Acute Kidney Injury Risk Recognition in Resource-Sufficient Versus Resource-Limited Regions

Nooshin Dalili,[1,2] Kianoush Kashani[3,4]

[1]Department of Nephrology, Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Chronic Kidney Disease Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Division of Nephrology and Hypertension, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA
[4]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA

Acute kidney injury is a very common complication of acute illnesses with dire consequences. There are significant differences in incidence, etiology, severity, and clinical impact of acute kidney injury between resource-sufficient and resource-limited regions. Awareness of such differences would potentially allow clinicians and policymakers to devise and provide region-specific interventions to decrease the incidence of acute kidney injury and mitigate its complications. In this review article, we describe the similarities and differences of acute kidney injury risk factors and risk stratifications based on the level of resource availability in different regions. We also outline differences between community- and hospital-acquired acute kidney injury in different countries. In the end, we outline the potential steps need to be taken to mitigate incidence and clinical impacts of acute kidney injury in both resource-sufficient and resource-limited regions.

INTRODUCTION

Acute kidney injury (AKI) is a very common complication of critical illnesses with significant burden both at individual and society levels. The cost of care for AKI among high-income countries reaches to about 1 billion dollars per year.[1] Acute kidney injury occurs in approximately 2 million individuals within developed countries, of whom about 10% to 15% die, and among survivors, end-stage kidney disease is observed in 10%, and another 20% develop advanced chronic kidney disease (CKD). This impact is even more palpable in the developing countries as the care of about 11.3 million patients with AKI annually leads to 5.6 billion dollars cost of care for patients with advanced CKD an end-stage kidney disease. This additional cost among the developing countries can impact the economy of these regions and the quality of care provided to all individuals.[1]

Susantitaphong and coworkers conducted a meta-analysis to assess the incidence of AKI across the globe. By including more than 300 studies, mostly from north hemisphere and high-income countries (82%), and the inclusion of nearly 50 million patients the AKI incidence was estimated to be 21.6% in adults with associated mortality rates of about 23.9%.[2] The authors showed by accepting the Kidney Disease: Improving Global Outcomes definition for AKI, about 1 in 5 adults end up with AKI during each hospitalization. Considering the significant burden of AKI, it is only rational to devise interventions to avoid AKI development and mitigate its consequences. In order to achieve this objective, identifying patients who are at risk for AKI is one of the most necessary first steps. In this review article, we summarize and compare the current literature focused on AKI prediction and risk stratification in resource-sufficient versus resource-limited global regions.

ACUTE KIDNEY INJURY RISK FACTORS

In the recent Acute Disease Quality Initiative consensus conference held in Hyderabad, India, the participants suggested AKI risk factors to

be divided into 4 levels (population, healthcare system, provider, and patient), and 5 dimensions (inherent risk factors, exposures, processes of care, social economic and cultural, and environmental; Figure 1).[3] The inherent risk factors are mostly nonmodifiable comorbid conditions that can result in increased chances of AKI among patients that are exposed to injurious entities (eg, nephrotoxins, sepsis, and hypotension). Among the inherent risk factors, age is one of the most effective AKI risks. The impact of age on the development of AKI is so significant that among elderly patients, other risk factors (eg, chronic kidney disease, hypertension, and diabetes mellitus) have a reduced impact on risk of AKI development.[4] In addition, the number of risk factors for AKI increases with age.[5] Indeed, it seems using age alone could be as powerful predictor of AKI as many other models that include other risk factors.[5] The type of exposures and quality of care provided to the critically ill patient can significantly impact the risk of AKI.[6] While among developing countries

