Community-acquired acute kidney injury in tropical countries

Vivekanand Jha and Sreejith Parameswaran

Abstract | Community-acquired acute kidney injury (AKI) in developing tropical countries is markedly different from AKI in developed countries with a temperate climate, which exemplifies the influence that environment can have on the epidemiology of human diseases. The aetiology and presentation of AKI reflect the ethnicity, socioeconomic factors, climatic and ecological characteristics in tropical countries. Tropical zones are characterized by high year-round temperatures and the absence of frost, which supports the propagation of infections that can cause AKI, including malaria, leptospirosis, HIV and diarrhoeal diseases. Other major causes of AKI in tropical countries are envenomation; ingestion of toxic herbs or chemicals; poisoning; and obstetric complications. These factors are associated with low levels of income, poor access to treatment, and social or cultural practices (such as the use of traditional herbal medicines and treatments) that contribute to poor outcomes of patients with AKI. Most causes of AKI in developing tropical countries are preventable, but strategies to improve the outcomes and reduce the burden of tropical AKI require both improvements in basic public health, achieved through effective interventions, and increased access to effective medical care (especially for patients with established AKI).

Jha, V. & Parameswaran, S. *Nat. Rev. Nephrol.* **9**, 278–290 (2013); published online 5 March 2013; doi:10.1038/nrneph.2013.36

Introduction

The tropics can be defined in two ways: either geographically or ecologically. Geographically, the latitudes on either side of the equator where the sun is directly overhead at least once during the solar year (approximately 23° north–23° south) is defined as the tropical zone. In ecological or climatic terms, the tropics are characterized by the presence of high year-round temperatures and the absence of frost. Precipitation rates range from high rainfall throughout the year in tropical rainforests to very low rainfall in the arid deserts of Africa and the Middle East. Approximately 40% of the world population lives in the tropics; by 2060, the high birth rate in these regions is expected to increase this proportion to 60%.[1]

Countries in the tropics also differ from those in temperate climates in economic terms. Countries in temperate climates comprise approximately 8% of the world's inhabited land mass and 22% of the world's population, yet account for 52% of the world's gross national product (Figure 1).[2] Moreover, of the 30 economies classified as high income by the World Bank, only two small regions (Singapore and Hong Kong) are in the tropical region.[2] To a large extent, climate and ecology are thought to explain this economic difference.[3,4]

The disease burden in developing tropical countries is heavily influenced by local climatic and economic conditions. Thus, the spectrum of acute kidney injury (AKI) in developing tropical countries is fundamentally different to that described in affluent countries with temperate climates: in developed, temperate countries, where the disease burden is dominated by lifestyle-related chronic diseases and degenerative disorders in the elderly, AKI usually occurs as part of multiple organ involvement in an already hospitalized, elderly patient or after surgical or diagnostic interventions, and iatrogenic factors have an important role.[5] Hospital-acquired AKI is a serious medical problem in this population, as even apparently minor acute worsening of renal function contributes to increased mortality and morbidity.[6] By contrast, previously healthy, relatively young individuals (typically aged 37–47 years) who have developed AKI as a result of factors encountered in their environment dominate the tropical AKI population.[7,8] These patients usually present to hospitals with already reduced urine output and/or glomerular filtration rate (GFR).[9,10] Such patients are said to have community-acquired AKI.[11] Moreover, in contrast to the multifactorial origin of hospital-acquired AKI in temperate, developed countries, the aetiology of tropical, community-acquired AKI can usually be traced to a single cause, typically an infection, exposure to an environmental toxin, envenomation by snakes or insects, or complications of out-of-hospital childbirth.[9,10]

In this Review, we discuss the aetiology and pathogenesis of community-acquired AKI in tropical countries. We also describe factors that influence the availability and efficacy of treatment, and discuss how the burden of AKI in developing tropical countries might be decreased.

Postgraduate Institute of Medical Education and Research, Sector-12, Chandigarh 160 012, India (**V. Jha**). Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry 605 006, India (**S. Parameswaran**).

Correspondence to: V. Jha vjha@pginephro.org

Competing interests
The authors declare no competing interests.

Tropical ecology—a driver of disease

Environmental factors

Patients in the tropics continue to confront diseases that are secondary to public-health problems, such as poor sanitation, unsafe drinking water, a lack of infection control and out-of-hospital childbirth.[12]

Water quality has a major role in the ecosystem of disease in the tropics. Tropical soil is fragile; high temperatures and heavy precipitation leach minerals and organic compounds, which enter flowing water,[13] leading to waterlogging and contamination of grain fields. The end result is a high prevalence of water-borne diseases, many of which are associated with AKI. In most patients who develop infection-associated AKI in the tropics, the source of disease is closely linked to contact with contaminated water. The spread of diseases by direct transmission, such as in aerosols is also more likely in the tropics because of overcrowding and poor living conditions.

Tropical ecosystems also favour the proliferation of vermin and parasites. High temperatures, wet weather and high salinity favour the persistence of infection in animal reservoirs, intermediate hosts and vectors of parasitic diseases, as well as promote the survival of pathogenic microorganisms outside the human host, thereby increasing the population of vectors and transmission of water-borne disease.[14–16] The tropical climate also affects the incidence of snake bites. Flooding of snake burrows in the rainy (monsoon) season forces their inhabitants to come to the surface at times when large numbers of workers are in the fields for planting or harvesting crops, leading to a spike in the number of bite victims. Seasonal variation in snake envenomation is seen throughout the tropics.[17,18]

Socioeconomic factors

Individuals living in poverty are exposed to greater personal and environmental health risks, are less well nourished, have less information and are less able to access healthcare than are affluent individuals. Populations in the tropics are characterized by greater heterogeneity than in temperate climates in terms of socioeconomic status, lifestyle, level of education and access to goods, services and medical care. People living in affluent areas in these countries are less exposed to the environmental risks than those in poor rural areas, but are not completely protected. Moreover, almost all cities in tropical countries contain large slum areas and shanty towns where basic amenities are as limited as those in rural areas, making their disease patterns almost indistinguishable. Poverty and the lack of appropriate regulations also increase the risk of an encounter with industrial toxins that can cause AKI.[8]

The combined effect of a high disease burden and poor economic performance is reflected in the lower life expectancy, higher infant mortality and maternal mortality rates throughout the tropics compared with developed countries. Even after correction for the level of income, the infant mortality rate in the tropical zone is 52% higher and the life expectancy 8% lower than in temperate zones.[2] Tropical regions are often characterized by high fertility and high mortality,[2] which result in a high proportion of children in the population, but at the cost of fewer resources per child, limited opportunities for primary and higher education, and a lack of access to primary health care. Conversely, illness reduces productivity and household savings, decreases learning ability, and leads to a diminished quality of life, thereby perpetuating or even increasing poverty.[19] The developing tropical countries consequently lag behind those of the temperate zone in terms of scientific and technological innovation.[20]

Health-care systems in parts of the tropics are not well developed and specialized care is scarce or distributed unevenly. For cultural reasons, access to health care can be disproportionately restricted in certain sectors of society, for example women and children. Limited access to health care, suspicion of modern medical systems, high health-care costs, and spiritual and cultural beliefs result in continued reliance on traditional medical systems.

Key points

- Pests, animals and insects thrive in tropical countries owing to poor sanitation and climatic conditions, which result in unique forms of community-acquired acute kidney injury (AKI)
- Accurate data on the epidemiology of AKI in developing tropical countries are lacking; however, tropical AKI typically affects individuals aged 37–47 years and has a single aetiology
- AKI resulting from infectious diseases, obstetric complications and ingestion of chemical and plant toxins is more prevalent in developing countries than in developed countries
- Other challenges, such as the HIV epidemic, contribute to the burden of AKI in developing countries
- Limited access to medical care and a lack of infrastructure contribute to poor outcomes of community-acquired tropical AKI; addressing these factors could substantially improve or alleviate the burden of disease

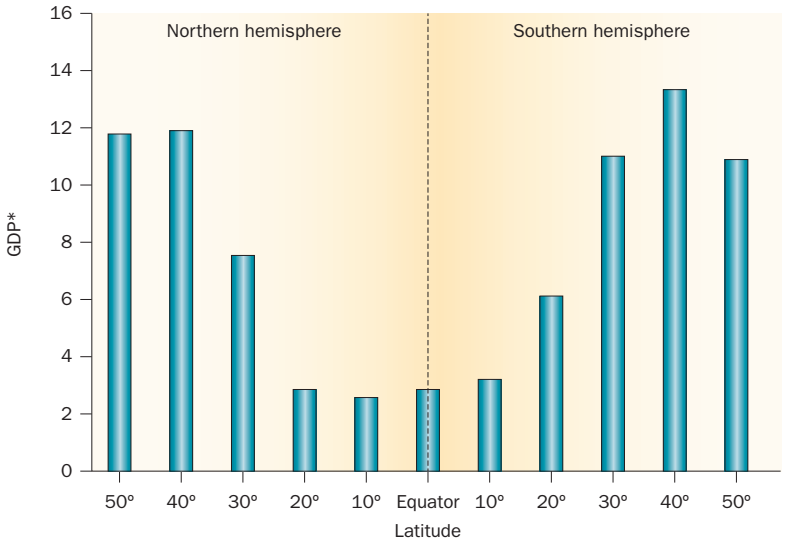

Figure 1 | Global GDP per capita by latitude. National GDP per capita is consistently lower in countries in tropical latitudes than in those in higher latitudes, in both the northern and southern hemispheres. Tropical countries with low GDP show consistently high prevalence of community-acquired acute kidney injury. *GDP values are given in 1990 US dollars adjusted by 1995 purchasing power parity. Abbreviation: GDP, gross domestic product. From "Tropical Underdevelopment" © 2001 by Jeffrey D. Sachs, used by permission of The Wiley Agency LLC.[2]

