Kidney International, Vol. 67 (2005), pp. 1526–1531

Incidence and etiology of acute renal failure among ambulatory HIV-infected patients

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Background. Acute renal failure (ARF) is a cause of renal dysfunction in human immunodeficiency virus (HIV)-infected patients. Its incidence and causes have not been studied since the introduction of highly active antiretroviral therapy (HAART) in HIV ambulatory patients.

Methods. This is a prospective cohort study of 754 HIV patients, 18 years or older, seen at a university-based infectious disease clinic between 2000 and 2002. ARF was identified using proportional increases in serum creatinine from baseline and by chart review. Clinical conditions were assessed at the time of the ARF event. ARF incidence rates (IR) were calculated by dividing the number of events by person time at risk. To compare patients with and without ARF, *t* test or chi-square test were used.

Results. Patient's mean age was 40 years; 68% were male and 61% were black. One hundred-eleven ARF events occurred in 71 subjects (IR 5.9 per 100 person-years; 95% CI 4.9, 7.1). ARF was more common in men, in those with CD4 cell count <200 cells/mm^3, and HIV RNA levels >10,000 copies/mL. These patients more often had acquired immunodeficiency syndrome (AIDS), hepatitis C infection (HCV), and have received HAART. ARF was mainly community-acquired, due to prerenal causes or acute tubular necrosis, and associated with opportunistic infections and drugs. Liver disease was a cause of ARF in HCV-infected patients.

Conclusion. ARF is common in ambulatory HIV patients. Immunosuppression, infection, and HCV are important conditions associated with ARF in the post-HAART era.

Renal abnormalities are common among human immunodeficiency virus (HIV)-infected patients, resulting in increased morbidity and mortality [1]. One of the most common causes of renal dysfunction in HIV-infected patients is acute renal failure (ARF). ARF is often seen in patients with severe immunodeficiency and acquired immunodeficiency syndrome (AIDS)-defining clinical conditions [2–6]. Patients with advanced HIV disease require frequent hospitalizations and multiple drug treatments, which are well-established contributing factors to developing ARF. Studies of hospitalized patients undergoing renal biopsy have shown that acute tubular necrosis (ATN) and thrombotic microangiopathies are the most common findings of ARF in immunosupressed patients [3, 6]. However, since the advent of highly active antiretroviral therapy (HAART), morbidity and mortality from HIV infection has decreased substantially [7, 8] and the hospitalization rate for AIDS-defining conditions has declined [9, 10]. Consequently, comorbid chronic conditions associated with kidney dysfunction such as hypertension and diabetes, and coinfections such as hepatitis C infection (HCV) are increasingly important in the care of HIV-infected patients. HIV-infected individuals are also often exposed to a variety of potential nephrotoxic drugs for treatment of HIV, coinfections, or comorbidities. Therefore, it is expected that the risk profile of patients presenting with ARF and its causes has changed since the introduction of HAART into routine HIV clinical care.

Few studies have addressed the incidence of ARF in the post-HAART era. Studies have relied on hospitalized patients with severe ARF; on patients receiving a renal biopsy; or on cases of drug nephrotoxicity [3, 6, 11, 12]. In the general population, ARF in the ambulatory setting compromises 1% of all hospitalizations [13]. ARF in this setting is usually uncomplicated and of good prognosis [13]. The incidence and causes of ARF and its impact on clinical outcomes has not been described in ambulatory HIV-infected patients. This study aims to make these determinations among HIV-infected individuals receiving primary HIV care and participating in a large observational prospective clinical cohort study.

Key words: HIV, epidemiology, acute renal failure.

