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Research Report

HEPATITIS C VIRUS INFECTION IN HEMODIALYSIS PATIENTS: COMPARISON OF THE SURABAYA DIALYSIS CENTER AND JUNTENDO UNIVERSITY HOSPITAL DIALYSIS CENTRE

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ABSTRACT

Hepatitis C virus infection is highly prevalence in chronic hemodialysis (HD) patients. The present study will compare prevalence of HCV positive population in difference countries where there are great contrasts in and diversity of care available to patients who have end stage renal disease. All serum samples of the 100 patients were tested for HCV antibodies, using third-generation enzyme immunoassay. The prevalence of anti-HCV was correlated with a history of blood transfusion and with duration of hemodialysis. HCV prevalences were 88% of Surabaya group and 6% of Juntendo Group, respectively. In Surabaya Group, prevalence of HCV positive was high and the risk factors are not only those of the Juntendo Group, but also a combination of poor living conditions, frequent blood transfusions, and lack of adherence. Much needs to be studied about the role of universal screening and effective techniques for primary prevention in Surabaya Group

Key words: epidemiology, hemodialysis, hepatitis C virus, risk factor

INTRODUCTION

Patients with end stage renal disease (ESRD) are at higher risk of acquiring HCV infection.^[1,2] Published prevalence data for HCV infection among hemodialysis (HD) patients in various countries in consistently higher than in healthy populations,^[3] ranging from 2 to 6% in northwestern Europe to more than 20% in Japan and over 60% in Saudi Arabia.^[4,5,6] These variations seem not only to reflect local prevalence of HCV but also to suggest that aspects of the dialytic process may expose patients to an increased risk of developing HCV. This means the geographical region of the study population, methods used for detection of hepatitis C and the study design lead to varied results, as it was recently suggested in UK.^[7]

Even though general epidemiological information has been obtained for HD populations that are increasing worldwide, a considerable regional variability has been reported.^[8,9,10,11] The present study will compare prevalence of HCV positive population in difference countries where there are great contrasts in and diversity

of care available to patients who have end stage renal disease. Using demographic and laboratory databases, the present incidence of HCV positive hemodialysis patients, environmental conditions, and availability of sophisticated dialysis programmes and care for these patients or the lack of treatment facilities will be compared.

SUBJECTS AND METHODS

Health conditions and Patients

There are two groups, Dr. Soetomo Hospital Dialysis Center, Surabaya, Indonesia and Juntendo University Hospital Dialysis Center, Tokyo, Japan.

Surabaya Group:

Fifty hemodialysis patients (41 males and 9 females). Informed consent was obtained from each patient enrolled in this study. Their mean age was 48.7±12.7 years (range 15–74 years). The causal diseases were divided into Diabetes Melitus by 24% and other diseases by 76%. The mean duration of HD treatment was 37.45 ± 33.46

months (range 7 months to 120 months) (Table 1). The patients were treated with standard HD for 4 hours twice weekly, for almost HD patients were applied acetate buffer, cuprophane dialyzer which were reused. Standard heparin (multi dose ampules) was used to prevent coagulation. There was no special area for hepatitis positive patients. Erythropoietin treatment was rare because the Surabaya group is economically disadvantaged with almost all patients coming from the low income population with poor sanitary conditions (Table 1). Hepatitis prevalence in the normal population of the region is very high. In Surabaya, there is a reservoir of HCV infected persons who can transmit the infection to others and who are at risk for HCV related chronic disease. During the time of unknown HCV transmission within the unit, the frequent sharing of facilities over a prolonged period resulted in accumulated risk. Surabaya patients frequently received multiple blood products. History family related HCV infections was not examined.

