Predictors of HCV Seroconversion Among End-stage Renal Disease Patients in Hemodialysis Unit

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Abstract

Background: In patients receiving dialysis, blood borne infections remains one of the most public causes of morbidity, hospitalization and death. Among dialysis patient’s long-term hemodialysis (HD) therapy, frequency of blood transfusions and multiple blood transfusions enhance the risk of acquiring blood-borne infections. Objective: The aim of the study was to identify predictors for HCV sero-conversion in HD patients. Method: Prospective observational study was conducted on 173 CKD patients undergoing HD. Anti HCV antibody testing was accomplished at the start of study and every 2-3 months subsequently. To identify seroconversion, patients who were sero-negative for HCV were monitored. Results: Prospective follow-up exposed an occurrence of seroconversion of 12.1% during study duration. On multivariate analysis, both increase in the duration on hemodialysis besides attending more than one center for HD were significantly associated with anti-HCV positivity (p < 0.05, OR 0.185), (p <0.05, OR 4.52) respectively. Risk factors blood transfusion and AST > 40IU/L also shows significant association for seroconversion (p<0.05). Conclusion: It is concluded that increase post dialysis incidence of HCV occurs as specific guidelines for HCV infected patients were not followed. Regular surveillance for HCV infection helps dramatically in decreasing the spread of HCV in hemodialysis unit.

Keywords: Hepatitis C virus; Hemodialysis; End stage renal disease; Chronic kidney disease.

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1. Introduction

Hepatitis C virus (HCV) infection is substantial reason of morbidity and mortality in hemodialysis patients [1, 2] and observed as major public health problem [3, 4] infecting 170 million people globally [5]. Patients who undergo maintenance hemodialysis (HD) treatment are at high risk of getting infections and have a greater prevalence of HCV than the general population [6-9]. Preceding current screening of blood donors, blood transfusions was related with HCV infection essential to recover the anaemia related with kidney syndrome [10, 11]. Multiple blood transfusions and prolonged vascular exposure increase the probability of getting blood-borne infections in patients experiencing HD. Among end stage renal disease (ESRD) patients, blood borne virus is predominantly higher because of illicit drug use, inadequate sterilization of medical equipment, invasive dialysis procedures, mode of dialysis, contaminated blood and blood products and duration of end stage kidney disease [12-17]. Second most recurrent source of HCV infection is the nosocomial transmission [18, 19]. Most incidences of HCV transmission are consequently due to patient-patient transmission in the hospital setting through invasive procedures, such as sharing of multi dose vials, sharing of dialysis equipment, insertion of an intravascular catheter, surgery and colonoscopy [20-24]. Inadvertent bacteria transmission to patients through environmental surfaces, contact with contaminated HD equipment and supplies during treatment [25, 26], use of multi dose medication vials, regular use of recombinant human erythropoietin and staff members has been revealed as the most significant cause of HCV [27, 28]. With this background, the current study aims to determine the incidence and possible risk factors of HCV infection in renal disease patients undergoing HD in tertiary care hospital of Pakistan.

2. Methodology

2.1. Study setting

This descriptive observational study was performed in HD center of a tertiary care hospital treating adult CKD patients from January to October 2018.

2.2. Study design

During study period, Step I of the study was to collect the cross-sectional facts in maintenance HD facility about all adult CKD patients. Patient demographics and medical information were attained from patient’s medical record such as patient’s age, gender, level of education, type and stage of kidney disease, HD period, therapeutic history and sero-positivity to HD along with laboratory results. HCV sero-positivity was termed as: identification of HCV antibodies by 3rd generation enzyme linked immunoassay (ELISA), carried out in limited laboratories. Furthermore, all CKD patients undergoing HD per shift were interviewed during study period about further probable risk factors for HCV infection. These comprised of associated comorbidity, status of anemia treatment, HCV status of sexual partner, history of blood transfusions (number and time of blood transfusion) and history of visits to another dialysis center for hemodialysis. Data related to infection control procedures was also obtained at HD unit. During follow-up, Step II of the current study was to prospectively observe and identify seroconversion to HCV in already sero-negative patients. This step covered a cohort of 173 CKD patients from a single tertiary care hospital. All seroconversions were documented and comprised whether
the patient was transplanted or expired. All HD patients were observed to guarantee the inclusion of every new seroconversion during the study duration and to approve the positive results; all new sero-conversions were retested.

