

REVIEW ARTICLE

COMPARISON OF THE EFFECTIVENESS OF RINGER'S LACTATE AND 0.9% NaCl ON MORTALITY IN ADULT SEPSIS PATIENTS: AN EVIDENCE-BASED CASE REPORT

Muhammad Raffi Ridwan^{1*}, Faras Khairunnisa Ridwan²,
Muhammad Ijlal Ridwan³, Surianty Susilo⁴

¹Undergraduate Medical Program, Faculty of Military Medicine, Universitas Pertahanan
Republik Indonesia, Bogor, Indonesia

²Undergraduate Medical Program, Faculty of Medicine, Universitas Lampung, Bandar Lampung, Indonesia

³State Senior High School 1 Pekanbaru, Pekanbaru, Indonesia

⁴Department of Radiology, Arifin Achmad General Hospital, Pekanbaru, Indonesia

*Corresponding Author : raffi.110803@gmail.com

ABSTRACT

Background: The selection of crystalloid fluid in sepsis resuscitation affects acid-base balance, organ perfusion, and mortality. The 0.9% NaCl (normal saline, NS) is the standard fluid, but its high chloride content has the potential to cause physiological disturbances. In contrast, balanced crystalloids such as Ringer's Lactate (RL) have an electrolyte composition closer to physiological plasma and are thought to provide better clinical outcomes. Recent evidence suggests a possible role for RL in reducing mortality in patients with sepsis, although some studies report mixed results. This study aims to evaluate the effectiveness of Ringer's Lactate compared to 0.9% NaCl on mortality in adult patients with sepsis, using an evidence-based case report approach to inform fluid resuscitation decisions.

Methods: A literature search was conducted in October 2025 through PubMed NCBI, Medline EBSCO, ScienceDirect, and Google Scholar. Four studies met the inclusion criteria (3 RCTs, 1 SR/MA of RCTs) and were

subsequently screened according to the Centre for Evidence-Based Medicine (CEBM) guidelines for critical appraisal, relative to validity, relevance, and practicality to the clinical scenario.

Results: Across the included studies, the direction of effect generally favored RL over NS with respect to mortality outcomes. However, effect estimates were reported using different measures, including risk ratios and hazard ratios, and not all observed differences reached statistical significance. Given methodological heterogeneity and identified risks of bias, quantitative pooling of results was not performed, and findings were interpreted qualitatively.

Conclusion: The use of Ringer's Lactate in adult patients with sepsis appears to be associated with a favorable direction of effect on mortality compared with 0.9 NaCl. Nevertheless, the certainty of this evidence is limited, and definitive conclusions regarding superiority cannot be drawn.

Keywords: NaCl, balanced crystalloid, normal saline, mortality, Ringer's lactate, sepsis

INTRODUCTION

A 55-year-old male was taken to the emergency department complaining of a high fever for the past three days, now complicated by decreased level of consciousness and hypotension. Upon arrival, his blood pressure was noted to be 80/50 mmHg, heart rate 120 bpm, and temperature 39 degrees Celsius with tachypnea. He was subsequently diagnosed with pneumonia-induced sepsis and was taken for immediate IV fluid resuscitation and empiric antibiotic treatment. The attending physician had to consider which crystalloid fluid would be most appropriate for his initial

fluid resuscitation.

In daily practice, 0.9% NaCl is often used as the standard resuscitation fluid. However, some literature suggests that Ringer's Lactate may provide better clinical outcomes by reducing the risk of hyperchloremic acidosis and improving tissue perfusion. The physician then considers whether the use of Ringer's Lactate is more effective than 0.9% NaCl in reducing mortality in sepsis patients?

Sepsis is a complex clinical syndrome resulting from an uncontrolled systemic immune response to infection, leading to organ dysfunction and potentially fatal

hemodynamic disturbances.^{1,2} According to the Sepsis-3 definition, sepsis is life-threatening organ dysfunction caused by dysregulation of the host response to infection. Diagnostic criteria for sepsis include suspected or confirmed infection and an increase in Sequential Organ Failure Assessment (SOFA) score of ≥ 2 points from baseline, which represents acute organ dysfunction.^{3,4} In the Emergency Department, the quick SOFA (qSOFA) is a rapid screening tool that consists of: respiratory rate ≥ 22 breaths/minute, systolic blood pressure ≤ 100 mmHg, altered mental status, with a qSOFA score ≥ 2 reflecting high risk of severe sepsis and/or septic shock that requires subsequent immediate fluid resuscitation.^{1,5}

Ringer's Lactate (RL) is a balanced crystalloid fluid that preserves an electrolyte composition resembling that of plasma, sodium, potassium, calcium, and chloride in appropriate concentrations.^{6,7} Lactate, as found in RL, also acts as a buffer. Lactate in RL is converted in the liver to bicarbonate, which subsequently meaning that RL helps buffer against metabolic acidosis, which typically occurs in sepsis due to tissue hypo-perfusion creating excess lactate production. Similarly, the relatively lower chloride content of RL prevents hyperchloremia, which compromises renal perfusion and causes renal afferent vasoconstriction.⁸ Physiologically, RL better champions acid-base balance and fluid equilibrium with microcirculation stability and endothelial function preservation, which are all needed for tissue re-perfusion recuperation.⁹

