HEPATITIS B, DELTA AND HUMAN IMMUNODEFICIENCY VIRUS INFECTIONS AMONG OMANI PATIENTS WITH RENAL DISEASES: A SEROPREVALENCE STUDY

Said H. S. Al-Dhahry, MD, PhD; Prabhakar N. Aghanashinikar, MBBS, DSM; Hamoud A. Al-Marhuby, MBBS, DSM; Mads R. Buhl, MD, PhD; Abdullah S. Daar, FRCS, MRCP, PhD; Mohammed K. Al-Hasani, MD, MRCP

The prevalence of hepatitis B virus (HBV), hepatitis delta virus (HDV), and human immunodeficiency virus (HIV) infections were determined in 102 patients on regular hemodialysis, 82 kidney recipients and 103 nondialyzed, nontransplanted patients with various renal diseases. The prevalence rates of hepatitis B surface antigen (HBsAg) in dialysis and renal transplant patients (12.7% and 11.0% respectively) were significantly higher than the rate in a control group of patients who had never been dialyzed nor transplanted (2.9%, $P<0.05$). In patients who were HBsAg positive, evidence of HDV infection was found in one dialysis and two transplant patients only. HIV infection was confirmed in only two of 102 (2.0%) and three of 82 (3.7%) hemodialysis and kidney recipients respectively. These data indicate that hepatitis B, delta and HIV infections are major health problems among hemodialysis and renal transplant patients in the Sultanate of Oman. *Ann Saudi Med 1994;14(4):312-315.*

Soon after long-term dialysis became standard treatment for chronic renal failure, it was apparent that infectious hepatitis was a major problem for both patients and personnel staffing the units. In a 1972 serological survey of 15 dialysis centers in the United States, the Center for Disease Control (CDC) found the prevalence of markers of hepatitis B virus (HBV) to be 55% among patients and 33% among staff.[1] The introduction of mandatory screening of potential blood donors for hepatitis B surface antigen (HBsAg) in the mid 1970s, together with infection control measures, including isolation of HBsAg positive patients, resulted in a dramatic decrease in the incidence of hepatitis B in dialysis units.[2,3] Nonetheless, the availability of serological tests for the major agent causing non-A, non-B hepatitis (hepatitis C virus, HCV) has shown that HCV infection is common among dialysis patients.[4-9]

There is no published data on the frequency of hepatitis B, hepatitis C and other viral infections in dialysis patients in the Sultanate of Oman. We determined the prevalence of viral hepatitis B, C, and D and HIV infections in hemodialysis patients, and in two related groups of patients - those with kidney transplants and those with kidney diseases but who had never been dialyzed nor transplanted. Our findings on hepatitis C virus infection have been reported previously.[10]

From the Departments of Microbiology (Dr. Al-Dhahry), Medicine (Dr. Buhl), Surgery (Prof. Daar), College of Medicine, Sultan Qaboos University, and the Department of Nephrology (Drs. Aghanashinikar, Al-Marhuby, Al-Hasani), Royal Hospital, Muscat, Sultanate of Oman.

Address reprints and correspondence to Dr. Al-Dhahry: Department of Microbiology, College of Medicine, P.O. Box 35, Al-Khod, Muscat 123, Sultanate of Oman.

Accepted for publication 19 September 1993.

Subjects

Patients

Three groups of patients, treated at the Royal Hospital in Muscat, Sultanate of Oman, were included in this study. Serum samples were obtained from patients in the outpatient nephrology and transplant clinics or dialysis unit. A) Nephrology Clinic Patients - This category consisted of 103 consecutive patients (49 M, 54 F, mean age 39 years, range 8 to 74). Of these patients, 42 suffered from chronic but not end stage renal failure, 22 had glomerulonephritis, 20 had hypertensive kidney diseases, and 19 suffered from other kidney related diseases. None of the patients in this group was on dialysis. B) Hemodialysis Patients - 102 consecutive patients (46 M, 56 F, mean age 42 years, range 14 to 71) on hemodialysis due to end stage renal failure were studied. The duration of dialysis varied from four months to six years (mean 35 months). Of these 102 patients, four (3.9%) were already HBsAg positive on entering the hemodialysis program. C) Renal Transplant Patients - 82 patients (44 M, 38 F, mean age 33 years, range 5 to 61), regularly followed up in the clinic, were studied. Forty-five patients were transplanted in India, 22 in the United Kingdom, 10 in Oman and five in three other countries. Thirty-eight patients received kidneys from living related donors, 41 from living nonrelated donors, and three from cadavers. Prior to kidney transplantation, 98% of the patients had been dialyzed for a mean duration of nine months (range one month to three years).

