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ORIGINAL STUDIES

Factors Associated to the Prevalence of Antibodies to Hepatitis C Virus Among Patients Receiving Hemodialysis at Selected Dialysis Centers in Puerto Rico, 2005

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***Background*:** Limited information about the epidemiology of hepatitis C virus (HCV) infection is available in hemodialysis patients in Puerto Rico. We assessed the factors associated to the prevalence of antibodies to HCV (anti-HCV) among patients receiving hemodialysis in eight dialysis centers in Puerto Rico.

***Methods*:** A systematic sampling design was employed to select a sample of 150 hemodialysis patients (30 anti-HCV + and 120 anti-HCV -) 21 years and older during 2005. A total of 110 (81.5%) from 135 eligible patients completed a face-to-face interview that gathered data on demographics, and self-reported risk behaviors followed by a clinical record review. Variables that were marginally or significantly associated with the prevalence of anti-HCV (p<0.10) in the bivariate analyses were considered for inclusion into the multiple logistic regression model to estimate the adjusted prevalence odds ratio (POR).

***Results*:** Bivariate analysis revealed that age ($P\hat{O}R_C$=3.65, p=0.05), blood transfusions prior to 1992 ($P\hat{O}R_C$=5.13, p=0.05), tattooing practices ($P\hat{O}R_C$=13.29, p=0.04), and illegal drug use ($P\hat{O}R_C$ =4.53, p=0.01) were associated with anti-HCV. Multivariate analysis revealed that blood transfusions prior to 1992 ($P\hat{O}R_A$ = 11.05; p=0.04) remained significantly associated with anti-HCV after adjusting for age, tattooing practices, illegal drug use and dialysis center. Age ($P\hat{O}R_A$=5.40; p=0.06) was marginally associated with anti-HCV after adjusting for blood transfusions prior to 1992, tattooing practices, illegal drug use and dialysis center.

***Conclusions*:** The present study showed that the profile of risk factors for the hemodialysis population was similar to the profile of risk factors reported in the general population.

Key words: Hepatitis C, Hemodialysis patients, Risk factors, Puerto Rico

Hepatitis C virus (HCV) infection is the leading cause of chronic liver disease and liver transplant in the United States (U.S.) (1). Established risk factors for HCV infection include injection drug use, blood transfusion, and solid organ transplantation from infected donors prior to July 1992, receipt of blood clotting products before 1987, occupational injury, and vertical transmission. Other potential exposures for infection that have been investigated in epidemiologic studies include history of intranasal cocaine use, sharing of contaminated equipment and personal care items, tattooing, body piercing, imprisonment, acupuncture, and use of contaminated healthcare instruments (2).

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HCV infection is a persistent public health concern in hemodialysis (HD) patients. HD patients are vulnerable to HCV infection because of the risk for exposure to HCV associated with the dialysis procedure (3). Epidemiologic studies have shown that risk factors for HCV infection among HD patients include number of blood transfusions, duration of end-stage renal disease (ESRD), prevalence of HCV infection in the dialysis unit, history of organ transplantation, intravenous drug abuse and male sex (4). Other factors that may affect the risk of transmission of HCV to patients in dialysis centers include breakdown in standard infection control practices by the healthcare workers that are in direct contact with the patient (5-6), physical proximity to an infected patient, and dialysis machines (7-8). Several reports have linked a high incidence of HCV infection in dialysis patients who share dialysis machines in the hemodialysis unit (9-10). Nonetheless, the use of dedicated machines and isolated areas for anti-HCV positive patients along with strict enforcement of universal precautions has been associated with a decrease in the incidence of HCV seroconversion (8, 11). Therefore, risk factors for HCV

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infection in patients receiving HD can be categorized as either extrinsic or intrinsic to the dialysis unit.

