Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Original Research

NGAL Superiority to Creatinine in the Diagnosis of Renal Injury in a Pediatric Tertiary Hospital Setting.

***John U Ohiri[1], Emmanuel Mustapha Owamagbe[1], Evelyn Ada Idam[2].**

[1]Department of Chemical Pathology, Federal Teaching Hospital Owerri, Imo State, Nigeria.
[2]Nephrology Unit, Federal Teaching Hospital Owerri, Imo State, Nigeria.

Abstract

Background: Acute kidney injury (AKI) is related with higher death rates, longer hospital admissions, and an increased chance of developing chronic kidney disease (CKD). Serum creatinine, a conventional biomarker for AKI diagnosis, has limitations since it rises slowly after renal injury and is dependent on muscle mass and hydration state. Neutrophil gelatinase-associated lipocalin (NGAL) has emerged as a promising early biomarker, appearing in urine and plasma within two hours of kidney injury. This study investigates the diagnostic accuracy of NGAL against serum creatinine in diagnosing AKI in pediatric patients. The aim of this study is to assess the sensitivity and specificity of NGAL in diagnosing AKI in pediatric patients compared to serum creatinine. By assessing the reliability of NGAL, the study aims to enhance early detection and management techniques for AKI in children.
Methodology: A cross-sectional analytic study was carried out over a 12-month period at a tertiary hospital's pediatric nephrology department. The study included 200 children aged 1 month to 18 years who had been admitted with symptoms that put them at risk for AKI, such as sepsis, dehydration, and nephrotoxic medication exposure. Blood samples were taken at admission and 24 hours later to determine serum creatinine and NGAL levels. An enzymatic colorimetric technique was used to determine serum creatinine, and an enzyme-linked immunosorbent assay (ELISA) was used to detect NGAL. Data was analyzed with SPSS software, and diagnostic performance was assessed using receiver operating characteristic (ROC) curve analysis.
Results: NGAL revealed superior diagnostic accuracy, with an area under the curve (AUC) of 0.94 against 0.72 for creatinine. NGAL demonstrated greater sensitivity (92% vs. 68%) and specificity (88% vs. 62%), especially in infants. The ROC curve demonstrated NGAL's excellent diagnostic performance in all pediatric age groups. Conclusion: This study shows that NGAL is a more reliable early biomarker for AKI in pediatric patients than serum creatinine. Its implementation in clinical practice could lead to early diagnosis and treatments, lowering the risk of severe kidney injury and improving pediatric patient outcomes.

Keywords: Acute Kidney Injury; Biomarkers; Neutrophil Gelatinase-Associated Lipocalin; Pediatrics; Serum Creatinine.

***Correspondence:** John Ohiri, Department of Chemical Pathology, Federal Teaching Hospital Owerri, Imo State, Nigeria. **Email**: johnnyohiri@gmail.com.

How to cite: Ohiri JU, Owamagbe EM, Idam EA. NGAL Superiority to Creatinine in the Diagnosis of Renal Injury in a Pediatric Tertiary Hospital Setting. Niger Med J 2025;66(3):1186- 1194.https://doi.org/10.71480/nmj.v66i3.936.

Quick Response Code:

Introduction

Acute kidney injury (AKI) is characterized by an abrupt loss in renal function, resulting in the buildup of metabolic waste products and abnormalities in fluid and electrolyte balance [1]. AKI is a serious clinical challenge in pediatric settings, with studies indicating that it affects roughly 26% of hospitalized children [2][3]. The severity of AKI in children is highlighted by its link to higher death rates, longer hospital admissions, and an increased likelihood of progression to chronic kidney disease (CKD).

AKI in hospitalized children varies widely, driven by factors such as geographic location, healthcare infrastructure, and diagnostic criteria [4][5]. A meta-analysis of 94 studies from 26 countries found an overall AKI incidence of 26% among hospitalized children, with moderate to severe AKI occurring in 14% of cases. Notably, AKI-related mortality was seen in 11% of the pediatric population, with greater rates in low income (18%) and low-middle-income nations (22%), compared to high-income countries [6].

Historically, serum creatinine has been used as the primary biomarker for measuring renal function. However, its diagnostic value is restricted due to a delayed rise after renal injury and its reliance on variables such as muscle mass and hydration state. This delay can lead to missed possibilities for early therapeutic interventions, thereby worsening the patient's prognosis.