Healthy Subjects

Serum samples that were collected from 134 medical students as part of a vaccination program against hepatitis B and from 564 blood donors were tested.

Methods

Serological Testing - Sera were kept frozen at -20°C in multiple aliquots until assayed. The samples had not previously been thawed. All sera were tested for HBsAg and hepatitis B core antibody (anti-HBc) by commercial ELISAs (AUSZYME and CORZYME respectively, Abbott Laboratories). Sera that were HBsAg positive were tested for the "e" antigen (HBeAg), antibody to HBeAg (anti-HBe), anti-HBc IgM, and antibody to hepatitis delta virus (anti-delta) by ELISAs (HBe [rDNA] EIA, CORZYME-M, anti-delta respectively, Abbott Laboratories). HBsAg positive sera were also tested for hepatitis delta antigen (HDAg, Wellcome Diagnostics).

Testing for HIV antibody was performed on patients' sera only by a second generation ELISA (recombinant HIV-1/HIV-2 EIA, Abbott GmbH Diagnostica) with Western blot (Novopath HIV-1, Biorad, and New LavBlot II -HIV-2, Diagnostics Pasteur) for confirmation.

Statistical Analysis - The chi-square test with Yates' correction was used to evaluate the significance of differences within and among groups. A $P<0.05$ was considered to indicate statistical significance.

Results

Table 1 shows results of serological testing for HBsAg and anti-HBc. Among patients, the prevalence of HBsAg was significantly higher in hemodialysis and renal transplant patients than in nephrology clinic patients ($P<0.05$). In the latter group of patients, HBsAg prevalence rate (2.9%) was not statistically different from the prevalence in medical students (4.5%) and blood donors (5.1%).

Although nephrology clinic patients had a comparatively low prevalence of HBsAg, previous exposure to HBV, defined here as anti-HBc seropositivity without HBsAg, was found in 48 of 103 (46.6%) nephrology clinic patients, compared with 53 out of 102 (52%) hemodialysis patients and 43 of 82 (52.4%) renal transplant patients (Table 1, $P>0.05$). The prevalence rates of past HBV infection in medical students (23.1%) and blood donors (27.1%) were significantly lower than the rate in any of the patient groups ($P<0.001$).

The "e" antigen of HBV correlates closely with the concentration of Dane particles in serum and relative infectivity. We determined the prevalence of this antigen and its corresponding antibody (anti-HBe) in all subjects who were HBsAg positive (Table 2). Of the 14 HBeAg positive subjects, six (44.4%) were dialysis patients. The majority of patients (64%) and healthy subjects (71%) had anti-HBe.

Interpretation of HBV serological patterns[11,12] of patients and healthy subjects who were HBsAg positive suggests that 10% were either in the incubation period of hepatitis B or in early acute hepatitis B, 8% had acute hepatitis B, and 82% were persistent (i.e., chronic) carriers of HBV. Alanine aminotransferase activity, estimated in patients' sera only, was slightly elevated in four patients.[10] Two of these had serological evidence of acute hepatitis B and the other two were persistent carriers.

In an assessment of risk factors for acquiring hepatitis B, we found that seven of 103 (6.8%) nephrology clinic patients, 81 of 102 (79%) hemodialysis patients, and all kidney transplant recipients had been transfused in the past. However, further analysis of data from dialysis patients revealed no correlation between HBsAg positivity and frequency of blood transfusions or duration of dialysis (Table 3). None of the patients had a history of intravenous drug abuse.

In HBsAg positive subjects, serological evidence of HDV infection was found in one of 13 (7.7%) patients on dialysis and two of nine (22.2%) kidney transplant recipients only (Table 2). All three HDV-infected patients had been transfused in the past.