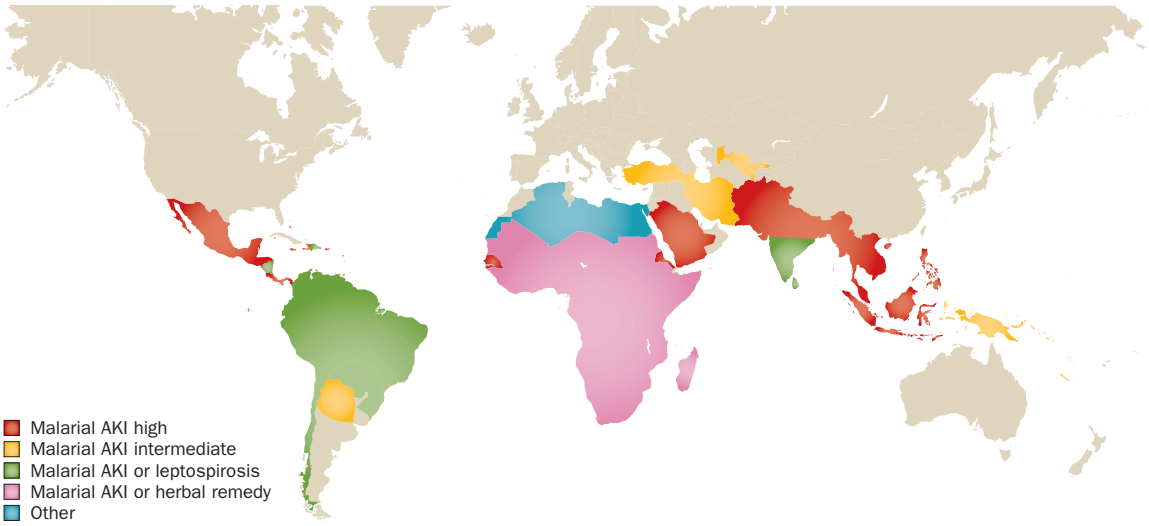

Figure 2 | Prevalence estimates of community-acquired AKI. Malaria-associated AKI has a high-to-intermediate prevalence in the tropical zones of Southeast Asia and Central America. AKI caused by malaria or leptospirosis has a similar prevalence in South America and India. Countries of Sub-Saharan Africa have a high prevalence of malarial and herbal-remedy-induced AKI. AKI as a result of other causes, such as diarrhoea, toxins or obstetric complications has a low prevalence in North Africa. Abbreviation: AKI, acute kidney injury.

The use of potentially harmful indigenous tropical remedies contributes to the development or exacerbation of AKI.[21,22] The reliance on nontraditional medical care also contributes to delayed presentation of these individuals to a hospital or treatment centre, which often results in life-threatening complications in those with already established AKI. Economic considerations can also prevent the implementation of technological solutions that might be feasible in more affluent countries; for example, technologically advanced and expensive treatments, such as continuous renal replacement therapy, are eschewed in favour of cheaper and less complex peritoneal dialysis, in developing tropical countries.[23]

Epidemiology of AKI in the tropics

Few studies have been published on the epidemiology of AKI in tropical countries.[24] Most published data are from single-centre studies conducted in urban areas and might not reflect the true prevalence of AKI, especially in rural areas;[25] many rural patients who develop AKI do not reach urban hospitals. Furthermore, the available studies have used different denominators to calculate the incidence of AKI, making comparisons difficult.[5,26–30] Thus, the reported incidence of AKI in tropical countries ranges from 0.31 cases per thousand hospital discharges[30] to 7.9 cases per thousand hospital admissions.[31] Approximately 0.10–0.25% of all admissions to Thai and Indian hospitals are for the management of severe AKI that requires dialysis. In one study, 0.6% of all patients at admission in a US hospital had AKI, but only 5% of them needed renal replacement therapy.[32] AKI is recognized as the most commonly encountered community-acquired renal emergency in tropical countries.[33,34] Areas with a high prevalence of community-acquired AKI as a result of infection or ingestion of toxins in different parts of the tropics (Figure 2).

The population of patients with AKI in developing tropical countries is younger (mean age 37–47 years) than that reported in developed temperate countries (mean age 68 years).[32,34–36] Most patients with AKI in developing tropical countries do not have pre-existing comorbidities, such as hypertension, diabetes or chronic kidney disease (CKD), which are characteristically found in patients with AKI in the hospitals of temperate countries.

Aetiology of AKI in the tropics

The causes of AKI in tropical countries can be broadly divided into those caused by infections, animal and plant toxins, chemicals or obstetric complications (Table 1, Box 1). Some of these causes have been well characterized and studied, whereas for others, the numbers of affected patients are small and a cause-and-effect relationship is suggested only by a temporal association.

Reliable estimates of the importance of the different causes of AKI are difficult to make, as these vary from region to region. For example, diarrhoeal and infectious diseases (including *Plasmodium falciparum* malaria) are a major public health concern in most tropical countries; leptospirosis, typhus, and envenomation are the main causes of AKI in South Asia;[8] malaria and indigenous herbal remedies are the most common causes of AKI in Africa;[28] and leptospirosis, dengue fever, envenomation and obstetric complications are the main causes of AKI in Latin American countries.[37]

Pathophysiology of tropical AKI

The pathogenesis of tropical community-acquired AKI varies according to its cause.

Direct kidney damage

Direct invasion of the kidney by a pathogen, as occurs in leptospirosis, induces injury through a local

inflammatory reaction, cellular proliferation and infiltration. Membrane components of *Leptospira* spirochaetes are directly nephrotoxic to the renal tubule, as are ingestion of raw bile of the grass carp, poisonous mushrooms and cottonseed oil.[38] Specific plant chemicals filtered by the kidneys are precipitated in the concentrated and acidic urine in the distal tubule. For example, AKI can be caused by djenkolic acid crystals formed after ingestion of djenkol beans, as well as by oxalate crystals formed after the ingestion of star fruit juice and *Averrhoa bilimbi* (irumban puli) juice.[38,39] *Daboia russelii* (Russell viper) venom and pit viper venom are also toxic to the vascular and glomerular endothelium and renal tubules.[40–42] Direct injury to the glomerular endothelium as a result of the interaction between erythrocytes parasitized by *P. falciparum* and the microvascular endothelium (cytoadherence) is well recognized.[43]

Indirect kidney damage

AKI can also be caused indirectly—through the breakdown of myoglobin (rhabdomyolysis), haemoglobin (haemolysis), increased concentration of bile acids, release of oxygen free radicals, enzymes (phospholipases and proteases) and generation of complement products—for example, as a result of a snake bite or insect sting.[44–46]

Haemodynamic alterations after tropical infections and toxin exposure are similar to those observed in sepsis.[47] Generalized arterial vasodilatation with a reduction in systemic vascular resistance, the haemodynamic hallmark of sepsis, occurs in patients with malaria, leptospirosis, scrub typhus and hantavirosis. This vasodilation leads to activation of the neurohumoral axis, sympathetic nervous system and renin–angiotensin–aldosterone system, which is associated with the nonosmotic release of vasopressin. The result is intrarenal vasoconstriction with systemic vasodilatation, which contribute to AKI.[48,49] Hypovolaemia in patients with severe infections (such as diarrhoeal diseases and dengue haemorrhagic fever, two common causes of severe hypovolaemia in the tropics[7,37]) is caused by increased vascular permeability and fluid loss from the intravascular compartment, which contribute to ischaemic AKI in patients with tropical diseases.

Acute cortical necrosis

Acute cortical necrosis (ACN) is a rare form of AKI that develops after obstetric complications, snake bite and haemolytic uraemic syndrome,[50,51] conditions encountered almost exclusively in tropical countries. ACN is rarely, if ever, encountered in temperate zone countries.[52] The necrosis of renal cortical tissue can be patchy or diffuse, and the patient's clinical course is determined by the extent of renal involvement.[50,51] In the 1960s and 1970s, ACN was diagnosed in 7.4% of patients with AKI in India.[51] Obstetric complications were the cause of ACN in 37–71% of these individuals. Other common causes of ACN were snake bite, pancreatitis and haemolytic uraemic syndrome.[50,51]

ACN should be suspected in patient with AKI (especially after snake bite or obstetric complication) who exhibit prolonged oliguria. Renal histology is the gold standard for diagnosis of ACN, and shows ischaemic necrosis of the cortical tissue, sometimes with thrombotic microangiopathy. However, contrast-enhanced CT has emerged as a reliable noninvasive diagnostic technique in this setting (Figure 3).[53] When the cortical involvement is diffuse, kidney function will fail to recover and the patient requires lifelong renal replacement therapy.

Table 1 | Comparative frequency of causes of AKI in tropical countries*

Reference(s)	Country	Number of patients	Medical (% patients)	Surgical (% patients)	Obstetric (% patients)
Firmat & Pas (1975)[140]	Argentina	1,000	58	28	14
Sitprija & Benyajati (1975)[141]	Thailand	162	61	15	24
Adu *et al.* (1976)[142]	Ghana	50	62	24	4
Chugh *et al.* (1978)[143]	India	325	67	22	11
Shah *et al.* (1985)[144]	India	816	56	32	21
Chugh *et al.* (1987)[81]	India	1,862	60	25	15
Muthusethupathi & Shivakumar (1987)[145]	India	187	85	9	6
Bamgboye *et al.* (1993)[146]	Nigeria	175	52	23	26
Seedat & Nathoo (1993)[28]	South Africa	226	77	9	14
Firmat *et al.* (1994)[119]	Argentina	500	52	16	32
Ramachandran (1994)[147]	Sri Lanka	317	79	15	6
Olowu & Adelusola (2004)[148]	Nigeria	123	91	8	0
Vukusich *et al.* (2004)[30]	Chile	114	70	30	0
Jayakumar *et al.* (2006)[34]	India	1,112	88	9	3
Al Rohani *et al.* (2011)[149]	Yemen	203	91	6	3
Daher *et al.* (2012)[9]	Brazil	491	85	13	2
Kaul *et al.* (2012)[10]	India	240	78	8	14
Guru & Jha (unpublished work)	India	1,114	79	15	6

*In many studies of AKI from tropical countries, aetiology is categorized as medical, surgical or obstetric. These data suggest that the epidemiology of tropical AKI is changing; in general, obstetric and diarrhoeal AKI seems to be declining in prevalence. Abbreviation: AKI, acute kidney injury. Reproduced by permission of Oxford University Press © Chugh, K. S. *et al.* The Oxford Textbook of Clinical Nephrology, 3rd edn 1614–1630 (2005).[7]

