Unraveling Urinary Sepsis in Pediatrics: A Scope Review

Desvendando a Sepse com Foco Urinário na Pediatria: Uma Revisão de Escopo
Desentrañando la Sepsis Urinaria en Pediatría: Una Revisión de Scope

RESUMO
Objetivo: Mapear os principais indicadores clínicos e laboratoriais relacionados à urosepse pediátrica, contribuindo para a prática baseada em evidências. **Métodos:** Trata-se de uma revisão de escopo, a qual apropriou-se das bases *Medical Literature Analysis and Retrieval System Online* – MEDLINE/PubMed, Cochrane, LILACS, BDENF e Embase, com intervalo temporal de 2020 a 2025, em qualquer idioma. Foram excluídos os artigos repetidos e aqueles cujo a temática não era compatível com os do objetivo do trabalho. **Resultados:** Dos 641 artigos identificados inicialmente, 17 foram selecionados após triagem detalhada. A maioria dos estudos era de coorte e apresentava nível de evidência IV. Os critérios KDIGO foram amplamente utilizados para diagnóstico de insuficiência renal aguda, um dos principais desfechos associados à urosepse. Biomarcadores como uCXCL10 e DKK3 urinária mostraram-se promissores na predição de IRA séptica e mortalidade em crianças gravemente doentes. **Conclusão:** A gravidade da IRA é determinada pela alteração na creatinina sérica e débito urinário, sendo essencial o diagnóstico precoce para melhorar o prognóstico. Além disso, estratégias como atenuação da sobrecarga hídrica precoce e uso de biomarcadores podem auxiliar na redução da mortalidade. Reforça-se a importância da abordagem multidisciplinar no manejo da urosepse pediátrica e sugere que avanços na classificação e identificação precoce de biomarcadores podem contribuir significativamente para melhores resultados clínicos.
DESCRITORES: Sepse. Pediatria. Infecções Urinárias.

ABSTRACT
Objective: To map the main clinical and laboratory indicators related to pediatric urosepsis, contributing to evidence-based practice. **Methods:** A scoping review was conducted using five databases (MEDLINE/PubMed, Cochrane, LILACS, BDENF, and Embase) covering studies from 2020 to 2025 in any language. Duplicate articles and those unrelated to the study's objective were excluded. **Results:** Out of 641 initially identified articles, 17 were selected after detailed screening. Most studies were cohort-based and had a level IV evidence rating. The Kidney Disease Improving Global Outcomes (KDIGO) criteria were widely used for diagnosing acute kidney injury (AKI), a key outcome associated with urosepsis. Biomarkers such as urinary uCXCL10 and DKK3 showed promise in predicting septic AKI and mortality in critically ill children. **Conclusion:** AKI severity is determined by changes in serum creatinine levels and urine output, emphasizing the importance of early diagnosis for better prognosis. Strategies like early fluid overload management and biomarker utilization can help reduce mortality. The study highlights the importance of a multidisciplinary approach in managing pediatric urosepsis and suggests that advancements in biomarker identification could significantly improve clinical outcomes.
DESCRIPTORS: Sepsis. Pediatrics. Urinary Tract Infections.

RESUMEN
Objetivo: Mapear los principales indicadores clínicos y de laboratorio relacionados con la sepsis urinaria pediátrica, contribuyendo a la práctica basada en la evidencia. **Métodos:** Se realizó una revisión exploratoria utilizando cinco bases de datos (MEDLINE/PubMed, Cochrane, LILACS, BDENF y Embase) que abarcaron estudios de 2020 a 2025 en cualquier idioma. Se excluyeron los artículos duplicados y aquellos no relacionados con el objetivo del estudio. **Resultados:** De los 641 artículos identificados inicialmente, 17 fueron seleccionados tras una revisión exhaustiva. La mayoría de los estudios se basaron en cohortes y obtuvieron una calificación de evidencia de nivel IV. Los criterios KDIGO (Kidney

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Disease Improving Global Outcomes) se utilizaron ampliamente para el diagnóstico de la lesión renal aguda (LRA), un resultado clave asociado con la sepsis urinaria. Biomarcadores como uCXCL10 y DKK3 urinarios mostraron ser prometedores en la predicción de la LRA séptica y la mortalidad en niños en estado crítico. **Conclusión:** La gravedad de la IRA se determina por los cambios en los niveles séricos de creatinina y la diuresis, lo que resalta la importancia del diagnóstico precoz para un mejor pronóstico. Estrategias como el manejo temprano de la sobrecarga hídrica y el uso de biomarcadores pueden ayudar a reducir la mortalidad. El estudio destaca la importancia de un enfoque multidisciplinario en el manejo de la sepsis urinaria pediátrica y sugiere que los avances en la identificación de biomarcadores podrían mejorar significativamente los resultados clínicos.
DESCRIPTORES: Sepsis. Pediatría. Infecciones del tracto urinario.