Juntendo Group:

There were 50 hemodialysis patients (33 males and 17 females), with a mean age 65.4 ± 14.7 years (range 30 to 89 years). The length of time on dialysis treatment was 110.3 ± 61.65 months (range 32.5 months to 249 months, median of 90.9 months). All patients were on HD thrice weekly. The duration of the dialysis procedure ranged from 4 to 5 hours per session. The blood flow was between 200 and 250 ml/min and dialysate flow was 500 ml/min. Almost all HD patients received bicarbonate buffer and recombinant human erythropoietin. Underlying renal diseases were: diabetes (34%) and other diseases (66%). Information on duration of hemodialysis, and number of blood transfusions was obtained from medical records (Table 1). The unit concerned provides two dialysis shifts daily. Dialysis machines are not moved, and wherever possible, patients occupy the same dialysis station. A few specified machines

were used to dialyzed all known HCV positive patients and a few patients with hepatitis B were dialyzed within the unit. Dialysis was carried out using Nipro machines in all patients. Between dialysis sessions, machine sterilization was carried out according to manufactured recommendations. The sterilization procedures were based on the instructions of the manufacturers. Application of universal precautions to prevent staff members from facilitating transmission of HCV between patients and also to limit the risk of contracting HCV themselves were carried out according to standard infection control practices. All HD patients and staff members were regularly tested for hepatitis B and C. Almost all patients did not any receive blood. Dialyzers used were either cuprophane or polysulfone. Disposable equipment was used for dialysis and dialyzers were not reused. Single use heparin vials were used to administer bolus and continuous heparin infusions. Informed consent was also obtained from each patient enrolled in this study.

Laboratory tests

All serum samples of the 100 patients were tested for HCV antibodies using the INNO-test Ab III enzyme immunoassay (EIA) for the presence of antibodies to HCV. All tests were carried out and interpreted strictly in accordance with the manufacturer's instructions. The liver tests, which included determinations of aspartate aminotransferase and alanine aminotransferase, were performed using the Hitachi analyzer (Boehringer-Mannheim, Germany).

Statistical analysis.

Epidemiological data are presented as means \pm SD and percentages of the mean. Further statistical analysis of risk factors for HCV infection (duration of hemodialysis, and number of blood transfusions) was also performed.

Table 1. Characteristics of anti-HCV-positive in two groups

Patient characteristics	Surabaya Group		Juntendo Group		p
	Anti HCV-	Anti HCV +	Anti HCV-	Anti HCV +	
Sex					
Male	41		33		
Female	9		17		
Hemoglobin concentration (gr/dl)	7.34 + 1.66		10.2 + 0.77		<0.001
Age (Years)	48.7 + 12.7		65.4 + 14.7		<0.001
Standard hemodialysis for 4 hours	Twice/week		Thrice/week		
Dialyzer	Reused		Disposable		
Median duration of HD treatment (months)	37.45 \pm 33.46		110.3 \pm 61.65		<0.001
Underlying renal diseases					
DM/Non-DM	24% / 76%		34% / 66%		
Standard infection control practices	\pm (Incomplete)		+ (Complete)		
Erythropoietin Treatment	Not any/rare		+		

RESULTS

Serum sample were collected from a total of 100 dialysis patients (Surabaya and Juntendo Groups). The collected sera were subjected to serological tests. Of those tested for hepatitis C virus antibodies by third generation ELISA, 44 were positive (88%) in the Surabaya Group and 3 were positive (6%) in the Juntendo Group. Statistically, there was significant differences between the two groups. The Surabaya Group had a significantly higher prevalence than that in Juntendo Group ($p < 0.0001$)(Fig. 1).

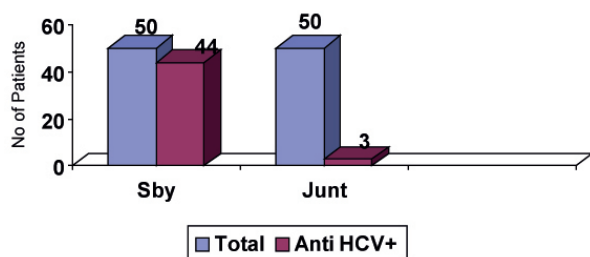


Figure 1. Prevalence of anti HCV positive in hemodialysis patients, Surabaya: Juntendo University Hospital Dialysis Center.

