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International Society of Nephrology's 0by25 initiative (zero preventable deaths from acute kidney injury by 2025): focus on diagnosis of acute kidney injury in low-income countries

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Abstract

In developing countries with limited medical infrastructure, preservation and recovery of renal function following acute kidney injury (AKI) is difficult. In conjunction with clinical presentation, rapid measurement of renal function is essential for early diagnosis and management. Especially in low- and middle-income countries, simple interventions such as hydration and avoidance of toxins have the highest probability of recovery. In such contexts, measurement of urine volume and osmolality and serum creatinine with point-of-care devices and saliva urea nitrogen dipsticks can be valuable. This review aims to identify currently available methodologies to assist in reaching the ambitious goal of the 0by25 initiative to eliminate all preventable deaths from AKI by 2025.

Key words: AKI, biomarkers, blood and saliva urea nitrogen, creatinine, guidelines, intensive care, systematic review

Introduction

Acute kidney injury (AKI) is increasingly recognized as a major public health challenge, particularly in less privileged areas of the world. Despite technological progress and substantial preventive efforts, the incidence of AKI in these countries remains high with an estimated 13.3 million cases per year (85% of which in developing countries), and it was further estimated that around 1.7 million deaths can be attributed to AKI [1–4]. Although AKI in developed countries with sophisticated medical infrastructure is predominantly a disease found in hospitalized, elderly and very sick patients, in low- and middle-income countries (LMIC) it is largely a community-acquired condition [1, 5], with dehydration and hypotension being the most common cause in recently published data [3].

In LMIC, a large fraction of newly occurring community-acquired AKI is due to causes, which have a substantial potential of reversibility with simple interventions [2, 5]. Infectious diseases (mainly gastroenteritis associated with diarrhea, malaria and leptospirosis) and obstetric complications are the leading causes of AKI, followed by animal venoms and natural herbal medicines [2]. Although treating the underlying cause is of prime importance, death as a consequence of AKI may often be prevented by simple interventions such as oral rehydration or immediate temporary dialysis. Given the potential

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reversibility of AKI with early intervention, early diagnosis is of particular importance. However, given the possibility of causing an even greater risk of adverse outcomes by fluid overloading patients where rehydration is not indicated [6], accurate diagnostic tools are central to safely intervene at an early stage. Provision and utilization of early diagnostic tools in remote areas without an adequately trained medical and nursing infrastructure and often lacking power sources is a major deterrent to change [7, 8]. Even when diagnostic tools and therapeutic devices are available, specific training of primary healthcare providers can be difficult. A detailed review on risk factors, management and all associated challenges has recently been published [9].

The International Society of Nephrology's AKI initiative aims to prevent all avoidable death from AKI by 2025 (0by25) [2]. A recently conducted and published Global Snapshot study assessed during a 10-week period the whole range of AKI as reported by 322 caregivers from all over the world on 4018 diagnosed patients [3]. Currently, pilot projects are being designed and launched that aim to assess the management of AKI in a real-life setting in low-income countries and to identify areas of improvement.

In the context of the International Society of Nephrology's 0by25 initiative, this report aims to evaluate currently available methods for early diagnosis of AKI in remote areas with inadequate medical infrastructure.

Point-of-care testing

This manuscript will focus on point-of-care testing (POCT) only. Thus, we will not discuss other potential methods of measuring renal function that are expensive and are not used on a routine basis for clinical care, including low molecular weight proteins such as cystatin C, up-regulated proteins such as NGAL, KIM-1, LFABP and IL-18, and tubular enzymes that are excreted in the urine as a results of tubular acute injury. Additionally, a new generation of biomarkers useful in the diagnosis of AKI, the cell cycle arrest biomarkers, require mentioning and are currently under intensive research will not be discussed in this manuscript [10].