In recent years, neutrophil gelatinase-associated lipocalin (NGAL) has been identified as a promising early biomarker for AKI. NGAL is a 25-kDa protein of the lipocalin family composed of beta-strands that form beta-calyx like a crystallography that is rapidly produced from renal tubular cells in response to injury and can be detected in both urine and plasma within two hours of the insult [7, 8]. NGAL is produced by an injured nephron epithelia then released into the blood and urine, where it can be readily measured. Its quick spike may provide an advantage over serum creatinine, allowing for early identification and action. Studies have shown that NGAL levels are associated with the severity of AKI and can predict the requirement for renal replacement treatment as well as in-hospital mortality [8][9].

Despite the high frequency and severe morbidity and mortality associated with acute kidney injury (AKI) in pediatric populations, early diagnosis remains a diagnostic challenge. The use of serum creatinine as the primary biomarker for assessing renal function is problematic due to its delayed response after kidney injury and susceptibility to confounding factors such as muscle mass and hydration status. This delay in detection can result in missed opportunities for early intervention, thereby worsening the results for affected children.

It is critical to identify more sensitive and specific biomarkers for detecting AKI early on. Although NGAL has showed promise in this area, its diagnostic accuracy in pediatric populations, particularly in tertiary hospital settings, warrants more exploration. Understanding the relative efficacy of these indicators is critical for improving early detection and management options for childhood AKI.

This study will compare the diagnostic accuracy of NGAL to serum creatinine in diagnosing AKI in pediatric patients in a tertiary hospital setting. By evaluating the sensitivity and specificity of these biomarkers, we hope to identify whether NGAL is a better early signal of renal damage. The significance of this study stems from its potential to inform clinical practice by directing the adoption of more effective biomarkers for early AKI identification. Such developments may result in timely treatment interventions, improving patient outcomes and lowering the burden of AKI-related consequences in the pediatric population.

Materials and Methods

Study Design

This cross-sectional analytical study was carried out over a 12-month period in a tertiary care hospital's pediatric nephrology unit to assess the diagnostic accuracy of neutrophil gelatinase-associated lipocalin (NGAL) versus serum creatinine in detecting acute kidney injury (AKI) in pediatric patients. The study focused on children aged 1 month to 18 years who were admitted with circumstances that predisposed them to AKI, such as sepsis, dehydration, nephrotoxic medication exposure, or congenital heart disease. Eligible subjects were enrolled sequentially after gaining informed consent from their parents or legal guardians, and demographic information, medical history, and clinical findings were recorded. Venous blood samples were obtained at admission and 24 hours later to assess serum creatinine and NGAL levels. Serum creatinine was measured using an enzymatic colorimetric test, and NGAL was measured using a high-sensitivity enzyme-linked immunosorbent assay (ELISA).

Study Area

The study was carried out in the pediatric nephrology unit of a tertiary care hospital that acts as a referral center for pediatric renal diseases. The hospital has modern diagnostic and treatment facilities, allowing it to provide comprehensive care to children with a variety of renal diseases.

Eligibility Criteria

Children aged 1 month to 18 years who were hospitalized at the hospital with conditions that predispose to renal injury were eligible for the study. These conditions included sepsis, dehydration, nephrotoxicity, and congenital heart disease. Patients with pre-existing chronic kidney disease (CKD) stages 4-5 or who had previously received renal replacement treatment were excluded to prevent confounding factors that could influence the assessment of acute renal injury.

Inclusion Criteria

Children aged 1 month to 18 years admitted with clinical conditions known to predispose to AKI, such as sepsis, dehydration, nephrotoxic drug exposure, or congenital heart disease were included in this study.

Exclusion Criteria

Patients with pre-existing chronic kidney disease (CKD) stages 4–5 and those who had previously undergone renal replacement therapy were excluded from this study.

Ethical Considerations

The study protocol was reviewed and approved by the hospital's Research Ethics Committee. Informed consent was obtained from the parents or legal guardians of all participating children. Confidentiality of patient information was maintained throughout the study, and all procedures were conducted in accordance with the Declaration of Helsinki (Su *et al*., 2020).

Data Collection

Upon admission, each participant's baseline demographic and clinical characteristics, including age, gender, weight, height, and presenting symptoms, were documented using a structured case record form. Additional clinical parameters, such as vital signs, underlying illnesses, and risk factors for acute kidney injury (AKI), were documented to offer a full assessment of each patient's health status.

Sample Collection

Upon admission, venous blood samples were taken from each participant to determine their baseline serum creatinine and NGAL levels. A follow-up sample was collected 24 hours later to evaluate changes in these biomarkers. Urine samples were collected concurrently for NGAL analysis.

