Impact of hepatitis C in mortality in patients on hemodialysis

Authors

Cristian Paul Leon Rabanal[1]

Javier Cieza Zevallos[2]

Roberto Cieza Cusato[1]

[1]Universidad Peruana Cayetano Heredia
[2]Service of Nephrology Hospital Nacional Cayetano Heredia, Lima – Peru

ABSTRACT

Objective: Cardiovascular diseases are the most important causes of mortality in patients with end-stage renal disease. However, viral infections (hepatitis B and C) have acquired great importance for patients undergoing hemodialysis, because they affect patients' survival and increase morbidity and mortality. This study aimed at assessing the influence of hepatitis C on the mortality of patients undergoing hemodialysis. **Methods:** This is a non-concurrent cohort study during a period of ten years. **Results:** Each cohort comprised 74 patients. Hepatitis C did not increase the risk of death, and the survival of infected patients was better than that of patients without hepatitis C. The one-year and five-year survivals of non-infected patients were 93.9% and 52.3%, respectively, while those of non-infected patients were 95.5% and 73.1%, respectively (Cox-Mantel log-rank, p = 0.02). **Conclusion:** No increase in mortality risk was observed. Hepatitis C did not correlate with an increase in mortality in patients with end-stage renal disease undergoing hemodialysis.

Keywords: chronic kidney failure, hepatitis C, mortality, renal dialysis.

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Corresponding author:
Dr. Cristian León Rabanal
Hospital Nacional Cayetano Heredia. Servicio de Nefrología. Universidad Peruana Cayetano Heredia.
Av. Honorio Delgado 430, San Martín de Porres
Lima – Perú.
E-mail: cristianleonr27@hotmail.com

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INTRODUCTION

In the past 20 years, cardiovascular complications were recognized as the major cause of mortality in hemodialysis (HD) patients. The presence of chronic infection has generated a series of speculations about its importance for the final status of patients undergoing that type of renal replacement therapy. Of the chronic infections, those caused by different hepatitis viruses have gained attention. Regarding the hepatitis B virus, policies of systematic vaccination and the establishment of strict biosafety measures in HD units related to hepatitis B have succeeded in controlling that infection with the virtual elimination of the problem among patients undergoing chronic dialysis. The same did not occur with hepatitis C, initially described as hepatitis non-A, non-B, and later, in 1989, identified as C. [1,2]

The accuracy of the test for detecting the hepatitis C viral DNA in past years has allowed for the successful identification of that virus in the epidemiological chain of blood banks and the limitation of its transmission in chronic patients undergoing HD. Nevertheless, it could neither prevent a period of rapid spread of the disease in HD units, nor recognize other relevant aspects for the transmission that do not depend on blood transfusion and that could not be interfered with.[2]

Although those problems have been solved, the effect of hepatitis C on the mortality of chronic patients undergoing HD has been studied and, apparently, that effect is controversial or does not exist. However, some studies have shown an increase in the mortality risk as compared with that of patients with no hepatitis C. That risk is associated with an increase in cardiovascular mortality in patients under the age of 65 years. Whether that effect is due to inflammation or to liver disease has not been clarified.[3,4,5,6]

Chronic patients undergoing HD have shown characteristics specific to each country and population. Such differences

can be established to each regional and local level, and, thus, the effect on lethality can differ according to each particular situation.[6]

In Peru, some specific situations related to hepatitis C in HD services should be emphasized. For example, the epidemics characterized by infection rates of as much as 70% or more in the 1990s [12] has drastically decreased in past years because of the health policies established to improve laboratory services provided to groups of potential blood donors infected with hepatitis C virus (HCV). Another measure was the isolation of patients with HCV infection in special units, generating HD units intended for the exclusive treatment of either infected or non-infected patients, limiting the number of infected patients in each unit.[12,13,14]

That policy, initially made in a intuitive manner, was successful, as previously reported.[14] Now we need to study, in our population, the effect of seropositivity for hepatitis C on lethality, controlling critical variables, using a study of cohorts, because the previous study assessed a small number of individuals with a low incidence of seroconversion (from negative to positive).

The problem of prevalence of hepatitis C and its effect on time in populations like ours need to be solved, so that pharmacological actions to enhance survival can be initiated, even though that intervention is controversial in the international literature.

