Profile of Hepatitis B Virus, Hepatitis C Virus, Hepatitis D Virus and Human Immunodeficiency Virus Infections in Hemodialysis Patients of a Tertiary Care Hospital in Uttarakhand

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Background and aim: **Viral hepatitis and human immunodeficiency virus (HIV) infection are important causes of morbidity and mortality in hemodialysis (HD) patients. The present study was performed to assess the prevalence of hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and HIV infections in hemodialysis patients of a tertiary care hospital in Uttarakhand.** ***Methods:*** **All patients undergoing maintenance HD at our center were screened for hepatitis B surface antigen (HBsAg), antibody to HCV (anti-HCV), antibody to HDV (anti-HDV) and HIV antibody by ELISA. Detailed history regarding age, sex, duration of dialysis, blood transfusions, number of dialysis centers, dialyzer reuse and laboratory data was recorded.** ***Results:*** **A total of 118 patients (79 males and 39 females) were followed for 18 months with screening for the presence of HBV, HCV and HIV infections. At baseline, 12 (10.2%) patients were positive for HBsAg, 19 (16.1%) for anti-HCV and 2 (1.7%) for HIV antibody. Over 18 months, one additional patient became HBsAg positive and an additional 17 became anti-HCV-positive to give a total of 36 HCV-positive patients. Dual HBV and HCV infection was seen in 5 (4.2%) and anti-HDV antibodies were found in 1 (0.9%) patient. History of blood transfusions, duration of HD, dialyzer reuse and dialysis at multiple centers were found to be important risk factors for anti-HCV positivity.** ***Conclusions:*** **Implementation and adherence to universal work precautions by dialysis staff is imperative to prevent transmission of these infections. (J Clin Exp Hepatol 2013;3:24–28)**

Haemodialysis (HD) is an important modality of therapy for the patients of end-stage renal disease (ESRD). Being an extracorporeal mode of therapy the dialysis patients have an increased risk of exposure to parenterally transmitted hepatitis viruses and human immunodeficiency virus (HIV). Both, viral hepatitis (hepatitis B virus [HBV], hepatitis C virus [HCV], hepatitis D virus [HDV]) and human immunodeficiency virus (HIV) infection are important causes of mortality and morbidity in these patients treated with HD.[1,2] The prevalence of these infections is known to vary widely in different regions of the world. Even within India, a very wide range of prevalence rates for HBV (3.4–45%) and HCV (4.3–45.2%) in the dialysis population have been reported.[3] These prevalence rates are higher than the average prevalence rates estimated for the general population in India (4.7% and 1.85% for HBV and HCV respectively).[4,5]

HBV infection is less prevalent than HCV in HD units.[6] Introduction of HBV vaccination, isolation of HBV positive patients, use of dedicated dialysis machines and regular surveillance for HBV infection have dramatically reduced the spread of HBV in this setting.[7] The prevalence of HCV infection among HD is high and varies between countries and between dialysis units within a single country.[8] Dual infection with HBV and HCV leads to more aggressive liver disease in patients with ESRD on HD.[9]

The present study was undertaken to estimate the prevalence of HBV, HCV, HDV and HIV infection among haemodialysis patients.

METHODS

Patients

A total of 118 patients undergoing HD at HIMS were initially screened and subsequently every 3–4 months for HBsAg, anti-HCV, anti-HIV upto a period of 18 months. Patients were enrolled after written informed consent. Detailed history regarding age, sex, cause of ESRD, duration of HD, history of blood transfusion, history of dialysis

Keywords: hepatitis C, hepatitis B, hepatitis D, HIV, hemodialysis
Received: 13.1.2013; *Accepted:* 2.2.2013; *Available online:* 10.2.2013
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Abbreviations: HD: haemodialysis; ESRD: end-stage renal disease; HBsAg: hepatitis B surface antigen; HIV: human immunodeficiency virus; HBV: hepatitis B virus; HCV: hepatitis C virus; HDV: hepatitis D virus
http://dx.doi.org/10.1016/j.jceh.2013.02.003

outside our institution, reuse/non-reuse of dialyzer and tubing, and erythropoietin therapy was recorded. At our center, we do not use dedicated machines for HCV-positive patients however dialyzers are reused in these patients. We do not reuse dialyzers in HIV and HBsAg positive patients and apply universal work precautions for infection control.

