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Brief communication (Original)

Seroprevalence of hepatitis B and C virus in patients who undergo hemodialysis in Antalya province, Turkey

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Background: Chronic hepatitis B (HBV) and C virus (HCV) infections are important causes of morbidity and mortality in patients who undergo hemodialysis (HD).

Objectives: To define seroprevalence of HBV and HCV in patients who underwent HD in Antalya province, Turkey.

Methods: We included 1347 patients with end-stage renal failure who underwent HD at one of the 23 centers in Antalya province from January 01 to March 31, 2014 in this retrospective cross-sectional study. Hepatitis B surface antigen (HBsAg) and anti-HCV seropositivity were assessed clinically using a third-generation enzyme-linked immunosorbent assay. HBV DNA and HCV RNA were determined in HBsAg positive and anti-HCV positive HD patients respectively.

Results: Of the patients included, 805 (59.8%) were male. Mean age (± standard deviation) of the patients was 53.9 ±17.0 (range 17–89) years. The sera of 2.4% patients was positive for HBsAg, and the sera of 5.5% of the patients was positive for anti-HCV. The sera of 56% of patients positive for HBsAg was also positive for HBV DNA, and the sera of 43% of patients positive for anti-HCV was also positive for HCV RNA. Coexistence of HBsAg and anti-HCV was 1.02%.

Conclusion: The present study showed that the prevalence of chronic HBV and HCV infection in patients who underwent HD in Antalya province was moderate-to-low for Turkey. Compliance of HD centers with infection control rules, isolation of HBsAg positive patients, isolation of the equipment used for HBV susceptible patients, and active surveillance of the HD patients may have resulted in lower prevalence rates.

Keywords: HBsAg, HBV, HCV, hemodialysis, seroprevalence

In recent years, there has been an increase in risk factors such as hypertension and diabetes mellitus, and as a consequence, chronic kidney disease has become a major healthcare problem worldwide.

Patients who have undergone hemodialysis (HD) for end-stage renal failure are at a higher risk for infections that are transmitted by blood and blood products [1]. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are important causes of morbidity and mortality in these patients [2-5]. Studies have demonstrated that anti-HCV seropositivity is associated with increased mortality of HD patients [3]. In a meta-analysis including 6 studies, hepatitis B surface antigen (HBsAg) seropositivity was an independent and important risk factor for mortality and graft loss after renal transplantation [6].

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HBV infection in patients who underwent HD

HBV is transmitted by contact of infectious blood or other body fluids with skin or mucous membranes with impaired integrity. HBV can survive on environmental surfaces for up to 7 days at room temperature. In studies conducted at centers for HD, HBV was detected on surgical equipment, control buttons of HD machines, and on door handles [7]. Transmission from environmental surfaces, equipment, and healthcare workers plays a major role in transmission of HBV [8, 9].

HBV causes acute or chronic infection. Adults with normal immunity experience infection at a rate of 94%–98% after exposure to the virus and acquire permanent immunity with neutralizing antibodies. However, immunosuppressed individuals, such as patients who are infected often develop a chronic infection [10].

Common application of HBV vaccination, use of erythropoietin to treat anemia and to reduce the need of transfusion, the widespread use of new generation diagnostic assays, and isolation of HBsAg seropositive patients has led to a decrease in the prevalence of HBV seropositivity among patients who undergo HD. Nevertheless, prevalence remains high compared to normal populations [1, 8, 11, 12].

Isolation of HBsAg seropositive patients and the equipment used for patients with susceptibility for HBV may decrease prevalence of HBV infection by up to 70%–80% [8, 12]. Vaccination programs and limitation of blood transfusion may also play an important role in the decreased prevalence [13, 14].

Vaccination at 0, 1, and 6 months is recommended as routine HBV prophylaxis before HD, whereas one scheme for post exposure prophylaxis is vaccination at 0, 1, 2, and 6 months. Some centers recommend a high dose of 40 μg vaccine for HD patients at 0, 1, 2 and 6 months [1, 8].

HCV infection in patients who underwent HD

Like HBV, HCV is also transmitted percutaneously, but horizontal transmission is also possible in HD units from environmental surfaces, equipment, and healthcare workers [1, 8].

The incubation period for HCV infection varies from 14 to 180 days. Following acute infection, which is usually asymptomatic or occurs as a mild clinical disease, chronic HCV infection develops in 75%–85% of patients [1, 15].

For diagnosis, anti-HCV serology is used routinely. After exposure to HCV, seroconversion occurs in 8–9 weeks. Sera is positive for anti-HCV in 80% of cases within 15 weeks, and more than 97% within 6 months after the exposure [1, 8]. However, anti-HCV serology may not distinguish acute, chronic or past infections, and it often exists for a lifetime. However, it may not provide protection against reinfection [1, 8]. Currently, third generation enzyme-linked immunosorbent assays (ELISAs), which detect antibodies against core, NS3, and NS5 regions of HCV are used. Active HCV infection is established by detection of HCV RNA with *polymerase chain reaction* (PCR) methods. HCV RNA is detectable in the blood 1–2 weeks after exposure. New methods have been developed to detect of HCV nucleocapsid antigen [1, 8]. The U.S. Center for Disease Control and Prevention (CDC) recommends to use ELISA for initial anti-HCV serology screening of patients who undergo HD. Positive outcomes must be confirmed with HCV RNA testing [8]. Whereas, Kidney Disease Improving Global Outcomes (KDIGO) recommends that patients who undergo HD must be screened with molecular tests at first admission to HD units and again at transfer to another center because of the high HCV seroprevalence in HD units [16].