This study aimed at assessing the existence of an association between the presence of positive markers for hepatitis C and mortality in our population.

Methods

This is a non-concurrent cohort study involving two cohorts of patients undergoing chronic HD at a HD center in the city of Lima, Peru, from January first, 1985, to December 31st, 2007. We assumed that hepatitis C could increase the relative risk of death by one and a half time, accepting a mortality rate of the general population of 50% during a five-year follow-up in the HD program.

The calculated sample was 65 patients in each cohort, with one exposed patient (HCV-infected) to one non-exposed patient (non HCV-infected), and the sample was increased in 10% to prevent bias with data loss. Thus, the final size of each cohort was defined as 74 patients.

Analysis of mortality adjusted to the variables sex, age, and etiology of the underlying disease was performed to avoid biases that could influence mortality. Analysis of survival was performed by use of the Kaplan Meier risk curve, log-rank test, and Cox multivariate analysis. The results that achieved a statistically significant value ($p < 0.05$) are shown in tables and survival curves.

Results

Seventy-four patients were studied in each cohort. The general data of the cohorts are shown in Table 1. No statistically significant difference was observed in the control variables of the cohorts. Thus, there are two comparable groups for analysis in the model of adjusted mortality, in which the variables that could influence the final result were controlled.

Table 1 General characteristics of the cohort

Variable	Exposed patients†	Control patients††	P value
Sex			> 0.05
Men	46	44	
Women	28	26	
Age			> 0.05
< 60 years	38	27	
> 60 years	40	40	
Etiology of CKD*			>0.05
Glomerulonephritis	21	16	
Hypertension	14	11	
Interstitial nephropathy	11	6	
Diabetic nephropathy	15	22	
Others etiologies	13	8	

*Chronic kidney disease; † HCV infected; †† Non-HCV infected

The hospitalization period of the patients in dialysis differed in the cohorts. This is the effect of the increase in the number of HCV-infected patients after the year 2000 (Table 2).

On univariate analysis, no variable was associated with the risk of death ($p > 0.05$). However, Table 3 shows an inverse relation between HCV infection and risk of death (Cox proportional hazards regression model). That analysis was performed by adjusting the variables that could influence the result.

Table 2 Time elapsed since beginning the hemodialysis program and starting the follow-up in the cohorts

Period of the program	HCV infected patients†	Control patients††
1985-1990	7	3
1991-1995	5	0
1996-2000	35	13
2001-2005	18	29
2005-2007	9	25

† HCV infected; †† Non-HCV infected

Table 3 Cox multivariate analysis – all variables

Variables	B	SE	p	Exponential (β)
HCV	- 0.553	0.364	0.129	0.575
Sex	0.330	0.318	0.300	1.391
Year of entrance	0.042	0.038	0.267	1.043
age ? 60	0.620	0.366	0.090	1.858
Diagnosis	0.004	0.046	0.235	1.004

p = 0.035

Figure 1 shows the overall survival curve of infected patients in accordance with data of the international literature. Figure 2 shows the survival curves of the generations, in which survival of patients with hepatitis C is better than that of patients without hepatitis C. Figure 3 shows the cumulative risk of death of HCV-infected and non HCV-infected patients, which is similar to the previous result.

Figure 1. General survival of the population.

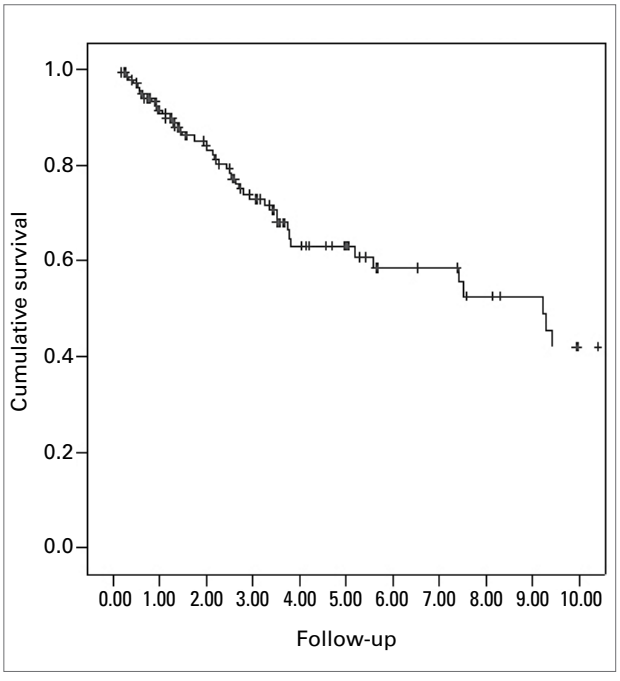


Figure 2. Survival according to the presence or absence of HCV infection.