Time on hemodialysis in the Surabaya patients was $37.45 \pm$ months less than that in the Juntendo Group ($110.3 + 61.7$ months) with a significant difference (Table.1). The Surabaya HCV antibody positive patients showed a significantly lower mean level of hemoglobin (7.34 ± 1.66 gr/dl) than the Juntendo Group, whose Hb values were 10.2 ± 0.77 gr/dl) ($p < 0.0001$) (Table 1). Many Surabaya antibody positive patients one to multiple blood transfusions but no Juntendo patients received any transfusions (Table 2).

Table 2. Relationship between parameters and prevalences of anti-HCV positive patients.

Parameter	Surabaya		Juntendo	
	Anti-HCV positive	Anti-HCV negative	Anti-HCV positive	Anti-HCV negative
Sex				
Male	36 (81.81%)	5 (83.33%)	2 (66.66%)	31 (65.95%)
Female	8 (18.19%)	1 (16.67%)	1 (33.34%)	16 (34.05%)
Elevated				
ALT	5	1	0	0
AST	5	2	0	0

Data obtained from this study demonstrated that prevalence of anti HCV antibodies in the Surabaya Group was much higher than in those in the Juntendo Group, which may be attributed to several risk factors, including blood transfusion, duration of dialysis, and a lack of access to dialysis treatment due to limited health care resources. The prevalence rate of positive anti-HCV antibody in Surabaya Group was 88%, with a positive correlation between anti-HCV positive cases and longer duration on dialysis

Table 3. Relationship between the duration of HD and the prevalence of anti HCV Positive among HD Patients in Surabaya and Juntendo

Parameter	Surabaya		Juntendo	
	Anti-HCV positive (n = 44)	Anti-HCV negative (n = 6)	Anti-HCV positive (n = 3)	Anti-HCV negative (n = 47)
Duration of hemodialysis (months)				
<12	8 (18.18%)	5 (83.3%)	0 (0%)	0 (0%)
12–48	8 (18.18%)	1 (16.7%)	0 (0%)	6 (12.77%)
>48	28 (63.64%)	0 (0%)	3 (100%)	41 (87.23%)
Duration on hemodialysis (months)	42.04±34.06	9.7±2.5	148.5±70.5	108.7±62.5

Table 4. Relationship between HD Patients Previously with Blood Transfusion, with No Blood Transfusion and Prevalence Anti HCV Positive In Surabaya Centre

HD Patients	Anti HCV (+)	Anti HCV (-)	
Previously with Blood Transfusion	36 (81,82%)	6 (100%)	42 (84%)
Previously with no blood transfusion	8(18,18%)	0 (0%)	8 (16%)
Total	44	6	50

Prevalence anti HCV + Among HD Patients: $42/50 = 84\%$
 Prevalence Anti HCV + Among HD with Blood Transfusion: $36/43 = 81,81\%$
 Prevalence Anti HCV + Among HD with no Blood Transfusion : $8/43 = 18,18\%$

($p = 0.0001$) and blood transfusion ($p = 0.001$), suggesting the presence of clear regional differences within populations in the incidence of HCV antibody. The relationship between HCV infection and transfusion in the Surabaya subgroup is more complex since subgroup I patients (time on dialysis < 1 year) and subgroup II patients (> 3 years) have the same frequency and those in subgroup III have a higher frequency than those with intermediate values (Table 3). HCV positive patients attributed to transfusion were observed in patients on dialysis with both short and long times.