AKI happens mostly on younger individuals due to infection, envenomation, or obstetrics-related issues, within the developed countries, using nephrotoxins, sepsis with multiorgan failure in the setting of a significant number of comorbid conditions among older individuals attributes to the majority of AKI cases.[3] The impact of each specific exposure on the AKI risk could be different based on the resource availability. For example, sepsis-associated AKI among patients who have access to health insurance, and tertiary hospital potentially is associated with a better outcome in comparison with the areas that have very limited resources to provide appropriate care to such patients, given similar risk profile among the two examples. The factors that make these differences are mainly focused on socioeconomic, cultural, and environmental factors. Therefore, interventions to mitigate this kind of risk factors among developing countries at the population level may provide more benefit than focusing on inherent risk factors. In contrast, within the developed countries where
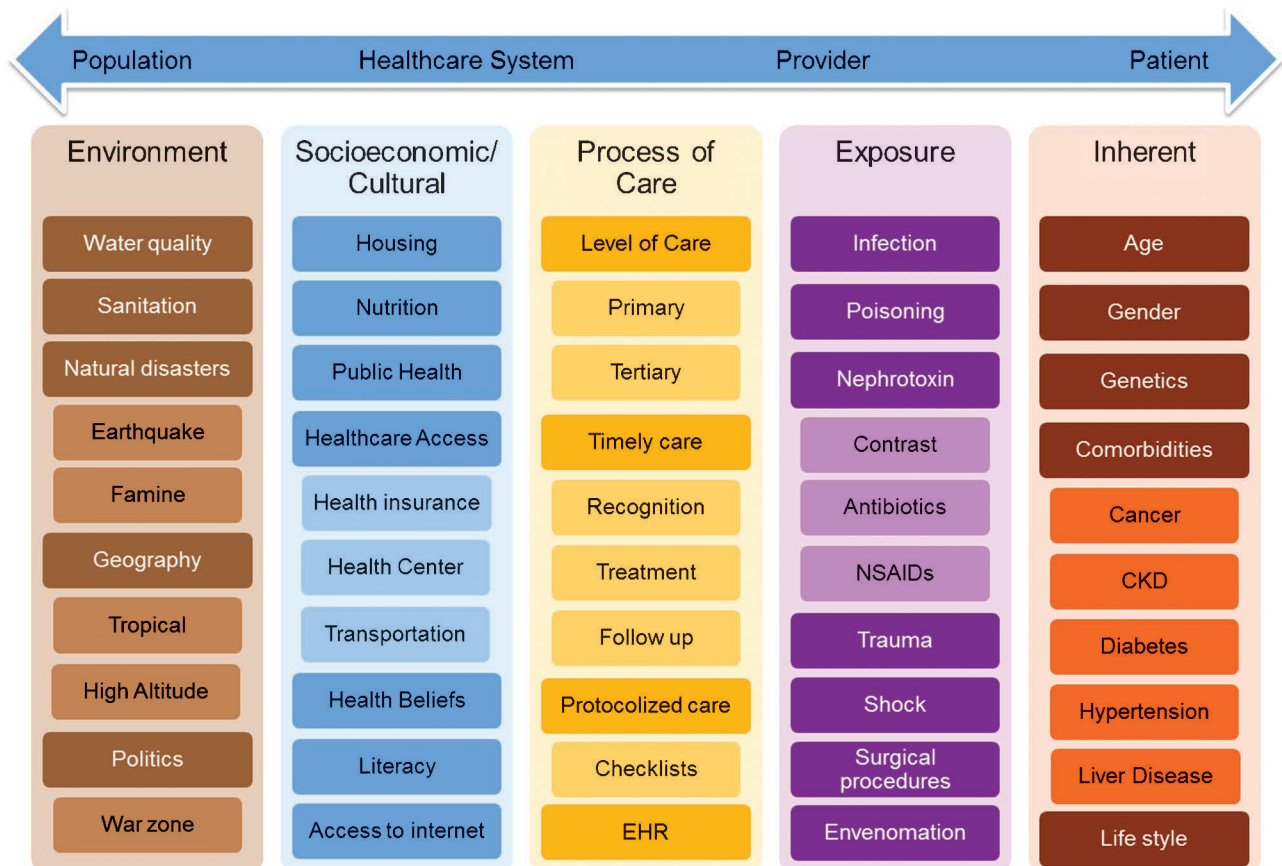

Figure 1. Acute kidney injury risk levels and dimensions. Adapted from the Acute Disease Quality Initiative with permission.[3] CKD indicates chronic kidney disease; NSAID, nonsteroidal anti-inflammatory drugs; and EHR, electronic health records.

access to health care is widely available, the impact of inherent risk factors on the incidence of AKI is more palpable.