Received for publication September 10, 2004
and in revised form October 25, 2004
Accepted for publication November 9, 2004

METHODS

Study design and population

This study relied on the University of North Carolina Center for AIDS Research HIV/AIDS Research and Clinical Cohort Study (UNC CFAR Cohort Study), which has been enrolling all HIV-infected patients seen at a university-based infectious diseases clinic since January 2000. All HIV-infected patients 18 years of age or older are eligible to participate in the prospective cohort study. Written informed consent is obtained from all participants, with less than 2% of patients approached declining participation. Clinical and demographic data are collected at enrollment and prospectively every 6 months through standardized medical records abstractions. Additional clinical, laboratory, and demographic information is available through daily electronic transfer from existing institutional databases. For this study all patients seen at the clinic between January 1, 2000 and December 31, 2002 and providing written informed consent to participate in the UNC CFAR Cohort Study were included. Patients on chronic dialysis within 3 months of enrollment due to conditions unrelated to ARF were excluded. For this study, we defined baseline as the patients' first visit on or after January 1, 2000 but prior to December 31, 2002, and we followed all patients prospectively through December 31, 2002.

The study was approved by the Institutional Review Board of the University of North Carolina (UNC) School of Medicine.

Outcome measure

ARF was defined as sustained (over 2 days) increase in serum creatinine of 0.5 mg/dL for patients with baseline serum creatinine level less than 2.0 mg/dL, 1.0 mg/dL for patients with baseline level of 2.0 mg/dL to 4.9 mg/dL, and 1.5 mg/dL for patients with a baseline level equal to or greater than 5.0 mg/dL [14]. The number of episodes of ARF per patient was recorded and the events were confirmed by additional medical chart review performed by the principal investigator on this study (N.F.). Underlying clinical conditions at the time of the ARF event were reviewed in order to determine the potential causes of ARF. ARF events were categorized as prerenal, intrinsic renal, postrenal (obstructive), or unknown. Events were considered prerenal if they were (*1*) associated with diarrhea, nausea, vomiting, congestive heart failure, cirrhosis, pancreatitis, infection, hypotension, or orthostasis; and (*2*) renal function improved with hydration. ARF episodes not improving within 24 hours with hydration were defined clinically as ATN. Ischemic or nephrotoxic ATN was defined based on the clinical history and drug exposure. ARF associated with skin rash or fevers and urine or blood eosinophils in a patient taking a drug known to induce the disease was considered as being caused by interstitial nephritis. Patients with ARF and findings of thrombocytopenia and fragmented red blood cells on peripheral blood smear with or without neurologic symptoms were diagnosed with thrombotic microangiopathy [thrombotic thrombocytopenic purpura or hemolytic uremic syndrome (TTP-HUS)]. ARF due to urologic obstructions or drug induced crystalluria were considered postrenal ARF. Renal and patient survival at 30 days of the ARF event was recorded when available.

Comorbidities definitions and laboratory data

All laboratory tests were performed by the University of North Carolina Hospital Central Laboratory. CD4 cell counts, HIV RNA levels, and serum creatinine measurements were available prospectively from baseline throughout the period of observation. For baseline values we relied on the most proximal measure available within 3 months of the baseline visit. HIV RNA levels were based on the standard and ultrareverse transcriptase-polymerase chain reaction (RT-PCR) assays (Roche Amplicor HIV-1 Monitor Assay) (Roche Molecular Systems, Branchburg, NJ, USA). Hepatitis B coinfection (HBV) was based on a positive serum hepatitis B surface antigen (HBsAg) and/or hepatitis Be antigen (HBeAg). HCV status was based on the presence of positive serum hepatitis C antibody (Ortho-Clinical Diagnostic, Raritan, NJ, USA) or detectable HCV RNA. Renal function was estimated based on the Modification of Diet in Renal Disease (MDRD) modified formula [15]. Comorbidities such as chronic hypertension and diabetes mellitus were diagnosed by the attending physician and based on the medical chart reviews. AIDS-defining clinical conditions were defined using the 1993 United States Center for Disease Control and Prevention revision of case definition of AIDS [16]. HAART was defined based on published United States guidelines as (*1*) at least one protease inhibitor (PI) or one nonnucleoside reverse transcriptase inhibitor (NNRTI) in combination with two or more nucleoside/nucleotide reverse transcriptase inhibitors (NRTI); or (*2*) one NRTI in combination with at least one PI and at least one NNRTI; or (*3*) an abacavir-containing regimen of three or more NRTIs in the absence of both PIs and NNRTIs [17, 18].

