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Chaos in the diagnosis of hepatitis C virus in hemodialysis patients

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Abstract

Background: In India, a broad range of prevalence of Hepatitis C virus (HCV) infection in hemodialysis (HD) patients was reported. Variations in screening methods and regional differences in the HCV genome render challenges in the accurate detection of HCV. In this background, the present study was undertaken to assess the prevalence of HCV by HCV RNA PCR (Ribose nucleic acid Polymerase Chain Reaction) and HCV antibody detection by immunochromatography (ICT) and ELISA (Enzyme Linked Immuno-Sorbent Assay). **Methods**: A total of 50 patients with chronic kidney disease (CKD) on maintenance HD for more than six months were included in the study. Blood sample was collected and subjected to HCV RNA PCR, and HCV antibody by ICT and ELISA. **Results**: Of the 50 samples tested, ICT for HCV antibody was detected in 22 (44%) patients. They were positive for ELISA also. HCV RNA was positive in 15 (30%) patients. PCR positive was also positive for HCV antibody. **Conclusions**: This study concludes, that HCV antibody screening should be performed monthly and RNA PCR once every three months among HD patients.

Keywords: Hepatitis C virus; Hemodialysis; Antibody detection; Molecular method

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Introduction

Hepatitis C virus (HCV) is the most common infection which causes constant public health threats among patients on maintenance hemodialysis (HD) owing to its high risk of progression to chronic liver disease, aftereffects in renal transplantation and resulting in death. The prevalence of HCV infection varies widely in different geographic locations globally. In India, a very broad range of prevalence of HCV infection in HD patients was reported [1]. Because dialysis procedures carry a risk of HCV exposure, they are more likely to acquire infection. Unlike with hepatitis B, there is no vaccine available for HCV. Variations in screening methods and regional differences in the HCV genome render challenges in the accurate detection of HCV [2]. However, there is a paucity of studies on the prevalence of HCV by PCR among HD patients. In this background, the present study was undertaken to assess the prevalence of HCV by HCV RNA PCR and HCV antibody detection by immunochromatography (ICT) and ELISA. In addition, this study assessed the risk factors associated with the transmission of HCV among these high-risk populations.

Material and methods

This descriptive cross-sectional study was conducted in the Department of Microbiology & Virology, Tertiary Care Hospital for a period of six months between May and October 2023. A total of 50 patients with CKD on maintenance HD for more than six months were included in the study. Socio-demographic data such as age, gender, duration of illness, history of jaundice, blood transfusion, and details of co-morbid illness of these patients were collected using a detailed proforma. Each participant was allotted a unique laboratory ID. Under sterile aseptic precautions, 5 mL of venous blood was collected, and the serum was utilized for ICT (9557TG, Bioline Diagnostics, Mumbai, India) and ELISA (ErbaLISA HCV GEN 3 (v2), TCG 32203, Transasia Bio-Medicals, Daman, India). Another 5 mL of blood was collected in an EDTA (Ethylene Diamine Tetra-acetic Acid) tube used for molecular study (CP00003-C-0522001, MyLab Discovery solutions, Pune, India) and the samples were stored at −80 ℃ until the tests were performed.

Statistical analysis

Data obtained was entered in Microsoft Excel and results were analyzed using the SPSS software version 27.0, IBM Corporation, Armonk, NY, USA. Mean and standard deviation were calculated for continuous variables, and data for categorical variables were expressed as percentages. Statistical analyses were performed using the Chi-Square test and Fisher's exact test for the categorical values. Statistical significance was calculated with a probability value (*p*-value) of less than 0.05.

Inclusion criteria

Patients >18 years of age who have undergone HD for more than six months.

Exclusion criteria

Patients who have undergone HD for less than six months.

Pregnant women were excluded from the study.

Patients who were HCV positive before the study period.

Results

Of the 50 patients, 29 (58%) were between 38–57 years. 37 (74%) were male. The mean age of the study participants was 41.3 ± 13.47 years. History of blood transfusion was recorded in 11 (22%). Comorbid conditions such as diabetes and hypertension were noted in 15 (30%). The frequency of HD >3 sessions/week was reported in 36 (72%) participants (Table 1).

