Original Article

Nephrology Section

Prevalence and Risk Factors of Hepatitis C among Maintenance Hemodialysis Patients at a Tertiary-Care Hospital in Coimbatore, India

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ABSTRACT

Background: Haemodialysis (HD) patients are at an increased risk of Hepatitis C virus (HCV) infection, which is significantly associated with increased morbidity and mortality. This study was conducted to determine the prevalence of HCV infection among patients who were put on maintenance HD and its associated risk factors.

Methods: A total of 145 patients (102 males and 43 females) were included in the study. The medical records were reviewed for details regarding history, age, sex, duration of dialysis, dialyzer reuse, blood transfusions, number of dialysis centers and other biochemical data.

Results: Out of 145 patients 18 (12.4%) patients were found to be anti-HCV positive. The mean age of the HCV positive patients was 45.8 ± 13.9 years. There were 13 (72.2%) males in the HCV positive group and 89 (70.1%) males in the HCV negative group. The mean duration of the dialysis among HCV positive group was 36.6 ± 31.6 months, while it was 18.5 ± 21.2 months for HCV negative ones. The duration of dialysis was significantly longer in HCV positive patients ($p = 0.002$). Similarly, patients who had dialysis at more than one centre had a higher (55.56%) positivity, which was statistically significant ($p = 0.001$). Binary logistic regression analysis showed that the duration of dialysis and dialysis at more than one centre were the significant variables for increased positivity.

Conclusion: The patients on HD had 12.4% positivity for anti-HCV in our dialysis unit. Further, the present study demonstrated that the duration of haemodialysis and getting the dialysis done at more than one centre were the important risk factors for acquiring HCV infection in these patients.

Key Words: Maintenance haemodialysis; Hepatitis C; Duration of dialysis, Anti-HCV

INTRODUCTION

Hepatitis C virus (HCV) infection is prevalent among patients who undergo maintenance haemodialysis (HD) and is a particular concern because of the high risk for chronic liver disease, complications in renal transplantation and death in these patients [1]. The prevalence of this infection is known to vary widely in different regions of the world. In India, a very wide range of prevalence rates for HCV (4.3-45.2%) in the HD population have been reported [2-7].

A number of risk factors have been identified for HCV infection among the dialysis patients, which include cross infections from the sharing of dialysis machines and the dialysis equipment, the reprocessing of dialyzers and blood lines and the increased requirement of blood transfusions [8, 9]. Among this, dialytic age has been considered as a powerful predictor for the risk of the acquisition of the HCV infection. A significant association between the dialytic age and anti-HCV positivity has been reported in several studies [10, 11]. Similarly, it has been suggested that the HCV infection occurs among HD patients during repeated dialysis, but not through the equipment [12]. However, the situation differs in the developed countries, regarding the prevalence of HCV infection in dialysis patients. The disease in such countries is less prevalent due to many factors including socioeconomic factors, better infection control measures, the use of erythropoietin instead of blood transfusion to treat anaemia and the lower prevalence of the HCV infection among the general population [13].

As far as the literature conveys, the prevalence of HCV infection among the HD patients varies between countries and between the dialysis units within a single country. So far, studies have reported the prevalence of HCV infection in these patients in different regions including the central, western and the northern parts of the country. However, data from the southern part of India on the prevalence of HCV among the HD patients are scanty [6, 7]. Hence, the present study was undertaken to assess the occurrence of the HCV infection in patients on maintenance HD. Furthermore, we also evaluated the risk factors which could facilitate the development of an effective strategy to minimize HCV spread among these vulnerable patients.

MATERIALS AND METHODS

Patients: A total of 145 patients who were on maintenance HD for more than three months were included in the study. Of the 145 patients 102 were males and 43 were females, with a median age of 45 years and an age range of 24-72 years. The medical records were examined for details regarding the duration of HD, the frequency of dialysis, blood transfusions in the past one year, the number of dialysis centres which were visited and the reuse of the dialyzer. The causes of renal failure were diabetes, hypertension, chronic glomerulonephritis and other diseases. Patients with acute renal failure who underwent dialysis were excluded from the study. The Institutional Human Ethics Committee approved the study protocol and written informed consent was obtained from all the patients.