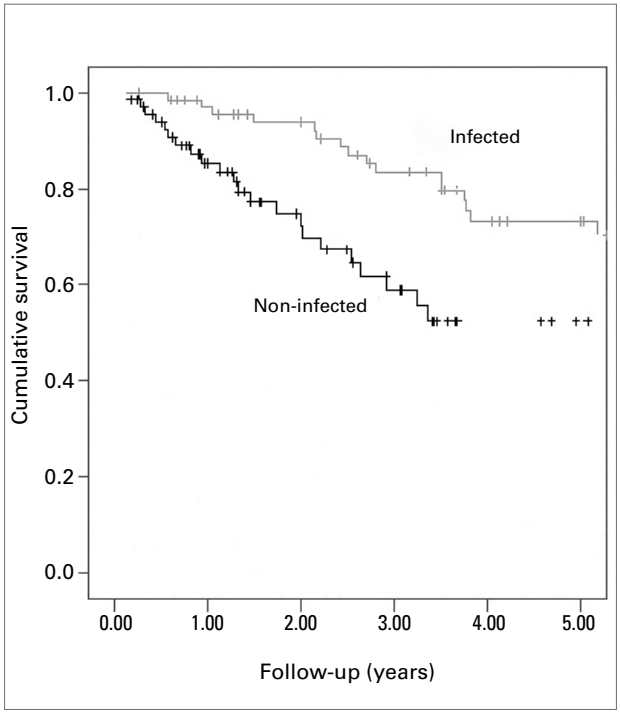
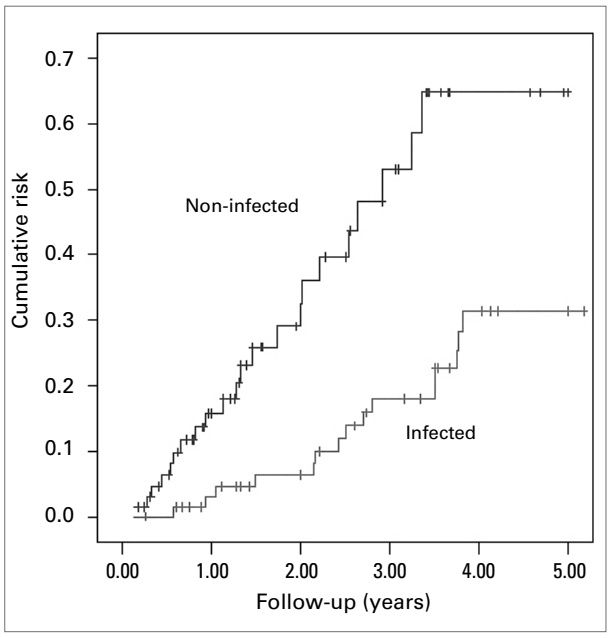


Figure 3. Cumulative risk of death of HCV-infected and non-HCV infected patients.



Discussion

Our results show that the risk of mortality among patients with kidney failure undergoing HD does not negatively correlate with hepatitis C; paradoxically, survival is higher among those patients, which is not in accordance with other studies on the subject.[7,10,16,18]

Our project controlled important confounding variables that can affect the results, such as underlying disease, sex, and age. The results have shown that HCV infection did not influence negatively the survival of our patients undergoing chronic HD, as described in previous studies[7,10,16], and, paradoxically, the survival curves and risk of death were better in infected patients.

The HCV infection has been shown to have a negative effect in the survival of individuals with no kidney disease.[2] However, in patients undergoing chronic HD, the HCV infection does not seem to have the same negative effect. The literature is controversial and data should be carefully analyzed.[6,7,8]

The mechanisms potentially involved in the protective effect of HCV infection are yet to be clarified, but it is possible that patients with that disease are more closely followed up and, thus, the complications are earlier detected.

