	Negative (n=93)	Positive (n=3)	
Age			
Mean±Sd	62.89±18.23	54.00±13.11	
Median (Min-Max)	64.5 (17-92)	56 (40-66)	
Gender			
Male	52 (55.9)	2 (66.7)	^a 1.000
Female	41 (44.1)	1 (33.3)	
Duration of dialysis			
≤3 months	45 (48.4)	0 (0)	^d 0.201
3 months - 3 years	18 (19.4)	1 (33.3)	
≥3 years	30 (32.3)	2 (66.7)	
Dialysis application site			
Fistula	43 (46.2)	2 (66.7)	^a 0.598
Catheter	50 (53.8)	1 (33.3)	
Alcohol use			
Surgical intervention	43 (46.2)	2 (66.7)	^a 1.000
No	43 (46.2)	2 (66.7)	^a 1.000
Yes	50 (53.8)	1 (33.3)	
Blood transfusion			
No	43 (46.2)	2 (66.7)	^a 0.247
Yes	50 (53.8)	1 (33.3)	

^aFisher's Exact Test, ^dFisher Freeman Halton Test

Table 3. Comparison of patients' anti-HIV status according to their demographic characteristics

	Anti-HIV		P
	Negative (n=94)	Positive (n=2)	
Age			
Mean±Sd	62.80±18.22	54.00±11.31	
Median (Min-Max)	64.5 (17-92)	54 (46-62)	
Gender			
Male	52 (55.3)	2 (100)	^a 0.503
Female	42 (44.7)	0 (0)	
Duration of dialysis			
≤3 months	45 (47.9)	0 (0)	^d 0.276
3 months - 3 years	18 (19.1)	1 (50)	
≥3 years	31 (33)	1 (50)	
Dialysis application site			
Fistula	43 (45.7)	2 (100)	^a 0.217
Catheter	51 (54.3)	0 (0)	
Alcohol use			
Surgical intervention	52 (55.3)	2 (100)	^a 1.000
No	23 (24.5)	0 (0)	^a 1.000
Yes	71 (75.5)	2 (100)	
Blood transfusion			
No	43 (45.7)	1 (50)	^a 1.000
Yes	51 (54.3)	1 (50)	

^aFisher's Exact Test, ^dFisher Freeman Halton Test

The only HbsAg positive patient had been receiving hepatitis B treatment for ten years and his HBV DNA was undetectable. Two patients who were positive for anti-HCV had negative HCV RNA and one of them became negative after antiviral treatment. The HCV RNA value of the other anti-HCV positive patient was 74.858 IU/mL. One of the anti-HIV positive patients had received

HIV treatment for two years and the other for nine years. Both patients had undetectable HIV RNA levels.

There was a statistically significant relationship between anti-HBs positivity and duration of dialysis (p=0.001; p<0.01). The rate of being negative for anti-HBs was higher in the patients with dialysis duration of 3 months or less, and the rate of being positive for anti-HBs was higher in those with dialysis duration between 3 months and 3 years and those with dialysis duration of 3 years and above. The rate of being positive for anti-HBs was statistically significantly higher in the patients with fistula than in those with catheter (p=0.001; p<0.01). In addition, anti-HBs positivity was statistically significantly higher in the patients who underwent surgery than in those who did not (p=0.001; p<0.01).

Laboratory characteristics of the study patients are presented in **Table 4.**

Table 4. Laboratory characteristics of the patients

	Median (Min-Max)
Kt/V (min: 1.2)	1.5 (0.5-2.9)
WBC (4000-10.000/uL)	7.000 (2.700-49.300)
Hemoglobin (13.5-17 g/dl)	10.35 (6.1-14.5)
Plt (100.000-400.000/uL)	194.000 (48.000-513.000)
ALT(0-41 U/L)	12 (2-756)
Albumin (35-52 gr/dL)	36.5 (2-94)
Glucose (74-106 mg/dL)	103 (46-258)

Kt/V: dialyzer clearance urea, dialysis time/ volume of distribution of urea; WBC: White blood cell; Plt: platelet; ALT: Alanine aminotransferase

DISCUSSION

It is estimated that worldwide at least 350 million people are chronically infected with HBV, 170 million with HCV and 38 million with HIV, and these infections still cause significant public health problems across the world (7,8). Blood is one of the most common routes of transmission of these infections. Patients with end-stage renal disease are at risk due to intravenous exposures, frequent use of blood and blood products, and frequent hospitalizations. In addition, susceptibility to infections due to impaired immune system increases, while vaccine responses decrease. Among these patients, deaths due to infections rank number two following cardiovascular diseases (9-11).

As in the world, hemodialysis is the most frequently applied renal replacement therapy (RRT) in patients with end-stage kidney disease in our country (12,13). As of the end of 2019, there are 61,341 patients in the hemodialysis program in Turkey. These patients are followed in 886 centers, 6.21% of which are hemodialysis units in university hospitals. According to the Joint Report of the Ministry of Health and the Turkish Society of Nephrology, the number of hemodialysis patients continues to increase over the years. According to the

latest data, 2.57% (n=1574) of these patients were positive for HBsAg, 3.14% (n=1928) for anti-HCV positivity, 0.43% (n= 263) for both HBsAg and anti-HCV positivity, and 0.11% (n=67) for anti-HIV positivity (13).

In our study, HBsAg positivity was found only in 1% of our patients. This low rate may be due to several reasons including Hepatitis B vaccine programs' implementation for hemodialysis patients, Hepatitis B vaccine's being added to childhood vaccines since 1998, screening of patients regularly for viral infections in accordance with the guidelines, using separate machines in isolations for HBsAg positive patients, hygiene and infection control rules' being followed by both patients and health professionals, and provision of good in-service training for health workers.