0.9% NaCl (Normal Saline, NS) is the standard crystalloid isotonic solution and has historically been the widely utilized resuscitation fluid. It is inexpensive and easy to access, but its ionic composition is non-physiological; even RL's sodium content is lower at 130 mmol/L; 154 mmol/L of NaCl and Cl⁻ means that NS delivers an unnecessary chloride load.^{6,10} This increases glomerular filtration as demonstrated by tubuloglomerular feedback and vasodilation of renal afferent arterioles.⁸ Moreover, NS complications include a non-physiological acid-base balance response via hyperchloremic metabolic acidosis seen in patients receiving large volume infusions, leading to acid-base disturbances, which further complicate renal function and microvasculature in septic patients.^{11,12}

While physiologically, RL has a profile closer to that of plasma and is "safer" than NS, the real question in practical application comes down to how much these compositional variances truly impact sepsis patients' clinical sequelae, with mortality in mind for such a diverse population, and what this means for smaller, more resource-limited health centers. Additionally, guidelines such as the Surviving Sepsis Campaign still provide "weak" recommendations for choosing RL over NS due to evidence deemed of moderate quality.¹³ Therefore, this evidence-based case report aims to address a specific clinical question arising from the

presented case by evaluating the best available evidence comparing Ringer's Lactate and 0.9% NaCl in terms of mortality outcomes in adult patients with sepsis, in order to inform clinical decision-making regarding initial fluid resuscitation.

METHODS

Search Strategy

A focused literature search was conducted in October 2025 to identify the best available evidence relevant to the clinical question arising from the presented case. The search was performed using four major electronic databases, namely PubMed NCBI, Medline EBSCO, ScienceDirect, and Google Scholar, covering the last five years. The search process used a combination of keywords tailored to the focus of this study, including: "sepsis or septic or septicemia", "ringer lactate or ringer's lactate or balanced crystalloid or balanced crystalloids or lactated ringer", "normal saline or saline or 0.9% sodium chloride", "mortality or death or deaths". These keywords were combined using Boolean AND and OR operators, resulting in the following final syntax: ((sepsis or septic or septicemia) AND (ringer lactate or ringer's lactate or balanced crystalloid or balanced crystalloids or lactated ringer) AND (normal saline or saline or 0.9% sodium chloride) AND (mortality or death or deaths)). The search format was slightly adjusted to suit the structure of each database.

To ensure clinical relevance and contemporary applicability, the search was limited to studies published within the last five years. The search was intentionally limited to the last five years to prioritize contemporary evidence relevant to current sepsis management practices. Additional eligibility restrictions included articles available in full text and published in English or Indonesian. These limits were applied to facilitate critical appraisal and interpretation within the context of the EBCR framework. All retrieved records were screened by title and abstract for relevance to the clinical question, followed by full-text assessment of potentially eligible articles.

Eligibility Criteria

The eligibility criteria were defined to identify clinically relevant and high-quality evidence applicable to the presented case. The target population included adult patients (≥ 18 years) diagnosed with sepsis, broadly consistent with contemporary definitions of sepsis, including Sepsis-3 criteria and closely related earlier definitions used in major clinical trials. Eligible study designs included randomized controlled trials (RCTs) and systematic reviews or meta-analyses of RCTs that compared Ringer's Lactate or other balanced crystalloids with 0.9% NaCl for intravenous fluid resuscitation in adult patients

with sepsis, and reported mortality as a primary or secondary outcome.

Studies involving pediatric populations, non-comparative designs, case reports, case series, editorials, and commentaries were excluded, as they were not considered sufficiently informative for addressing the clinical question. To facilitate critical appraisal within the EBCR framework, inclusion was limited to full-text articles published in English or Indonesian. These eligibility criteria were applied pragmatically to ensure the feasibility of appraisal and interpretation, and are acknowledged as potential sources of language and publication bias.

Critical Appraisal

The methodological quality of each article was evaluated using the assessment sheet from the Centre for Evidence-Based Medicine (CEBM).¹⁴ This instrument was selected because it offers a consistent and standardized approach to evaluation for assessing the quality of scientific evidence across mixed research designs. The evaluation process involved two appraisal sheets: CEBM Appraisal Sheet for RCT's and CEBM Appraisal Sheet for Systematic Reviews. Study selection and critical appraisal were performed by two independent reviewers, with disagreements resolved by discussion.

