J. Dhaka National Med. Coll. Hos. 2014; 20 (01): 9-14

Original article

HCV infection in haemodialysis patients: Prevalence and risk factor analysis.

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Abstract:

Introduction: Dialysis patients have a higher rate of HCV infection.[2] This study was carried out to find out the prevalence of HCV infection in patients on chronic haemodialysis and to identify the risk factors for HCV transmission in this patient group. Methods: This prospective cross sectional study was carried out in the haemodialysis units and the department of Gastrointestinal, Hepatobiliary and pancreatic disorders (GHPD) of BIRDEM hospital, during the period of March 2006 to March 2007. A total of 72 end stage renal disease patients of both sexes and all ages on maintenance heamodialysis for more than three months were enrolled. A pre-designed questionnaire comprising demographic, dialysis-specific, medical history and life style variables was filled up. Predialysis five (5) ml blood were taken from the arterial channel for anti-HCV (ELISA) test. P-value <0.05 was considered as significant. Results: The prevalence of HCV infection in patients on chronic haemodialysis was 23.6%. There was no statistical significance ($p=0.133^{ns}$) between anti-HCV positivity and age and sex distribution. The association between HCV status and the total number of units of blood transfused, mean duration of haemodialysis and life-style risk factors for HCV transmission were statistically significant. Conclusion: In our study, the prevalence of HCV infection in patients on chronic haemodialysis was 23.6%. The haemodialysis patients in our dialysis unit have an infection rate 8-12 fold more than general population. The association between the total number of units of blood transfused, mean duration of haemodialysis, and presence of one or more risk factors and HCV positivity were statistically significant.

Keywords: Haemodialysis, Hepatitis C.

Introduction:

Hepatitis C virus continues to be a major disease burden on the world. It is an RNA virus, a member of the Flaviviridae family. The virus is the principal etiologic agent responsible for more than 90% of post-transfusion non-A, non-B hepatitis.[1]

It has been well documented that dialysis patients have a higher rate of HCV infection.[2] The prevalence of HCV infection among haemodialysis is high and varies between countries and between dialysis units within a single country.[3] HCV infection is now recognized as the principal cause of liver diseases in adults with renal failure on chronic dialysis treatment and thus an

important cause of morbidity and mortality in haemodialysis patients.[4]

The identity of the exact 'vector' for transmission remains unclear although two overlapping theories exist. The first is that viable virus can survive regular sterilization and pass on to the next patient despite use of disposable dialysis equipment. The second proposed mode of transmission is through environmental contamination, with breakdown in preventive measures facilitating person-to-person spread.[3]

Chronic haemodialysis patients are at high risk for infection because the process of haemodialysis requires vascular access for prolonged periods. In an environment where multiple patients receive dialysis concurrently, repeated opportunities exist for person-to-person transmission of infectious agents via contaminated devices, equipment and supplies, environmental surfaces, or hands of personnel. Furthermore, heamodialysis patients are immunosuppressed,[5] which increases their susceptibility to nosocomial infections.

The detection of anti-HCV antibodies using third generation ELISA is a convenient and conventional mode of documenting present or past HCV infection.[6] Determination of viremia (HCV-RNA) can be obtained by polymerase chain reaction (PCR).

Materials and Methods:

This was a prospective cross sectional study. This study was carried out in the haemodialysis units and the department of Gastrointestinal, Hepatobiliary and pancreatic disorders (GHPD) of BIRDEM hospital, during the period of March 2006 to March 2007. A total of 72 end stage renal disease patients having maintenance heamodialysis for more than three months were enrolled in this study. Patients of all ages and both sexsx were included. All patients of end stage renal disease (patients of chronic renal failure who are permanently dependent upon renal replacement therapy) on chronic haemodialysis treatment (on maintenance haemodialysis for more than three months) were enrolled in this study. Patients on maintenance haemodialysis for less than three months were excluded from the study. Haemodialysis patients who were not interested to participate in the study were excluded.

