

Original Article

Prevalence and Risk Factors for Hepatitis B and C Among End-stage Renal Disease Patients on Hemodialysis in Gaborone, Botswana

P Mahupe^{1,2}, OJ Molefe-Baikai^{1,2}, G Saleshando³, GM Rwegerera^{1,2}

¹Department of Internal Medicine, University of Botswana, ²Department of Medicine, Princess Marina Hospital, ³Nephrology Unit, Bokamoso Private Hospital and Renal Care Unit, Gaborone, Botswana

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ABSTRACT

Background: Patients on maintenance hemodialysis (HD) are at risk of blood transmitted infections such as hepatitis B and C. **Objectives:** To determine the prevalence and risk factors for hepatitis B and hepatitis C virus infections among end-stage renal disease (ESRD) patients on maintenance hemodialysis in Gaborone, Botswana. **Materials and Methods:** A cross-sectional study with a retrospective longitudinal approach involving all eligible public patients undergoing hemodialysis was carried out for a period of 3 months. Data on socio-demographic, clinical characteristics, and hepatitis serology was collected using a case report form. Statistical Software Package for Social Sciences (SPSS) version 24 was used for data entry, cleaning, and analysis. The risk factors associated with Hepatitis B and C infections were determined using bivariate logistic regression analyses. A *P* value of less than 0.05 was considered statistically significant. **Results:** Of the 168 participants, 5 (2.98%) were HBsAg seropositive at the initiation of hemodialysis, whereas 2 (1.19%) were seropositive for anti-HCV antibodies at the initiation of hemodialysis. Two patients out of 163 (1.23%) were found to have seroconverted to HBsAg positivity during hemodialysis. One out of 166 patients (0.61%) seroconverted to HCV antibodies positivity during hemodialysis. The duration of hemodialysis, history of invasive procedures, HIV status, frequency of hospitalization, and blood transfusion were not associated with seroconversion for both Hepatitis B and C. **Conclusions:** The prevalence hepatitis B and C infections among ESRD patients on hemodialysis is low. There was no significant association between the identified risk factors and HBV/HCV infection. Regular audits on seroconversion status for hepatitis B and C are recommended as a way of assessing and supporting the current strategies for infection control among HD patients.

KEYWORDS: Botswana, Gaborone, hemodialysis, hepatitis B, hepatitis C, prevalence, risk factors

INTRODUCTION

About 2 million people worldwide were estimated to be on renal replacement therapy (RRT) in order to survive by 2010.^[1] In low-and middle-income countries such as Botswana the number of patients requiring RRT is growing due to an increasing prevalence of risk factors for chronic kidney disease, which includes diabetes and hypertension.^[2] Kidney transplantation is an uncommon option in Botswana due to limited resources and lack of suitable donors; hence, the vast majority of

patients who are on RRT remain on dialysis permanently. Hemodialysis (HD) is a risk factor for exposure of patients on dialysis to blood-borne infections such as hepatitis B virus and hepatitis C virus.^[3] Hepatitis B and

Address for correspondence: Prof. GM Rwegerera, Faculty of Medicine, University of Botswana, Private Bag 00713, Gaborone, Botswana.
E-mail: grwege@yahoo.com

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C viruses are the main causes of chronic viral hepatitis, which may ultimately complicate to liver cirrhosis and hepatocellular carcinoma.^[4]

In sub-Saharan Africa, the most common route of HCV transmission is iatrogenic; through blood transfusions and invasive procedures.^[5,6] The nosocomial transmission of hepatitis B infection between patients through cross contacts has also been demonstrated.^[7] As a result, most studies recommend strict infection control measures in hemodialysis units in order to limit the nosocomial spread of viral hepatitis.^[8,9] Other recommendations include vaccinations of patients and healthcare workers against hepatitis B while patients who are infected with hepatitis B or C should be dialyzed in isolation.^[8,9]

This study aimed to determine the prevalence of hepatitis B and C viral infections among end-stage renal disease (ESRD) patients on hemodialysis in Gaborone; also to identify the risk factors for infection with hepatitis B and C virus in such patients.

MATERIALS AND METHODS

Study area

This study was conducted at the Renal Care Institute (RCI) and Bokamoso Private Hospital dialysis unit. These two centers are private facilities which provide hemodialysis services to public patients, with the cost being covered by the Government of Botswana. Patients dialyzed in these facilities are followed up routinely at Princess Marina Hospital (PMH), Gaborone, Botswana. PMH is the largest tertiary and academic hospital in Botswana where most of the University of Botswana (Faculty of medicine) teaching occurs. Most of the patients are dialyzed three times weekly while a minority of them are dialyzed two times weekly.

