Epidemiology of Acute Kidney Injury in Africa

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Summary: Acute kidney injury (AKI) is a challenging problem in Africa because of the burden of disease (especially human immunodeficiency virus [HIV]-related AKI in sub-Saharan Africa, diarrheal disease, malaria, and nephrotoxins), late presentation of patients to health care facilities, and the lack of resources to support patients with established AKI in many countries. The pattern of AKI is vastly different from that in more developed countries. There are no reliable statistics about the incidence of AKI in Africa. Infections (malaria, HIV, diarrheal diseases, and others), nephrotoxins, and obstetric and surgical complications are the major etiologies in Africa. AKI in hospitalized antiretroviral therapy (ART)-naive HIV-1–infected patients is associated with a 6-fold higher risk of in-hospital mortality. The most common risk factors are severe immunosuppression (CD4 count, <200 cells/mm^3) and opportunistic infection. The most common causes are acute tubular necrosis and thrombotic microangiopathy. In the post-ART era, HIV-1–infected patients with AKI still have an increased risk of in-hospital mortality and these episodes of AKI seem more frequent in the first year of ART. Subsequently, survival is comparable in those with and without HIV infection. More resources are required to prevent AKI and to provide renal support for those patients requiring dialytic therapy.

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Acute kidney injury (AKI) is a challenging problem in Africa—a diverse continent with regards to population and financial and medical resources. There are no reliable statistics about the incidence of AKI in Africa. Based on sporadic regional publications the incidence has been estimated at 150 per million population.[1] In addition to infectious diseases; toxins play a major etiologic role in AKI.

MAJOR CAUSES OF AKI BY REGION

The major causes of AKI in Africa were obtained from a survey of colleagues in nephrology practice in different regions in Africa and are presented in Table 1. Infections (malaria, human immunodeficiency virus [HIV], diarrheal diseases, and others), nephrotoxins, and obstetric and surgical complications were reported as the major etiologies in all regions.

AKI IN SPECIFIC COUNTRIES

South Africa

Seedat[2] reported in 1978 that medical causes were the dominant cause of AKI, occurring in 65% of patients in Durban, followed by gynecologic (17%), surgical (10%), and obstetric (7.3%) causes, with an overall mortality rate of 35%. The most common causes were nephrotoxins, mainly herbal remedies. A subsequent study

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Table 1. Major Causes of AKI by Region

Country	Causes of AKI
North Africa	
Algeria	Toxins, trauma/surgery, urologic
Egypt	Surgical, toxins, obstructive
Morocco	Hemodynamic, sepsis, obstructive
West Africa	
Cameroon	Malaria, obstetric, toxins
Cote d'Ivoire	Malaria, HIV, toxins
Nigeria	Sepsis, obstetric, toxins
Senegal	Obstetric, malaria, herbal toxins
Democratic Republic of Congo	Infections (especially malaria), hypovolemia, toxins
East Africa	
Kenya	Infection, obstetric, surgical
Burundi	Malaria, dehydration (HIV, diarrhea)
Rwanda	Infections, trauma, toxins
Ethiopia	Malaria, surgical, acute glomerulonephritis
Eritrea	Infection
Sudan	Infection, toxins
Southern Africa	
South Africa	Infections (including HIV), toxins, pregnancy
Mozambique	Malaria, dehydration, HIV
Zimbabwe	Prerenal (HIV), malaria, obstetric
Zambia	Malaria, obstetric
Malawi	Diarrheal diseases, malaria, sepsis

(1986-1988) from the same region reported that sepsis replaced nephrotoxins as the predominant cause of AKI.[3] A recent survey of patients presenting to the acute renal service at Johannesburg hospital over a 1-year period from November 2005 to October 2006 showed that 122 of 700 patients (17.4%) were HIV positive, with a mean age of 37 years: 80% were medical, 6% were surgical, 4% were obstetric and gynecologic, and 10% were in the intensive care unit (ICU). The mean CD4 was 134 cells/mm^3 and there were less than 50 cells/mm^3 in 42% of patients. Mortality occurred in 25 of 122 (20%) of the HIV-positive patients (Vachiat et al; unpublished data).