2.3. Ethical approval of study

Permission to carry out the study was approved from the respective tertiary care center on their letter head and signed from respective authorities. The project was permitted by the Bio-Ethics Committee of research institute. Patients inclusion was made after a written informed consent.

3. Statistical Investigation

Information were accomplished and evaluated using SPSS version 2.1 (IBM). A multinomial logistic regression (MLR) model was used to investigate the possible predictors for HCV seroconversion. Study was emphasised on patients with seroconversion, that was compared to patients having no conversion in their status to classify the reasons causative of seroconversion throughout the HD treatment. Independent variables included number of blood transfusions, hemodialysis duration, number of altered hemodialysis units visited for cure and lab values of AST and AST were entered in the model. Alpha was fixed at 5% level.

4. Results

4.1. Influencing factors

173 participants undergo hemodialysis during the study duration. The mean age of the HD patients included was 46.4 years (SD ± 13.37) and the age range was 16 to 71 years. Among those 15.6 % of the patients were of 18-30 years, 28.9 % of 31-45 years, 42.2 % of 46-60 years and 13.3 % of 61-75 years. The highest numbers of ESRD incidences were seen in the patient with advanced age (46-60). Just over half (63.6%) of the participants were male and most (83.8%) married. Majority of people were those who suffer from chronic kidney disease have low education level (72.3%). Based on HD treatment duration, from which 13.3% undergoing HD from 3 months and 86.7% from >3 months (ranging from three to 60 months). Study included those participants who were 100.0% HCV negative before the initiation of HD and all of the patients undergoing HD were of chronic renal failure. None of the patient was co-infected by HCV and HBV. Over half (56.6%, 98/173) of all patients had conventional blood transfusions and 50.9% (88/173) were known to have received management at different HD units. Causes of ESRD included hypertension, diabetes mellitus and other unknown causes, among which (55.5%, 96/173) participants had two or less than two comorbid condition while (44.5%, 77/173) had more than two comorbidities. Table 1 illustrate the demographics of the studied people consequently. Study revealed that seroconversion occurred in 21 patients out of 173 patients (12.1%) among which 38.1% were of 31-45 years of age, majority of them were male (71.4%) and 85.7% were married, even though no variations were detected in HCV infection status of remaining 152 patients. Seroconversion was not considerably related with sexual characteristics and marital status of the patient. In age groups of the participants only 18-30 year of age showed significant association (p= 0.006, OR 0.095, CI 0.018-0.508) while advancing age proven to be a risk factor for seroconversion (p>0.05, OR 0.625, CI 0.053-7.32).
### Table 1: Characteristics of hemodialysis patients and evaluation of factors associated with seroconversion during dialysis treatment by regression analysis (n=173)