Tropical AKI in children

In addition to the causes described above, postinfectious glomerulonephritis contributes to paediatric AKI in many tropical countries. Haemolytic uraemic syndrome is the underlying cause of AKI in 25–55% of all cases of this disease in preschool children in tropical countries.[54–57] In contrast to countries of temperate climates, where *Escherichia coli* is the primary causative agent, *Shigella* infection is the primary cause of post-diarrhoeal haemolytic uraemic syndrome in paediatric patients with AKI in the Indian subcontinent.[58] Renal histology in these patients indicates a disproportionately high involvement of arterioles and small arteries, with severe intimal proliferation and luminal stenosis. Up to 40% of paediatric patients with haemolytic uraemic syndrome develop ACN.[56] Various forms of postinfection glomerulonephritis constitute approximately 10% of

Box 1 | Causes of acute kidney injury in the tropics

Vector-borne infections
Malaria (*Plasmodium falciparum*, transmitted by *Anopheles* mosquito)
Dengue fever (Dengue virus, transmitted by *Aedes* mosquito)
Scrub typhus (*Orientia tsutsugamushi*, transmitted by trombiculid mites)
Haemorrhagic Rift valley fever (RVF virus, transmitted by *Aedes* or *Culex* mosquitoes)
Direct infections
Leptospirosis (*Leptospira interrogans*)
Hantavirosis, also known as haemorrhagic fever with renal syndrome (puumala and hantaan hantaviruses)
Zygomycosis
Diarrhoeal diseases for example, *Escherichia coli*, amoebic (*Entamoeba histolytica*) and bacillary (*Shigella*) dysentery, cholera and viral gastroenteritis
Melioidosis (*Burkholderia pseudomallei*)
Typhoid (*Salmonella typhi*)
Chlamydia (*Chlamydia trachomatis*)
Legionellosis (*Legionella pneumophila*)

Plant and fungal toxins
Herbal medicines
Impila food plants
Djenkol beans
Marking nut
Mushroom
Plant-derived toxins used as insecticides and to kill fish
Animal poisons
Snake bites
Wasp, hornet and bee stings
Spider bite
Jellyfish sting
Scorpion sting
Carp gallbladder or bile

Chemical nephrotoxins
Ethylene glycol
N,*N*'-dimethyl-4,4'-bipyridinium dichloride
Ethylene dibromide
Copper sulphate
Chromic acid

Environmental factors
Heat stroke
Natural disasters

Other causes
Intravascular haemolysis resulting from glucose-6-phosphate 1-dehydrogenase deficiency
Obstetric complications

all cases of paediatric AKI in the tropics,[59] although the incidence of postinfection glomerulonephritis is declining in several tropical countries because of early detection and treatment of respiratory infections and improvement in hygienic conditions that limits the spread of infection.[38]

Important causes of tropical AKI

The following sections describe some of the most common causes of community-acquired AKI.

Infections

AKI has been described in association with a large number of tropical infections. The usual presentation is an acute febrile illness with severe headache, myalgia and involvement of other organ systems to a variable extent; jaundice, intravascular haemolysis and thrombocytopenia often accompany these early symptoms. Associated metabolic disturbances include lactic acidosis, hypoglycaemia, hyponatraemia and hyperkalaemia. However, the similarity of the clinical presentations of the various forms of infection-associated AKI makes identifying the different underlying tropical infections on the basis of clinical features alone difficult. Timely diagnosis, therefore, requires a good knowledge of the local epidemiology of community-acquired AKI and the availability of sensitive and diagnostic tests for specific pathogens.

For some infectious aetiologies of AKI, the number of affected patients is too few to draw any meaningful conclusions about the natural history or pathogenesis, but a few common infections, highlighted below, are associated with a substantial burden of AKI.

Malaria

Severe malaria is a medical emergency. Malaria is estimated to account for 60% of outpatient visits, 30–50% of hospital admissions and 40% of public health expenditure in countries with a high burden of malarial disease.[60] In 2010, 216 million people had malaria and an estimated 655,000 deaths were caused by this disease worldwide.[61] 98% of deaths due to malaria occur in 35 countries, of which 30 are in sub-Saharan Africa and the rest are in Asia.

Most cases of malaria-associated AKI occur in the context of *P. falciparum* infection, although a few reports describe AKI in association with *P. vivax* infection.[62,63] Approximately 1–4% of patients with *P. falciparum* malaria develop AKI, and the incidence of AKI increases to 60% in those with severe malarial disease.[62,64] Patients with severe parasitaemia and children under the age of 5 years, pregnant women, and individuals with HIV or AIDS are at an increased risk of AKI if they get malaria.[43,65] Approximately 45% of people with malaria-induced AKI die.[43] The mortality rate is particularly high in children in Africa, where a child dies every minute from malaria and 22% of all childhood deaths are due to malaria.[60] A diagnosis of malaria is made by the demonstration of the asexual forms of the parasite in a thick peripheral blood smear. Simple card tests using antibodies against specific *P. falciparum* antigens are now available and can be used for quick diagnosis when microscopy facilities or trained personnel are not available. The sensitivity and specificity of these tests are variable and light microscopy remains the gold standard for malaria diagnosis. Artemisinin-based combination therapies are the recommended treatment for *P. falciparum* malaria.[66] Early antimalarial treatment and dialysis is associated with improved survival and recovery of renal function in patients with malaria-induced AKI.[67,68]

Leptospirosis

Leptospirosis, the most prevalent zoonosis in the world, is found in the tropical countries of Southeast Asia, South America and Africa.[69] The annual incidence is

estimated to be 10–100 cases per 100,000 of the population in tropical countries. Seasonal outbreaks occur after heavy rainfall and flooding.[70,71] The major reservoirs of infection are rodents and dogs in urban areas, and cattle, wild rodents and opossums in rural areas and villages. Leptospira are excreted in the urine of infected animals. Human infection occurs accidentally from exposure to water contaminated with infected urine and may occur in farm or abattoir workers as a result of occupational exposure or in other groups from exposure during leisure-time activities.

Classic leptospirosis is biphasic: the initial leptospiremic phase lasts 4–7 days and can be either asymptomatic or associated with transient flu-like symptoms that resolve completely. The leptospiremic phase is followed by the immune phase, characterized by an increase in IgM antibodies, cytokinaemia and the development of disease manifestations in various organ systems. Approximately 20–85% of patients with second-phase leptospirosis develop AKI,[72–75] as well as jaundice, meningitis, upper gastrointestinal bleeding and pulmonary haemorrhage. Some patients might not have obvious symptoms in the first phase and present in the second phase depending on the intensity of the immune response.

Serology is the most common method for confirming the diagnosis of leptospirosis. The antibody-based microagglutination test is the gold standard for this purpose, but requires maintenance of cultures of live spirochaetes from representative serogroups, which are available only in reference laboratories. The organism can be cultured from patients' blood during the first phase and from their urine during the second phase. Dark-field microscopy has been used to detect spirochaetes in serum and cerebrospinal fluid; however, this test is insensitive and not useful for clinical application.[76] Nucleic acid tests (such as PCR) are highly sensitive and highly specific, and can detect *Leptospira* infection several days before antibody-based tests,[77] but are only available in research laboratories.

Leptospirosis is usually self-limiting, and requires only supportive measures such as correction of dyselectrolytemias and adequate fluid replacement. Penicillin or doxycycline shorten the duration of fever and hospital stay, and might hasten the resolution of leptospiruria.[72] Sequencing of the *L. interrogans* genome has been completed and substantial research efforts are directed toward vaccine development.[78]

Diarrhoeal diseases

AKI secondary to diarrhoeal diseases continues to be a major problem in tropical countries, particularly in the paediatric population. However, adult patients are also seen, especially when rehydration is suboptimal.[79] Diarrhoea-related AKI is most frequent in rural areas and urban slums where sanitation is poor and safe drinking water is not available. The incidence of diarrhoea-related AKI increases during summer and rainy seasons. During the 1980s, studies in India showed that 35–50% of all children who required dialysis treatment for AKI had diarrhoea-related AKI,[80,81] but almost a decade later the incidence of diarrhoea-related AKI requiring dialysis had declined to 17% as a result of the widespread use of oral rehydration solutions.[56]

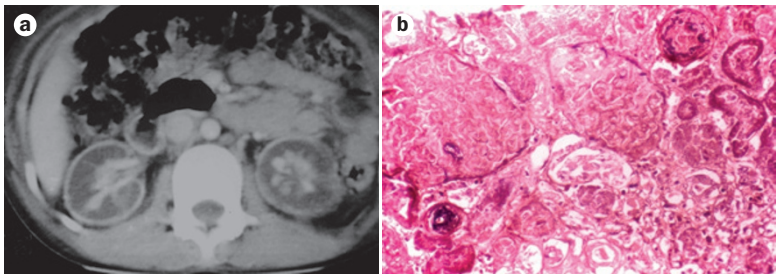

Figure 3 | Imaging findings in patients with community-acquired acute kidney injury. **a** | Contrast-enhanced axial CT scan at the level of the kidneys in a 26-year-old patient with acute cortical necrosis. The subcapsular region shows a rim of contrast enhancement (white). Enhancement is completely absent in the renal cortex of both kidneys, and normal in the medulla. No excreted contrast agent can be observed in the collecting system. **b** | Photomicrograph of kidney tissue showing complete necrosis indicated by loss of cellular details and nuclei of all structures in the renal cortex. Haematoxylin and eosin stain.

The patient's clinical symptoms might provide clues as to the identity of the causative pathogen in diarrhoea-related AKI. Early vomiting is a feature of rotavirus infection. Loose, watery stools indicate infection with enterotoxigenic *E. coli* or *Vibrio cholerae*. Fever, cramps and tenesmus accompanied by blood and mucus in the stool, suggest infection with *Shigella*, *Salmonella*, or enteroinvasive *E. coli* species. A diagnosis of cholera can be confirmed by the demonstration of motile vibrios in a hanging-drop stool preparation; for other organisms, cell culture is necessary to confirm the diagnosis.

