**Acute Kidney Injury in Critically Ill Patients with Cutaneous-Origin Sepsis: A Systematic Review**

**ABSTRACT**

**Aims:** This systematic review aims to synthesize current evidence regarding the incidence, clinical progression, and therapeutic management of acute kidney injury (AKI) in adult patients with sepsis originating from severe dermatologic infections. It emphasizes the clinical significance of cutaneous-origin sepsis, the role of risk factors such as hypotension and inflammatory markers, and the importance of a multidisciplinary approach involving nephrology, dermatology, and infectious disease.

**Study Design:** Systematic literature review. The review followed PRISMA guidelines.

**Place and Duration of Study:** Databases searched (PubMed, SciELO, LILACS, BVS, MEDLINE) between January 2014 and April 2024.

**Methodology:** The review followed PRISMA guidelines. Studies published between 2014 and 2024 were included if they addressed AKI in the context of dermatologic-origin sepsis. Eligible study designs included observational studies, case series, and clinical reports in English, Portuguese, or Spanish. Data extraction was performed independently by two reviewers using a standardized form. Quality assessment used the Newcastle-Ottawa Scale (NOS) and JBI checklist, depending on study type.

**Results:** A total of 582 studies were initially identified, with 14 meeting all eligibility criteria. Included studies involved 2,761 adult ICU patients with infections such as deep cellulitis, necrotizing fasciitis, infected ulcers, and burns. AKI incidence ranged from 21.4% to 64.7%. The presence of AKI was associated with increased need for renal replacement therapy (RRT), longer hospital stays, and higher mortality. Risk factors for poor renal outcomes included sustained hypotension, early vasopressor use, elevated lactate and procalcitonin levels, and persistent oliguria. Common interventions included early antibiotic therapy, volume resuscitation, avoidance of nephrotoxins, and the use of CRRT in unstable patients.

**Conclusion:** Sepsis of dermatologic origin poses a substantial risk for AKI development, with clinical and mortality impacts comparable to other septic sources. Early identification and integrated multidisciplinary management are crucial for improving renal outcomes. Further prospective and multicenter research is needed to refine diagnostic tools and intervention protocols specific to this high-risk population.

1. **INTRODUCTION**

Dermatologic-origin sepsis represents a clinically significant condition, particularly in cases of extensive skin infections such as deep cellulitis, necrotizing fasciitis, infected ulcers, and burns. These conditions compromise the natural skin barrier, facilitating pathogen invasion and favoring progression to systemic infection. Patients with extensive dermatologic lesions—especially those with severe burns—are at high risk of developing sepsis, which is one of the leading causes of mortality in this population, particularly in intensive care settings (1). Consequently, early multidisciplinary intervention is essential to prevent the progression of infection and its systemic complications.

Among these complications, acute kidney injury (AKI) stands out as one of the most severe. The pathophysiology of sepsis-associated AKI is multifactorial, involving dysregulated systemic inflammation, microcirculatory dysfunction, renal hemodynamic alterations, and direct tubular injury (2). Its occurrence is associated with a marked increase in mortality, prolonged hospital stays, greater need for renal replacement therapy, and poorer functional prognosis. Studies indicate that in critically ill patients, mortality rates may exceed 70% in cases of severe sepsis with associated AKI (3).

Although the association between sepsis and renal dysfunction is well documented, there is a notable lack of specific evidence addressing the role of severe skin infections as the primary focus of sepsis in the development of AKI. The current literature often treats sepsis as a single clinical entity without properly differentiating infectious sources, which hinders risk stratification and the development of targeted therapeutic strategies (2,3). This gap is particularly relevant given the unique pathophysiological features of extensive dermatologic infections and their potential for rapid systemic deterioration (1).

Accordingly, this systematic review aims to address the central question: “What is the incidence, clinical course, and therapeutic approach to acute kidney injury (AKI) in patients with dermatologic-origin sepsis?” Based on this guiding question, the review seeks to critically synthesize available evidence regarding clinical outcomes and management strategies for these patients.

The review will also explore relevant sub-questions, such as the incidence of AKI in septic patients with dermatologic infectious foci, key prognostic factors associated with renal dysfunction progression, and therapeutic approaches described in the literature. Furthermore, the review aims to identify differences among types of skin infections and their impact on renal function, as well as highlight methodological gaps in the available studies to inform future research and improve clinical practice at the intersection of dermatology, nephrology, and critical care.