In contrast with the hepatitis B virus (HBV), no vaccine is available for HCV (12). HCV infection in patients with ESRD has been associated with greater morbidity and mortality (3). According to the National Surveillance of Dialysis-Associated Diseases in 2002, HCV infection affects approximately 7.8% of chronic HD patients in the U.S. (13). The prevalence of anti-HCV among ESRD networks in the U.S. in 2002 ranged from 5.5% to 9.8%, where the prevalence of anti-HCV for Puerto Rico and New Jersey (ESRD network #3) was the highest (9.8%). Moreover, the incidence rate was 0.34%, similar to the rate observed in 2001 (0.29%). Reasons for the higher prevalence of HCV among ESRD patients in Puerto Rico and New Jersey are unknown; however, networks with higher anti-HCV prevalence are more likely to test their patients for anti-HCV. The percent of centers testing for anti-HCV ranged from 50% (ESRD network #15 and #16) to 80% (ESRD network #3). In 2001, routine testing of HD patients for anti-HCV on admission and every 6 months was recommended (14), thus differences in the percent of centers testing for anti-HCV may explain these differences.

A study in three hemodialysis units in the western region of Puerto Rico revealed a prevalence of 2% (15). Information about the epidemiology of HCV infection in chronic HD patients in Puerto Rico is limited. We assessed the factors associated to the prevalence of antibodies to anti-HCV in a sample of eight dialysis centers in Puerto Rico.

Methods

Sample

A stratified sampling design was employed to select a random sample of 150 patients among 666 HD patients 21 years and older attending eight dialysis centers throughout the island during 2005. The first stratum consisted of all anti-HCV positive patients (n=30). The second stratum consisted of 120 anti-HCV negative patients (four anti-HCV negative patients per each anti-HCV positive patient) selected in a systematic fashion (16).

Data collection

After obtaining written informed consent, all HD patients completed a structured face-to-face interview to gather data on demographics and self-reported risk behaviors followed by a clinical record review. Patients were interviewed after undergoing HD at one of the three shifts available per day (6 AM, 10 AM, 4 PM). The questionnaire covered demographics, drug use and sexual risk practices measured over the lifetime, tattooing practices, body piercing, receipt of blood transfusions and organ transplant, and self-reported medical history. The clinical record review gathered information on primary and secondary causes of ESRD, years on HD treatment, history of HBV vaccination, and results of laboratory tests for the detection of anti-HCV (ADVIA Centaur HCV assay, Bayer HealthCare LLC for Ortho-Clinical Diagnostics, Tarrytown, NY, USA) during 2005. The study protocol was approved by the Institutional Review Board of the University of Puerto Rico Medical Sciences Campus.

Statistical analysis

Frequency distributions were computed to describe demographics and high-risk behaviors of the study group. To evaluate the association between high-risk behaviors and anti-HCV prevalence, unadjusted prevalence odds ratios (POR) were computed. Variables that were marginally or significantly associated with anti-HCV (p<0.10) in the bivariate analyses were considered for inclusion into the multiple logistic regression model to estimate the adjusted POR. All possible first-order interactions were assessed in the model. All unadjusted and adjusted parameters were estimated using generalized estimating equations (GEE) method to control for the adjusted intra-class correlation ($\hat{\rho}$= 0.4749) among patients of the same dialysis center. Data management and statistical analyses were performed using Stata (Version 9.0, College Station, TX, USA).

Results

Of the estimated 150 patients required for the study, 15 were excluded for various reasons: 6 were too ill to be interviewed (4 anti-HCV+, 2 anti-HCV-), 8 died before being approached (6 anti-HCV+, 2 anti-HCV-), and 1 had an indeterminate anti-HCV result. Of the remaining 135 eligible patients, 25 patients (3 anti-HCV+, 22 anti-HCV-) refused to participate in the face-to-face interview due to the hour of HD treatment (6 AM) (Figure 1).