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Lucas Dalvi Armond Rezende
Nurse from the Federal University of Espírito Santo (UFES). Master's student in Medicine in the discipline of Endocrinology from the Federal University of Rio de Janeiro (UFRJ). Professor at the Salesian University Center, assigned to the Nursing Board of the Salesian University Center, Vitória, ES - BR. Federal University of Rio de Janeiro, Postgraduate Program in Medicine (Endocrinology), Department of Endocrinology, School of Medicine - Rio de Janeiro, RJ - BR.
ORCID: https://orcid.org/0000-0002-3313-852X

Victória Gabriel Passos
Undergraduate in Medicine at Multivix College. Vitória, ES – BR.
ORCID: https://orcid.org/0000-0003-3392-2872

Pedro Massaroni Peçanha
Doctor from the University of Vassouras. Residency in Pediatrics from the General Hospital of Nova Iguaçu. Residency in Pediatric Infectology from the Oswaldo Cruz Foundation (FIOCRUZ). Master in Research Applied to Children's and Women's Health from FIOCRUZ. Associated with the Department of Medicine of the Higher School of Sciences of the Santa Casa de Misericórdia de Vitória (EMESCAM), Vitória, ES – BR.
ORCID: https://orcid.org/0000-0002-4151-5508

Rafaela Gava Secchin
Undergraduate in Medicine at Multivix College. Vitória, ES – BR.
ORCID: https://orcid.org/0009-0009-8155-6230

Lucas Zon Andrade de Assis
Doctor from the Higher School of Sciences of the Santa Casa de Misericórdia de Vitória (EMESCAM). Linked to the Medical Residency Program in Internal Medicine at the Santa Casa de Misericórdia Hospital of São Paulo (HSCMSP), São Paulo, SP – Brazil.
ORCID: https://orcid.org/0009-0002-0536-1633

Marco Antônio Oliveira Brito
Undergraduate in Medicine from the Higher School of Sciences of the Santa Casa de Misericórdia de Vitória (EMESCAM). Vitória, ES – BR.
ORCID: https://orcid.org/0009-0001-5711-0353

Leonardo Gomes da Silva
Nurse from the Higher School of Sciences of the Santa Casa de Misericórdia de Vitória (EMESCAM). Master and Doctoral student in Public Health from the Federal University of Espírito Santo (UFES). Professor at the Department of Medicine and Nursing of the Higher School of Sciences of the Santa Casa de Misericórdia de Vitória (EMESCAM). Vitória, ES – BR.
ORCID: https://orcid.org/0000-0002-1820-8075

Lavínya Moreira Silva Funabashi
Nurse from the Federal University of Espírito Santo (UFES). Resident in the Cardiology Nursing Residency Program at the Dante Pazzanese Institute of Cardiology (IDPC), São Paulo, SP – BR.
ORCID: https://orcid.org/0000-0003-4832-3143

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INTRODUCTION

The currently accepted definitions of sepsis, severe sepsis, and septic shock were developed to help identify, treat, and study patients with infections who are at increased risk for significant morbidity and mortality. [1-3]

The foci of childhood sepsis can be the most varied, including pharyngotonsillitis, meningitis, and upper and lower urinary tract infections. The general prognosis of childhood sepsis is unfavorable when diagnosed late, and when specifically addressing childhood urosepsis, the prognosis does not become more favorable, with reported mortality rates of 20 to 40% for severe urosepsis. [2,4]

The pathophysiology of childhood urosepsis results from infection leading to the release of pathogens and molecular patterns associated with damage, which bind to pattern recognition receptors on the surface of defense cells, endothelial and urothelial cells, with the ability to hyperreactively modulate the immune response through pro- and anti-inflammatory mediators and biomarkers, generating an imbalance in the homeostasis and hemodynamics of the affected child. [2,5]

Thus, considering its importance in clinical practice, the objective of this article is to map the clinical and laboratory indicators, as well as the main evidence in the literature about childhood urosepsis, seeking to contribute to evidence-based practice.