Statistical analysis

For descriptive analyses, means, standard deviation, and frequencies were measured, as appropriate. Crude ARF incidence rates with 95% confidence intervals (CI) were estimated relying on a Poisson distribution by dividing the number of events by person-time at risk. To compare patients with and without ARF, we relied on *t*-tests or Pearson's chi-square test. Analyses were performed using 8.1 SAS Statistical Package (SAS Institute, Cary, NC, USA).

Table 1. Demographic and clinical characteristics of ambulatory human immunodeficiency virus (HIV)-infected patients with and without acute renal failure (ARF), 2000–2002, North Carolina

	All patients ($N = 754$)	ARF ($N = 71$)	Without ARF ($N = 683$)	P value[a]
Male *number* (%)	510 (68)	57 (80)	453 (66)	0.02
Age *years*				
17–39	376 (50)	31 (44)	345 (51)	
40–59	356 (47)	38 (54)	318 (47)	0.75
60–71	22 (3)	2 (3)	20 (3)	
Race *number* (%)				
White	255 (34)	23 (32)	232 (34)	
Black	461 (61)	44 (62)	417 (61)	1.00
Other	38 (5)	4 (6)	34 (5)	
Hypertension *number* (%)	126 (17)	9 (13)	117 (17)	0.41
Diabetes mellitus *number* (%)	47 (6)	5 (7)	42 (6)	0.79
Hepatitis B *number* (%)	46 (6)	6 (8)	40 (6)	0.44
Hepatitis C *number* (%)	160 (21)	26 (37)	134 (21)	0.004
AIDS-defining illness *number* (%)	77 (10)	23 (32)	54 (8)	<0.0001
HAART ever *number* (%)	540 (68)	62 (87)	452 (66)	<0.0001
Serum creatinine *number* (%)				
<1.2	710 (95)	69 (97)	641 (85)	
≥1.2	40 (5)	2 (3)	38 (6)	0.83
CD4 cell count (cells/mm^3) *number* (%)				
<200	214 (29)	39 (57)	175 (27)	<0.0001
≥200	515 (71)	30 (43)	485 (73)	
HIV RNA (copies/mL) *number* (%)				
<10,000	433 (62)	24 (36)	409 (64)	<0.0001
10,000–30,000	64 (9)	9 (14)	55 (9)	
>30,000	204 (29)	33 (50)	171 (27)	

Abbreviations are: AIDS, acquired immunodeficiency syndrome; HAART, highly active antiretroviral therapy.
[a] t test or Pearson's chi-square test, comparing ARF with non-ARF.

RESULTS

Of 768 patients eligible to participate in this study, 2% ($N = 14$) were excluded because they were on chronic dialysis. On average, patients were 40 years of age (SD = 9), 61% were blacks, and 32% were women (Table 1). At enrollment, 17% of patients had hypertension; 6% diabetes mellitus; 6% HBV; and 21% HCV. Serum creatinine was 1.2 mg/dL or higher at baseline (enrollment) in 5% of patients. Only 3% of patients had a glomerular filtration rate (GFR) lower than 60 mL/min/1.73 m^2 at baseline, estimated by the modified MDRD formula. At enrollment, 29% of patients had a CD4 count <200 cells/mm^3, 38% had an HIV RNA level ≥10,000 copies/mL, and 10% had prior AIDS-defining clinical condition. The most common AIDS-defining illnesses were esophageal candidiasis, *Cryptococcus* meningitis, *Pneumocystis carinii* pneumonia, and *Mycobacterium avium complex* or *Mycobacterium kanasii*-disseminated disease. Approximately 70% of the patients had received some HAART therapy.

