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Important Tips on Acute Kidney Injury for Primary Care Physicians in Sub-Sahara Africa

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ABSTRACT
The number of Nephrology Specialists continue to lag desperately behind the standard requirements for the Nigerian populace, a situation that is replicated in most sub-Saharan countries in Africa. This has resulted in unfavourable impact on clinical outcomes among patients who present with life-threatening renal diseases that require early recognition and prompt intervention such as acute kidney injury, nephrogenic pulmonary oedema and acute dyselelctrolaemia.

It has been shown that early intervention by primary care physicians portends better outcomes for patients with acute kidney injury through early recognition of the disease, prompt intervention and (where necessary) referral to the Nephrologist.

However, recent studies indicate that majority of primary care physicians are inadequately equipped with knowledge of the disease thus defeating the purpose of primary care physicians having early contact with such patients. In this article, we aimed to present primary care physicians working in sub-Sahara Africa and other third world countries some simplified but current and practical tips on early recognition of acute kidney injury and the necessary first steps to take during interventions.

One of the take home points in this article is the relevance of focused history taking in identifying the aetiological agent(s) of acute kidney injury across the major sub-specialties in contemporary times in sub-Sahara African hospitals as most patients cannot afford hi-tech, sophisticated investigations when and where they are available.

Keywords: *Acute kidney injury, primary care physicians, diagnosis, tips, Africa*

INTRODUCTION

The number of Nephrology Specialists continue to lag desperately behind the standard requirements for the Nigerian populace, a situation that is replicated in most sub-Saharan countries in Africa. This has resulted in unfavourable impact on clinical outcomes among patients who present with life-threatening renal diseases that require early recognition and prompt intervention such as acute kidney injury (AKI), nephrogenic pulmonary oedema and acute dyselelctrolaemia.

A country by country analysis showed that African countries rank among those with the lowest Nephrologist-to-patient ratio; for instance, with the exemption of Tunisia and Egypt with seven Nephrologists per million population (pmp), other countries have $\leq$ 1 Nephrologist pmp (figures 1 and 2).[1-2]

To be more specific, Nigeria currently has an estimated 160 Nephrologists (spread across 149 dialysis centres) who are serving about 200 million people.[3] Added to this is the shrinking global Nephrology workforce with many Nephrologists already approaching the age of retirement.[2] This has led to calls for primary care physicians (PCPs) to be involved in the care of patients with kidney diseases in order to improve outcomes through early

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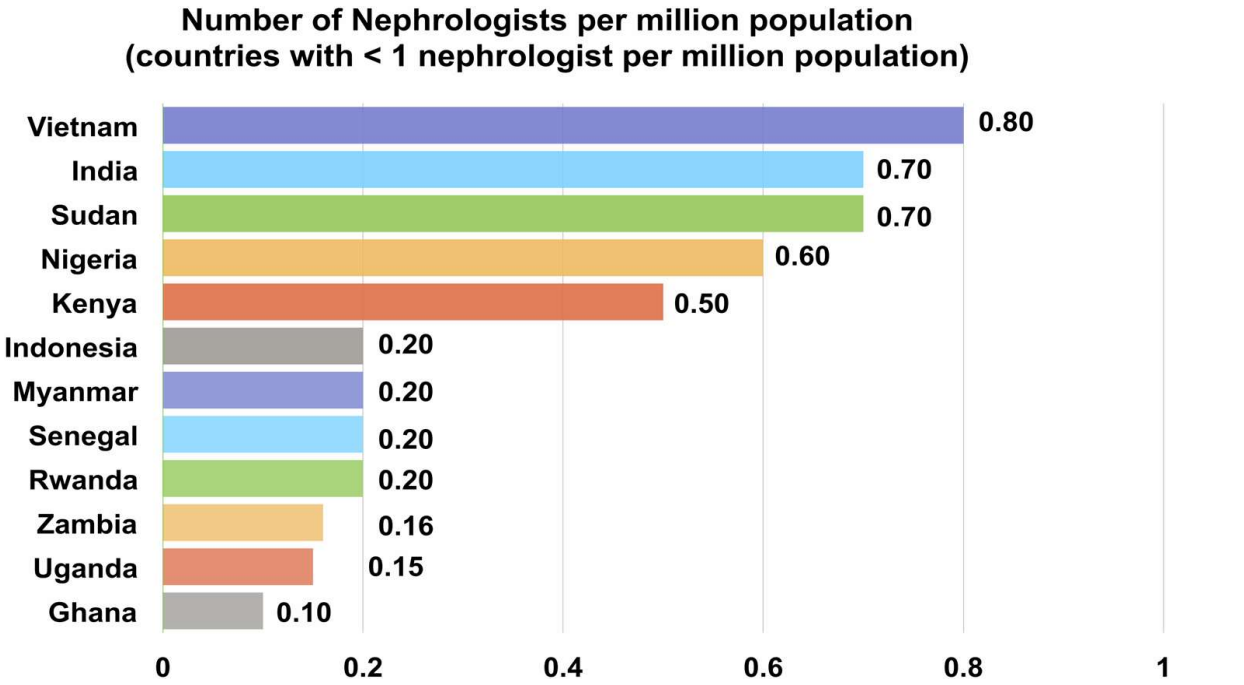

