# STUDY ON HEPATITIS B AND HEPATITIS C IN HAEMODIALYSIS PATIENTS OF NATIONAL INSTITUTE OF KIDNEY DISEASES AND UROLOGY (NIKDU), DHAKA

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### **Abstract**

Hepatitis viral infections are important causes of morbidity and mortality in haemodialysis patients. The present study was undertaken to estimate the prevalence of HBV and HCV and dual infection among haemodialysis patients attending at National Institute of Kidney Diseases and Urology (NIKDU), Sher –E–Bangla Nagar, Dhaka during the period between January 2012 to April 2013. One hundred and fifty patients attending haemodialysis unit were screened for the presence of HBV and HCV infections. 22 (14.67%) patients were HCV positive while 18 (12%) patients had HBV infection. A dual infection with both the viruses was observed in 1 patient (.67%).

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## Introduction

HBV and HCV share a common route of transmission and can coexist with each other. Haemodialysis patients are at high risk for hepatitis viral infections due to the high number of blood transfusions, prolonged vascular access and the potential for exposure to infected patients and contaminated equipment. Patients with chronic HBV and HCV concurrent infection show a reciprocal inhibition of viral genomes, an association with a severe clinical presentation and an infrequent response to interferon alfa treatment. <sup>2</sup>

Significant immune status disturbances were registered in haemodialysis patients infected with both HBV and HCV compared to patients with HCV alone. A significant risk of cirrhosis development and decompensation of liver function is observed in HBV and HCV infected haemodialysis patients. Dialysis is a recognised risk factor for transmission of hepatitis B (HBV) which is the most commonly transmitted blood-borne virus in the healthcare setting. Following acute infection, 5-90% of patients become chronic carriers, depending on age and immune competence. Chronic carriage has significant risks of chronic liver disease, cirrhosis, hepatocellular carcinoma and ultimately death. Since 1982 hepatitis

B vaccination has been recommended for susceptible HbsAg negative patients. This has reduced the incidence of HBV infection amongst haemodialysis patients. <sup>4, 5.</sup>

Chronic hepatitis C is the most common chronic liver disease at present and chronic hepatitis C virus infection is found with variable prevalence in dialysis populations in different parts of the world. There is currently no vaccination available for HCV, which should tend to reinforce the importance of strategies to prevent transmission of HCV in the dialysis room. An important reported risk factor for acquiring hepatitis C is the proximity of patient to patient, with high risk documented for a patient dialysed adjacent to an anti- HCV positive patient <sup>6</sup>. The lowest incidence of HCV infection is in haemodialysis units which isolate anti-HCV positive patients in separate rooms, ideally with separate machines <sup>7,8</sup>.

The above evidence should provide impetus for more widespread institution of isolation dialysis for HCV positive patients; given that there is no protective vaccine, HCV exposure leads to chronic infection in approximately 85% of those infected, the disease has a very high risk of chronic morbidity and mortality .

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# Methodology

One hundred and fifty chronic renal failure patients undergoing haemodialysis in the dialysis unit of the nephrology department of National Institute of Kidney Diseases and Urology (NIKDU), Sher-E-Bangla Nagar, Dhaka, during the period between January 2012 to April 2013, were included in the present study. The dialysis unit has 14 haemodialysis machines. Among these, 2 machines are dedicated for HBV and 4 machines are dedicated for HCV positive patients. 6 machines are placed away from the rest(8) of the machines in two isolated rooms, so as to avoid cross contamination. The dialyzers of the patients are reused. Reprocessing of the dialyzers of the HBV / HCV positive patients are done in a separate room, away from the rest of the patients. Dedicated nursing staff look after each patient during the dialysis session. Blood samples were drawn from the patients before the start of the first haemodialysis and every 3 months thereafter. The serum samples were screened for HBsAg and anti HCV antibody. All the HBsAg negative patients were given HBV vaccination. Any patient positive for HBsAg or anti HCV or to both were dialyzed on the dedicated machines. Testing of the serum samples of the patient was done by the commercially available Anti HCV (ICT) and HBsAg (ICT) in the Transfusion Medicine department of our institute. The results are also checked by ELISA method in department of immunology of NIKDU.