Serology

Blood samples were screened for hepatitis B surface antigen (HBsAg), antibody to HCV (anti-HCV) and anti-HIV antibodies at the time of undergoing HD for the first time during inclusion in the study. The above serological tests were repeated every 3–4 month to look for any seroconversion. Patients found to be positive for HBsAg were also tested for antibody to HDV (anti-HDV antibody).

Hepatitis B Surface Antigen

HBsAg was assessed in our study using a direct immunoenzymatic assay of the "sandwich" type (Hepanostika HBsAg Ultra, Biomerieux, Netherlands).

Antibody to Hepatitis C Virus

A third generation ELISA was used to detect antibodies against HCV using cut-off OD value = 0.27 × PCx (PCx = mean value of positive controls) as described by the manufacturer (Hepanostika HCV Ultra, Biomerieux, Netherlands). The test detected antibodies against highly antigenic segments of core, NS3, NS4 and NS5 regions of hepatitis C virus.

Antibody to Human Immunodeficiency Virus

A fourth generation ELISA based on one-step "sandwich principle" was used to detect HIV-1 p24 antigen and antibodies against HIV-1 gp160, HIV-1 ant70 peptide, HIV-2 env peptide (Vironostika HIV uniform II, Biomerieux, Netherlands).

Antibody to Hepatitis D Virus

Anti-HDV was assessed using commercially available ELISA kit based on "competitive" ELISA method (Wantai Hep D, Wantai Biologicals, Beijing).

Institutional ethical committee approved the study protocol.

Statistical Analysis

The data are presented as number (%) and relative risk (RR) with 95% confidence interval (CI). A χ^2 test was used to compare differences in categorical variables; Yates correlation was applied when required. A two-tailed *P* value of less than 0.05 was considered statistically significant. Statistical analysis was performed with EPI info (version 3.5.1; Aug 2008) from CDC Atlanta, Georgia.

RESULTS

A total of 118 patients undergoing HD at HIMS (79 males and 39 females) were initially screened and subsequently every 3–4 months for HBsAg, anti-HCV, anti-HIV upto a period of 18 months. The underlying cause of chronic renal failure in these patients was mainly chronic glomerulonephritis 36 (30.5%) and diabetic nephropathy 31 (26.3%) followed by hypertensive nephropathy 23 (19.5%). The demographic profile of patients is shown in Table 1.

Majority of our patients remained asymptomatic for liver disease during the short term period of follow-up in the present study.

Prevalence of Viral Hepatitis and HIV Infection

Baseline

Initial screening at the beginning of HD, demonstrated that 12 (10.2%) patients were positive for HBsAg, 19 (16.1%) for anti-HCV and 2 (1.7%) for HIV antibody. Among 12 patients with HBsAg, 1 (8.3%) was also positive for anti-HDV (Table 2).

Follow-up

All patients were followed up for a total of 18 months. After 18 months of follow-up, screening of 118 patients for various viral markers revealed that, 13 (11%) patients were HBsAg positive, and 36 (30.5%) were positive for anti-HCV (Table 2). Whereas dual infection i.e. HBV and HCV was seen in 5 (4.2%) patients, HBV and HDV was seen in 1 (0.9%) patient and HCV and HIV was seen in 2 (1.7%) patients. 74 patients (62.7%) were negative for all viral markers.

Table 1 Demographic profile of patients.

Parameter	Number (%)
Age[a]	50.02 years (17–83)
Male:female	79 (66.9):39 (33.1)
History of blood transfusion	68 (57.6)
Dialyzer reuse	36 (30.5)
History of intravenous drug abuse	1 (0.85)
Duration of HD	
<1 year	71 (60.2)
>1 year	47 (39.8)
Baseline hemoglobin (g/dL)[a]	8.65 (5.2–13.5)
Baseline serum urea (mg/dL)[a]	149.8 (50–350)
Baseline serum creatinine (mg/dL)[a]	9.6 (4.6–24.4)
Baseline serum alanine aminotransferase (IU/mL)[a]	51.10 (15–227)
Baseline serum aspartate aminotransferase (IU/mL)[a]	39.21 (12–221)

[a]Mean (range).

Table 2 Prevalence of viral hepatitis and HIV infection.