The nosocomial pathway plays a primary role in HCV transmission in HD units. There is also the knowledge that HCV is not transmitted from dialysis membrane directly. Two large prospective observational studies, the DOPPS and an Italian study, concluded that isolation does not protect against HCV after multivariate adjustment for potential confounders [17, 18]. The CDC and KDIGO emphasize strict adherence to infection control precautions, but there is no recommendation for the isolation of anti-HCV positive patients [1, 8, 16]. By contrast, there are several studies demonstrating that HCV seroconversion was decreased with the isolation of anti-HCV positive patients. Seroconversion was reported to decrease from 10% to 0% by Shebeb et al. [19], from 21.6% to 6.8% by Gallego et al. [20], from 14.4% to 4.5% by Alavian et al. [21], and from 42% to 4% by Agarwal et al. [22].

We still have no vaccine against HCV and even more importantly diagnostic assays for early detection of HCV available in HD units. Acute HCV infection can be treated effectively with early antiviral therapy [1, 23].

In the present study, we aimed to define the seroprevalence of HBV and HCV in patients how have undergone HD in Antalya province, Turkey.

Materials and methods

Antalya, with a population of 1,900,000, is the seventh largest city of Turkey and is located on the Mediterranean coast. HD services in Antalya are delivered by 23 centers including one university hospital, 11 public hospitals, and 11 private dialysis centers. After approval (No. 64/10) by the administrative board of the Clinical Research Ethics Committee of the Antalya Training and Research Hospital we revised the records

of 1347 patients with end-stage renal failure who underwent HD in 23 centers in Antalya between January 01 and March 31, 2014 in this retrospective cross-sectional study. Personal and historical information, HBsAg and anti-HCV status of patients were evaluated retrospectively while preserving the anonymity of the patients included in this study. In all centers, HBsAg and anti-HCV serology was performed using a third-generation ELISA (Abbott Laboratories, North Chicago, IL, USA). Assays for HBV DNA and HCV RNA were used to assess the HBsAg seropositive and anti-HCV seropositive HD patients further. Serum HBV DNA was determined using a quantitative polymerase chain reaction (PCR) assay (COBAS TaqMan HBV test, detection limit 12 IU/ml; Roche Diagnostics, Indianapolis, IN, USA), and HCV RNA in sera was determined using a real-time PCR assay (Real Time HCV, detection limit 12 IU/ml; Abbott Molecular, Des Plaines IL, USA).

Results

Of the 1,347 patients included, 805 (59.8%) were male, and 547 (40.2%) were female. The mean age (± standard deviation) of the patients was 53.9 ±17.0 (range 17–89) years. Thirty-two patients (2.4%) received HD in the university hospital, 316 (23.4%) in public hospitals, and 999 (74.2%) in private HD centers. Sera were determined to be positive for HBsAg and anti-HCV a rate of 0% and 12.5% in the university hospital; 2.2% and 2.2% in public hospitals; and 2.5% and 6.3% in private centers for HD, respectively.

The sera of 2.4% patients who underwent HD in Antalya province was positive for HBsAg, and the sera of 5.5% of the patients was positive for anti-HCV. The sera of 56% of patients positive for HBsAg was also positive for HBV DNA, and the sera of 43% of patients positive for anti-HCV was also positive for HCV RNA.

Coexistence of HBsAg and anti-HCV was 1.02%. The mean age, sex, dialysis duration, and history of blood transfusion into patients positive for HBsAg and anti-HCV are listed in **Table 1**.

Discussion

HBV and HCV infections are important causes of morbidity and mortality in patients who undergo HD [13, 17]. These infections may lead to acute or chronic hepatitis, cirrhosis, or hepatocellular carcinoma. Patients who undergo HD are vulnerable to and at risk for HBV and HCV infections because of the immunosuppressive effects of renal failure, increased exposure to blood transfusion, and breakdown of standard infection control and isolation rules [13]. In addition, insufficient antibody response against infections leads to diagnostic problems in these patients. Early diagnosis is important to identify nosocomial transmission and damage to the liver can be prevented by early treatment of acute infection.

Since 1982, we have an effective vaccine for HBV, yet over 350 million people worldwide are estimated to be chronic HBV carriers. The majority of these carriers live in undeveloped or developing countries [13]. Chronic HBV infection is seen as highly endemic (>8%) in Southeast Asia, Sub-Saharan Africa, Central Asia, and some Eastern European countries. In these regions, the incidence of HBV infection before the age of 40 years remains high [1, 9]. In developed countries like North America, Western and Northern Europe, Australia, and some parts of South America, HBV seroprevalence is below 2% [1, 9]. Turkey is intermediate to highly endemic with rates of HBsAg seropositivity between 3.9% and 12.5% varying in different regions [24, 25].