Early and adequate fluid replacement is the cornerstone of management for all diarrhoeal diseases. The WHO recommends the use of oral rehydration as soon as symptoms appear. Intravenous rehydration might be required in patients with severe dehydration, persistent vomiting, or paralytic ileus. Hypokalaemia, secondary to the metabolic acidosis worsens as dehydration is corrected by fluid replacement therapy and should also be monitored and treated with potassium supplementation. However, the mortality rate associated with diarrhoea-related AKI remains high. In a study from Malaysia, the mortality rate was 2.1 in 1,000 admissions; women, infants and patients with severe dehydration at admission were at increased risk.[82]

HIV infection

HIV infection is one of the leading causes of infectious-disease-related mortality, and has accounted for approximately 25 million deaths in the past 30 years. The number of AIDS-related deaths has been declining steadily, 1.7 million people died of AIDS-related causes in 2011, a reduction of 25% from the peak in 2005.[83] In 2010, approximately 34 million people worldwide were living with HIV infection; sub-Saharan Africa is home to over 60% of them. Associated infections, especially tuberculosis, volume depletion, the use of nephrotoxic antiretroviral drugs and contrast agents for medical

imaging all increase the risk of AKI in these patients. Thrombotic microangiopathy caused by HIV infection can present with AKI. AKI is, therefore, common in hospitalized patients with HIV infection.[84] AKI in patients with HIV has consequences that extend beyond the acute episode, including an increased risk of cardiovascular events, end-stage renal disease (ESRD) and increased mortality.[85] Antiretroviral drugs used in highly active antiretroviral therapy (HAART), such as tenofovir disoproxil and indinavir, can also cause AKI.[86] AKI in HIV-infected patients (in the HAART era) is associated with a sixfold increase in mortality.[84] Prevention of AKI requires attention to common risk factors, for example volume depletion and avoidance of nephrotoxic drugs, especially in individuals with pre-existing CKD. Therapeutic management entails the use of a high index of suspicion, correction of volume deficit and attention to the list of medications.

Plant, animal and fungal nephrotoxin exposure

AKI resulting from intentional ingestion of animal, plant and fungal nephrotoxins is common throughout sub-Saharan Africa and in parts of Asia.[87] A number of renal lesions, including acute tubular necrosis, ACN and interstitial nephritis, have been described in individuals with these forms of AKI (Table 1).[88,89]

Some commonly ingested tropical plant foods can have toxic effects if consumed without proper preparation. One example is the consumption of beans from the djenkol plant, which are considered a delicacy in several Southeast Asian countries.[90] Ingestion of a large amount of uncooked beans, especially in individuals with a low fluid intake, can cause dysuria, lumbar pain, hypertension, haematuria and oliguria secondary to the intratubular formation of djenkolic acid crystals.[90,91] The breath and urine of these patients have a characteristic, sulphurous odour, and the needle-like crystals can be seen in urine under light microscopy. Increased fluid intake and urinary alkalinization with sodium bicarbonate help to dissolve the crystals.[91] With appropriate management, most victims recover within 2 weeks.[92]

More than 75% of all deaths from acute poisoning, and 25–60% of all cases of AKI related to medical (that is, not surgical or obstetric) causes in South African hospitals are, however, associated with the use of traditional medicines (Table 1).[88,89] Indigenous medical systems based on remedies derived from local plants and animals flourish in tropical countries (Table 2). Medicines are prepared by herbalists under nonstandard conditions and are not tested for efficacy and safety.[87] The ingredients are variable and the dosage and route of administration are not standardized. Many of these remedies contain potentially nephrotoxic molecules. Furthermore, potentially toxic substances, such as paint thinners, turpentine, chloroxylenol, ginger, pepper, soap, vinegar, copper sulphate and potassium permanganate, are often added to the plant extracts to increase their effect.[89] The most common cause of AKI related to the use of traditional herbal medicines in Africa is the use of extracts of the tubers of *Callilepis laureola* (impila), which are taken either orally or as an enema for their purgative and vermifugal effects by black Africans.[93] Symptoms appear 1–4 days after consumption and include abdominal pain, vomiting, seizures, oliguria and jaundice. The active agent is thought to be atractyloside, an alkaloid that inhibits ATP synthesis. The mortality rate for impila-related AKI is over 50%.[94]

The raw gallbladder or bile of sheep, freshwater carp and grass carp are used for medicinal purposes in rural areas of the Middle East and Southeast Asia, respectively.[95,96] A syndrome of acute hepatic failure and renal failure has been reported after consumption of these items. AKI with oliguria develops within 48 h and lasts 2–3 weeks. Susceptibility to AKI is probably related to differences in the species of fish used, the amount of bile ingested and patient-specific factors; for example, an association has been found between the size of the fish and the severity of the toxic effect. The prognosis of patients with AKI resulting from bile ingestion is usually good, and death usually occurs only in those who present late and already have multiorgan failure.[96]

A temporal relationship between the use of traditional medicines and the onset of clinical symptoms can help to establish a cause-and-effect relationship. Information on the use of traditional medicines is often not volunteered by the patient, and might be missed if not specifically sought when obtaining the patient's history.

Envenomation

Snake bite

Of the ~2,000 species of snake found worldwide, ~450 are venomous. At least 421,000 instances of envenomation are attributed to snake bite every year, the majority of which occur in tropical countries in Asia, Africa and Latin America.[97] The highest number of snake-bite-related deaths— approximately 45, 900 every year—is reported in India.[98]

AKI develops in about 12–30% of patients who have been bitten by a venomous snake. Most of these patients have received a bite with venom that is haemotoxic or myotoxic. The clinical manifestations depend upon the species and the dose of venom injected. Common features after viper bites are local pain and swelling, blistering, tender regional lymphadenopathy, local or systemic bleeding and hypotension. Individuals bitten by sea snakes develop severe myalgia and muscle weakness secondary to rhabdomyolysis. Onset of AKI can occur within 4–6 h after the bite, or may be delayed for 3–4 days.[18] Grossly, the kidney is swollen and shows petechial haemorrhages. Light microscopy of renal biopsy samples shows acute tubular necrosis with intratubular pigment casts in 70–80% of patients with snake-bite-related AKI. Other changes include thrombotic microangiopathy, mesangiolysis, interstitial inflammation, glomerulonephritis, vasculitis and renal infarction. ACN is seen in approximately 20–25% of patients after a *D. russelii* (Russell viper) or *Echis carinatus* (saw-scaled viper) bite.[99]

Management of patients with snake-bite-related AKI consists of local wound care, administration of

Table 2 | Plant and fungal nephrotoxins reported to cause AKI in tropical countries

Plant (common or local name)	Country	Active molecule	Renal manifestations	Other manifestations
Averrhoa bilimbi (irumban puli)	South India	Oxalic acid	Intratubular obstruction	None
Callilepis laureola (impila)	Sub-Saharan Africa	Atractyloside	Acute tubular necrosis	Abdominal pain, diarrhoea, vomiting, jaundice, seizures and coma
Catha edulis (khat leaf)	East Africa and Arabian peninsula	*S*-cathinone and ephedrine	Acute tubular necrosis	Hepatotoxic effects
Cleistanthus collinus (oduvan)	India	Cleistanthin A and B, and dyphylline	AKI	Hypotension, hypokalaemia and arrhythmia
Colchicum autumnale (autumn crocus)	Turkey	Colchicine	Acute tubular necrosis	Haemorrhagic gastroenteritis, muscle paralysis and respiratory failure
Crotalaria laburnifolia (bird flower)	Zimbabwe and Sri Lanka	Pyrrolizidine alkaloids	Acute tubular necrosis and hepatorenal syndrome	Hepatic veno-occlusive disease, pulmonary injury and thrombocytopenia
Dioscorea quartiniana (yam)	Africa and Asia	Dioscorine and dioscin	Acute tubular necrosis	Convulsions
Pithecellobium lobatum and *Pithecellobium jiringa* (djenkol beans)	Southeast Asia	Djenkolic acid	Intratubular obstruction and acute tubular necrosis	Lumbar and lower abdominal pain, hypertension
Dodonaea angustifolia (sand olive)	South Africa	Unknown	Acute interstitial nephritis	Pulmonary embolism
Euphorbia metabelensis (spurge)	Zimbabwe	Irritant chemicals in plant latex	Acute tubular necrosis	Thrombocytopenia
Larrea tridentate (chaparral)	Chile and South Africa	Nordihydroguaiaretic acid and *S*-quinone	Renal cysts, renal cell carcinoma	Hepatic failure
Propolis (resin)	Brazil	Unknown	Acute interstitial nephritis	Contact dermatitis
Rhizoma rhei (rhubarb)	Hong Kong	Anthraquinones (emodin, aloe-emodin)	Acute interstitial nephritis	None
Securidaca longepedunculata (violet tree, or wild wisteria)	Congo, Zambia and Zimbabwe	Methyl salicylate, securinine, saponins	Acute tubular necrosis	Vomiting and diarrhoea
Sutherlandia frufescens (cancer brush)	South Africa	Unknown	Acute interstitial nephritis	Pulmonary embolism
Takaout roumia	Morocco and Sudan	Paraphenylenediamine	Acute tubular necrosis	Rhabdomyolysis
Semecarpus anacardium (marking nut)	India	Unknown	Acute tubular necrosis and acute cortical necrosis	Corrosive blisters in pharynx, gastrointestinal irritation, shock and coma
Taxus celebica (Chinese yew)	Asia	Flavonoid	Acute tubular necrosis and acute interstitial nephritis	Hepatitis, haemolysis and disseminated intravascular coagulation
Thevetia peruviana (yellow oleander)	India and Sri Lanka	Cardiac glycosides	Acute tubular necrosis	Liver failure and cardiac arrhythmias
Tripterygium wilfordii Hook. f. (thunder-god vine)	Taiwan	Triptolide	Acute tubular necrosis	Diarrhoea and shock
Uncara tomentosa (cat's claw)	Peru	Alkaloids and flavonols	Acute tubular necrosis	Diarrhoea, hypotension, bruising and bleeding gums

Abbreviation: AKI, acute kidney injury. Reproduced by permission of Oxford University Press © Jha, V. The Oxford Textbook of Medicine, 5th edn, 4084–4092 (2011) and modified from Comprehensive Clinical Nephrology, 4th edn, Burdmann, E. *et al.* Acute kidney injury in the tropics. 813–820 © (2011) with permission from Elsevier.[150]

antivenom and supportive treatment. Early administration of antivenom prevents or attenuates the development of haematological abnormalities or rhabdomyolysis and AKI. Antivenom therapy is continued until the systemic effects of envenomation subside; the usual method of monitoring haemotoxic bites is serial measurements of the whole-blood clotting time. Supportive measures include administration of fresh frozen plasma to correct coagulopathy, blood transfusion (in patients with substantial haemorrhage) and inoculation with antitetanus immunoglobulin. Patients bitten by myotoxic snakes need aggressive fluid therapy and urinary alkalinization to prevent intratubular precipitation of myoglobin.[100] Mortality from snake bite envenomation is estimated to be up to 35%.[17,99,101] The prognosis of snake-bite-related AKI is, however, favourable in patients who receive early medical attention and adequate doses of antivenom.

