HIV Transmission at a Saudi Arabia Hemodialysis Unit

Faisal Mashragi,1 Robert S. Bernstein,2 Mohammad Al-Mazroa,1 Jaffar A. Al-Tawfiq,3 Sanaa Filemban,1 Abdullah Assiri,1 Elaine Furukawa,1 Mohammad Al Hazmi,1 Abdullah Alzahrani,1 Gwen Stephens,1 and Ziad A. Memish1,4

1Ministry of Health, Riyadh, Kingdom of Saudi Arabia; 2Bureau of Epidemiology, Florida Department of Health, Tallahassee; and 3Saudi Aramco Medical Services Organization, Dhahran, and 4College of Medicine, Alfaisal University, Riyadh, Kingdom of Saudi Arabia

Background. Hemodialysis is associated with increased risk of healthcare-associated infections but considered a low-risk setting for human immunodeficiency virus (HIV) transmission. We investigated 3 hemodialysis unit (HDU) patients with new HIV infections to determine whether transmission was hemodialysis-associated and to correct factors that contributed to transmission.

Methods. Each patient was evaluated for HIV risk factors. Blood samples were tested to determine relatedness of HIV strains. Clinical data (gathered over 18 months) was reviewed to identify seroconversions at 12 HDUs. Infection prevention and control practices were evaluated at 14 HDUs.

Findings. No other HIV seroconversions were identified during the study. HIV gag, pol, and env gene sequences were consistent with a clonal relationship. HIV and hepatitis C virus prevalence rates at one HDU 1 (5.7% and 6.5%, respectively) were higher than for 11 other HDUs (0% and 0.15%, respectively).

Conclusions. Sequencing supports either patient-to-patient or common-source transmission. Infections occurred despite Saudi Arabia’s low HIV prevalence and national dialysis policies that emphasize stringent infection prevention and control practices.

Keywords. hemodialysis; healthcare-associated infections; epidemic outbreak; HIV; HCV.

Endemic transmission and epidemic outbreaks of healthcare-associated infections (HAIs) are frequent threats to patient safety, causing substantial morbidity, disability, mortality, and economic losses worldwide [1, 2]. Patients on chronic hemodialysis are highly vulnerable to HAIs for many reasons [3]. In the hemodialysis setting, failure to use proper hand hygiene, cross-contamination of instruments and medications, mishandling or inadequate disinfection of dialysis equipment, and failures to adhere to infection prevention and control (IPC) standard practices place dialysis patients at increased risk of HAIs, notably to infection by blood-borne viruses (BBVs) [3–7].

Although hemodialysis has been associated with increased risk of healthcare-associated hepatitis C virus (HCV) and hepatitis B virus (HBV) infections [2, 3], it is considered to be a low-risk setting for human immunodeficiency virus (HIV) transmission [3]. Five outbreaks of hemodialysis-associated HIV occurred from 1990 to 1994 in 3 developing countries [4–7]. In these outbreaks, epidemiologic findings supporting hemodialysis-associated HIV transmission were linked with directly observed or reliably reported evidence of egregious breaks in IPC practices. Consistency in the molecular sequencing of the epidemic strain of HIV further supported the epidemiologic findings in the 1993 outbreak in Egypt [7].

In early 2012, the Directorate of Health Affairs in the Jizan Region of the Kingdom of Saudi Arabia (KSA) informed the Ministry of Health that 2 patients (patient numbers 2 and 3) at hemodialysis unit (HDU) 1 had become HIV positive. A preliminary investigation
suggested that their infections might be healthcare associated and linked to an HIV-infected patient (patient 1) referred to HDU 1 on 4 November 2011, from HDUs 13 and 14 in Abha Region. A team investigated the reported cluster to identify and correct factors contributing to the outbreak.

METHODS

Case Definition
A case of hemodialysis healthcare-associated HIV infection was defined as a patient among the 35 undergoing treatment at HDU 1 from 1 November 2011 to 31 December 2011, who seroconverted during this period to HIV-positive status and whose self-reported behaviors did not include HIV risk factors (extramarital sexual relations or injection drug use), and whose spouse was seronegative for HIV. Oral informed consent was obtained prior to confidential interviews, examinations, and serology testing [2, 8].