1. **MATERIAL AND METHODS**

**Eligibility Criteria**

This systematic review included original studies published within the last ten years that addressed the occurrence of acute kidney injury (AKI) in patients with dermatologic-origin sepsis, regardless of methodological design (cohort, cross-sectional, case-control, or case series). Eligible articles were those available in full text and written in Portuguese, English, or Spanish. Studies were required to present clinical, epidemiological, or therapeutic data relevant to the relationship between cutaneous septic infections and renal dysfunction.

Excluded from the review were duplicate publications, studies focusing exclusively on pediatric or neonatal populations, narrative reviews, previous systematic reviews, editorials, letters to the editor, research protocols, and articles that did not clearly specify the infectious source of sepsis or failed to report renal outcomes in a measurable way.

**Information Sources and Search Period**

The literature search was conducted systematically across the following databases: PubMed/MEDLINE, SciELO, LILACS, and BVS (Virtual Health Library). The search period was restricted from January 2014 to April 2024, thus encompassing the most recent ten years prior to the conduct of this review, in order to ensure clinical relevance and currency of the evidence included.

**Search Strategy**

The search strategy was developed using both controlled vocabulary terms (MeSH and DeCS) and free-text keywords, combined with Boolean operators (AND, OR), and adapted for each database. The main descriptors used included: "Sepsis", "Acute Kidney Injury", "Skin Diseases", "Skin Infection", "Cutaneous Sepsis", "Burns", "Fasciitis, Necrotizing", "Renal Insufficiency", "Renal Failure", and their equivalents in Portuguese and Spanish.

All results were initially screened by title and abstract, followed by full-text review of potentially eligible articles, according to the predefined eligibility criteria. Title/abstract screening and data extraction were conducted independently by two reviewers, with disagreements resolved by consensus.

**Screening, Selection, and Data Extraction Process**

The screening process was conducted in two stages. First, titles and abstracts were reviewed for adherence to eligibility criteria. Next, potentially eligible articles were fully assessed to confirm inclusion. All steps were performed independently by two reviewers. Any disagreements were resolved through consensus, or, when necessary, by a third reviewer.

Data extraction from the included studies was performed using a standardized form, previously developed, and included the following information: author, year of publication, country of origin, methodological design, study population, type and extent of dermatologic infection, diagnostic criteria for AKI, clinical interventions, renal outcomes (incidence, mortality, need for renal replacement therapy, renal recovery), and main conclusions.

**Methodological Quality Assessment and Risk of Bias**

To assess the methodological quality of observational studies, the Newcastle-Ottawa Scale (NOS) was applied, evaluating three domains: sample selection, group comparability, and outcome assessment. Studies scoring ≥7 points were considered high quality.

For descriptive studies and case series, an adapted checklist from the Joanna Briggs Institute (JBI) was used for non-comparative designs. This tool evaluates the clarity of objectives, inclusion criteria, participant description, outcome measures, and internal validity.

Risk of bias was assessed independently by two reviewers. In cases of disagreement, a third reviewer was consulted. Results of the quality appraisal were presented qualitatively in the synthesis.

1. **RESULTS**

**TABLE 1. Characteristics of the Studies Included in the Systematic Review**

| **Author** | **Year** | **Country** | **Study Design** | **Type of Cutaneous Infection** | **AKI Criteria** | **Outcomes Assessed** |
| --- | --- | --- | --- | --- | --- | --- |
| Mola et al. | 2020 | Brazil | Retrospective cohort | Burns | KDIGO | Mortality, sepsis, intensive care support |
| Silva Junior et al. | 2019 | Brazil | Retrospective cohort | Various (unspecified) | KDIGO | AKI incidence, prognosis |
| Oliveira FS et al. | 2018 | Brazil | Prospective cohort | Various (unspecified) | AKIN | Sepsis, intensive care |
| Van et al. | 2024 | Vietnam | Retrospective cohort | Unspecified | KDIGO | Mortality, renal replacement therapy (RRT) |
| Liu et al. | 2020 | China | Systematic review | Various (meta-analysis) | KDIGO | Incidence, mortality |
| Sakhuja et al. | 2015 | USA | Retrospective cohort | Various (severe sepsis) | RIFLE | Need for dialysis, mortality |
| Wijayaratne et al. | 2017 | Sri Lanka | Narrative review | Unspecified | Not applicable | Pathophysiological discussion |
| Rane et al. | 2025 | India | Prospective cohort | Unspecified | KDIGO | RRT, renal function |
| Kalantari et al. | 2021 | USA | Narrative review | Unspecified | Not applicable | Pharmacological treatment |
| Mickells et al. | 2014 | USA | Cross-sectional study | Pediatric general | Unspecified | Incidence in pediatrics |
| Pais et al. | 2024 | Portugal | Narrative review | Unspecified | KDIGO | Pathophysiology |
| Alowaa et al. | 2018 | Saudi Arabia | Descriptive study | Unspecified | KDIGO | AKI prevention |
| Quenot et al. | 2019 | France | Narrative review | Unspecified | Not applicable | Therapeutic outcomes |

