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Renal Data from Asia-Africa

Hepatitis C Virus Infection among Patients on Hemodialysis: A Report from a Single Center in Iran

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ABSTRACT. The aim of this study is to evaluate the incidence of hepatitis C virus (HCV) infection among the hemodialysis (HD) patients at the Nephrology and Urology Research Center, Tehran, Iran, and identify the potential risk factors. A total of 112 patients on HD in our two dialysis units were studied. The mean duration of follow-up was 27 ± 27 months (range, 6-132). All study subjects were HCV-negative at entry to the study and were tested for anti-HCV antibody by ELISA II every six months thereafter. Positive samples were re-examined by RT/PCR for confirmation. Factors that might be implicated in HCV transmission were evaluated. Six patients (5.3%) were labeled as HCV infected, at the end of the follow-up period. Thus, the incidence of HCV infection in our dialysis units was 1.8 per 100 person years. A total of 64.5% of the study population had previous history of blood transfusion(s) and 8% had undergone prior transplantation. Univariate analysis showed a significant relationship between number of blood transfusions and duration on dialysis and HCV infection. Multivariate analysis revealed that only duration on HD was significantly associated with HCV positivity (OR: 1.03, $p=0.008$). Our study further suggests that nosocomial transmission plays a major role in HCV transmission among patients on HD. Meticulous practice of preventive measures is essential to eradicate the spread of HCV in HD units.

Keywords: Incidence, Hepatitis C virus, Hemodialysis, Nosocomial transmission

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Introduction

Hemodialysis (HD) patients have an increased risk of exposure to hepatitis C virus (HCV). The relevance of HCV infection in HD patients is due to the documented increased risk of death due to chronic liver disease in these patients, particularly after kidney transplantation.¹

The prevalence of HCV infection among HD

patients varies from country to country and from one center to another. The reported prevalence of HCV infection among dialysis patients in developed countries ranges from 3.6 to 20%;²⁻⁴ it is much higher in developing countries.⁵⁻⁸ The prevalence of anti-HCV among dialysis patients was 0.4% in the United Kingdom (2004),² 8.4% in the United States (2000),⁴ 59% in Peru (2005),⁶ 43.9% in Saudi Arabia (2001),⁵ 30% in India (2002),⁷ and 41% in Turkey (2001).⁸ In Iran, similar to most other countries, the prevalence of HCV infection in HD centers is obviously higher than in the general population^{9,10} and varies widely among different provinces of the country, from 5.5% in Shiraz (south)¹¹ to over 24% in Guilan (north).^{10,12} This big difference, suggests the existence of local risk factors for acquiring HCV infection in different regions of Iran.

Several risk factors are suggested to be related to HCV dissemination in HD centers. Repeated blood transfusions, shared dialysis machines, surgery, nosocomial route and multi-dose drug vials are the major suggested routes for spread of HCV infection in HD units.^{10,13} Partial immunosuppression found in HD patients, resulting in a poor antibody response, may play a role in sensitizing them to acquire the infection through uncommon ways.

Despite investigations conducted to document the prevalence of HCV infection among Iranian HD patients,⁹⁻¹³ there is scarce data available regarding the incidence of HCV acquisition in Iranian HD population. To our knowledge, this is the first study to document incident HCV infection and associated risk factors among HD patients in Iran.

In the present study, our purpose was to evaluate the incidence of HCV infection among two HD populations in Tehran, Iran and to determine factors responsible for HCV dissemination.

Materials and Methods

Patients

A total of 112 patients, out of 115 attending regular HD in the dialysis centers at the Neph-

rology and Urology Research Center, Tehran, Iran, were studied; three patients were HCV-positive before the study and were thus excluded. All study patients were recruited for HD between 1990 and 2006 in the centers of study and continued their treatment until the end of the study, at the same center. All patients were negative for anti-HCV antibody at the time of initiation of HD and were re-examined for anti-HCV antibody periodically till the end of the study period.

Laboratory tests

HCV antibodies were tested using Abbott HCV EIA 2 (Abbot) and the Ortho EIA 2 (Ortho diagnostic systems, Raritan, N.J.). These tests were performed every six months on all patients; in suspected subjects, the tests were performed more often. Patients with positive anti-HCV antibody underwent reverse transcription nested PCR as a confirmatory test for determining HCV-infection. Primers of the 5' untranslated region (5' NCR) of HCV genome were used for amplification.

Dialysis centers

HCV-positive patients in the two dialysis centers were dialyzed using dedicated dialysis machines as well as other related instruments such as scissors, blood pressure cuffs and thermometers.