Study design

This cross-sectional study with a retrospective longitudinal approach was conducted among end-stage renal disease (ESRD) patients on chronic hemodialysis for a period of 3 months from 1st May 2016 to 31st July 2016. Study population: All stable ambulatory patients with end-stage renal disease on hemodialysis for at least 6 months attended at renal care institute and Bokamoso renal unit during the study period who gave informed consent to participate in the study were included.

Sample size estimation

We did not perform sampling as the intention was to recruit all eligible patients who would consent; ultimately this study involved all 168 patients with ESRD on hemodialysis for at least 6 months. The sample included all the patients (88) undergoing chronic hemodialysis at RCI and 80 public patients

who were dialyzing at Bokamoso Private Hospital dialysis unit.

Data collection

Data collection was done by trained research assistance nurse using a structured case report form; it involved collecting demographic characteristics such as age, gender, and marital status. The history of previous admissions, blood transfusion, duration of hemodialysis, and previous invasive procedures such as surgery, gastroscopy, and dental extraction was also obtained through a coordinated semi-structured tool. On the other hand, patients' history of prior vaccination for hepatitis B infection was solicited and cross-checked from medical records. HIV status was recorded as positive/negative or unknown depending on available information. For the HIV positive patients, recent CD4 count was recorded either from medical records or Integrated Patient Management System (IPMS). All patients who gave consent to participate in the study had their medical charts and records at dialysis units reviewed for hepatitis B and C serology status at the initiation of hemodialysis and throughout the entire duration of hemodialysis. The results for hepatitis B or C serology that had been recorded within 3 months of the study period were recorded as the current serology status since patients are routinely tested on a 3-monthly basis. The same information was explored from Integrated Patient Management System (IPMS).

Patients who had no records of hepatitis serology and the ones who tested negative for either of hepatitis B or C at the initiation of HD were asked for venesection procedure under aseptic techniques to obtain 5 mL of blood in plain tubes. Blood was stored in a cooler box and transferred to the Private laboratory where a test for anti-HCV antibodies was performed using the ARCHITECT anti HCV assay. The Government through the Ministry of Health covered the costs for the blood tests since routine testing for these infections is carried out as part of standard clinical care required at the dialysis units. Rapid HBsAg test was performed in the dialysis units using the SD BIOLINE HBsAg test kits.

Data management

Statistical Package for the Social Sciences [IBM SPSS Statistics] software version 24^[10] was used for data entry, cleaning, and analysis. Frequency, percentage, mean, and standard deviation were used to describe the data. Chi-squared test and Fisher exact test with a 95% confidence interval were employed to analyze the associations of categorical variables. The risk factors associated with hepatitis B and hepatitis C infections

were determined using bivariate logistic regression analysis. A *P* value of less than 0.05 was considered statistically significant.

Ethical consideration

Ethical clearance to conduct the study was obtained from the University of Botswana Institutional Review Board, Princess Marina Hospital Ethics Committee, and Botswana Ministry of Health Research Unit. The participants were informed of the study aspects that included interviews and phlebotomy to obtain blood for hepatitis serology as necessary; they were assured of the minimal risks associated with phlebotomy as less than 5 mL would be drawn. They were told that it is possible to feel tired or faint as a worst-case scenario after the procedure, hence encouraged to take rest and drink plenty of fluids after the procedure. Phlebotomy was done under an aseptic technique. All participants signed informed written consent and they were told that they can choose to withdraw consent at any point with the decision not affecting their medical care.

RESULTS

Socio-demographic characteristics of study participants

A total of 168 patients with end-stage renal disease on hemodialysis were enrolled in the study providing a response rate of 100%. The mean age (standard deviation) (SD) of the patients was 50.5 (12.7) years, with a range of 18–86 years. Almost half (47%) of the patients were within the 51–70 years age group. Male patients were majority constituting 68.5% of the study population [Table 1].

Clinical characteristics of study participants

The majority (91.1%) of the study participants had been on dialysis for less than 60 months. The mean hemodialysis duration (SD) was 30.1 (19.4) months, ranging from 6–80 months. Over half of the patients (58.3%) had received blood transfusion 1–5 times. Over two-thirds of the patients (67.9%) had undergone invasive surgical procedures such as arteriovenous (AV) fistula, AV graft, and other general surgical and dental procedures. Almost a quarter of patients (24.4%) were HIV positive. All patients had been admitted to hospital with the majority (78.6%) having been previously hospitalized up to 5 times. The mean hospitalization frequency (SD) was 4.2 (3.1) days. Almost two thirds (58.8%) of the HIV positive patients had well-controlled disease with CD4 counts above 350 $\mu\text{mol/L}$. Over half of the patients (53.0%) had not been vaccinated against hepatitis B infection [Table 1].