The development of new generation diagnostic devices and biomarkers has widened the available methodologies needed to make early diagnosis outside of hospitals. However, their use demands the development of a new infrastructure to operate the devices and communicate results. Some diagnostic elements, such as urine dipsticks, remain available and are invaluable for screening purposes or in the detection of suspected disease. Finally, with the advancement of technology and strong consumer support of the 'smaller is better' concept, use of devices with a substantially smaller footprint has become possible in remote environments. Some of these POCT devices can be utilized in conjunction with smart phones, which automatically digitize results and communicate via text message or the world-wide-web. These devices are available to measure biomarkers of a broad range of diseases and can be used in blood, plasma, sweat, urine and saliva specimens. In combination with medical history and examination, and routine diagnostic instruments, point-of-care techniques reveal a wide range of applications and enable care to be delivered to a large number of patients in LMIC. As current diagnostic measures are based, in part, on the use of serum creatinine (RIFLE [11], AKIN [12] and KDIGO Guidelines [13]), measurement of this parameter is crucial.

Point-of-care devices have already found use in the monitoring of the administration of nephrotoxic agents in radiologic facilities [14], during surgery, to monitor the effects of exposure to nephrotoxic drugs in oncology or to dose antibiotics [14, 15]. Experience with these devices in remote areas without technical and medical infrastructure corroborates their usefulness [16]. However, it is imperative that the use of POCT devices in developing countries needs to be consistent with practices in the developed world ([17]; Table 1). Furthermore, it is important that POCT devices need to be able to connect to commonly used data processing devices (i.e. smartphones, tabloids, computers) in order to transmit or store data for future use, such as clinical observation and monitoring, and/or clinical research.

Diagnosis of AKI

AKI diagnosis is mainly based on changes in urine volume, plasma creatinine and blood urea nitrogen (BUN). Assessments of urine osmolality (or specific gravity), urinary sodium concentration and fractional excretion of sodium and urea possibly have value to diagnose conditions such as dehydration and hypotension (particularly important for developing countries where these conditions are the most common cause of AKI). Current KDIGO recommendations (Table 2) have found broad acceptance [13]. However, the need for blood draws and urine collection is generally difficult in remote villages.

Herein, we briefly discuss clinical presentation, and urine-, blood- and saliva-based biomarkers of interest for the diagnosis and assessment of severity of AKI.

Clinical presentation and medical history

The clinical history is essential in the diagnosis of AKI, usually preceded by infection-related vomiting and diarrhea leading to dehydration and hypovolemia, or ingestion of drugs (including

Table 1. Practice recommendations of the American Association for Clinical Chemistry and the National Academy for Clinical Biochemistry on the use of point-of-care technology devices

- Development and maintenance of a comprehensive quality assurance program, including operator training and competency assessment, quality control, equipment maintenance, reagent storage, periodic correlation of results with a central laboratory and troubleshooting of significant discrepancies or errors.
- An interdisciplinary work group including physicians and laboratory professionals. Close collaboration between the laboratory director and POCT users to monitor testing and to investigate deviations, complaints or incidents is essential.
- Training programs and continuing education of those involved on dissemination of knowledge of recent innovations and limitations in POCT devices and testing.
- Data management as a mechanism to improve the quality of POCT. Concurrent central laboratory creatinine testing of the same samples is recommended for the early stages of program development and conduct of regular quality assurance studies.

Table 2. KDIGO: definition and classification of AKI

AKI stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline[a] OR ≥0.3 mg/dL (≥26.5 mmol/L) increase[b]	<0.5 mL/kg/h for 6–12 h
2	2.0–2.9 times baseline[a]	<0.5 mL/kg/h for ≥12 h
3	3.0 times baseline[a] OR Increase in serum creatinine to ≥4.0 mg/dL (≥353.6 mmol/L) OR Initiation of renal replacement therapy OR In patients <18 years, decrease in eGFR to <35 mL/min/1.73 m^2	<0.3 mL/kg/h for ≥24 h OR Anuria for ≥12 h

[a]Known or presumed to have occurred during the prior 7 days.
[b]Within the preceding 48 h.
[c]eGFR, estimated glomerular filtration rate.

herbal medicines), snake bites, parasitic diseases such as malaria, obstetric complications and other etiologies. Often, the clinical presentation is dominated by the underlying disease and the AKI-specific symptoms are lost within a myriad of disease-specific symptoms [4, 18].