Haemodialysis Unit: The HD unit had two routine HD unit areas and one isolated area each for HCV positive and HBV positive patients. The routine HD area had eight machines in each area, the HCV positive area had three machines and the HBV positive area had two machines. All the patients underwent serological testing for HCV, HBV and HIV before initiating the dialysis. Patients who were negative for HCV before initiating the dialysis were dialyzed by using the routine dialysis machines and those who were HCV positive were dialyzed on dedicated machines in the isolated areas. Patients who were seroconverted during the haemodialysis treatment were shifted to the respective isolated area. None of the staff members in the dialysis unit had a history of blood transfusion, drug abuse, or a history of hepatitis B or C infection.

All the patients were essentially treated with three sessions of routine conventional bicarbonate HD each week (3 to 4 h/session) by using standard polysulfone (PS) membranes (Fresenius F-6, 40 mm thick of 1.32 m^2 surface area). A dialysate with a standard composition, with bicarbonate buffer was used in all the patients. The blood flow rate was 200 mL/min and the dialysate flow rate was 500 mL/min. The dose of the dialysis was individually adjusted to maintain a Kt/V which was >1.2. All the HD machines were chemically disinfected between each dialysis session. The dialyzers were reused in all the patients.

Specimen collection and Laboratory data: The samples of blood were collected from the patients by using vacutainers (BD, USA), they were centrifuged for 15 min at 2000 rpm and the serum was separated and stored at –20^{0}C until analysis. The data regarding the liver function tests were recorded from the patients' dialysis records and the data was maintained anonymously. The anti-HCV assay was performed by a enhanced chemiluminescence immunoassay (Ortho/ECi), by using the vitros reagent pack and the immunodiagnostic calibrator on the vitros ECi immunodiagnostic system. The Ortho/ECi anti-HCV assay is a two-step sandwich chemiluminescence assay for the qualitative detection of human antibodies in serum or plasma to various proteins of HCV, with a total incubation time of 45 min. The Ortho/ECi system uses a small sample volume (20 µl) for each determination. The results were calculated as a normalized signal relative to the cutoff value (signal/cutoff [S/C] ratio). The patient samples with a single S/C ratio of ≥1.00 were considered to be test positive. If the S/C ratio was <0.90, the sample was considered as negative. Samples with an S/C ratio of ≥0.90 and <1.00 were retested in duplicate, based on the manufacturer's recommendations.

STATISTICAL ANALYSIS

The data analysis was performed by determining the frequencies and the percentages for the variables under study. The unpaired Students "t" test was used to compare the quantitative parameters between the anti-HCV negative and the anti-HCV positive group. The Chi-square test was used for the categorical data. A 'p' value which was <0.05 was considered to be statistically significant. Logistic regression analysis was done to determine the risk factors by taking anti HCV as a dependent variable. The statistical analysis was performed by using the statistical software, SPSS version 16.0.

RESULTS

The patients included in this study were divided into two groups, anti-HCV positive and anti-HCV negative. The demographic and the clinical characteristics of these patients are shown in [Table/Fig-1]. Among the 145 patients on HD, 18 patients (12.4%) were found to be anti-HCV positive. There were 13 (72.2%) males in the HCV positive group and 89 (70.1%) males in the HCV negative group. Anti-HCV antibodies were present prior to the dialysis in only eight of the patients who were included in the study population. Ten (10) of them acquired the antibodies during the course of the study. The anti-HCV positivity was 8.6% in patients who underwent dialysis at one centre, whereas the patients who had dialysis at more than one centre had a higher positivity (56%).

A comparison between the two groups, the anti-HCV positive and the anti-HCV negative groups, is shown in [Table/Fig-2]. The mean duration of the dialysis among the HCV positive patients was 36.67 ± 31.68 months, while in the HCV negative patients, it was 18.50 ± 21.29 months, which was statistically significant (p = 0.002). Similarly, patients who had the dialysis at more than one centre had a higher (55.56%) positivity, which was statistically significant (p = 0.001). The proportion of surgeries was higher in the anti-HCV positive group (100.0%) as compared to that in the negative group (90.55%), (p = 0.017). There was no statistically significant difference between the two groups with regards to other risk factors (ALT, AST, ALP and blood transfusion which were received in one year).