Results

**Table-I**Distribution by age

Class interval	No of patients	%
11-20	05	3.33
21-30	19	12.67
31-40	21	14.00
41-50	29	19.33
51-60	57	38.00
61-70	16	10.67
71-80	03	2.00
Total	150	100.00

**Table-II**Distribution by sex

Sex	No of patients	%
Male	98	65.33
Female	52	34.67
Total	150	100.00

**Table-III**Distribution by blood group

Blood group	No of patients	%
A	36	24.00
В	64	42.67
O	41	27.33
AB	09	6.00
Total	150	100.00

**Table-IV**Distribution by unit of blood transfused

Unit of blood	No of patients	%
0	36	24.00
1-5	52	34.67
6-10	38	25.33
11-15	18	12.00
16-20	06	4.00
Total	150	100.00

**Table-V**Distribution by frequency of dialysis

frequency of dialysis	No of patients	%
Twice weekly	136	90.67
Thrice weekly	14	9.33
Total	150	100.00

**Table-VI**Distribution by screening positive

Screening	No of patients	%
HBsAg	18	12.00
Anti-HCV	22	14.67
Dual (HBsAg, Anti-HCV)	01	67
Total	41	27.34

# Discussion

Hepatitis B (HBV) and hepatitis C (HCV) viral infections are important causes of morbidity and mortality in haemodialysis patients<sup>9</sup> and pose problems in the management of the patients in the renal dialysis units. Chronic renal failure patients do not clear these viral infections efficiently. Several outbreaks of hepatitis have occurred in these settings.<sup>10</sup>

In this study, 22 (14.67%) patients were HCV positive while 18 (12%) patients had HBV infection. A dual infection with both the viruses was observed in 1 patient (.67%). This result coincide with other studies in different countries.

HBV infection is less prevalent than HCV in haemodialysis units. <sup>11</sup> Introduction of HBV vaccination, isolation of HBV positive patients, use of dedicated dialysis machines and regular surveillance for HBV infection dramatically reduced the spread of HBV in this setting. <sup>12</sup> The prevalence of HCV infection among haemodialysis is high and varies between countries (2% to 60%) and between dialysis units within a single country. <sup>13</sup> Dual infection with HBV and HCV leads to more aggressive liver disease. <sup>14</sup> There are very few reports on the prevalence of such dual infections in haemodialysis patients.

Prevalence of HBV and HCV co-infection in non-haemodialysis patients was reported by several authors and ranged between 3 to  $56\%.^{15,16}$  A simultaneous study carried out on 75 patients with chronic liver disease by the gastroenterology department of our institute showed a prevalence rate of dual infection of  $4\%.^{15,16}$ 

Studies on prevalence of HCV and HBV coinfection in haemodialysis are rare. Kara *et al* reported dual infection in three patients out of 67 haemodialysis patients. Han et al reported dual infection of 30.4% and it was higher than non haemodialysis patients which was only 3.8%. In their series . In one study, they found 3.7% prevalence of dual infection in haemodialysis patients, which was higher than among the non-haemodialysis patients (0.09%). Out of 134 patients, eight were positive for only anti HCV (5.9%), two patients were positive for HBsAg (1.4%) and dual infection was observed in another five patients (3.7%). All the five patients had a risk factor of history of 2-4 units of blood transfusion before becoming positive. In

Another study showed higher prevalence of HCV (9.240%) than HBsAg (5.88%) in Bahrainis. Higher prevalence of anti-HCV (14.7%) than HBsAg (11.8%) were seen among Saudi patients.<sup>20</sup>

In a study of 1286 hemodialysis patients with anti-HCV and/or HCV-PCR testing, 69 (5.4%) tested positive. Two HCV genotype 4 seroconversions were identified. HCV incidence rate on dialysis was 78.8 cases per 100,000 person-years. Younger age, history of renal transplant and past HBV infection were associated with HCV infection. No occult infection was identified using HCV-