Thus, the study sample size comprised 110 patients (16 anti-HCV+, 94 anti-HCV-), attaining an overall response rate of 81.5%. The number of anti-HCV positive patients varied significantly (p<0.0001) by dialysis center, with a greater number of anti-HCV patients observed in center 2 (Table 1). Therefore, the dialysis centers were grouped as follows: center 2 versus other centers (1, 3, 4, 5, 6, 7, 8). Participation rates by center were similar (p>0.05) by sex (Table 2). However, participation rates in other dialysis centers significantly (p < 0.0001) differed by age. The main reasons for non-participation among patients receiving HD
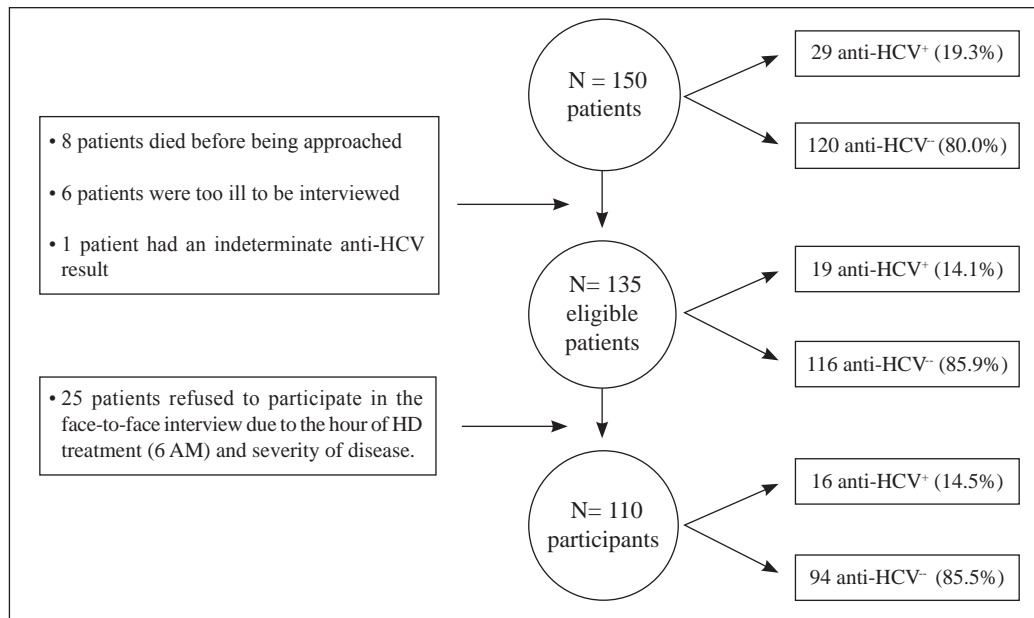
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Figure 1. Selection of study group

Table 1. Anti-HCV positive patients by dialysis center (n=110).

Dialysis center	Number of patients	Number (%) of anti-HCV positive patients
1	14	0 (0.0%)
2	17	10 (58.8%)
3	16	2 (12.5%)
4	10	1 (10.0%)
5	16	1 (6.3%)
6	13	1 (7.7%)
7	13	1 (7.7%)
8	11	0 (0.0%)
Total	**110**	**16 (14.5%)**

Table 2. Comparison between participants and non-participants by dialysis center (n=135).

	Center 2			Other centers (1, 3-8)		
	Participants f_i (%)*	Non-participants f_i (%)*	p-value†	Participants f_i (%)*	Non-participants f_i (%)*	p-value†
Sex						
Female	5 (29.4)	0 (0.0)		34 (36.6)	6 (28.6)	
Male	12 (70.6)	4 (100.0)		59 (63.4)	15 (71.4)	
Total	17	4	p=0.53	93	21	p=0.62
Age in years						
≤ 60	10 (58.8)	0 (0.0)		54 (58.1)	0 (0.0)	
> 60	7 (41.2)	4 (100.0)		39 (41.9)	21 (100.0)	
Total	17	4	p=0.09	93	21	p<0.0001

*f_i indicates frequency   †Fisher's exact test

in other centers were hour of HD treatment (6 AM) and severity of disease. Among the 110 HD patients, 64.5% were males, 58.2% were 60 years or younger, 51.8% had been in HD treatment for 32 months or less, and 49.1% had diabetes mellitus as the primary cause of ERSD (Table 3). Three (2.7%) patients reported tattooing practices, 1 (1.0%) reported ear or other body piercing, 17 (15.5%) reported illegal drug use, 44 (40.0%) reported an early age (<18 years) at first sexual intercourse, 69 (62.7%) reported two or more sexual partners over their lifetime, 7 (6.4%) reported blood transfusions prior to 1992, and 2 (1.8%) reported an organ transplant prior to 1992. The following variables were significantly associated with anti-HCV in the bivariate analysis: blood transfusions prior to 1992

