Prevalence of Hepatitis B, Hepatitis C and HIV Infections among Chronic Renal Failure Patients on Hemodialysis

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ABSTRACT

Though practices to minimize viral transmission have been used in hemodialysis units for many years, many studies have shown that incidences of viral transmission continue to occur in hemodialysis centers and the prevalence and seroconversion greatly vary among hemodialysis facilities. More recent studies in some hemodialysis facilities have shown decline in seroconversion, where as the transmission of these diseases continues to persist within several dialysis units. However, there are no published data on prevalence and seroconversion of these diseases in patients undergoing maintenance hemodialysis in Nepal. So this study was conducted to evaluate the prevalence and seroconversion of hepatitis B, hepatitis C and HIV infection among Nepalese hemodialysis population.

The study was a prospective hospital based study done in 54 end-stage renal disease (ESRD) patients on maintenance hemodialysis (MHD). Serological tests for HBsAg, anti HCV antibodies and anti HIV-1 & 2 antibodies, using third generation Enzyme-Linked immunosorbent assay (ELISA) were done. These serological tests were repeated to see any seroconversion after 18 months. The mean age of the HD patients was 47.52 (±13.54) years. The causes of ESRD were chronic glomerulonephritis (CGN) (40%), diabetes (20%), hypertension (9%) and others (ADPKD, obstructive uropathy and unknown) (31%). The mean HD duration was 32.32 (± 22.61) months. Seroconversion of HBV, HCV and HIV was nil during 18 months follow up. The zero seroconversion of the mentioned viral diseases in our hemodialysis units might be due to several factors such as strict adherence to standard infection control practice, vaccination of all the patients for hepatitis B, segregation of patients, regular screening of the patients for the viral disease, use of erythropoietin. Though there was no seroconversion of HBV, HCV or HIV in our dialysis population, this should not lead to compromise in standard infection control practice and screening for these potentially lethal complications.

Key words: Chronic renal failure, hemodialysis, hepatitis B and C

INTRODUCTION

Chronic hemodialysis patients are at high risk for transmission of viral infections. In an environment where multiple patients receive dialysis concurrently, repeated opportunities exist for person-to-person transmission of infectious agents, directly or indirectly via contaminated devices, equipment and supplies, environmental surfaces, or hands of personnel. The worldwide data suggest that the prevalence of hepatitis viruses among chronic renal failure (CRF) patients could be as high as 80%. The number of patients with end-stage renal disease (ESRD) treated by maintenance hemodialysis in the United States has increased sharply during the past 30 years. Between 1973 and 1999 there was a more than 30-fold increase in the number of patients enrolled in the Medicare funded end-stage renal disease (ESRD) program in US, from approximately 10,000 to 340,000. In 1999, more than 3,000 hemodialysis centers had >190,000 chronic hemodialysis patients and >60,000 staff members. The increasing incidence and prevalence of ESRD and chronic kidney disease (CKD) is a global trend not just confined to the United States. India had a total...
of more than 700,000 renal failure cases by the turn of the century. In Bir hospital in 2001, total of 2635 sessions of hemodialysis was given to 43 new and 11 old cases continued from previous year.

Various studies from different parts of the world have shown higher prevalence of hepatitis B, hepatitis C and HIV among CRF patients on hemodialysis in spite of screening and preventive measures. However, data on the prevalence of hepatitis viruses among such population in Nepal is unknown as such study has not been conducted in Nepal. Thus this study was conducted at nephrology department of National Academy of Medical Sciences, Bir Hospital, and Shree Birendra hospital, Kathmandu with the aim of to study the prevalence of HBsAg, anti-HCV and anti HIV antibodies among chronic renal failure patients, who are at higher risk of acquiring such infections because of hemodialysis, as well as demographic parameters of the chronic renal failure patients attending nephrology department in the year 2005/2006. The result of this study was aimed to help to show the extent of the problem, provide an insight to our preventive measures and highlight the need to take the appropriate measures for the prevention and treatment of such complications if there were any.

MATERIALS & METHODS

Type of study:

This prospective study was conducted at nephrology department of National Academy of Medical Sciences, Bir Hospital and Shree Birendra hospital, Kathmandu. Nephrology units of National Academy of Medical Sciences, Bir Hospital and Shree Birendra hospital, Kathmandu have six and three hemodialysis machines respectively. Both units provide dialysis services to HBsAg, anti HCV and HIV non reactive subjects only. Patients who were already on maintenance hemodialysis and patients going to start maintenance hemodialysis were included in the study. Where as patient who are infected with hepatitis B, hepatitis C and HIV are excluded from the study.

Patients who are already hepatitis B, hepatitis C or HIV positive. Patient without valid consent.

