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WHAT'S NEW IN INTENSIVE CARE

Paediatric acute kidney injury: can we match therapy with resources around the world?

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Acute kidney injury (AKI) is a global public health problem with high rates of morbidity and mortality. In 2014, the International Society of Nephrology (ISN) conducted the Global Snapshot of AKI [1], demonstrating that the burden of AKI falls disproportionately on low- and lower-middle income countries (LLMICs), with increased levels of mortality compared to high-income countries (HICs). The Global Snapshot further revealed that nearly 10% of patients in need of renal replacement therapy (RRT) did not receive it. In addition to the lack of resources to diagnose and an inability to afford the therapy, there was also a scarcity of data addressing the epidemiology and causes of AKI in developing countries and poor awareness of the impact of AKI on patient outcomes. ISN has developed the 0 by 25 initiative to address this worldwide concern with the goal that by 2025, no one would die of preventable and treatable AKI.

Children are not exempt from AKI risks. The AWARE [2] and AWAKEN [3] studies demonstrated the high incidence of AKI in critically ill children (27%) and neonates (25%), with AKI being an independent risk factor for mortality. The ISN Global Snapshot indicated that the most common causes for AKI in the worldwide pediatric population are dehydration (32%), hypotension (32%), infection (29%) and nephrotoxin exposure (20%) [1]. There is significant geographic variation; specific diagnoses in LLMICs associated with pediatric AKI include infectious Diarrhoea and envenomation while children living in HICs are more likely to develop AKI in association with complex hospital care and multi-organ dysfunction. Like their adult counterparts identified in the Global Snapshot, many children in need of RRT do not receive it, especially where resources are limited.

In the face of this public health concern, what tools do we have at our disposal to address AKI in hospitalized patients and how do we reconcile the health-related need with the global variation in resources? Figure 1 summarizes various diagnostic and therapeutic measures which are available in LLMICs and HICs. Given the findings of the ISN Global Snapshot, optimization of volume status and blood pressure is primary. Where indicated, one should provide necessary volume expansion using enteral or intravenous routes, as available [4]. Thought and care must guide fluid resuscitation; clinical observation and reports demonstrate risks associated with excessive fluid delivery [5, 6], while physiological studies suggest that AKI and subsequent recovery may depend more on microcirculatory changes, in combination with inflammatory/oxidative stress, coagulation cascade activation, and variation in cell energetics [7]. A simple bedside scoring system, the Renal Angina Index (RAI) [8], can identify those critically ill patients at greater risk to develop AKI, permitting more focused review. In settings with higher resources, the use of biomarkers such as neutrophil gelatinase-associated lipocalin, kidney injury molecule 1 or insulin-like growth factor binding protein 7 and tissue inhibitor of metalloproteinases 2 can further identify and map the course of patients with AKI; combining biomarkers with the RAI may improve predictive models [9]. Nephrotoxic medications are a significant source of AKI; limitation or withdrawal, an intervention we should consider in any resource setting, mitigates AKI severity, as documented in a quality improvement program from the United States [10].