The RCT appraisal sheet assesses study quality relative to internal validity, a measure that encompasses whether a study was randomized, if a baseline level of similarity was established, if intervention and control groups were equally treated, if intention to treat was established, and if blinding was enabled. In addition, an assessment is made of the importance as seen from the strength and clinical significance of the reported findings. Meanwhile, in the appraisal sheet for systematic reviews, the assessment focuses on the FAAT components (focus question clarity, appropriate searching, appropriate inclusion criteria, study validity, and result similarity). In addition, the meta-analysis results are evaluated through a 95% confidence interval, heterogeneity level, and overall effect to assess the consistency and significance of the findings between studies.

RESULTS

Search Results

As shown in Figure 1, a literature search of four electronic databases using pre-designed keywords yielded 624 potentially relevant publications (Table 1). After the identification process, 73 duplicate articles were found and subsequently removed. Of the remaining 551 unique articles, a screening based on title and abstract was conducted to assess suitability with the research focus. This stage resulted in the elimination of 538 articles that did not meet the eligibility criteria, including not discussing the

main topic, involving populations with inappropriate characteristics, not evaluating the desired outcomes, or having an inappropriate research design. A total of 13 articles that passed the initial stage were then further analyzed through full-text review, but 9 of them were excluded because they did not meet the inclusion criteria, such as the unavailability of full text, involving an inappropriate population, or not being an RCT, systematic review, or meta-analysis. Thus, 4 studies were deemed eligible for inclusion in this EBCR analysis, consisting of one systematic review with meta-analysis and three controlled clinical studies. Of the three primary clinical studies, two employed randomized controlled trial designs, while one was a controlled study without clear random allocation.

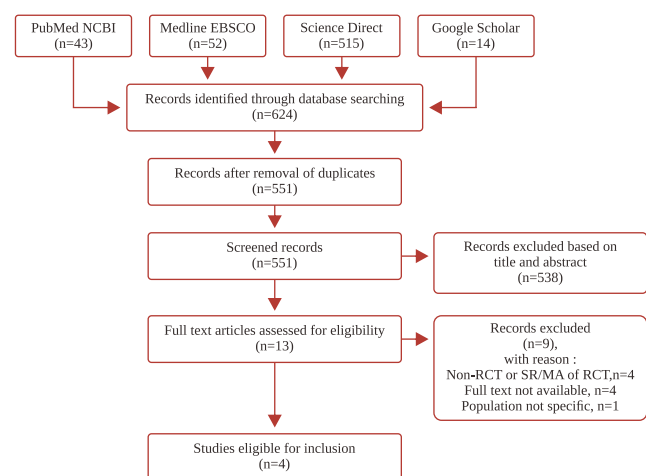


Figure 1. PRISMA flowchart outlining the process of article selection

Critical Appraisal

Of the four studies that met the inclusion criteria, three were controlled clinical studies, and one was a systematic review that included a meta-analysis of several RCTs comparing the use of Ringer's Lactate versus 0.9% NaCl in adult patients with sepsis. Among the three primary clinical studies included in this review, two were randomized controlled trials with clearly reported randomization procedures, while one study did not clearly describe random allocation of participants. Accordingly, this study was considered to have a higher risk of selection bias and was interpreted with greater caution in the overall synthesis of evidence. The methodological quality of all studies was assessed using the CEBM University of Oxford assessment sheet to evaluate aspects of internal validity, clinical relevance, and the strength of research results.¹⁴

Selection bias was the main concern in the non-randomized controlled study, as the absence of clear random allocation may have resulted in baseline differences between intervention groups. In contrast, the two randomized controlled trials reported adequate randomization

procedures and generally comparable baseline characteristics, thereby reducing the risk of selection bias in those studies. Performance bias was present across all included primary clinical studies, as none implemented blinding of participants or treating clinicians. This open-label design may have influenced aspects of patient management; however, its impact on the primary outcome was considered limited. With regard to detection bias, the primary outcome assessed across studies was mortality, which represents an objective and clinically definitive endpoint. Therefore, despite the lack of blinding, the risk of detection bias was considered low. No major concerns related to selective reporting bias were identified, as the outcomes reported were consistent with those described in the study objectives and methods. Additionally, the use of different effect measures (RR versus HR) across studies further limits direct comparability of effect sizes and reinforces the need for cautious, qualitative interpretation of the mortality findings. Overall, these methodological limitations were taken into account when interpreting the mortality outcomes and reduced the certainty of causal inferences regarding the effect of Ringer's Lactate compared with 0.9% NaCl in adult patients with sepsis.

Of the three RCTs analyzed, two demonstrated good internal validity, with clear study designs that included proper randomization processes, baseline similarity between groups, and the application of the intention-to-treat principle

in outcome analysis (Table 2). Meanwhile, one study, namely Gelbenegger et al,¹⁵ did not carry out a randomization process in its research. Another study, Golla et al,¹⁶ also did not explain in detail the equality of treatment between intervention groups during the study, which could affect the consistency of results between groups. In addition, the three RCTs analyzed did not apply blinding to either the researchers or the participants, so the potential for bias cannot be completely ruled out.