Total fifty four patients who were already on maintenance hemodialysis or new patients going for maintenance hemodialysis were included in this study from July 2005. A uniform protocol was followed for all of the subjects. On enrollment, demographic and clinical data collected were age, gender, diabetic status, etiology of end-stage renal disease (ESRD), date of starting of dialysis and seropositivity to hepatitis B, hepatitis C and human immunodeficiency virus (HIV). As per the protocol, the patients were screened for various parameters (renal function tests, seromarkers of hepatitis B and hepatitis C viruses, HIV) at the time of entry. The frequencies of dialysis were fixed on the basis of BUN and creatinine levels. After initial HBsAg screening, all of the HBsAg-nonreactive subjects were to be advised to receive immunization against hepatitis B if not already vaccinated. In those cases involving the repeated use of items (e.g., dialyzers and tubings), the items will be decontaminated and reserved for the individual patients for subsequent use. When required, the patients were to receive blood transfusions involving blood units that were stringently screened for HBsAg, HIV, and HCV. All the enrolled patients were followed up for 18 months (Dec 31, 2006) and were screened for HBsAg, anti HCV, HIV I and II antibodies every three monthly. No patient was an intravenous drug abuser.

A new case of HCV infection was defined as seroconversion by a patient from HCV antibody negativity at initial testing to HCV antibody positivity in the reporting center during the study period. Similarly a new case of HBV infection was defined as seroconversion by HBsAg negative status to HBsAg positive status during the study period and a new case of HIV infection was defined as presence antibody to HIV I or II during the study period.

The End Point

If the patient becomes seropositive for hepatitis B, hepatitis C or HIV, go for renal transplant or death of the patient during the study period.

SEROLOGICAL ANALYSIS

Serological analysis were carried out using 3rd generation enzyme linked immunosorbent assay (ELISA from standard laboratory), for all three tests, i.e., HBsAg, anti HCV and anti HIV I and II. These tests were performed in the laboratories of National Academy of Medical Sciences, Bir Hospital and Shree Birendra hospital, Kathmandu.
The sensitivity of anti HCV by third generation ELISA is approximately 97%. It is detected in 80% of patients within 15 weeks, in >90% within 5 months, in >97% by 6 months after exposure or 2–3 months after increase in ALT. The sensitivity and specificity of anti HIV by the third generation ELISA are approximately 99.6% and 97.5% respectively.

DATA ANALYSIS AND STATISTICAL ANALYSIS

A structured questionnaire and format was used to enter the data. Data was analyzed using SPSS v 11.5 (Statistical Package for Social Science, SPSS Inc. Chicago) and MS Excel.

RESULTS

A total of 54 cases on maintenance hemodialysis, meeting the inclusion criteria, were included in this study. They were screened for HBsAg, anti HCV and HIV 1 and 2 at the beginning of the study and other demographic data were collected. At the end of the study, the patients were again screened for above mentioned viral markers. The seroconversion of the above mentioned viral disease was nil during the study period.

Mean age of the patients was 47.52 years (range 20 to 72 years). Among the patients, thirty-seven percent were female with mean age 42.10 (± 11.48) years and sixty three were male with the mean age of 50.71(± 13.79).

The commonest cause of ESRD was chronic glomerulonephritis (40%) followed by diabetic nephropathy (20%), hypertensive nephropathy (9%) and other causes (31%) (unknown, obstructive uropathy, ADPKD and chronic allograft nephropathy).

The mean duration of hemodialysis was 32.32 (± 22.61) months with maximum being 107 months.

Out of 54 patients, the majority of the patients were anemic with the mean PCV value of 27.43 (±5.12). The mean serum calcium and phosphorus levels were 8.25 (± 0.94) and 4.85 (± 1.41) respectively.
Among the total patients 39% of the patients were receiving injection erythropoietin while rest were receiving blood transfusion for the correction of anemia. And the patients who were receiving erythropoietin had higher hemoglobin level with p value <0.001.

<table>
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<tr>
<th>Table 1. Showing serological results</th>
<th>At the beginning of study</th>
<th>At the end of study</th>
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<tr>
<td>Total no. of patients with non reactive HBsAg</td>
<td>54</td>
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<tr>
<td>Total no. of patients with non reactive Anti HCV</td>
<td>54</td>
<td>54</td>
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<tr>
<td>Total no. of patients with non reactive HIV</td>
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Patients were screened for HBsAg, anti HCV and HIV at the time of enrollment and non reactive patients were included for the study. At the end of the study, these viral markers were still non reactive.

At the end of the study period, among the 54 patients, 71 percent of the patients were still continuing hemodialysis while 9 percent of the patients went for renal transplant and 20 percent of the patient expired.