Oliguria is not always present in AKI, but when present provides valuable information. KDIGO guidelines define a reduction of urine volume as an independent criterion for AKI diagnosis (Table 2). It has been reported that mortality is highest when both creatinine elevation and oliguria are present [19]. A recent publication in critically ill patients showed that an assessment of urine volume over a 6 h period was equivalent to hourly assessments for the diagnosis of oliguria and subsequently AKI [20]. This is of great importance in the diagnosis of a patient with oliguria in a remote area, where, apart from the history and examination, specific gravity and urine output may be all that is available for the diagnosis and assessment of AKI.

Urine color may change according to ingested food (e.g. beetroot will turn the urine red). Turbidity and odor may also be of diagnostic value for specific causes of renal dysfunction.

The first contact between village healthcare providers and trained professionals could initially be telephonic reporting history, blood pressure measurements or digital transmission of imaging from portable sonography.

Urine microscopy

Microscopic examination of centrifuged fresh urine for red cells and polymorphonuclear leucocytes, tubular cells, and red cell and tubular cell casts may be of value for the diagnosis of non-AKI causes of oliguria such as glomerular or interstitial diseases, infection or obstruction (see below [21]). Urine microscopy is a useful diagnostic tool in every context of renal disease, with a remarkable specificity as shown in a recent assessment of its diagnostic accuracy [22] and a recently developed urinary sediment scoring system diagnosing based on the number of renal tubular epithelial cells and granular casts has shown to be able to predict worsening of AKI during hospitalization [23]. However, diagnoses made based on microscopy not only require the tool *per se* but also highly specialized training, which does render these diagnostic methods less practical in remote settings. It may, however, be envisioned that future technological innovations such as one allowing the imaging of helminth eggs using mini-microscopes constructed from webcams and mobile phone cameras [24] will one day allow for affordable urinary microscopy in remote settings in developing countries. It may further be envisioned that more sophisticated approaches, possibly with electronic transfer of images or automated methods of diagnosis, could at one point enable the routine use of urinary microscopy in medically isolated settings.

Table 3. Pathophysiological correlates of urine discoloration (based on [20])

Pink	Hematuria, hemoglobinuria and myoglobinuria; massive uric acid crystalluria
Red	Hematuria, hemoglobinuria and myoglobinuria; porphyrinuria and alkaptonuria (turns black on standing)
Brown	Hematuria, hemoglobinuria and myoglobinuria; jaundice
Black	Hematuria, hemoglobinuria and myoglobinuria
White (milky)	Chyluria
Velvet	Urinary infection (certain strains of *Escherichia coli*)

Urine osmolality/specific gravity

Reports of changes in frequency of urination and urinary volume and color provide valuable information (see Table 3; [25]) and it is well established that dehydration causes increases in serum and urine osmolality. Work using the diagnostic value of color scales to diagnose urinary osmolality and possible dehydration deserves mentioning in this context [26]. Measurement of urinary osmolality requires an osmometer or a refractometer. Specific gravity, measurable by a hygrometer or by commercially available dry strips also reflects changes in osmolality, however their usefulness to diagnose dehydration has been questioned because a dehydrated patient will unlikely start to urinate prior to initiation of rehydration and secondly because the change in specific gravity will substantially lag behind the actual change in hydration status [27–29].

Point-of-care testing

The first available POCT methods had a low level of accuracy and precision, but recent developments demonstrate good agreement between results using currently marketed POCT devices and standard laboratory methods [21].

The most frequently used laboratory method for measuring creatinine is based on the color change induced by the reaction of creatinine with picric acid in the Jaffe reaction. The presence of so-called pseudo-chromogens (molecules such as ketones, glucose and bilirubin in the plasma reacting with the picric acid) reduce the accuracy of this method. Newer enzymatic methods eliminate this problem [30] and have permitted the development of smaller devices useable at the bedside [30] without any problems conferred by the pseudo-chromogens in the plasma. However, it is of note that these methods are generally more costly, which is reflected in the price for each measurement (Table 4).