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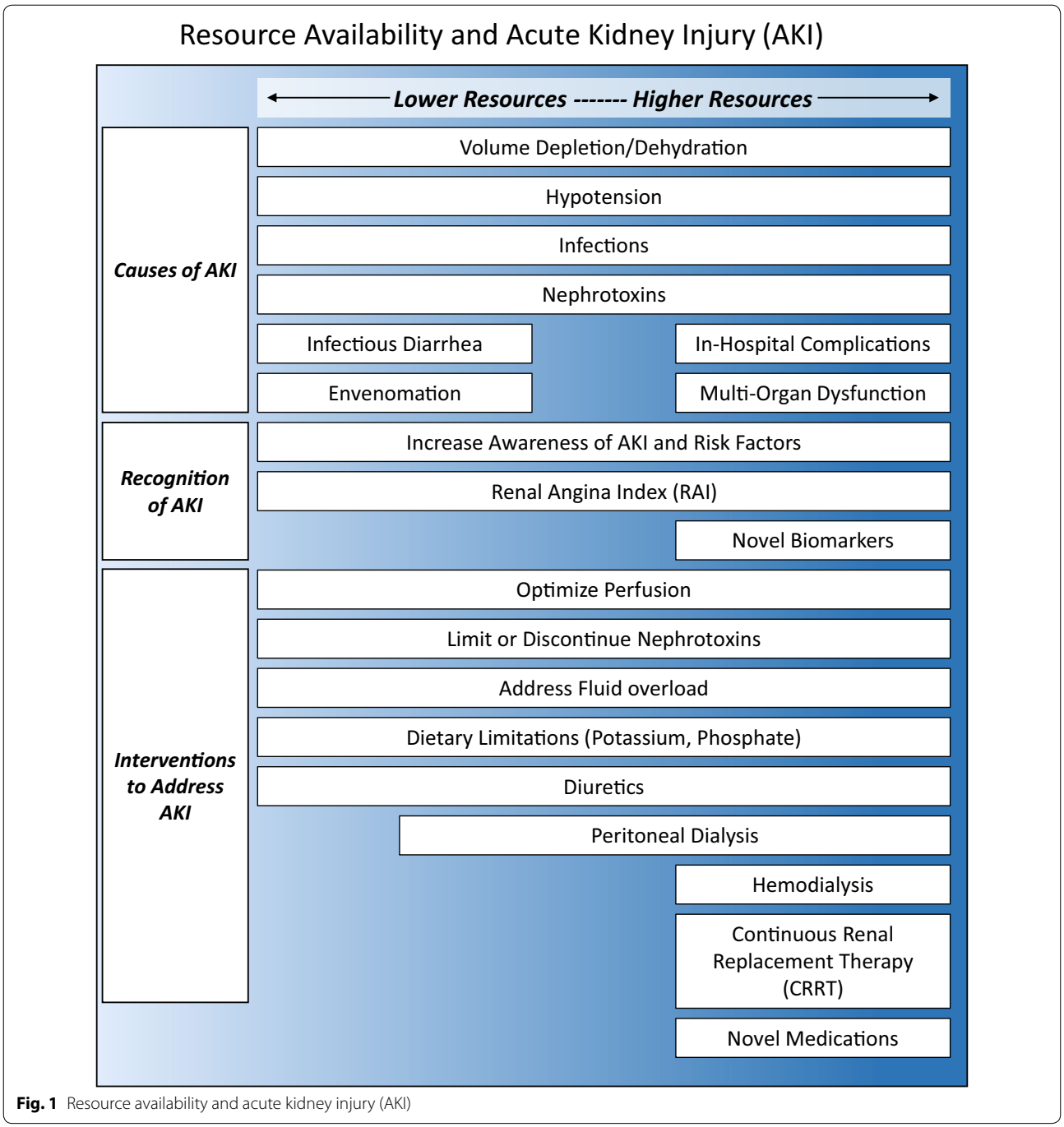

Fig. 1 Resource availability and acute kidney injury (AKI)

When AKI develops, care remains largely supportive as specific pharmacological interventions to address established AKI have, to date, proven ineffective. With reduced glomerular filtration rate and oliguria, one may institute conservative management with fluid and electrolyte restriction to limit volume overload and acute metabolic imbalances; such maneuvers can be deployed in any resource setting. Diuretics can augment urinary output and improve fluid balance; as they are relatively inexpensive, diuretics can aid in the care of AKI patients in settings of lower and higher resource.

Renal replacement therapy serves as the mainstay of supportive management for those who develop severe AKI. Peritoneal dialysis (PD), hemodialysis, and continuous renal replacement therapy (CRRT) have all proven successful in pediatric AKI at correcting

metabolic imbalances and volume overload. Hemodialysis and CRRT for children has required the adapted use of devices made for adult patients; recently, neonatal-specific CRRT machines with lower priming volumes, easy-to-obtain access and innovative anticoagulation protocols to maximize filter lives have become available [11], expanding our ability to provide this therapy to our youngest patients. Complex dialytic technology may only be available in HICs; for those patients who require renal replacement where hemodialysis or CRRT is unavailable, PD remains an essential and effective modality. Where resources are more limited, even PD may prove challenging—there may be no commercially prepared PD solutions nor surgeons with experience to place a PD catheter. The Saving Young Lives project spearheads a sustainable program to train local practitioners in low-resourced settings to provide PD to children with AKI [12]. Pediatricians and nurses learn to place improvised PD catheters and to employ extemporized PD solutions with the aim that no child should die of AKI without an attempt at acute PD.

Recent advances in our understanding of renal injury and repair have led to the development of targeted pharmaceuticals. These new drugs include anti-inflammatory agents, anti-oxidants (iron chelators, hemearginate), vasodilators (levosimendan), apoptosis inhibitors (QPI-1002), and repair agents (THR-184, BB-3, mesenchymal stem cells) [13]. Given the multifactorial pathophysiology of human AKI, it is unlikely that any single agent will elicit a consistent salutary response. Future pharmacotherapy for AKI will need to be individualized, based on etiology and primary mechanism. Cost and limited availability of these agents in low-resource countries raise concerns.

Pediatric AKI remains a challenge around the world, and the resources to combat it vary greatly. Scrupulous attention to fluid balance, careful consideration of electrolyte delivery, and thoughtful use of pharmacological interventions are important maneuvers in the care of any critically ill patient with AKI, regardless of resources, and will aid in optimizing outcomes. Greater sharing of knowledge, coordination with industry to develop more economical methods for renal replacement, and efforts to identify and prevent AKI would serve all our patients well. Global efforts, such as those of ISN's 0by25 [14] initiative, can help to mitigate the worldwide burden of AKI for children and adults alike.

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Compliance with ethical standards

Conflicts of interest
On behalf of all authors, the corresponding author states that there is no conflict of interest.

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