METHOD

This is a scoping review with high compliance with the JBI Manual for Evidence Synthesis, and the Preferred Reporting Items for Systematic Review and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) statement was used to summarize the study selection process and its steps. [6-8] This scoping review had its research protocol registered in the Open Science Framework (DOI 10.17605/OSF.IO/8EXS2)

The nine steps for conducting a scoping review include: 1) elaboration of the guiding question; 2) definition of inclusion and exclusion criteria according to the guiding question; 3) planning the search strategy, selection of articles and presentation of results; 4) designing a clear and reproducible search strategy; 5) selection of studies; 6) extraction of data; 7) evaluation of evidence; 8) presentation of the evidence gathered; and 9) summary of results according to the objectives of the review. [7,9]

The search strategy was carried out in January 2023, in five electronic databases: Medical Literature Analysis and Retrieval System Online - MEDLINE/PubMed, Cochrane Central Register of Controlled Trials, Latin American and Caribbean Literature in Health Sciences, Nursing Database and Embase. The acronym PECO (Population/Exposure/Comparison/Outcomes) was used to develop the guiding question of the research, considering P = (Pediatric patients with urinary tract infection), E = (Symptoms and changes common to the septic condition), C = (Pediatric patients with urinary tract infection without sepsis) and O = (Patient prognosis and knowledge of the main changes). [10,11] Thus, the research question was: "What scientific evidence is available on clinical and laboratory indicators for sepsis with urinary focus in pediatric patients?".

Mendeley - Reference Management Software was used to organize and manage the studies found in the databases. The selection of studies was performed by three researchers independently and in a double-blind manner, using the Rayyan™ application. The Boolean operators "AND" and "OR" were used to obtain restrictive and additive combinations, and to combine the Health Sciences Descriptors/Medical Subjective Headings (DeCS/MeSH), namely: "Sepse" ("Sepsis"), "Infeção de Trato Urinário" ("Urinary Tract Infections"), "Pielonefrite" ("Pyelonephritis"), "Glomerulonefrite" ("Glomerulonephritis"), "Injúria Renal Aguda" ("Acute Kidney Injury") e "Pediatria" ("Pediatrics").

Eligibility criteria

All published observational, experimental, qualitative study designs and literature reviews were included, as well as studies covering pediatric urosepsis and kidney infections that progress to septic shock/septicemia.

Regarding exclusions, preprints, e-books and articles that addressed the population aged 18 or older were removed. According to the language of the articles, productions in the following languages were selected: English, Portuguese, Spanish and French. Regarding the time criterion, a time cut-off of 5 years was used for the search in the electronic databases.

Study selection

All files examined were imported into Mendeley - Reference Management Software, and duplicate studies were removed. Three independent researchers searched and filtered the records by abstract and title using the Rayyan™ application. After the first screening, the full texts of the retrieved studies were assessed for inclusion or exclusion using the same application. In case of disagreement between the authors, a fourth author was consulted to make the selection. [6]

Data extraction and synthesis

Three authors performed data extraction for each included study based on a previously published form. The extracted data included: 1) type of methodological study; 2) population, if applicable; 3) recruitment method; 4) measurement/follow-up time; 5) main findings; 6) relevance to clinical practice. [11-13]

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Assessment of included studies

The level of evidence was identified according to the hierarchy of evidence, a strategy chosen because it is widely used and effective for classifying evidence for literature reviews. This system is divided into seven hierarchical levels, and in this review we consider levels I to III as strong, IV to VI as moderate and VII as weak, namely: I - Systematic reviews or meta-analyses of randomized clinical trials; II - Well-designed randomized controlled clinical trial; III - Well-designed controlled clinical trial without randomization; IV - Cohort study, case-control, or well-designed cross-sectional study; V - Systematic review of qualitative studies and descriptive studies; VI - Single descriptive or qualitative study; VII - Authority opinion and/or expert report. [13,14]