| Patient information | HCV negative | Seroconversion to HCV positive | Multi logistic OR | p-value |
|---------------------|--------------|-------------------------------|------------------|---------|
|                     | N (%)        | N (%)                         |                  |         |
|                     | n = 152      | n = 21                        |                  |         |
| Age groups          |              |                               |                  |         |
| 18-30               | 25 (16.4)    | 2 (9.5)                       | 0.095            | 0.006   |
| 31-45               | 42 (27.6)    | 8 (38.1)                      | 0.625            | 0.708   |
| 46-60               | 66 (43.4)    | 7 (33.3)                      | 0.497            | 0.609   |
| 61-75               | 19 (12.5)    | 4 (19.0)                      | 0.997            | 0.998   |
| Gender              |              |                               |                  |         |
| Male                | 95 (62.5)    | 15 (71.4)                     | 1.609            | 0.400   |
| Female              | 57 (37.5)    | 6 (28.6)                      |                  |         |
| Marital status      |              |                               |                  |         |
| Married             | 127 (83.6)   | 18 (85.7)                     | 0.158            | 0.171   |
| Unmarried           | 25 (16.4)    | 3 (14.3)                      |                  |         |
| Education           |              |                               |                  |         |
| Educated            | 43 (28.3)    | 5 (23.8)                      | 0.332            | 0.165   |
| Uneducated          | 109 (71.7)   | 16 (72.6)                     |                  |         |
| Employment          |              |                               |                  |         |
| Employed            | 15 (9.9)     | 5 (23.8)                      | 5.556            | 0.036   |
| Unemployed          | 137 (90.1)   | 16 (72.6)                     |                  |         |
| Hemodialysis duration |          |                               |                  |         |
| 3 months            | 23 (15.1)    | 7 (33.3)                      | 0.629            | 0.434   |
| >3 months           | 129 (84.9)   | 14 (66.7)                     | 0.185            | 0.000   |
| Associated comorbidity |            |                               |                  |         |
| <2 or 2 morbidities | 85 (55.9)    | 11 (52.4)                     | 0.939            | 0.129   |
| >2 morbidities      |              |                               |                  |         |
| Anaemia treatment   |              |                               |                  |         |
| Blood transfusion   | 13 (8.6)     | 3 (14.3)                      | 0.684            | 0.620   |
| Erythropoietin      |              |                               |                  |         |
| treatment          |              |                               |                  |         |
| Blood transfusion & erythropoietin | 74 (48.7) | 3 (14.3) | 0.150 | 0.006 |
| No. of Blood       |              |                               |                  |         |
| transusions <5 or = 5 |        |                               |                  |         |
| 34 (22.4)           | 5 (23.8)     | 0.147            | 0.000   |
| >5                  | 43 (28.3)    | 15 (71.4)                     | 0.349            | 0.000   |
| Vaccination for hepatitis B | 52 (34.2) | 6 (28.6) | 0.121 | 0.152 |
| No                  | 100 (65.8)   | 15 (71.4)                     | 0.171            | 0.208   |
| Yes                 |              |                               |                  |         |
| Recent surgery      |              |                               |                  |         |
| No                  | 131 (86.2)   | 7 (33.3)                      | 0.113            | 0.000   |
| Yes                 | 21 (13.8)    | 14 (66.7)                     |                  |         |
| Screening of blood donor |            |                               |                  |         |
| Yes                 | 58 (38.2)    | 9 (42.9)                      | 5.662            | 0.121   |
| Don’t know          | 19 (12.5)    | 11 (52.4)                     | 21.33            | 0.006   |
| No donor            | 75 (49.3)    | 1 (4.8)                       |                  |         |
| Family history of HCV |           |                               |                  |         |
| Positive            | 131 (86.2)   | 12 (57.1)                     | 0.443            | 0.173   |
| History of medication use other than allopathic | 21 (13.8) | 9 (42.9) | . . | . . |
| No                  | 90 (59.2)    | 8 (38.1)                      | 1.271            | 0.702   |
| Yes                 | 62 (40.8)    | 13 (61.9)                     |                  |         |
| History of piercing and acupuncture |            |                               |                  |         |
| No                  | 137 (90.1)   | 17 (81.0)                     | 0.939            | 0.933   |
| Yes                 | 15 (9.9)     | 4 (19.0)                      |                  |         |

HBV vaccine had been directed in 115 of 173 patients however post vaccination antibody levels were not tested.

HBV immunization showed non-significant association with seroconversion status (p>0.05). Vaccination was
routinely practiced at the unit; 71.4% seroconverted patients were vaccinated.

