



## Editorial Editorial on the Special Issue "Advances in Pediatric Acute Kidney Injury"

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Acute kidney injury (AKI) refers to a swift decline in kidney function, marked by the reduced excretion of waste products and disturbances in fluid and electrolyte balance [1,2]. The Kidney Disease/Improving Global Outcome (KDIGO) guidelines identify AKI based on elevated serum creatinine levels or decreased urine outputs [2].

Despite its significant impact on long-term kidney health [3,4], AKI often goes unnoticed in pediatric cases [5,6]. The severity of AKI is closely associated with both short- and long-term adverse outcomes [7–10], with animal studies indicating potential long-term structural changes such as renal fibrosis [11]. This leads to a doubled risk of chronic kidney disease (CKD) even with mild AKI; the risk rises exponentially with AKI severity [3]. However, AKI is commonly observed in hospitalized children, complicating 1–25% of intensive care unit (ICU) admissions and 1–7% of total hospital admissions [12]. This Special Issue, entitled "Advances in pediatric acute kidney injury", aims to enhance our understanding of AKI in children and neonates. This Editorial focuses on the innovations presented in the articles featured in this Special Issue.

AKI can complicate various common pediatric conditions [13–20]. For example, children with type one diabetes mellitus (T1DM) may undergo kidney damage in both chronic and acute settings [21,22]. Osmotic polyuria from hyperglycemia during T1DM onset can lead to dehydration, hypovolemia, and kidney hypoperfusion, resulting in tubular damage [21].

During T1DM onset, AKI may occur in 43.8% of patients, reaching 65% in those with diabetic ketoacidosis [16]. Acidosis can expedite tubular damage deterioration [21].

The baseline serum creatinine (bSCr) level is critical for AKI diagnosis, and when the measured bSCr (mbSCr) is unavailable, estimated bSCr (ebSCr) based on height can serve as a viable substitute [23]. Depending on the method used to quantify creatinine, the revised Schwartz equation [24] or the original Schwartz equation [25] is employed.

In this context, Guarino et al. assessed whether the ebSCr, calculated based on height, could serve as a viable alternative for diagnosing AKI compared with the mbSCr. This investigation was conducted within a cohort of individuals experiencing onset of T1DM, as presented in this Special Issue [23]. Notably, the study revealed a substantial 90% agreement between ebSCr and the established gold standard, the mbSCr value [23]. This underscores the potential use of ebSCr based on height as a screening tool for identifying AKI in patients experiencing T1DM onset, especially in situations where mbSCr is unavailable, such as in critically ill children in pediatric intensive care units (PICUs). Additionally, the study recommended using the revised Schwartz equation [24] for the retrocalculation of creatinine based on height when the creatinine is determined using the IDMS-traceable technique [eb-SCr (mg/dL) = (0.413 height [cm])/baseline estimated glomerular filtration rate (eGFR)]. However, if the Jaffe technique is employed to quantify creatinine, use of the original Schwartz equation [25] is advised [23].



**Citation:** Rivetti, G.; Montaldo, P.; Marzuillo, P. Editorial on the Special Issue "Advances in Pediatric Acute Kidney Injury". *Children* **2024**, *11*, 195. https://doi.org/10.3390/ children11020195

Received: 8 December 2023 Accepted: 2 February 2024 Published: 3 February 2024



**Copyright:** © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). In a concise report by Marzuillo et al., the prevalence and risk factors associated with AKI in a cohort of patients with acute appendicitis (AA) were explored. Among 122 children hospitalized for AA, AKI occurred in 7.4%, and it was associated with vomiting, 5% dehydration, axillary body temperature  $\geq$  38.5 °C, and elevated levels of C-reactive protein and neutrophils [13].

As mentioned earlier, AKI doubles the risk of chronic kidney disease [3], and conditions linked to reduced nephronic mass significantly contribute to AKI development [15].

For example, very-low-birth-weight babies are at an increased risk due to insufficient renal reserves, stressful postnatal events, and medication exposures [26]. Lazarovits et al. reported a 21% prevalence of AKI in 152 infants with very low birth weight, with predictors including the use of vasopressors, patent ductus arteriosus, and bloodstream infection [26]. Neonatal mortality and AKI were strongly correlated [26]. Various methods exist to diagnose AKI [9,27], such as the widely used risk, injury, failure, loss, and end-stage (RIFLE) criteria [28]. The "Acute Kidney Injury Network" (AKIN) developed a classification system which evaluates changes in kidney function within 48 h to increase the sensitivity of the RIFLE detection approach [29].

