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EDITORIAL

# A shield against a monster: Hepatitis C in hemodialysis patients

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# Abstract

Hepatitis C virus (HCV) infection is highly prevalent among patients on hemodialysis (HD). The prevalence of HCV infection in HD patients varies markedly from country to country. Some factors are especially related to these high prevalence rates, such as blood transfusions and length of dialysis time. Nosocomial routes of transmission including the use of contaminated equipment and patient-to-patient exposure is considered more important. Several prophylactic measures have been suggested to avoid infection by HCV in the HD environment.

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**Key words:** Dialysis; Epidemiology; Hepatitis C virus; Incidence; Isolation; Nosocomial transmission; Prevalence; Prevention; Universal precaution

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# INTRODUCTION

Hepatitis C virus (HCV) infection is considered a major public health problem worldwide. Patients with chronic renal failure who are on hemodialysis (HD) have a high prevalence of HCV. They are among the highest risk groups for the acquisition of HCV infection<sup>[1-3]</sup>. Prevalence of HCV infection has decreased in this group in recent years<sup>[4]</sup>, but still remains a significant public health concern. HCV-infected patients on HD have significant liver disease and a decreased life expectancy<sup>[5,6]</sup>. The relative risk for death in HCVinfected patients on HD compared with non-infected patients is greater than 1.4<sup>[6-8]</sup>. In addition, HCV infection leads to decreased graft and patient survival in renal transplant recipients<sup>[9,10]</sup>. On the other hand, due to the increased prevalence of non-communicable diseases such as diabetes mellitus and hypertension, and their complications, chronic renal failure has become a more serious health issue throughout the world<sup>[11]</sup>. Therefore, the clinical importance of HCV has been increasingly recognized in the dialysis community.

## PREVALENCE AND INCIDENCE

HCV prevalence in HD varies geographically, both within and between countries<sup>[12]</sup>. The reported anti-HCV seropositivity since 1999 ranges from low (1.9%) in the Slovenian 2001 Annual Report<sup>[13]</sup> to high (80%) in Senegal<sup>[14]</sup>. HCV seroprevalence in the HD population was 59% in Bosnia and Herzegovina<sup>[15]</sup>, 6.8% in Belgium<sup>[16]</sup>, 16.3% in France<sup>[2]</sup>, 6.1% in Germany<sup>[17]</sup>, 10%-29% in Greece<sup>[18-20]</sup>, 22.5%-32.1% in Italy<sup>[21,22]</sup>, 1070-2976 in Greece 1, 22.570-52.176 in Italy 17, 75% in Moldavia<sup>[23]</sup>, 3.4% in the Netherlands<sup>[24]</sup>, 1.9% in Slovenia<sup>[13]</sup>, 11% in Sweden<sup>[25]</sup>, 7%-23.3% in the USA<sup>[26-30]</sup>, 4% in the UK<sup>[31]</sup> 20.5% in Libya<sup>[32]</sup>, 71% in Kuwait<sup>[31]</sup> 80% in Senegal<sup>[14]</sup>, 23.7% in Sudan<sup>[33]</sup>, 19%-41.7% in Tunisia<sup>[34,55]</sup>, 8.4%-43.2% in Brazil<sup>[36-39]</sup>, 6.7% in Mexico<sup>[40]</sup>, 59.3% in Peru<sup>[41]</sup>, 3.5% in Puerto Rico<sup>[42]</sup> and 13.2% in Iran<sup>[43]</sup>. Some investigators have suggested a decline in HCV prevalence among HD patients in recent years, mostly attributable to strict adherence to universal precautions with<sup>[16,44-49]</sup> or without<sup>[50,51]</sup> observing isolation measures. This decrease is more significant in the USA and European countries<sup>[4,16,47,52]</sup>. Studies that have prospectively followed HD patients for their HCV serostatus have yielded annual incidence rates of de novo HCV infection of 0.4% in France<sup>[53]</sup>, 0.5% in Tunisia<sup>[54]</sup>, 0.5% in the Netherlands<sup>[24]</sup>, 0.83% in Italy<sup>[55]</sup>,  $1.38\%^{[56]}$  and  $2.1\%^{[57]}$  in the USA,  $0.33\%^{[58]}$ ,  $2.59\%^{[59]}$ , 3.1% in Japan<sup>[60]</sup>,  $3.7\%^{[61]}$ , 5.5% in Brazil<sup>[62]</sup>, and 6.2%in Greece<sup>[20]</sup>. This variation in different countries and different centers underlines the importance of infection

control. New infection was evidently more frequent at centers that had higher anti-HCV prevalence and failure in infection control measures. In some countries, both prevalence and incidence remain very high, indicating major ongoing nosocomial transmission, probably due to the limited resources available to treat a rapidly growing HD population<sup>[63,64]</sup>.