Insect stings

Stinging insects, such as honeybees, wasps, yellow jackets and hornets are common throughout the tropical zone. AKI, proteinuria, and nephritic and nephrotic syndromes have been reported in some individuals after insect stings.[102–105] AKI usually develops in individuals who have received a large dose of venom, typically after multiple stings by a swarm of insects, but can also develop after only a single sting in patients who experience an anaphylactic reaction.[104] The diagnosis is obvious, and the management entails prompt reversal of symptoms with short course of steroids, antihistamines and fluid replacement.

Chemical poisons

Accidental, intentional (suicidal and nonsuicidal) or occupational exposure to chemicals that induce AKI is well documented in the tropics. AKI occurs after the

ingestion of chemicals, such as *N*,*N*'-dimethyl-4,4'-bipyridinium dichloride-containing pesticides, copper sulphate or ethylene dibromide for suicidal purposes.[7] Chemical intoxication is, therefore, often regarded as a suicide attempt but may also be the result of occupational exposure, given the inadequacy of environmental protection measures in factories in many tropical regions. AKI can also be caused by consumption of chemicals such as ethylene glycol, for example when car antifreeze solution is consumed as a substitute for alcoholic drinks, or when it is used as a vehicle in cough syrups in the place of the more expensive propylene glycol.[106,107]

Genetic factors

Environmental factors have favoured some unique genetic traits in tropical populations. One example is the well-known protection that heterozygous carriers of the sickle-cell trait have against *P. falciparum* malaria in West Africa. However, homozygous carriers of this trait develop sickle-cell disease, which can cause AKI through sickle-cell crises.

Glucose-6-phosphate 1-dehydrogenase (G6PD) is a key enzyme in the hexose monophosphate pathway that protects erythrocytes from oxidative stress. Mutations in the *G6PD* gene can reduce or abolish the activity of this enzyme, rendering erythrocytes susceptible to oxidative stress, which causes haemolysis.[108] A deficiency in this enzyme is encountered with high frequency in black South Africans and Brazilians, and in parts of India. A haemolytic crisis, manifested by the passage of dark-coloured urine, develops within a couple of hours of exposure to oxidative stress, and is most commonly induced by drugs, toxins or infections. AKI occurs in 5–10% of patients with haemolytic crisis.[109–111] Assays that estimate G6PD activity in erythrocytes can confirm the presence of a deficiency in this enzyme, but these tests are misleading (often falsely suggesting enzyme levels are normal) during a haemolytic episode because the surviving newly produced erythrocytes show normal enzyme activity, which rapidly declines as the red blood cells age. Consequently, the test should be repeated after the patient has recovered from the acute haemolytic episode. All individuals known to have the deficiency should be given a list of drugs that are likely to precipitate haemolysis so that they can be avoided. Also, patients who need to be started on a drug known to precipitate haemolysis, such as dapsone or primaquine should be tested for G6PD deficiency.

Obstetric complications

Advances in health care and socioeconomic development have eliminated pregnancy-related AKI in developed countries[52]. However, obstetric AKI continues to be encountered in the tropics, mostly as a consequence of suboptimal antenatal care, out-of-hospital childbirth and unsafe abortion practices.[112,113] The incidence of obstetric AKI shows a bimodal distribution; the first peak is accounted for by hyperemesis gravidarum or septic abortion in women late in their first trimester of pregnancy, whereas pre-eclampsia, eclampsia, placental abruption, postpartum haemorrhage and puerperal sepsis in women in their third trimester account for the second peak.

Legalization of abortion and improvements in antenatal care reduced the incidence of obstetric AKI in India from 22% of all cases of AKI in the 1960s and 1970s to approximately 8% of all cases of AKI in the 1990s.[33] Obstetric AKI, however, continues to be prevalent and has a poor prognosis in many parts of the tropics even today.[112–117] Septic abortion is the cause of AKI in 52% of patients in Ethiopia,[118] and in Argentina and Nigeria, gynaecological and obstetric complications still account for about one-third of patients with AKI.[112,113,119] In one hospital in Pakistan, of 100 patients with obstetric AKI seen over a 3-year period, over 90% needed dialysis, 7% died in hospital, and only 44% were off dialysis at discharge.[114]

Long-term consequences of tropical AKI

In addition to the high mortality rate, patients who survive an episode of AKI might not enjoy a complete return to health.[120] Among patients who survived an episode of AKI, 10% had developed ESRD at 3.0–3.5 years.[121] In a cohort of children with AKI discharged from a public-sector hospital in India, proteinuria, hypertension, haematuria or reduced GFR were present in 32% of patients after 6 months and in 38% of patients after 10 years.[122] Snake-bite-induced AKI, need for dialysis, and prolonged oliguria are associated with adverse outcomes. The risk of the future development of CKD is exacerbated by the late presentation of AKI.[123] Moreover, as tropical community-acquired AKI predominantly affects young people, who are often the primary breadwinner of the family, this disease extracts a high economic cost from families and societies as well as the individual concerned. Community-acquired AKI leads to catastrophic or impoverishing health expenditure (defined as expenditure that endangers a household's ability to maintain its customary standard of living, set at 5–20% of total household income).[124] Thus, patients with tropical community-acquired AKI, though believed to have lower mortality rates than their counterparts with hospital-acquired AKI in developed, temperate countries, contribute not only to poor productivity, but also to an increased health-care burden in the long term.

Prevention and treatment of AKI

Prevention

As discussed above, community-acquired tropical AKI is largely preventable, but doing so requires an integrated approach to reduce the disease burden. Such an approach requires a radical change in public policy and a change in focus away from hospital-based care and towards improvement of basic health needs, such as the provision of safe drinking water and improved sanitation, as well as improvements in the conditions of farm workers and the provision of obstetric care. Indeed, the epidemiology of AKI seems to be changing

over time as these factors are addressed. For countries in which multiple studies have been conducted, a decline in obstetric and diarrhoeal causes of AKI is generally evident, which is attributed to improved maternal care and the widespread use of oral rehydration solution (Table 1).[125,126] However, global warming and climate change are expected to reduce the availability of clean air, safe drinking water and sufficient food and secure shelter in the future.[127,128] The prevalence of diarrhoeal diseases, malnutrition and vector-borne infections, which are major preventable causes of AKI and death in the tropics, is highly sensitive to climate change and is, therefore, expected to increase in response to climate change.[15,128] Areas with a weak public health infrastructure are expected to be the worst affected.

Vector control is the most effective way to prevent transmission of vector-borne-diseases. In the tropics, however, vector-borne diseases are notoriously difficult to control.[129] In the 1950s and 1960s, vector eradication relied on the use of chemical insecticides.[130] However, concerns about the effects of these pesticides on tropical ecosystems (for example, reduced biodiversity), acute as well as long-term adverse effects of pesticide exposure on human health, and the prospect that vectors could develop resistance to these pesticides resulted in the abandonment of this strategy[131] and its replacement by an integrated management approach. This approach uses a range of interventions, including the rational use of pesticides and mosquito nets on the basis of local knowledge about the vectors, diseases and disease determinants, and engagement with local communities and other stakeholders within a public health regulatory and legislative framework.[132] Integrated vector management requires additional organizational and economic resources for implementation. Not all countries that followed WHO recommendations have reported uniform success.[133] The distribution of mosquito nets impregnated with long-lasting insecticide and indoor spraying of residual insecticides led to ≥50% reduction in the number of patients with malaria in 43 of the 99 countries with ongoing transmission of vector-borne diseases, and a 25–50% reduction was observed in another eight of these countries between 2000 and 2010.[61] Since 2000, the estimated global incidence of malaria and malaria-specific mortality has decreased by 17% and 26%, respectively.[61] However, modern technological tools, such as remote sensing using satellite-derived imagery[134] and novel biological methods such as the use of larvivorous fish[135] are now being utilized for eradication of tropical disease-causing organisms and vectors.

Public awareness of the need for use of safe water, safe handling and use of pesticides and other nephrotoxins should be increased by including these issues in school curricula, and by sustained campaigns in mass media.

Treatment

The preventive measures described above need to be coupled with improvements in the training of healthcare workers, to enable prompt identification of patients with suspected AKI who might be candidates for referral to centres that have facilities for specialized care. With the exception of a few sub-Saharan African nations, dialysis is available in most tropical countries. However, haemodialysis facilities are concentrated in urban centres and are often unable to cope with the huge demand for their services. Peritoneal dialysis is, therefore, often the only form of dialysis available, especially in remote areas[136] and for small children.[137] Peritoneal dialysis has equivalent efficacy to more expensive continuous renal replacement therapy modalities, especially when high fluid volumes are used, administered to patients through a soft catheter.[138,139] Advances in dialysis technology that permit use of haemodialysis in remote areas using simple machines and resin systems to regenerate water, and development of mobile dialysis platforms will be likely to improve outcomes.