DISCUSSION

Prevalence of anti-HCV antibodies among patients on dialysis is consistently higher than in healthy populations,^[3] suggesting that dialysis patients may be at higher risk of acquiring HCV infection.^[1,2] In different countries, prevalence of this disease among dialysis patients shows wide variations.^[12,13,14] Studies performed in a selected group of dialysis centers showed that the prevalence of

HCV infections among hemodialysis (HD) patients, is much higher than that among healthy donors,^[3] ranging from 2 to 6% in northwestern Europe to more than 20% in Japan and over 60% in Saudi Arabia.^[4,5,6] Many factors are involved in these variations which may explain the differences in prevalence of anti-HCV positivity among the dialysis units.^[5] The increased requirement for blood transfusion in the dialysis population^[10,15,16,17,18] and duration of hemodialysis are risk factors for HCV infection (independent of previous transfusions), transmission within the dialysis unit,^[17] the mode of transmission is through environmental contamination.^[19,20] Data obtained from this study demonstrated that prevalence of anti HCV antibodies in the Surabaya Group was very different from than in the Juntendo Group. The low prevalence of HCV infection among the Juntendo Group has to be contrasted with the 88% prevalence of infection found in the Surabaya Group. Such the high variations have also been reported by other authors.^[5] Using these estimates and assuming that the incidence is related to many factors for developing HCV infection in the population, this study proposes a several mechanisms explaining the difference in prevalence in the two groups. The reason for this difference may be explained by the unique condition in the two countries

Epidemiologically, the different prevalence of HCV infections in HD patients in both countries, suggests an increase in the number of patients at higher risk for the development of HCV infection and such regional variability has been reported.^[21] In fact the hepatitis C prevalence in the general population of the region is higher,^[22] suggesting infection from a common source. A dramatically higher prevalence is anti HCV positive HD patients in the Surabaya Group has been found, which has made it a significant health burden in the Surabaya Group.

It is well known that administration of blood products is the main risk factor for developing hepatitis C.^[15] In Indonesia including Surabaya, blood and blood products are important factors in the transmission of HCV infection, because hepatitis C virus is still the major cause of post-transfusion hepatitis. Therefore, multiple blood transfusions seemed to be an important risk factor for HD patients in the acquisition of HCV infection in the Surabaya Group, as recently stressed by other authors.^[23] The fact that these patients had never received erythropoietin suggest that the need for blood transfusion has still continued to correct renal anemia in hemodialysis patients.

The introduction of erythropoietin and screening of blood products for anti HCV infection can be highly effective in preventing transmission of HCV infection. In the present study of the Juntendo Group, patients had almost no HCV infection (only 6%) and the number of transfusions in dialysis patients was much lower. In contrast to the Juntendo Group with availability of a sophisticated dialysis program, the Surabaya Group had a prevalence of HCV positive patients of more than 87%. The nonrandom distribution of HCV infection in the Surabaya Group indicated that local factors may play

a role in the epidemiology of HCV. The reason for this phenomenon is not entirely clear, but there are several proposed mechanisms to explain the high prevalence of HCV infection in the Surabaya group. Undoubtedly, the use of blood products was a major contributory factor, with this mode of transmission is now largely historical in Japan, especially in the Juntendo University Hospital Dialysis Centre. This condition is supported by evidence of the prevalence rate varied between 0 and 53% on a multicentre study in 11 centres in Japan.^[22] In the present study, anti-HCV positive HD patients received significantly more units of blood products than anti-HCV negative patients. Frequent blood transfusions (multiple blood transfusions) over a prolonged period may result in an accumulated risk and the present study found a positive correlation between blood transfusions and the risk of infection by HCV, as recently stressed by other authors.^[24]

The major risk factor is longer duration of dialysis. In Surabaya Group, the risk factors are not only those of the Juntendo Group, but also a combination of poor living conditions, frequent blood transfusions, and lack of adherence to universal infection precautions including poor infection control practices, sharing of instruments or medication, nurses not regularly wearing gloves, spread through blood spillage, and presence of other levels of hygienic standards that make dialysis prone to hepatitis C viral infection. The such high prevalence is a burden on the health care system especially for the Surabaya Group. HCV is major health problem in HD patients in the Surabaya Centre. Identifiable risk factors may be longer duration of dialysis, blood transfusion, and the lack of adherence to universal infection precautions. The major difference in prevalence of anti-HCV antibody in the Surabaya and Juntendo Groups illustrates the diversity of care available to patients in developing and developed countries.

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