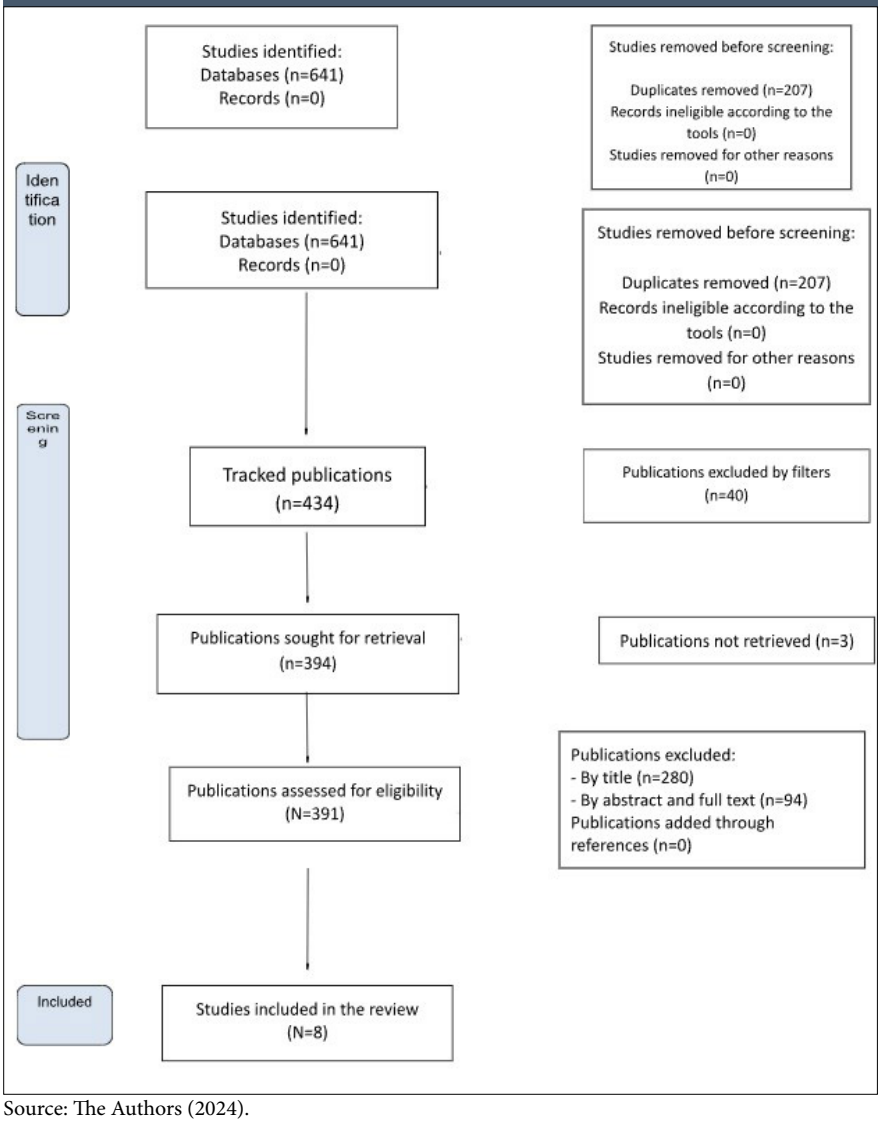
Regarding data synthesis, the characteristics of the studies were summarized and presented in tables, and the results will be presented according to the study design. Tables 1 and 2 contain: (a) citation; (b) country of origin; (c) objective; (d) main results; (e) level of evidence; and (f) clinical applicability.

In addition, the quantitative tool described in Peters et al., (2015) 15, was used, which includes 12 criteria for assessing the methodological quality of the studies selected for the review. A score of 1 or 0 was established for each criterion assessed by the tool and converted to a percentage for interpretation. Thus, a study with a score of 100% is considered a methodologically good study. The scores of each study were assessed by a nurse and a physician experienced in the area of pediatrics, and in the scoping review method.

RESULTS

The search stage identified 641 articles in the databases chosen for the review. Of these, we found 207 duplicates, which were excluded using the Rayyan IA selection application. The selection phase continued with 434 articles, of which 280 articles were excluded based on their title, and 93 articles were analyzed by abstract and full reading. Forty-one articles were excluded because they did not address the guiding question, totaling 17 articles for the review synthesis. Diagram 1 below demonstrates the selection steps for this scoping review.

Scheme 1 - Steps for selection according to PRISMA - Extension for Scoping Reviews (PRISMA-ScR)



Source: The Authors (2024).

When addressing the classification for medical diagnosis of Acute Renal Failure, almost all productions used the Kidney Disease Improving Global Outcomes (KDIGO) criteria (N=16 / 94.12%), with only one production not indicating the AKI classification method (N=1 / 5.88%).

To attribute the diagnosis of acute renal failure, some criteria established by the Kidney Disease Improving Global

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Outcomes (KDIGO) must be followed, namely: 1) increase in serum creatinine by at least 0.3 mg/dL in 48 hours; 2) increase in creatinine at least 1.5 times the baseline value in up to 7 days; and; 3) urine volume less than 0.5 ml/kg/h for 6 hours.[15-19]

In general, the severity of AKI is determined according to the greatest change in serum creatinine concentration. Values below stage 1 were designated as absence of injury; stage 1 as mild AKI; and stages 2 and 3 are categorized as severe AKI. When serum creatinine and urine output criteria led to different stages, all studies prioritized the most advanced stage of the classification.

Table 2 - Systematization of studies included in the review.