Among studies conducted with hemodialysis patients in Turkey, Sayar et al. (14) did not detect HBsAg positivity in Van province. Similarly, both Temiz et al. (15) and Yüksel et al. (16) did not detect HBsAg positivity in Diyarbakır province. However, HBsAg positivity rate was found as 0.9% by Asgin et al. (17) in Karabük province, 3.6% by Evirgen et al. in Hatay province (18), 5.5% by Çopur Çiçek et al. (4) in Rize province, 5.8% by Eser Karlıdağ et al. (19) in Elazığ province, 8.7% by Sirmatel et al. in Gaziantep province, and 0.7% by Güvenir et al. (20) in the Turkish Republic of Northern Cyprus. In our neighbors, this rate was found to be 3.2% for Iraq and 2% for Iran (21,22). In countries from different continents, the prevalence of HBV positivity was found as 2.98% for Botswana, 16.1% for Pakistan, 0% for Brazil, 12% for Kosovo, and 1.03% for Spain (21-27). As seen, the rates vary from by country and even in different geographical regions of one country.

Turkey is a country with low prevalence of HCV. This may be because intravenous drug use, which is the most important route of transmission in developed countries, is low in our country and blood donors have been tested for HCV since 1996 (3, 28, 29). Nevertheless, the rate can be higher in hemodialysis patients due to frequent parenteral interventions and lack of a protective vaccine as in Hepatitis B. In our study, HCV positivity was 3.1%, two of the patients positive for anti-HCV had negative HCV RNA, and one of them became negative after antiviral treatment. In addition, one male patient could not receive antiviral treatment due to his foreign nationality and his HCV RNA value was detectable.

Studies conducted in our country have shown that hemodialysis patients have anti-HCV positivity at rates ranging from 1.2% to 16% (2,4,14-19). Among international studies, the prevalence of anti-HCV was determined as 4.3% by Ibrahim et al. (21) in Iraq, 8.3% by Roushan et al. (22) in Iran, 43% by Telaku et al. (24) in

Kosovo, and 43.2% by Lodhi et al. (26) in Pakistan. Our anti-HCV rate was close to Turkey's average.

Hemodialysis process also carries a significant risk in terms of HIV transmission. HIV transmissions originating from overseas hemodialysis units have been reported in the past years. In 1990, 33 kidney patients were infected with HIV in a dialysis center in Cordoba, Argentina, where same hemodialysis filters were used repeatedly for different patients (30). Similarly, an HIV infection outbreak was reported among 39 patients in two dialysis centers in Egypt in 1993 (31). Although similar incidents are no longer encountered, these outbreaks show how disruptions in infection control measures can cause severe health consequences.

Our study found anti-HIV positivity as 2.1%. Sayar et al. (14), Temiz et al. (15), Yüksel et al. (16), and Eser Karlıdağ et al. (19) found no anti-HIV positivity in their hemodialysis study populations. Güvenir et al. (20) reported anti-HIV positivity for only one patient (0.7%). The rate of anti-HIV positivity in our dialysis center is higher than those reported in other Turkish studies. In the report of the Turkish Society of Nephrology published in 2019, anti-HIV positivity was determined as 0.11% for hemodialysis patients. Although Turkey is not a country with high HIV prevalence, the rates were high in our study. As we have a machine reserved for HIV-positive patients and a specific clinic to which HIV-positive individuals in our region are referred in need, which probably results in a higher frequency of HIV positive dialysis patients.

Anti-HBs positivity was observed in 59.4% (n=57) of the patients. The rate was significantly high for patients who have been on dialysis for more than 3 months. Patients in need of renal replacement therapy usually were tested and included in the vaccination program as soon as possible, preferably before starting dialysis. Six patients who were known to have antibodies against Hepatitis B before, were tested negative for Hepatitis B antibodies. Low antibody response and seroconversion may develop in patients with advanced kidney disease and their vaccine responses may be less permanent than healthy individuals. Whether a booster dose is needed for patients with end stage kidney disease should be evaluated regularly with annual anti-HBs titer checks (32, 33). It should be kept in mind that Anti-HBs titers may decrease more rapidly in these patients, and a revaccination plan should be recommended for patients without adequate antibody response (Anti-HBs < 10IU/ml) to protect them from the risk of hepatitis B infection (32, 34). A booster dose was administered to these six patients whose antibodies were found to be negative. The patients undergoing dialysis from fistula had high anti-HBs positivity. Before surgical

procedures, hepatitis B, C and HIV status are usually checked, they probably were administered a hepatitis B vaccine booster dose if needed after an antibody control before the fistula was created.

According to the annual joint reports of the Turkish Society of Nephrology, both HBsAg, anti-HCV and anti-HIV positivity have decreased over the years. Experienced health personnel, regular staff and patient training and high compliance with hygiene rules have a significant contribution to this decline. No additional risk factor that would cause HBsAg, anti-HCV, and anti-HIV positivity was encountered in our study. This was attributed to proper observance of infection control measures and careful work of healthcare professionals.

Limitation: Since this was a retrospective study, all patient data could not be reached in our study. Also our dialysis center is based in a tertiary hospital, which may cause a selection bias and therefore our results may not reflect other dialysis centers, especially centers not affiliated with hospitals.

CONCLUSION

Hemodialysis patients may be at an increased risk for hepatitis B, hepatitis C and HIV infection than the general population if infection control guidelines are not followed strictly. In addition to complying with these guidelines, both health workers and patients should be trained constantly, patients' virological indicators should be tested, patients should be vaccinated as soon as possible and hepatitis B vaccine should be re-administered to hemodialysis patients without seroconversion or if their antibody responses change.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Medeniyet University Göztepe Training and Research Hospital Ethics Committee (Date: 02.09.2020, Decision No: 2020/0551).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

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