Table 1: Socio-demographic and clinical characteristics of study participants

Variable	Frequency	Percentage
Age in years		
Mean \pm SD, Range	50.5 \pm 12.7, 18-86	
<30	11	6.5
31-50	71	42.3
51-70	79	47.0
\geq 71	7	4.2
Gender		
Male	115	68.5
Female	53	31.5
Marital status		
Single	69	41.1
Married	86	51.2
Divorced	4	2.4
Widowed	9	5.4
Duration of dialysis (months)		
Mean \pm SD, Range	30.1 \pm 19.4, 6-80	
<60	153	91.1
\geq 60	15	8.9
Frequency of blood transfusion		
0	62	36.9
1-5	98	58.3
6-10	6	3.6
11-15	2	1.2
Frequency of previous hospitalization (Mean \pm SD)		
Mean \pm SD	4.2 \pm 3.1	
1-5	132	78.6
6-10	32	19.0
>10	4	2.4
History of invasive procedure		
Yes	114	67.9
No	54	32.1
HIV status		
Positive	41	24.4
Negative	127	75.6
CD4 count*		
<200	8	23.5
200-350	6	17.7
>350	20	58.8
Hepatitis B vaccination status		
Yes	79	47.0
No	89	53.0

*Of the 41 HIV positive patients, 7 had missing CD4 results

Prevalence of patients with HBsAg and HCV antibodies at the initiation of HD and while on hemodialysis

Overall, 5/168 (2.98%) and 2/168 (1.19%) were seropositive for HBsAg and anti HCV antibodies,

Table 2: Prevalence of hepatitis B and C positive serology at initiation and while on hemodialysis

Hepatitis serology	Frequency hepatitis positivity at initiation of hemodialysis	Frequency of seroconversion while on hemodialysis
HBsAg		
Positive	5 (2.98%)	2 (1.23%)
Negative	163	161
Total	168	163
Anti HCV Ab		
Positive	2 (1.19%)	1 (0.61%)
Negative	166	165
Total	168	166

respectively at the initiation of hemodialysis. The number of patients that were seroconverted after initiating hemodialysis was 2/163 (1.23%) and 1/166 (0.61%) for HBsAg and anti HCV antibodies, respectively [Table 2]

Association between socio-demographic/clinical characteristics and hepatitis B seroconversion

Two (2) patients who were HBsAg negative at the initiation of HD seroconverted: one male and one female aged 31–50 and 51–70 years, respectively. The two patients shared similar characteristics in that they were all on HD for less than 60 months, had undergone invasive procedures, and had not been vaccinated against hepatitis B infection. The

Table 3: Bivariate logistic regression analysis to show factors associated with Hepatitis B infection seroconversion (n=163)

Variables	Hepatitis B serology seroconversion		P	COR (95%CI)
	Positive	Negative		
Age				
<30	0	11	1 (Ref)	1 (Ref)
31-50	1	68	0.999	-
51-70	1	75	0.999	-
≥71	0	7	1.000	0.4 (0.00-)
Gender				
Male	1	109	1 (Ref)	1 (Ref)
Female	1	52	0.360	2.8 (0.3-24.9)
Marital status				
Single	0	66	1 (Ref)	1 (Ref)
Married	1	84	0.170	3.5 (0.6-21.8)
Divorced	0	3	0.330	0.27 (0.02-3.5)
Widowed	1	8	0.999	-
Duration of dialysis (months)				
<60	2	146	1 (Ref)	1 (Ref)
≥60	0	15	0.999	(0.00)
Frequency of blood transfusion				
0	1	57	1 (Ref)	1 (Ref)
1-5	0	97	0.050	11 (0.95-131.0)
6-10	0	6	0.999	-
11-15	1	1	0.999	-
Frequency of previous hospitalizations				
1-5	1	127	1 (Ref)	1 (Ref)
6-10	0	31	0.700	0.6 (0.05-7.3)
>10	1	3	0.999	-
History of invasive procedure				
Yes	2	110	1 (Ref)	1 (Ref)
No	0	51	0.927	1.1 (0.18-6.7)
HIV status				
Positive	1	40	1 (Ref)	1 (Ref)
Negative	1	121	0.550	2.2 (0.17-28.0)
History of Vaccination for Hepatitis B				
Yes	0	78	0.09	1 (Ref)
No	2	83		0.12 (0.01--.4)