Routine Serology Testing for HIV, HBV, and HCV Infections
Saudi Arabia Dialysis Safety guidelines [9] require all new hemodialysis referrals and patients transferred to new HDUs to be tested for HIV, HCV, and HBV prior to treatment. Saudi Arabia employs a fourth-generation HIV enzyme immunoassay (Bio-Rad Laboratories Genscreen [10]) to detect HIV type 1 (HIV-1) p24 antigen, plus antibody to HIV-1 (groups M and O) and HIV type 2 (HIV-2). Positive specimens are confirmed by the Western blot method and by HIV RNA polymerase chain reaction (PCR) in the event of discrepancies. HIV status of seronegative patients is monitored at intervals that vary from a few months to semiannually depending on the unit.

HBV infection is confirmed for patients who are repeatedly reactive for hepatitis B surface antigen (HBsAg) by Bio-Rad Monolisa HBsAg ULTRA assay [10]. Patients with ambiguous HBV markers are reflexed to HBV DNA testing for definitive diagnosis.

HCV status is determined by a qualitative enzyme immunoassay test that detects both anti-HCV antibody and HCV core antigen (Bio-Rad Monolisa HCV Ag-Ab ULTRA [10]). Specimens with equivocal results are resolved by HCV RNA PCR testing.

Molecular Analyses
All 3 patients were known to be HCV seropositive. Sequencing studies were used to determine relatedness of HCV and HIV viruses for each patient in the cluster. For HCV, a 328-nucleotide fragment of the NS5B subgenomic region was amplified and then sequenced to determine a conventional genotype. For HIV, population sequencing of PCR products for pol, gag, and env genes was done. Maximum likelihood methods were used to carry out a phylogenetic analysis. Because there were too few KSA pol sequences available from public databases, 80 from other Middle Eastern countries were used as controls.

Fifty-five gag sequences from KSA were downloaded from public databases and used as controls.

Case Finding and Epidemiologic Analyses
Results of routine BBV surveillance tests for all patients in 14 Ministry of Health HDUs—HDU 1 plus 5 others in Jizan, 2 in Abha, and 6 in the Capital Region of Riyadh—were reviewed. All HIV- and HCV-seronegative patients from HDU 1 and HDU 14 were retested to check for interval seroconversions. We compared prevalence rates and relative risk of acquiring HIV and HCV infection for patients treated at HDU 1 with those treated at the other 11 HDUs [11].

IPC Practices in 14 HDUs
Using a structured IPC checklist assessment protocol (a copy of the Maryland HDU Assessment Tool is available from Dr Priti Patel at priti.patel@cdc.hhs.gov; for an example of its previous use, see [12]), an infectious disease consultant, an infection control practitioner, and 3 medical epidemiologists assessed the HDU facilities, audited staff practices, and interviewed the 3 new HIV-positive patients. Interviews, observations, and record reviews were carried out in HDU 1, and in another 13 Ministry of Health HDUs in Jizan and Riyadh, including both HDUs in Abha where patient 1 had been treated between September and November 2011 when she became infected with HIV. The evaluation teams investigated HDU practices for compliance with Saudi Arabia/Gulf Cooperation Council (GCC) dialysis safety procedures. Local dialysis policies are based on international recommendations [9, 13–17]. The IPC supervisor, nurse/nurse manager, and dialysis technician of each HDU were interviewed and IPC practices were evaluated. Supervisory staff were asked about the methods and frequency of IPC feedback, whether not a system of competency-based IPC training was in use [3, 9, 13–18].

RESULTS

Case Finding
Investigations were initiated 16 November 2011 at HDU 1 on receipt of patient 1’s positive HIV test result. A confirmatory Western blot result followed 22 November, along with a viral load report of 4 million copies/mL. Although Ministry of Health policy requires each HDU to conduct preadmission BBV testing prior to initiating dialysis at a new unit, patient 1’s first specimen from 4 November was unsatisfactory, and a second serum was sent. A rapid HIV point-of-care test had been done prior to treatment; however, the result was indeterminate.