Conclusions

Community-acquired AKI is a major problem in developing tropical countries. The prevalence and epidemiology of this form of AKI is closely linked to other public health problems, such as infections, unclean water, a predominantly rural population, suboptimal antenatal care, poor regulation of indigenous medical practices, and unsafe births and abortions. Many patients in tropical countries who have infection-associated AKI present with similar features and patterns of organ involvement, which makes identification of the underlying cause difficult on the basis of clinical findings alone. Additionally, the lack of easy access to hospitals can delay diagnosis and management of AKI, which culminates in the high mortality rates for this condition reported in developing countries. The long-term renal prognosis is poor in a large number of AKI survivors, especially those with unfavourable histological lesions, such as ACN. Community-acquired AKI in tropical countries is, however, potentially preventable. Prevention requires adopting a public health approach, including provision of safe water, infection control, vector management, better obstetric care and campaigns to raise awareness about safe use of herbs, pesticides and chemicals. Timely referral of patients with established AKI to centres with dialysis facilities will improve outcomes.

Review criteria

The PubMed database was searched using the terms "acute renal failure", "acute kidney injury", "acute renal insufficiency", "kidney injury", "acute", and "acute kidney failure". This search was refined using the terms "kidney failure", "acute/economics", "acute/epidemiology", "kidney failure" and "acute/aetiology". Full-text articles were obtained for all relevant publications relating to humans. In addition, textbooks, conference presentations and position statement papers were reviewed. Online resources were searched for material relevant to the impact of climate on health care and further information was obtained by checking cross-references. Data on economic development and general health indicators were obtained from the World Bank and WHO websites.

1. United Nations Department of Economic and Social Affairs. *United Nations Population Division Home Page* [online], http://www.un.org/esa/population/unpop.html (2012).
2. Sachs, J. M. Why tropical countries are underdeveloped. *The National Bureau of Economic Research Working Paper Series* [online], http://www.nber.org/w8119.html (2001).
3. Diamond, J. *Guns, germs and steel: the fates of human societies*. (W. W. Norton and Co., New York, 1997).
4. Engerman, S. & Sokoloff, K. in *How Latin America fell* (ed. Harber, S.) 260–304 (Stanford University Press, Stanford, 1997).
5. Jha, V., Malhotra, H. S., Sakhuja, V. & Chugh, K. S. Spectrum of hospital-acquired acute renal failure in the developing countries–Chandigarh study. *Q. J. Med.* **83**, 497–505 (1992).
6. Chertow, G. M., Burdick, E., Honour, M., Bonventre, J. V. & Bates, D. W. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J. Am. Soc. Nephrol.* **16**, 3365–3370 (2005).
7. Chugh, K. S., Sitprija, V. & Jha, V. in *Oxford Textbook of Nephrology* (eds Davison, A. M. *et al.*) 1614–1630 (Oxford University Press, Oxford, 2005).
8. Jha, V. & Chugh, K. S. Community-acquired acute kidney injury in Asia. *Semin. Nephrol.* **28**, 330–347 (2008).
9. Daher, E. F. *et al.* Differences in community, hospital and intensive care unit-acquired acute kidney injury: observational study in a nephrology service of a developing country. *Clin. Nephrol.* **78**, 449–455 (2012).
10. Kaul, A. *et al.* Spectrum of community-acquired acute kidney injury in India: a retrospective study. *Saudi J. Kidney Dis. Transpl.* **23**, 619–628 (2012).
11. Kaufman, J., Dhakal, M., Patel, B. & Hamburger, R. Community-acquired acute renal failure. *Am. J. Kidney Dis.* **17**, 191–198 (1991).
12. Schoolwerth, A. C. *et al.* Chronic kidney disease: a public health problem that needs a public health action plan. *Prev. Chronic Dis.* **3**, A57 (2006).
13. Tiessen, H., Cuevas, E. & Salcedo, I. H. Organic matter stability and nutrient availability under temperate and tropical conditions. *Advances in GeoEcology* **31**, 415–422 (1997).
14. Gomes, A. F., Nobre, A. A. & Cruz, O. G. Temporal analysis of the relationship between dengue and meteorological variables in the city of Rio de Janeiro, Brazil, 2001–2009. *Cad. Saúde Publica* **28**, 2189–97 (2012).
15. Githeko, A. K., Ototo, E. N. & Guiyun, Y. Progress towards understanding the ecology and epidemiology of malaria in the western Kenya highlands: opportunities and challenges for control under climate change risk. *Acta Trop.* **121**, 19–25 (2012).
16. Haque, U. *et al.* The role of climate variability in the spread of malaria in Bangladeshi highlands. *PLoS ONE* **5**, e14341 (2010).
17. Rodrigues Sgrignolli, L., Florido Mendes, G. E., Carlos, C. P. & Burdmann, E. A. Acute kidney injury caused by bothrops snake venom. *Nephron Clin. Pract.* **119**, c131–c136; discussion c137 (2011).
18. Chugh, K. S. Snake-bite-induced acute renal failure in India. *Kidney Int.* **35**, 891–907 (1989).
19. WHO. *Health Topics* [online], http://www.who.int/topics/poverty/en/ (2011).
20. Jaffe, A. B. & Trajtenberg, M. *International knowledge flows: evidence from patent citations* [online], http://www.nber.org/papers/w6507.pdf (2013).
21. Hegde, H. V., Hegde, G. R. & Kholkute, S. D. Herbal care for reproductive health: ethno medicobotany from Uttara Kannada district in Karnataka, India. *Complement Ther. Clin. Pract.* **13**, 38–45 (2007).
22. Puckree, T., Mkhize, M., Mgobhozi, Z. & Lin, J. African traditional healers: what health care professionals need to know. *Int. J. Rehabil. Res.* **25**, 247–251 (2002).
23. Chugh, K. S., Jha, V. & Chugh, S. Economics of dialysis and renal transplantation in the developing world. *Transplant. Proc.* **31**, 3275–3277 (1999).
24. Cerda, J. *et al.* Epidemiology of acute kidney injury. *Clin. J. Am. Soc. Nephrol.* **3**, 881–886 (2008).
25. Cerda, J., Bagga, A., Kher, V. & Chakravarthi, R. M. The contrasting characteristics of acute kidney injury in developed and developing countries. *Nat. Clin. Pract. Nephrol.* **4**, 138–153 (2008).
26. Abraham, G., Gupta, R. K., Senthilselvan, A., van der Meulen, J. & Johny, K. V. Cause and prognosis of acute renal failure in Kuwait: a 2-year prospective study. *J. Trop. Med. Hyg.* **92**, 325–329 (1989).
27. Al-Homrany, M. Epidemiology of acute renal failure in hospitalized patients: experience from southern Saudi Arabia. *East. Mediterr. Health J.* **9**, 1061–1067 (2003).
28. Seedat, Y. K. & Nathoo, B. C. Acute renal failure in blacks and Indians in South Africa–comparison after 10 years. *Nephron* **64**, 198–201 (1993).
29. Thomas, C. N. *et al.* Coronary artery bypass graft outcome: the Trinidad and Tobago experience. *West Indian Med. J.* **49**, 290–293 (2000).
30. Vukusich, A. *et al.* Epidemiology of severe acute renal failure in Metropolitan Santiago [Spanish]. *Rev. Med. Chil.* **132**, 1355–1361 (2004).
31. Noronha, I. L. *et al.* Nephrology, dialysis and transplantation in Brazil. *Nephrol. Dial. Transplant.* **12**, 2234–2243 (1997).
32. Schissler, M. M. *et al.* Characteristics and Outcomes in Community-Acquired Versus Hospital-Acquired Acute Kidney Injury. *Nephrology (Carlton)* http://dx.doi:10.1111/nep.12036.
33. Chugh, K. S., Sakhuja, V., Malhotra, H. S. & Pereira, B. J. Changing trends in acute renal failure in third-world countries–Chandigarh study. *Q. J. Med.* **73**, 1117–1123 (1989).
34. Jayakumar, M. *et al.* Epidemiologic trend changes in acute renal failure–a tertiary center experience from South India. *Ren. Fail.* **28**, 405–410 (2006).
35. Basu, G. *et al.* Acute kidney injury in tropical acute febrile illness in a tertiary care centre–RIFLE criteria validation. *Nephrol. Dial. Transplant.* **26**, 524–531 (2011).
36. Dharan, K. S., John, G. T., Antonisamy, B., Kirubakaran, M. G. & Jacob, C. K. Prediction of mortality in acute renal failure in the tropics. *Ren. Fail.* **27**, 289–296 (2005).
37. Lombardi, R., Yu, L., Younes-Ibrahim, M., Schor, N. & Burdmann, E. A. Epidemiology of acute kidney injury in Latin America. *Semin. Nephrol.* **28**, 320–329 (2008).
38. Chugh, K. S. & Sakhuja, V. Glomerular diseases in the tropics. *Am. J. Nephrol.* **10**, 437–450 (1990).
39. Unni, V. N. Acute oxalate nephropathy due to 'Averrhoa bilimbi' fruit juice ingestion–A case series. *Indian J. Nephrol.* (in press).
40. Sitprija, V. & Boonpucknavig, V. The kidney in tropical snakebite. *Clin. Nephrol.* **8**, 377–383 (1977).
41. Ratcliffe, P. J., Pukrittayakamee, S., Ledingham, J. G. & Warrell, D. A. Direct nephrotoxicity of Russell's viper venom demonstrated in the isolated perfused rat kidney. *Am. J. Trop. Med. Hyg.* **40**, 312–319 (1989).
42. Gunatilake, M., Jayakody, R. L., Angunawela, P. & de Tissera, A. Direct nephrotoxic effects produced by venoms of Sri Lankan cobra, Russell's viper and hump nosed viper. *Ceylon J. Med. Sci.* **46**, 61–66 (2003).
43. Mishra, S. K. & Das, B. S. Malaria and acute kidney injury. *Semin. Nephrol.* **28**, 395–408 (2008).
44. Zager, R. A. Myoglobin depletes renal adenine nucleotide pools in the presence and absence of shock. *Kidney Int.* **39**, 111–119 (1991).
45. Mahasandana, S., Rungruxsirivorn, Y. & Chantarangkul, V. Clinical manifestations of bleeding following Russell's viper and Green pit viper bites in adults. *Southeast Asian J. Trop. Med. Public Health* **11**, 285–293 (1980).
46. Sitprija, V. & Boonpucknavig, V. in *Renal pathology with clinical and functional correlations* (eds Tisher, C. C. & Brenner, B. M.) 575 (Lippincott, Philadelphia, 1989).
47. Barosum, R. S. & Sitprija, V. Tropical Nephrology. in *Diseases of the Kidney and Urinary tract* (ed. Schrier, R. W.) 2013–2055 (Philadelphia, Lippincott, 2007).
48. Lameire, N., Van Biesen, W. & Vanholder, R. Acute renal failure. *Lancet* **365**, 417–430 (2005).
49. Schrier, R. W. & Wang, W. Acute renal failure and sepsis. *N. Engl. J. Med.* **351**, 159–169 (2004).
50. Chugh, K. S., Jha, V., Sakhuja, V. & Joshi, K. Acute renal cortical necrosis–a study of 113 patients. *Ren. Fail.* **16**, 37–47 (1994).
51. Chugh, K. S. *et al.* Spectrum of acute cortical necrosis in Indian patients. *Am. J. Med. Sci.* **286**, 10–20 (1983).
52. Gurrieri, C. *et al.* Kidney injury during pregnancy: associated comorbid conditions and outcomes. *Arch. Gynecol. Obstet.* **286**, 567–573 (2012).
53. Jha, V. & Sakhuja, V. Postpartum renal cortical necrosis. *Nephrol. Dial. Transplant.* **20**, 1010 (2005).
54. Bonetti, V. *et al.* Hemolytic-Uremic Syndrome in Uberländia, MG, Brazil. *ISRN Pediatr.* **2011**, 651–749 (2011).
55. Otukesh, H. *et al.* Prognosis of acute renal failure in children. *Pediatr. Nephrol.* **21**, 1873–1878 (2006).
56. Srivastava, R. N., Bagga, A. & Moudgil, A. Acute renal failure in north Indian children. *Indian J. Med. Res.* **92**, 404–408 (1990).
57. Jamal, A. & Ramzan, A. Renal and post-renal causes of acute renal failure in children. *J. Coll. Physicians Surg. Pak.* **14**, 411–415 (2004).
58. Date, A., Raghupathy, P., Jadhav, M., Pereira, S. M. & Shastry, J. C. Outcome of the haemolytic-uraemic syndrome complicating bacillary dysentery. *Ann. Trop. Paediatr.* **2**, 1–6 (1982).
59. Prakash, J. *et al.* Acute renal failure due to intrinsic renal diseases: review of 1122 cases. *Ren. Fail.* **25**, 225–233 (2003).
60. WHO. *WHO Fact sheet on Malaria* [online], http://www.who.int/mediacentre/factsheets/fs094/en/ (2011).
61. WHO. *World malaria report* [online], http://www.who.int/malaria/world_malaria_report_2011/9789241564403_eng.pdf (2011).
62. Naqvi, R., Ahmad, E., Akhtar, F., Naqvi, A. & Rizvi, A. Outcome in severe acute renal failure associated with malaria. *Nephrol. Dial. Transplant.* **18**, 1820–1823 (2003).

