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Prevalence of Hepatitis C Virus Infection among Hemodialysis Patients at a Tertiary-Care Hospital in Mexico City, Mexico

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We determined the prevalence of hepatitis C virus (HCV) in hemodialysis patients by antibody testing and HCV RNA determination by PCR. A total of 149 patients with kidney failure with replacement therapy were tested. The prevalence of anti-HCV was 6.7% (10 of 149 patients), and viremia was detectable in 8 of 149 (5%) patients. Three of 149 patients (2%) were anti-HCV negative with detectable HCV RNA.

Hepatitis C virus (HCV) is an RNA virus member of the family *Flaviviridae* (9). Approximately 170 million people in the world are infected with HCV (13). In Mexico its prevalence is approximately 1.2% (25). High prevalence of HCV infection is observed in transfusion recipients (before 1989); intravenous drug abusers; health providers; incarcerated, institutionalized, and homeless persons; and people with a history of cocaine and marijuana use or high-risk sexual behavior (1, 9, 14).

HCV infection is frequent in patients undergoing chronic hemodialysis (HD), with a prevalence between 8 and 10%, and there is a particular concern because of the high risk for chronic liver disease, complications in renal transplantation, and death in these patients (18, 19). The extensive use of recombinant erythropoietin to correct renal anemia in HD patients resulted in a significant reduction in blood transfusions. However, previous studies have shown that de novo infections in single HD units may still occur in the absence of other parenteral risk factors (7). It has been suggested that infection could be transmitted from patient to patient in the hospital, and there is now indirect evidence that HCV infection occurs among HD patients during repeated dialysis procedures, but not through the equipment, probably due to procedural errors (15).

The health minister of Mexico recommends screening for HCV infection in chronic HD patients with elevated levels of aspartate aminotransferase, alanine aminotransferase, and anti-HCV antibodies monthly (21). Alanine aminotransferase levels in HD patients with HCV infection typically are within the normal laboratory range despite hepatitis C viremia and histological disease (19). In this study we determined the prevalence of HCV infection by detecting HCV RNA in an HD unit. Participants were interviewed, and data were extracted from their medical records. Serum specimens from all patients were screened for anti-HCV (confirmed by blind repeated analyses) with the Axsyum system, HCV version 3.0 (Abbott Laboratories Ltd., Wiesbaden, Germany). HCV RNA was also screened in all sera (confirmed by blind repeated analyses) by qualitative PCR to confirm active infection and by quantitative real-time PCR using a modified procedure from Roche (50 to 7,000,000 IU/ml). In HCV RNA-positive patients, genotyping was performed by using the HCV RNA Genotype Duplitype assay (Quest Diagnostics), a DNA sequencing technology, to subtype two regions of the HCV genome: the CORE gene and NS5B region. Also, the serum specimens from all patients were screened for anti-hepatitis B virus surface (HBs) antibodies by using an anti-HBs antibody assay kit (Abbott; RIA kit) and for human immunodeficiency virus (HIV) by using the automated Axsym HIV 1/2gO assay (Abbott Diagnostics Division, Delkenheim, Germany). The results are expressed as a means ± standard deviations.

One hundred forty-nine patients with kidney failure with replacement therapy (KFRT) on HD were included; 79 (53%) were male and 70 (43%) were female, and the mean age was 51 ± 17 years.

The prevalence of anti-HCV-positive patients was 6.7% (n = 10), and HCV RNA was detected in eight (5%) patients. Three patients (2%) were HCV RNA positive with no detectable antibodies. The quantitative HCV RNA range was from undetectable to 953,000 IU/ml. The main causes of KFRT were diabetic nephropathy, reflux nephropathy, and glomerulonephritis.

Serum HCV RNA from one patient could not be sent for quantitative PCR and genotyping because of patient death. Genotypes were detected as follows: four patients had 1a, two patients had 1b, and the other genotype could not be detected because of a low viral load. None of the anti-HCV-positive patients were HBs antibody positive, and all subjects were HIV negative.

Patients on chronic HD have a high prevalence of HCV infection, which is now recognized as the principal cause of liver disease in adults with KFRT (3, 8). In a previous study Gonzalez-Michaca et al. (10) found an anti-HCV positivity prevalence of 10.2% in Mexican patients in KFRT with HD. In the present study we found a prevalence of 6.7% seropositive patients. In HD and immunocompromised subjects the sensitivity of the anti-HCV antibody enzyme immunoassay is lower, ranging from 50 to 95%, depending most likely on the depth of

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immunosuppression (5), and it may be appropriate to determine the presence of the virus itself in the circulation by detecting HCV RNA (6).

Although HCV viremia in HD patients is lower than that in HCV patients without KFRT (7, 24), probably because of the destruction of viral particles by the HD procedure (16), RNA testing is widely accepted as the "gold standard" in HCV detection in the HD population (19).

Hinrichsen et al. (11) in a multicenter study found an HCV RNA positivity prevalence of 4%; 21.6% of patients were seronegative. In the present study we found an HCV RNA positivity prevalence of 5% and three (2%) patients were seronegative. In a previous study Sheu et al. (23) found similar data for a Taiwan population where, of the 47 HCV RNA-positive cases, only 83.0% were positive by a second-generation anti-HCV immunoassay. Bukh et al. (2) in a Danish study found that eight dialysis patients ($n = 340$) had detectable levels of HCV RNA but were seronegative by second-generation enzyme-linked immunosorbent assays. Finally Schroter et al. (20) found in a German population that, among the 238 seronegative patients, HCV infection was detected in 12 cases (5.0%), exclusively by PCR. Contrariwise, Dalekos et al. (4) found that none of the anti-HCV-negative HD patients ($n = 81$) were shown to be viremic by the combined reverse transcriptase PCR and DNA enzyme immunoassay method. Additionally Kelley et al. (12) showed that, in an American population, none of the 233 HCV antibody-negative patients were viremic by PCR. These findings show the importance of HCV RNA testing for detection of HCV infection.

In the United States, the vast majority of the patients are infected with HCV genotypes 1a and 1b (17). In this study we found genotype 1a to be the most prevalent genotype in the patients studied (four patients), followed by genotype 1b (two patients). There is a clear relationship between HCV genotype and response to interferon therapy (6). HCV of genotype 1 is less amenable to treatment than HCV of genotypes 2 and 3 (22).

In conclusion, early detection of HCV infection is important in patients with KFRT undergoing HD because of the high prevalence of infection. This early detection could result in better management of patients and a reduction in patient-to-patient transfer of HCV infection in HD units. The results of this study confirm that detection of the anti-HCV antibody alone does not exclude the possibility of HCV infection in HD patients and the importance of HCV RNA detection by PCR in screening for HCV infection in these patients.

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