In general, the three RCTs showed consistent results, with the RL group having a lower mortality risk than the NS group, although not all of them reached statistical significance. The study with the largest number of participants, by Gelbenegger et al,¹⁵ showed a 90-day mortality reduction (12.2% vs 15.9%; RR = 0.77; 95% CI = 0.51–0.99) with a Number Needed to Treat (NNT) of 27 patients to prevent one death. Similar results were also seen in Golla et al,¹⁶ which reported a trend toward a decrease in 30-day mortality (36.3% vs 43.8%) in the RL group compared to the NS group, although the difference in mortality did not reach $p < 0.05$. Meanwhile, Zhang et al,¹⁷ showed no statistically significant difference in 90-day mortality (33.8% vs. 37.5%; HR = 0.9; 95% CI = 0.4–1.9), but the clinical trend still pointed toward the benefit of RL in reducing the incidence of hyperchloremia and kidney dysfunction.

Table 1. Search strategy in searching for evidence articles

| Database | Search strategy (key terms) | Hits | Selected articles |
|----------------|---|------|-------------------|
| PubMed NCBI | ((sepsis OR septic OR septicemia)AND (Ringer's lactate OR balanced crystalloid OR lactated Ringer)AND ("normal saline" OR "0.9% NaCl" OR "isotonic saline")AND (mortality OR death) | 43 | 2 |
| Medline EBSCO | ((sepsis or septic or septicemia) AND (Ringer's lactate or balanced crystalloid or lactated Ringer's) AND (normal saline or saline or 0.9% sodium chloride) AND (mortality or death or deaths) | 52 | 1 |
| ScienceDirect | ((sepsis OR septic) AND (Ringer's lactate OR balanced crystalloid OR balanced crystalloids) AND ("normal saline" OR "0.9% NaCl") AND (mortality OR death)) | 515 | 0 |
| Google Scholar | ((sepsis or septic or septicemia) AND (Ringer's lactate or balanced crystalloid or lactated crystalloid or lactated Ringer's solution) AND (normal saline or saline or 0.9% sodium chloride) AND (mortality or death or deaths) | 14 | 1 |

Analysis of the Systematic Review and Meta-Analysis by Chen et al,¹⁸ showed a high level of validity based on the FAAT CEBM criteria (Table 3), with a clear PICO, comprehensive search strategy, and adequate assessment of study quality. The meta-analysis results involved several large RCTs and found that the use of balanced crystalloids significantly reduced the risk of mortality in sepsis patients compared to saline (RR = 0.91; 95% CI = 0.85–0.99; $p =$

0.02), with very low heterogeneity ($I^2 = 0\%$). This indicates consistency of results across studies and strengthens the reliability of the findings.

Administration Mode and Dosage of Ringer's Lactate (RL)

In all the RCTs assessed, RL was the only crystalloid fluid used in early sepsis resuscitation, administered intravenously. Differences existed among total volume, rate,

and duration, as per institutional standards and acuity. Gelbenegger et al,¹⁵ researched the use of RL in an early resuscitation volume of 1–3L, which accounts for ≥95% of the total early IV fluid requirement for those patients in the ED and ICU only. Golla et al,¹⁶, researched the use of RL within the first 24 hours as per the Surviving Sepsis Campaign (SSC) guidelines, although the volume was at a clinician's discretion to fit the resuscitation needs for early resuscitation and fluid maintenance. Zhang et al,¹⁷ assessed Ringer's Acetate Solution (RAS), a balanced crystalloid comparable to RL, delivered at an average dose of 30 mL/kg over the first three hours and a median total volume of about 2500 mL (1300–3000 mL) administered over five days. All studies have used RL as the only or primary fluid for intravenous resuscitation therapy, with differences in doses and time lengths in each study.

Administration Mode and Dosage of 0.9% NaCl

In every study presented, NS (0.9% NaCl; Normal Saline) was the crystalloid fluid of choice and the comparator to RL. The volume and rate of administration were generally appropriate to resuscitation goals according to international guidelines on sepsis resuscitation, most effectively the SSC, to maintain intervention equivalence between groups. For example, in Gelbenegger et al, NS was administered at ±1–3 liters as the resuscitation fluid of choice and constituted ≥95% of volume given in the first 24 hours of admission.¹⁵ Golla et al. (2022) utilized a similar approach, giving intravenous NS according to hemodynamic needs in the first 24 hours, whereas Zhang et al, administered an initial bolus of 30mL/kg in the first three hours, with a total average volume of 1,900mL (1,000–3,000 mL) over five days.^{16–17} Ultimately, all studies maintained fluid regimen equivalence between NS and RL groups so that differences in clinical outcomes were more reflective of physiological differences of fluids instead of volumetric disparities.