Table 1. Demographic characteristics of patients positive for HBsAg and anti-HCV

	HBsAg positive n = 32	Anti-HCV positive n = 74
Mean age (year ± SD)	57.1 ± 11.79	53.5 ± 9.89
Sex, n (%)		
Male	14 (44%)	42 (57%)
Female	18 (56%)	32 (43%)
Dialysis Duration n (%)		
<5 years	12 (38%)	45 (61%)
≥5 years	20 (62%)	29 (39%)
Blood transfusion n (%)		
Yes	18 (56%)	30 (41%)
No	14 (44%)	44 (59%)

In developed countries, HBV prevalence among patients who undergo HD is low (0–10%), whereas the prevalence is higher in developing countries (2%20%) [26]. In Turkey, according to national data from the Turkish Society of Nephrology's (TSN), HBsAg seropositivity in HD patients was 11.1% in 1997, 6.8% in 2006, and 4.3% in 2011 [27, 28]. In the present study, the rate of 2.37% was lower than the TSN data in Antalya province. Another study including 201 HD patients from Antalya province reported similar rates of HBsAg positivity (2.5%) [29].

In 2005, strict rules by the Turkish Ministry of Health (TMH) came into force that govern HD centers. Precautions such as isolation of HBsAg positive HD patients in separate rooms, segregation of dialysis machines of anti-HCV positive patients, infection control programs and surveillance of chronical hepatitis B and C disease with vaccination of the susceptible patients mandatory [30]. The reduce of HBsAg seropositivity in TSN data and the low seroprevalence in present study may be the result of the isolation precautions and effective infection control programs [8, 12].

Prevalence of HCV infection is about 3% worldwide and nearly 170 million people are infected. Incidence of HCV infection is higher in HD patients compared to the normal population. HCV seroprevalence in HD patients differs among countries and among HD units in the same country between 4–60% [1, 31]. HCV seroprevalence was reported as 1%–5% in Brasil, Eastern Europe, Mediterranean countries, India, and some Asian and African countries [32]. In DOPPS study, HCV seroprevalence among HD patients in countries including France, Germany, Italy, Japan, Spain, United Kingdom and USA was reported between 2.6% and 22.9% with a mean value of 13.5% [17]. In another registry study in 2009, the seroprevalence was reported as 7.9% in Asia-Pacific countries; below 5% in Australia, New Zealand, Korea, Japan and Thailand; 5%–15% in Hong Kong, Taiwan and Malaysia and over 15% in China [11].

In Turkey, according to a surveillance study conducted in 2001, TMH reported that anti-HCV was found in 23.9% of 21127 HD patients [33]. Additionally, TSN reported that HCV seroprevalence among HD patients was 54.6% in 1997, 15.9% in 2006 and 7.9% in 2011 [27, 28]. In present study we determined HCV seroprevalence as 5.5%, which is similar to the 5.9% reported in Turkish by Daglar et al. in 2014 [29] after a much smaller study, and is lower than the rates reported by the TSN in 1997, 2006, 2011, and of TMH in 2001. The new directives published in 2005 might have had an effect in lowering the rate.

Coexistence of HBsAg and anti-HCV seropositivity among patients who undergo HD in Antalya province was 1.02%, again similar to the 0.9% found in the study by Daglar et al., whereas the rate in Turkey overall was 1.5% according to 2004 TSN data [29, 34].

In the present study, 56% of patients seropositive for HBsAg were also seropositive for HBV DNA, whereas 43% of patients seropositive for anti-HCV were also positive for HCV RNA. In 2003, Sirmatel et al. reported [35] that of 289 patients undergoing HD in Turkey 30% of patients seropositive for HBsAg were also seropositive for HBV DNA, and 25.6% of patients seropositive for anti-HCV were also seropositive for HCV RNA. In an Iranian study reported by Zahedi et al. [36], including 228 patients who underwent HD 37.5% of patients who were seropositive for HBsAg and 43% of patients who were seropositive for anti-HCV had a positive qualitative PCR test [36]. In a more recent study conducted in Taiwan, 57.8% of patients seropositive for HBsAg were also seropositive for HBV DNA, 73.8% of patients seropositive for anti-HCV were also seropositive for HCV RNA [37]. The results of the present study are consistent with the literature, but viral nucleic acid assays were not conducted in every patient, therefore the sensitivity and specificity of serological and virologic tests, and occult hepatitis B and C status could not be shown.

The prevalence of chronic HBV and HCV infection in patients who received HD in Antalya province is moderate-to-low for Turkey. The prevalence has decreased since the 2005 directives of the TMH. Infection control rules, compliance of HD centers with the directives, and active surveillance of patients who undergo HD may have an effect on decreasing rates.

Conflict of interest statement

The authors declare that there is no conflict of interest in this research.

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