POCT devices not only allow the assessment of serum creatinine for AKI diagnosis but may also be helpful to diagnose electrolyte derangements such as increases in serum potassium. Serial measurements with a POCT may be of particular value to monitor AKI patients. Other parameters measurable

Table 4. POCT devices for serum creatinine

Device	Manufacturer	Sample type	Sample volume	Consumable	Supply storage temperature	Dimensions (width × length × height); portability and weight	Power	Time to result	Price[a]	Price per test
i-STAT	Abbott	Whole blood	65 μL	Cartridge	6–8°C	7.7 × 23.5 × 7.2 cm; handheld, 0.7 kg	AC or battery	2 min	≈15 000–20 000 USD	≈15–20 USD
Stat Sensor	Nova Biomedical	Whole blood, capillary blood	1 μL	Dry strip	4–8°C	15.3 × 8.3 × 4.6 cm; handheld, 0.4 kg	AC or battery	0.5 min	≈3995 USD	≈6 USD
LabGeo-PT10 Smart Blood Analyzer	Samsung	Whole blood	70 μL	Cartridge	n/a	140 × 205 × 206 mm, handheld, 2.0 kg	AC or battery	7 min	≈8000 USD	≈15–20 USD
IRMA TRUpoint	ITC	Whole blood, capillary blood	200 μL or 125 μL in capillary collection kit	Cartridge	2–8°C	29.2 × 24.1 × 12.7 cm; portable, 2.4 kg	AC or battery	1 min	≈8–10 000 USD	≈10–15 USD
Reflotron	Roche	Whole blood, serum, plasma	30 μL	Dry strip	n/a	21 × 30 × 35 cm; benchtop but portable, 5 kg	AC, optional battery operation	2–3 min	≈6500 USD	≈4–5 USD
Piccolo xpress	Abraxis	Whole blood, serum or plasma	9 μL	Self-contained multi-analyte reagent disc	2–8°C	32.4 × 15.2 × 20.3 cm; benchtop, 5 kg	AC or battery	≈12 min	≈18 000 USD	≈20 USD
Spotchem EZ	Arkray	Whole blood, serum or plasma	250 μL	Dry strip	<30°C	33.8 × 20 × 16.3; benchtop; 5.5 kg	AC or battery	8–15 min	≈8500 USD	≈ 6 USD

[a]Prices are estimates based on research results online at various distributors in the USA and Europe and may vary by region, vendor, etc. These estimates only have the purpose to approximate the costs associated with the purchase and use and are by no means replacing a cost estimate by a vendor.

with POCTs range from general chemistry measurements (electrolytes, glucose, urea nitrogen, blood gases) to enzymes such as glutamate pyruvate transaminase (GPT), gamma-glutamyl transferase (GGT), glutamic oxaloacetic transaminase (GOT) and creatine phosphokinase (CPK). Due to considerably higher costs, these latter methods are not widely used.

Handheld devices

Abbott iStat (handheld)

The hand held, battery-operated (two 9 V alkaline lithium batteries) iStat (Table 4), weighing 0.7 kg, measures creatinine and is established as a popular useful device in situations such as disaster relief [16] or radiology units using contrast agents [31]. Measurements require a small cartridge that can be inserted into the iStat. Within 2 min, the device can measure an entire panel of laboratories or just creatinine. Although the iStat can measure substances in plasma and serum samples, the manufacturer recommends the use of whole blood for creatinine (iStat Manual ART: 714446-00H, REV. DATE 17 February 2011). The limitations include that cartridges need to be stored between 2°C and 8°C, need a warm-up time of around 10 min and cannot be cooled again after exposure to ambient temperature. They need to be used within 2 weeks after exposure to temperatures >8°C. An additional downside is the manufacturer's recommendation to not use the device at ambient temperatures >30°C. In terms of accuracy and precision, the iStat overestimates creatinine measurements with a systematic bias of 0.16 mg/dL compared with the Roche Jaffe method, and 0.23 mg/dL compared with a Roche enzymatic method, respectively [32]. Reproducibility of the replicate samples was acceptable with a coefficient of variation of 3.2% [32].