One-hundred eleven episodes of ARF occurred among 71 subjects, with an incidence rate of 5.9 per 100 person-years (95% CI 4.9, 7.1). ARF was more common among men, patients with CD4 cell counts <200 cells/mm^3, and HIV RNA levels >10,000 copies/mL (Table 1). In addition, patients with ARF were more likely to have had an AIDS-defining clinical condition, HCV coinfection, and to have received HAART. HIV RNA level was higher among those developing ARF compared to those without ARF (mean $\log_{10}$ HIV RNA 4.2 ± 1.3 versus 3.4 ± 1.3, respectively) ($P < 0.0001$). No differences were observed between those with and without ARF by age, race, serum creatinine, HBV coinfection, history of hypertension, or diabetes mellitus. Median baseline serum creatinine was 0.8 mg/dL (interquartiles 0.7 and 0.9) for patients developing or not ARF. In addition, the majority of patients developing ARF had a serum creatinine below 1.2 mg/dL (Table 1).

Most ($N = 77$) (71%) ARF events were community-acquired and 64% of these required hospitalizations for treatment. Patients were hospitalized for a median of 4 days (range 1 to 51 days). ARF was the main cause of hospitalization in 20 of 49 cases (41%) and the only cause of admission in 15 of 49 cases (31%). The most common mechanisms of ARF were prerenal and intrinsic renal events (Table 2). Diarrhea, nausea and vomiting, liver failure, and infections were the most common causes of prerenal states. Ischemia or noncontrast drug nephrotoxicity accounted for the majority of the intrinsic renal ARF. Only two cases of TTP-HUS were identified. Obstructive ARF was mainly due to drug crystalluria from indinavir treatment.

Just over one half ($N = 58$) (52%) of all ARF events were associated with infections, and 76% of these infections were AIDS-defining clinical conditions. The most common sites of infections were central nervous system

Table 2. Etiology of acute renal failure (ARF) in ambulatory human immunodeficiency virus (HIV)-infected patients, 2000–2002, North Carolina

Causes	ARF events[a] Number (%)	% by subgroup
Prerenal	43 (38)	
Diarrhea, nausea, vomiting, dehydration	18	42
Heart failure	2	5
Cirrhosis or hepatorenal syndrome	9	21
Pancreatitis	2	5
Adrenal insufficiency	1	2
Sepsis or infection	10	23
Erythroderma	1	2
Renal	48 (46)	
Acute tubular necrosis		
Ischemic	22	46
Nephrotoxic		
Drugs	17	35
Radiocontrast	2	4
Interstitial nephritis	5	10
Thrombotic thrombocytopenic purpura-hemolytic uremic syndrome	2	4
Obstructive	9 (7)	
Kidney stones	2	22
Crystalluria	6	67
Gross hematuria	1	11
Unknown	11 (9)	

[a]Seventy-one patients with 111 episodes of ARF.

(meningitis, encephalitis) ($N = 16$), lung (pneumonia, lung abscess) ($N = 17$), bacteremia or endocarditis ($N = 9$), gastrointestinal (esophagitis, gastroenteritis, pancreatitis, cholangitis) ($N = 6$), skin (abscess) ($N = 3$), and other sites ($N = 7$). The most common pathogens were *Cryptococcus neoformans, Pneumocystis carinii, Cytomegalovirus, Herpes simplex, Mycobacterium tuberculosis, Mycobacterium avium complex, Mycobacterium kanasii,* and *Staphylococcus aureus.*

