

Occult Hepatitis C Virus Infection in Chronic Kidney Disease on HemodialysisShiv Parshad Mittal^{1*}, Satish Kumar Jaiswal²¹Assist Professor, Department of Medicine, MM Medical College & Hospital Kumarhatti, (Solani) - Himachal Pradesh, India²Professor, Department of Microbiology, MM Medical College & Hospital Kumarhatti, (Solani) – Himachal Pradesh, India**Original Research Article*****Corresponding author**

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Abstract: Patients undergoing hemodialysis are prone to Hepatitis C Virus (HCV) infection. Elevation of serum Alanine Amino Transaminase (ALT) is suspected to correlate with the occult HCV infection. Our study is based on this observation to substantiate the findings or otherwise. This hospital randomized retrospective and prospective of about 2 years study, recruited 74 patients (55 males and 19 females) of stage – 5 chronic kidney diseases (CKD). After clinical evaluation, relevant laboratory tests, viral markers (HIV, HBV and HCV) and hepatic enzymes patients were followed after each hemodialysis. Patients with elevated ALT were subjected to HCV testing. Results analyzed. Preliminary data suggest a high frequency of occult HCV infection in dialysis patients with elevated liver enzymes who are anti-HCV antibody and HCV RNA negative.

Keywords: Occult Hepatitis C Virus Infection; Serum Alanine Amino Transaminase; Chronic kidney Diseases; Hemodialysis.

INTRODUCTION

Hepatitis C Virus (HCV) infection is an insidious, mostly asymptomatic, recurrent & occult hepatitis. If not diagnosed and treated timely it progresses to cirrhosis and hepato-cellular carcinoma. HCV found in patients with different presentations i.e. Liver transplantation [1]; Chronic Hepatitis, Cirrhosis or persistent liver dysfunction of unknown etiology, patients receiving antiviral therapy, Chronic Kidney Diseases (CKD) on Hemodialysis (HD) and even in screened blood transfusion from blood donors HCV infection is 1 in 103000 [2].

Patient vulnerability to HCV infection during HD depends on: the duration of dialysis, associated Hepatitis B Virus (HBV) infection, diabetes, blood transfusions, alcohol, I/V substance abuse, nosocomial HCV transmission and male gender [3-5]. Some patients on HD have propensity to develop elevated serum Alanine Amino transferase (ALT). New genomic studies detected HCV in these patients [6, 7]. In view of this, this study is undertaken to detect occult HCV infection in patients with raised Serum ALT so that early effective therapeutic and preventive measures can ameliorate the risk of HCV transmission.

METHOD

Study design: This hospital based cross – sectional, open, randomized, retrospective and prospective study was undertaken jointly by Department of Medicine and Microbiology of Maharishi Markandeshaver Medical College and Hospital Kumarhatti– Himachal Pradesh.

Study duration: From May 2014 to Mar 2016.

Patients

Consecutive patients of Stage - 5 CKD (Glomerular Filtration Rate \leq 15 ml / min per 1.73 m²), due to any cause, requiring maintenance HD were included in this study. Total patients were 74 patients (55 males and 19 females, male: female 3:1).

Exclusion criteria

(1) Liver dysfunction due to causes other than viral hepatitis, (2) Patients receiving steroids or immunosuppressants and (3) Patients were not available for follow up.

Patients enrolled in this study were clinically evaluated: detail history taken including relevant family history, especially for Diabetes mellitus, hypertension and other risk factor, life style, substance abuse including I/V drug abuse, blood transfusion, extra marital sexual contact and health care consciousness. Physical examination included: measurement of blood pressure and other relevant vital parameters; presence

of anemia, edema, cardiovascular state especially bruit over renal arteries and other systemic examination.

After clinical examination, on 1st predialysis day (when patient is taken for dialysis in this hospital), blood samples were taken for Hemoglobin (Hb), Total (TLC) & Differential Leukocyte Count (DLC), Urine routine examination and, if required, urine for culture and sensitivity; blood for biochemical profile mandatory for HD, serum HBV, HCV & HIV viruses and Liver function tests including Aspartate Aminotransferase (AST) and Alanine Aminotranferase (ALT). USG Abdomen was taken, especially, for Liver & renal areas. After HD, patients were advised to continue medication for Hypertension (HTN), DM & other appropriate symptomatic treatment and recommended follow up. Follow up was decided based on serum creatinine level (> 7 mg%), symptomatic fluid overload, concurrent infection with increase catabolism and/or systemic complications of uremia. On subsequent maintenance HD, each patient, apart from

clinical examination, was subjected to required laboratory tests. Medicine renewed. Three monthly, patient was screened for HCV, HBV and HIV.