Parameter	HBsAg (+)	anti-HCV (+)	anti-HDV (+)	HIV (+)
At initial screening (*N* = 118)	12 (10.2%)	19 (16.1%)	1 (8.3%)[a]	2 (1.7%)
Subsequent screenings (*N* = 118)	13 (11%)	36 (30.5%)	1 (7.7%)[b]	2 (1.7%)
Sex: Males (*N* = 79)	9 (11.4%)	26 (32.9%)	1 (1.3%)	2 (2.6%)
Females (*N* = 39)	4 (10.3%)	10 (25.6%)	0 (0%)	0 (0%)
History of blood transfusion (*N* = 68)	9 (13.2%)	26 (38.2%)	0 (0%)	2 (2.9%)
Duration of HD				
<1 year (*N* = 71)	7 (9.9%)	13 (18.3%)	1 (1.4%)	2 (2.8%)
>1 year (*N* = 47)	6 (12.8%)	23 (48.9%)	0 (0%)	0 (0%)

[a]1 patient of 12 HBsAg positive patients.
[b]1 patient of 13 HBsAg positive patients.

Out of 13 HBsAg positive patients, 12 were found to be HBsAg positive at the beginning of the study and 1 more patient became positive in subsequent screenings. Of 36 patients positive for anti-HCV, 19 were found to be positive at the beginning of the study and subsequent screenings of 99 patients revealed 17 anti-HCV seroconversions by the end of the study (Table 2).

Only 1 (0.9%) patient was found to be positive for anti-HDV. HIV infection (anti-HIV and/or p24 Ag) was found in 2 patients (1.7%) undergoing HD. Both were males and had dual infection with HIV and HCV. Only one revealed risk factor of drug abuse and both gave history of past blood transfusions (Table 2).

History of blood transfusion was seen in 9/13 (69.2%) of HBsAg positive cases [RR 1.6 (95% CI 0.53–5.0), χ^2 = 0.36, P = 0.39]; 26/36 (72.2%) of anti-HCV-positive cases [RR 1.9 (95% CI 0.69–2.38), χ^2 = 3.7, P = 0.04]; and both the HIV positive cases. Seventy-one patients out of 118 had taken HD for less than 1 year and 47 had taken HD for more than a year. In case of 36 anti-HCV-positive patients, 13 had undergone HD for less than a year (36.1%) and 23 patients had undergone HD for more than a year (63.9%) [RR 2.7 (95% CI 1.53–4.7), χ^2 = 11.1, P = 0.0005]. Whereas in case of HBsAg positive patients, 7 had undergone HD for less than a year and 6 patients underwent HD for more than a year [RR = 1.2 (95% CI 0.46–3.61), χ^2 = 0.04, P = 0.70]. Though correlation of duration of HD and viral markers positivity was found to be statistically significant in anti-HCV-positive patients, the same could not be established in HBsAg positive, HIV positive or anti-HDV positive patients (Table 2). Out of 17 patients who underwent anti-HCV seroconversion, 14 gave history of dialyzer reuse and 3 did not (χ^2 = 13.4; P = 0.001).

Out of 118 patients 34 gave history of HD at another dialysis center and 84 did not. Out of 17 patients seroconverted for anti-HCV antibodies, 10 gave history of receiving HD at some other dialysis center (χ^2 = 8.72; P = 0.003).

DISCUSSION

HD patients are at high risk for viral hepatitis infections due to the high number of blood transfusion sessions, prolonged vascular access and the potential for exposure to infected patients and contaminated equipment.[10,11]

In India the HCV prevalence rate in the general population is 1.85%.[3] An earlier report from our hospital has shown an anti-HCV prevalence of 0.74% in voluntary blood donors.[12] Literature available from different sources regarding anti-HCV prevalence in HD patients is highly variable ranging from 0.4% to 59% worldwide.[13–16] Estimates provided from several Indian studies in HD also reflect wide variation in anti-HCV prevalence in individual HD units across the country from 4.3% to 46%.[17,18]

In our study, anti-HCV antibodies were found in 30.5% of patients at the end of 18 months of our study period, which is lower than studies conducted by Chandra et al (46%)[19] but was higher than studies conducted by Jain (29%)[20] and Jasuja (22%).[21] Our hospital is a tertiary care center where many patients are referred for HD from other HD centers of Uttarakhand and patients registered at our center did take HD at other centers as per their convenience. Out of 17 patients seroconverting for anti-HCV antibodies, 10 gave history of receiving HD at some other dialysis center. This difference was found to be statistically significant (χ^2 = 8.72; P = 0.003). Out of 84 patients with no history of taking HD at another dialysis center 7 (8.3%) became anti-HCV-positive. These variations may reflect differences in adherence to infection control policies in individual HD units.