The conflicting results have likely been subjected to confounding variables that may not have been considered, such as nutritional or cardiovascular functional status, that may play a different role depending on where the observation is made. Our population has a high rate of undernourished patients, who may have undergone pre-selection, generating undetectable biases in the sample.

In Peru, HCV infection is still a severe problem in HD units, although its prevalence has decreased dramatically in recent years due to health policies aimed at controlling the disease.[12,13]

A previous study has shown that HCV infection is associated with certain risk factors typical of the health policy for patients undergoing chronic HD in Peru, where the HD service is provided by the private sector (hired by the government), differing from that provided by direct public auxiliary services (use of blood, hospitalization, management of vascular access, and solution for emergency situations and surgical treatments). That fact along with the policy encouraging the high turnover of patients are factors that affect the high prevalence of HCV infection in our country and have been progressively corrected.[14]

In such a context of high prevalence of HCV infection, it is worth emphasizing the importance of minimizing the number of infected patients in HD units. That should not exceed a certain threshold (close to 50%), because this leads to a rapid increase in the incidence of HCV infection occurs, in addition to complying with the biosafety measures internationally accepted.

One limitation of the study may have been not considering other variables, such as metabolic bone disease or nutritional status; however, the most important variables were controlled.

In conclusion, hemodialysis patients with hepatitis C do not have an increase in the likelihood of death. Other specific variables than HCV infection are likely to exert a greater effect on patients undergoing HD.

References

1. Terrés-Speziale AM. Hepatitis C. Historia natural y estado actual de su manejo. Rev Mex Patol Clin 2003; 50:179-189.
2. Lauer GM, Walker BD. Hepatitis C virus infection. N Engl J Med 2001; 345:41–52.
3. Zacks SL, Fried MW. Hepatitis B and C and renal failure. Infec Dis Clin North Am 2001; 15:877-99.
4. Martin P, Fabrizi F. Hepatitis C virus and kidney disease. J Hepatol 2008; 49:613-24.
5. Johnson W, Dent H. Frequencies of hepatitis B and C infections among haemodialysis and peritoneal dialysis patients in Asia-Pacific countries: analysis of registry data. Nephrol Dial Transplant 2009; 24:1598-603.
6. Fabrizi F, Bunnapradist S, Lunghi G, Aucella F, Martin P. Epidemiology and clinical significance of hepatotropic infections in dialysis patients. Recent evidence. Minerva Urol Nefrol 2004; 56:249-57.
7. Santoro D, Mazzaglia G. Hepatitis status and mortality in hemodialysis population. Renal Failure 2009; 31:6-12.

8. Fabrizi F, Poordad FF. Hepatitis C infection and the patient with end-stage renal disease. Hepatology 2002; 36:3-10.
9. Fabrizi F, Lunghi G. Hepatitis C virus infection and the dialysis patient. Semin Dial 2007; 20:416-22.
10. Fabrizi F, Takkouche B. The impact of hepatitis C virus infection on survival in dialysis patients: meta-analysis of observational studies. J Viral Hepat 2007; 14:697-703.
11. Mello LA. Hepatitis C serum prevalence in hemodialyzed patients. Rev Soc Bras Med Trop 2007; 40:290-4.
12. Javier Cieza Z, Pinares A. Factores de riesgo para infección por hepatitis C en dos unidades de diálisis de Lima-Perú. Rev Med Exp 2001; 18:5-8.
13. De los Ríos R, Miyahira J. Prevalencia de anticuerpos anti-hepatitis C en pacientes en hemodiálisis crónica. Rev Medica Herediana 1997; 8:67-71.
14. Valencia Y, Cieza Z. Factors associated with Hepatitis C infection in patients with chronic hemodyalisis. Rev Gastroenterol 2009; 29:11-6.
15. Perico N, Cattaneo D. Hepatitis C infection and chronic renal diseases Clin J Am Soc Nephrol 2009; 4:207-20.
16. Butt AA, Skanderson M, McGinnis KA. Impact of hepatitis C virus infection and other comorbidities on survival in patients on dialysis. J Viral Hepat 2007; 14:688-96.
17. Meyers CM, Seeff LB, Stehman-Breen CO, Hoofnagle JH. Hepatitis C and renal disease: an update. Am J Kidney Dis 2003; 42:631-57.
18. Butt AA, Xiaoqiang W. Hepatitis C virus infection and the risk of coronary disease. Clin Infect Dis 2009; 49:225-32.