Figure 1: Number of nephrologists per million population by countries with <1 nephrologist per million population[1]

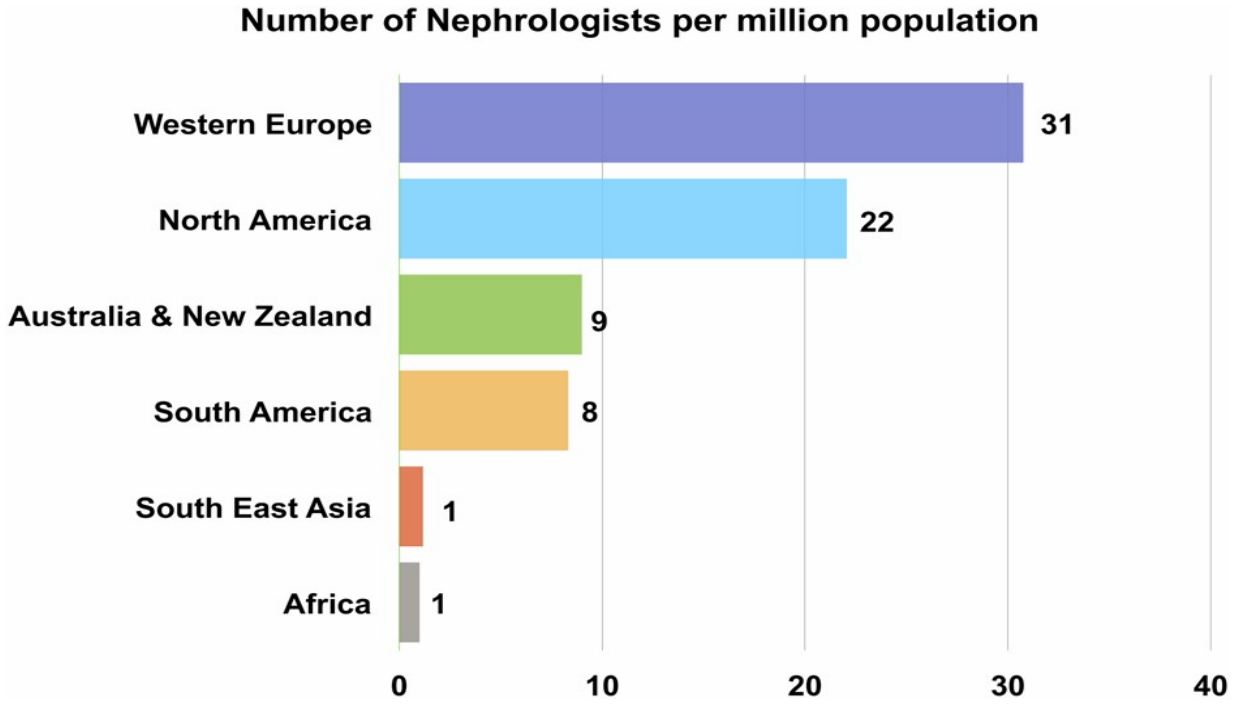

Figure 2: Number of nephrologists per million population by continent [2]

recognition of life threatening events, early intervention and (where necessary) referral to the Nephrologist.[4]

However, unless PCPs are adequately equipped with updated knowledge on current management of AKI, these objectives may not be achievable. For instance, in a study carried out among non-renal doctors in Southwest Nigeria, only 1.2% of the respondents had good knowledge of AKI with mode of presentation, risk factors, and criteria for definition and staging identified among the key areas of knowledge deficiencies[5] with similar findings

described among doctors and other healthcare workers in some other parts of SSA.[6-7]

The purpose of this article is to offer PCPs who are working in SSA and other third world countries some simplified but current tips on early recognition of AKI and necessary first steps to take during interventions.

