Editorial:

Rising incidence of acute kidney injury – the emerging significance of "pill" burden

Acute kidney injury (AKI) is defined as a sudden fall in kidney function (over hours to days) resulting in accumulation of nitrogenous waste products and fluids in the body. It is at times a devastating syndrome with high costs to patients and health care systems.[1] Most studies of AKI detection are based on serum creatinine levels with or without urine output measurements. The limitation of serum creatinine as a biomarker of AKI is well understood.[2] The quest for novel biomarkers is on. These biomarkers should be able to segregate tissue injury from changes in function. This is one area in AKI where knowledge gap exists. The Risk, Injury, Failure, Loss of Function, End stage renal disease (RIFLE) criteria in 2004,[3] Acute Kidney Injury Network (AKIN) criteria in 2007[4] and Kidney Disease Improving Global Outcomes (KDIGO) criteria in 2012[5] represent substantial advance in our efforts to standardize the definition of AKI.

Over the past 2 decades, dramatic increase in the incidence of AKI has been reported. Ali et al [6] reported an incidence of 2147 per million population per year in Scotland. A community study[7] in Northern California documented an incidence of 3841 and 244 per million population per year respectively of non-dialysis requiring and dialysis requiring AKI.[7] Unfortunately no such data are available from developing countries. Data from developed countries have reported AKI to constitute 3.2%-9.6% of hospital admissions.[1] The potential reasons for the increase in AKI could be increase in comorbidity burden and illness severity. Other reasons for the rise in incidence of AKI could be the underlying precipitants,[8] sepsis, acute decompensated cardiac failure, higher frequency of invasive procedures and underlying chronic kidney disease (CKD) to name a few.

Decades ago single-centre studies[9,10] suggested an important role of medications in the changing epidemiology of AKI. Further studies[9,10] reported that drug-induced AKI grew from 7% to 16% over a span of 17 years in their two centres. Today medications are the reason for severe AKI in 20% of adults.[11] The same is true for AKI in paediatric practice too.[12]

The ever expanding repertoire of antimicrobial agents comes with the risk of nephrotoxicity. In 1979, aminoglycosides accounted for 82% of the drug induced AKI; however, by 1996, they accounted for only 26% of drug related AKI.[6] Today interventions which were considered benign hitherto are being implicated as potential causes of AKI. These include intravenous fluid formulations like hydroxylethyl starch[13] and chloride rich solutions.[14] Hydroxyethyl starch is no longer recommended for initial volume expansion in view of its potential nephrotoxicity. Chloride rich solutions and their association with increased risk of AKI and need for renal replacement therapy needs to be validated in large randomized clinical trials. Early and aggressive fluid resuscitation is considered standard of care in diseases like sepsis. So the safety of intravenous fluids used for volume resuscitation needs to be scrutinized like any other medicine.

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In the community, more number of medicines are now being recognized for their nephrotoxic potential. Non-steroidal anti-inflammatory drugs (NSAIDs) in particular continue to be a problem in patients at high risk for AKI.[15] Plenty of literature is available with regards to adverse renal effects of NSAIDs. Proton pump inhibitors (PPI),[15] highly active antiretroviral therapy,[16] statins[17] and fluoroquinolones[18] have all been associated with AKI.

Renin angiotensin aldosterone system (RAAS) blockade has been proven to have renoprotective effects by lowering intraglomerular pressure. This class of medication has been widely integrated into the treatments of multiple chronic conditions like CKD, congestive heart failure (CHF), proteinuric states, hypertension etc. However, they may lower the threshold for developing or worsening of already set-in AKI in susceptible individuals. Cox et al[19] observed that RAAS blockers were most commonly associated with AKI in hospitalized patients.

Cancer related mortality has been reduced by 20% over the past two decades. This is because of improvements in prevention, detection and treatment of cancers. As a result the ever increasing numbers of cancer survivors are at risk of developing AKI.[20] Recent data published using creatinine based definitions suggest AKI incidence in cancer patients to be as high as 12%.[21] The aetiologies of AKI in cancer patients varies widely from traditional risk factors like volume depletion, sepsis, antibiotic use, tumour lysis syndrome to a new spectrum of potentially nephrotoxic chemotherapy and myeloablative protocols.[22] Onco-nephrology is a promising new field.

The availability of new biomarkers of kidney damage and functional change is giving us an opportunity to improve our understanding of this syndrome. It is likely to help us develop new strategies for diagnosis and intervention in AKI. It will be interesting to see which of the new biomarkers will ultimately replace serum creatinine.

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