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The Prevalence of Hepatitis B Surface Antigen and Hepatitis D Virus Antibody Positivity Among Hemodialysis Patients and Patients With Beta-Thalassemia Major

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Abstract

Background: Patients, who receive hemodialysis and patients with beta-thalassemia major are at great risk for blood-borne viral infections, chiefly different types of hepatitis.
Objectives: This study aimed at assessing the prevalence of hepatitis B and D among hemodialysis patients and patients with beta-thalassemia major in Kashan, Iran.
Methods: This cross-sectional study was conducted in 2016 on 108 patients on hemodialysis and 34 patients with beta-thalassemia major in Kashan, Iran. After explaining the aim of the study to the participants and securing their informed consents, data on their demographic and health-related characteristics were collected through a questionnaire. Then, a five-milliliter venous blood sample was obtained from each participant and tested using enzyme-linked immunosorbent assay technique for hepatitis B surface antigen and hepatitis D virus antibody. The data were entered in the SPSS program (v. 16.0) and analyzed using the Chi-square and the independent-sample t tests.
Results: The prevalence of hepatitis B surface antigen positivity among patients on hemodialysis and patients with beta-thalassemia major was 3.7% and 8.8%, respectively. Moreover, the prevalence of hepatitis D virus antibody positivity among these patients was 2.9% and 1.9%, respectively. The prevalence of hepatitis B surface antigen positivity among patients on hemodialysis had a significant relationship with history of addiction and history of unprotected sex.
Conclusions: The prevalence of hepatitis B and D was respectively 3.7% and 8.8% among hemodialysis patients and 2.9% and 1.9% among patients with beta-thalassemia major. Effective strategies should be employed to minimize the risks of hepatitis B and D transmission among hemodialysis patients and patients with beta-thalassemia major. Moreover, regular screening programs are needed for early diagnosis and treatment of viral hepatitis among these patients.

Keywords: Hepatitis B Surface Antigen, Hepatitis D Virus Antibody, Hemodialysis, Beta-Thalassemia Major

1. Background

Patients, who receive hemodialysis and patients with beta-thalassemia major (BTM) need frequent hospitalizations. Moreover, they undergo different invasive procedures throughout the course of their treatments. They also experience complex health conditions, which can impair their immunity. Therefore, they are at great risk for blood-borne infections, particularly different types of hepatitis, such as hepatitis B and D (1-3).

Hepatitis B is a global health problem with varying prevalence in different areas of the world. Currently, there are 350 million patients with hepatitis B around the world, 15 to 20 million of whom (around 5%) have hepatitis D as well (4, 5).

Hepatitis D results from the highly virulent hepatitis D virus (HDV) and is the most aggressive type of viral hepatitis with rapid progression to liver cirrhosis and failure (4). Furthermore, HDV replication occurs only when hepatitis B virus (HBV) is present (5). There is no credible information about the global prevalence of hepatitis D (4, 5). It's primary reported prevalence was 20% to 30%. However, it has significantly decreased since the onset of HBV immunization in 1980. Hepatitis D has a global distribution with varying prevalence in different areas of the world. Of course, its distribution pattern is not the same as hepatitis B. Its prevalence in the United States and the North of Europe is low, while its prevalence in other areas of Europe is

8.1% to 11%, with the highest prevalence in Eastern Europe (4, 5). Hepatitis D is endemic in the Mediterranean Basin, Middle East, Turkey, Central Africa, and some areas of South America (4).

Studies in different areas of Iran reported varying prevalences of hepatitis D. For instance, a study from Mashhad found that eighteen out of 200 patients (9%) with hepatitis B surface antigen (HBsAg) positivity had anti-HDV antibody (HDVAb) in their serum (6). In another study on 606 HBsAg-positive patients in Mashhad, HDVAb was found in the serum of 35 patients, representing a prevalence of around 5.8% (7). Another study on patients, who were receiving hemodialysis in Tehran found that 7.5% of the cases were HBsAg-positive and 33.3% of HBsAg-positive patients were HDVAb-positive (8). However, a study on 153 hemodialysis patients in the south of Iran showed that nine (5.88%) were HBsAg-positive and none suffered from hepatitis D (9).