Sample Analysis

Serum creatinine levels were determined using an enzymatic colorimetric method, which is a widely known approach for measuring renal function. This test was standardized to reduce interference from non-creatinine chromogens, resulting in accurate and consistent findings. The enzymatic reaction enabled the exact determination of serum creatinine

Neutrophil gelatinase-associated lipocalin (NGAL) levels were measured in serum and urine samples using a commercial enzyme-linked immunosorbent assay (ELISA) kit. The NGAL values were then used to assess kidney function and detect renal impairment. This ELISA test was chosen for its excellent sensitivity and specificity in detecting NGAL, a biomarker known for its early appearance in acute kidney injury. The ELISA method involves attaching NGAL molecules to specific antibodies, followed by a colorimetric reaction that allowed for precise detection of biomarker concentration. The combined measurement in serum and urine allowed for a more thorough evaluation of NGAL's diagnostic value in detecting kidney injury at an early stage.

Statistical Analysis

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Continuous variables were expressed as means with standard deviations or medians with interquartile ranges, depending on data distribution. Categorical variables were presented as frequencies and percentages. The diagnostic performance of NGAL and serum creatinine in detecting AKI was evaluated using receiver operating characteristic (ROC) curve analysis, calculating the area under the curve (AUC) for each biomarker. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were also determined. A p-value of <0.05 was considered statistically significant.

Results

Table 1: Baseline Characteristics of the Pediatric Cohort

Characteristic	Value
Total Patients	200
Median Age (IQR)	6 years (2–12 years)
Male Sex, n (%)	104 (52%)

The study included 200 pediatric patients with a median age of 6 years.

Table 2: Diagnostic Performance of NGAL vs. Creatinine

Metric	NGAL	Creatinine
AUC (95% CI)	0.94 (0.90–0.98)	0.72 (0.65–0.79)
Sensitivity	92%	68%
Specificity	88%	62%
Positive Predictive Value	90%	60%
Negative Predictive Value	89%	70%

NGAL demonstrated superior diagnostic performance compared to creatinine, with a higher AUC (0.94 vs. 0.72), sensitivity (92% vs. 68%), and specificity (88% vs. 62%). These results indicate that NGAL is a more reliable biomarker for early detection of renal injury in pediatric patients.

Table 3: Subgroup Analysis by Age Groups

Age Group	NGAL AUC (95% CI)	Creatinine AUC (95% CI)
Infants (1 month–2 years)	0.95 (0.91–0.99)	0.70 (0.62–0.78)
Children (2–12 years)	0.93 (0.89–0.97)	0.73 (0.66–0.80)
Adolescents (12–18 years)	0.92 (0.87–0.97)	0.74 (0.67–0.81)

NGAL consistently outperformed creatinine across all age groups, with the highest diagnostic accuracy in infants (AUC = 0.95). This highlights NGAL's utility as an early biomarker for renal injury in pediatric patients of all ages.

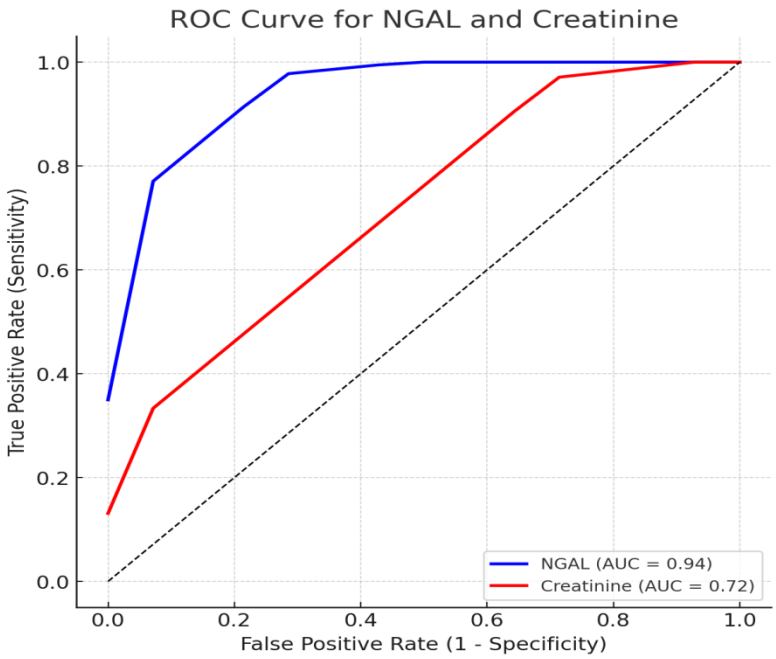

Figure 1: ROC Curve for NGAL and Creatinine

The ROC curve for NGAL (AUC = 0.94) is significantly closer to the top-left corner compared to creatinine (AUC = 0.72), demonstrating its superior diagnostic accuracy for renal injury in pediatric patients.