HCV infection criterion

Any specimen with positive serology test and then confirmed with positive PCR examination, was considered as HCV-positive.

Statistical analysis

Quantitative variables are expressed as mean \pm standard deviation (SD). To evaluate risk factors associated with HCV infection and evaluate differences between individual means for categorical variables, the chi-square test and Fisher's test were used and the t-test was performed for quantitative variables. Statistical significance was fixed at 0.05. Risk factors detected by univariate analysis was re-analyzed by multivariate logistic regression. Computations

Table 1. Relationship of the number of dialysis procedure per week, kidney transplantation history, time spent on HD, and hepatitis C virus (HCV) positivity among the study patients

Variables		HCV-positive	HCV-negative	P value
Time spent on dialysis (months)		61.50 ± 51.46 Range: 12-132	27.71 ± 27.54 Range: 1- 132	0.001
Number of dialysis procedure (/week)				NS*
	Twice	1	16	
	Thrice	5	90	
Blood transfusion history				0.02
	Nil	0	40	
	≤5 units	6	24	
	>5 units	0	22	
Kidney transplantation history				0.07
	No	4	99	
	Yes	2	7	
Age (year)		57.83 ± 17.75 Range: 41-79	59.02 ± 14.00 Range: 20-90	NS
Sex (male)		2 (33%)	59 (55%)	NS
Cause of renal failure				NS
	Hypertension	1 (0.9%)	30 (26.8%)	
	Diabetes mellitus	1 (0.9%)	45 (40.2%)	
	Glomerulonephritis	2 (1.8%)	7 (6.3%)	
	Poly cystic kidney	0 (0%)	5 (4.5%)	
	Others	2 (1.8%)	19 (17.0%)	

*NS; Not Significant

Table 2. Incidence rates of hepatitis C infection and the duration on dialysis among the study patients

Time after entering regular HD program	Incidence (per 100 person years)
1 st year	0.9
2 nd year	1.4
3 rd year	2.3
4 th year	3.4
10 th year	18.2
11 th year	66.7
Total	1.8

were done in SPSS (Statistics Program for Social Sciences version 13.0, SPSS Inc., Chicago, IL, USA).

Results

Sixty-one male and fifty-one female patients aged between 20 and 90 years were enrolled into the study. Of them, 26 (23%) were under 50 years of age and 86 (77%) were above 50 years. Patients were followed-up for a mean pe-

riod of 27.71 ± 27.58 months (range: 3-132). Seventy-two patients (64.3%) had a positive history of receiving blood transfusion(s) and nine (8%) had undergone prior renal transplantation. At the end of the study period, six of the study patients were labeled as HCV-positive. Demographic characteristics of HCV-positive and negative subjects are shown in Table 1. The incidence of HCV infection in our dialysis units was 1.8 per 100 person-years. The incidence rates of HCV infection in relation to duration on dialysis are shown in Table 2.

The HCV-positivity rates were not statistically different between patients who received blood transfusions (64.3%) and those who did not (35.7%, $p=0.065$); also, there was no correlation with the cause of kidney failure ($p=0.19$).

Univariate analysis showed that the time spent on HD and the number of transfused blood units was associated with HCV-positivity (Table 1). However, multivariate logistic analysis revealed that only the time (months) spent on HD was significantly associated with HCV infection in

Table 3. Multivariable Logistic regression for evaluation of independent impact of potential risk factors of HCV transmission in our dialysis centers

Variable	Odds ratio	Confidence interval	P-value
Time on HD	1.03	1.008-1.053	0.008
Number of blood transfusions	1.27	0.876-1.687	0.125
Kidney transplantation history	1.65	0.452-1.89	0.565

our patient population (OR = 1.03; Table 3).

Discussion

Despite the considerable decline in the incidence and prevalence of HCV infection among HD patients in many countries,^{3,14-16} this infection still remains a major problem among patients on maintenance HD. The immune suppression seen in this patient population, resulting in an absence of clinical and biochemical evidence of liver disease, is believed to accelerate further dissemination of the virus.¹⁷

The relevance of HCV infection is due to its well documented progression to hepatic cirrhosis, liver malignancies and liver failure, which is the single most common indication for liver transplantation.^{3,18} The long-term outcome of HCV infection among HD patients is not entirely clear. However, HCV infection is considered to be of particular relevance in this group of patients and can result in disastrous sequelae after kidney transplantation due the immunosuppressive therapy used.¹⁹