In the HD setting, cross-contamination to patients via environmental surfaces, supplies, equipment, multiple-dose medication vials and staff members is mainly responsible for both HBV and HCV transmission. The incidence and prevalence of HBV in HD centers have dropped markedly as a result of isolation strategy for HBsAg positive patients, the implementation of infection control measures and the introduction of HBV vaccine. The incidence and prevalence of HCV infection among HD patients remain higher than the corresponding general population..<sup>22</sup>

Of the 353 patients enrolled in the study, HBsAg and anti-HCV was detected in 16 (4.5%) and 30 (8.5%) patients, respectively. None of the transfused and anti-HCV eropositivity, multivariate analysis showed no association between age, sex, level of education, istory of surgery or number of units of blood transfused and anti CV seropositivity.<sup>23</sup>

Chronic hepatitis C is the most common chronic liver disease at present and chronic hepatitis C virus infection is found with variable prevalence in dialysis populations in different parts of the world. Using firstgeneration ELISA, the highest prevalence was 42-71% in the Middle East<sup>24,25</sup> with prevalence of approximately 4-14% in the UK<sup>26,27</sup>. Intermediate prevalences are reported from Mediterranean countries. The prevalence in Australia and New Zealand is 1.2-10%.28, with significant regional variability. The prevalence of HCV is consistently higher in dialysis populations than in healthy populations. The prevalence of HCV increases with age, the number of blood transfusions received, the mode of dialysis and the time on dialysis. <sup>29,30</sup> Usage of erythropoietin to reduce numbers of blood transfusions and screening of the blood donor population for anti HCV has reduced the incidence of hepatitis C infection. 31

The prevalence of anti HCV in patients on continuous ambulatory peritoneal dialysis (CAPD) appears much lower <sup>32</sup>, even though HCV has been identified in the peritoneal dialysis effluent. <sup>33</sup> There are multiple reports of patient to patient transmission on haemodialysis, with use of genotypic analysis and molecular typing revealing ongoing nosocomial transmission of hepatitis C in modern dialysis units. <sup>334,35,336,37,38</sup> The risk of acquiring infection is higher for those patients treated in units with a high prevalence of HCV infection.<sup>39</sup>

Acquiring HCV on dialysis has significant implications in regard to morbidity and mortality, with a high incidence of progressive chronic liver disease and its sequelae. Renal patients with HCV antibody detected

by serology or HCV RNA testing have been found to have an increased relative risk of death approaching 1.8 to 2.0, respectively. 40,41

A total of 142 haemodialysis patients participated in this study, 11 were anti-HCV positive and 7 were HBsAg positive.<sup>42</sup>

The prevalence of a positive antihepatitis C virus (HCV) test among dialysis patients was 5.4% in a large prospective multicenter trial in Germany<sup>43</sup> and up to 9.8% in the US dialysis population.<sup>44</sup> However, in southern Europe and Asia, the prevalence may be even higher with rates up to 22.9%<sup>45</sup>. In contrast, hepatitis B virus (HBV) infection prevalence among dialysis population ranges between 2.1 and 4.6% in western countries<sup>46</sup>.

In conclusion, dual infection with HBV and HCV, though rare, occurs more frequently in certain risk groups. The risk is greater among the CKD patients due to the frequent exposure to blood from transfusions and extracorporeal circulation during haemodialysis. Immunization with HBV vaccine before beginning the dialysis will reduce infection of HBV and strict adherence to universal precautions in the dialysis units may help to decrease the prevalence of both infections among these high-risk patients. These patients should be identified early and managed appropriately so as to reduce the risk of long term complications like cirrhosis.

# Conclusion

Prevention of transmission of HBV and HCV in the HD setting warrants a multi-faceted approach. Not enough stress can be placed on the importance of adequate infection control practices for the prevention of both infections. Prevention of HBV transmission is augmented by correct implementation of isolation strategies and the universal vaccination of susceptible patients.