ACUTE KIDNEY INJURY RISK ASSESSMENT

There are several AKI risk stratification models used for specific subgroups of patients. Mehran and colleagues published a simple model of risk prediction score in 2004 for contrast-associated AKI following percutaneous coronary intervention. This model includes 8 variables including hypotension, use of intra-aortic balloon pump, history of congestive heart failure, CKD or diabetes mellitus, an age greater than 75 years, presence of anemia, and volume of used contrast media as independent risk factors with an area under the curve (AUC) of receiver operating characteristic of about 0.67. This model uses a few variables indicating exposure including the use of intra-aortic balloon pump and the dose of contrast, while the other variables are among chronic and non-modifiable comorbid conditions.[7] Thakar and coworkers described a risk stratification model for cardiovascular surgery-associated AKI. Among variables used in this model female sex, a left ventricular ejection fraction less than 35%, chronic obstructive pulmonary disease, insulin-requiring diabetes mellitus, congestive heart failure, history of previous cardiac surgery, and preoperative creatinine level are all nonmodifiable comorbid conditions. The only exposure variables in this model include the perioperative use of intra-aortic balloon pump and emergency nature of the procedure, along with the type of surgery. The investigators reported AUC of this model as 0.82. [8] In a large-scale study of individuals who underwent general surgical procedures the incidence of AKI was found to be about 1%. To identify patients at higher risk of AKI a model including an age greater than 56 years, male sex, emergency nature of the procedure, intraperitoneal surgery, diabetes mellitus treated with oral agents, insulin-dependent diabetes mellitus, history of congestive heart failure and hypertension, presence of ascites, and mild or moderate preoperative CKD was reported to provide good performance with AUC of 0.80. About 9% of patients who had 6 or more risk factors developed AKI. Like previously mentioned models this model also includes a significant number of nonmodifiable comorbid conditions.[9]

Recently, there have been several clinical models that could be applied to all intensive care unit or hospital patients with excellent performance in AKI prediction. These models use extant clinical data within the medical records. Malhotra and coworkers reported a very simple clinical model for all intensive care unit (ICU) patients including chronic comorbid conditions in acute exposures for AKI prediction that was externally validated. This clinical model included chronic conditions (ie, CKD, chronic liver disease, congestive heart failure, hypertension, and atherosclerosis coronary vascular disease) along with acute variables (ie, pH < 7.3, nephrotoxin exposure, severe infection or sepsis, need for mechanical ventilation, and anemia) and was able to provide AUC of 0.81.[10] Koyner and colleagues described the derivation and validation of several AKI risk stratification models for patients were admitted to the hospital. These models included easily available clinical, demographic, laboratory, and hemodynamic variables. They evaluated the performance of the model for different levels of AKI severity. Their highest performer model for AKI stage 3 had AUC of 0.83.[11] The same lead investigator and colleagues recently reported a machine learning model for prediction of inpatient AKI stages 2 and 3 by using clinically extant data including changes in serum creatinine and blood urea nitrogen. The performance of this model was found to be excellent with AUC of 0.93 for prediction of AKI stage 3.[12] Flechet and coworkers reported another clinical model for all ICU patients using machine learning tools (random forest model) to devise 4 separate models based on the availability of data and found an excellent performance for these models in AKI prediction.[13] One of the important features of the more modern models is the fact that they can be calculated automatically.

Despite significant progress that has been made over the course of last 2 decades in development and validation of AKI risk stratification models, the current models still suffer from substantial limitations (Table 1). The majority of current models are disease specific (eg, cardiovascular surgery, contrast exposure, etc). In addition, a greater number of them have been validated within areas with sufficient resource availability and focused on hospital-acquired AKI. Concentration on inherent risk factors and limited use of variables related to

Table 1. Limitations of Current Acute Kidney Injury Risk Prediction Models

Limitations
● Disease-specific
● Mostly from developed countries
● Mostly for hospital-acquired acute kidney injury
● Mostly focused on inherent risk factors
● Limited evaluation of providers, healthcare systems, and population-level factors
● Limited use of the process of care quality indexes

the quality of care are among the other limitations of such models. Most of the current models focus on patients risks and do not emphasize the role of providers, healthcare systems, and populations on the development and progress of AKI. Hence, the future studies should focus on combining the current AKI risk stratification models with factors that can impact AKI risks on other dimensions and levels of care (Figure 2). For example, the future models should assign different AKI risk score to diabetic patients with chronic kidney disease who seeks medical attention due to septic shock

in places that have different levels of access to healthcare systems.[3]

COMMUNITY- VERSUS HOSPITAL-ACQUIRED ACUTE KIDNEY INJURY

There are significant differences between community- and hospital-acquired AKI. As shown in Table 2, in developing regions, community acquired in comparison with hospital-acquired AKI is more common and happens mostly among younger individuals with limited comorbid conditions due to exposures like infection, venoms, dehydration, nephrotoxic agents and obstetrical issues (post-delivery bleeding) which leads to single organ failure with a higher chance of recovery.[14,15] In contrary, in resource-sufficient regions, AKI cases occur mainly as a complication of hospitalization and mostly seen in older patients with multiple comorbid conditions due to sepsis and multi-organ failure.[16]