Author	Country	Clinical applicability
HUANG et al., 2022 / A[20]	China	It revealed that higher uCXCL10 levels may be predictive of septic AKI and PICU mortality in critically ill children.
AL GHARAIBEH et al., 2022 / B[21]	USA	Attenuating AKI and early fluid overload may reduce mortality in sepsis.
COGGINS et al., 2021 / C[22]	USA	Children with late-onset sepsis had higher odds of AKI and greater severity within 7 days of sepsis.
FORMECK et al., 2021 / D[17]	USA	Acute kidney injury is associated with an increased risk of subsequent infection in critically ill children.
NINMER et al., 2022 / E[23]	USA	In children with severe sepsis, the degree of hemodynamic support measured by vasoactive-inotropic score and the presence of fluid overload may identify patients at increased risk of developing severe AKI.
WANG et al., 2020/ G[18]	China	Metabolic analysis could be a promising approach to identify diagnostic biomarkers of pediatric septic AKI and helped elucidate the pathological mechanisms involved.
STANSKI et al., 2020 / H[16]	USA	Among children with septic shock, PERSEVERE biomarkers predict and identify patients with early AKI who are likely to recover.
STARR et al., 2020 / I[15]	USA	Sepsis survivors with severe acute injury were more likely to have persistent and severe deterioration in health-related quality of life at 3 months.
OZKAYA et al., 2023 / J[24]	Turkey	Although the incidence of AKI was similar among the three classifications, pRIFLE was the most successful classification for distinguishing the AKI state.
BASU et al., 2021 / R[19]	USA	Refinement of the AKI classification may allow enrichment of the population, facilitating biological analysis, trial design, and targeted therapy.
LAI et al., 2022 / L[25]	China	Fluid overload prior to CRRT may increase mortality in children with sepsis-associated AKI, and CRRT should be performed for these children as early as possible.
WEISS et al., 2019 / M[26]	USA	In children with sepsis, major adverse renal events within 30 days are common and feasible to measure.
HU et al., 2022 / N[27]	China	Urinary DKK3 may be an early biomarker for predicting mortality from acute kidney injury, sepsis-associated acute kidney injury, and critically ill children in pediatric intensive care units.
EL-GAMASY et al., 2018 / O[28]	Egypt	HSP60 may play a role in the pathogenesis of sepsis in pediatric patients, being elevated in patients with sepsis-associated AKI and decreased in children without these pathologies or healthy subjects.
STANSKI et al., 2021 / P[29]	USA	The RAI appears to be a sensitive and reliable tool for predicting severe AKI in children with septic shock, although the use of a recalibrated sepsis-specific RAI using a higher cutoff and platelet count may be beneficial.
TOMAR et al., 2021 / Q[31]	India	Compared with standard PD, early PD in sepsis-associated acute kidney injury resulted in favorable renal outcome, decreased PD duration, and earlier dialysis discontinuation.

Source: Author (2024). Caption: AKI – Acute Kidney Injury; PICU – Pediatric Intensive Care Unit; CRRT – Continuous Renal Replacement Therapy; RAI – Renal Angina Index; PD – Peritoneal Dialysis.

When assessing the methodological design of the included articles, a greater number of studies with a cohort study design were noted (N=9 / 52.94%). When assessing other methodological designs, we found a well-defined prospective cross-sectional study (N=4 / 23.53%), a well-defined retrospective cross-sectional study (N=1 / 5.88%), a descriptive study (N=2 / 11.76%) and a case-control study (N=1 / 5.88%).

In addition, when researching the level of evidence of the publications included in the article, it was noted that the vast majority were classified as LE IV (N=16 / 94.12%) and only one article was classified as LE VI (N=1 / 5.88%). The methodological evaluation of the study and level of evidence were shown in Table 3 below.

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Table 3 - Methodological evaluation of the study and level of evidence

Study	Methodological design	Level of evidence	Journal impact factor
A	Well-defined prospective cross-sectional study	IV	3.756
B	Cohort study	IV	3.714
C	Cohort study	IV	5.94
D	Cohort study	IV	3.971
E	Cohort study	IV	3.971
F	Cohort study	IV	0.156
G	Descriptive study	VI	4.361
H	Well-defined prospective cross-sectional study	IV	21.405
I	Descriptive study	IV	3.971
J	Cohort study	IV	0.415
K	Well-defined prospective cross-sectional study	IV	3.971
L	Cohort study	IV	0.75
M	Well-defined prospective cross-sectional study	IV	4.964
N	Cohort study	IV	3.756
O	Case-control study	IV	0.268
P	Well-defined prospective cross-sectional study	IV	4.164
Q	Cohort study	IV	1.43

Source: Authors (2024).

Regarding the methodological quality of the 17 studies, based on the generic quantitative assessment tool, we obtained 16 productions considered to be of good quality, with only one of moderate quality. The assessment was made in agreement with the authors of Peters et al., (2021) [14], as well as removing the evaluation score in cases of non-applicability of the criterion. The evaluation was described in table 4 below.