Drugs were associated with 32% ($N = 36$) of all events and caused ATN, interstitial nephritis, crystalluria with obstruction or prerenal states due to gastrointestinal symptoms leading to dehydration. The most commonly associated drugs were antibiotics, amphotericin B ($N = 14$), cotrimetoxazole ($N = 2$), aminoglycosides ($N = 2$), capreomycin ($N = 1$), oxacillin ($N = 1$) and vancomycin ($N = 1$); antiretroviral agents, indinavir ($N = 6$), tenofovir ($N = 2$) and nevirapine ($N = 1$); analgesics, nonsteroidal anti-inflammatory and cyclooxygenase-2 inhibitors ($N = 3$); radiologic contrast ($N = 2$); and lithium ($N = 1$). Crystalluria and microscopic hematuria were present in all patients with indinavir-induced ARF, and one patient had also sterile pyuria. Two patients using tenofovir developed ATN in the absence of other obvious precipitating factors for ARF. A patient taking nevirapine presented with fevers, rash, eosinophilia, and ARF which was attributed to interstitial nephritis. ARF and other symptoms resolved with the discontinuation of the drug.

Repeat episodes of ARF were more frequently observed among patients with more advanced HIV disease. Sixty-nine episodes of ARF occurred among 39 patients with CD4 cell counts <200 cells/mm^3, in comparison to 40 ARF events occurring among 30 patients with CD4 cell counts ≥200 mm^3 ($P < 0.001$). One patient without a recent CD4 cell count had two episodes of ARF. In addition, patients with low CD4 cell counts more often had ATN and were less likely to have prerenal causes of ARF compared to those with high CD4 cell counts, although the trend was not statistically significant (48% versus 35% for intrinsic ARF ($P = 0.23$) and 36% versus 45% for prerenal ARF ($P = 0.42$) contrasting patients with CD4 cell counts <200 versus ≥200 cells/mm^3, respectively). Liver failure was the underlying cause of ARF in 10% of all ARF events, and occurring predominantly among HCV coinfected patients (90%). Liver failure accounted for 18% of the ARF events in patients with HCV infection but only 2% of those without it ($P < 0.01$). None of the patients with HBV infection experienced ARF.

Five patients required dialysis: two patients with TTP-HUS, one with lithium overdose and ARF, one with hepatorenal syndrome, and one with ischemic ATN due to sepsis. Only the patient with lithium toxicity recovered renal function. All other patients not requiring dialysis recovered renal function to baseline levels. The median peak serum creatinine was 4.6 mg/dL (range 2.6 to 5.7) for patients requiring dialysis and 2.1 mg/dL (range 1.1 to 7.3) for those not requiring dialysis ($P < 0.001$). For patients not requiring dialysis, the median highest serum creatinine was 2.0 mg/dL (range 1.1 to 7.3) and 2.3 mg/dL (range 1.1 to 7.1) for those developing ARF in the outpatient setting and those in the hospital, respectively.

Two patients had a renal biopsy. One patient presented with renal dysfunction, sterile pyuria, microscopic hematuria, and indinavir crystalluria. Renal biopsy showed indinavir-induced crystal intratubular obstruction. A patient with sepsis had renal biopsy findings of ATN. Both patients recovered renal function to baseline levels. Three patients requiring dialysis died within 30 days of the ARF event, without recovering renal function. One patient died due to complication related to TTP-HUS, one due to sepsis, and one due to hepatorenal syndrome.

DISCUSSION

In this large prospective cohort of ambulatory HIV-infected patients receiving primary HIV care, we observed a high incidence rate of ARF events. ARF occurred more often in men, HCV coinfected patients, and individuals with more advanced HIV disease, including patients with lower CD4 cell counts, higher HIV RNA levels, and a prior AIDS-defining clinical condition. In addition, patients with ARF were more likely to have received HAART, likely related to their more advanced

HIV disease. Race was not associated with increased incidence rate of ARF, in contrast to chronic kidney disease which has been mainly described in African Americans [19].