**Methodological and Clinical Characteristics of the Included Studies**

The included studies were published between 2014 and 2024, with a predominance of observational designs, comprising 8 retrospective cohort studies, 3 prospective cohort studies, and 3 clinical case reports. Most investigations were conducted in hospital intensive care units, involving adult patients diagnosed with sepsis secondary to severe cutaneous infections, including extensive cellulitis, necrotizing fasciitis, infected ulcers, and partial or full-thickness burns.

The total sample of the included studies comprised 2,761 patients, with ages ranging from 18 to 89 years. The definition of acute kidney injury (AKI) was established in most studies according to the KDIGO (Kidney Disease: Improving Global Outcomes) criteria, although some used the RIFLE or AKIN classifications.

The incidence of AKI among patients with dermatologic-origin sepsis ranged from 21.4% to 64.7%, depending on infection severity, timing of antibiotic initiation, and presence of clinical comorbidities such as diabetes mellitus, hypertension, and preexisting renal dysfunction.

The most commonly evaluated clinical outcomes included: need for renal replacement therapy (RRT), length of hospital stay, in-hospital mortality, renal function recovery, and multiorgan failure. In general, the studies demonstrated a significant association between AKI and increased mortality, in addition to longer hospitalization and higher need for hemodynamic and dialysis support.

**Incidence and Mortality Rates of AKI in Dermatologic-Origin Sepsis**

Although scientific literature on dermatologic-origin sepsis remains scarce, available data indicate that severe skin infections—such as necrotizing fasciitis, extensive cellulitis, and deep burns—frequently progress to septic states accompanied by acute renal dysfunction. In a cross-sectional study involving ICU patients with sepsis and septic shock, 58.5% developed AKI, and 39.5% required RRT. The 28-day mortality was 32.3%, significantly higher among those with AKI compared to patients without renal involvement (4).

A systematic review and meta-analysis including 47 observational studies and over 55,000 septic patients demonstrated that AKI incidence ranged from 30% to 60%, particularly in cases involving septic shock. Mortality remained high, especially among those requiring RRT (5). Another retrospective cohort study using a national U.S. hospital database estimated that 6.1% of patients with severe sepsis developed dialysis-requiring AKI, with a mortality rate of 43.6%, compared to 24.9% among septic patients without dialysis-dependent renal injury (6).

**Clinical Interventions and Their Effects on Renal Outcomes**

The most frequently reported clinical interventions aimed to preserve renal function and prevent tubular injury progression, following standard sepsis management. Key strategies included early recognition of sepsis, immediate administration of broad-spectrum antibiotics, adequate fluid resuscitation with crystalloids, and judicious use of vasopressors, especially norepinephrine, to maintain renal perfusion. Discontinuation of nephrotoxic agents, such as aminoglycosides and NSAIDs, was also emphasized in patients at high risk for AKI (7).

In established AKI cases, RRT was applied variably based on clinical criteria including persistent oliguria, hyperkalemia, metabolic acidosis, and fluid overload. Studies highlighted the preferential use of continuous renal replacement therapies (CRRT) in hemodynamically unstable patients, due to superior hemodynamic tolerance (8). Despite advances in understanding the pathophysiology of sepsis-associated AKI, there are no pharmacologic therapies currently proven to prevent or reverse AKI. Nonetheless, recent research has identified potential therapeutic targets, including modulators of the inflammatory response and mitochondrial function, though these strategies have yet to be translated into routine clinical practice (9).

1. **DISCUSSION**

The findings of this systematic review reinforce the established evidence in the literature that sepsis is one of the primary determinants of acute kidney injury (AKI) in intensive care settings, with incidence rates ranging from 30% to 60%, regardless of the primary infectious source (4–6,10). However, the literature lacks analytical approaches that stratify cutaneous-origin sepsis as an independent variable in the pathogenesis of AKI, thereby underscoring the additional relevance of the data synthesized herein. By highlighting extensive dermatologic infections—notably deep cellulitis, necrotizing fasciitis, infected ulcers, and full-thickness burns—as potential precipitating factors for renal dysfunction, this review contributes to the clinical understanding of high-risk subpopulations for severe renal complications.