Patient 1 was a 46-year-old married female with end-stage renal disease who had been referred to Jizan from HDUs 13 and 14 in Abha Region, where she had received dialysis treatment for 12 years. All previous BBV tests confirmed she was HIV negative from commencement of dialysis treatment
through 4 September 2011, the date of her last HIV serology at HDU 14. She had no self-reported behavioral risk factors for HIV infection, and her husband was HIV negative. Twice in September and October 2011, she was admitted to a hospital in Abha Region, first for treatment of sepsis and abdominal pain and later for treatment of ascites, pleural effusion, lymphadenopathy, fever, and anemia. She was transfused with 3 units of blood in the first admission and 2 units in the second admission. All 5 units and contributing donors tested negative for HBV, HCV, and HIV using American Association of Blood Banks–compliant procedures.

Among the 35 patients at HDU 1, 2 additional patients met the case definition for hemodialysis HAI. Patient 2 was a 70-year-old married woman who had been undergoing hemodialysis for 20 years at HDU 1. Prior to December 2011, she was HCV positive and seronegative for HIV. Patient 3 was a 30-year-old married woman with end-stage renal disease and several disabling congenital conditions. Both patients 2 and 3 denied extramarital sexual relations; neither had ever engaged in injection drug use. The husbands of patients 1, 2, and 3 tested HIV negative.

Initial interviews with patients 1, 2, and 3 confirmed that patient 1 had an initial dialysis on 14 November, at HDU 1 in a room reserved for HCV-seropositive patients. This date coincided with the acute stage of her HIV infection. She shared the same dialysis nurse and was dialyzed on the same shift as patient 2. This machine was later used to dialyze patient 3. Breaches of IPC dialysis protocol included a 15-minute disinfection cycle rather than the required 45 minutes of the dialysis machine shared by patients 1 and 3, a nurse who used blood-spattered gloves to handle vascular access lines of multiple patients, and the use of a shared syringe to access a multidose vial of heparin. All 3 patients had been dialyzed in the same (22.4 m² 3-bed) room.

**HDU Facilities and Practices in 3 KSA Health Regions**

Table 1 summarizes compliance audits for the 14 HDUs in Jizan and Riyadh, plus 2 additional HDUs in Abha Region (HDUs 13 and 14) where patient 1 was treated before November 2011.

In all HDUs except for the one in Riyadh, multidose heparin vials were shared with multiple patients (Table 1). Disposable gloves were used before drawing of heparin, but disinfection of the vial septum was observed in only a few of the 14 HDUs. At all HDUs, sharps were appropriately disposed of in puncture-resistant sharps containers.

Blood-spill competence was evaluated by questioning nurses in each unit about measures they would take in such instances [19–21]. Nurses were often unsure of proper blood-spill cleaning procedures, and many were not aware of the location of written infection control guidance materials in the HDU.

In all HDUs, a diluted bleach solution was used to clean and disinfect chairs and external surfaces of the dialysis machines; however, monitoring of disinfectant concentration was not done. The dialysis water system was routinely disinfected every month in a third of the HDUs and every 3–6 months in the other two-thirds. Filters were changed every 3–6 months in all HDUs. Dialyzers are single-use devices in KSA.

**HDU Staffing and IPC Staff Training in 3 Regions**

Each HDU had 1 head nurse to supervise nursing staff. The average number of nurses per patient varied from 1 to 3 in both Jizan and Riyadh. All HDUs have an explicit infection control training program, and copies of the GCC/Certified Infection Control Guidelines on site. IPC policies and practices were immediately available to staff; however, the frequency and nature of IPC training varied across all HDUs. Neither IPC competencies nor compliance with dialysis standards and guidelines were routinely audited by supervisors [9, 18].

**Medical Record Reviews**

Monitoring of HCV- and HIV-seronegative patients was done at all HDUs in accordance with KSA/GCC hemodialysis guidelines. Five HDUs in Jizan tested patients every 3 months, and 1 HDU tested every 6 months. In January 2011, HCV prevalence for 698 patients being treated at 6 Jizan HDUs was 16.2% (Table 2). During an 18-month period between 1 January 2011 and 30 June 2012, HCV seroconversions occurred at 2 Jizan HDUs; incidence rates were revised to 0.9% for HDU 2.