RL and NS Administration on Sepsis Patient Mortality

The three RCT studies and one systematic review analyzed as a whole showed consistent results, namely that the use of RL provided better clinical outcomes than NS in adult patients with sepsis. This improvement was particularly evident in the reduction in mortality rates, both 30-day and 90-day mortality.

A large-scale study by Gelbenegger et al, found the most significant results, showing that 90-day mortality was lower in the RL group than in the NS group (12.2% vs. 15.9%) with a hazard ratio (HR) of 0.71 [95% CI 0.51–0.99; $p = 0.043$], and a number needed to treat (NNT) of 27.¹⁵ These findings support that the use of fluids with balanced electrolyte composition can improve tissue perfusion and reduce the risk of death. Golla et al, also reported a lower mortality trend in the RL group, although it did not reach statistical significance.¹⁶ Meanwhile, Zhang et al. (2024) found no significant difference in 90-day mortality (33.8%

vs. 37.5%; HR = 0.9 [95% CI 0.4–1.9]).¹⁷ The included studies reported mortality outcomes using different effect measures. Two studies presented effect estimates as risk ratios (RR), while one study reported hazard ratios (HR) derived from time-to-event analysis. Given the fundamental methodological differences between RR and HR, no quantitative pooling or direct numerical comparison of effect sizes was performed. Instead, the direction and consistency of the reported effects were interpreted qualitatively.

A meta-analysis by Chen et al, encompassing several large RCTs reinforced this evidence by showing that balanced crystalloids significantly reduced the risk of mortality in sepsis patients (RR = 0.91; 95% CI = 0.85–0.99; $p = 0.02$) compared to saline, with very low heterogeneity ($I^2 = 0\%$).¹⁸ This consistency indicates that the observed effect is not limited to specific populations or conditions but can be generally applied to sepsis patients undergoing fluid resuscitation across various levels of care, including the ICU and emergency department.

Physiologically, these results are consistent with the theory that the high chloride load in 0.9% NaCl can cause hyperchloremic metabolic acidosis and renal afferent vasoconstriction, which impairs renal perfusion and increases the risk of organ dysfunction.¹¹ In contrast, Ringer's Lactate provides an electrolyte composition closer to physiological plasma, with lactate content that is metabolized into bicarbonate and acts as a buffer to neutralize acidosis.^{8,19} Therefore, although some results did not reach statistical significance, consistent clinical trends indicate that RL provides better physiological and prognostic benefits compared to NS, particularly in reducing mortality in sepsis patients.

DISCUSSION

This evidence-based case report examined the best available evidence comparing Ringer's Lactate and 0.9% NaCl for fluid resuscitation in adult patients with sepsis, prompted by a specific clinical scenario. Overall, the included studies suggest a consistent direction of effect favoring balanced crystalloids, including Ringer's Lactate, with respect to mortality outcomes; however, the strength of this evidence remains limited. This reduction in mortality is evident in large-scale studies such as Gelbenegger et al, which reported lower 90-day mortality in the RL group (12.2%) compared to the NS group (15.9%), with a hazard ratio of 0.71 (95% CI 0.51–0.99).¹⁵ These findings are consistent with the results of a recent meta-analysis by Chen et al, involving a population of sepsis patients from various RCTs, showing that balanced crystalloids significantly reduce the risk of mortality (RR = 0.91; 95% CI = 0.85–0.99; $p = 0.02$), with very low heterogeneity ($I^2 = 0\%$).¹⁸

Interpretation of these findings must consider important methodological limitations. One included study lacked clear randomization, and none of the primary clinical studies implemented blinding, introducing potential selection and performance bias. In addition, mortality outcomes were reported using different effect measures, including risk ratios and hazard ratios, which are not directly interchangeable. Consequently, quantitative comparison of effect sizes was not performed, and conclusions were based on qualitative assessment of the direction and consistency of effects.

Despite these limitations, the observed trend toward lower mortality with balanced crystalloids is biologically plausible. Physiologically, this effect can be explained by the mechanism that RL, with an ionic composition close to physiological plasma, is able to maintain microcirculatory hemodynamic stability and tissue oxygenation better than NS.^{20,21} The administration of RL prevents electrolyte imbalance and extreme changes in plasma tonicity that can impair perfusion of vital tissues. Improvements in tissue

perfusion and oxygenation contribute to a reduction in multiple organ dysfunction, which is the primary determinant of mortality in sepsis patients.^{8,9} Thus, the benefits of RL in reducing mortality stem not only from intravascular volume correction but also from its positive impact on the physiological homeostasis of critically ill patients.

However, it should be noted that not all clinical trials have found statistically significant differences in mortality between RL and NS. Other RCT studies, such as Golla et al, and Zhang et al, reported non-significant results, although the direction of the effect still favored RL.^{16,17} This variation in results is likely due to differences in population, clinical setting, and the amount of fluid administered. Therefore, interpretation of results must consider the clinical context and patient characteristics, with an emphasis that the trend of RL's benefit on mortality is sufficiently consistent clinically and biologically rational.