In a study by Wonnacott and colleagues, investigators used electronic medical records to
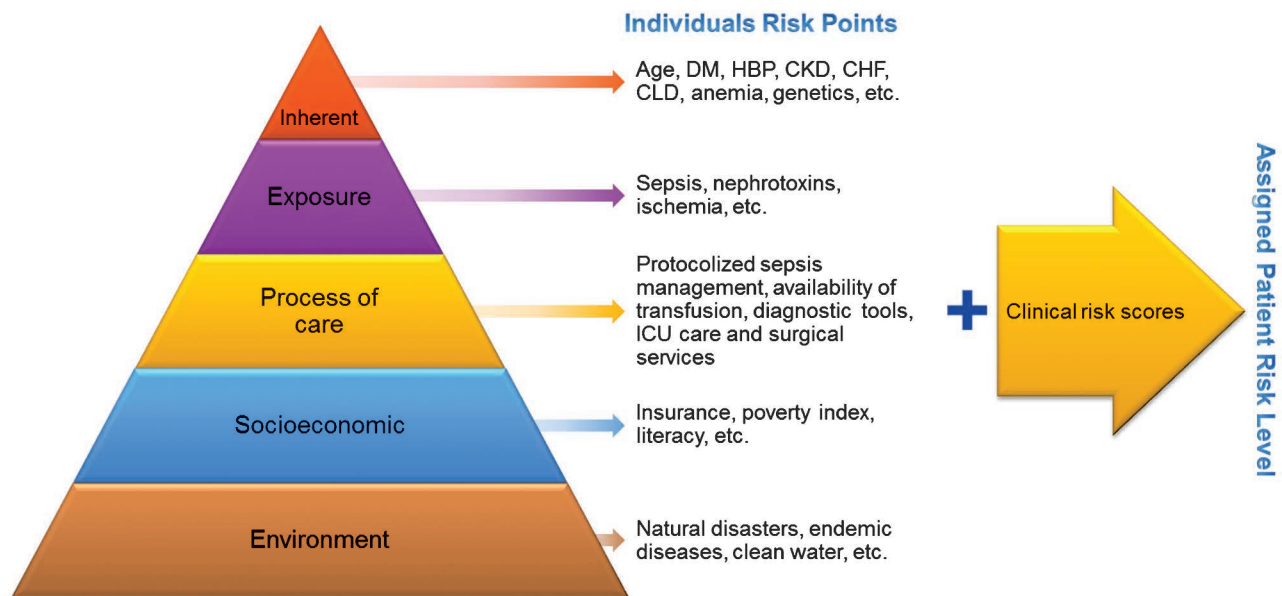

Figure 2. Acute kidney injury risk stratification. Adapted from the Acute Disease Quality Initiative with permission.[3] DM indicates diabetes mellitus; HBP, high blood pressure; CKD, chronic kidney disease; CHF, congestive heart failure; CLD, chronic liver disease; and ICU, intensive care unit.

Table 2. Differences in Acute Kidney Injury Among Low Resource Versus High Resource Availability Regions

Low Resource Availability	High Resource Availability
Mostly community-acquired	Combination of community- and hospital-acquired
Majority of patients being young with limited comorbidities	Majority of patients being older with more comorbidities
Due to infections (tropical, etc), envenomation, nephrotoxins, or obstetric-related issues	Due to hospital complication, sepsis, multi-organ failure, and high-risk procedures

assess differences between these two types of AKI in the United Kingdom. Among 15 976 adult patients who were screened over the course of 6 months, 4.3% had community-acquired AKI and 2.1% found to have hospital-acquired AKI. Investigators also noted the severity of AKI was higher among those who developed AKI in the community (P = .03). In addition, they were younger by about 2 years (P = .01), had higher rate of kidney function recovery (54.8 versus 45.5%; P = .01), and also had a trend towards higher incidence of de novo CKD (P = .06), but less likely to be admitted in the ICU when they were compared with those with hospital-acquired AKI.[17] Also, patients with community-acquired AKI have less risk of long-term mortality regardless of the severity of the original AKI.[2]