Of 287 patients and 698 healthy subjects tested, a double viral infection of HBV and HCV was found in only four hemodialysis and two transplant patients.[10] HIV

TABLE 1. *Serological status for hepatitis B and HIV among patients with renal diseases and healthy subjects.*

Group	No. tested	HBsAg +ve	(%)	Anti-HBc[a] +ve	(%)	Anti-HIV +ve	(%)
Patients							
Nephrology clinic	103	3	(2.9)	48	(46.6)	0	(0)
Hemodialysis	102	13	(12.7)	53	(52.0)	2	(2.0)
Renal transplant	82	9	(11.0)	43	(52.4)	3	(3.7)
Healthy Subjects							
Medical students	134	6	(4.5)	31	(23.1)	NT	
Blood donors	564	29	(5.1)	152	(27.1)	NT	

[a]=anti-HBc seropositivity in subjects without HBsAg as a marker of past infection; NT=not tested

TABLE 2. *Serological status for HBeAg, anti HBe, and HDV in subjects positive for HBsAg.*

Group	No. tested	HBeAg +ve	Anti-HBe +ve	HDV +ve
Patients				
Nephrology clinic	3	0	2	0
Hemodialysis	13	6	7	1
Renal transplant	9	1	7	2
Healthy Subjects				
Medical students	6	2	4	0
Blood donors	29	5	21	0

TABLE 3. *Relationship between blood transfusion, duration of dialysis and HBsAg seropositivity in hemodialysis patients.*

Number of transfusion	HbsAg+ve (%)
0	3/22 (14)
1 - 5	7/50 (14)
6 - 10	3/12 (25)
11 - 15	0/8 (0)
> 15	0/10 (0)
Duration of dialysis (y)	
< 1	1/32 (3)
1 - 3	6/22 (27)
4 - 6	6/48 (13)

infection was confirmed in five patients (Table 1). Their ages ranged from 28 years to 60 years. The three HIV positive transplant patients seroconverted between three and nine months following kidney transplantation abroad. Prior to that, they had been consistently HIV negative. Similarly, the two HIV positive hemodialysis patients seroconverted after repeated dialysis and multiple blood transfusions abroad, where they had primarily gone for kidney transplantation.

Discussion

Our study shows that the prevalence of HBV infection in Omani patients with renal diseases is high. Approximately 50% of all patients studied had serological evidence of current or past infection. However, the prevalence of HBsAg was significantly higher in hemodialysis and renal transplant patients than in patients with kidney diseases but who had never been dialyzed nor transplanted. In the latter group of patients, the prevalence of HBsAg was comparable to that of healthy subjects. It has been suggested that patients on regular hemodialysis acquire hepatitis B through multiple blood transfusions, environmental contamination of dialysis units, and contact between patients.[3] Kidney transplant patients are infected through similar routes but, in addition, the transplanted kidney may be the source of infection.[13] Results of this study suggest that in our dialysis and transplant patients, hepatitis B is acquired through similar routes, as well as through routes that are unrelated to hemodialysis, transfusion and transplantation.

In healthy subjects, the prevalence of HBsAg was approximately 5%; an additional 25% had evidence of past infection. In a parallel study of 2000 women who attended antenatal clinics in all regions of the Sultanate of Oman, the prevalence of HBsAg and anti-HBs was 9% and 38% respectively.[14] These results place Oman among countries with high endemicity of hepatitis B. In these countries, the reported prevalence of HBsAg in dialysis patients varies from 7% to 26%.[15-17]

On the basis of serological patterns of HBV markers, 82% of the HBsAg positive subjects had chronic hepatitis. Since liver histology was not done in any of these subjects, the type(s) of chronic hepatitis remains unknown.

Hepatitis delta infection has been reported to be common in the Middle East.[18,19] In a recent study from neighboring Saudi Arabia, anti-HDV was detected in 17% (5/30) of HBsAg positive renal transplant patients.[17] Sixteen of 36 (44.5%) HBsAg positive hemodialysis patients in Iran had anti-delta.[20] Although our population samples of HBsAg positive dialysis and transplant patients are small, the prevalence of HDV infection in these two groups of Omani patients appears to be high.

In contrast, none of the 35 HBsAg positive healthy subjects (i.e., medical students and blood donors) had serological evidence of delta infection.

The main risk factor for acquiring HIV infection in the five patients who were confirmed positive was probably multiple blood transfusions. However, HIV may be acquired through kidney transplantation.[21] HIV infection in Omani patients following renal transplantation abroad has been reported previously.[22]

Figures from the Gulf countries indicate that there was a definite risk, approximately 1:12, of HIV seroconversion following transplantation in Bombay, India during the period of this study. In transplanted patients, acquisition of HIV infection is almost uniformly devastating, with the majority of patients either dying or losing their kidneys through, surprisingly, chronic rejection.[23]

Acknowledgment

We thank Miss J. Dongbo for technical assistance and Miss T. P. Cahanding for preparation of the typescript.