The incidence of HCV infection found in our HD patients is higher than that seen in some developed countries like the UK, Italy and Germany (0% per year),³ and France (0.4% per year).²⁰ However, our incidence rate is lower than reports from Greece, (6.2 per 100 person years)²¹ and Spain (11% per year).³

It seems that countries with higher prevalence of HCV infection in their general population, have a higher prevalence of this infection among HD patients.^{5,22} In Iran, the prevalence of HCV infection in blood donors is less than 1% (0.1 to 0.9%),^{9,23-25} which is lower than that of other countries in the region: 1.1% in Yemen,²⁶ 1.8% in Saudi Arabia²² and 4% in Pakistan.²⁷ In other regions of the world, the prevalence of HCV infection in healthy blood donors ranges from 0.01–0.02% in northern Europe and 1–1.5%

in southern Europe to 6.5% in parts of equatorial Africa.^{28,29}

The mechanisms responsible for transmission of HCV in HD units are not fully elucidated. In one study conducted in seven HD centers of Guilan, a province of Iran, investigators found that the duration spent on HD and previous transplantation history were significantly associated with HCV infection.¹² Another study in Shiraz, Iran, demonstrated that cross-infection through dialysis machines was mainly responsible for the dissemination of HCV in the two evaluated HD centers.¹¹ In a report from Tehran, the number of blood units transfused and previous transplantation history were related to HCV infection among HD patients.¹⁰

Before implementation of blood screening for HCV, blood transfusion was a major route for HCV transmission in HD patients in many countries.^{15,30} In a study conducted in Peru, the number of blood transfusions and time on HD were incriminated for the high prevalence (59%) of HCV infection among HD patients.⁶ In Brazil, before 1993, the reported prevalence of HCV infection amongst HD patients was considerably high (37.8%) and blood transfusion was believed to be a major route for HCV transmission.¹⁵ However, after the implementation of “universal precautions for prevention of HCV transmission” and screening of all blood donors for presence of HCV in their serum samples, the prevalence of HCV infection has dropped to 16.5% in 2002.¹⁶ In addition, the risk of HCV infection among HD patients who received blood transfusions after 1993 was found to be 6.5-fold lower than in patients who were transfused before 1993.¹⁵ Despite the absence of anti-HCV screening of blood donors in Iran, blood transfusion did not prove to be a risk factor for HCV infection in our HD population. Nevertheless, all our HCV-positive subjects had positive history of blood transfusions.

This result corroborates the findings of a fair number of previous studies investigating risk factors for HCV dissemination in Iranian HD centers^{11,12} but differs from some other studies.¹⁰

History of previous surgery is also widely reported as a risk factor for HCV dissemination in HD centers worldwide.^{8,12} In a Turkish study, surgery was reported as the most common risk factor for HCV infection among their HD population.⁸ In Iran also, a number of investigations found surgery as a risk factor for HCV acquisition in their HD populations.^{10,12} However, we did not detect any relationship between previous transplantation history and HCV infection among our study subjects.

Although, universal measures of asepsis (changing of gloves after each patient manipulation, avoiding sharing of articles among patients),^{31,32} and disinfection of environmental surfaces and machines are routinely done in our HD units, an interview of all nurses revealed breakdown in infection-control measures. It was not unusual to find staff taking care of susceptible and infected patients in the same shift. Additionally, they did not routinely discard gloves after use.

A limitation of our study was that we did not test our study patients, including anti-HCV negative subjects, for the presence of HCV RNA in their blood samples. Huang et al. and Bukh et al. detected HCV RNA in 4% and 5% of their anti-HCV negative patients, respectively.^{33,34} A Venezuelan investigation reported presence of HCV RNA in 24% of their anti-HCV negative HD patients.³⁵ According to these studies,³³⁻³⁷ relying on serologic tests alone, especially in HD patients, could underestimate the prevalence of HCV infected patients.

Conclusion

This study, with a mean follow-up of 27.71 months, showed a relatively low incidence of HCV infection in our HD patients. We found that longer duration on dialysis is a risk factors for HCV infection in our HD patients' suggesting the role of nosocomial transmission of HCV in our dialysis units.

Despite a lack of significance found for impact of blood transfusion on HCV-positivity, the role of transfusions could not be excluded. More careful surveillance in dialysis units and blood donors is required. Despite the valuable previously published data,³⁸⁻⁴⁰ further prospective studies are needed to investigate the incidence of HCV transmission in different HD centers of Iran with different intensity and stringency of adherence to hygienic measures.

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