The majority of clinical risk stratification models focus on hospital-acquired acute kidney injury. This is while community-acquired AKI remains very common and continues to have dire consequences. Availability of information for patients who are admitted to the hospital in comparison with individuals in the community is one of the reasons that majority of studies have focused on hospital-acquired AKI.[2] Among developed countries, about half of the cases of AKI happen within the community while between low-income countries 80% of AKI cases occur in the community.[18,19] Despite its clinical relevance and significant financial burden on healthcare systems, it is known that AKI among resource-limited areas is significantly underreported.[20] Lack of access to health centers, scarcity of reporting systems, limited awareness of AKI and its clinical impacts, and limitations in access to the laboratory are amongst reasons that community-acquired AKI among developing countries is substantially underreported.[18,19] In a systematic review, it was described that the AKI incidence in the developed world is 3000 to 5000 person per million per year, against only 20 person per million per year for developing countries.[20] In a prospective study of 892 patients in Malawi, investigators noted during the first medical encounter kidney disease existed among 21% of admitted patients of which 81% had confirmed AKI. The investigators also reported that the most common etiology of AKI was sepsis, gastroenteritis, and tuberculosis.[21]

FUTURE STEPS

In order to improve the AKI outcomes within resource-sufficient and resource-limited regions, the following steps are needed to be considered[6]:

Phase I: Identification of Region-Specific Acute Kidney Injury Risk Factors

As it was suggested by the Acute Disease Quality Initiative group, AKI risk factors are needed to be evaluated in all 5 dimensions (inherent, processes of care, exposures, social, economic, or cultural, and environmental risk factors) within each region based on the resource availability.[3] Evaluating risk factor dimensions can provide a clearer path to prevent AKI within each region. For example, if tropical infections including malaria are among very common risk factors in a region, providing mosquito nets may have a significantly higher impact on the AKI incidence than management of inherent risk factors.

Phase II: Patient Risk Stratification

Using available clinical risk stratification model combined with other regional risk factors could potentially provide an improved avenue to detect patients or populations at higher risk of AKI (Figure 2).

Phase III: Implementation of Preventive Measures

After recognition of higher risk individuals and populations, the very next step is to provide appropriate preventive measures to avoid AKI occurrence and progress. These measures could be divided into before and after the medical encounter. Prior to the medical encounter, raising awareness among the population, policymakers, and providers about AKI risk factors, signs and symptoms, and outcomes at the community level is one of the most important, yet substantially ignored steps.[1] Managing environmental risk factors (eg, providing clean water, and mosquito control), improving access to healthcare, correcting harmful cultural beliefs, limiting risk exposures (eg, controlling tropical infections and providing access to prenatal care), enhancing provider knowledge regarding to the processes of care to avoid AKI are important interventions prior to each medical encounter to mitigate the risk of AKI development, its progress, and dire consequences.

After the medical encounter preventive measures could be divided into one of the following 3 categories[22]:

Primary AKI prevention. These interventions rely on appropriate AKI risk stratification among patients who have not developed AKI yet. Limiting nephrotoxin exposure, avoiding high-risk procedures, optimizing hemodynamics states, and eliminating other modifiable risk factors could impact the AKI incidence.[22]

Secondary AKI prevention. After AKI development, close monitoring of kidney function, performing noninvasive and invasive diagnostic tests to detect etiology of AKI, adjusting doses of medications cleared by the kidneys, and avoiding nephrotoxins are considered preventive interventions that may impact AKI outcomes.[23,24]

Tertiary AKI prevention. Mitigating complications of AKI is an important step in the management of these patients. Dialysis-related adverse events, CKD (de novo or progression), anemia, chronic inflammatory state, cardiorenal syndrome type IV, and chronic volume retention or hypertension are amongst complications of AKI. The timeline between AKI development and the first ninety days is called acute kidney disease.[25] In this timeline, monitoring serum creatinine and urine albumin allows clinicians to evaluate kidney function recovery and determine the risk of CKD development. During AKD period, individualized risk-based management, adjustment in doses of medication excreted from the kidneys, avoiding nephrotoxin and reintroducing renoprotective medications are considered important steps. For patients with stage III AKI who have been initiated on renal replacement therapy using specific renal replacement therapy techniques to improve chances of kidney recovery are recommended (eg, avoid intradialytic hypotension and significant intravascular volume swing, and frequent evaluations of potential kidney recovery for renal replacement therapy liberation).[25]

CONCLUSIONS

There are significant differences between resource-sufficient versus resource-limited regions in the AKI risks and its related complication. Raising awareness regarding these differences would allow clinicians and policymakers to implement region-specific interventions to decrease the incidence of AKI and alleviate its complications.

CONFLICT OF INTEREST

None declared.

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Correspondence to:
Kianoush Kashani, MD, MSc
Division of Nephrology and Hypertension, Mayo Clinic, 200 First St SW, Rochester, MN 55905
Tel: +1 507 266 7093
Fax: +1 507 266 7891
E-mail: kashani.kianoush@mayo.edu