Nova StatSensor

The StatSensor (Table 4) is a battery-operated (3.7 V Li polymer rechargeable or replaceable), handheld POCT device measuring creatinine; it weighs 0.4 kg. The StatSensor can utilize whole blood (arterial and venous) and capillary blood obtained by fingerprick. After the sample is applied on a test strip and inserted for measurement, it provides a result within 30 s. Similar to the iStat, cartridges have to be stored at a temperature between 6°C and 8°C, but the operational temperature is between 15°C and 40°C [33]. In a recent study of 100 subjects, venous whole blood samples were measured with the StatSensor and compared with an enzymatic creatinine assay as the reference method. The correlation was good R^2 of 0.93; standard error of the estimate was 0.22 mg/dL and a negative proportional bias of −30% [34]. When creatinine measurements were performed using a fingerprick sample, the results suggest an underestimation of 0.54 mg/dL compared with the factory setting [35].

A more recent analysis evaluated the performance of the slightly smaller and more specific StatSensor Xpress creatinine analyzer (not available in the USA). It reported good agreement compared with a standard laboratory enzymatic method (concordance correlation coefficient of 0.97 with a systematic bias of −0.12; $N = 60$), except at higher creatinine levels, where agreement was worse (systematic bias −0.23; $N = 15$ [33]).

Another analyzer from the same company is the Stat Profile pHOx Series. However, while some classify it as a POCT device, it is not a preferred tool for use in remote settings given its dimension (30 × 30 × 37.5 cm) and weight of 9 kg.

Non-handheld devices

LabGeo-PT10 Smart Blood Analyzer

The LabGeo PT10 by Samsung is a device weighing about 2 kg that does require electrical power supply (AC 100 ∼ 240 V/50 ∼ 60 Hz). The device operates between 15°C and 32°C. Application of whole blood is on a dry test cartridge (not requiring cooling), which, by application of pressure via a plunger, separates cells from plasma, and measures creatinine as one of the analyses on two different multi-analyte cartridges. It delivers a creatinine reading within 7 min. In a recent comparison, the LabGeo PT10 showed good reproducibility and agreement with serum and whole-blood specimen measurements using the Roche Cobas 8000 modular analyzer (Roche, Switzerland [36]).

IRMA TRUpoint

The IRMA TRUpoint Blood Gas analyzer is portable and weighs approximately 2.4 kg. The device operates at temperatures between 12°C and 30°C and at a humidity not exceeding 80%. Cartridges, designed to measure arterial or venous whole blood (or alternatively capillary blood when collected with a lithium-heparin-containing capillary collection device supplied by the manufacturer), need to be stored between 2°C and 8°C and need a warm-up time of 15 min. The comparison between the IRMA TRUpoint and the Jaffe and enzymatic methods showed that the device results are reproducible: replicate differences of 0.01 (ranging from −0.2 to 0.6) mg/dL and accurate (systematic bias of −0.05 mg/dL) and precise (coefficient of variation 6.1%) in clinical settings. Compared with the reference method the IRMA TRUpoint did not show a significant bias [32].

Reflotron

The Reflotron Plus Chemistry analysis weighs around 5 kg. It can optionally be battery-operated (i.e. car battery at 12/24 V DC voltage) and measures creatinine after application of the sample (whole blood, plasma or serum) on a dry test strip. The strip separates plasma from whole blood but through a separation pad, which allows a measurement in only 2–3 min. The manufacturer recommends an operational temperature of between 15°C and 34°C with a maximum humidity of 90%. A recent analysis showed small bias and good precision (0.12 mg/dL (95% 0.07–0.17) for creatinine levels lower than 5.7 mg/dL and −0.59 (−0.77 to −0.40) with higher creatinine levels [37].

Piccolo xpress

The Abraxis Piccolo xpress weighs around 5 kg and can optionally be battery-operated (i.e. car battery at 15 V DC, 5.0 A). It measures creatinine in whole blood, serum or plasma after application to a self-contained multi-analyte reagent disc. The device can operate at temperatures between 15°C and 32°C and the cartridges are storable for up to 18 months at a temperature between 2°C and 8°C. Once a disc is removed from refrigeration (and left unopened) it must be used within a few hours. The Piccolo xpress uses centrifugation prior to measuring, which delays the measurement to 12 min. At the time of this writing no *in-vivo* data on creatinine testing was found; however, data provided by the manufacturer reports minimal bias and acceptable accuracy when compared with reference methods.