## Recommendation

Gloves should be used by staff with washing of hands and changing gloves between patients.

Use of protective eye wear or a face mask and gowns where blood or infective fluids may splash.

Provision of adequate space between each dialysis patient.

No sharing of instruments, medications between patients, regardless of serologic status.

Medications should be prepared and distributed from a centralised separate, clean area.

Contaminated supplies, equipment or blood samples

etc should not be handled or stored in areas where medications and clean equipment and stores are handled.

Dialysis machines should be effectively disinfected after each patient. The exterior of the machine should also cleaned and disinfected using protocols following manufacturers instructions.

Blood spills should be promptly and effectively attended using bleach .

Cleaning of isolation rooms should be undertaken after each dialysis.

Regular testing of HBV susceptibility and immunity leading to aggressive Hepatitis B vaccination of all susceptible patients and staff.

Separation of HBs Ag +ve patients by room, machine, instruments, supplies and staff.

Regular serologic testing for HCV and HIV of all susceptible patients and prompt review of results.

HbsAg / HbsAb 3-6 monthly, HCV Ab 3-6 monthly and HIV annually.

Hepatitis B immunisation programs should be undertaken aggressively.

Patients with chronic active viral infection should be referred for potential anti-viral treatment.

Liver function tests monthly.

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# References

- Meyers CM, Seeff LB, Stehman-Breen CO, Hoofnagle JH. Hepatitis C and Renal Disease: An update. Am J Kidney Diseases 2003;42(4): 631-658.
- Sangelli E, Coppola N, Messina V, Di Caprio D, Marrocco C, Marotta A, Onofrio M, Scolastic C, Filippini P. HBV superinfection in Hepatitis C virus chronic carriers, viral interaction, and clinical course. Hepatology 2002;36(5):1285-1291.
- Fabrizio F, Martin P. Hepatitis B virus infection in dialysis patients. Am J. Nephrol 2000; 20:1-11
- Tokars J I, Alter M J, Favero M S, et al. National surveillance of dialysis associated diseases in the United States ASAIO J 1991; 39:966-975
- Stevens CE, Alter H J, Taylor P E, et al. Hepatitis B vaccine in patients receiving haemodialysis. NEJM 1984; 311:496-501
- Jadoul M, Cornu C, van Ypersele de Strihou C, the UCL Collaborative group: Incidence and risk factors

- for hepatitis C seroconversion in haemodialysis: A prospective study. Kid. Int. 1993; 44:1322-1326.
- Izopet J, Rostaing L, Ton Then H. Incidence of HCV infection in haemodialysis units with or without patients isolation. J. Am. Soc. Nephrol. 1995; 6:537
- 8. Zamir, D, Storch S, et al. Hepatitis C virus seroconversion and phenotype prevalence in patients and staff on chronic haemodialysis. J Clin Gastro 1999;28:23-28
- 9. Saha D, Agarwal SK. Hepatitis and HIV infection During Haemodialysis. J Indian Med Assoc 2001;99(4):194- 199.
- 10 . Moreira R, Pinho JRR, Fares J, Oba IT, Cardoso MR, Saraceni CP, Granato C. Prospective Study Of Hepatitis C Virus infection in haemodialysis patients by monthly analysis of HCV RNA and antibodies. Canadian J Microbiol 2003; 49 (8):503-507.
- Oesterreicher C, Hammer J, Koch U, Pfeffel F, Sunder-Plassmann G, Petermann D, Muller C. HBV and HCV genome in peripheral blood mononuclear cells in patients undergoing chronic hemodialysis. Kidney International 1995; 48:1967-1971.
- Fabrizi F, Poordad F, Martin P. Hepatitis C Infection and the patients with end-stage renal disease. Hepatology 2002; 36(1): 3-10.
- 13. Delarocque-Astagneau E, Baffoy N, Thiers V, Simon N, de Valk H, Laperche S, Courouce AM, Astagmeau P, Buisson C, Desenclos JC. Outbreak of Hepatitis C Virus infection in an haemodialysis unit: Potential transmission by haemodialysis machine?. Infection Control And Hospital Epidemiology 2002;23(6):328-334
- 14. Devi KS, Singh NB, Mara J, Singh TB, Singh YM. Seroprevalence of Hepatitis B V virus and Hepatitis C Virus among hepatic disorders and injecting drug users in Manipur- A preliminary report. Ind J Medical Microbiol 2004;22(2):136-137.
- Anima X, Kumar M, Minz M. Sharma HP, Shahi SK. Prevalence of Hepatitis B and Hepatitis C virus coinfection in chronic liver disease. Indian J Pathol Microbiol 2001; 44(3):253-255.
- Berry N, Chakravati A, Sharma VK, Mathur MD. Coinfection with HBV and HIV in HCV infected chronic liver disease. Indian J Med Microbiol 1998;16(1):44
- 17. Kara IH, Yilmaz ME, Sari, Y, Diizen.S, Usul.Y, Isikoglu B. Seroprevalence and risk factors of HCV in dialysis patients in a University haemodialysis center of south east Anatolia, Turkey. Dialysis and Transplantation 2001;30(11):748-755.
- 18. Hung KY, Chen WY, Yang CS, Lee SH, Wu DJ. Hepatitis B and Hepatitis C in haemodialysis patients. Dialysis and Transplantation 1995; 24(3): 135-139.