RESULTS

This study included 74 patients of Stage – 5 CKD (55 male and 19 female. Male & Female ratio 3:1). They constituted both Indoor and OPD patients. Out of 55 males 30 (54.55 %) had HTN, 10 (18.18%) DM, 12 (21.82%) both HTN & DM and 3 (5.9%) pyelonephritis. Out of 19 females 15 (78.95%) had HTN, 1(5.56%) DM and 3 (16.67%) both HTN and DM (Table – 1)

Based on exclusion criteria 5 patients [1 = predialysis positive for HCV (male); 1 = HIV positive (male); 1 = terminally ill (male) and 2 = continue to receive multidisciplinary therapies (1 Male & 1 Female)] were excluded. Details of patient’s age and sex – wise distribution of CKD patients (51 Males and 18 Females) given in Table – 1.

Table-1: Age & Sex – wise Distribution of CKD patients

Sex	Male				Female			
	< 30	31 – 50	51 – 70	>70	<30	31 – 50	51 – 70	>70
HTN	2	9	19		1	8	6	
DM		3	7			1		
HTN & DM		2	10				3	
Misc (?Pyelonephritis)		2	1					
Total	2	16	37		1	9	9	

(Note: DM = Diabetes mellitus; HTN = Hypertension; Misc = Miscellaneous. Diagnosis of Pyelonephritis was assumed in a patient with history of recurrent fever, general symptoms and urinary tract infection in setting of nephrolithiasis)

Sixty one patients [47 (85.45%) males and 14 (73.68 %) females] were with rural background inhabiting in remote hilly areas and financially backward. Almost all were irregular in follow up for HD because of financial constraint, ignorance about the nature of the disease and wrong notion that HD is an ultimate cure of CKD and hence probably accepted multidisciplinary treatment including holistic medicine for the disease before being diagnosed as CKD. None of the patient was I/V substance abuser, though 48 (87.27%) males consumed country – made alcohol in moderation during healthy life. Fifty two (97 %) males and 9 (47.39%) females were smokers in moderation and for many years. No past history of jaundice or infusion of blood of blood products.. Whether HTN is the cause or complication of CKD cannot be substantiated authentically as patients had no previous medical record. Many HTN patients were diagnosed CKD on initial examination. CKD was found to be more prevalent in males being highest in age group 51 – 60 and lesser in 31- 50 years in females and detected about a decade earlier in females. Same trend was seen with DM or DM and HTN. CKD in young seems likely to be of infective in origin. Age at which CKD was diagnosed / HD initiated shown in Table – 1 & depicted in Fig – 1.

During initial evaluation and subsequent follow up, 25 [17 (24.64%) males and 8 (11.59%) females] patients were found abnormally raised ALT and AST either before or during HD follow up, except 1 male patient where ALT was disproportionately high and AST normal. Follow up revealed that elevated hepatic enzymes, especially ALT, were not related to the duration of HD, age of patient and number of blood transfusions, if any. Males have shown greater propensity towards hepatic enzyme elevation than females. One patient turned positive for HCV during 1 year of maintenance HD with abnormally raised ALT when initially level was normal. None of the patient with raised ALT had features of overt hepatitis or its complications. Secondly, none of CKD patient has undergone renal transplantation which could have necessitated immunosuppressant therapy and activating occult HCV hepatitis to overt hepatitis. Because of limitations, this study could not perform hepatic fibroscan, liver biopsy and / or HCV RNA genomic study to substantiate or rule out hepatic changes in occult HCV infection. This study has observed that during follow up almost all the patients failed to adhere to prescribe conservative therapy at home and reporting with deranged serum electrolytes, raised blood urea and

serum creatinine, appreciable fluid retention and / or

uncontrolled DM and HTN and infections.

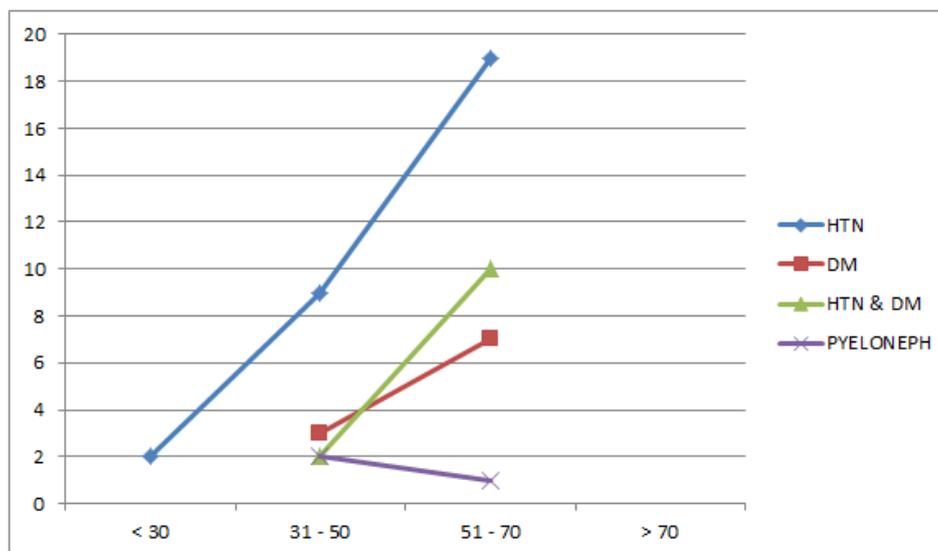


Fig-1: Age of Male CKD patients reporting for HD)

