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Investigationof The Change in Seroprevalence of Viral Hepatitis in Patients Receiving Hemodialysis Treatment Over The Years: A Single-Center Study

Safiye Koçulu Demir[1*], Tülin Akagün[2]

[1]*Demiroglu Bilim University Medical School, Department of İnfection Disease and Clinical Microbiology, Istanbul, Turkey*

[2]*Giresun University Medical School. Department of Nephrology, Giresun, Turkey*

Abstract

In this study, it was aimed to evaluate HBV, HCV, and HIV seroprevalence and their 9-year changes in patients receiving hemodialysis (HD) treatment in the Giresun province in Turkey. A total of 607 patients over the age of 18 who received hemodialysis treatment in Giresun – Turkey, provincial and district hospitals in 2013 and 2022 were included in our study. The files of the patients were reviewed retrospectively. Demographic characteristics of the patients and serology results of HBV, HCV, HDV, and HIV were recorded. The data was evaluated using the IBM SPSS Statistics 25.0 program. A total of 607 patients, 385 of whom received HD treatment in 2013 and 222 who received HD treatment in 2022, were included in the study. Two hundred thirty (59.7%) in 2013 and 135 (60.8%) in 2022 of male patients. While the mean age of the patients was 60.26±14 years in 2013, it was 63.08±13.18 years in 2022. In 2013, HBsAg positivity was detected in 9 (2.3%), HBV-DNA positivity in 4 (44.4%), anti-HCV positivity in 31 (8.1%), and HCV-RNA positivity in 8 (25.8%) patients. In 2022, HBsAg positivity was detected in 4 (1.8%), HBV DNA positivity in 2 (50%), and anti-HCV positivity in 31 (8.1%) patients. Compared with dialysis duration, the anti-HCV positivity rate was significantly increased in patients with long dialysis duration ($p<0.001$). In line with the health policies, the epidemiological data obtained support a decrease in the population's seroprevalence of HBV and HCV. However, according to the results of our study, it was determined that there was no significant decrease in HBsAg seroprevalence in patients who received HD treatment over nine years. As a result, it was concluded that it would be beneficial to closely monitor the seroprevalence of viral hepatitis in patients receiving HD treatment.

***Key words**: Hemodialysis, HBV, HCV, HIV, Seroprevalence*

*Corresponding author: Safiye Koçulu Demir, E-mail: safiyekoculu@gmail.com, ORCID ID: 0000-0003-4918-2258

Introduction

Hemodialysis (HD) remains the most common method of renal replacement therapy for patients with the end-stage renal disease worldwide (1). Hemodialysis patients are at high risk for infections due to the immunosuppressive effect of chronic renal failure, the need for frequent blood transfusions, and the possibility of nosocomial transmission. Especially, hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV), which are viral infections transmitted through blood and blood products, cause significant mortality and morbidity (2).

The World Health Organization (WHO) declared the Global Health Sector Strategy on Viral Hepatitis (GHSS) in 2016 to prevent the transmission of hepatitis viruses, reduce complications and deaths related to viral hepatitis, improve patient care and reduce its negative socio-economic effects. In addition, WHO aims to eliminate viral hepatitis as a public health risk by 2030; it aims to reduce the risk of new infections by 90%, reduce the number of hepatitis patients who can be treated by 80%, and reduce the hepatitis-related mortality rate to 65% (3, 4).

HIV, HBV, and HCV prevalence in HD patients; geographic location, socioeconomic status, and even change over time. The prevalence of hepatitis B and C in Turkey has been reported as 4.0% and 0.3-1.0% (5, 6).

This study aims to evaluate the data on HBV, HCV, and HIV seroprevalence of patients undergoing hemodialysis in Giresun province in Turkey from 2013 to 2022 and the change in 9 years.