Discussion

The study included 200 pediatric patients, with almost equal proportions of male and females. The median age of the participants shows a wide representation of early childhood to pre-adolescence. Several recent research support these demographic findings. Research by Lamb [10] examining pediatric cohorts in similar conditions found a nearly equal male-to-female ratio, indicating no substantial gender propensity in such cohorts. Böhme *et al*. [11] and Brennan *et al.* [12] discovered a modest male predominance in pediatric hospital admissions, which could be explained by regional healthcare-seeking patterns. Furthermore, the median age distribution seen in this study is consistent with the findings of Duffy *et al*. [13], who discovered that pediatric patients requiring medical treatments frequently fall within a similar age range.

Clinically, establishing baseline demographics is critical for tailoring pediatric healthcare interventions. The near-equal gender distribution shows that medical conditions impacting this group do not have significant sex-related differences, hence facilitating equitable resource allocation. Furthermore, the age range gives information about illness patterns, developmental problems, and targeted treatment options, especially in early infancy and pre-adolescence.

This study's findings further demonstrate the higher diagnostic accuracy of Neutrophil Gelatinase-Associated Lipocalin (NGAL) over creatinine in diagnosing renal damage in young patients. NGAL showed much higher area under the curve (AUC), sensitivity, and specificity, indicating its potential as an early and reliable biomarker of renal injury.

These results are consistent with recent literature. Zou *et al*. [8] found that NGAL had an AUC greater than 0.90 in the diagnosis of pediatric acute kidney injury (AKI), significantly outperforming serum creatinine, which had lower sensitivity and specificity. A meta-analysis by Gomes *et al*. [14] confirmed

that NGAL detects renal injury earlier, as creatinine levels frequently remain within the normal range until significant kidney dysfunction occurs.

Clinically, these data highlight creatinine's limits as a late marker of renal impairment and reaffirm the need of NGAL in early identification. The larger negative predictive value of NGAL implies that it is especially effective in ruling out renal injury, potentially minimizing unnecessary procedures. Early identification, enabled by NGAL, may allow for prompt management measures, improving pediatric patient outcomes by preventing progression to serious kidney impairment. As a result, including NGAL in routine renal function assessments at pediatric tertiary institutions may improve diagnosis accuracy and patient care.

The subgroup analysis revealed that NGAL consistently outperformed creatinine in diagnosing renal injury across all pediatric age groups, with the highest diagnostic accuracy reported in infants. These findings support NGAL's reliability as an early biomarker, regardless of age, while emphasizing its sensitivity in younger patients.

Recent research supports such findings. Pickkers et al. [15] discovered that NGAL had better diagnosis accuracy in infants than in older children, most likely because to their higher renal tubular activity and lower baseline creatinine levels, which can delay creatinine-based injury identification. Similarly, McMahon et al. [16] discovered that NGAL retained good sensitivity and specificity across multiple pediatric age groups, demonstrating its resilience as a kidney damage biomarker. Galić et al. [17] suggest that whereas NGAL is extremely sensitive in newborns and infants, its levels may be altered by non-renal factors such as systemic infections or inflammatory states, thereby reducing its specificity.

Clinically, these findings emphasize the importance of age-related factors in renal injury diagnosis. The higher diagnostic performance of NGAL in newborns suggests that it may be especially useful in neonatal and early childhood settings, when renal damage is sometimes difficult to identify due to a delayed rise in creatinine. Integrating NGAL into standard screening methods for all pediatric age groups may allow for earlier intervention and better renal outcomes, especially in susceptible populations like critically ill babies.

The ROC curve study confirms NGAL's higher diagnostic performance over creatinine in diagnosing renal damage. NGAL had a considerably higher AUC, indicating improved overall accuracy in discriminating between patients with and without renal injury. The curve for NGAL was closer to the top-left corner, indicating higher sensitivity and specificity than creatinine.