The mean age of HCV-positive patients was 42.71 ± 10.96 years. History of blood transfusion in three (12.5%) and comorbid conditions such as both diabetes and hypertension in eight (33%) and hypertension alone in 14 (58%) were observed among the HCV-positive individuals. Nine (20%) had Alanine aminotransferase (ALT) >40 IU/mL and Aspartate aminotransferase (AST) >35 IU/mL. The frequency of HD >3

Table 1. Basic characteristics of the haemodialysis patients.

Categories	Variables	HCV-negative patients (n = 26)	HCV-positive patients (n = 24) (%)	*p*-value < 0.05
Gender				
	Male	18	19 (79.2)	0.423581
	Female	8	5 (20.8)	Not significant
Age group (yr)				
	18–37	9	7 (29.2)	-
	38–57	13	16 (66.6)	-
	≥58	4	1 (4.2)	-
	Mean ± SD	40.00 ± 15.77	42.71 ± 10.96	
Co-morbid conditions				
	SHT alone	14	14 (58.3)	-
	DM alone	0	0	-
	SHT & DM	7	8 (33.3)	-
	No comorbidity	5	2 (8.3)	-
Blood transfusion				
	Yes	8	3 (12.5)	0.1754
	No	18	21 (87.5)	Not significant
Duration of HD				
	6 to 12 mon	11	19 (79.0)	0.0101
	≥13 mon	15	5 (21.0)	Significant
Frequency of HD				
	≤2 sessions/wk	5	9 (37.5)	0.2109
	≥3 sessions/wk	21	15 (62.5)	Not significant
AST				
	Elevated	1	9 (37.5)	0.004
	Normal	25	15 (62.5)	Significant
ALT				
	Elevated	2	9 (37.5)	0.0164
	Normal	24	15 (62.5)	Significant

SHT: systemic hypertension; DM: diabetes mellitus; SD: Standard deviation; HCV: Hepatitis C Virus; HD: Hemodialysis; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase.

sessions/week was noted in 15 (63%) of HCV-positive patients (Table 1).

Of the 50 samples tested, ICT for HCV antibody was detected in 22 (44%) patients. They were positive for HCV antibody by ELISA also. HCV RNA was positive in 15 (30%) patients of which 13 were positive and 2 were negative by ELISA/ICT. PCR positive was also positive for HCV antibody (Table 2). There was no discordance observed between ELISA & ICT in detecting the HCV antibodies. The sensitivity and specificity of the ICT and ELISA used were 59.1% and 92.9% respectively and the positive predictive and negative predictive values were 86.7% and 74.3% respectively in comparison with the gold standard method of HCV RNA testing. The Chi-square test value is 0.000069 with Kappa Coefficient of 0.538. These results indicate moderate agreement between RT-PCR (Reverse Transcriptase-Polymerase Chain Reaction) and ELISA & ICT for HCV testing. The mean duration of HD among HCV-positive cases was 11.79 ± 3.82 months. There is a statistical association between duration of HD and HCV seropositivity.

Table 2. Association between RT-PCR, ELISA & ICT in HCV.

RT-PCR	ELISA & ICT		Total
	Positive	Negative	
Positive	13	2	15
Negative	9	26	35
Total	22	28	50

RT-PCR: Reverse Transcriptase-Polymerase Chain Reaction; ELISA: Enzyme Linked ImmunoSorbent Assay; ICT: Immuno-Chromatographic Test.

Discussion

Patients with end-stage renal disease (ESRD) who have HCV infection have been linked to higher rates of morbidity and mortality as well as further complications following renal transplantation [1]. Worldwide estimates recorded that between 4.7 and 10.9 million people in India had HCV viremia in 2015, with a prevalence rate of 0.5%. Based on anti-HCV antibodies, a meta-analysis of 327 studies estimated that the prevalence rate of HCV in India was 0.85% in the general population, 0.44% in asymptomatic blood donors, and 0.88% in pregnant women. The prevalence rate among attendees of sexually transmitted disease clinics was recorded as 3.5–44.7% [3].