Table 4: Bivariate logistic regression analysis to show factors associated with Anti-HCV antibodies seroconversion (n=166)

Variables	Anti-HCV antibodies seroconversion		P	COR (95%CI)
	Positive	Negative		
Age				
<30	0	11	1 (Ref)	1 (Ref)
31-50	1	69	1.000	0.00
51-70	0	78	0.999	0.84 (0.00-)
≥71	0	7	0.999	0.78 (0.00-)
Gender				
Male	1	112	1 (Ref)	1 (Ref)
Female	0	53	0.500	0.3 (0.02-5.8)
Marital status				
Single	1	67	1 (Ref)	1 (Ref)
Married	0	85	0.770	0.7 (0.04-11.0)
Divorced	0	4	0.999	0.00
Widowed	0	9	0.999	0.00
Duration of dialysis (months)				
<60	1	150	1 (Ref)	1 (Ref)
≥60	0	15	0.998	-
Frequency of blood transfusion				
0	0	62	1 (Ref)	1 (Ref)
1-5	1	95	0.997	0.00
6-10	0	6	0.999	0.00
11-15	0	2	1.000	0.88 (0.00-)
Frequency of previous hospitalizations				
1-5	1	129	1 (Ref)	1 (Ref)
6-10	0	32	0.998	4.2 (0.00-)
>10	0	4	1.000	0.00
History of invasive procedure				
Yes	1	112	1 (Ref)	1 (Ref)
No	0	53	0.997	-
HIV status				
Positive	1	40	1 (Ref)	1 (Ref)
Negative	0	125	0.760	0.08--9.0)

studied factors were however not significantly associated with HBV seroconversion [Table 3]

Association between socio-demographic/clinical characteristics and anti-HCV seroconversion

One patient seroconverted for anti- HCV antibodies over the course of HD. This patient was a male of 31–50 years category who was HIV positive, had a history of invasive procedure and had been on hemodialysis for less than 60 months. Overall studied factors were not associated with anti-HCV antibodies [Table 4].

DISCUSSION

The prevalence of hepatitis B and hepatitis C in hemodialysis patients in Botswana has not been documented previously.

Five out of one hundred and sixty-eight (2.98%) patients were found to be seropositive for HBsAg positive at the initiation of hemodialysis. This is close to the prevalence found in HD patients of other regions, for instance; 1% in the USA 1%^[11] and 1.3%–14.6% in Asia Pacific countries.^[12] This, however, is lower than the prevalence across most African countries, which range between 5%–68%.^[13,14] Compared to other available data on hepatitis B prevalence in Botswana, this study showed a lower prevalence; a study done in an HIV center in Botswana between 2005 to 2009 reported 5.3% prevalence among HIV co-infected people^[15] and one done between 2004 and 2013 at various antenatal clinics in Botswana showed a prevalence of 3.8%.^[16] The possible reason for lower prevalence in our study

is different population characteristics; the majority of the patients in our study were HIV negative as compared to the other Botswana studies, which were done mainly on HIV positive patients.

Two out of one hundred and sixty-eight (1.19%) patients were seropositive for anti-HCV antibodies at the initiation of HD; this low prevalence is in agreement with previous studies that showed that in sub-Saharan Africa HCV infection rates range between 1.5% and 3.5%.^[17] The low sero-prevalence in our study could be due to strict adherence to infection control measures and proper training of medical staff members in the dialysis units. Furthermore, the isolation of patients with HBV and HCV infection is common practice in our dialysis units, which could have contributed to the low prevalence, as it is recommended that the isolation of patients with HCV in dialysis patients could be an additional strategy to reduce seroconversion.^[18] Male gender comprised the majority, 2/3 (66.7%) of patients who seroconverted for HBV and HCV infection in our study, this is probably a reflection of global statistics where the majority of patients with ESRD are male; as reported elsewhere in the United Kingdom and USA.^[19]

Two out of one hundred and sixty-three (1.23%) patients were found to have seroconverted to HBsAg positivity having tested negative at the initiation of HD. This is slightly higher than what was found in a previous study done in Libya, which showed an incidence of 0.6%;^[20] this could be due to the low vaccination rates in our study HD centers as both patients that seroconverted had not been vaccinated against HBV.