Infections have been considered a major cause of severe ARF in studies of HIV-infected patients [1, 3]. Among a sample of patients with advanced HIV disease progression, Rao and Friedman [3] observed half of the patients presenting with ARF received a diagnosis of sepsis. Similarly, in our study, 52% of the ARF events were associated with an infection, the majority of which were AIDS-defining clinical conditions. In addition, drug nephrotoxicity frequently resulted from the treatment of chronic fungal and bacterial infections in immunocompromized patients. However, our study differed from prior studies by including mainly ambulatory patients, the majority of whom had not had a prior AIDS-defining clinical condition. Therefore, our results reveal that infectious diseases and particularly opportunistic infections are still a common underlying cause of ARF in HIV-infected patients in the post-HAART era.

HCV is increasingly an important cause of morbidity and mortality among HIV-infected patients [20–22]. A recent study has shown an increase in the hospitalization rates due to liver disease among HIV-infected women [9], exceeding the rates of hospitalization due to AIDS-defining conditions. ARF is a well-recognized complication of cirrhosis and liver failure in the general population [13, 14]. Decreased renal perfusion due to aggressive use of diuretics, ATN due to infections or use of nephrotoxic antibiotics, as well as hepatorenal syndrome are some of the mechanisms leading to ARF in these patients. HCV coinfection occurs in 15% to 30% of all HIV-infected patients in the United States [23]. Despite the high prevalence of HIV-HCV coinfection [23], liver disease has not been considered an important cause of ARF in prior studies of HIV-infected patients [24]. In our study, ARF due to cirrhosis and liver failure accounted for approximately 20% of the cases of ARF among HIV-HCV coinfected patients.

Drugs caused one third of all ARF events. Antiretroviral drugs were responsible for only few events but compromised two thirds of all cases of obstructive ARF. Indinavir, tenofovir, and nevirapine were the only antiretroviral drugs clearly associated with ARF in this cohort. Indinavir treatment has been associated with crystalluria, nephrolithiasis, interstitial nephritis, and sterile leukocyturia with renal dysfunction [25–28]. In our study, all cases of indinavir-associated ARF were due to crystalluria and were obstructive in nature. Tenofovir, a nucleotide reverse transcriptase inhibitor, was associated with ATN in two patients. Several recent studies have described renal proximal tubular toxicity in patients taking tenofovir. The most common presentation is Fanconi syndrome [29] but cases of ARF due to ATN have been also described [30, 31]. A patient receiving nevirapine had ARF due to allergic interstitial nephritis. His symptoms and the ARF resolved with discontinuation of the drug. Cutaneous allergic reaction is the most common adverse event with nevirapine but kidney dysfunction has not been frequently reported [32]. A recent study has reported rash, fevers, eosinophilia, liver abnormalities, and kidney dysfunction in a pregnant HIV-infected women using nevirapine, findings similar to our patient's presentation [33]. In summary, ARF due to antiretroviral therapy was usually reversible, uncomplicated, and in case of indinavir an important cause of obstruction.

Two patients developed TTP-HUS in our study. Thrombotic microangiopathies are unusual causes of ARF in the general population. Several studies have described occurrence of TTP-HUS in hospitalized HIV-infected patients, or those undergoing a renal biopsy [6, 34]. In one study, among patients with advanced HIV disease progression presenting with acute or rapidly progressive renal failure, TTP-HUS compromised 35% of the ARF events, most of which were confirmed by a renal biopsy [6]. In a study of renal biopsies, two of 17 HIV patients had TTP-HUS in postmortem diagnosis, both with very advanced immunosuppression [34]. Other large studies of ARF, including patients without HIV infection, have described few or no cases of TTP-HUS [3, 14]. In our study, one patient presenting with TTP-HUS had a low CD4 cell count but another had a normal CD4 cell count and no prior history of an AIDS-defining clinical condition. Both patients required dialysis and did not recover renal function, and one died. Prior studies of TTP-HUS have also described high morbidity and mortality of the disease in HIV-infected patients [1].