Risk factors associated with HCV infection among dialysis patients include cross infections due to sharing of dialysis machines, reprocessing of dialyzers, longer duration of dialysis, bloodlines, repeated blood transfusions, HIV, hepatitis B virus, history of cirrhosis and glomerulonephritis [4]. Three persons (12.5%) had a history of blood transfusion among HCV-positive cases. It was statistically not significant among HCV-positive and negative cases. In this centre, sharing dialysis machines and reprocessing of dialyzers are practised routinely. The most common comorbid condition noted was hypertension in 22 (92%) cases. Altinawe *et al.* [5] reported that 84% of HCV positives had hypertension.

Centre for Disease Control (CDC) advises persons at increased risk of HCV infection should be screened routinely. HCV antibody detection by ICT/ELISA failed to detect all the cases in the acute phase of infection [6]. The window period in the HD patients may be prolonged, because of the immunocompromised state, leading to false negative results. Seroconversion to HCV antibodies may not occur in all HD patients, as stated by Dharmesti *et al.* [7]. Hence, a reactive, indeterminate, equivocal, weakly reactive antibody detection method should be confirmed by HCV RNA detection in serum. Whereas, the demonstration of HCV RNA in hepatocytes or peripheral blood mononuclear cells should be performed to rule out occult HCV infection [8]. Due to the high PCR assay cost, repeated PCR testing among HD patients is limited resulting in a high rate of false negatives.

Most of the Indian studies perform HCV antibody by ICT/ELISA, reported a prevalence of 1.38–12.4% among HD patients in the last decade. Data on the prevalence of HCV by PCR is scarce [9]. Reddy *et al.* [10] and Medhi *et al.* [11] observed a prevalence of 13.23% and 17.2% among HD patients by HCV core antigen ELISA. In the present study, HCV antibody was detected in 22 (44%) patients which is concordant to study by Kerollos *et al.* [12], stated 34.8% of HCV seroprevalence among HD patients. In the present study, high seroprevalence was noted due to the persistence of anti-HCV antibodies for a longer duration. HCV RNA was positive in 15 (30%) patients of which 13 were positive and 2 negative by ELISA/ICT. Studies mentioned that HCV viremia in HD patients is lower than that in HCV patients without kidney failure replacement therapy probably because of the destruction of viral particles by the HD procedure [13]. There are certain instances where an individual with an active HCV infection may have a negative HCV RNA. Viral load decreases during acute infection while anti-HCV titer increases, which may lead to negative HCV RNA [14].

Routine screening of dialysis patients by PCR-based methods, effective blood bank screening protocols, use of erythropoiesis-stimulating agents instead of blood transfusions and strict adherence to infection control measures in dialysis units will reduce the prevalence of HCV among HD patients. This study emphasizes all HD patients should undergo HCV antibody testing every month with RNA PCR once in three months.

PCR-positive samples were not sent for sequencing and genotyping due to financial constraints.

Conclusions

Of the 50 samples tested, ICT for HCV antibody was detected in 22 (44%) patients. They were also positive for ELISA. HCV RNA was positive in 15 (30%) patients. The most important risk factor observed in the study was renal failure requiring HD for a longer duration, sharing dialysis machines and reprocessing of dialyzers are practised routinely. Hence, this study concludes that HCV antibody screening should be performed monthly and RNA PCR once every three months among HD patients.

Availability of Data and Materials

The data are contained within this article.

Author contributions

AI and SKP—designed the research study, wrote the manuscript and analysed the data. GV—wrote the manuscript. KMK—provided help and advice on the preparation of the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from all the participants using the form approved by the Institutional Ethics Committee of Tirunelveli Medical College, Tirunelveli, Tamilnadu, India (TIREC ID: 20232686, dated 21 March 2023) before the study commencement.

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Conflict of interest

The authors declare no potential conflicts of interest with respect to research, authorship and/or publication of this article.

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