Aanemia was universal in patients in this study. Severe anemia was present in 42 [37 (72.5%) males and 5 (27.8%) females]; moderate in 19 [11 (21.57%) males and 8 (44.44%) females] and mild in 8 [2 (3.92%) males and 6 (33.33%)].

DISCUSSION

In general population HCV infection is common in 30 to 49 years of age with male preponderance [8, 9]. Significant routes of HCV transmission are intravenous drug abuse, hemodialysis, blood and blood products transfusion. In more than 40% of cases, source and mode of transmission cannot be identified, suggesting other unidentified modes of transmission. Since HCV infection is mostly asymptomatic, it remains undiagnosed and 50 – 85% of these patients gradually progress to cirrhosis, hepatic failure and Hepatocellular carcinoma.

Occult HCV infection is recently described entity which means absence of conventional anti-HCV antibody and HCV-RNA in peripheral blood but evidence of HCV viremia (HCV RNA) in hepatocytes or peripheral blood mononuclear cells (PMNCs). Apart from hepatotropic nature of HCV, it can also replicate in extrahepatic sites, including PMNCs [12, 13].

The prevalence of occult HCV infection is high in HD patients with persistently abnormal values of alanine aminotransferase of unknown cause [6, 18, 20, 21].

Very little is known about the potential transmission risks of occult HCV infection, especially, in patients on maintenance dialysis [10]. In some centres, the prevalence of anti-HCV is estimated to be 8% among chronic hemodialysis patients, nosocomial

transmission mode is common [11], HCV infection increases the risk for death among patients receiving chronic hemodialysis treatment and after renal transplantation. Despite stringent guidelines to prevent HCV transmission in HD units, HD - related HCV infections do occur; may be due to breaches in infection control.

Even Centers for Disease Control (CDC) recommends initial anti HCV screening upon admission for all chronic HD patients. For HCV-susceptible patients, periodic testing for ALT; anti-HCV screening should be obtained semiannually thereafter and in response to unexplained elevations in ALT, to facilitate early detection of transmission of HCV in HD units and implementation of control measures [14]. In the presence of elevated levels of liver enzymes, dialysis patients are usually tested for the major hepatitis viruses (hepatitis B virus [HBV] and HCV). Some patients (3%) on maintenance HD have elevated liver enzymes with unclear cause [15]. Information about occult HCV infection in patients on maintenance dialysis is limited [16, 17].

Apart from nosocomial spread, clinical consequences of Occult HCV infected patient include risk of transmitting HCV to others within HD units.

Limitations

This study has limitations due to technical or financial reasons for not performing liver biopsy, Fibroscan liver and HCV – RNA genomic study.

Study was purely based on biochemical signs of liver disease (raised ALT) of unknown cause probably due to HCV infection (based on various studies data implicating HCV in raised ALT); follow up

not adequate to the end point (development of Hepatitis C, death) and finally some studies have shown that HCV-related liver disease in CKD patients is characterized by spuriously low aminotransferases even in the presence of active infection (?).

If it is expected that occult HCV infection does transmit HCV within dialysis units, so current measures should be adequate to control spread of HCV, even if not evaluated by PCR or nucleic acid technology. But more information is needed to substantiate this speculation and to define the risk, if any, for HCV transmission in HD units. Renal transplant recipients get HBV infection from donors with positive HBV serologies (hepatitis B surface antigen–negative/anti–hepatitis sB core antigen antibody–positive kidney donors) indicative only of previous infection [17]. There is theoretical speculation that CRF patients have low immunity therapy enhances HCV replication in HD contact patients. Detection of occult HCV infection not uncovered by routine diagnostic methods may have an important bearing on the development of new screening strategies and therapeutic interventions for HCV infection in these patients. Some screening strategies for HCV detection have shown hopes to confirm HCV infection i.e. detection of HCV-RNA in Peripheral Blood Mononuclear Cells [18] and if not identified in peripheral blood mononuclear cells then detection of HCV-RNA in liver cells. Liver biopsy for HCV not routinely contemplated except in patients undertaken for liver transplantation [6].

In conclusion, preliminary data suggest a high frequency of occult HCV infection in dialysis patients with elevated liver enzymes who are anti-HCV antibody and HCV RNA negative. Further studies are needed to assess the clinical consequences of occult HCV infection in dialysis patients and renal transplant recipient

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