Sudan

AKI is a common health problem in Sudan owing to the widespread prevalence of infectious diseases, the use of traditional remedies, and certain social habits. Kaballo et al[4] studied 89 patients who were referred with AKI over a period of 1 year to the renal unit of a tertiary hospital in Khartoum. Patients with surgical conditions were excluded from the study. Sixty-four percent were males and 36% were females. Acute tubular necrosis was diagnosed in 50 patients (56.1%) and was caused by infections, mainly malaria and typhoid fever (28 patients); acute hair dye poisoning (12 patients); drug nephrotoxicity (5 patients); and snake bites (5 patients). Other causes of AKI were obstructive uropathy mainly caused by urinary calculi in 12% of patients, and acute glomerulonephritis in 9%. In 19% of the patients the etiology of AKI was unknown. The AKI caused by hair dyes is attributed to paraphenylene-diamine (PPD), a component in some of those cosmetics. In addition to its nephrotoxicity, it causes other manifestations that are discussed later. The toxic injury was caused by ingestion of the hair dyes in suicide attempts. The patients who required dialysis usually were treated initially with acute peritoneal dialysis. Those who re-

quired prolonged dialysis were shifted to hemodialysis, which is available in the main cities. Fifty-nine percent of the patients had complete recovery, 7% progressed to chronic kidney disease, 18% died, and 16% were lost to follow-up evaluation.

Morocco

There is a lack of epidemiologic studies to estimate the importance of AKI in Morocco, but some hospital reports indicate that it is a common health problem. In these hospital series, the pattern of AKI was dominated by late referral and severity of clinical symptoms (mean blood urea nitrogen level, 41 mmol/L; mean serum creatinine level, 905 μmol/L).[5,6] Acute tubular necrosis represents the majority of cases (44%), mainly of infectious (sepsis and leptospirosis) and toxic origin (rhabdomyolysis), followed by glomerulonephritis (20%) and obstructive causes (12%). In rare cases, it was reported to be caused by an imported form of malarial AKI.[7] The obstructive etiologies are dominated by lithiasis in 68% and cancers in 25% of cases.[8] Prerenal AKI in these hospital series represents only 11%. Renal biopsy was rarely needed for an etiologic diagnosis and was performed in about 13% of the patients disclosing as AKI cause glomerulonephritis, vasculitis, and interstitial nephritis.[9] In this hospital series, dialysis was performed frequently, in about 80% of the patients. Peritoneal dialysis usually was used in children and hemodialysis was used in the majority of adults. The mortality rate was about 30%, and total recovery of renal function occurred in 57%.

AKI IN SPECIFIC CONDITIONS

AKI in HIV Infection

AKI is a common complication in ambulatory HIV-infected patients treated with highly active antiretroviral therapy, with an odds ratio of 2.82.[10] Patients hospitalized with complications of HIV may be at increased risk of AKI related to volume depletion, hemodynamic stress, infections, and administration of nephrotoxic medication or radiocontrast. HIV-related renal disease can present as AKI or chronic kidney disease (CKD). AKI in hospitalized (antiretroviral therapy) ART-naive HIV-1–infected patients is associated with a 6-fold higher risk of in-hospital mortality.[10] The most common risk factors are severe levels of immunosuppression (CD4 count, <200 cells/mm^3) and opportunistic infection. The most common causes are acute tubular necrosis and thrombotic microangiopathy. In the post-ART era, HIV-1–infected patients with AKI still have an increased risk of in-hospital mortality and these episodes of AKI seem more frequent in the first year of ART. In this group, AKI has been associated with infection, antibiotics, and antifungal agents, and risk factors are low CD4 count, co-infection with hepatitis C, acute or chronic liver injury, diabetes mellitus, and underlying CKD. Kidney injury related to ART occurs in less than 10% of patients. Data on AKI with HIV infection in developing countries are scarce.

In our experience in South Africa, hospitalized patients are at advanced stages of immunosuppression and many causes of AKI are in fact prerenal, implying that with aggressive and appropriate management the AKI is potentially reversible, even if there is an underlying chronic component. This concept is critical for those managing patients in circumstances where there is limited/no access to intensive or high levels of care and/or acute dialysis (unpublished data). Glomerular disease in HIV also can present as AKI. Glomerular diseases may be unrelated to HIV (lupus nephritis, poststreptococcal glomerulonephritis) or may be the underlying condition on which an additional acute insult has precipitated a decline in kidney function. Herbal toxin ingestion, sepsis, or severe gastroenteritis with dehydration commonly results in AKI in our setting. In addition to managing the acute component, clinicians also must be aware that CKD does co-exist, which places patients at additional risk and needs to be managed.