AKI: New definitions and diagnostic criteria

First and foremost, PCPs should be aware of the paradigm shift in the definition and approach to diagnosis of acute renal failure (ARF). Since the 1940s, the term ARF was used loosely to represent sudden and rapid deterioration in kidney function which traditionally had a time frame of 'days to weeks'. This used to be defined clinically by the presence of oliguria (urine output <400ml) or anuria (urine output <200ml), uraemic symptoms (nausea, vomiting, pruritus etc.) and deranged blood urea nitrogen levels. However, the new term, acute kidney injury (AKI) which was introduced in the 1990s is based on newer evidence that kidney failure begins indeed with subtle, sub-clinical changes in serum creatinine and/or decrease in urinary output with the time frame now modified to 'within hours to days' thus effectively eliminating the necessity to wait for overt clinical features before making a diagnosis of renal failure (table 1).[8]

AKI: Relevance of adequate history taking

PCPs in SSA need to pay close attention to focused history taking when attending to cases of suspected AKI as a step-wise history taking (which takes into consideration important risk factors) is useful in identifying individuals who stand a high risk of developing AKI. It must be emphasized that in SSA where hi-tech investigations may not be readily available in many hospitals, or where available the costs of care presents a burden to the patients and their relatives who mainly pay out-of-pocket to access medical services, a focused history of the illness remains a relevant tool in arriving at a diagnosis.[10-11] The PCP should carefully clerk for underlying risk factors and/or aetiologies of AKI even in the absence of reduction in urine output or other overt features of renal failure in order not to miss evolving renal failure.

The PCP should look for co-occurrence of multiple aetiologies such as sepsis and fluid depletion, trauma and sepsis, sepsis and herbal usage, abortion and sepsis, etc. Where a referral note or e-mail is available, the PCP should check if the serum creatinine is reported as this is useful as a "baseline tool" for assessing progression of the disease, its severity and prognostication.

Table 1: Definition of Acute Kidney Injury according to the "Acute Kidney Injury Network" (AKIN) criteria [8]

Stage	Changes in serum creatinine	Changes in urine output
1.	1.5-2 times baseline OR 0.3 mg/dL increase from baseline	<0.5 ml/kg/hr for >6 hours
2.	2-3 times baseline	<0.5 ml/kg/hr for >12 hours
3.	3 times baseline OR 0.5 mg/dl increase if baseline>4mg/dL OR any renal replacement therapy given	<0.3 ml/kg/hr for >24 hours OR anuria for >12 hours

Kg/hr: kilogram/hour

The diagnosis of AKI therefore requires a high index of suspicion in order to provide clinicians (be it PCPs or Nephrologists) with sufficient time to offer prompt intervention with a view to achieving reversal of the process of kidney injury before overt renal failure sets in. This approach therefore presents the benefit of reducing the risk for developing chronic kidney disease (CKD) among patients with AKI.[9]

AKI: Sepsis and fluid depletion

During clinical evaluation (history taking and physical examination), every PCP in SSA should be acutely aware that sepsis from any portal of entry and fluid depletion or a combination of the two are the most common causes of pre-renal AKI in SSA.[12-14] The PCP must have a high index of suspicion for AKI in all patients presenting with sepsis. The suspicion

should be further heightened when it is accompanied by fluid depletion as a result of vomiting, diarrhoea or anorexia. Assessment of patients with fever and altered sensorium for AKI should be conducted as soon as they are admitted; this is important as PCPs are most likely to be distracted by the more dramatic features (and required emergency care) that often accompany the high-dependent, unconscious patient. Usually, prompt treatment of the underlying cause(s) of the sepsis and correction of the fluid depletion (by use of crystals, colloids, or blood and blood products) results in reversal of the AKI with no need for dialysis.