Table 1. Summary of Observed Breaks in Compliance With Standard Infection Prevention and Control Practices, 14 Hemodialysis Units in Jizan, Riyadh, and Abha Regions, Saudi Arabia, June 2012

<table>
<thead>
<tr>
<th>Break</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region</td>
<td>Jizan</td>
<td>Jizan</td>
<td>Jizan</td>
<td>Jizan</td>
<td>Jizan</td>
<td>Riyadh</td>
<td>Riyadh</td>
<td>Riyadh</td>
<td>Riyadh</td>
<td>Riyadh</td>
<td>Riyadh</td>
<td>Riyadh</td>
<td>Riyadh</td>
<td>Abha</td>
</tr>
<tr>
<td>Practice breaks</td>
<td>1, 2, 3, 4, 5</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td>1, 2, 3, 4</td>
<td></td>
</tr>
</tbody>
</table>

* Explanation of symbols: A: inconsistent or noncompliance with manufacturer’s recommended procedures for cleaning, disinfecting, maintaining, and storing dialyzers and dialyzer machines; B: absence of designated medication preparation area removed from patient’s station; C: malfunctioning of hand-washing sinks; 1: common cross-use of one normal saline bag for dilution of multidose injectable vials; 2: alcohol swabs were not used for cleaning the ports of multidose injectable vials; 3: drawing of medication beside the patient station; 4: carrying of medication from station to station; and 5: patients reported too short (15-minute) disinfection of dialyzers and bloody gloves used to handle vascular access lines.
Table 2. Summary of Hepatitis C Virus Seroconversions Among Chronic Renal Dialysis Patients in 12 Hemodialysis Units in Jizan and Riyadh Regions, January 2011–June 2012

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HDU 1</td>
<td>Jizan</td>
<td>35</td>
<td>4 (11%)</td>
<td>31</td>
<td>2</td>
<td>6.45%</td>
</tr>
<tr>
<td>HDU 2</td>
<td>Jizan</td>
<td>271</td>
<td>54 (20%)</td>
<td>217</td>
<td>2</td>
<td>0.92%</td>
</tr>
<tr>
<td>HDUs 3–6</td>
<td>Jizan</td>
<td>392</td>
<td>55 (6%–19%)</td>
<td>337</td>
<td>0</td>
<td>0.00%</td>
</tr>
<tr>
<td>HDUs 1–6</td>
<td>Jizan</td>
<td>698</td>
<td>113 (0%–20%)</td>
<td>585</td>
<td>4</td>
<td>0.68%</td>
</tr>
<tr>
<td>HDUs 7–12</td>
<td>Riyadh</td>
<td>1065</td>
<td>262 (11%–41%)</td>
<td>803</td>
<td>0</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

Abbreviations: HCV, hepatitis C virus; HDU, hemodialysis unit.

and 6.5% for HDU 1, where HIV transmission occurred in patients 2 and 3 (Table 2).

In Riyadh, HCV-negative patients are retested every 6 months, and HIV is checked semiannually. In January 2011, the overall HCV prevalence for the 6 HDUs with a population of 1065 patients was 24.6% (range, 11.3%–40.9%; Table 2). There were no HCV or HIV seroconversions between 1 January 2011 and 30 June 2012.

The rates of HIV and HCV seroconversions at HDU 1 (5.7% and 6.5%, respectively) were higher than for the other 5 Jizan HDUs (0%, Fisher exact test 2-tailed $P = .005$; and 0.4%, $P = .03$). Differences were of even greater statistical significance when compared with HIV and HCV seroconversion rates at the 11 other HDUs in Jizan and Riyadh (0%, Fisher exact test 2-tailed $P = .0008$; and 0.15%, $P = .006$, respectively).

Molecular Phylogenetic Analyses

HIV pol, gag, and env gene sequences aligned in single clusters, indicating a clonal relationship consistent with recent transmission (Supplementary Figures 1–3). HCV genotypes for patients 1, 2, and 3 were identified as 3a, 4a, and 1a, respectively, by sequencing of an NS5B gene fragment (Supplementary Figure 4). This confirms that for these three patients, the HCV infections were unlinked and independent events.