Logistic Regression analysis was done by taking anti-HCV positivity as a dependant variable and other suspected variables (diabetes, haemodialysis duration, dialysis at more than one centre and blood transfusions) as independent variables or risk factors (Table/Fig-3). For the analysis, 145 patients were considered, as these patients contained the values of these independent variables. The duration of dialysis (p = 0.034) and the dialysis at more than one centre (p = 019) were found to be statistically significant. The basic disease diagnosis (diabetic or nondiabetic) and the blood transfusions were found to be statistically insignificant.

DISCUSSION

It is well known that HD patients are at a high risk for the development of HCV infection. The prevalence of the HCV infection varies widely from 8% to 45% in these patients [2-7]. Reddy et al (2005) reported 13.3% [7], Chandra et al (2004) reported 43% [6], Agarwal et al (1999) reported 42% [3], and recently, Jasuja et al (2009) reported 27.7 % [2]. The highest reported incidence from a single HD unit was 43% [6]. The reason for this variation in the prevalence rates of HCV among the HD patients which were reported from different parts is unknown. However, Reddy et al

S.No	Variable	Anti-HCV Positive (%)	Anti-HCV Negative (%)	Total (%)
1.	Total cases (n)	18 (12.4)	127 (87.6)	145 (100)
2.	Sex			
	Females	05 (27.8)	38 (29.9)	43 (29.7)
	Males	13 (72.2)	89 (70.1)	102 (70.3)
3.	Diagnosis			
	Diabetic	15 (83.3)	80 (63.0)	95 (65.5)
	Non-diabetic	03 (16.7)	47 (37.0)	50 (34.5)
4.	Dialyzer			
	Reuse	18 (100.0)	127 (100.0)	145(100.0)
	Non-Reuse	–	–	–
5.	Dialyzed at			
	One centre	08 (8.6)	85 (91.4)	93 (64.2)
	Two centre	04 (10.0)	35 (90.0)	39 (26.9)
	Three/ More	06 (46.0)	07 (54.0)	13 (8.9)

[Table/Fig-1]: Baseline characteristics of hemodialysis patients

S. No	Parameter	n	Anti-HCV positive	n	Anti-HCV negative	p-value
Quantitative†						
1.	Age (Years)	18	47.11 ± 14.40	127	45.86 ± 13.99	0.654
2.	Duration of hemodialysis (M)	18	36.67 ± 31.68	127	18.50 ± 21.29	0.002*
3.	AST (IU/L)	18	46.65 ± 51.64	127	38.50 ± 39.45	0.587
4.	ALT (IU/L)	18	53.67 ± 65.57	127	44.80 ± 55.59	0.464
5.	ALP (IU/L)	18	177.80 ± 15.59	127	146.67 ± 13.57	0.078
Qualitative						
1.	Males	18	13 (72.22)	127	89 (70.08)	0.547
2.	No of surgeries	18	18 (100.0)	127	115 (90.55)	0.017*
3.	No of blood transfusions					
	Ours	18	04 (22.22)	127	49 (38.58)	0.645
	Outside	18	00 (0.00)	127	08 (06.29)	0.753
4.	Dialysis at more than one centre	18	10 (55.56)	127	42 (33.07)	0.001*

[Table/Fig-2]: Comparison of Groups 1 (anti-HCV positive) and 2 (anti-HCV negative)

† Values are Mean ± SD; * (compared to anti-HCV positive); Figures in parenthesis indicate percentage; ALT: alanine Aminotransferase; AST: aspartate Aminotransferase; ALP: alkaline phosphatase.

S. No	Variable	n	Beta coefficient	Adjusted odds ratio	95% CI of odds ratio	P value
1.	Diabetes	50	–1.163	0.269	0.045–1.507	0.145
2.	Duration	145	–0.019	0.981	0.964–0.999	0.034*
3.	Dialysis more than one center (>1)	52	–0.834	0.434	0.217–0.879	0.019*
4.	Blood Transfusions	61	-1.103	0.179	0.063–1.507	0.298

[Table/Fig-3]: Logistic Regression analysis

† Anti-HCV positivity as dependant variable and others as independent variables (risk factors)

(2005) reported that stringent blood testing and the isolation of the dialysis machines have helped in the reduction of the transmission of hepatitis C among HD patients and that this was the reason for the low prevalence of HCV [7]. In the present study, we found a low anti-HCV prevalence among the maintenance HD patients at our dialysis centre (12.4% and 72.2% in males and 27.8% in females), which was in harmony with the results of the study which was done by Reddy et al (2005) (13.3%) [7]. Strict adherence to infection control measures in the dialysis setting, the use of dedicated machines, equipments and isolated areas and separate washing areas for the positive patients may be the reason for the low prevalence (12.4%) in our dialysis unit. Similarly, we found a low sero-conversion rate (7.44%) at our dialysis centre. Only 10 of the included patients became seropositive after the initiation of haemodialysis. However, the acquisition of the infection by some individuals after the initiation of dialysis was possibly because of the breach in the infection control strategies during the dialysis.