Blood-based diagnosis summary

The above-listed devices were intentionally chosen to include only those with a maximal weight of 5 kg. We believe that size and weight are important parameters to determine whether the

device is practical for use in remote settings. The Abbott i-STAT and the Nova StatSensor are hand held devices operated with batteries and their advantage for use in remote villages is clear. Others are benchtop devices, weighing up to 5 kg; they are nevertheless portable (or at the very least, transportable), and seem to be fit for the purpose from the logistic point of view. Machines heavier than 5 kg and designed for benchtop use are suitable for secondary or tertiary healthcare settings. As long as it fit into a car, can be carried and runs on (preferably rechargeable) batteries, the device has a clear advantage in the proposed application compared with those being used only on benchtop.

Although the diagnostic accuracy of the enzymatic methods that are being used in the measurement methods of the POCT devices are unaffected by pseudo-chromogens and thus are of uncompromised usability even in cases of hyperbilirubinemia as found in malaria patients, practicability in terms of storage and transportability of the test strips or cartridges used for measurement require consideration. The enzymatic methods used in POCT devices require storage at cool temperature and special considerations in terms of cooling and warming up prior to use. This, in conjunction with their operating temperatures, provides logistic and practical challenges.

The measurement medium is another area of concern. Most POCT devices measure creatinine (as the only parameter discussed) in whole blood (Table 4). The Reflotron Plus and the Piccolo xpress can measure creatinine in plasma [38], while the manufacturer of the Nova StatSensor and the IRMA TRUpoint, also claim that their device allows the measurement of creatinine with collection of capillary blood, which may however, result in less precision [39].

It is important to note that most laboratory routine and reference methods also show biases between each other. The accuracy of most of the POCT analyzers shows a small positive bias compared with the studied reference methods [15, 35, 38, 39], but with regard to the aforementioned biases of most references methods to the 'gold standard', these biases of POCT devices, and their direction and magnitude, may differ compared with the reference method used in the local laboratory. This emphasizes the importance of regular confirmatory studies and the necessity to validate the proper use and functionality of the POCT device (Table 1 [35]).

Saliva-based biomarker

Salivary urea nitrogen

BUN accumulates in the blood when renal function decreases. Although BUN is a suboptimal biomarker for the diagnosis of AKI because its concentration is dependent on non-renal factors independent of kidney function (e.g. renal tubular handling, protein intake, protein catabolism, liver diseases, gastrointestinal bleeding, volume status and therapy with high-dose steroids) [40], nevertheless it was reported in the Program to Improve Care in Acute Renal Disease study that acute dialysis initiation at a higher level of BUN associates with an increased risk of death [41, 42]. It may be argued that particularly in developing countries, where many patients may potentially suffer from malnutrition due to low protein intake and consequent low baseline BUN, a sudden increase may be particularly worrisome.

Urea is equally distributed in the total body water including exocrine secretions such as saliva, tears and sweat. It has been known since the 19th century that saliva urea nitrogen (SUN) reflects BUN [43] and it was first proposed as a marker of renal function in the early 20th century [44], and since the 1960s as a useful tool to monitor BUN clearance during hemodialysis [45].

