Available online at http://inakidneyhypertension.co.id Official Journal of the Indonesian Society of Nephrology
Indonesian Journal of Kidney & Hypertension InaKidney

Editorial

Sepsis and Acute Kidney Injury (AKI): Which is More Important, Sepsis Biomarkers or AKI Biomarkers?

Nur Samsu[1]

[1]Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

Corresponding Author:
Nur Samsu, Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Brawijaya, dr. Saiful Anwar-General Hospital, Malang, Indonesia, nur_samsu.fk@ub.ac.id

Sepsis and acute kidney injury (AKI) are two major global health problems and are strongly associated with poor outcomes. Although often used interchangeably in clinical practice, there are conditions associated with sepsis and AKI that are fundamentally different in their underlying pathophysiology. Sepsis-associated AKI (SA-AKI), which is AKI that occurs concurrently with or within 7 days of the diagnosis of sepsis[1], and sepsis-induced AKI (SI-AKI), which is a sub-phenotype of SA-AKI in which sepsis serves as the primary and dominant trigger for kidney injury.[2] In SA-AKI, sepsis is not always the sole direct cause of AKI. The occurrence of AKI can be exacerbated by the use of nephrotoxic drugs during treatment or other comorbid medical conditions. On the other hand, in SI-AKI, AKI occurs directly due to mechanisms triggered by sepsis, such as cytokine storm, impaired renal microcirculation, and oxidative stress in renal tubular cells.

Which biomarker is more important to evaluate in critically ill patients: biomarkers for sepsis or biomarkers for AKI?

In a clinical context, evaluating sepsis biomarkers or AKI biomarkers is equally important, but they have different roles depending on the purpose. Whether the evaluation is performed to detect the cause of AKI or to detect the presence or absence of kidney disorders. However, sepsis and AKI can also occur simultaneously. Clearly, the prognosis of both SA-AKI and SI-AKI is worse than that of sepsis and AKI separately.[3] Patients with AKI due to sepsis have worse outcomes than patients with AKI due to other causes (i.e., non-septic AKI). Conversely, patients with sepsis and AKI who experience improvements in urine output, serum urea levels, and creatinine levels 48 hours after hospital admission have lower mortality rates than patients with the opposite conditions.[4] Therefore, rapid and appropriate intervention will result in good outcomes. Therefore, early detection of SA-AKI and SI-AKI is crucial so that preventive measures and early treatment can be initiated promptly. A major problem to date is the lack of tools to help diagnose sepsis and AKI early and accurately.

Sepsis biomarker evaluation aims to confirm the presence of bacterial infection and determine how aggressive antibiotic therapy should be administered. Therefore, the primary priority is to identify and manage sepsis as early as possible to prevent organ damage and/or progression. Meanwhile, AKI biomarker evaluation aims to detect kidney impairment early, even at subclinical stages, and monitor the severity and risk of permanent kidney disease. Recognizing kidney stress increases physicians'

Cite this as:
Samsu N. Sepsis and Acute Kidney Injury (AKI): Which is More Important, Sepsis Biomarkers or AKI Biomarkers? InaKidney. 2026;3(1):151-153. doi:10.32867/inakidney.v3i1.248

caution in prescribing medications or managing fluids to avoid worsening kidney conditions.

Use of AKI and Sepsis Biomarkers in Critically Ill Patients

The role of biomarkers in identifying sepsis and AKI is crucial for the diagnosis, treatment, and prognosis of these conditions. However, to date, no single biomarker has demonstrated sufficient specificity or discriminatory value to be used decisively and reliably in the diagnosis and/or prognosis of these disorders.[5] There is no ideal sepsis screening tool that achieves both high sensitivity and specificity.[6] Sepsis remains a clinical diagnosis and should neither be confirmed nor excluded on the basis of a single biomarker or diagnostic test alone. On the other hand, sepsis treatment is highly time-dependent.[7] Patients with untreated sepsis or early sepsis are at higher risk of developing SI-AKI.[8] Similarly, in patients with AKI, early diagnosis remains challenging. Creatinine has many limitations, while early biomarkers are not yet widely accessible in clinical practice. Therefore, there is a need for early, easily accessible biomarkers to diagnose structural damage before functional injury occurs. This early identification will facilitate the application of targeted therapeutic interventions, with the potential to alter the natural course of the disease.