63. Prakash, J., Singh, A. K., Kumar, N. S. & Saxena, R. K. Acute renal failure in Plasmodium vivax malaria. *J. Assoc. Physicians India* **51**, 265–267 (2003).
64. Mehta, K. S. *et al.* Severe acute renal failure in malaria. *J. Postgrad. Med.* **47**, 24–26 (2001).
65. Jha, V. & Chugh, K. S. in *Critical Care Nephrology* (eds Ronco, C., Bellomo, R. & Kellum, J.) 850–856 (Saunders Elsevier, Philadelphia, 2009).
66. WHO. *Guidelines for the treatment of malaria* [online], http://whqlibdoc.who.int/publications/2010/9789241547925_eng.pdf (2010).
67. Koh, K. H., Chew, P. H. & Kiyu, A. A retrospective study of malaria infections in an intensive care unit of a general hospital in Malaysia. *Singapore Med. J.* **45**, 28–36 (2004).
68. Zinna, S., Vathsala, A. & Woo, K. T. A case series of falciparum malaria-induced acute renal failure. *Ann. Acad. Med. Singapore* **28**, 578–582 (1999).
69. WHO. *Leptospirosis situation in the WHO South East Asia region* [online], http://209.61.208.233/LinkFiles/Communicable_Diseases_Surveillance_and_response_SEA-CD-216.pdf (2013).
70. WHO. *Leptosiposis fact sheet* [online], http://new.paho.org/HQ/index.php?option=com_content&view=article&id=7821&Itemid=39696&lang=en (2013).
71. Ricaldi, J. N. & Vinetz, J. M. Leptospirosis in the tropics and in travelers. *Curr. Infect. Dis. Rep.* **8**, 51–58 (2006).
72. Andrade, L., de Francesco Daher, E. & Seguro, A. C. Leptospiral nephropathy. *Semin. Nephrol.* **28**, 383–394 (2008).
73. Ittyachen, A. M., Krishnapillai, T. V., Nair, M. C. & Rajan, A. R. Retrospective study of severe cases of leptospirosis admitted in the intensive care unit. *J. Postgrad. Med.* **53**, 232–235 (2007).
74. Muthusethupathi, M. A. *et al.* Leptospirosis in Madras–a clinical and serological study. *J. Assoc. Physicians India* **43**, 456–458 (1995).
75. Sitprija, V., Losuwanrak, K. & Kanjanabuch, T. Leptospiral nephropathy. *Semin. Nephrol.* **23**, 42–48 (2003).
76. Levett, P. N. in *Manual of Clinical Microbiology* (ed. Murray, P. R.) 929–936 (ASM Press, Washington DC, 2003).
77. Ahmed, A., Engelberts, M. F., Boer, K. R., Ahmed, N. & Hartskeerl, R. A. Development and validation of a real-time PCR for detection of pathogenic leptospira species in clinical materials. *PLoS ONE* **4**, e7093 (2009).
78. McBride, A. J., Athanazio, D. A., Reis, M. G. & Ko, A. I. Leptospirosis. *Curr. Opin. Infect. Dis.* **18**, 376–386 (2005).
79. Hayat, A. *et al.* Peritoneal dialysis for adults with acute renal failure: an underutilized modality. *Saudi J. Kidney Dis. Transpl.* **18**, 195–199 (2007).
80. Choudhry, V. P., Srivastava, R. N., Vellodi, A., Bhuyan, U. N. & Ghai, O. P. A study of acute renal failure. *Indian Pediatr.* **17**, 405–410 (1980).
81. Chugh, K. S. *et al.* Acute renal failure amongst children in a tropical environment. *Int. J. Artif. Organs* **10**, 97–101 (1987).
82. Lee, W. S. & Ooi, T. L. Deaths following acute diarrhoeal diseases among hospitalised infants in Kuala Lumpur. *Med. J. Malaysia* **54**, 303–309 (1999).
83. UNAIDS. *Report on the Global AIDS Epidemic* [online], http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120_UNAIDS_Global_Report_2012_en.pdf (2012).
84. Wyatt, C. M., Arons, R. R., Klotman, P. E. & Klotman, M. E. Acute renal failure in hospitalized patients with HIV: risk factors and impact on in-hospital mortality. *AIDS* **20**, 561–565 (2006).
85. Choi, A. I., Li, Y., Parikh, C., Volberding, P. A. & Shlipak, M. G. Long-term clinical consequences of acute kidney injury in the HIV-infected. *Kidney Int.* **78**, 478–485 (2010).
86. Kalim, S., Szczech, L. A. & Wyatt, C. M. Acute kidney injury in HIV-infected patients. *Semin. Nephrol.* **28**, 556–562 (2008).
87. Jha, V. & Rathi, M. Natural medicines causing acute kidney injury. *Semin. Nephrol.* **28**, 416–428 (2008).
88. Adelekun, T. A., Ekwere, T. R. & Akinsola, A. The pattern of acute toxic nephropathy in Ife, Nigeria. *West Afr. J. Med.* **18**, 60–63 (1999).
89. Luyckx, V. A., Steenkamp, V. & Stewart, M. J. Acute renal failure associated with the use of traditional folk remedies in South Africa. *Ren. Fail.* **27**, 35–43 (2005).
90. Segasothy, M., Swaminathan, M., Kong, N. C. & Bennett, W. M. Djenkol bean poisoning (djenkolism): an unusual cause of acute renal failure. *Am. J. Kidney Dis.* **25**, 63–66 (1995).
91. Areekul, S. & Kirdudom, P. Studies on the chemical components and toxic substances in niang beans. *J. Med. Assoc. Thai.* **60**, 3–8 (1977).
92. West, C. E., Perrin, D. D., Shaw, D. C., Heap, G. H. & Soemanto. Djenkol bean poisoning (djenkolism): proposals for treatment and prevention. *Southeast Asian J. Trop. Med. Public Health* **4**, 564–570 (1973).
93. Hutchings, A. & Terblanche, S. E. Observations on the use of some known and suspected toxic Liliiflorae in Zulu and Xhosa medicine. *S. Afr. Med. J.* **75**, 62–69 (1989).
94. Steenkamp, V. & Stewart, M. J. Nephrotoxicity associated with exposure to plant toxins, with particular reference to Africa. *Ther. Drug Monit.* **27**, 270–277 (2005).
95. Centers for Disease Control and Prevention. Hepatic and renal toxicity among patients ingesting sheep bile as an unconventional remedy for diabetes mellitus-Saudi Arabia-1995. *MMWR Morb. Mortal. Wkly Rep.* **45**, 941–943 (1996).
96. Park, S. K. *et al.* Toxic acute renal failure and hepatitis after ingestion of raw carp bile. *Nephron* **56**, 188–193 (1990).
97. Kasturiratne, A. *et al.* The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Med.* **5**, e218 (2008).
98. Mohapatra, B. *et al.* Snakebite mortality in India: a nationally representative mortality survey. *PLoS Negl. Trop. Dis.* **5**, e1018 (2011).
99. Chugh, K. S. *et al.* Acute renal failure following poisonous snakebite. *Am. J. Kidney Dis.* **4**, 30–38 (1984).
100. Kanjanabuch, T. & Sitprija, V. Snakebite nephrotoxicity in Asia. *Semin. Nephrol.* **28**, 363–372 (2008).
101. Pinho, F. M., Zanetta, D. M. & Burdmann, E. A. Acute renal failure after Crotalus durissus snakebite: a prospective survey on 100 patients. *Kidney Int.* **67**, 659–667 (2005).
102. Abdulkader, R. C., Barbaro, K. C., Barros, E. J. & Burdmann, E. A. Nephrotoxicity of insect and spider venoms in Latin America. *Semin. Nephrol.* **28**, 373–382 (2008).
103. Cuoghi, D., Venturi, P. & Cheli, E. Bee sting and relapse of nephrotic syndrome. *Child Nephrol. Urol.* **9**, 82–83 (1988).
104. Kumar, V. *et al.* acute kidney injury due to acute cortical necrosis following a single wasp sting. *Ren. Fail.* **35**, 170–172 (2013).
105. Vikrant, S. & Patial, R. K. Acute renal failure following multiple honeybee stings. *Indian J. Med. Sci.* **60**, 202–204 (2006).
106. Okuonghae, H. O., Ighogboja, I. S., Lawson, J. O. & Nwana, E. J. Diethylene glycol poisoning in Nigerian children. *Ann. Trop. Paediatr.* **12**, 235–238 (1992).
107. Singh, J. *et al.* Diethylene glycol poisoning in Gurgaon, India, 1998. *Bull. World Health Organ.* **79**, 88–95 (2001).
108. Khan, M. Glucose 6 phosphate dehydrogenase deficiency in adults. *J. Coll. Physicians Surg. Pak.* **14**, 400–403 (2004).
109. Chugh, K. S. *et al.* Acute renal failure due to intravascular hemolysis in the North Indian patients. *Am. J. Med. Sci.* **274**, 139–146 (1977).
110. Sarkar, S. *et al.* Acute intravascular haemolysis in glucose-6-phosphate dehydrogenase deficiency. *Ann. Trop. Paediatr.* **13**, 391–394 (1993).
111. Wanachiwanawin, W. & Piankijagum, A. Severe hyperbilirubinemia in glucose-6-phosphate dehydrogenase deficient patients during viral hepatitis. *J. Med. Assoc. Thai* **73**, 552–555 (1990).
112. Chijioke, A., Makusidi, A. M. & Rafiu, M. O. Factors influencing hemodialysis and outcome in severe acute renal failure from Ilorin, Nigeria. *Saudi J. Kidney Dis. Transpl.* **23**, 391–396 (2012).
113. Okunola, O. O., Ayodele, O. E. & Adekanle, A. D. Acute kidney injury requiring hemodialysis in the tropics. *Saudi J. Kidney Dis. Transpl.* **23**, 1315–1319 (2012).
114. Ali, A., Ali, M. A., Ali, M. U. & Mohammad, S. Hospital outcomes of obstetrical-related acute renal failure in a tertiary care teaching hospital. *Ren. Fail.* **33**, 285–290 (2011).
115. Bentata, Y., Housni, B., Mimouni, A., Azzouzi, A. & Abouqal, R. Acute kidney injury related to pregnancy in developing countries: etiology and risk factors in an intensive care unit. *J. Nephrol.* **25**, 764–775 (2012).
116. Erdemoglu, M., Kuyumcuoglu, U., Kale, A. & Akdeniz, N. Pregnancy-related acute renal failure in the southeast region of Turkey: analysis of 75 cases. *Clin. Exp. Obstet. Gynecol.* **37**, 148–149 (2010).
117. Sivakumar, V. *et al.* Pregnancy-related acute renal failure: a ten-year experience. *Saudi J. Kidney Dis. Transpl.* **22**, 352–353 (2011).
118. Zewdu, W. Acute renal failure in Addis Abeba, Ethiopia: a prospective study of 136 patients. *Ethiop. Med. J.* **32**, 79–87 (1994).
119. Firmat, J., Zucchini, A., Martin, R. & Aguirre, C. A study of 500 cases of acute renal failure (1978–1991). *Ren. Fail.* **16**, 91–99 (1994).
120. Ponte, B., Felipe, C., Muriel, A., Tenorio, M. T. & Liano, F. Long-term functional evolution after an acute kidney injury: a 10-year study. *Nephrol. Dial. Transplant.* **23**, 3859–3866 (2008).
121. Triverio, P. A. *et al.* Long-term prognosis after acute kidney injury requiring renal replacement therapy. *Nephrol. Dial. Transplant.* **24**, 2186–2189 (2009).
122. Sinha, R., Nandi, M., Tullus, K., Marks, S. D. & Taraphder, A. Ten-year follow-up of children after acute renal failure from a developing country. *Nephrol. Dial. Transplant.* **24**, 829–833 (2009).
123. Coca, S. G., Singanamala, S. & Parikh, C. R. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. *Kidney Int.* **81**, 442–448 (2012).
124. Xu, K. *et al.* Household catastrophic health expenditure: a multicountry analysis. *Lancet* **362**, 111–117 (2003).
125. Sakhuja, V. & Kohli, H. S. in *Brenner and Rector's The Kidney* (eds Taal, M. *et al.*) 2770–2785 (Saunders, 2011).
126. Chugh, K. S. Changing spectrum of community acquired AKI in Asia. Presented at the 8th Asian pacific Congress of Nephrology.