AKI: Trauma and haemorrhage

AKI is a frequent complication of severe trauma and is associated with prolonged hospital length of stay and increased mortality.[15] Intravascular volume contraction can occur in the setting of excessive blood loss from traumatic injury, which may be penetrating or blunt in nature. PCPs should be more alert to blunt injuries (usually abdomen and/or chest) as patients may develop AKI from undetected, massive haemorrhage into the third space. For example, the peritoneum can accommodate up to more than 5 litres of blood before clinical manifestation of exanguination (by which time the patient would have developed shock, a major risk factor for AKI). Rhabdomyolysis, direct renal injury, abdominal compartment syndrome, or nephrotoxic effects of treatment are some of the risk factors which may contribute to the onset and progression of AKI in the trauma setting.[16] Older age, greater injury severity, presence of shock, greater requirements for blood transfusion (especially in the first 24 hours of injury) and higher admission serum creatinine are also important factors for the PCP to consider.[16]

The time taken for AKI to set in the setting of intravascular contraction ranges from hours to days depending on the quantity of haemorrhage and the time taken. The PCP should monitor hourly urine output and target a range of 0.5-1.0ml/kg/hour for at least the first 6 to 12 hours of admission. The earlier internal bleeding is detected and arrested, the greater the chances of preventing onset of AKI. In the same vein, every pregnant woman with significant blood loss from antepartum, peripartum or postpartum haemorrhage must be assessed within 6 to 12 hours for AKI.

AKI: herbs as a trigger

Herbal remedies account for about 35% of AKI in the developing world.[17] Most Africans believe and practice herbal medication therapy hence many sick persons would most invariably have consumed herbal concoction before presenting to the hospital. The PCP should therefore search for detailed history of herbal use in the days leading to the onset of AKI. In a study by Kadiri et al, nephrotoxicity resulting from use of traditional herbal remedies (37.5%) was higher than septicaemia (17.5%) among the most commonly identified precipitating factors of AKI.[18] Due to cultural beliefs and practices, family members and relatives are known to "smuggle" herbal concoction into the hospital wards. PCPs and their managing teams should be at alert to prevent this from happening.

Another important point to note is that some of the patients presenting to the hospital with AKI may have been using herbs to manage some chronic illnesses.[19] Herbal mixtures have been known to act as second-hit in the progression of CKD among patients with underlying risk factors/aetiologies such as hypertension, diabetes mellitus, obstructive uropathy, cystic kidney diseases etc. PCPs must be at alert to obtain information on herbal usage among all their clients and such medications must be stopped at once as they may interfere with patient compliance, drug metabolism or even worsen the on-going background renal damage.[20]

AKI in the Obstetrics and Gynaecological setting

The prevalence and pattern of AKI in pregnancy depends on the trimester. In developing countries, sepsis and intravascular volume contraction from ante- and peri-partum haemorrhage account for the highest number of AKI.[21-23] PCPs should also be aware of the trimester during which particular aetiologies of AKI can set in; for instance, septic abortion is the most common cause of AKI in early trimester while preeclampsia and haemorrhage occur more frequently in late pregnancy.[24-25]

All pregnant women must be assessed for hypertension and at least a urinalysis carried out. Women with minimum proteinuria of 2+ should be screened to details for preeclampsia. This step is important because preeclampsia can act as a smokescreen for other causes of AKI stemming from intrinsic damage to the renal vasculature such as

thrombotic thrombocytopaenia, thrombotic microangiopathy or acute fatty liver of pregnancy.[26] AKI secondary to preeclampsia must be considered an emergency and the Nephrologist (where available) should be involved in the management as early as possible, otherwise such a patient should be referred to a facility where she can be co-managed with a Nephrologist. Determination of termination of pregnancy (or not) depends greatly on the assessment, clinical experience and intervention of the Nephrologist.

The PCP must be alert to the fact that some female patients may insert herbal medications in the form of pessaries into their vagina to treat fibroids, utero-vaginal prolapse, induce fertility act as an abortifacient.[27-28] Young ladies presenting to the emergency room with sepsis and/or vaginal bleeding are the usual suspects; they must undergo vaginal examination for unhealthy discharge and/or presence of herbal vaginal pessaries. Usually, they deny usage, so the PCP must be at alert to cross-check by way of clinical examination. Women with other listed problems as stated above should also be assessed for use of vaginal pessaries though this is less common among them. Prompt removal of the pessaries and treatment of associated pelvic infection and/or sepsis usually reverse the AKI.

