Raising awareness of acute kidney injury: a global perspective of a silent killer

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Worldwide, acute kidney injury (AKI) is associated with poor patient outcomes. Over the last few years, collaborative efforts, enabled by a common definition of AKI, have provided a description of the epidemiology, natural history, and outcomes of this disease and improved our understanding of the pathophysiology. There is increased recognition that AKI is encountered in multiple settings and in all age groups, and that its course and outcomes are influenced by the severity and duration of the event. The effect of AKI on an individual patient and the resulting societal burden that ensues from the long-term effects of the disease, including development of chronic kidney disease (CKD) and end-stage renal disease (ESRD), is attracting increasing scrutiny. There is evidence of marked variation in the management of AKI, which is, to a large extent, due to a lack of awareness and an absence of standards for prevention, early recognition, and intervention. These emerging data point to an urgent need for a global effort to highlight that AKI is preventable, its course is modifiable, and its treatment can improve outcomes. In this article, we provide a framework of reference and propose specific strategies to raise awareness of AKI globally, with the goal to ultimately improve outcomes from this devastating disease.

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Acute kidney injury (AKI) is now well established as a common, often underrecognized disorder, which is associated with a high risk for mortality, development of chronic kidney disease (CKD), and other organ dysfunction. This condition has both short- and long-term effects on functional status, and leads to increased resource utilization.[1–3] Several studies have confirmed that although the course of AKI is variable based on the setting where it occurs, the severity and duration of AKI determines outcomes, including dialysis requirement, renal functional recovery, and survival.[4,5] There is increasing recognition of both the effect of AKI on the individual patient and the resulting societal burden ensuing from its long-term effects, including development of CKD and end-stage renal disease (ESRD) requiring dialysis or transplantation.[6]

Data derived from high-income (HI) countries, using standardized definitions for diagnosis and staging of AKI, have facilitated comparisons of incidence and outcomes in different clinical settings.[7] Conversely, a paucity of information on the prevalence, course, and outcomes of AKI in low- and middle-income (LMI) countries contributes to a somewhat biased view of AKI as a disease of hospitalized patients. In LMI countries, although the majority of urban cases occur in the context of acute illness, usually in association with hypovolemia and sepsis, AKI occurring in the community (for example, diarrheal states, malaria) is underrecognized.[8,9]

Despite emerging data and increasing interest in AKI as a major contributor to adverse outcomes, there is still considerable lack of understanding of the condition among physicians, allied personnel, and the lay public. As a result, systematic efforts have been limited and few resources have been allocated to inform health-care professionals and the public of the importance of AKI as a preventable and treatable disease. Recent publications have highlighted deficiencies and wide variation in the care of AKI patients worldwide.[10,11] These reports have demonstrated missed opportunities to prevent and detect AKI, and suboptimal management.

AKI is encountered in multiple settings and is commonly first encountered by nonspecialized health-care providers, either in the community or the hospital setting. As AKI is not associated with any specific symptoms and the diagnosis is

largely based on measurement of lab parameters, it is essential that caregivers be educated on the risks for AKI and equipped with the knowledge for early recognition, timely intervention, and effective follow-up.

This article provides a rationale and a proposal for a calibrated approach to raise awareness of the incidence and consequences of AKI to all potential stakeholders, including patients. Our ultimate goal is to improve the recognition and timely management of this silent killer, and to emphasize the need for collaboration among all those involved in the care of these patients.

WHY DO WE NEED TO RAISE AWARENESS OF THE IMPORTANCE OF AKI?