To enhance the sensitivity of RIFLE, the AKIN introduced a categorization system to assess changes in kidney function within a 48 h period [29]. Leblebici et al. conducted a study comparing AKIN with pediatric RIFLE (pRIFLE) AKI classifications and PICU scoring methods. In the original article by Leblebici et al., it was revealed that 8.7% of the PICU patients developed kidney injury according to pRIFLE and AKIN classifications, significantly impacting mortality [29]. Renal injury incidence exhibited a strong statistical correlation with elevated Pediatric Mortality Risk Score (PRISM III), Pediatric Logistic Organ Dysfunction-2 (PELOD-2), and Pediatric Sequential Organ Failure Assessment (pSOFA) scores. When comparing AKIN criteria stages with PRISM III, PELOD-2, and pSOFA scores, a significant difference was observed between patients without AKI and those with stage 1, stage 2, and stage 3 kidney injury. However, for PRISM III, PELOD-2, and pSOFA scores, no significant differences were found between stages, according to AKIN criteria [29]. Notably, a substantial difference emerged between patients without AKI and those in the risk, injury, and failure plus loss stages according to pRIFLE criteria. According to the Pediatric Mortality Index (PIM-2) ratio and pRIFLE criteria, a statistically significant difference was identified between patients in the injury and failure plus loss stages and those without AKI [29].

The association between kidney impairment and COVID-19 infection has also been acknowledged [30–32]. In their systematic review, Wu et al. shared findings from a thorough literature investigation on renal complications arising from COVID-19 in children and adolescents. The most commonly reported manifestation was nephrotic syndrome, and there were additional instances involving diverse glomerulonephritides [33]. Furthermore, individuals with transplanted kidneys who tested positive for COVID-19 displayed T-cell-mediated rejection and moderate tubular interstitial infiltration [33].

Finally, in a separate comprehensive investigation, Wu et al. documented the potential negative impacts of COVID-19 vaccination on the kidneys within a restricted group of vaccinated children and adolescents, a subset of the wider vaccinated population. They emphasized that, unless specific circumstances dictate otherwise, there is currently no justification to abstain from vaccination, given that the advantages far exceed any potential risks [34]. The authors particularly advocated for the careful monitoring of all children and adolescents undergoing COVID-19 vaccination [34].

We hope readers are satisfied with the new evidence in this area of research.

Conflicts of Interest: The authors declare no conflict of interest.