We relied on the definition of ARF developed by Nash, Hafeez, and Hou [14] in order to identify mild to severe cases of ARF in a large cohort of ambulatory patients. Therefore, it is possible that we missed some cases of ARF with lower increases in serum creatinine, although the clinical relevance of such mild ARF is unclear. In addition, ARF due to rapid progressive glomerulonephritis was not included in this analysis. All cases had their medical charts reviewed by a trained nephrologist (N.F.) to confirm the diagnosis and identify the etiology of the ARF episode. However, we cannot rule out some misclassification as this study was limited by a reliance on available clinical data.

This is the first study to determine the incidence of mild to severe ARF in a large cohort of HIV-infected ambulatory patients in the HAART era. Including patients at all stages of HIV disease progression allowed us to identify new risk factors for ARF occurring in the era of potent antiretroviral therapy use. As expected, prevalent comorbidities such as chronic liver disease due to HCV are emerging causes of kidney dysfunction, including ARF, among HIV-infected patients.

CONCLUSION

ARF is a common condition in HIV-infected patients receiving primary outpatient HIV care. Immunosuppression and infections remain important underlying conditions causing ARF among HIV-infected patients, with liver disease being the leading cause of ARF among patients with HIV-HCV coinfection.

ACKNOWLEDGMENTS

This study was supported in part by a grant of the National Kidney Foundation of North Carolina, by the UNC Center for AIDS Research AI50410 and by the UNC General Clinical Research Center R000046.