**DISCUSSION**

Practices to minimize virus transmission have been used in hemodialysis units for many years. Even so, many studies have shown that incidences of viral transmission continue to occur in hemodialysis centers and the prevalence and seroconversion greatly vary among hemodialysis facilities. More recent studies in some hemodialysis facilities have shown sharp decline in seroconversion, even to zero, where as the transmission of these diseases continues to persist within several dialysis units. However, there are no published data on prevalence and seroconversion of these diseases in patients undergoing maintenance dialysis in Nepal. So the aim of the present study was to assess the prevalence and seroconversion of hepatitis B, hepatitis C and HIV infection among ESRD patient on maintenance hemodialysis in two centers in Kathmandu.

Consensus regarding the need for hemodialysis patients’ isolation and dedicated dialysis machines to prevent HCV transmission, in addition to blood-borne precautions, does not exist in the nephrology community. Several investigators report that strict implementation of universal precautions is sufficient. Other investigators focus on isolation of HCV-positive patients and have shown that hemodialysis units without isolation of HCV-positive patients have higher rates of HCV infection.

Convincing data are available that demonstrate an increased risk of anti-HCV seroconversion associated with both a failure to strictly follow infection control procedures and the performance of dialysis at a station immediately adjacent to that of a patient testing positive for anti-HCV. Units using dedicated machines have shown a decreased incidence of seroconversion. The literature provides conflicting data on the likelihood of passage of HCV RNA into dialysis ultrafiltrate and the risk of contamination by reprocessing filters.

In the Dialysis Outcomes and Practice Patterns Study (DOPPS), it is notable that isolation of HBV positive patients was associated with smaller risk of HCV seroconversion. It is possible that hemodialysis staff members in the unit that isolate HBV positive patient have a higher level of attention to specific infection control procedures, such as hand-washing and vigilance regarding blood contamination.

Following the successful experience of segregation of hepatitis B virus (HBV) (+) patients, which led to a drastic fall of HBV transmission before the vaccination era, several authors have advocated the isolation of anti-HCV (+) patients in a separate HD room. Other authors have stressed that nosocomial transmission probably resulted mainly from an inadequate application of the universal precautions delineated by the Centers for Disease Control (Atlanta, GA USA), and concluded that prevention of HCV nosocomial transmission would be better achieved by strict adherence to the universal precaution by staff members, than by the cumbersome, not fully secure, segregation of patients.
Otedo AE et al. conducted a study in Kenya and found a low seroprevalence of HBV and HCV in their dialysis population and concluded that the longer duration of dialysis and the number of blood transfusions were associated with an increased seroprevalence of HBV and HCV.23

A recent study in Spain found that the prevalence of hepatitis C virus (HCV) infection in hemodialysis (HD) patients has decreased significantly in the course of the past decade in most HD units. Causes implicated in the reduction in prevalence of HCV infection in HD patients are a greater mortality rate, stabilization of the incidence of acute HCV infection, and a low percentage of HCV infection in predialysis patients. And the authors concluded that by the end of 2006, the rate of HCV infection in HD patients will be very close to that of the predialysis population.24

The benefit of isolation of HBV, HCV infected dialysis patients remains controversial. But various studies have shown use of dedicated machine decrease the transmission among patients. The segregation of HBsAg-positive patients and their equipment from HBV-susceptible patients resulted in 70%–80% reductions in incidence of HBV infection among hemodialysis patients.25 Low prevalence of HCV infection (HCV antibodies) in a HD unit in Istanbul (4.7%) showed that patient isolation and use of dedicated dialysis machines for seropositive patients decrease the transmission of HCV infection in HD centers.26 Data derived from another study in Turkey demonstrated that nosocomial spread of HCV in HD units in which both seropositive and seronegative patients were treated together were higher than that of units with dedicated machines.27 A study in Lebanon has shown that infection by HCV may be dialysis machine-related, rather than transfusion-related.28 Another study showed a significant decline of hepatitis C infection among end-stage renal disease patients in Central Brazil, ratifying the importance of public health strategies such as screening for anti-HCV in blood banks and infection control measures for control and prevention of hepatitis C in the hemodialysis environment.29

The zero seroconversion of the mentioned viral diseases in our hemodialysis units might be due to several factors such as strict adherence to standard infection control practice, 100% vaccination of the patients for hepatitis B, segregation of patients, regular screening of the patients for the viral disease. Besides many patients were getting erythropoietin (39 %), thus decreasing the requirement of blood transfusions.

The absence of seroconversion of above mentioned viral disease among our hemodialysis units are in par with the study reported by the E. Rist Medical Center in Paris, where a 0% incidence has been maintained over several years despite a high HCV prevalence and the absence of isolation.30 Introduction of rigorous infection-control strategies has led to a remarkable decline in the spread of HBV infection in dialysis units.