Table 4 - Quantitative evaluation of the studies included in the review

Reference	Criteria*												Score	%
	1	2	3	4	5	6	7	8	9	10	11	12	10/10	100
A	Y	Y	Y	Y	Y	NA	NA	Y	Y	Y	Y	Y	7/10	70
B	Y	Y	Y	N	N	NA	NA	Y	Y	Y	N	Y	9/10	90
C	Y	Y	Y	Y	N	NA	NA	Y	Y	Y	Y	Y	9/10	90
D	Y	Y	Y	Y	Y	NA	NA	Y	Y	Y	N	Y	7/10	70
E	Y	Y	Y	N	Y	NA	NA	Y	N	Y	N	Y	9/10	90
F	Y	Y	Y	Y	Y	NA	NA	Y	Y	Y	NR	Y	9/10	90
G	Y	Y	Y	Y	Y	NA	NA	Y	Y	Y	N	Y	9/10	90
H	Y	Y	Y	Y	Y	NA	NA	Y	Y	Y	N	Y	9/10	90
I	Y	Y	Y	N	Y	NA	NA	Y	Y	Y	S	Y	6/10	60
J	Y	Y	Y	N	Y	NA	NA	N	Y	Y	N	Y	9/10	90
K	Y	Y	Y	Y	Y	NA	NA	Y	Y	Y	N	Y	10/12	83,3
L	Y	Y	Y	Y	Y	S	N	Y	Y	Y	N	Y	7/10	70

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O	Y	Y	Y	N	Y	NA	N	Y	Y	Y	N	Y	9/10	90
P	Y	Y	Y	Y	Y	NA	NA	Y	Y	Y	N	Y	9/10	90
Q	Y	Y	Y	Y	Y	NA	NA	Y	Y	Y	N	Y		

*Criteria: 1 = Objective of the study; 2 = Relevant background; 3 = Sample description; 4 = Justification of sample size; 5 = Reliability and validity of outcome measures; 6 = Description of the intervention; 7 = Contamination and co-intervention; 8 = Statistical significance; 9 = Adequate analyses; 10 = Clinical-Epidemiological significance; 11 = Reported dropouts; 12 = Appropriate conclusions. *N = No; NA = Not applicable; NR = Not reported; Y = Yes. Study classification: ≥70% = Good quality; ≥50% and <70% = Moderate quality; <50% = Poor quality.
Source: Authors (2024)

DISCUSSION

Despite the relevance of the topic of pediatric sepsis, until 2005 there was no consensus regarding definitions for the pediatric population. This difficulty is related to the dynamic and complex nature of the disease associated with the peculiarities of pediatrics, such as physiological variations in vital signs, different infectious agents and predisposing factors to the dichotomies of the adult population. It was only in 2005 that the members of the International Pediatric Sepsis Consensus Conference (IPSCC) published exclusive definitions for the pediatric age group. [30-32]

For better understanding, the discussion was subdivided into biomarkers for pediatric urinary sepsis, renal replacement therapy in pediatric urinary sepsis, and epidemiological data on pediatric urinary sepsis.

Biomarkers in pediatric urinary sepsis

During the last years, studies on AKI have mainly focused on identifying new biomarkers for detecting kidney injury even before serum creatinine rises, optimizing clinical outcomes in AKI. However, although many urinary biomarkers have been reported in children, they have not been widely accepted and implemented in daily clinical practice. [16,31]

Urinary sepsis is one of the main well-known causes of AKI in critically ill patients, thus, for the purpose of early detection, the presence of cellular biomarkers has become the target of research. Huang et al (2021) evaluated the biomarker called motif chemokine ligand 10 (CXCL10) in the urine of children admitted to an ICU. Under normal conditions, CXCL10 is expressed at low renal levels, with its expression levels regulated by exposure to ischemia, nephrotoxic and inflammatory stress. [31,33]

When urinary CXCL10 (uCXCL10) levels were evaluated, it was noted that in critically ill children with urinary sepsis, their levels were higher, suggesting that uCXCL10 levels were influenced by inflammation and infection. Furthermore, urinary CXCL10 remained independently associated with sepsis and AKI, indicating that increases in CXCL10 due to AKI and sepsis are additive. [16,33]

Urinary CXCL10 levels were independently associated with an increased risk of AKI, sepsis, septic AKI, and PICU mortality, even after adjustment for confounding factors with serum creatinine. Higher uCXCL10 may be predictive of septic AKI and PICU mortality in critically ill children. [23,24]

Other biomarkers were measured and showed promise, such as glycerophospholipid, DKK3 and heat shock protein 60 (HSP60). [18,27,28] The activation of the immune system during sepsis, associated with nutritional insufficiency, induces a catabolic response, such as increased glycolysis, generating greater lipid oxidation. Therefore, the increase in glycerophosphocholine observed in septic AKI is explained by the activation of phospholipase A2 and increased lipid oxidation. Thus, the measurement of glycerophospholipids, especially glycerophosphocholine, appears to play a vital role in the early detection and control of sepsis treatment. [18]

Furthermore, Wang et al., (2020) revealed that the metabolism of glyoxylate and dicarboxylate were significantly altered in septic AKI; however, the role of glyoxylate and dicarboxylate metabolism in pediatric patients with septic AKI remains unclear. Furthermore, reduced L-glutamine levels were noted, in favor of the study by Hu et al., (2021), which revealed that the administration of a single dose of glutamine during sepsis contributed to balanced immune regulation and attenuation of systemic and renal inflammation; however, there are no further studies that prove the benefit of this administration.