Many factors may have contributed to the prevalence of the positive anti-HCV in the HD patients. Some of these have been confirmed in the present study. Of the risk factors for the HCV transmission during HD, blood transfusion was an important factor. Several studies [14-16] showed that the risk of acquiring the HCV infection increased with an increase in the number of units of blood which were transfused. However, in the present study, we found no significant association between the blood transfusions and the anti-HCV positivity. Few other investigators [2, 17] have also forwarded similar results and have suggested that an association between dialysis-associated hepatitis and transfusion does not imply a causal relationship, but that rather it is related to the duration of the dialysis.

Most studies concur that the duration of dialysis is closely related to a positive anti-HCV rate [2, 15, 18]. The prevalence of HCV infection in the HD patients in our setup was low (12.4%). However, its association with the duration of dialysis was found to be statistically significant. Our results also emphasized that the longer dialysis duration was a significant risk factor for acquiring HCV infection. Interestingly, in the present study, we found a significant association between the anti-HCV positivity and patients who had dialysis at more than one centre, which was a new finding of the study. Furthermore, there are few studies [19, 20] which have reported a higher incidence of HCV infection in the presence of reuse of the dialyzer. In our study, there was no significant impact of the dialyzer reuse.

As per the literature review, anti-HCV positive patients had significantly elevated levels of liver enzymes than the HCV negative patients [15, 21, 22]. In a recent study, Jasuja et.al [2] (2009) reported a significant correlation of HCV RNA positivity with elevated levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Moreover, the study found that ALT was a significant risk factor for HCV RNA positivity. However, in the present study, the values of ALT and AST were similar in both the groups. Transaminase levels are rarely used for the detection of liver disease in these patients, because they are usually low even in patients with a normal hepatic function and histology, who are on dialysis. Hence, the presence of similar values in positive and negative patients in this study should not be considered as being unusual.

The main limitation of the present study was the inability to adopt HCV RNA PCR as a screening test due to the high costs. We used enhanced chemiluminescence immunoassay as a screening test for the HCV infection. This was more sensitive and specific than the third generation ELISA and we used strong cutoff points to detect the HCV positivity [23].

In conclusion, although the prevalence of the HCV infection among patients on HD at our dialysis centre was lower than that in other parts of the country, it still remains high. We believe that preventive measures and the adherence to 'universal precautions for HCV control' remain a priority. Hence, we recommend the use of dedicated dialysis equipment, spaces, nursing staff, separate washing areas and the screening of the patients once in 3 months, for preventing cross-infection. Furthermore, the present study demonstrated that along with the duration of HD, dialysis at more than one centre was also an important risk-factor for acquiring the HCV infection.

REFERENCES

[1] Petrosillo N, Gilli P, Serraino D, Dentico P, Mele A, Ragni P. et.al. Prevalence of infected patients and understaffing have a role in hepatitis C virus transmission in dialysis. *Am J Kidney Dis* 2001; 37:1004-1010.

[2] Jasuja S, Gupta AK, Choudhary R, Kher V, Agarwal DK, Misra A. et.al. Prevalence and association of hepatitis C viremia in hemodialysis patients at a tertiary care hospital. *Indian J Nephrol* 2009; 19: 62-68.

[3] Agarwal SK, Dash SC, Irshad MC. Hepatitis C virus infection during hemodialysis in India. *J Assoc Physicians India* 1999; 47:1139-43.

[4] Jaiswal S, Chitnis D, Salgia P, Sepaha A, Pandit C. Prevalence of the hepatitis virus among chronic renal failure patients on hemodialysis in central India. *Dialysis Transplant* 2002; 31: 234-38.

[5] Saha D, Agarwal SK. Hepatitis and HIV infection in hemodialysis patients. *J Indian Med Assoc* 2001; 99: 194-9,203,213.