The objectives of the study were explained and verbal consent was taken from each patient prior to data collection. All patients were interviewed by the same interviewer using a pre-designed questionnaire comprising demographic, dialysis-specific, medical history and life style variables. The demographic variables were age, sex and occupation. Medical variables included a history of blood transfusion, use of erythropoietin injection, surgery, jaundice and abnormal liver function. Life-style risk factors included body piercing (i.e. ear or nose), tattooing, shaving in saloon, injection drug use, house hold contact with an injection drug user, sexual contact with a injection drug user, sexual contact with a known hepatitis case, a history of sexually transmitted disease, any history of unusual sexual behavior, dental procedure, hospitalization, surgery, needle stick injury and occupational exposure to blood and blood products. Dialysis-specific variables included duration on chronic dialysis, frequency of dialysis per week, hours of dialysis per seating and any history of peritoneal dialysis. Adequate precautions were taken accordingly during sample collection procedure. Predialysis five (5) ml blood were taken from the arterial channel immediately after pricking the fistula and labeled with a known serial number for each patient. Serum for ELISA test were stored at -20^{0}C till the collection of sample from all patients. All samples and reagents were brought to room temperature thirty minutes before performing the tests.

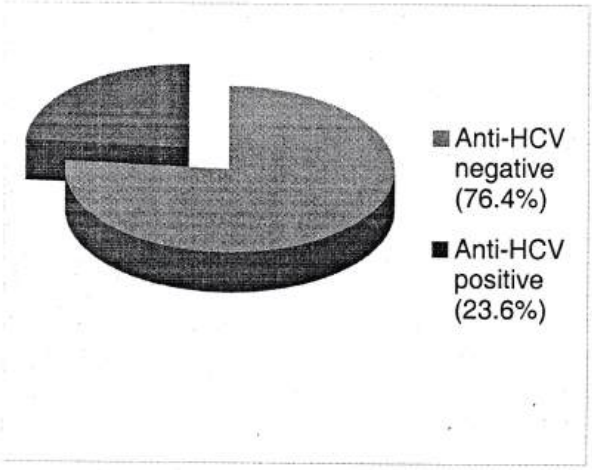
All parametric variables were expressed as mean ± SD unless otherwise stated. For statistical analysis unpaired student's 't' test, Paired student's 't' test, Chi-square test and Z-test were performed. P-value <0.05 was considered as significant. Appropriate statistical analysis of collected data were done using computer based statistical package SPSS version 11 and appropriate statistical methods were used to arrive at conclusion making necessary graphs and tables used to write the thesis.

Results :

There were 41(56.9%) male and 31(43.1%) female patients between the ages of 19-76 years (mean age-52.85).

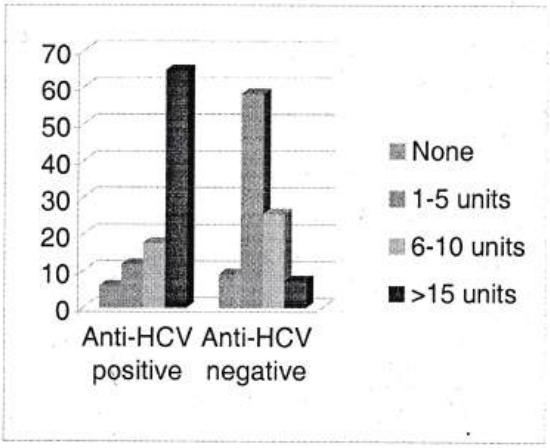
Among 72 patients 17 (23.6%) were positive and 55 (76.4%) were negative for anti-HCV by third generation ELISA method. Six (06) anti-HCV negative patients had persistently elevated serum ALT level estimated six months apart; qualitative HCV RNA tests were performed but none of them were positive for HCV.

Figure-1: Prevalence of HCV infection among the study population (N=72).



Among anti-HCV positive patients 11.8% (n=02) belonged to .21-40 years age group, 70.6% (n=12) belonged to 41-60 years age group and 17.6% (n=03) belonged to 61-80 years age group. The association between different age groups and anti-HCV status in our study population was statistically not significant. 41.2% (n=07) of anti-HCV positive group was represented by male and 58.8% (n=10) by female patients. There was no statistical significance ($p=0.133^{ns}$) between anti-HCV positivity and sex distribution. In HCV positive population 5.9% (n=1) patient had no blood transfusion, 11.8% (n=2) patients had 1-5 units of blood transfusion, 17.6% (n=3) patients had 6-15 units of blood transfusion and 64.7% (n=11) patients had more than 15 units of blood transfusion. Chi-square test revealed that the association between HCV status and the total number of units of blood transfused is statistically highly significant ($p<0.001^{***}$).