There is limited information about the prevalence of hepatitis B and D among hemodialysis and BTM patients in some areas of Iran, including Kashan. This study aimed at assessing the prevalence of hepatitis B and D among patients on hemodialysis and patients with BTM in Kashan, Iran.

2. Methods

This cross-sectional study was conducted during year 2016 on 108 hemodialysis patients and 34 patients with BTM in Kashan, Iran. Eligible patients were identified, provided with information about the study aims, and invited to complete a demographic and health-related characteristics questionnaire. The items of the questionnaire were on marital and employment status, educational level, place of residence, underlying conditions, history of injection drug abuse, and history of unprotected sex. After that, a five-milliliter venous blood sample was obtained from each participant. Blood samples were sent to a local laboratory for serological assessments, respecting HBsAg and HDVAb. Furthermore, HBsAg testing was performed using the DIAPRO kit (manufactured in Italy), enzyme-linked immunosorbent assay technique (ELISA), and Lab-Systems multiskan ELISA reader (manufactured in Italy). The HDVAb testing was also performed using the PRD kit (No. 20128; DIA company, Italy). The HDVAb kits were kept at a temperature of 2 to 8°C. All blood samples were also kept at a temperature of -20°C until all samples were collected. Finally, all serological assessments were performed on samples in the same condition and using the same technique.

Collected data were entered in the SPSS program (version 16.0). The frequency and prevalence values were calculated for HBsAg and HDVAb positivity. Then, the Chi-square and the independent-sample t tests were conducted to compare patients in different groupings of demographic and health-related characteristics, respecting HBsAg and HDVAb positivity. P values less than 0.05 were considered statistically significant.

This study was approved by the Institutional review board and the ethics committee of Kashan University of Medical Sciences, Kashan, Iran. Reliable up-to-date data collection and analysis methods were used to produce reliable results. Participants' data were handled confidentially and their informed consents were obtained.

3. Results

This study was conducted on 108 patients on hemodialysis and 34 patients with BTM in Kashan, Iran. Mean age in these two groups of patients was 59.4 $\pm$ 21.44 and 17.55 $\pm$ 8.52, respectively. Patients on hemodialysis included 74 males (68.5%) and 34 females (31.5%), while patients with BTM included 17 males (50%) and 17 females (50%).

The prevalence of hepatitis B (diagnosed based on HBsAg positivity) among hemodialysis and beta-thalassemia patients was 3.7% (four out of 108) and 8.8% (three out of 34), respectively. There was no statistically significant difference between hemodialysis and BTM patients regarding hepatitis B prevalence (P = 0.2). The prevalence of hepatitis D among these patients was respectively 2.9% and 1.9%, with no significant between-group difference (P = 0.7; Table 1).

Table 1. Comparison of Prevalence of Hepatitis B and D Among Patients on Hemodialysis and Patients with Beta-Thalassemia Major

Test Results	Patients with Beta-Thalassemia Major, No. (%)	Hemodialysis Patients, No. (%)	P Value
HBs Ag-negative	31 (91.2)	104 (96.3)	0.22
HBs Ag-positive	3 (8.8)	4 (3.7)	
HDVAb-negative	33 (97.1)	106 (98.1)	0.7
HDVAb-positive	1 (2.9)	2 (1.9)	

Two out of four HBsAg-positive hemodialysis patients and one out of three HBsAg-positive BTM patients were HDVAb-positive. The prevalence of hepatitis B and D among hemodialysis patients had a significant relationship with history of addiction and unprotected sex (P < 0.05) and no significant relationship with other characteristics (P > 0.05; Table 2). On the other hand, the prevalence

of hepatitis B and D among patients with BTM had significant relationships with their marital status and age ($P < 0.05$), yet had no significant relationship with their other characteristics ($P > 0.05$; Table 3). Moreover, the prevalence of hepatitis B and D coinfection among hemodialysis patients had no significant relationship with their demographic and health-related characteristics ($P > 0.05$).