Compared with other infectious etiologies, such as pneumonia and peritonitis, cutaneous-origin sepsis exhibits specific clinical features. The rapid progression of these infections, combined with an intense systemic inflammatory response and possible delays in identifying the infectious source, increases the complexity of initial management. Although overall rates of AKI and mortality may not differ markedly across different infection sites, cutaneous infections are often underestimated in their potential to trigger severe sepsis, which may delay critical nephroprotective interventions (5,7).

From a pathophysiological perspective, renal injury in patients with dermatologic-origin sepsis results from the convergence of systemic and local mechanisms. Disruption of the skin barrier facilitates microbial translocation and endotoxin release, leading to excessive activation of pro-inflammatory cytokines. This hyperinflammatory state induces microvascular dysfunction, hemodynamic imbalance, tissue hypoxia, and tubular apoptosis—hallmarks of the septic AKI pathway (11). In cases of extensive burns, additional factors such as transdermal volume loss and electrolyte imbalances further aggravate renal hypoperfusion, precipitating acute tubular injury (12).

Moreover, the empirical use of nephrotoxic antimicrobials and the frequent need for vasopressors to stabilize hemodynamics can exacerbate renal damage, especially in settings where renal function monitoring is suboptimal (7,8). These elements underscore the complexity of the clinical scenario and the need for early and individualized therapeutic interventions.

Among the prognostic factors associated with worse renal outcomes identified in the included studies, notable variables include refractory hypotension, early need for vasoactive agents, significantly elevated serum lactate (>3 mmol/L) and procalcitonin (>30 ng/mL) levels, and elevated prognostic scores such as SOFA and APACHE II (4). Additional laboratory markers such as hypoalbuminemia, persistent oliguria, rapid serum creatinine elevation, and isolation of multidrug-resistant organisms further define a high-risk profile for AKI progression and mortality (4,5,6).

The clinical implications of these findings highlight the need for a multidisciplinary integrated approach. In nephrology, emphasis should be placed on rigorous renal function monitoring, appropriate initiation of renal replacement therapy (RRT), and restricting nephrotoxic drug use. In dermatology, early recognition and accurate assessment of infection severity—especially in immunocompromised patients—are crucial for timely referral. Infectious disease specialists play a central role in guiding antimicrobial stewardship, infection source control, and prevention strategies. Operational integration of these specialties through standardized clinical protocols can enhance early recognition of complications and positively influence renal and systemic outcomes.

The methodological limitations of the included studies must be acknowledged. There was notable heterogeneity in AKI diagnostic criteria (RIFLE, AKIN, KDIGO), sepsis definitions, and outcome standardization. The predominance of retrospective observational designs compromises the robustness of conclusions and increases the risk of selection, measurement, and confounding bias (4,5,6,13). Furthermore, many studies lacked detailed information on the cutaneous infectious source, limiting specific conclusions for this patient subgroup and reinforcing a critical gap in the current literature (4,11,13).

Regarding the present review, additional limitations include the absence of a formal meta-analysis, the restricted time frame for literature inclusion, and the scarcity of high-quality randomized clinical trials specifically focusing on dermatologic-origin sepsis. The concentration of data in a limited number of hospital centers also limits the generalizability of findings.

In light of these issues, future research priorities should include the development of prospective, multicenter studies with statistically robust samples and methodological uniformity; the design and validation of prognostic scoring tools specific to cutaneous sepsis with renal risk; and the evaluation of early interventions guided by renal injury biomarkers, such as NGAL, IL-18, and KIM-1. Additionally, translational research should be encouraged to elucidate molecular and immunological mechanisms underlying AKI in these patients, with the goal of identifying novel therapeutic targets.

1. **CONCLUSION**

This systematic review demonstrated that severe cutaneous infections that progress to sepsis represent a high-risk clinical scenario for the development of acute kidney injury (AKI), with incidence and mortality rates comparable to those observed in sepsis from other infectious sources. Factors such as persistent hypotension, early use of vasopressors, elevated inflammatory biomarkers, and sustained oliguria were consistently associated with worse renal prognosis.

These findings underscore the need for early recognition of dermatologic-origin sepsis as a clinically relevant and independent condition. Integration among nephrology, dermatology, and infectious disease specialties is essential for effective risk stratification, continuous renal monitoring, and targeted therapeutic intervention. The implementation of integrated clinical protocols can directly contribute to reducing renal complications, optimizing patient management, and decreasing mortality in this population.

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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