($P\hat{O}R_C$=5.13; 95% CI: 1.03-25.59), tattooing practices ($P\hat{O}R_C$=13.29; 95% CI: 1.13-156.34), and illegal drug use ($P\hat{O}R_C$=4.53; 95% CI: 1.38-14.91). Age ($P\hat{O}R_C$= 3.65; 95% CI: 0.98-13.68) was marginally associated with anti-HCV (Table 4). First-order interaction terms were not statistically significant (p>0.10). Multivariate analysis revealed that blood transfusions prior to 1992 ($P\hat{O}R_A$= 11.05; 95% CI: 1.15-105.68) remained significantly associated with anti-HCV after adjusting for age, tattooing practices, illegal drug use and dialysis center. Age ($P\hat{O}R_A$= 5.40; 95% CI: 0.94-30.99) was marginally associated with anti-HCV after adjusting for blood transfusions prior to 1992, tattooing practices, illegal drug use and dialysis center.

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Table 3. Demographic and risk-related characteristics of the study group (n=110).

Characteristics	Number	%
Sex		
Female	39	35.5
Male	71	64.5
Age in years		
≤ 60	64	58.2
> 60	46	41.8
Mean (SD): 56.9 ± 11.9 years		
Time in dialysis (months)		
≤ 32	57	51.8
> 32	53	48.2
Mean (SD): 46.9 ± 43.5 months		
Primary cause of ESRD		
Diabetes mellitus	54	49.1
Hypertension	38	34.6
Glomerulonephritis	13	11.8
Other	5	4.5
Tattooing practices		
Yes	3	2.7
No	107	97.3
Ear or other body piercing		
Yes	1	1.0
No	109	99.0
Illegal drug use*		
Yes	17	15.5
No	93	84.5
Age at first sexual intercourse in years (n=104)		
< 18	44	40.0
≥ 18	60	54.6
Lifetime number of sexual partners		
≥ 2	69	62.7
0-1	41	37.3
Blood transfusion prior to 1992		
Yes	7	6.4
No	103	93.6
Organ transplant prior to 1992		
Yes	2	1.8
No	108	98.2

*Illegal drug use was defined as lifetime use of marijuana, cocaine, heroin, crack or injection drug use.

Conclusions

This is the first epidemiological study that assessed the factors associated with the prevalence of antibodies to HCV in patients receiving HD in a sample of dialysis centers in Puerto Rico. A previous study in three dialysis units in the western region of Puerto Rico reported blood transfusions, organ transplantation and illicit intravenous drug use as major risk factors for HCV infection (15). Our data evidenced that multiple risk factors were found to be present in HD patients; however, only a history of blood transfusions prior to 1992 (p<0.05) was significantly associated to anti-HCV after adjusting for age, tattooing practices, illegal drug use and dialysis center. Age was marginally associated to anti-HCV after adjusting for blood transfusions prior to 1992, tattooing practices, illegal drug use and dialysis center.

Some studies have revealed that anti-HCV positive HD patients had received significantly more units of blood products than anti-HCV negative patients (17). In our study, history of blood transfusions prior to 1992 was significantly correlated with anti-HCV; however, the number of blood products transfused was not consistently documented in all medical records. Increased prevalence of HCV infection in HD patients with a history of illegal drug use has been previously reported (18). Not surprisingly, in our study, a history of illegal drug use was associated with anti-HCV in the bivariate analysis. However, it did not remain an independent risk factor for anti-HCV in the multivariate analysis. History of organ transplantation prior to 1992 is a known risk factor for HCV infection in patients receiving dialysis (18). In our study, history of organ transplantation was not evaluated because only two patients reported such a history. A history of tattooing practices was the strongest risk factor associated with anti-HCV in the bivariate analysis; however, this variable did not reach statistical significance in the multivariate analysis since only three patients reported this practice.

Male sex, duration of dialysis and other risk factors such as lifetime number of sexual partners and age at the first sexual intercourse were not significantly associated with anti-HCV in the present study. These results may be partially explained by the limited number of anti-HCV positive patients included in the study.