[6] Chandra M, Khaja MN, Hussain MM, Poduri CD, Farees N, Habeeb MA, et.al. Prevalence of hepatitis B and hepatitis C viral infections in Indian patients with chronic renal failure. *Intervirology* 2004; 47: 374-376.

[7] Reddy GA, Dakishnamurthy KV, Neelaprasad P, Gangadhar T, Lakshmi V. Prevalence of HBV and HCV dual infection in patients on hemodialysis. *Indian J Med Microbiol* 2005; 23: 41-43.

[8] Salama G, Rostaing L, Sandres K, Izopet J. Hepatitis C infection in a French hemodialysis unit; a multicenter study. *J Med Virol* 2000; 61: 44-51.

[9] Jaiswal SP, Chitnis DS, Naik G, Artwani KK, Pandit CS, Salgia et al. Prevalence of anti-HCV antibodies in central India. *Indian J Med Res* 1996; 104:177-81.

[10] Hardy NM, Sandroni S, Danielson S, Wilsom WJ. The antibody to the Hepatitis C Virus increases with time on hemodialysis. *Clin Nephrol* 1992; 38:44-48.

[11] Niu MT, Coleman PJ, Alter MJ. A multicenter study on the hepatitis C virus infection in chronic hemodialysis patients and hemodialysis staff members. *Am J Kidney Dis* 1993; 22:568-573.

[12] Okuda K, Hayashi H, Kobayashi S, Irie Y. The mode of the hepatitis C infection is not associated with blood transfusion among chronic hemodialysis patients. *J Hepatol* 1995; 23:28-31.

[13] Kalantar-Zadeh K, McAllister CJ, Miller LG. Clinical characteristics and mortality in hepatitis C-positive haemodialysis patients: a population based study. *Nephrol Dial Transplant* 2005; 20: 1662-1669.

[14] Saab S, Martion P, Brezina M, Gitrich G, Yee HF Jr. Serum alanine aminotransferase in hepatitis C screening of the patients on hemodialysis. *Am J Kidney Dis* 2001; 37: 308-15.

[15] Dentico P, Buogiorno R; Volpe A. Prevalence and incidence of hepatitis C virus (HCV) in hemodialysis patients: study of risk factors. *Clin Nephrol* 1992; 38:49-52.

[16] Alfurayh O, Sobh M, Buali A, Ali MA, Barri Y, Qunibi W, et al. Hepatitis C virus infection in chronic hemodialysis patients: A Clinicopathological study. *Nephrol Dialysis Transplant* 1992; 7:327-332.

[17] Hardy NM, Sandroni S, Danielson S, Wilson WJ. The antibody to the hepatitis C virus increases with time on hemodialysis. *Clin Nephrol* 1992; 38: 44-48.

[18] Donahue JG, Munoz A, Ness PM, Brown DE Jr, Yawn DH, McAllister HA Jr, et.al. The declining risk of the post transfusion hepatitis C virus infection. *N Engl J Med* 1992; 327:369-73.

[19] dos Santos JP, Loureiro A, Cendoroglo Neto M, Pereira BJ. The impact of the dialysis room and reuse strategies on the incidence of the hepatitis C infection in hemodialysis units. *Nephrol Dial Transplant* 1996; 11:2017-22.

[20] Jadoul M, Cornu C, van Ypersele de Strihou C. Incidence and risk factors for hepatitis C seroconversions hemodialysis: A Prospective study. *Kidney Int* 1993; 44:1322-6.

[21] Natov SN, Lau JY, Bouthot BA, Murthy BV, Ruthazer R, Schmid CH, et al. Serological and virological profiles of the hepatitis C infection in renal transplant candidates. *Am J Kidney Dis* 1998; 31: 920-927.

[22] Herrine SK, Michael B, Na WL, Rossi S, Dunn SR, Hyslop T. Development of an HCV infection risk stratification algorithm for patients on chronic hemodialysis. *Am J Gastroenterol* 2002; 97: 2619-22.

[23] Sherman KE, Rouster SD, Horn PS. Comparison of the Methodologies for the Quantification of the Hepatitis C Virus (HCV) RNA in Patients who are Co infected with the HCV and the Human Immunodeficiency Viruses. *Clin Infect Dis* 2002; 35:482-7.

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