127. Anonymous. *Climate Change and Health Impacts* [online], http://www.cleanairchampions.ca/database/files/bg_climatechangeandhealth.pdf (2012).
128. WHO. *Climate change and health* [online], http://www.who.int/mediacentre/factsheets/fs266/en/ (2012).
129. Hamoudi, A. & Sachs, J. D. The changing global distribution of malaria: A review. Harvard Kennedy School [online], http://www.hks.harvard.edu/var/ezp_site/storage/fckeditor/file/pdfs/centers-programs/centers/cid/publications/faculty/wp/002.pdf (2013).
130. National Institute of Health and Family Welfare. *National Anti-malaria Program* [online], http://www.nihfw.org/NDC/DocumentationServices/NationalHealthProgramme/NATIONALANTI-MALARIAPROGRAMME.html (2012).
131. WHO. *Malaria Control: the power of integrated action* [online], http://www.who.int/heli/risks/vectors/malariacontrol/en/ (2012).
132. WHO. *Handbook for integrated vector management* [online], http://whqlibdoc.who.int/publications/2012/9789241502801_eng.pdf (2013).
133. van den Berg, H. *et al.* Status of pesticide management in the practice of vector control: a global survey in countries at risk of malaria or other major vector-borne diseases. *Malar. J.* **10**, 125 (2011).
134. Clennon, J. A., Kamanga, A., Musapa, M., Shiff, C. & Glass, G. E. Identifying malaria vector breeding habitats with remote sensing data and terrain-based landscape indices in Zambia. *Int. J. Health Geogr.* **9**, 58 (2010).
135. Lou, Y. & Zhao, X. Q. Modelling malaria control by introduction of larvivorous fish. *Bull. Math. Biol.* **73**, 2384–2407 (2011).
136. Mohandas, N. & Chellapandian, D. Value of intermittent peritoneal dialysis in rural setup. *Indian J. Perit. Dial.* **6**, 19–20 (2004).
137. Kohli, H. S. *et al.* Daily peritoneal dialysis using a surgically placed Tenckhoff catheter for acute renal failure in children. *Ren. Fail.* **17**, 51–56 (1995).
138. Gabriel, D. P., Caramori, J. T., Martim, L. C., Barretti, P. & Balbi, A. L. High volume peritoneal dialysis vs daily hemodialysis: a randomized, controlled trial in patients with acute kidney injury. *Kidney Int. Suppl.* **108**, S87–S93 (2008).
139. George, J. *et al.* Comparing continuous venovenous hemodiafiltration and peritoneal dialysis in critically ill patients with acute kidney injury: a pilot study. *Perit. Dial. Int.* **31**, 422–429 (2011).
140. Firmat, J. & Pas, R. 1000 patients with acute renal failure—clinical and pathological observations. Presented at the VI International Congress of Nephrology.
141. Sitprija, V. & Benyajati, C. Tropical diseases and acute renal failure. *Ann. Acad. Med. Singapore* **4** (Suppl. 4), 112–114 (1975).
142. Adu, D. *et al.* Acute renal failure in tropical Africa. *Br. Med. J.* **1**, 890–892 (1976).
143. Chugh, K. S. *et al.* Spectrum of acute renal failure in North India. *J. Assoc. Physicians India* **26**, 147–154 (1978).
144. Shah, P. P., Trivedi, H. L., Sharma, R. K., Shah, P. R. & Joshi, M. N. Acute renal failure, experience of 816 patients in the tropics. Presented at the XVth Annual Conference of the Indian Society of Nephrology.
145. Muthusethupathi, M. A. & Shivakumar, S. Acute renal failure in south India. Our experience with 187 patients. *J. Assoc. Physicians India* **35**, 504–507 (1987).
146. Bamgboye, E. L., Mabayoje, M. O., Odutola, T. A. & Mabadeje, A. F. Acute renal failure at the Lagos University Teaching Hospital: a 10-year review. *Ren. Fail.* **15**, 77–80 (1993).
147. Ramachandran, S. in *Asian Nephrology* (ed. Chugh, K. S.) 378–383 (Oxford University Press, New Delhi, 1994).
148. Olowu, W. A. & Adelusola, K. A. Pediatric acute renal failure in southwestern Nigeria. *Kidney Int.* **66**, 1541–1548 (2004).
149. Al Rohani, M., Aljawshaei, H. & Aduolimi, E. Acute renal failure in Yemeni patients. *Saudi J. Kidney Dis. Transpl.* **22**, 829–833 (2011).
150. Burdmann, E., Jha, V. & Sitprija, V. in *Comprehensive Clinical Nephrology* 4th edn Ch. 67 (eds Floege, J., Johnson, R. J. & Feehally, J.) 813–820 (Saunders Elsevier, St Louis, 2011).

Author contributions
V. Jha and S. Parameswaran contributed equally to discussion of content for the article, researching data for and writing the manuscript. V. Jha reviewed and edited the manuscript before submission.