Those with *hyperemesis gravidarum* must also be watched for reduction in urine output and/or rise in serum creatinine as in situations of prolonged hyperemesis, the patient may end up in the dialysis room.[29] PCPs must admit the patient, institute the appropriate intravenous infusion as early as possible and administer anti-emetics. Gynaecologists and Anaesthesiologists must take care during pelvic surgery in females to watch out against ureteric ligation, which will manifest as anuria immediately after surgery. Usually, these patients do not make urine within the theatre and during the immediate post-operative window. Such patients must be taken back for release of ligature immediately before permanent renal damage sets in.[30]

AKI and nephrotoxins

Another key area which the PCP should assess during history-taking is the use of medications, especially administration aminoglycosides during illness. In Africa, there exists a group of "healthcare workers" referred to as *auxiliary nurses* and another group, *Health Assistants* who have assumed the role of "medical doctors/nurses" in the community. They are seen by the people as easily accessible and cheaper alternatives to board certified medical and nursing professionals. During the course of a serious fever, often referred to as "typhoid fever" by these quacks, they would most likely have administered high dose gentamycin to the patient as it is cheap and most times considered effective for most "infections". For the same reasons, the use of gentamycin is also common among PCPs in the private sector as it is considered "good business" by some. However, in combination with other factors, high dose gentamycin is likely to result in AKI when used without following dosage guidelines.[31-33]

While gentamycin generally has a low rate of microbial resistance and high clinical effectiveness, PCPs must be aware that it may not work in all settings. It is advised that PCPs have a strong indication for the use of aminoglycosides by way of culture sensitivity result. Other conditions that promote AKI from gentamycin such as elevated trough gentamicin levels, plasma concentration-time area under the curve, duration of treatment on aminoglycoside, concomitant vancomycin, frusemide use, volume depletion, elevated baseline serum creatinine, increasing age, presence of co-morbidities, liver dysfunction, sepsis, hypokalemia, hypomagnesaemia, type of aminoglycoside, frequency of aminoglycoside dosing, and the timing of aminoglycoside administration should be sought.[32-33]

It is critical for PCPs to pay attention to a history of home care, and check the available medications or their package (if exhausted). The same caution applies to the use of over the counter analgesic mixture (asapo, akapo) as, in most cases, the patient would have first and foremost visited the local pharmacy (aka "Chemists") for self-care.[34] While it is uncommon, PCPs should note that suicide attempt by ingestion of chemicals can result in AKI.[35]

AKI and malignant hypertension

Accelerated hypertension this can be tricky, can finish the kidneys in no time. From our personal experience, many patients present to the PCP with unexplained, recurrent headache, "fever" (which is actually internal heat/discomfort) and insomnia. Unfortunately, this is termed as "typhoid fever" by some PCPs and quacks. For every episode of malignant hypertension, there is some form of nephron damage from intravascular bleeding and fibrinoid necrosis. Young

women with malignant hypertension should be assessed for renal artery stenosis and AGN at the least.

AKI and rhabdomyolysis

AKI is known to result from trauma due to rhabdomyolysis during which there is direct sarcolemmic injury with release of myoglobin into the circulation. Not all cases of rhabdomyolysis is associated with myoglobinuria and renal tubular injury except in situations where there is massive destruction of myocytes and renal threshold of myoglobin is exceeded (>0.5-1.5mg/dL).[36] PCPs should be on the look-out for cases of crush injury such as in road traffic accidents (RTA), severe physical assault, electrocution, alcoholism, heat or cold exposure which are most likely to cause massive muscle cell destruction.[37-40] Intervention should begin immediately the muscle injury begins with early and aggressive fluid replacement of up to 10 litres of intravenous fluid, though this should be adjusted in accordance to severity of the rhabdomyolysis. This is required because of sequestration of water in the injured muscles.

Other important considerations

PCPs should also be aware of some other not-so-common causes of AKI in SSA such as acute glomerulonephritis (acute GN). They may present with anuria/oligo-anuria, high blood pressure and smoky urine. The PCP should conduct urine microscopy for all patients with suspected AKI in order to identify this category of patients or co-existence of AKI and acute GN. At best, this group of patients should be referred to the Nephrologist immediately as early biopsy-proven histological diagnosis is useful in guiding appropriate therapy. Patients with heart failure should also be evaluated regularly for AKI which may develop from hypoperfusion.

CONCLUSION

The PCP plays a key role in survival among patients with AKI. Continuing medical education is required for PCPs on a regular basis in order to boost their confidence when faced with patients who present with AKI. Early recognition, intervention and referral to the Nephrologist (where available) can go a long way to reduce morbidity and mortality among patients with AKI.

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