One out of one hundred and sixty-six patients (0.61%) seroconverted to HCV antibody positivity having tested negative at the initiation of hemodialysis. In comparison to a previous study done in Libya, which showed a seroconversion rate of 7.1%;^[20] we found a markedly lower proportion. This is likely due to the low prevalence rates of HCV in this region as depicted previously.^[15,17]

Of the two patients (1.23%) that seroconverted to HBsAg positivity after starting HD, one was a male and the other a female; there was no significant relationship between gender and seroconversion. This is in agreement with previous studies, which did not show any significant relationship between gender and seroconversion.^[20,21] The patients that seroconverted for both HCV and HBV were within the age range of 30–70 years, however, there was no significant relationship between age and seroconversion, which is in agreement with previous studies.^[20,22] On the other hand, this study revealed a lack of significant association between marital status and HBV and HCV seroconversion. There was no literature

to compare our findings on the marital status association to HBV and HCV seroconversion.

Blood transfusion is one of the risk factors implicated in the transmission of viral hepatitis in HD patients.^[23] However, in this study, 1 in 2 (50%) of patients who seroconverted for HBsAg had not been transfused; and the only one seroconverted HCV patient received blood transfusion albeit less frequently (1–5 times). Overall, over a third (36.9%) of the study population had never received a blood transfusion. There was no significant relationship between the history of blood transfusion and the seroconversion of HBsAg and anti-HCV antibodies. This is in contrast with a study done in Senegal, which stated that a univariate analysis showed a significant relationship between HCV infection and the number of blood transfusions.^[18] However, our findings were in agreement with other studies,^[21,24] which showed no association between the history of blood transfusion and HBV infection in HD patients.

The lack of association between blood transfusion and HBV and HCV infections could be due to excellent blood screening methods for viral hepatitis in the country. The higher number of nontransfused patients (36.9%) as compared to literature may imply liberal the use of erythropoietin and iron supplements to treat anemia in HD patients in our dialysis units.

The duration of HD has been indicated as one of the main risk factors for the spread of HCV in HD patients.^[25] A study done in Cameroon^[26] showed that HD duration was significantly associated with the increased risk of HCV infection. Another study done in Rabat, Morocco concluded that HD duration of 10.6 years \pm 5.17 years was a major risk factor for HCV infection.^[22] In this study, the two patients that seroconverted to HBsAg became positive within 18 months and 21 months, respectively. The patient that seroconverted to anti HCV antibodies became positive within 21 months of HD. There was no significant association between dialysis duration and seroprevalence of HBV and HCV infection in this study. The lack of association with the duration of HD may partly be explained by the fact that the majority of our patients (91.1%) have been on HD for less than 60 months as public dialysis units were established only six years ago.

In some studies, it has been postulated that the history of invasive procedures is a risk factor for HBV infection,^[27] however, some studies have shown no association between the history of invasive procedure and HBV infection as it was found in this study.

A previous study done in Botswana showed that HBV infection as opposed to HCV infection was relatively

more common among HIV infected patients.^[15] The results of this study differ from previous findings as 2 in 7 (28.6%) HBsAg positive patients were HIV-infected as compared to 1 in 3 (33.3%) who were seropositive for anti-HCV antibodies. This may partly be explained by the fact that this study had fewer HIV positive patients, unlike the previous study that was among the HIV-infected population.

It is generally recommended to vaccinate ESRD patients on HD, as protection against HBV infection as immune memory remains for up to 20 years despite the declining antibody levels.^[28] In this study, only 47% of the patients were immunized against HBV. Notably, all patients who had been vaccinated did not seroconvert while the seropositive patients had no history of immunization against HBV, which agrees with the notion that vaccination does protect the majority of HD patients against HBV infection.

This study had several limitations; it included public center patients in the southern part of Botswana; patients dialyzing at dialysis unit on the northern part of the country were not included; hence it may be difficult to generalize the findings to the whole of Botswana. On the other hand, this being a cross-sectional study design; it can all show association and it is difficult to trace causation. Another study limitation is the laboratory tests used; the use of HBsAg as the marker for HBV may have missed some of the occult infections that could have been picked by other serological tests such as HBcAb or HBV DNA. Similarly, for HCV detection genotyping or PCR is more sensitive to establish infection as compared to anti-HCV antibodies.

In conclusion, this study revealed that the prevalence of hepatitis B and C among ESRD patients on hemodialysis at Princess Marina Hospital is low, which could be due to good hygienic infection control practices in the dialysis units in Botswana. There was no significant association between the duration of dialysis, frequency of blood transfusion, history of invasive procedures, or history of hospitalization and the seroconversion for either HBsAg or anti HCV antibodies. Routine vaccination against HBV infection is advised for all the patients on HD to reduce the risk of seroconversion. Regular audits on seroconversion status for hepatitis B and C are also recommended as a way of assessing and supporting the current strategies for infection control among HD patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and

other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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