### 4.2. Risk Aspects for HCV infection

With HCV seroconversion risk factors (vulnerable sexual interaction, inoculating drug use, history of recent surgery, sharing of toothbrush razor or blade used by barber and tattooing) were not considerably related. Out of 21 seroconverted patients, 9 (42.9%) described to have HCV positive sexual companion. Since HCV spread through blood and blood products and blood transfusion is one of the most important possible factor in HCV transmission. In our present study, 15(71.4%) out of 21 seroconverted patients had received beyond 5 times of blood transfusion, remaining 23.8% were received less than 5 transfusions. Seroconversion was greater in patients with history of blood transfusion and seroconverted patients were considerably more probably have received greater number of blood transfusions (P= 0.000, OR 0.349, 95% CI 0.194-0.628) and significantly more likely to have more than two altered HD units (P= 0.000, OR 4.52, CI 2.76-7.40) compared with HCV negative patients. 52.4% patients were unfamiliar about the effective screening of blood donor. Poor blood donor screening was observed as risk factor for HCV acquisition (P= 0.06, OR 21.3 CI 2.3-192.7). Based on the duration of HD, 14 (66.7%) out of seroconverted patients undergo HD for >3 months so the hemodialysis duration was significantly longer in patients with seroconversion (P= 0.000, OR 0.185, CI 0.08-0.38). As described in Table 2, a non-significant relationship (p>0.05) was detected among the hazard of seroconversion with a history of associated comorbidity, piercing and acupuncture, history of medication use other than allopathic, as well as family history of HCV of study participants. After removing potential predictors such as cirrhosis, alcohol and herbal intake that can rise liver enzyme, higher levels of aspartate aminotransferase (AST) and alanine transaminase (ALT) were observed in 12.1% (21/173) of study participants. AST > 40 IU/L (P = 0.000, OR 0.927, CI 0.889-0.967) and ALT > 56IU/L (p= 0.009, OR 1.051, CI 1.013-1.091) were associated with HCV positivity.

| Continuous variables | Binary logistic | Multivariate |
|----------------------|-----------------|--------------|
| Mean ±S.D            | OR p-value      | OR p-value   |
| Dialysis from other centre | 3.210 0.000 | 4.523 0.000 |
| ALT levels           | 26.66 ±28.40   | 0.996 0.352  |
| AST levels           | 26.16 ±23.38   | 0.991 0.049  |