Follow-up

The 2 HIV-infected HDU 1 patients were counseled and started on highly active antiretroviral therapy. Patient 1 died of AIDS within 6 months. No additional HIV infections have been diagnosed.

DISCUSSION

Hemodialysis patients are at greater risk of HAI than other hospitalized patients, particularly for BBV transmission. Patient safety has benefited from continuous improvements in dialysis machine design, equipment safety, diagnostic assays, vaccines, and guidelines that emphasize evidence-based infection prevention strategies.

KSA/GCC hemodialysis policies incorporate recommendations from multiple international guidelines and share an emphasis on universal precautions and strict measures to prevent transfer of contaminated materials between patients. Units with dedicated equipment and machines are available for HCV- as well as HBV-infected patients. Although many centers reuse dialyzers for the same patient, these are single-use devices in KSA, discarded at the end of treatment along with needles and bloodlines. Single-pass hemodialysis machines are in use in all units; this ensures that internal fluid pathways are not subject to contamination with blood. Because contact transmission is known to be a major route by which patients acquire BBV, IPC practices, in particular hand hygiene and contact precautions, are emphasized in KSA/GCC hemodialysis policies and training.

Our investigation of the available evidence implicates non-compliant IPC practices as a cause of the outbreak. Using epidemiological methods, we were able to demonstrate a biologically plausible association between breaks in IPC practices and the transmission of HIV infections in HDU 1. The most likely index case was patient 1, given an HIV seroconversion window between September and November 2011, and an acute illness between October and November. This finding coincides with an acute HIV syndrome typically associated with high viral loads, increased risk of transmission, and higher rates of false-negative HIV tests. On November 14, the index case was dialedyzed in proximity to both secondary cases. Risk factors for transmission include a multidose heparin vial from which injections were shared by all 3 patients, inadequately disinfected hemodialysis equipment, and dialysis staff who used blood-contaminated gloves to manipulate vascular access for multiple patients. The patients were dialyzed in close proximity despite a known association of increased infections linked in these settings [19–24]. Hemodialysis-associated HIV transmission has not been reported in developed countries [3], and did not recur in the 3 countries where it was previously reported [4–7];
thus, strengthening IPC programs can prevent hemodialysis-associated infections [1–3, 16, 17]. Similar to the current study, sequence analyses of the HIV nucleotide, a common source of exposure, was evident in half of the reported cases [4–6]. During visits to each HDU, individual healthcare workers were asked to provide feedback on IPC practices, and intensified measures to educate all hemodialysis staff about IPC practices were conducted [9, 14–17]. After 1 month, HDUs 1 and 14 were compliant with the corrective actions. A national system of competency-based IPC training was developed [25], and a national healthcare safety program was initiated based on international recommendations [9, 14, 17, 26]. The program includes a system of (1) auditing hand hygiene and other IPC practices with immediate feedback and (2) surveillance and response for the occurrence of adverse dialysis-associated events in accordance with the literature [13, 16, 17]. An international workforce requires a standardized approach to staff training and adherence to KSA dialysis safety standards. Procedures and practices for IPC training, supervision, and monitoring of HAIs are particularly important [1–3, 9, 13, 17].

The genetic analysis of HCV did not reveal a cross-transmission among the 3 patients. Hemodialysis-associated HCV infection was documented to occur in centers with a high rate of HCV-positive patients and in relation to a low staff-to-patient ratio.

This study has acknowledged limitations including an inability to evaluate the role of staff education, training, and supervision in the outbreak. IPC deficiencies may have been underestimated in other centers given the tendency for staff to alter practices while being audited [25, 28]. Potential contributing factors that may have played a role but are difficult to evaluate include the multiplicity of nationalities with different educational and training backgrounds represented in the ranks of KSA dialysis staff. This has confounded efforts to standardize practice and emphasizes the importance of continuous quality improvement processes [29].

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Acknowledgments. The authors express their gratitude for the molecular phylogenetic analyses of viral isolates, which were carried out by the following experts at the UK Health Protection Agency: Dr Patricia Cane, Dr Tamyo Mbisa, Dr Siew-Lin Ngui, and Dr Richard Tedder.

Financial support. The work was supported by the Kingdom of Saudi Arabia Ministry of Health.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References