Table 2. Critical appraisal of RCTs using the CEBM tool by the University of Oxford

| Author | Number of Participants | Level of Evidence | Internal Validity* | | | | | Importance** | | | | |
|---------------------------|------------------------|-------------------|--------------------|---------------------|-----------------|--------------------|----------|--------------|---------|---------|------|--------------|
| | | | Randomization | Baseline Similarity | Equally Treated | Intention to Treat | Blinding | RR | ARR (%) | RRR (%) | NNT | 95% CI |
| Gelbenegger et al. (2025) | 1312 | 2 | - | + | + | + | - | 0.77 | 3.72 | 23.3 | 26.8 | (0.51, 0.99) |
| Golla et al. (2022) | 160 | 2 | + | + | ? | + | - | 0.83 | 7.5 | 17 | 13.3 | (0.57, 1.21) |
| Zhang et al. (2024) | 116 | 2 | + | + | + | + | - | 0.86 | 4.75 | 0.14 | 21.1 | (0.40, 1.90) |

* Internal validity indicated by + stated clearly in the article; - not being done; ? not stated clearly

** Importance was calculated based on the incidence of mortality.

Table 3. Critical appraisal of the systematic reviews using the CEBM tool by the University of Oxford.

| Author | FAAT | | | | | Results | | |
|--------------------|------------|-----------------------|--------------------------------|----------------|-------------------|----------------------|---|---------------------|
| | Clear PICO | Appropriate searching | Appropriate inclusion criteria | Study validity | Result similarity | Total 95% CI | Heterogeneity | Overall effect |
| Chen et al. (2023) | + | + | + | + | + | RR 0.91 [0.85, 0.99] | I ² = 0%, τ^2 = 0, p = 0.93 | Z = 2.36 (p = 0.02) |

FAAT indicated by + stated clearly in the article; - not being done; ? not stated clearly.

Table 4. Summary of included randomized controlled trials.

| Author | Study population | Ringer's Lactate (method of administration, dose) | Normal saline (method of administration, dose) | Outcome measure | Results |
|---------------------------|--|--|---|---|--|
| Gelbenegger et al. (2025) | Adult patients with sepsis in ICUs and emergency departments in 60 U.S. centers from March 2018 to January 2022 (n = 1312) | Ringer's Lactate administered intravenously as initial resuscitation fluid ($\pm 1-3$ L), $\geq 95\%$ of total initial fluid. | Normal saline administered intravenously as initial resuscitation fluid ($\pm 1-3$ L), $\geq 95\%$ of total initial fluid. | Primary: 90-day mortality. Secondary: hospital-free days, AKI, electrolyte levels. | Primary: lower mortality in RL (12.2%) compared to NS (15.9%), HR 0.71 [95% CI 0.51–0.99], p = 0.043. Secondary: higher hospital-free days in RL compared to NS (16.6 ± 10.8 vs. 15.4 ± 11.4 , respectively; adjusted mean difference, 1.6 d [95% CI, 0.4–2.8 d; p = 0.009]) |

| | | | | | |
|---------------------|--|---|--|--|---|
| Golla et al. (2022) | Adult patients with sepsis in Emergency Medical Services and Emergency Departments at a tertiary hospital, India (n = 160) | Ringer's Lactate intravenous infusion according to the Surviving Sepsis Campaign (SSC) protocol during the first 24 hours | 0.9% NaCl intravenous infusion according to the SSC protocol during the first 24 hours | Primary: hyperchloremia. Secondary: AKI and mortality (in-hospital mortality and 30-day mortality). | Primary: RL (48.8%) reduced hyperchloremia compared to NS (75%), p = 0.001. Secondary: AKI (24 hours): NS 23.8% vs RL 10.0%, p = 0.020; AKI (48 hours): NS 29.1% vs RL 15.4%, p = 0.039; Hospital mortality: NS 37.5% vs RL 28.8%, p = 0.240; 30-day mortality: NS 43.8% vs RL 36.3%, p = 0.418 |
| Zhang et al. (2024) | Adult patients with sepsis in the ICU of Zhongnan Hospital of Wuhan University (n = 116) | Ringer's Acetate Solution (RAS) 30 mL/kg of IV crystalloid fluid within the first 3 hours. During the 5-day intervention, the median dose was 2,500 mL (1,300–3,000 mL) | Normal Saline Solution (NSS) 30 mL/kg of IV crystalloid fluid within the first 3 hours. During the 5-day intervention, the median dose was 1,900 mL (1,000–3,000 mL) | Primary: Major Adverse Kidney Events within 28 days (MAKE28). Secondary: 30-day and 90-day mortality, AKI, and hyperchloremia. | Primary: MAKE28 did not differ significantly between RAS (23.3%) and NSS (27.3%), OR 0.82 [95% CI 0.35–1.94], p = 0.65. Secondary: 90-day mortality: RAS 33.8% vs NSS 37.5%, HR 0.9 [95% CI 0.4–1.9], p = 0.70; AKI: RAS 58.3% vs NSS 56.8%, p = 0.87; hyperchloremia: RAS 12.5% vs NSS 23.3%, p = 0.14 |

ICU: Intensive Care Unit, IV: Intravenous, AKI: Acute Kidney Injury.