- GA Reddy, KV Dakshinamurthy, P Neelaprasad, T Gangadhar, V Lakshmi ,Prevalence of HBV and HCV dual infection in patients on haemodialysis.Indian Journal of Microbiology 2005; 23(1):41-43.
- 20. Almawi WY, Qadi AA, Tamim H, Ameen G, Bu-Ali A, Arrayid S, Abou Jaoude MM. Seroprevalence of hepatitis C virus and hepatitis B virus among dialysis patients in Bahrain and Saudi Arabia. Pubmed transplant Proc. 2004 Jul-Aug;36(6): 1824-6
- 21. Andrew W Tu, Jane A Buxton, Mandy Whitlock, Ognjenka Djurdjev, Mei Chong, Mel Krajden, Monica Beaulieu, Adeera Levin, Prevalence and incidence of hepatitis C virus in hemodialysis patients in British Columbia: Follow-up after a possible breach in hemodialysis machines. Can J Infect Dis Med Microbiol. 2009 Summer; 20(2): 19-23.
- 22. Elamin S, Abu-Aisha H. Prevention of hepatitis B virus and hepatitis C virus transmission in hemodialysis centers: review of current international recommendations. Arab J Nephrol Transplant. 2011 Jan;4(1):35-47.
- 23. Gasim I. Gasim, Hamdan Z. Hamdan, Sumaia Z. Hamdan, and Ishag Adam. Epidemiology of Hepatitis B and Hepatitis C VirusInfections Among Hemodialysis Patients in Khartoum, Sudan. . Journal of Medical Virology 84:52-55 (2012)
- 24. Al Nasser M N, al Mugeiren M A and Assuhaimi S A. Seropositivity to hepatitis C virus in Saudi haemodialysis patients. Vox Sang 1992; 62, 94-97
- 25. Ayoola E A, Huraib S, Arif M, et al. Prevalence and significance of antibodies to hepatitis C virus among Saudi haemodialysis patients. J. Med. Virol 1991; 35, 155-159
- Corcoran G D, Brink N S, Millar C G, et al.. Hepatitis C virus infection in haemodialysis patients: a clinical and virological study. J. Infect. 1994; 28, 279-285
- 27. Conway M, Catterall A P, Brown E A, et al. Prevalence of antibodies to hepatitis C in dialysis patients and transplant recipients with possible routes of transmission (see comments). Nephrol. Dial. Transplant 1992; 7, 1226-1229
- Pereira B J, Levey A.S, Hepatitis C infection in dialysis and renal transplantation Kid. Int. 1997; 51:981-9999
- 29. Dentico P, Buongiorno R, Volpe A, et al. Prevalence and incidence of hepatitis C virus (HCV) in haemodialysis patients: study of risk factors. Clin. Nephrol. 1992; 38(1):49-52
- Hardy N M, Sandroni S, Danielson S, et al. Antibody to hepatitis C virus increases with time on dialysis. Clin. Nephrol. 1992; 38(1)44-48