Several studies from developed countries have shown HBsAg prevalence rates to range from 4% to 15% in HD patients.[22,23] In India, HBV prevalence in HD patients ranged from 3.4% to 45% which is clearly in excess to the prevalence of 4.7% in the general population.[3] Prevalence of 11% HBsAg positivity in our study is similar to a recent report from Jaipur (11%).[20] HBV is less prevalent than HCV in HD units because of HBV vaccination, isolation of HBV positive patients, use of dedicated dialysis machines and regular surveillance.[9]

Dual infection of HBV and HCV was found to be 4.47% in Turkey[13] and as high as 30.4% by Hung et al from SE Asia.[24] In India dual infection of HBV and HCV was seen in 3%–3.7% of patients undergoing HD,[9,20] which is in accordance to our findings (4.2%). In our study, HCV and HIV infection together was found in 1.7%. It is not surprising to find this co-infection since both the viruses share the same routes of transmission.[17]

Approximately 5% of HBsAg carriers are infected with HDV all around the world. Various studies conducted worldwide show wide variation in HDV prevalence in HD patients. A study from France shows an anti-HDV prevalence of 0%[25] whereas Pujol et al[2] from Venezeula showed an anti-HDV prevalence of 2% in HBsAg positive HD patients in a particular unit. No Indian data was available in this group of patients. Our study shows a prevalence of 0.9% in HD patients.

In addition to the 12 HBsAg positive patients included in our study, one more patient became positive (0.9%) during the course of study. Effective HBV vaccination, isolation measures, use of dedicated dialysis machine, use of erythropoietin and no reuse of dialyzer in HBsAg positive patients may have contributed to a low incidence of HBsAg at our hospital.

Consensus regarding need for HD patient isolation and dedicated dialysis machines to prevent HCV transmission, in addition to universal work precautions, does not exist in the nephrology community. The observed persistence of HCV seroconversion within dialysis units makes re-examination of infection control practice patterns highly relevant.[26]

Center for Disease Control and Prevention in the United States (CDC) does not recommend dedicated machines, patient isolation, or a ban on reuse of dialyzer in HD patients with HCV infection. Strict adherence to universal precautions, careful attention to hygiene, and strict sterilization of dialysis machines have been shown to prevent transmission of infection.[27]

We do not isolate HCV-positive patients and they are not dialyzed on dedicated machines. Isolation of these patients is difficult because of administrative problems, cross-transmission of various genotypes among the segregated HCV-positive patients and inability to adopt HCV RNA PCR as screening test due to high cost. Though reprocessing of dialyzers of anti-HCV-positive patients is done on a dedicated reprocessor, the reprocessing of both anti-HCV-positive and negative patients is done in the same room. Thus cross contamination cannot be ruled out.

Although universal measures of asepsis (changing of gloves after each patient manipulation, avoiding sharing of articles among patients, hand washing), disinfection of environmental surfaces and machines are routinely done in our HD units, it was not unusual to find staff taking care of susceptible and infected patients in the same shift, as has also been mentioned by Nemati et al[28] A study from Saudi Arabia showed the presence of HCV RNA in significant numbers of hands of dialysis personnel, indicating that hands were a potential mode for facilitating transmission of HCV between HD patients.[29]

As far as we know no Indian study and very few International studies mention the pattern of HBV, HCV, HDV and HIV infection in HD patients. However a limitation of our study was that we did not test our study patients, including anti-HCV negative subjects for the presence of HCV RNA in their blood samples due to high cost. Relying on serologic tests alone, especially in HD patients, could underestimate the prevalence of HCV infected patients.

In conclusion, history of blood transfusion, duration of HD, dialyzer reuse and dialysis at multiple centers were found to be important risk factors for anti-HCV positivity. Screening of blood products for HCV/HIV/HBV by nucleic acid amplification testing should be seriously considered in all blood banks because of limitations of serology based assays. As recommended by KDOQI guidelines,[30] strict implementation and adherence to standard work precautions by dialysis staff is imperative to reduce transmission of these infections in such a setting.

CONFLICTS OF INTEREST

All authors have none to declare.

ACKNOWLEDGMENTS

The authors acknowledge the help of Dr. S.L. Jethani (Med. Superintendent), Dr. Deepak Goel (Dy. Med. Superintendent) and Dr. Prakash Keshaviah (Director Nephrology) from HIMS in completion of this manuscript.

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