4. Discussion

The prevalence of HBsAg and HDVAb positivity among 34 patients with BTM in the present study was 8.8% and 1.9%, respectively. The prevalence of HBsAg positivity among patients with BTM in the two studies in India was reported to be 20% (10) and 45% (11), while this rate in a study from Ahvaz, Iran, was 19% (12). These rates are much higher than the rate found by the current study. However, the prevalence of HBsAg positivity in several studies was less than the current study. For instance, a study from India reported that this rate was 3.8% (13). Moreover, two studies from Qazvin and Zahedan, Iran, reported only one case of HBsAg positivity among patients with BTM (14, 15) and two studies in East Azerbaijan province and Markazi province in Iran found no HBsAg positivity among patients with BTM (16, 17). On the other hand, the prevalence rates of HDVAb positivity were 3% in Iran (18) and 16.7% in India (11), which are greater than the prevalence rate of the current study. However, none of the patients in the Indian study were HDVAb-positive (10).

The current findings also showed that the prevalence of HBsAg positivity among 108 hemodialysis patients was 3.7%. Previous studies in Iran reported that 5.88% to 7.5% of hemodialysis patients were HBsAg-positive (8, 9, 19, 20). This rate among 76 hemodialysis and BTM patients in Iran was 7.89% (21). A study from India also reported that 10.2% of high-risk hemodialysis patients were HBsAg-positive (22). The prevalence of HBsAg positivity was also reported to be 8% in Kenya (23), 4.5% in Sudan (24), and 29.8% and 45% in Brazil (25, 26). All these rates were greater than the rate of the current study. However, two studies from Iran reported that the prevalence of HBsAg positivity among hemodialysis patients was 3% in Birjand (27) and 1.4% in Gilan (28). A large-scale study on 4110 patients at 103 dialysis centers in Tehran, Iran, also reported an HBsAg positivity prevalence rate of 2.1% (29). A review study also reported that the prevalence of latent hepatitis B among hemodialysis patients was 2.07% (30). These rates are less than the rate found by the current study. The overall prevalence of hepatitis B among hemodialysis patients varies from 0% to 58% (9). Of course, this prevalence decreased from 3.8% in 1999 to 2.6% in 2006 (29).

The prevalence of HDVAb positivity among patients on hemodialysis in the present study was 2.9%. This rate in previous studies from Iran was 8% (31), 14% (18), and 8.7%, which is much higher than the rate of the current study. However, the prevalence of HDVAb positivity was as low as 0.9% in a study from India (22) and 0% in two studies from Iran (9, 19).

The prevalence rates of hepatitis B (based on HBsAg positivity) and hepatitis D (based on HDVAb positivity) in the present study were different from the rates reported in other areas of Iran. This difference may be due to the more intense screening and immunization programs for hemodialysis and BTM patients. It is noteworthy to mention that the prevalence of blood-borne viral hepatitis in each population depends on the success of health-related and preventive measures (32).

Another finding of the present study was the insignificant relationship of hepatitis B prevalence with patients' gender, marital and employment status, educational level, immunization history, place of residence, and affliction by hyperlipidemia, hypertension, and diabetes mellitus. Moreover, although the HBsAg-positive participants were older than their HBsAg-negative counterparts, the difference was not statistically significant. The results of previous studies regarding the relationship of age and hepatitis B prevalence are contradictory. Some studies reported higher prevalence of the disease among older adults (5, 14, 33), while a study found that afflicted patients were younger than their non-afflicted counterparts (34).

