

# NGAL and Early AKI Detection, Call for Action!

**Abbreviations:** AKI: Acute Kidney Injury; SCr: Serum Creatinine; ATN: Acute Tubular Necrosis; NGAL: Neutrophil Gelatinase-Associated Lipocalin; DGF: Delayed Graft Function

## Editorial

Acute Kidney Injury (AKI) is defined as rapid reduction in kidney function because of multiple causes. Its incidence is increasing in hospitalized patients, especially in critical illness. Worldwide AKI incidence was estimated to be 21.6% in adults and 33.7% in children [1]. AKI is diagnosed only when significant nephron damage occurs, serum creatinine (SCr) rises  $\geq 0.3$  mg/dL or oliguria is present. It remains important to recognize the limitations imposed by the use of SCr and urine output for the detection of AKI. SCr concentration may increase slowly, perhaps only following a major kidney damage. SCr is also influenced by factors such as age, gender, and muscle mass and nutritional status. It is also unable to differentiate pre-renal AKI from intrinsic renal AKI like acute tubular necrosis (ATN). AKI should be diagnosed earlier in order to protect against adverse outcomes. There is increasing evidence for adverse outcomes associated with AKI including, longer hospital length of stay, significant complication rates (including infection), risk of CKD, development of cardiovascular disease and higher mortality. The risk of worsening or de novo CKD following an episode of AKI (even if renal functions returned back to normal) remains high [2]. Fast and accurate AKI biomarkers will significantly improve morbidity and mortality by providing early diagnosis. This is particularly important for effective patient management in AKI. Neutrophil gelatinase-associated lipocalin (NGAL) seem to represent a suitable option to accomplish this task and replace SCr in AKI diagnosis.

Neutrophil gelatinase-associated lipocalin (NGAL) is a 25-kDa glycoprotein produced by epithelial tissues in several organs. NGAL is excreted via glomerular filtration and completely reabsorbed by tubular cells. Urinary NGAL is sensitive and specific for early ATN (not increased in pre-renal AKI). It rises 2-4h post-AKI. Plasma NGAL may also help to predict likelihood of renal recovery. NGAL has been validated in different AKI settings including; pediatric AKI, Sepsis-induced AKI, Delayed Graft Function in Kidney Transplantation from Extended Criteria Donors, in fluid resuscitation of severely burned patients and others [3]. For example, in a cross-sectional study, adults in the intensive care unit with established AKI (defined as a doubling of the SCr) due to sepsis, ischemia, or nephrotoxins displayed a more than 10-fold increase in plasma NGAL and more than a 100-fold increase in urine NGAL by Western blotting when compared to normal controls. Both plasma and urine NGAL correlated highly with serum creatinine levels. These results identified NGAL as a sensitive biomarker to established AKI in humans [4].

Also, in children undergoing cardiopulmonary bypass, NGAL measurement by Western blotting and ELISA showed a 10-fold or more increase in the urine and plasma within 2-6 h of surgery in patients who subsequently developed AKI (diagnosed using

SCr after 1-3 days following surgery). Both urine and plasma NGAL were powerful independent predictors of AKI [5]. Again, NGAL has also been evaluated as a biomarker of delayed graft function (DGF) in kidney transplantation. A significant correlation between NGAL staining intensity (in biopsies obtained one hour after vascular anastomosis) and the subsequent development of DGF was found [6].

Benefits of early AKI diagnosis are countless. It allow for therapeutic intervention either by stopping an offending drug or correcting an underlying condition or for example starting a CRRT. Furthermore, biomarkers like NGAL are able to distinguish causes of AKI (increase in ATN, Normal in pre-renal AKI). Also, therapeutic intervention for early AKI couldn't be applied early except after detecting and defining early AKI even before urine output decreases or creatinine increases.

In summary, NGAL is emerging as an early, sensitive biomarker in the field of AKI. Strong evidence has been provided for the predictability of NGAL in a variety of AKI settings. NGAL should start to pave its way into clinical practice (suggested approach for NGAL start of use in clinical practice is summarized in Figure 1). Benefits of such a diagnostic tool will surely exceed the costs for its implementation. And advancements in nephrology practice will certainly take place with the routine use of NGAL.

### Suggested Approach for the Start of Clinical Use of NGAL:

1. Standardization of measuring technique.
2. Defining cut off values for normal range in different population, cut off values categorized according to RIFLE/AKIN or KDIGO staging.
3. Starting the clinical use of biomarkers for early AKI identification.
4. Assigning clinical interventions according to best available evidence in large cohorts.
5. Reflection (Does early diagnosis of AKI improved outcomes?)
6. Modifying therapeutic interventions according to feedback.
7. Validation of these intervention results through RCTs.

**Figure 1:** A suggested approach for NGAL use in clinical practice.

## References

1. Susantitaphong P, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, et al. (2013) World incidence of AKI: a meta-analysis. Clin J Am Soc Nephrol 8(9): 1482-1493.

Editorial

Volume 3 Issue 3 - 2016

**Mohamed E Elrggal\***

*Kidney & Urology Center, Egypt*

**\*Corresponding author:** Mohamed E Elrggal, Kidney & Urology Center, Alexandria, Egypt, Tel: +2-01005038467; Email: m\_elrggal@hotmail.com

**Received:** April 28, 2016 | **Published:** April 29, 2016

2. Bucaloiu ID, Kirchner HL, Norfolk ER, Hartle JE, Perkins RM (2012) Increased risk of death and de novo chronic kidney disease following reversible acute kidney injury. *Kidney Int* 81(5): 477-485.
3. Ronco C, Legrand M, Goldstein SL, Hur M, Tran N, et al. (2014) Neutrophil gelatinase-associated lipocalin: ready for routine clinical use? An international perspective. *Blood Purif* 37(4): 271-285.
4. Mori K, Lee HT, Rapoport D, Drexler IR, Foster K, et al. (2005) Endocytic delivery of lipocalin-siderophore-iron complex rescues the kidney from ischemia-reperfusion injury. *J Clin Invest* 115(3): 610-621.
5. Mishra J, Dent C, Tarabishi R, Mitsnefes MM, Ma Q, et al. (2005) Neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker for acute renal injury after cardiac surgery. *Lancet* 365(9466): 1231-1238.
6. Mishra J, Ma Q, Kelly C, Mitsnefes M, Mori K, et al. (2006) Kidney NGAL is a novel early marker of acute injury following transplantation. *Pediatr Nephrol* 21(6): 856-863.