Material and method

This study includes 607 adult patients, 385 of whom were treated with HD in 2013 and 222 with HD in 2022, in Giresun city center and district hospitals. Patients with end-stage renal disease over 18 years of age who underwent long-term hemodialysis were included in the study. Demographic and serological data of the patients were obtained from hospital automation systems and patient files and scanned retrospectively. HBsAg, anti-HBs, anti-HCV, and anti-HIV tests of all patients were evaluated. HBV-DNA was investigated in HBsAg-positive patients and HCV RNA in anti-HCV-positive patients. HBsAg, anti-HCV, and anti-HIV were tested by electrochemiluminescence immunoassay (ECLIA) method in Cobas e 601 (Roche Diagnostics, Germany). HBV DNA and HCV RNA were investigated by real-time polymerase chain reaction (Real-time PCR) using the RealTime System (QIAGEN, Germany).

Statistical analysis

Statistical data were created using the IBM SPSS Statistics 25.0 program. Data were defined by calculating frequency, percentage, median, arithmetic mean, and standard deviation. Discrete variables were evaluated using $\chi 2$ and Fisher's exact test. The conformity of continuous variables to normal distribution was tested with Kolmogorov Smirnov. Variables with normal distribution were evaluated with the Student-T test and those not with the Mann Whitney-U test. A p-value of ≤ 0.05 was considered significant.

Results

A total of 607 patients, 385 of whom were treated with HD in 2013 and 222 with HD in 2022, were included in the study. Of the patients, 230 (59.7%) in 2013 and 135 (60.8%) in 2022 consisted of male patients. While the mean age of the patients was 60.26±14 years in 2013, it was 63.08±13.18 years in 2022. When the years were compared with each other, no

significant difference was found between the genders in the age of dialysis.

The duration of dialysis was 60 (24-96) months in 2013 and 39 (20-81) months in 2022. A statistically significant difference was found when 2013 and 2022 were compared in terms of the duration of dialysis (p=0.009). When the demographic data of the patients (Table 1) were examined, it was accepted that the rate of hypertension (p=0.001) and heart failure (p=0.03) among the underlying diseases increased in 2022 compared to 2013.

The serological results of the patients were evaluated by years (Table 2). In 2013, HBsAg-positivity was detected in 9 (2.3%) patients. Six of these patients had negative HBV DNA, two were $\leq 10^4$ copies/ml, and one was $>3.6x10^6$ copies/ml. In 2022, HBsAg-positivity was detected in 4 (1.8%) patients. Among these patients, one of the two patients with negative HBV DNA was not receiving treatment and the other was using entecavir. Two patients with positive HBV DNA ($<10^4$ IU/ml and $12x10^8$ IU/ml) were not receiving treatment. When HbsAg-positivity and anti-HBs rates were compared according to years, no significant difference was found.

Table 1: Demographic data of patients

	2013 year (n=385)	2022 (n=222)	**P**	**OR**	**95% confidence interval**
Gender					
Male n(%)	230 (59.7%)	135 (60.8%)	0.79	1.04	0.74-1.46
Female n(%)	155 (40.3%)	87 (39.2%)			
Age years (average±SS)	60.26±14	63.08±13.18	**0.02***		
Dialysis time (months), median (IQR)	60 (24-96)	39 (20-81)	**0.009***		
HT n (%)	222 (57.7%)	171 (77%)	**0.000***	2.46	1.69-3.57
DM, n (%)	165 (42.9%)	86 (38.7%)	0.32	0.84	0.60-1.18
CHF, n (%)	7 (1.8%)	11 (5%)	**0.03***	2.81	1.07-7.37
CAD, n (%)	14 (3.6%)	6 (2.7%)	0.53	0.73	0.27-1.94
COPD, n (%)	5 (1.3%)	4 (1.8%)	0.73	1.39	0.37-5.24

n: number of patients, OR: Odd ratio, SD: standard deviation, * P<0.05 significant according to Pearson Chi-square test, IQR: interquartile range, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure

Table 2: Serological outcomes of patients by the year

	2013 n(%)	**2022 n(%)**	**P value**	**OR**	**95% confidence interval**
HBsAg-positive	9 (2.3)	4 (1.8)	0.66	0.76	0.23-2.51
Anti-HBs -positive	321(83.4)	191 (86)	0.38	1.22	0.77-1.95
Anti-HCV -positive	31 (8.1)	7 (3.2)	**0.02***	0.37	0.16-0.85
Anti-HDV-positive	0 (0)	0 (0)			
Anti-HIV -positive	0 (0)	0 (0)			
HBV DNA -positive	4(44,4)	2 (50)	1		
HCV RNA -positive	8 (25,8)	0 (0)	0.14	0.70	0.54-0.91

n: number of patiens, OR: Odd ratio, SS: standard deviation, HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, HDV: Hepatitis D virus, * P<0.05 significant according to Pearson Chi-square test

Anti-HCV-positivity was detected in 31 (8.1%) patients in 2013, and anti HCV positivity was detected in 7 (3.2%) patients in 2022, and a statistically significant decrease was observed when compared according to years (p=0.02). In 2013, 8 (25.8%) of the patients who were anti-HCV positive were positive for HCV-RNA. In 2022, the HCV RNA of all patients positive for anti-HCV was found to be negative. It was determined that 6 of the patients received treatment and 1 did not receive any treatment.

When the vaccination status of the patients in 2013 and 2022 was questioned, there were 2 patients who could not be vaccinated in both groups. There were 317 (89.8%) and 190 (88%) patients who were vaccinated, and 36 (10.2%) and 26 (12%) patients who were not immunized with the vaccine, respectively. There was no statistical difference between years (p=0.492).

Tables 3 and 4 show HBsAg and anti-HCV positive patients according to HD duration and gender. When HBsAg and anti-HCV-positivity rates were compared according to genders, no significant difference was found. Although there was no significant difference in HBsAg-positivity rate when compared with dialysis duration, the anti-HCV-positivity rate was found to be significantly higher in patients with long dialysis duration (p<0.001).

Table 3: Comparison of HbsAg-positive patients with negative ones

	HBsAg positive (n=13)	HBsAg negative (n=594)	p
Dialysis time, months, median (IQR)	36 (12-108)	48 (24-96)	0.46
Gender, n (%)			
Woman	5 (38.5%)	237 (39.9%)	0.91
Male	8 (61.5%)	357 (60.1%)	

n: number of patients, *: According to Pearson Chi-square test p<0.05 significant

Table 4: Comparison of Anti-HCV-positive patients with negative ones

	Anti-HCV-positive (n=38)	Anti-HCV-negative (n=569)	p
Dialysis time, months, median (IQR)	108 (36-203)	48 (24-89)	<0,001
Gender, n (%)			
Woman	13 (34.2)	229 (40.2)	0.46
Male	25 (65.8)	340 (59.8)	

n: number of patiens , *: According to Pearson Chi-square test p<0.05 significant

Discussion

Viral hepatitis continues to be a significant risk for both patients and staff in hemodialysis units. Despite the availability of effective vaccines since 1982, HBV infection has remained endemic in many countries. WHO estimates that approximately 296 million people worldwide are living with chronic hepatitis B infection in 2019 (4). HBsAg positivity rates in dialysis patients are 1% in the United States, 1.3-14.6% in the Asia Pacific region (lower rates in countries such as Australia, Japan, and New Zealand; higher rates in countries such as Mongolia, Philippines, and China) (7, 8), 0% in Brazil (9), 1.03% in Spain (10), 16.1% in Pakistan (11), 3.2% in Iraq (12), Iran% 2 (13) have been reported.

Turkey is located in the middle endemic region in terms of HBV infection (14). HBsAg positivity rates in articles published for HD patients were found 8.1% by Kaygusuz et al. in 2007 (15), 8.7% by Sırmatel et al. in 2008 (16), 3.6% by Evirgen et al. in 2010 (17), 5.5% by Çiçek Çopur et al. in 2013 (18) and, 5.8% by Karlıdağ et al. in 2017 (19). Temiz et al. (20), Yüksel et al. (21) and Sayar et al. found HBsAg negative in all HD patients while Furuncuoglu et al. (23) found HBsAg positivity rate as 4.2% and anti-

HBs positivity rate as 16.8% in 26.001 adult patients. In the study, when the 20-years was divided into three periods and analyzed separately (1995-2002, 2003-2009, 2010-2015), it was reported that the HBsAg positivity rate decreased from 5.3% to 4.8% and 3.1%. In our study, it was determined that the HBsAg positivity rate was 2.3% in 2013 and decreased to 1.8% in 2022. As in other studies, the decrease in our study over the years is remarkable.