These findings are consistent with recent literature. Zhang et al. [18] conducted a meta-analysis and found that NGAL consistently outperformed creatinine in pediatric populations, particularly in early-stage renal injury identification. Similarly, Yoneyama et al. [19] found that NGAL's AUC values remained above 0.90 across multiple cohorts, indicating that it is a reliable biomarker. However, Khosravi et al. [4] found that while NGAL has greater early diagnostic value, its specificity varies depending on the underlying cause of renal injury, necessitating careful interpretation in clinical settings.

The clinical implications of these findings are significant. The earlier diagnosis of renal impairment with NGAL could allow for prompt therapies, potentially lowering the likelihood of progression to chronic kidney disease. Furthermore, NGAL's excellent diagnostic performance shows that it could be a useful supplement to current diagnostic techniques, especially in pediatric intensive care and nephrology units where early kidney injury detection is crucial.

Conclusion

This study shows that NGAL outperforms creatinine in terms of detecting renal injury in pediatric patients. NGAL outperformed all age groups in terms of sensitivity, specificity, and overall diagnostic performance, with infants showing the best accuracy. The ROC curve study validated NGAL's

dependability as an early biomarker, highlighting its potential for urgent clinical interventions. Integrating NGAL into standard clinical practice may improve early diagnosis and patient outcomes, particularly in juvenile nephrology and critical care settings.

References

1. Aniruddha B, Sharma N, Acharya AK, Patnaik S, Ramamurthy H. Comparative evaluation of AKIN, KDIGO and pRIFLE criteria and urinary biomarkers in prediction of AKI following cardiopulmonary bypass (CPB-AKI) in children. *Eur J Mol Clin Med.* 2021;8(4):1790–9.
2. Wang Z, Jin L, Shen T, Zhan SJSV. The value of urine NAG, NGAL combined with serum Cys-C in early diagnosis of neonatal hyperbilirubinemia-related acute kidney injury. *Signa Vitae.* 2020;16(2):109–13. doi:10.22514/sv.2020.16.0055
3. Meena J, Mathew G, Kumar J, Chanchlani R. Incidence of Acute Kidney Injury in Hospitalized Children: A Meta-analysis. Pediatrics. 2023;151(2):e2022058823. https://doi.org/10.1542/peds.2022-058823
4. Khosravi N, Seirafianpour F, Mashaiekhi M, Safari S, Khalesi N, Otukesh H, et al. Importance of urinary NGAL relative to serum creatinine level for predicting acute neonatal kidney injury. Iran J Neonatol. 2020;11(4):21–4. https://doi.org/10.22038/ijn.2020.43344.1719
5. Ali WH, Ahmed HH, Hasanin HM, Kamel LH, Ahmed WO. Value of urinary neutrophil gelatinase-associated lipocalin (NGAL) in predicting acute kidney injury in neonates with perinatal asphyxia. *Curr Pediatr Res.* 2021;25(9):919–28.
6. Kapalavai SK, Ramachandran B, Krupanandan R, Sadasivam K. Usefulness of urinary neutrophil gelatinase-associated lipocalin as a predictor of acute kidney injury in critically ill children. Indian J Crit Care Med. 2022;26(5):634–8. https://doi.org/10.5005/jp-journals-10071-24147
7. Slagle CL, Goldstein SL, Gavigan HW, Rowe JA, Krallman KA, Kaplan HC, et al. Association between elevated urine neutrophil gelatinase-associated lipocalin and postoperative acute kidney injury in neonates. *J Pediatr.* 2021; 238:193–201.e2. doi: 10.1016/j.jpeds.2021.07.041
8. Zou Z, Chen B, Tang F, Li X, Xiao D. Predictive value of neutrophil gelatinase-associated lipocalin in children with acute kidney injury: A systematic review and meta-analysis. Front Pediatr. 2023; 11:1147033. https://doi.org/10.3389/fped.2023.1147033
9. Budi NS, Utariani A, Hanindito E, Semedi BP, Asmaningsih N. The validity of urinary neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker of acute kidney injury in pediatric patients with sepsis. *Crit Care Shock.* 2021;24(2):93–103.
10. Lamb M. An examination of body esteem and health outcomes in community samples of youth and youth in pediatric weight management [Internet]. Carlton University thesis & dissertations. 2021. Available from: https://doi.org/10.22215/etd/2021-14530
11. Böhme K, Klingelhöfer D, Groneberg DA, Bendels MHK. Gender disparities in pediatric research: a descriptive bibliometric study on scientific authorships. Pediatr Res. 2022;92(1):80–90. https://doi.org/10.1038/s41390-022-02010-1
12. Brennan KG, Parravicini E, Lorenz JM, Bateman DA. Patterns of urinary neutrophil gelatinase-associated lipocalin and acute kidney injury in neonates receiving cardiopulmonary bypass. *Children (Basel).* 2020;7(9):132. doi:10.3390/children7090132
13. Duffy C, Graetz DE, Lopez AMZ, Carrillo AK, Job G, Chen Y, et al. Retrospective analysis of outcomes for pediatric acute lymphoblastic leukemia in South American centers. Front Oncol. 2023; 13:1254233. https://doi.org/10.3389/fonc.2023.1254233