### 5. Discussion

The current study assessed HCV seroconversion in ESRD patients undergoing HD and its relationship with risk factors and facility specific practice patterns. In patients receiving HD treatment, the seroconversion rate for HCV infection and incidence of anti-HCV antibodies is remarkably significantly greater than the general population [16-29]. Our study reports that 21 seroconversions for HCV infection during study duration through eventual follow-up of sero negative HD patients providing a general incidence of 12.1% of total patients. In
Libya, similar high occurrence of new HCV infections was observed during 1 year surveillance period (7.2%) [6]. The prevalence rate of prevalence rate of seroconversion was found to be higher among men than women and in employed, older patients and it is correlated with literature [9]. One must proceed into consideration that this concluding study had a relatively less sample size (n=173) and all patients were recruited from a distinct HD center. Our study shows that ESRD patients of 18-30 years of age revealed significant association with seroconversion while greater incidence of HCV sero-positivity was observed in elder patients of age 31-75. On average older age prove to be a best predictor for acquiring HCV infection in patients undergo HD treatment. This observation is in agreement with other studies [30, 31]. Conversely HCV seroconversion was significantly associated with length of time on HD. Study participants undergo hemodialysis for longer duration was more prone towards HCVacquisition. It is dependable with nosocomial spread associated to dialysis; meanwhile extensive duration of dialysis treatment signifies a longer period at hazard of attaining an infection. Related observation have been stated by different authors [5]. Another study in 2006 showed that in HD patients the frequency of HCV was associated with longer period of HD therapy, this study also revealed that those HCV negative patients who have longer period of HD treatment became seroconverted. These outcomes are compatible with the findings of other studies [2]. It is of vital importance to prevent nosocomial transmission in Pakistan such as HCV antiviral treatment is costly, and its accessibility is restricted to only limited centers. On the other hand ESRD patients require blood transfusion and erythropoietin for anemia treatment [10], study revealed that patients receiving erythropoietin treatment only are less susceptible towards acquiring HCV whereas a progressive history of blood transfusions along with number of blood transfusions was identified as risk factor for HCV spread. Strong association of blood transfusion with HCV infection was reported by other studies [9, 32]. In transmission of HCV infection through contaminated needles or syringes and blood transfusion, medical interventions play the most important role [18]. Poor screening of blood donors was documented as principal basis of HCV infection preceding to the institution of history of blood transfusions. Our study reported that a greater percentage of patients had formerly received blood transfusions without effective screening of blood donor (52.4%). In agreement with other studies HCV infection was further predominant in patients with poor screening of donor blood [6-19]. Moreover, it is probable that approximate blood donors infected with HCV are neglected by present screening measures and these might be essential for re-evaluation. Current study raised additional concern that there is a significant association of HCV infection with a history of HD from alternative centers. For social reasons, many patients travel but after starting dialysis some also moved to another dialysis center as an emergency providing acute services. HBV infection relationship with travel proposes the hazard of nosocomial infection during follow up of seroconverted patients. Other studies support this incidence [2, 6, 20]. These interpretations highlight the significance of separating patients following their return and observing them for seroconversion. In addition, history of recent surgery found to be more prominent in our study in seroconverted patients (66.7%) in comparison with sero negative group (13.8%). In the present study there was no association between seroconversion with history of renal transplantation, but we just found statistically significant relation with any recent surgical intervention of patients. These conclusions are compatible with the findings of other studies [5, 33]. On the other hand, the use of Multidose vials was mutual and is probable to have been an essential basis of nosocomial infections. Without being vaccinated against HBV many patients started HD treatment. Even the antibody level was not evaluated in vaccinated patients. In seroconverted patients, mean values for Aspartate Aminotransferase and Alanine Aminotransferase were greater
in spite of being within the normal range. HCV infections are related with increased transaminase levels [10-19]. Nevertheless in chronic dialysis patients with viral hepatitis infection, elevation of transaminases (>40 IU/L) is not permanently exist [34]. We institute that AST > 40 show significant association with HCV infection. This recommends that an inexplicable or minor rise in AST could be used to indicate initial HCV seroconversion. As per the significant role of blood transfusion, behaviors like for each patient changing gloves after touching HD machines, paying careful attention to hand hygiene after contact with different patients, complete disinfection of HD machines, and declining the use of blood products to the minimum level are suggested to avoid transmission of blood borne infections. Some breaches in infection control practices were identified through investigation of local records. Particularly, the risk valuation was missing for prevention of infection and there were no explicit control measures for the dialysis facility as well as education and training of nursing staff were estimated inadequate. There were no written procedures for sterilization and cleaning of working surfaces and for safe direction of parenteral medication were missing. HCV infection was said to be scrutinized but there was no accessibility to written practices on HCV screening and on management of seroconverted patient.

6. Study limitation

Some boundaries of this study ought to be agreed. Repeatedly incomplete medical histories and further clinical facts was regularly attained by questioning HD staff and patients. In local laboratories serological analysis was performed and it is probable that there was variance in the quality of testing. To detect anti-HCV antibodies, HCV testing depend on a third generation ELISA and was not established by the finding of HCV RNA in blood samples. Genotyping or validation with PCR is presently not accessible in maximum centers. This study also reported that seroconversion was most likely to occur in patients undergo HD greater than three months. Though, serologic assessments were not done frequently in every patient, consequently these outcomes are subjective as the infection might be done far ahead.

7. Conclusion

This study concluded that patients on continuous HD treatment have a high prevalence and incidence of HCV infection. Study revealed post dialysis occurrence of HCV within HD units. Vital action is required in HD centers to enhance and develop infection control actions and to diminish reliance on blood transfusions aimed at the management of anemia. Regular surveillance for HCV infection helps significantly in decreasing the spread of HCV in HD unit. Poor practices of nursing staff and high level of non-adherence to infection control strategies were observed. Adherence of health care workers to infection control competencies can be improved by providing continuous education, supervision and monitoring

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8. Conflict of interest declaration

None stated.

9. Funding sources

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