AKI and Toxins

Among the nephrotoxic agents encountered in some African countries, especially in East Africa and Maghreb, are some hair dye preparations that contain PPD. Some of those hair dyes are added to henna, which is a traditional cosmetic agent applied to the upper and lower limbs, to

increase its skin-staining effect. PPD can be absorbed from the skin but more severe intoxication is produced by ingestion of the hair dyes, mostly in suicide attempts. In 1983 a case of a patient with hair dye poisoning who developed AKI was reported.[11] Renal biopsy showed acute tubular necrosis. In 1992, PPD poisoning was reported in 31 Sudanese children, 5 of whom developed AKI and required peritoneal dialysis but made a full recovery.[12] In addition to acute tubular necrosis, AKI can be caused by rhabdomyolysis and hemoglobinuria, which occurs with PPD poisoning. In 2006, Motaouakkil et al[13] reported a cohort study of 315 cases over 6 years. The mean age was 23 ± 9 years, with a clear female predominance (sex ratio = 9.86). The intoxication was owing to suicide attempts in 93.3% of the patients. Mortality usually is caused by other manifestations of the poisoning, namely angioedema, which occurs early, and arrhythmias caused by direct cardiotoxicity of the chemical.[14] There is no known antidote. Accordingly, it is recommended to start dialysis early to remove the toxin. PPD poisoning continues to represent a major cause of toxic rhabdomyolysis in Morocco and is responsible for its high mortality rate (47%) despite standard clinical management in the ICU.[13]

Plant toxins may cause AKI when they are used as traditional medicines. Common nephrotoxic plants include Impila (*Callilepis laureola*), found in South Africa, Democratic Republic of Congo, Zimbabwe, and Zambia.[15,16] Other identified plant toxins are fava beans, poisonous mushrooms, and *Euphorbia matabalensis*. Nephrotoxicity can occur because of direct renal injury with acute tubular necrosis and acute interstitial nephritis or by indirect mechanisms such as intravascular hemolysis and dehydration as a result of diarrhea.

Animal toxins are an important cause of AKI in Africa. Snake bites cause AKI secondary to systemic manifestations including intravascular hemolysis, hypotension, blood hyperviscosity, myoglobinuria, and hemorrhage. Various renal lesions may be produced as a result of snake bites including acute tubular necrosis, cortical necrosis, acute interstitial nephritis, and diffuse proliferative glomerulonephritis. Scorpion stings cause AKI in some patients owing to disseminated intravascular coagulation and hemorrhage.

Pregnancy-Related AKI

Obstetric AKI has become a rare complication during pregnancy in industrialized countries, although it continues to be a frequent clinical problem in African countries such as Morocco, mainly secondary to pre-eclampsia and eclampsia (74.5%), to septic conditions (11%), and to obstetric hemorrhage (7.2%) as reported by Hachim et al.[17] Dialysis was required for this clinical condition in 74.5% of patients.

During a prospective study of 178 consecutive women with eclampsia, Mjahed et al[18] found that the incidence of AKI (serum creatinine concentration, >140 μmol/L) was 25.8%. Dialysis was needed in a third of patients and AKI was associated with a higher mortality rate (32.6% versus 9.1%). Pregnancy-related disorders were responsible for 16% of all AKIs requiring dialysis from 1990 to 1992 in South Africa, with pre-eclampsia–eclampsia, septic abortion, and herbal toxins being the major causes. The maternal mortality rate was reported to be 5% in this study.[19]

AKI in the ICU

Meyers et al[20] reported on risk factors and mortality rates in patients requiring dialysis for AKI in Johannesburg in 3 cohorts: 1968 to 1972 (110 patients), 1975 to 1984 (520 patients), and 1998 to 1999 (335 patients). The incidence of AKI was calculated as 48 per million population per year. The mortality rate was 32% in medical patients, 84% in surgical patients, and 36% in obstetric patients, with a mortality rate of 75% in septic abortions. The overall mortality rate in ICU patients was 73% compared with 27% in non-ICU patients. Ezekiel et al[21] reported on outcomes of 174 patients dialyzed for AKI in the ICU in Johannesburg from January 2003 to December 2004. Fifty-three percent of patients using continuous veno-venous hemodialysis died, compared with 38% treated with intermittent hemodialysis, a reflection of more severe illness in the former group.[21] ICU survival rates were similar in those with and without HIV-related disease.[22]

THERAPY FOR AKI

As with many conditions in nephrology, AKI may be preventable in many instances. Education regarding avoidance of nephrotoxins, prompt treatment of infections, and fluid replacement are important facets of therapy. This is vital because many countries in Africa are not able to provide renal replacement therapy. The majority of patients who are supported with dialysis receive hemodialysis, with acute peritoneal dialysis provided in a few countries, especially for pediatric patients. Continuous renal replacement therapies and slow efficiency dialysis are provided for ICU patients who are hemodynamically unstable.

CONCLUSIONS

AKI is a challenging problem in Africa because of the burden of disease (especially HIV-related AKI in sub-Saharan Africa, diarrheal disease, malaria, and nephrotoxins), late presentation of patients to health care facilities, and the lack of resources to support patients with established AKI in many countries. The pattern of AKI is vastly different from that in more industrialized countries. More resources are required to prevent AKI and to provide renal support for those patients requiring dialytic therapy.

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