Globally, approximately 115 million people (1.6%) have chronic HCV infection (24). HCV infection is more common in dialysis patients than in healthy populations. In a meta-analysis evaluating 1,302,167 HD patients and 407 studies, the highest prevalence of HCV infection was; in Africa (28%), Asia (22.3%), Europe (20.1%), South America (19.4%) and North America (16.5%) compared to 3% in Australia and New Zealand. 6, 0.18% in Iran. The highest prevalence (48.5%) was shown in low-income countries (13, 25).

Among the studies conducted in our country; Anti-HCV positivity was found 18.4% by Mountains et al. (26), 16% by Çiçek et al. (18), 4.1% by Temiz et al. (20), 3.1% by Ergen et al. (27) and 3.2% by Yüksel et al. (21). In our study, it was determined that while the rate of anti-HCV positivity was 8.1% in 2013, it decreased to 3.2% in 2022.

The prevalence of HIV infection in HD patients is not clearly defined, but available data suggest that it varies with the prevalence of HIV infection in the local population. According to 2017 data from a large dialysis center with 417,756 dialysis patients in the United States, the HIV prevalence was found to be 1.7%. When the patient populations with end-stage renal disease (ESRD) were compared with the lower-risk group, it was determined that the false-positive rate was higher in ESRD patients. According to the latest data from the Ministry of Health in our country; a total of 30293 HIV-infected individuals and HIV positivity in HD patients was reported below 0.5% (28-31). In our study, all patients were anti-HIV negative.

Patients with ESRD have a decreased response to the HBV vaccine. While over 90% response is obtained in patients without renal failure, antibody response develops in only 50-60% of patients with ESRD after HBV vaccination (32, 33). In our study, 89.8% and 88% of those who were vaccinated in 2013 and 2022, respectively, were 10.2% and 12% who were not vaccinated. While the antibody response against HBV was 83.6% in 2013, it was 86% in 2022.

Due to the immunosuppression that develops in hemodialysis patients, it is stated that in the diagnosis of HBV and HCV infections, HBV DNA and HCV RNA should be investigated by molecular methods as well as tests for antigen and antibody determination (34).

In dialysis patients; The incidence of HBV and HCV infection has decreased significantly due to screening of blood products for HBsAg and anti-HBc, effective HBV vaccination, implementation and monitoring of stricter infection control measures, less need for transfusion after the emergence of erythropoiesis-stimulating agents, and the emergence of new technological diagnostic tests. However, Turkey's nomads influence the prevalence of hepatitis in the country.

Access to diagnosis and treatment of HBV and HCV infection is limited in low-income countries. Currently, there is no effective vaccine against HCV, Turkey is on the migration route from Eastern European countries, Afghanistan, and other Central Asian countries, the existence of unpredictable geopolitical situations such as the war in neighboring countries, the employment of unregistered immigrants who cannot be followed in the service sector, and COVID- Uncertain economic

conditions predominately prevent viral hepatitis rates from reaching desired levels (35, 36).

Conclusion

The reduction in seroprevalances of HBV and HCV infections can be explained by elimination programs carried out by the Ministry of Health, screening of blood products for HBsAg and anti-HBc in dialysis patients, use of new generation tests with increased sensitivity HBV and HCV specific diagnosis, implementation and supervision of strict infection control measures, less need for transfusion by using new agents and effective HBV vaccination. This shows that the viral hepatitis elimination programs carried out by the Ministry of Health have a positive effect. However, it was shown that there was no significant difference in HBsAg seroprevalence in patients who received HD treatment in Giresun province over nine years. Therefore, the seroprevalence of viral hepatitis should be closely monitored, especially in HD patients.

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