## References

- 1. Sutherland, S.M.; Kwiatkowski, D.M. Acute Kidney Injury in Children. Adv. Chronic Kidney Dis. 2017, 24, 380–387. [CrossRef]
- 2. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int. 2012, 2 (Suppl. S1), 1–138. [CrossRef]
- 3. Coca, S.G.; Singanamala, S.; Parikh, C.R. Chronic kidney disease after acute kidney injury: A systematic review and meta-analysis. *Kidney Int.* 2012, *81*, 442–448. [CrossRef]
- Gameiro, J.; Marques, F.; Antó, J.; Lopes, N. Long-term consequences of acute kidney injury: A narrative review. *Clin. Kidney J.* 2020, 14, 789–804. [CrossRef]
- 5. Rivetti, G.; Marzuillo, P. Community-Acquired Acute Kidney Injury in Hospitalized Children: Do Not Miss the Diagnosis! *Indian Paediatr.* **2023**, *60*, 433–434. [CrossRef]
- Jones, K.; Neu, A.; Fadrowski, J. AKI in Hospitalized Children: Poorly Documented (and Underrecognized). Front. Pediatr. 2022, 9, 790509. [CrossRef]
- Susantitaphong, P.; Cruz, D.N.; Cerda, J.; Abulfaraj, M.; Alqahtani, F.; Koulouridis, I.; Jaber, B.L. World incidence of AKI: A meta-analysis. *Clin. J. Am. Soc. Nephrol.* 2013, *8*, 1482–1493. [CrossRef]
- 8. Chawla, L.S.; Amdur, R.L.; Amodeo, S.; Kimmel, P.L.; Palant, C.E. The severity of acute kidney injury predicts progression to chronic kidney disease. *Kidney Int.* 2011, *79*, 1361–1369. [CrossRef]
- 9. Sutherland, S.M.; Byrnes, J.J.; Kothari, M.; Longhurst, C.A.; Dutta, S.; Garcia, P.; Goldstein, S.L. AKI in hospitalized children: Comparing the pRIFLE, AKIN, and KDIGO definitions. *Clin. J. Am. Soc. Nephrol.* **2015**, *10*, 554–561. [CrossRef]
- 10. Macedo, E.; Cerdá, J.; Hingorani, S.; Hou, J.; Bagga, A.; Burdmann, E.A.; Rocco, V.M.; Mehta, L.R. Recognition and management of acute kidney injury in children: The ISN 0by25 Global Snapshot study. *PLoS ONE* **2018**, *13*, e0196586. [CrossRef] [PubMed]
- 11. Parr, S.K.; Siew, E.D. Delayed Consequences of Acute Kidney Injury. Adv. Chronic Kidney Dis. 2016, 23, 186–194. [CrossRef]
- 12. Stevens, L.A.; Lafayette, R.A.; Perrone, R.D.; Levey, A.S. Laboratory evaluation of kidney function. In *Diseases of the Kidney and Urinary Tract*, 8th ed.; Schrier, R.W., Ed.; Lippincott, Williams and Wilkins: Philadelphia, PA, USA, 2007; Volume 1–3.
- 13. Marzuillo, P.; Coppola, C.; Caiazzo, R.; Macchini, G.; Di Sessa, A.; Guarino, S.; Esposito, F.; del Giudice, E.M.; Tipo, V. Acute Kidney Injury in Children with Acute Appendicitis. *Children* **2022**, *9*, 620. [CrossRef]
- 14. Marzuillo, P.; Baldascino, M.; Guarino, S.; Perrotta, S.; del Giudice, E.M.; Nunziata, F. Acute kidney injury in children hospitalized for acute gastroenteritis: Prevalence and risk factors. *Pediatr. Nephrol.* **2021**, *36*, 1627–1635. [CrossRef]
- 15. Marzuillo, P.; Di Sessa, A.; Golino, R.; Tirelli, P.; De Lucia, M.; Rivetti, G.; del Giudice, E.M.; Guarino, S.; Nunziata, F. Acute kidney injury in infants hospitalized for viral bronchiolitis. *Eur. J. Pediatr.* **2023**, *182*, 3569–3576. [CrossRef]
- Marzuillo, P.; Iafusco, D.; Zanfardino, A.; Guarino, S.; Piscopo, A.; Casaburo, F.; Capalbo, D.; Ventre, M.; Arienzo, M.R.; Cirillo, G.; et al. Acute Kidney Injury and Renal Tubular Damage in Children with Type 1 Diabetes Mellitus Onset. *J. Clin. Endocrinol. Metab.* 2021, 106, E2720–E2737. [CrossRef]
- 17. Xiong, M.; Wang, L.; Su, L.; Luo, W.; Li, Y.; Li, L.; Nie, S.; Hou, F.F. Acute kidney injury among hospitalized children with cancer. *Pediatr. Nephrol.* **2021**, *36*, 171–179. [CrossRef]
- 18. Baddam, S.; Aban, I.; Hilliard, L.; Howard, T.; Askenazi, D.; Lebensburger, J.D. Acute kidney injury during a pediatric sickle cell vaso-occlusive pain crisis. *Pediatr. Nephrol.* **2017**, *32*, 1451–1456. [CrossRef]
- Sethi, S.K.; Rana, A.; Adnani, H.; McCulloch, M.; Alhasan, K.; Sultana, A.; Safadi, R.; Agrawal, N.; Raina, R. Kidney involvement in multisystem inflammatory syndrome in children: A pediatric nephrologist's perspective. *Clin. Kidney J.* 2021, 14, 2000–2011. [CrossRef]
- 20. Plumb, L.; Casula, A.; Sinha, M.D.; Inward, C.D.; Marks, S.D.; Medcalf, J.; Nitsch, D. Epidemiology of childhood acute kidney injury in England using e-alerts. *Clin. Kidney J.* 2023, *16*, 1288–1297. [CrossRef]
- 21. Rivetti, G.; Hursh, B.E.; Miraglia del Giudice, E.; Marzuillo, P. Acute and chronic kidney complications in children with type 1 diabetes mellitus. *Pediatr. Nephrol.* **2022**, *38*, 1449–1458. [CrossRef]
- 22. Hursh, B.E.; Ronsley, R.; Islam, N.; Mammen, C.; Panagiotopoulos, C. Acute kidney injury in children with type 1 diabetes hospitalized for diabetic ketoacidosis. *JAMA Pediatr.* 2017, 171, e170020. [CrossRef] [PubMed]
- Guarino, S.; Rivetti, G.; Di Sessa, A.; De Lucia, M.; Palma, P.L.; Miraglia del Giudice, E.; Polito, C.; Marzuillo, P. Diagnostic performance of height-estimated basal creatinine in diagnosing acute kidney injury in children with type 1 diabetes mellitus onset. *Children* 2022, *16*, 899. [CrossRef] [PubMed]
- 24. Schwartz, G.J.; Muñoz, A.; Schneider, M.F.; Mak, R.H.; Kaskel, F.; Warady, B.A.; Furth, S.L. New equations to estimate GFR in children with CKD. *J. Am. Soc. Nephrol.* 2009, 20, 629–637. [CrossRef] [PubMed]
- 25. Schwartz, G.J.; Brion, L.P.; Spitzer, A. The Use of Plasma Creatinine Concentration for Estimating Glomerular Filtration Rate in Infants, Children, and Adolescents. *Pediatr. Clin. N. Am.* **1987**, *34*, 571–590. [CrossRef] [PubMed]
- Lazarovits, G.; Ofek Shlomai, N.; Kheir, R.; Abram, T.B.; Friedman, S.E.; Volovelsky, O. Acute Kidney Injury in Very Low Birth Weight Infants: A Major Morbidity and Mortality Risk Factor. *Children* 2023, 10, 242. [CrossRef] [PubMed]
- Zappitelli, M.; Ambalavanan, N.; Askenazi, D.J.; Moxey-Mims, M.M.; Kimmel, P.L.; Star, R.A.; Abitbol, C.L.; Brophy, P.D.; Hidalgo, G.; Hanna, M.; et al. Developing a neonatal acute kidney injury research definition: A report from the NIDDK neonatal AKI workshop. *Pediatr. Res.* 2017, *82*, 569–573. [CrossRef] [PubMed]
- Bellomo, R.; Ronco, C.; Kellum, J.A.; Mehta, R.L.; Palevsky, P.; ADQI Workgroup. Open Access Acute renal failure-definition, outcome measures, animal models, fluid therapy and information technology needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI). *Group Crit. Care* 2004, *8*, R204–R212. [CrossRef]