Table 5. Summary of the included systematic review and meta-analyses of randomized controlled trials.

| Author | Study population | Ringer's Lactate (method of administration, dose) | Normal saline (method of administration, dose) | Results | Comments |
|--------------------|--|---|---|--|--|
| Chen et al. (2023) | Critically ill adult patients, including those with sepsis, who are treated in the ICU and require fluid resuscitation | Balanced Crystalloid (BC) was administered intravenously as initial resuscitation fluid | 0.9% saline was administered intravenously as the initial resuscitation fluid | Mortality in sepsis patients was lower with BC than with NS, RR 0.91 [95% CI 0.85–0.99], p = 0.02. | The authors support the use of Balanced Crystalloid over 0.9% Saline for fluid resuscitation in critically ill patients, especially in cases of sepsis. The results show a reduction in the risk of AKI and an improvement in overall composite mortality outcomes. These findings are important to guide clinical practice in the selection of safer and more effective IV fluids in the ICU. |

ICU: Intensive Care Unit, IV: Intravenous, AKI: Acute Kidney Injury.

In the context of the presented case, where initial fluid resuscitation was required in an adult patient with sepsis, the available evidence supports consideration of Ringer's Lactate as a reasonable alternative to 0.9% sodium chloride. This recommendation aligns with the 2021 Surviving Sepsis Campaign to use balanced crystalloid fluids as the initial resuscitation of choice, estimating an initial bolus of 30 mL/kg (adjusted per hemodynamic stabilization).¹³ However, given the limitations of the evidence base, this decision should be individualized and integrated with clinical judgment, patient characteristics, and local practice guidelines.

CONCLUSION

This evidence-based case report, conducted in response to a specific clinical scenario, suggests that the use of Ringer's Lactate for initial fluid resuscitation in adult patients with sepsis is associated with a favorable direction of effect on mortality when compared with 0.9% NaCl. However, the certainty of this evidence remains limited due to methodological heterogeneity among the included studies, including variations in study design, risk of bias, and the use of different effect measures such as risk ratios and hazard ratios. Given these limitations, the findings should be interpreted cautiously, and no definitive conclusions regarding the superiority of Ringer's Lactate over 0.9% NaCl can be drawn. Nevertheless, within the context of the presented case and the available evidence, Ringer's Lactate may be considered a reasonable option for fluid resuscitation

in adult patients with sepsis, alongside clinical judgment and existing guideline recommendations. Further well-designed randomized controlled trials are warranted to provide more robust and conclusive evidence on this topic.

STRENGTHS AND LIMITATION

This evidence-based review boasts a comprehensive yet concise overview of the current literature on Ringer's Lactate versus 0.9% NaCl for adult septic patients. One of its greatest strengths is the thorough literature selection and assessment process of the Centre for Evidence-Based Medicine (CEBM) a method that employs transparency and replicability to demonstrate author consistency and quality rating assessments of randomized controlled trials and systematic reviews. It combines a physiological and clinical understanding of the topic, which helps solidify appreciation for expert review findings as it bridges the gap between statistical findings and why certain mechanisms should impact fluid choice for septic resuscitation. Finally, much of the recent literature included comprises large-scale multicenter RCTs and multicenter meta-analyses that further lend credence and clinical relevance to the evidence compiled therein.

There are limitations to this review that should also be acknowledged. This evidence-based case report has several limitations. As an evidence-based case report, this study was designed to address a focused clinical question arising from a specific clinical scenario rather than to provide a comprehensive synthesis of evidence as in a full systematic review or meta-analysis. The literature search was intentionally limited to studies published within the last five years and to English-language full-text articles, which may have introduced selection and publication bias and resulted in the exclusion of potentially relevant studies. In addition, methodological heterogeneity was present among the included studies with respect to study design, patient populations, and reported effect measures, particularly the use of different mortality metrics such as risk ratios and hazard ratios that are not directly interchangeable. Consequently, quantitative pooling of effect estimates was not performed, and conclusions were based on qualitative assessment of the direction and consistency of effects. Furthermore, the risk-of-bias assessment identified limitations including unclear randomization procedures and lack of blinding, which may have introduced selection, performance, and detection bias. Finally, the limited number of included studies and the focused clinical context may restrict the generalizability of the findings, highlighting the need for further high-quality randomized controlled trials with standardized outcome reporting.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

ACKNOWLEDGMENTS

No declaration.

DECLARATION OF USING AI

The authors state that AI tools were involved in the writing process, but only to facilitate language use, including but not limited to, grammar checks, paraphrasing, and clarity improvement. No AI tools were utilized to produce initial drafts, analyze data, or interpret research results. The authors are responsible for all statements, interpretations, and conclusions of this manuscript.