The present study did not examine the relationship of hepatitis B prevalence with the length of hemodialysis, which is a significant factor behind affliction by hepatitis B in hemodialysis units. Another study showed that the use of the same dialysis equipment and machines strongly correlates with hepatitis B prevalence (9). Another study also reported a significant correlation between HDVAb positivity and the number of hemodialysis sessions per month (30). In addition, a study on thalassemia patients found that the number of transfused blood units was significantly correlated with hepatitis B prevalence (21). These correlations highlight the necessity of employing effective strategies for preventing nosocomial infections, particularly different types of hepatitis (33).

Among the limitations of the present study was the assessment of hepatitis B and D prevalence, solely based on HBsAg and HDVAb positivity. It is noteworthy to mention that latent hepatitis B can be diagnosed through hepatitis B core antibodies. However, because of budget deficits, this test could not be performed as part of the current study. Analysis of HDV genome was also not performed in the present study for the same reason. Large-scale studies with different serological assessment methods are needed to produce more credible results.

Table 2. Comparison of Prevalence of Hepatitis B and D Among Patients on Hemodialysis Based on Their Characteristics

Hepatitis		Negative, No. (%)	Positive, No. (%)	P Value
		Gender		
B				0.776
	Male	71 (95.9)	3 (4.1)	
	Female	33 (97.1)	1 (2.9)	
D				0.777
	Male	72 (97.3)	2 (2.7)	
	Female	34 (100)	0	
		Age (y)		
B				0.815
	< 40	21 (95.5)	1 (4.5)	
	> 40	83 (96.5)	3 (3.5)	
D				0.294
	< 40	21 (95.5)	1 (4.5)	
	> 40	85 (98.8)	1 (1.2)	
		Addiction		
B				< 0.001
	No	100 (98)	2 (2)	
	Yes	4 (66.7)	2 (33.3)	
D				0.006
	No	101 (99)	1 (1)	
	Yes	5 (83.3)	1 (16.7)	
		Unprotected sex		
B				< 0.001
	No	104 (97.2)	3 (2.8)	
	Yes	0	1 (100)	
D				< 0.001
	No	106 (99.1)	1 (.9)	
	Yes	0	1 (100)	
		Marital status		
B				0.649
	Single	17 (94.4)	1 (5.6)	
	Married	87 (96.7)	3 (3.3)	
D				
	Single	17 (94.4)	1 (5.6)	0.202
	Married	89 (98.9)	1 (1.1)	
		Place of residence		
B				0.153
	Urban areas	83 (97.6)	2 (2.4)	
	Rural areas	21 (91.3)	2 (8.7)	
D				0.006
	Urban areas	85 (100)	0	
	Rural areas	21 (91.3)	2 (8.7)	

Table 3. Comparison of Prevalence of Hepatitis B and D Among Patients with Beta-Thalassemia Major Based on Their Characteristics

Hepatitis		Negative, No. (%)	Positive, No. (%)	P Value
		Gender		
B				0.545
	Male	15 (88.2)	2 (11.8)	
	Female	16 (94.1)	1 (5.9)	
D				0.31
	Male	17 (100)	0	
	Female	16 (94.1)	1 (5.9)	
		Age (y)		
B				0.014
	< 20	22 (100)	0	
	> 20	9 (75)	3 (25)	
D				0.169
	< 20	22 (100)	0	
	> 20	11 (91.7)	1 (8.3)	
		Marital status		
B				0.034
	Single	30 (93.8)	2 (6.3)	
	Married	1 (50)	1 (50)	
D				< 0.001
	Single	32 (100)	0	
	Married	1 (50)	1 (50)	

4.1. Conclusions

The prevalence of hepatitis B among hemodialysis and BTM patients is 3.7% and 8.8% and the prevalence of hepatitis D among these patients is 2.9% and 1.9%, respectively. Therefore, effective strategies should be employed to minimize the risk of HBV and HDV transmission among these patients. Moreover, regular screening programs are needed for early diagnosis and treatment of viral hepatitis in these patient populations.

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