- Lin, L.; Deng, J.; Tan, W.; Li, J.; Wu, Z.; Zheng, L.; Yang, J. Pathogenesis and histological changes of nephropathy associated with COVID-19. J. Med. Virol. 2023, 95, e28311. [CrossRef]
  Palan, C.; Ciuhadami, T. Puhanak, Turani, S. J. Kidnay, Iniury in Critically, III Patients with COVID 10. From Pathophysical science
- Balan, C.; Ciuhodaru, T.; Bubenek-Turconi, S.-I. Kidney Injury in Critically Ill Patients with COVID-19-From Pathophysiological Mechanisms to a Personalized Therapeutic Model Published under CC BY 4.0 license. J. Crit. Care Med. 2023, 9, 148–161. [CrossRef]
- 32. Brogan, M.; Ross, M.J. Annual Review of Medicine COVID-19 and Kidney Disease. Annu. Rev. Med. 2022, 27, 1–13. [CrossRef]
- Wu, H.H.L.; Shenoy, M.; Kalra, P.A.; Chinnadurai, R. Intrinsic Kidney Pathology Following COVID-19 Infection in Children and Adolescents: A Systematic Review. *Children* 2022, 9, 3. [CrossRef] [PubMed]
- Wu, H.H.L.; Shenoy, M.; Kalra, P.A.; Chinnadurai, R. Intrinsic Kidney Pathology in Children and Adolescents Following COVID-19 Vaccination: A Systematic Review. *Children* 2022, 9, 1467. [CrossRef] [PubMed]

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