To date, there is no 100% specific biomarker for SA-AKI. What exists are AKI biomarkers that perform better in the context of sepsis. This is because SA-AKI is mediated through multiple pathways, including systemic and renal inflammation, complement activation, Renin-Angiotensin-Aldosterone System (RAAS) dysregulation, mitochondrial dysfunction, microcirculatory dysfunction, and macrocirculatory disturbances.[1]

Proenkephalin (PENK) is a newer glomerular filtration biomarker that is exclusively filtered in the glomerulus. PENK is a highly reliable indicator of glomerular filtration injury compared to creatinine. PENK is 48 hours earlier than serum creatinine in detecting severe AKI.[8] PENK is not a sepsis biomarker, but its performance appears to be superior in patients in the setting of sepsis. In this issue of InaKidney, Wahyudi et al. found that serum PENK levels ≥82.6 pmol/L have high accuracy in the early detection of AKI in sepsis.[9] In addition to early diagnosis, serum PENK levels can also determine the severity of AKI and appear to correlate strongly with GFR.[10]

It can be concluded that identifying sepsis biomarkers or AKI biomarkers in critically ill patients is equally important. However, if one must choose which to evaluate first, sepsis biomarkers appear to be the priority in critical care because they determine life-saving interventions. However, regular monitoring of AKI biomarkers is crucial in determining whether a patient will recover fully or end up with chronic kidney disease. The consensus report of the 28th Acute Disease Quality Initiative workgroup recommends using sepsis biomarkers alongside biomarkers of functional and tubular injury to improve prognosis in early or late SA-AKI.[1] Therefore, the best approach in AKI in the setting of sepsis is to use a combination of biomarkers, for example, PENK (biomarker of functional injury) and NGAL (biomarker of tubular injury). A thorough understanding of the underlying pathophysiology and the use of appropriate biomarkers can facilitate early diagnosis and potentially improve patient outcomes through targeted therapy.

Declarations

Competing interest

The author declares no conflict of interest.

References

1. Zarbock A, Nadim MHR, Pickkers P, Gomez H, Bell S, Joannidis M. Sepsis-associated acute kidney injury: consensus report of the 28th Acute Disease Quality Initiative workgroup. Nat Rev Nephrol. 2023;19(6):401–417. doi:10.1038/s41581-023-00683-3

2. Gist KM, Fuhrman D, Stanski N, Menon S, Soranno DE. Subphenotypes of acute kidney injury in children. Curr Opin Crit Care [Internet]. 2022;28(6):590–8.

Available from: https://journals.lww.com/10.1097/MCC.0000000000000986doi:10.1097/mcc.0000000000000986

3. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA [Internet] [Internet]. 2016;315(8):801–810. Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2016.0287doi:10.1001/jama.2016.0287

4. Samsu N, Marzuki MJ, Pratiwi IC, Pravitasari RA, Rifai A, Anshory M. Predictors in-hospital mortality of septic vs non-septic acute kidney injury patients: an observational cohort study. F1000Research [Internet] [Internet]. 2022;10:1184. Available from: https://f1000research.com/articles/10-1184/v2

5. Ferreira GS, Frota ML, Gonzaga MJD, FF VM, Lima C. The Role of Biomarkers in Diagnosis of Sepsis and Acute Kidney Injury. Biomedicines [Internet]. 2024;12(5):931. Available from: https://www.mdpi.com/2227-9059/12/5/931doi:10.3390/biomedicines12050931

6. Prescott HC, Antonelli M, Alhazzani W, Møller MH, Alshamsi F, Azevedo LCP. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026. Crit Care Med [Internet]. 2026;54(4):725–812. Available from: https://journals.lww.com/10.1097/CCM.0000000000007075doi:10.1097/ccm.0000000000007075

7. Gando S. Microvascular thrombosis and multiple organ dysfunction syndrome. Crit Care Med [Internet] [Internet]. 2010;38(2 Suppl):S35-42. Available from: http://journals.lww.com/00003246-201002001-00006doi:10.1097/ccm.0b013e3181c9e31d

8. Hotabilardus N, Anggraeni N. Differentiating of Sepsis-Associated and Sepsis-Induced Acute Kidney Injury in Intensive Care Unit Patients. Indones J Anesth Reanim [Internet] [Internet]. 2025;7(1):53–65. Available from: https://e-journal.unair.ac.id/IJAR/article/view/61812doi:10.20473/ijar.v7i12025.53-65

9. Wahyudi A, Priyono D, Viotra D. Diagnostic Value of Proenkephalin A 119–159 Serum in Early Detection of Sepsis-Associated Acute Kidney Injury. InaKidney. 2026;3(1):170–177.

10. Khorashadi M, Beunders R, Pickkers P, Legrand M. Proenkephalin: A New Biomarker for Glomerular Filtration Rate and Acute Kidney Injury. Nephron [Internet] [Internet]. 2020;144(12):655–61. Available from: https://karger.com/article/doi/10.1159/000509352doi:10.1159/000509352