#### **RISK FACTORS FOR HCV TRANSMISSION**

The high prevalence of HCV seropositivity among HD patients was initially attributed to blood transfusions for the treatment of uremic anemia in this population, which were often necessary<sup>[41,65-68]</sup>. Historically, the number of blood transfusions received was consistently reported in the literature to be associated with an increased prevalence of HCV-positive dialysis patients<sup>[31]</sup>. However, several recent reports have failed to recognize blood transfusion as an independent risk factor in HCV spread among HD subjects<sup>[2,20,23,24,30,33,62,69-74]</sup>. Indeed, from the late 1980s onward, the prescription of erythropoietin reduced the need for blood transfusion in HD patients. Furthermore, the introduction of sensitive tests for screening blood donors has markedly reduced the risk of HCV transmission through blood product transfusion. These two reasons may explain recent findings on the lack of association between blood transfusion and HCV infection. Nonetheless, considering the fact that new HCV infections do still occur in patients without a history of transfusion, the duration of HD is increasingly being considered as a risk factor for HCV infection<sup>[75,76]</sup>. Almost all recent surveys on the subject have congruently suggested that the length of time on HD is a risk factor for HCV seropositivity<sup>[17,20,23,29,30,33,36,39,43,60,69-71,77-80]</sup>. Nosocomial patient-to-patient transmission of HCV infection among HD patients has been suggested by several investigators who performed phylogenetic analysis of HCV viral isolates<sup>[24,25,53,54,81-84]</sup>. Lack of strict adherence to universal precautions by staff and sharing of articles such as multidose drugs might be the main mode of nosocomial HCV spread among HD patients<sup>[54,82,84-86]</sup>. Although some studies found that nosocomial spread of HCV declined when HCV-infected patients were treated in dedicated HD units<sup>[44-49,87,88]</sup>, other investigators could control nosocomial spread of HCV among HD patients by the strict application of hygienic precautions, without isolation of HCV-infected subjects or machine segregation<sup>[12,50,89]</sup>. Indeed, the observed efficacy of isolation might simply be due to the prevented sharing of articles between patients and might reflect a better implementation of other hygienic precautions.

The spread of HCV infection in HD units is mainly due to nosocomial transmission between patients<sup>[53,88,90-94]</sup>. The importance of this route of transmission is demonstrated by the high HCV prevalence in some HD units and by the lower infection rate in patients on peritoneal dialysis compared with those on HD. A high prevalence of patients with HCV infection in HD facilities has been considered a risk factor for transmission of the infection. However, there is no consensus on the necessity for infection control isolation of HCV-positive patients for at least two reasons: firstly, the infectivity of HCV is lower than that of the hepatitis B virus; and secondly, the criteria for patients to be isolated remain to be defined. On the contrary, some HD patients are infected with HCV but do not have antibodies. Detection of viral RNA by reversetranscription polymerase chain reaction (RT-PCR) is the only method to confirm HCV infection, however, this technique is not available at all centers.

## PREVENTIVE STRATEGIES

Several prophylactic measures have been suggested to avoid infection by HCV in the HD environment, and range from isolating patients with HCV infection<sup>[44,47,48,88,95]</sup>, to adopting a series of biosafety measures specific for HD, such as preparing medications in a separate area, cleaning and disinfecting dialysis station surfaces, washing hands and changing gloves between patient contacts, and items dedicated for use only with a single patient<sup>[12,39,50,96]</sup>. Strict adherence to universal infection control precautions seems to be enough to control the spread of disease in HD units<sup>[12,50,89,97-99]</sup>. Some reports have recommended the adoption of infection control isolation measures at centers with a high HCV prevalence<sup>[47,87,100,101]</sup> or if the staff/patient ratio at the center is lower than 28/100<sup>[102]</sup>. At centers with a high prevalence of HCV infection and in developing countries, universal precautions may not always be possible to implement. Thus isolation measures for HCV-positive patients should be implemented<sup>[47]</sup>. The CDC recommends that special precautions be observed in dialysis units including the wearing and changing of gloves and water-proof gowns between patients; systematic decontamination of the equipment, circuits, and surfaces after each patient treatment; no sharing of instruments (e.g. tourniquets) or medications (e.g. multiuse vials of heparin) among patients; and the assignment of patients to specific HD units<sup>[97]</sup>. Clearly, it is necessary to attempt, one step at a time, to minimize intradialytic or intracenter HCV transmission.

## CONCLUSION

In summary, despite the marked decrease in anti-HCV prevalence in HD patients in many countries, the disappearance of HCV from HD units should not be expected for decades. Universal infection control precautions are the keystone in the prevention of nosocomial HCV transmission in HD units; however, isolation measures, including health care monitoring of infected patients and providing care in a dedicated section of the unit, improve prevention results. Those HD units with a high HCV prevalence or in which there is no fulltime infection control personnel dedicated to the infected patients during HD sessions may have a greater risk of seroconversion. Therefore, isolation in

special units or dialyzing patients in specific sessions must be considered<sup>[44]</sup>. As HCV-infected HD patients serve as a reservoir of infection for other patients, HD staff, and the transplant team<sup>[28,103,104]</sup> at HD centers must be aware of new HCV infections in order to review their practices and increase vigilance. Public health authorities should be aware about the prevalence and incidence of HCV infection in HD patients in different cities in their respective countries, so that changes can be proposed and the risks of infection among patients can be assessed. Implementation of surveillance systems and continuing education of the unit's personnel on recommended infection control measures in HD units are necessary. The treatment of most HCV-infected patients with interferon alpha can significantly contribute to decreasing HCV infection in this group in the future<sup>[105]</sup>. Successful control of infection requires further studies to assess the effectiveness of different preventive policies.

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