FUNDING SOURCES

No funding was received.

REFERENCES

1. Harahap HM, Seruni D, Nasution M, Munandar F, Faradhiba Siregar N, Rizky R, et al. Tinjauan Pustaka Sepsis: Kriteria Diagnosa Dan Tatalaksana. *J Implementa Husada*. 2021;2(3):305–20.
2. Wiersinga WJ, van der Poll T. Immunopathophysiology of human sepsis. *eBioMedicine* [Internet]. 2022;86:104363. Available from: <https://doi.org/10.1016/j.ebiom.2022.104363>
3. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801–810.
4. Gauer R, Forbes D, Boyer N. Sepsis: Diagnosis and Management. *Am Fam Physician*. 2020;101(7):409–18.
5. Dugar S, Choudhary C, Duggal A. Sepsis and septic shock: Guideline-based management. *Cleve Clin J Med*. 2020;87(1):53–64.
6. Semler MW, Kellum JA. Balanced crystalloid solutions. *Am J Respir Crit Care Med*. 2019;199(8):952–60.
7. Khatua B, Yaron JR, El-Kurdi B, Kostenko S, Papachristou GI, Singh VP. Ringer's lactate prevents early organ failure by providing extracellular calcium. *J Clin Med*. 2020;9(1).
8. Maheshwari K, Turan A, Makarova N, Ma C, Esa WAS, Ruetzler K, et al. Saline versus Lactated Ringer's Solution: The Saline or Lactated Ringer's (SOLAR) Trial. *Anesthesiology*. 2020;132(4):614–24.
9. Chaussard M, Dépret F, Saint-Aubin O, Benyamina M, Coutrot M, Jully M, et al. Physiological response to fluid resuscitation with Ringer lactate versus

- Plasmalyte in critically ill burn patients. *J Appl Physiol*. 2020;128(3):709–14.
10. Chen L, Liu C, Zhang Z, Zhang Y, Feng X. Effects of normal saline versus lactated Ringer's solution on organ function and inflammatory responses to heatstroke in rats. *J Intensive Care* [Internet]. 2024;12(1):1–15. Available from: <https://doi.org/10.1186/s40560-024-00746-y>
11. Liu X, Lu M. Normal saline: Past, present, and future. *Sci Prog*. 2023;106(2):1–7.
12. Mikhael B, Steele DJR, Fenves AZ. In Defense of Normal Saline Our Perspective. *Clin J Am Soc Nephrol*. 2022;17(4):588–90.
13. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med* [Internet]. 2021;47(11):1181–247. Available from: <https://doi.org/10.1007/s00134-021-06506-y>
14. Nuffield Department of Primary Care Health Sciences. University of Oxford. Critical Appraisal tools CEBM.
15. Gelbenegger G, Shapiro NI, Zeitlinger M, Jilma B, Douglas IS, Jorda A. Lactated Ringer's or Normal Saline for Initial Fluid Resuscitation in Sepsis-Induced Hypotension. *Crit Care Med*. 2025;53(5):e1140–4.
16. Golla R, Kumar S, Dhibhar DP, Bhalla A, Sharma N. 0.9% saline V/S Ringer's lactate for fluid resuscitation in adult sepsis patients in emergency medical services: An open-label randomized controlled trial. *Hong Kong J Emerg Med*. 2022;29(5):271–80.
17. Zhang J, Liu F, Wu Z, Jiang J, Wang B, Qian Y, et al. Acetate Ringer's Solution Versus Normal Saline Solution in Sepsis: A Randomized, Controlled Trial. *Shock*. 2024;61(4):520–6.
18. Chen Y, Gao Y. Comparison of Balanced Crystalloids versus Normal Saline in Critically Ill Patients: A Systematic Review with Meta-Analysis and Trial Sequential Analysis of Randomized Controlled Trials. *Ther Clin Risk Manag*. 2023;19(August):783–99.
19. Rawat N, Sahni N, Yaddanapudi L. Comparison of commercially available balanced salt solution and ringer's lactate on extent of correction of metabolic acidosis in critically ill patients. *Indian J Crit Care Med*. 2020;24(7):539–43.
20. Moschopoulos CD, Dimopoulou D, Dimopoulou A, Dimopoulou K, Protopapas K, Zavras N, et al. New Insights into the Fluid Management in Patients with Septic Shock. *Gen Pharmacol* [Internet]. 2023;59(6):1047. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-0032126564&doi=10.1016%2FS0306-3623%2897%2900424-2&partnerID=40&md5=e70f13173e905d39509a5672ebc09801>
21. Malbrain MLNG, Wong A, Nasa P, Ghosh S. Rational use of intravenous fluids in critically Ill patients. *Rational Use of Intravenous Fluids in Critically Ill Patients*. 2023. 1–598 p.