DKK3, a glycoprotein synthesized by inflamed tubular epithelia, appears to be a possible biomarker in the early detection of septic AKI. Urinary Dickkopf-related protein 3 (DKK3) contributes to renal injury through multiple signaling pathways, significantly reducing total vessel length, percentage area, and number of capillary-like bifurcations. In rat models of AKI, DKK3 has been shown to worsen the clinical course of AKI by inhibiting Wnt/β-catenin signaling. [34,35]

In this regard, when investigating 73 children with septic AKI admitted to a PICU, it was noted that the urinary level of DKK3 was significantly associated with AKI, septic AKI and high mortality in the PICU, being predictive of the problems mentioned

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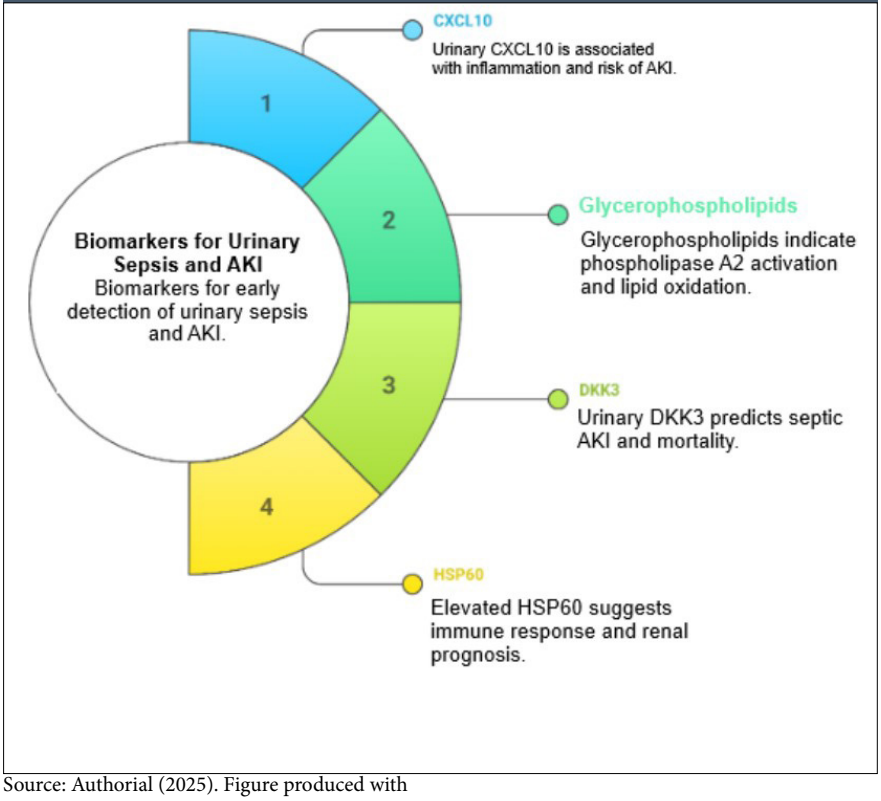
above in critically ill children. [27] Thus, DKK3 may be a rising laboratory biomarker in pediatrics.

Another biomarker studied and found in this review is HSP60. Heat shock proteins belong to the family of intracellular proteins, and are regulated by several stressors such as thermal, oxidative and chemical stress. Specifically, HSP60 is mostly located in mitochondrial tissue, and its function is the folding and assembly of mitochondrial proteins. [36]

It is proposed that HSP60 may be a biomarker for survival in the PICU, as well as an emerging marker for AKI in children with septic shock. Increased HSP60 levels in patients with AKI suggest an elevated immune response, contributing to the assessment of renal prognosis. Studies show that HSP60 has significant specificity and sensitivity for early detection of AKI, being a potentially valuable tool for the diagnosis and monitoring of renal function in pediatrics.

In a study with 120 critically ill children admitted to the PICU, HSP60 levels were evaluated in subgroups of 60 children with septic shock and AKI and a subgroup of 60 children without septic shock and AKI. It was noted that HSP60 values were significantly elevated, inferring that heat shock protein 60 may play an important role in the pathogenesis of urinary sepsis in pediatric patients, yet to be clarified. 28 Figure 1 below summarizes the main findings of the biomarkers.