More recent efforts have studied SUN with the use of a dipstick method [46–48], which is already in use in veterinary medicine. This method measures SUN after sample application on a test pad containing urease, which cleaves urea to ammonia and carbon dioxide, forming ammonium hydroxide. This increases the pH of the pad as shown by the color change of a pH indicator. This color can then be compared with a standardized block corresponding semi-quantitatively to the SUN concentration. This method was developed and is manufactured by Integrated Biomedical Technology (Elkhart, IN, USA). It has not yet received Food and Drug Administration approval for human use, but has been studied and validated in 62 subjects suffering from chronic kidney disease for the diagnosis of elevated BUN [48] and in a separate study of 44 subjects diagnosed with AKI, for the diagnosis of AKI severity [47]. SUN levels agree with BUN assessments, but it is insensitive to change and concentrations lower than 50 mg/dL. This does not affect the value of the method as a good discriminator of high versus low levels. In analyses investigating the discriminative abilities of the dipstick, the sensitivity to assess elevated BUN by means of SUN determination was between 0.77 and 0.85, and a specificity between 0.85 and 0.88. In AKI, the dipstick was studied simultaneously with BUN measurements to aid the discrimination of AKI at stage AKIN III from AKI at earlier stages with an acceptable performance with an area under the receiver operating characteristic curve of 0.76 (95% confidence interval 0.61–0.91) [47]. In a subsequent analysis, the agreement between SUN and BUN remained consistent over a period of 4 days [46]. The ease of use of the technique is the fact that no needle-stick is required and the low cost of the dipstick (<1 USD) are substantial advantages for use in remote areas. Downsides are of course the level of subjectivity conferred by the judgment of the color change and the lack of possibility to automatize measurement and data storage (the dipstick needs to be read after 1–2 min—readings after that will be invalid). In summary, more experience is needed with the SUN dipstick, which is in the process of being technically improved.

Discussion

In many countries, the distance to the next healthcare facility may be large and accessibility may be limited. Healthcare providers in remotely located communities need diagnostic autonomy. These constraints emphasize the importance of diagnostic tools that can be used in these settings. Such tools must be light, portable and moderately priced, require little maintenance, and be tolerant of temperature and humidity extremes.

On the next level (in regional or district healthcare settings), more advanced diagnostic tools are essential to establish the severity of disease and to decide which cases need referral to tertiary centers for immediate renal replacement therapy.

We suggest that the optimal AKI diagnostic tool must be chosen based on the existing infrastructure where the tool will be used. One must distinguish between use in a rural village with few or no trained healthcare workers, where urinary volume can be measured in a walk-in clinic and where training and maintenance of a portable point-of-care creatinine measurement is possible, or a more specialized second and third level health care facility where electrolyte estimations can be obtained.

Several considerations are necessary for choosing the right point-of-care device.

First, some of the currently available point-of-care devices to measure creatinine (Table 4) have the disadvantage of needing power supply. SUN assessment may be useful to overcome this limitation and to allow measurements in limited settings.

Second, most devices require that cartridges be stored in a cool environment and once the cooling chain is broken, the cartridges must be used within a defined period of time. This implies the need for electricity or solar power for refrigeration.

At the village level or in a remote rural area, a simple tool such as a urine dipstick detecting an ongoing pathological renal process may aid the decision to call and organize costly transport to a higher specialized facility. Confirmation of AKI by POCT devices would be ideal to confirm initial dipstick tests suggestive of AKI. One may envision the use of a simple technique such as the SUN dipstick in the rural villages in conjunction with the more accurate POCT devices (at higher levels of healthcare). The SUN dipstick would there serve, in combination with what is learned from anamnesis and clinical presentation, to maximize the information gain to accurately diagnose AKI.

Cost efficiency is an important consideration in the context of diagnosis of AKI in developing countries. Although POCT devices have the ability to determine serum creatinine at costs between 4000 and 20 000 USD, other approaches cost substantially less. In particularly, SUN dipsticks costing <1 USD require mentioning in this context. This is in sharp contrast to the cost of a measurement using a POCT device, where every single test runs at around 4–20 USD (and additionally requires refrigeration, which causes additional costs). Considering a child with suspected AKI requiring frequent assessments or a child diagnosed AKI where management is being monitored using a POCT device, this would quickly accumulate substantial costs.

Diagnostic is of immense importance for our endeavors to eliminate preventable deaths from AKI by 2025. In settings where maintenance renal replacement therapy or kidney transplantation is a challenge, the recovery and preservation of renal function is crucial. The measurement of parameters aiding the early diagnosis of pathologic renal conditions is of importance in order to counteract swiftly, possibly with only simple interventions such as hydration, and to have the highest probability of recovery.

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Conflicts of interest statement

None declared.

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