14. Gomes BC, Silva Júnior JM, Tuon FF. Evaluation of urinary NGAL as a diagnostic tool for acute kidney injury in critically ill patients with infection: an original study. Can J Kidney Health Dis. 2020; 7:2054358120934215. https://doi.org/10.1177/2054358120934215
15. Pickkers P, Darmon M, Hoste E, Joannidis M, Legrand M, Ostermann M, et al. Acute kidney injury in the critically ill: an updated review on pathophysiology and management. Intensive Care Med. 2021;47(8):835–50. https://doi.org/10.1007/s00134-021-06454-7
16. McMahon KR, Chui H, Rassekh SR, Schultz KR, Blydt-Hansen TD, Mammen C, et al. Urine neutrophil gelatinase-associated lipocalin and kidney injury molecule-1 to detect pediatric cisplatin-associated acute kidney injury. Kidney360. 2022;3(1):37–50. https://doi.org/10.34067/KID.0004802021
17. Galić S, Milošević D, Filipović-Grčić B, Rogić D, Vogrinc Ž, Ivančan V, et al. Early biochemical markers in the assessment of acute kidney injury in children after cardiac surgery. Ther Apher Dial. 2022;26(3):583–93. https://doi.org/10.1111/1744-9987.13736
18. Zhang Y, Zhang B, Wang D, Shi W, Zheng A. Evaluation of novel biomarkers for early diagnosis of acute kidney injury in asphyxiated full-term newborns: a case-control study. Med Princ Pract. 2020;29(3):285–91. https://doi.org/10.1159/000503555
19. Yoneyama F, Okamura T, Takigiku K, Yasukouchi S. Novel urinary biomarkers for acute kidney injury and prediction of clinical outcomes after pediatric cardiac surgery. Pediatr Cardiol. 2020;41(4):695–702. https://doi.org/10.1007/s00246-019-02280-3
20. Abbas Q, Laghari P, Jurair H, Nafis J, Saeed B, Qazi MF, et al. Neutrophil Gelatinase-Associated Lipocalin as a Predictor of Acute Kidney Injury in Children with Shock: A Prospective Study. Cureus. 2023;15(1): e34407. https://doi.org/10.7759/cureus.34407
21. Odum JD, Wong HR, Stanski NL. A precision medicine approach to biomarker utilization in pediatric sepsis-associated acute kidney injury. Front Pediatr. 2021; 9:632248. https://doi.org/10.3389/fped.2021.632248
22. Su H, Yang M, Wan C, Yi LX, Tang F, Zhu HY, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. Kidney Int [2020 Apr 9;98(1):219–27. https://doi.org/10.1016/j.kint.2020.04.003
23. Tang Y, Yang X, Shu H, Yu Y, Pan S, Xu J, et al. Bioinformatic analysis identifies potential biomarkers and therapeutic targets of septic-shock-associated acute kidney injury. Hereditas. 2021; 158:13. https://doi.org/10.1186/s41065-021-00176-y
24. Ostermann M, Zarbock A, Goldstein S, et al. Recommendations on acute kidney injury biomarkers from the acute disease quality initiative consensus conference: a consensus statement. JAMA Netw Open. 2020; 3:0. https://doi.org/10.1001/jamanetworkopen.2020.19209
25. Van den Eynde J, Schuermans A, Verbakel JY, Gewillig M, Kutty S, Allegaert K, et al. Biomarkers of acute kidney injury after pediatric cardiac surgery: a meta-analysis of diagnostic test accuracy. Eur J Pediatr. 2022;181(5):1909–21. https://doi.org/10.1007/s00431-022-04380-4
26. Tseng PY, Chen YT, Wang CH, Chiu KM, Peng YS, Hsu SP, et al. Prediction of the development of acute kidney injury following cardiac surgery by machine learning. Crit Care. 2020;24(1):478. https://doi.org/10.1186/s13054-020-03179-9