Similarly, in a Belgian multicentre study, the incidence of seroconversion for HCV in HD patients fell progressively to zero over a 54 month period. The authors had taken the practice of dedicated machine and universal precaution practice and they demonstrate the full prevention of HCV transmission. They proposed that suppression of HCV transmission resulted from the improved enforcement of universal precautions.31 The risk of transfusional transmission of HCV has clearly decreased with recent screening tests.32,33

Another study done in Monte Grande, Argentina in 2000, 7 of 14 (50.0%) patients who had been attending the unit before 1994 were anti-HCV-positive and non of 68 patients who had entered after 1994 were anti-HCV-positive (p < 0.001).34 Similarly, dialysis adhering to conventional infection control measures has been considered a low-risk setting for transmission of HIV. Even in centers with a high prevalence of HIV infection, no evidence of HIV transmission has been seen.35

The prevalence of hepatitis B was quite high (10%) in a Pakistani community but with increasing awareness and immunization, it has decreased considerably (3%). The seroconversion rate of hepatitis B in the dialysis population is around 3% in Pakistan.36

The decreasing incidence of hepatitis B infection among hemodialysis patients in recent years is due to better screening of the blood supply for evidence of this infection and decreased transfusion requirements due to the availability of erythropoietin. Introduction of vaccination, isolation of hepatitis B virus (HBV) positive patients, dedicated dialysis machines and regular surveillance for HBV infection dramatically reduced the spread of HBV infection.37 Transfusion of blood products remains necessary to treat the anemia of chronic renal disease. The most likely source of entry of HIV into dialysis centers may be blood products. Use
of erythropoietin should be preferred if possible to decrease the requirement of blood transfusion.

Regarding the etiology of the ESRD, chronic glomerulonephritis was the commonest cause (40%) followed by other causes (31%) (unknown, obstructive uropathy, ADPKD, chronic allograft nephropathy), diabetic nephropathy (20%) and hypertensive nephropathy (9%). This finding is similar to the previous data published in annual reports of Bir hospital. Chronic glomerulonephritis remains the most common cause of chronic renal failure in developing countries. A study in Pakistan shows chronic glomerulonephritis (33.56%) followed by diabetic nephropathy (33.28%), hypertension (12.67%) and calculus disease (7.24%) as the cause of ESRD. In this study the mortality during 18 months period was 20%. In a Pakistani study the mortality of hemodialysis patients was between 25 and 30% per year. In the United States, the mortality rate of the patients on dialysis is approximately 18% per year. Malnutrition and inadequate dialysis appear to be the major factors causing such high mortality.

There are some limitations of this study. Firstly, the average interval between exposure and seroconversion for HCV is 8–10 weeks; thus, the anti-HCV test will be negative in recently infected patients. The HCV infection can be detected by HCV RNA in serum as early as 1–2 weeks after infection. Although the antibody detection tests are considered important tools to assess the magnitude of HCV infection in patients on HD, the window phase in HD patients can be longer as these patients are immunocompromised and the anti HCV ELISA test alone may fail to detect the infected patients in the acute phase of the disease. But Bukh et al. reported that 2.6% of dialysis patients seronegative by second-generation enzyme-linked immunosorbent assay (ELISA) were viremic by PCR. However, the more recent introduction of third-generation anti-HCV assays has improved the accuracy of diagnostic testing. In one series of 81 dialysis patients, no false-negative serologies were found; however, in another report of 2,576 patients, 6 (0.23%) were seronegative but PCR positive. Most of the studies suggest that diagnosis of HCV infection in the HD patient need not include routine PCR testing. Secondly, the duration of the study was relatively shorter.

However rigorous implementation of precaution measures remains a cornerstone for prevention of HCV transmission among patients undergoing maintenance hemodialysis, but as unpredictable accidents can always take place in hemodialysis units; machine dedication may play a more important role in prevention of HCV transmission. Further studies are needed to evaluate the possible roles of machine dedication in the presence of strict adherence to hygienic precautions.

CONCLUSION

In this study the seroconversion of HBV, HCV and HIV in HD patients was nil during the study period. The zero seroconversion of the above mentioned viral diseases in our hemodialysis units might be due to several factors such as strict adherence to standard infection control practice, vaccination of all the patients for hepatitis B, segregation of patients, regular screening of the patients for the viral disease. Besides many patients were getting erythropoietin, thus decreasing the requirement of blood transfusions.

Additional studies may help to clarify the role of machine dedication in conjunction with application of universal precautions in reducing HBV, HCV and HIV transmission. Though there was no seroconversion of HBV, HCV or HIV in our dialysis population, this should not lead to compromise in standard infection control practice and screening for these potentially dangerous complications.

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