References

1. Szmuness W, Prince AM, Grady GF, et al. Hepatitis B infection: a point-prevalence study in 15 US hemodialysis centers. JAMA 1974;227:901-6.
2. Najem GR, Louria DB, Thind IS, et al. Control of hepatitis B infection: the role of surveillance and an isolation hemodialysis center. JAMA 1981;245:153-7.
3. Shusterman N, Singer I. Infectious hepatitis in dialysis patients. Am J Kid Dis 1987;9:447-55.
4. Mondelli MU, Cristina G, Rondanelli EG, et al. Anti-HCV positive patients in dialysis units? Lancet 1990;336:244.
5. Schlipkoter U, Roggendorf M, Ernst G, et al. Hepatitis C virus antibodies in hemodialysis patients. Lancet 1990;335:1409-10.
6. Ayoola EA, Huraib S, Arif M, et al. Prevalence and significance of antibodies to hepatitis C virus among Saudi hemodialysis patients. J Med Virol 1991;35:155-9.
7. Lin HH, Huang CC, Sheen IS, et al. Prevalence of antibodies to hepatitis C virus in the hemodialysis unit. Am J Nephrol 1991;11:192-4.
8. Tamura I, Koda T, Kobayashi Y, et al. Prevalence of four blood-borne viruses (HBV, HCV, HTLV-I, HIV-1) among hemodialysis patients in Japan. J Med Virol 1992;36:271-3.
9. Stempel CA, Lake J, Kuo G, Vincenti F. Hepatitis C - its prevalence in end-stage renal failure patients and clinical course after kidney transplantation. Transpl 1993;55:273-6.
10. Al-Dhahry SHS, Aghanashinikar PN, Al-Marhuby HA, et al. Antibodies to hepatitis C virus in Omani patients with renal disease. Transpl Proc 1992;24:1938-9.
11. Lutwick LI. Hepatitis B virus. In: Belshe RB, ed. Textbook of human virology, 2nd ed. St Louis: Mosby Year Book;1991:719-48.

12. Zuckerman AJ, Harrison TJ. Hepatitis B virus and hepatitis D virus. In: Principles and practice of clinical virology, 2nd ed. Zuckerman AJ, Banatvala JE, Pattison JR, eds. Chichester: John Wiley 1990;153-72.
13. Wolf JL, Perkins HA, Schreeder MT, Vincenti F. The transplanted kidney as a source of hepatitis B infection. Ann Intern Med 1979;91:412-3.
14. Al-Dhahry SHS. Seroprevalence of various infectious diseases in women attending antenatal clinics in the Sultanate of Oman. Report to the Director of Curative Services, Ministry of Health, Sultanate of Oman, 1991.
15. Sobeslavsky O. Prevalence of markers of hepatitis B virus infection in various countries. A WHO collaborative study. Bull WHO 1980;58:621-8.
16. Al-Faleh FZ. Hepatitis B infection in Saudi Arabia. Ann Saudi Med 1988;8:474-80.
17. Dhar JM, Al-Khader AA, Al-Sulaiman MH, Al-Hasani MK. The significance and implications of hepatitis B infection in renal transplant recipients. Transpl Proc 1991;23:1785-6.
18. Ponzetto A, Forzani B, Parravicini PP, et al. Epidemiology of hepatitis delta virus (HDV) infection. Eur J Epidemiol 1985;1:256-63.
19. Wright R. Viral hepatitis comparative epidemiology. Br Med Bull 1990;46:548-58.
20. Rezvan H, Forouzandeh B, Taroyan S, et al. A study on delta virus infection and its clinical impact in Iran. Infection 1990;18:26-8.
21. Quarto M, Germinario C, Fontana A, Barbuti S. HIV transmission through kidney transplantation from a living related donor. N Engl J Med 1989;320:1754.
22. Salahudeen AK, Woods HF, Pingle A, et al. High mortality among recipients of bought living unrelated donor kidneys. Lancet 1990;336:725-8.
23. Dalaney V, Sumrani N, Hong J, et al. The course of HIV disease in renal allograft recipients. Transplant Intern 1992;5(Suppl 1):S129-32.