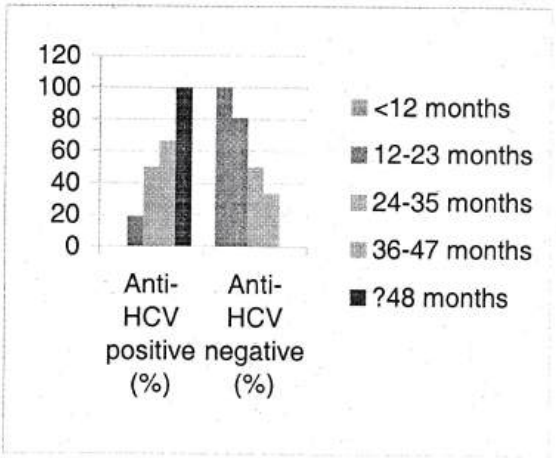
Figure-2: Percentage of anti-HCV positive and anti-HCV negative patients in relation to their number of blood transfusion (p<0.001%)



In anti-HCV positive group the duration on haemodialysis in months was 36.29 ± 20.06 (Mean ± SD) (range14-91 months). In anti-HCV negative group the duration on haemodialysis in months was 11.96 ± 8.20 (Mean ± SD) (range 4-42 months). Unpaired student's't' test revealed that the association between the mean duration of haemodialysis and HCV positivity is statistically highly significant ($p<0.001^{***}$) in our study population.

Figure-3: Percentages of anti-HCV positive and anti-HCV negative patients in relation to their duration on haemodialysis (p<0.001%*)**

In anti-HCV positive group 70.6% (n=12) had at least



one high risk life-style risk factor for HCV transmission and 29.4% (n=5) had no such identifiable high risk life-style risk factor. In anti-HCV negative population 36.4% (n=20) had at least one high risk life-style risk factor, where as 63.6% (n=35) had no identifiable high risk life-style risk factor for HCV transmission. Chi-square test revealed that the association between the presence of at least one high risk life-style risk factor for HCV transmission and anti-HCV positivity was statistically significant ($p<0.05^{*}$).

Table-1. HCV status in relation to presence of at least one high risk life-style risk factor for HCV transmission:

Risk factor	Anti-HCV positive (n=17)		Anti-HCV negative (n=55)		P value
	No.	(%)	No.	(%)	<0.05*
Present	12	70.6	20	36.6	
Absent	5	29.4	35	63.6	
Chi-square test * = Significant					

In anti-HCV positive group 58.8% (n=10) had two or more high risk life-style risk factors for HCV transmission and 41.2% (n=7) had no or less than two identifiable high risk life-style risk factor. In anti-HCV negative population 16.4% (n=9) had two or more high risk life-style risk factors for HCV transmission, where as, 83.6% (n=46) had no or less than two identifiable high risk life-style risk factor. Chi-square test revealed that the association between the presence of two or more high risk life-style risk factors for HCV transmission and HCV positivity is statistically highly significant ($p<0.001^{***}$) in our study group.

Table-2. HCV status in relation to presence of two or more high risk life-style behavior for HCV transmission

Risk factor	Anti-HCV positive (n=17)		Anti-HCV negative (n=55)		P value
	No.	(%)	No.	(%)	<0.0001***
Present	10	58.8	9	16.4	
Absent	7	41.2	46	83.6	
Chi-square test *** = Significant					

Among the study population 66 (91.7%) patients re-uses the dialyzer. In the anti-HCV positive population 100% (n=17) patients re-uses the dialyzer. In anti-HCV negative population 85.5% (n=47) patients re-uses dialyzer where as 14.5% (n=8) do not. Chi square test shows no statistical significance between HCV status and dialyzer re-uses in our study population ($p=0.095^{ns}$).