Figure 1 – Main findings about biomarkers.



Source: Authorial (2025). Figure produced with Napkin IA.

Renal replacement therapy and fluid (im)balance

Continuous renal replacement therapy (CRRT) plays a key role in the management of fluid balance in critically ill pediatric patients, particularly in those with acute kidney injury (AKI) associated with sepsis. Recent studies address the challenges and importance of maintaining adequate fluid balance in these patients to improve survival and clinical outcomes. [25,37]

In the study carried out by Lai et al. (2022), the effects of fluid overload in children undergoing CRRT with AKI associated with sepsis were analyzed. This study categorized patients into three groups according to the level of fluid load: low, high, and fluid overload, demonstrating that mortality was significantly higher among those with fluid overload, reaching 47%. This finding shows that fluid imbalance, particularly excess fluids, is strongly associated with worse prognoses. Furthermore, the article highlights that early implementation of CRRT in patients with fluid overload could mitigate the risk of mortality, suggesting that early intervention may have a protective impact on renal function and survival of these critically ill patients. [25,26,37]

Fluid overload in critically ill patients is a complex and challenging condition that can make accurate diagnosis of renal function difficult because of hemodilution of creatinine levels. This phenomenon masks the severity of renal injury and complicates monitoring and appropriate intervention. [24] Furthermore, fluid accumulation is associated with a higher incidence of acute kidney injury and the need for vasopressor support, suggesting a link between fluid imbalance and cardiac dysfunction in critically ill patients. [21] Fluid overload is an independent risk factor for increased mortality, highlighting the importance of rigorous fluid management strategies to minimize risk and improve prognosis in pediatric intensive care units. Early administration of continuous renal replacement therapy may be crucial to minimize the negative effects of fluid imbalance,

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preventing cardiac and renal complications and increasing survival. [21,25]

Epidemiology and associations of pediatric urosepsis

Pediatric urosepsis, especially in patients in Pediatric Intensive Care Units (PICUs), is frequently associated with acute kidney injury (AKI), a factor that significantly contributes to the worsening of infectious conditions and increases mortality. Studies indicate that late-onset sepsis in neonates increases the risk of developing AKI threefold compared with the absence of sepsis, and approximately 20% of neonates with sepsis developed kidney injury within 7 days of initial evaluation, while only 8% of neonates without sepsis developed the condition. In addition, the association of urosepsis tends to be more severe, increasing the risk of mortality within 30 days. [17,22]

In a study of 757 children with sepsis admitted to the PICU, approximately 40.6% presented some degree of AKI in the first 7 days of hospitalization. Among these, 22.3% developed the severe form of the disease and 18.2% presented a milder form. These data reflect the high prevalence of this condition in septic pediatric patients and indicate that the presence of sepsis significantly increases the risk of developing kidney injury. [19,23]

AKI also acts as a risk factor for the development of sepsis in critically ill children. Studies show that patients with severe AKI (stages 2 and 3) are more likely to develop sepsis compared to those with mild or no kidney injury, as this condition is associated with an immunocompromised state that increases susceptibility to infections. [17]

The classification of kidney injury into different phenotypes, considering severity and duration, reveals that children with this condition in a persistent form (lasting more than 48 hours) have worse outcomes, such as higher mortality and complexity in the use of ICU resources, compared to children with the transient form. The stratification of AKI, therefore, can help predict outcomes and personalize treatment according to the severity and time of evolution of the injury. [19]

Several factors contribute to the worsening of these cases in pediatrics, such as hypotension and advanced age within the pediatric spectrum, both associated with an increased risk of AKI and mortality. Conditions such as thrombocytopenia and changes in platelet count, common in urosepsis, reflect a dysregulated inflammatory response, which further aggravates the condition. In addition, septic shock increases the risk of multiple organ dysfunction, increasing mortality rates in cases of concomitant kidney injury, which can reach up to 70%. [24,29]

CONCLUSION

Pediatric urosepsis represents a complex challenge in pediatric intensive care medicine, given its intrinsic link with AKI and increased mortality. Early identification of biomarkers such as CXCL10, glycerophospholipids, DKK3, and HSP60 emerges as a promising area to optimize the diagnosis and monitoring of renal function, allowing faster and more targeted therapeutic interventions. Management of fluid balance, especially in patients undergoing CRRT, is crucial, since fluid overload worsens the prognosis.

In summary, a deeper understanding of the epidemiology of pediatric urosepsis and its associations with AKI, together with the continued search for effective biomarkers and fluid management strategies, are essential to improve clinical outcomes and reduce mortality in this vulnerable population. A multidisciplinary approach and the implementation of evidence-based protocols are essential to address the challenges posed by pediatric urinary sepsis and ensure the best possible care for critically ill children.

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