AKI is common worldwide and is encountered in multiple settings but remains poorly recognized

The incidence of AKI worldwide varies widely across different studies and is largely dependent on the setting (hospital-acquired (h-AKI) vs. community-acquired (c-AKI)) and the at-risk populations investigated. It affects between 7 and 18% of hospital inpatients[12–15] and ranges from 20 to 200 per million population in the community (Tables 1 and 2).[16] h-AKI is more common in the elderly; patients presenting with c-AKI are usually younger and healthier.[17] In HI countries, although mild AKI developing in the general hospital ward has become less common, more severe forms in the intensive care unit have become predominant. Among critically ill patients, the incidence of AKI varies between 30 and 70%; ~5% of intensive care unit admissions require renal replacement therapy (RRT).[18] In LMI countries, clinical presentation of AKI is dependent on location: whereas in larger cities, intensive care unit–acquired h-AKI predominates, in rural areas, c-AKI is more common.

The etiology of h-AKI in urban areas of both HI and LMI countries is similar, but treatment resources differ widely.[18–20] Hospital-acquired AKI develops in the intensive care unit, in the context of multiple organ failure, postcardiovascular procedures or sepsis, or as a complication of nephrotoxic medications. Patients affected are generally elderly, obese, and diabetic. Conversely, the etiology of c-AKI differs considerably between HI and LMI countries. In LMI countries, AKI is often a disease of the young, caused by specific infections or toxins resulting in diarrhea and hypovolemia. Etiology is dependent on geographical location and may be secondary to infectious agents such as malaria, leptospirosis, dengue, envenomation (snakes or arthropods), and be subject to seasonal variation. In those regions, HIV disease, obstetric complications (for example, septic abortion), or intoxications (often caused by traditional herbs or household products) are prevalent.[21–27]

A common factor across HI and LMI countries is that most cases of AKI are managed by nonnephrologists, who may be unfamiliar with the risk factors and early manifestations of the disease. This contributes to delayed recognition and suboptimal management. For instance, fluid accumulation decreases serum creatinine concentration by increasing total body water, thus contributing to delayed diagnosis and underestimation of the severity of AKI.[28,29]

The quality of care delivered to hospitalized patients with AKI has been recently reviewed in different studies and revealed large gaps in the care including delayed recognition, inadequate investigations, deficient monitoring, delayed and often flawed management, and lack of follow-up.[30,31] These findings were encountered even when nephrologists were available and illustrate the clear need for educating caregivers in all disciplines regarding this disorder.

In LMI countries, insufficient and late recognition is even more problematic in both community and hospital settings. Late recognition leads to delayed management, by which time associated morbidity and mortality have worsened considerably. Late recognition may account for the apparently 10-fold lower incidence in LMI countries: it is likely that AKI cases are underreported because of several factors, including access to appropriate medical care, lack of knowledge, and nonavailability of standard tests that are considered routine in the developed world (for example, serum creatinine). As an example, a recent report describes an 'epidemic' of kidney disease in Central America that is blamed for several deaths annually in impoverished sugarcane workers across Nicaragua, Costa Rica, El Salvador, and Guatemala. It is believed that the condition results from repetitive episodes of AKI secondary to dehydration. Standard work days of 12–14 h, with double shifts during the summer planting season when temperatures top 40 °C likely cause heat stroke, rhabdomyolysis, and AKI. Alternative mechanisms including environmental toxins and pesticides are being evaluated.[32] Survivors develop a disproportionate degree of CKD. Limited resources make chronic dialysis treatment unlikely, thus making the condition quite deadly.

AKI contributes to adverse outcomes including CKD and mortality

Several epidemiological studies have demonstrated the independent association of AKI with a higher risk of death. As severity increases so does mortality, which is highest among patients requiring RRT (50–60%) (Figure 1).[8] Duration and severity of AKI predict progression to CKD

Table 1 | Reported incidence of AKI in high-income (HI) and low- and middle-income (LMI) countries

	Community acquired	Change in incidence	Hospital acquired	Change in incidence
HI countries	200 PMP	51–62%	60–288/ 100,000 Pop	6.8 Times increase; 11%/year increase
LMI countries	20 PMP	No significant change	5.4/100,000 Pop	1.06 Increase over 5 years

Abbreviations: AKI, acute kidney injury; PMP, per million population; POP, population.
Modified from Cerda *et al.*[8]