Discussion:

Despite significant advancement in virology, including the identification of hepatitis C as the principal cause of NANB hepatitis,[7] our knowledge on the mode(s) of transmission of this virus and its health implications in the haemodialysis population remained incomplete. The HCV prevalence varies widely in haemodialysis patients between geographically and demographically dissimilar areas.

In our study, the prevalence of HCV infection in patients on chronic haemodialysis was 23.6%. Thorough review of all transfusion records and the use of highly sensitive tests for HCV infection permitted a valid assessment of HCV status. Prevalence data for HCV of the general population of Bangladesh (WHO) suggest that the rate is between 2-3%. Thus haemodialysis patients in our dialysis unit have an 8-12 fold increase in risk.

In another study, the prevalence of antibodies to HCV was estimated during the period of 2003-2004 in patients undergoing chronic haemodialysis in the Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. A total of 53 patients on chronic haemodialysis were studied with age ranging from 18 years to 65 years. The prevalence of HCV infection in that dialysis unit was 69.8%.[8] The wide variation in HCV prevalence between these two dialysis units within the same country reflects the opinion of many authors that in the dialysis population prevalence of HCV varies widely between countries and also with in the same country. These variations seem not simply to reflect local prevalence of HCV but rather suggest that some aspect(s) of dialytic process may expose patients to an increased risk of developing HCV. Besides, environmental contamination, with variable breakdown in infection control procedures may be responsible for such variations in HCV prevalence.

Several authors mentioned blood transfusion as an important factor in the transmission of HCV infection.[9] In our study the association of the total number of blood transfusion and HCV positivity was statistically highly significant (p<0.001%).

Out of 72 patients in our study only 4 patients were on injection erythropoietin from the very beginning of end stage renal failure and had never been transfused. Among those 25% were HCV positive indicating that mechanisms other than blood transfusion might operate. This finding is consistent with other investigators.[10]

In our study, out of 72 patients 6 had no history of blood transfusion. But 16.6% of them were HCV positive, which indicate that factors other than blood transfusion were contributory to spread infection. Whereas there is still no general agreement, cumulative evidence suggests that nosocomial transmission within the haemodialysis unit plays a key role in HCV transmission to these patient.[11]

Different literatures revealed the nosocomial transmission may have been facilitated either by close proximity allowing direct person-to-person spread through blood spillage and/or failure to strictly implement universal precautions recommended by CDC (Atlanta).[4] Patient to patient transmission was prospectively proved in several incidence studies in haemodialysis patients.[12] Occasional failure to observe strict measures of asepsis like changing of gloves after each patient manipulation, hand washing between two patient management, avoiding sharing of articles among patients, regular use of apron by the dialysis staffs, aseptic cleansing of blood spillage, disinfection of environmental surfaces and machines were observed in our haemodialysis unit and this factor might be incriminating.

In our study the relation between the duration of dialysis and HCV positivity was statistically highly significant (p<0.001). Similar results were found in some other studies in different countries, where authors mentioned that duration of haemodialysis is an independent risk factor for developing hepatitis C infection.[13]

There is little evidence supporting a significant role for the dialyzer reuses in HCV transmission.[14] We also found similar finding in our study. The association of dialyzer reuses and HCV positivity was statistically not significant in our study ($p=0.095^{ns}$).

In our study, we also looked for the association of high risk life-style risk factors with HCV positivity. Because the life-style factors were not mutually independent, and to facilitate the statistical analysis, the number of high risk life style risk factors per participants was calculated. A high risk life-style risk factors was defined as having engaged in any of the following activities: body piercing (i.e. ear or nose), tattooing, shaving in saloon, injection drug use, house hold contact with an injection drug user, sexual contact with a injection drug user, sexual contact with a known hepatitis case, a history of sexually transmitted disease, any history of unusual sexual behavior, history of dental procedure, history of hospitalization, history of surgery, history of needle stick injury and occupational exposure to blood and blood products. In our study, we found that the presence of at least one high risk life-style risk factor and HCV positivity was statistically significant (p<0.05) and the association between HCV positivity and presence of two or more high risk life-style risk factors was statistically highly significant (p<0.001). Other studies also showed similar correlation between high risk life-style risk factors and HCV positivity.

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