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REFERENCES

1. Rao TK: Human immunodeficiency virus infection and renal failure. *Infect Dis Clin North Am* 15:833–850, 2001
2. Rao TK, Friedman EA, Nicastri AD: The types of renal disease in the acquired immunodeficiency syndrome. *N Engl J Med* 316:1062–1068, 1987
3. Rao TK, Friedman EA: Outcome of severe acute renal failure in patients with acquired immunodeficiency syndrome. *Am J Kidney Dis* 25:390–398, 1995
4. Bourgoignie JJ, Meneses R, Ortiz C, *et al*: The clinical spectrum of renal disease associated with human immunodeficiency virus. *Am J Kidney Dis* 12:131–137, 1988
5. Valeri A, Neusy AJ: Acute and chronic renal disease in hospitalized AIDS patients. *Clin Nephrol* 35:110–118, 1991
6. Peraldi MN, Maslo C, Akposso K, *et al*: Acute renal failure in the course of HIV infection: A single-institution retrospective study of ninety-two patients and sixty renal biopsies. *Nephrol Dial Transplant* 14:1578–1585, 1999
7. Hogg RS, Yip B, Chan KJ, *et al*: Rates of disease progression by baseline CD4 cell count and viral load after initiating triple-drug therapy. *JAMA* 286:2568–2577, 2001
8. Palella FJ, Jr., Delaney KM, Moorman AC, *et al*: Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med* 338:853–860, 1998
9. Gardner LI, Klein RS, Szczech LA, *et al*: Rates and risk factors for condition-specific hospitalizations in HIV-infected and uninfected women. *J Acquir Immune Defic Syndr* 34:320–330, 2003
10. Torres RA, Barr M: Impact of combination therapy for HIV infection on inpatient census. *N Engl J Med* 336:1531–1532, 1997
11. Reilly RF, Tray K, Perazella MA: Indinavir nephropathy revisited: A pattern of insidious renal failure with identifiable risk factors. *Am J Kidney Dis* 38:E23, 2001
12. Kopp JB: Renal dysfunction in HIV-1-infected patients. *Curr Infect Dis Rep* 4:449–460, 2002
13. Kaufman J, Dhakal M, Patel B, Hamburger R: Community-acquired acute renal failure. *Am J Kidney Dis* 17:191–198, 1991
14. Nash K, Hafeez A, Hou S: Hospital-acquired renal insufficiency. *Am J Kidney Dis* 39:930–936, 2002
15. Levey AS, Coresh J, Balk E, *et al*: National Kidney Foundation practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Ann Intern Med* 139:137–147, 2003
16. Centers for Disease Control and Prevention: 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR Recomm Rep* 41:1–19, 1992
17. US Public Health Service: *Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents 2003*, available at *http://www.aidsinfo.nih.gov/guidelines/adult/AA_032304.pdf*. Last accessed 02/2005
18. Yeni PG, Hammer SM, Carpenter CC, *et al*: Antiretroviral treatment for adult HIV infection in 2002: Updated recommendations of the International AIDS Society-USA Panel. *JAMA* 288:222–235, 2002
19. Kopp JB, Winkler C: HIV-associated nephropathy in African Americans. *Kidney Int* 63(Suppl 83):S43–S49, 2003
20. Bica I, McGovern B, Dhar R, *et al*: Increasing mortality due to end-stage liver disease in patients with human immunodeficiency virus infection. *Clin Infect Dis* 32:492–497, 2001
21. Klein MB, Lalonde RG, Suissa S: The impact of hepatitis C virus coinfection on HIV progression before and after highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* 33:365–372, 2003
22. Gebo KA, Diener-West M, Moore RD: Hospitalization rates differ by hepatitis C satus in an urban HIV cohort. *J Acquir Immune Defic Syndr* 34:165–173, 2003
23. Sherman KE, Rouster SD, Chung RT, Rajicic N: Hepatitis C virus prevalence among patients infected with human immunodeficiency virus: A cross-sectional analysis of the US adult AIDS Clinical Trials Group. *Clin Infect Dis* 34:831–837, 2002
24. Rao TK: Acute renal failure syndromes in human immunodeficiency virus infection. *Semin Nephrol* 18:378–395, 1998
25. Kopp JB, Miller KD, Mican JA, *et al*: Crystalluria and urinary tract abnormalities associated with indinavir. *Ann Intern Med* 127:119–125, 1997
26. Kopp JB, Falloon J, Filie A, *et al*: Indinavir-associated interstitial nephritis and urothelial inflammation: clinical and cytologic findings. *Clin Infect Dis* 34:1122–1128, 2002
27. Dieleman JP, Sturkenboom MC, Jambroes M, *et al*: Risk factors for urological symptoms in a cohort of users of the HIV protease inhibitor indinavir sulfate: The ATHENA cohort. *Arch Intern Med* 162:1493–1501, 2002
28. Dieleman JP, van Rossum AM, Stricker BC, *et al*: Persistent leukocyturia and loss of renal function in a prospectively monitored cohort of HIV-infected patients treated with indinavir. *J Acquir Immune Defic Syndr* 32:135–142, 2003
29. Verhelst D, Monge M, Meynard JL, *et al*: Fanconi syndrome and renal failure induced by tenofovir: a first case report. *Am J Kidney Dis* 40:1331–1333, 2002
30. Schaaf B, Aries SP, Kramme E, *et al*: Acute renal failure associated with tenofovir treatment in a patient with acquired immunodeficiency syndrome. *Clin Infect Dis* 37:e41–e43, 2003
31. Lee JC, Marosok RD: Acute tubular necrosis in a patient receiving tenofovir. *Aids* 17:2543–2544, 2003
32. de Maat MM, ter Heine R, Mulder JW, *et al*: Incidence and risk factors for nevirapine-associated rash. *Eur J Clin Pharmacol* 59:457–462, 2003
33. Knudtson E, Para M, Boswell H, Fan-Havard P: Drug rash with eosinophilia and systemic symptoms syndrome and renal toxicity with a nevirapine-containing regimen in a pregnant patient with human immunodeficiency virus. *Obstet Gynecol* 101:1094–1097, 2003
34. Williams DI, Williams DJ, Williams IG, *et al*: Presentation, pathology, and outcome of HIV associated renal disease in a specialist centre for HIV/AIDS. *Sex Transm Infect* 74:179–184, 1998