Caution must be exercised in interpreting these results as generalizable to the HD population of Puerto Rico. In the first place, the present study was limited to the population of patients with ESRD receiving HD in eight dialysis centers in Puerto Rico. Second, the final sample size was reduced to 110 (73.3%), contributing to a greater imprecision in the POR estimation. Third, information of HCV risk factors may have been under-reported. Fourth, the cross-sectional nature of the investigation limits our ability to attribute a temporal relation between high-risk behaviors and prevalent HCV infection.

Further investigations with a representative sample of the HD population in Puerto Rico are needed to determine the incidence and prevalence of HCV infection, risk factors for viral acquisition, and awareness of HCV preventive practices among chronic HD patients. Such studies are essential for monitoring preventive strategies in dialysis settings. Finally, systematic implementation of the 2001 recommendations for preventing transmission of infections among chronic hemodialysis patients are

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Table 4. POR estimation to assess the association between anti-HCV and different variables (n=110).

Variable	Unadjusted $P\hat{O}R$* (95% CI)	Adjusted $P\hat{O}R$† (95% CI)	p-value‡
Age in years			
≤ 60	3.65 (0.98-13.68)	5.40 (0.94-30.99)	0.06
> 60§	1.00	1.00	
Blood transfusion prior to 1992			
Yes	5.13 (1.03-25.59)	11.05 (1.15-105.68)	0.04
No§	1.0	1.00	
Tattooing practices			
Yes	13.29 (1.13-156.34)	4.71 (0.16-135.16)	0.37
No§	1.0	1.00	
Illegal drug use			
Yes	4.53 (1.38-14.91)	1.35 (0.24-7.72)	0.73
No§	1.00	1.00	

*Unadjusted $P\hat{O}R$ was estimated using a simple logistic regression model through the GEE method.
†Adjusted $P\hat{O}R$ for dialysis center and all other listed variables was estimated using a multiple logistic regression model through the GEE method.
‡p-values from Wald test obtained in the multiple logistic regression model.
§Reference category

essential for evaluating the effectiveness of control practices in HD units in Puerto Rico (14).

The present study showed that the profile of risk factors for the HD population was similar to the profile of risk factors reported in the general population (1, 19). Routinely testing for HCV infection among HD patients provides the opportunity to reduce the risk of transmission of HCV in the dialysis setting and optimize patient's care.

Resumen

Los estudios epidemiológicos sobre la hepatitis C en pacientes de hemodiálisis en Puerto Rico son limitados. El presente estudio determinó los factores asociados a la prevalencia de anticuerpos para el virus de la hepatitis C (VHC) entre pacientes de hemodiálisis en ocho centros de diálisis en Puerto Rico. Se utilizó un muestreo sistemático para seleccionar a 150 pacientes mayores de 21 años que recibían hemodiálisis (30 anti-VHC+ y 120 anti-VHC -) durante 2005. Un total de 110 (81.5%) de 135 pacientes elegibles completaron la entrevista personal para obtener información sociodemográfica y factores de riesgo seguido por una revisión del expediente clínico. Las variables que se asociaron marginal o significativamente con la prevalencia de anti-VHC (p<0.10) en el análisis bivariado se incluyeron en el modelo de regresión logística múltiple para estimar el POR ajustado. El análisis bivariado reveló que la edad ($P\hat{O}R_C$=3.65, p=0.05), transfusión de sangre antes de 1992 ($P\hat{O}R_C$ =5.13, p=0.05), historial de tatuajes ($P\hat{O}R_C$ =13.29, p=0.04) y uso de drogas ilegales ($P\hat{O}R_C$= 4.53, p=0.01) se asociaron con la prevalencia de anti-VHC. El análisis multivariado reveló que las transfusiones de sangre antes de 1992 ($P\hat{O}R_A$= 11.05, p=0.04) fue el único factor que se asoció significativamente a la prevalencia de anti-VHC cuando se controla por edad, historial de tatuajes, uso de drogas ilegales y centro de diálisis. La edad se asoció marginalmente ($P\hat{O}R_A$= 5.40, p=0.06) a la prevalencia de anti-VHC cuando se controla por transfusiones de sangre antes de 1992, historial de tatuajes, uso de drogas ilegales y centro de diálisis. El presente estudio demuestra que el perfil de los factores de riesgo para la población de hemodiálisis es similar al perfil de los factores de riesgo informados para la población general.

Acknowledgements

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