- Schreiber G B, Busch M P, Kleinman S H, et al. The risk of transfusion-transmitted viral infections. NEJM 1996; 334:1685-90
- Katsulidou A, Praskevis D, et al. Molecular epidemiology of a hepatitis C virus outbreak in a haemodialysis unit. Nephrol Dial Transpl 1999;14:1188-1194
- Castelnovo C, Sampietro M et al. Diffusion of HCV through peritoneal membrane in HCV positive patients treated with continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant 1197:12:978
- 34. Le Pogam S, Le Chapois D, Christen R, et al. Hepatitis C in a haemodialysis unit: molecular evidence for nosocomial transmission. J. Clin. Micro 1998; 3040-3043
- 35. Norder H, Bergenstrom A, Uhnoo I, et al. Confirmation of nosocomial transmission of hepatitis C virus by phylogenetic analysis of the NS5-B region. J. Clin. Micro. 1998; 3066-3069
- Mizuno M, Higuchi T, Kanmatsuse K, et al. Genetic and serological evidence for multiple instances of unregionised transmission of hepatitis C virus in haemodialysis units. J. Clin. Micro. 1998; 2926-2931
- Sampietro M, Badalamenti S, Salvador S, et al. High prevalence of a rare hepatitis C virus in patients treated in the same haemodialysis unit: Evidence for nosocomial transmission of HCV. Kid. Int. 1995; 47:911-917
- 38. Katsoulidou A, Paraskuis D, Kalapothaki, et al. Molecular epidemiology of a hepatitis C outbreak in a haemodialysis unit. Nephrol Dial. Transplant 1999; 14:1188-1194.

- Kobayashi M, Tanaka E, Oguchi H, et al. Prospective follow up study of hepatitis C infection in patients undergoing maintenance haemodialysis: Comparison among dialysis units. J. Gastroenterol Hepatol. 1998; 13:604-609
- Stehman-Breen CO, Emerson S, et al. Risk of death among chronic dialysis patients infected with hepatitis C virus. Am J Kidney Dis 1998;32:629
- 41. Pereira BJ, Natov SN, et al. Effect of hepatitis C infection and renal transplantation on survival in end-stage renal disease. Kidney Int 1998;53:1374
- 42. Ingmar Mederacke, Matthias Meier, Johann B. Hans Schmidt-Gu"rtler, Regina Raupach,Ru"diger Horn-Wichmann1, Karsten Wursthorn1 Andrej Potthoff. Different kinetics of HBV and HCV during haemodialysis and absence of seronegative viral hepatitis in patients with end-stage renal disease. Nephrol Dial Transplant (2011) 0: 1–8
- 43. Ross RS, Viazov S, Clauberg R et al. Lack of de novo hepatitis C virus infections and absence of nosocomial transmissions of GB virus C in a large cohort of German haemodialysis patients. J Viral Hepat 2009; 16: 230–238
- 44. Finelli L, Miller JT, Tokars JI et al. National surveillance of dialysisassociated diseases in the United States, 2002. Semin Dial2005; 18: 52-61
- 45. Fissell RB, Bragg-Gresham JL, Woods JD et al. Patterns of hepatitis C prevalence and seroconversion in hemodialysis units from three continents: the DOPPS. Kidney Int 2004; 65: 2335-2342
- 46. Burdick RA, Bragg-Gresham JL, Woods JDet al. Patterns of hepatitis B prevalence and seroconversion in hemodialysis units from three continents: the DOPPS. Kidney Int 2003; 63: 2222-2229.