Review Article

Bull Emerg Trauma 2025;13(4):195-202.

Bulletin of Emergency And Trauma

The Role of Urine Alkalinization in Preventing Rhabdomyolysis-Induced Acute Kidney Injury and Need for Dialysis: A Systematic Review and Meta-Analysis

***Saeed Safari*[1,2], *Iraj Najafi*[3], *Seyed Hadi Aghili*[2,4,5], *Ali Jamshidi Kerachi*[2,6*], *Mohammad Amin Shahlaee*[6], *Alireza Sadeghi*[6,7], *Mehri Farhang Ranjbar*[2,8]**

[1]*Emergency Care Promotion Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[2]*Research Center for Trauma in Police Operations, Directorate of Health, Rescue and Treatment, Police Headquarters, Tehran, Iran*
[3]*Nephrology Department, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran*
[4]*Department of Neurosurgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran*
[5]*Department of Neurosurgery, Valiasr Hospital, Tehran, Iran*
[6]*Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran*
[7]*Gastroenterohepatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*
[8]*Department of Medical Surgical Nursing, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran*

***Corresponding author:** *Ali Jamshidi Kerachi*
Address: Research Center for Trauma in Police Operations, Directorate of Health, Rescue and Treatment, Police Headquarters, Tehran, Iran. **Tel:** +98 9211989915; **e-mail:** alijamshidi261375@gmail.com

Received: July 18, 2025
Revised: October 04, 2025
Accepted: October 06, 2025

ABSTRACT

Objective: This systematic review and meta-analysis aimed to evaluate the efficacy of urine alkalinization in preventing acute kidney injury (AKI) and the need for dialysis in patients with rhabdomyolysis.
Methods: This study was conducted in accordance with the PRISMA guideline. A systematic literature search of MEDLINE/ PubMed, Scopus, Web of Science, and Embase databases was conducted. No time or language restrictions were applied to maximize the scope of the results. After removing duplicates, the remaining articles were screened by title, abstract, and study criteria. Two researchers independently assessed the full texts of the remaining studies, with any discrepancies resolved through discussion. The risk of bias was assessed using the ROBINS-I tool, and studies with a critical risk of bias were excluded from the final analysis.
Results: Out of 9,230 initially identified articles, five studies met the inclusion criteria for the meta-analysis. The analysis revealed that urine alkalinization was not significantly effective in preventing AKI (OR: 2.11; 95% CI: 0.09-47.72; p=0.3), preventing acute renal failure (OR: 1.26; 95% CI: 0.86-1.84; p=0.36), or reducing the need for dialysis (OR: 4.25; 95% CI: 0-3.8e^{+07}; p=0.25).
Conclusion: The addition of sodium bicarbonate to fluid therapy solution did not appear to provide significant protection against AKI, acute renal failure, or the need for dialysis in patients with rhabdomyolysis. Further insight should be sought through controlled randomized clinical trials with larger sample sizes.

Keywords: Rhabdomyolysis, Crush injury, Urine alkalization, Sodium bicarbonate, Management.

Please cite this paper as:
Safari S, Najafi I, Aghili SH, Jamshidi Kerachi A, Shahlaee MA, Sadeghi AR, Farhang Ranjbar M. The Role of Urine Alkalinization in Preventing Rhabdomyolysis-Induced Acute Kidney Injury and Need for Dialysis: A Systematic Review and Meta-Analysis. *Bull Emerg Trauma*. 2025;13(4):195-202. doi: 10.30476/beat.2025.107657.1618.

Introduction

Rhabdomyolysis is a medical condition characterized by the breakdown of skeletal muscle tissue, leading to the release of intracellular components such as myoglobin, creatine kinase (CK), lactate dehydrogenase (LDH), and electrolytes into the bloodstream [1-3]. This process can trigger systemic complications, ranging from asymptomatic enzyme elevation to life-threatening conditions, including severe electrolyte disturbances, disseminated intravascular coagulation (DIC), and acute kidney injury (AKI) [4-6].

Muscle fiber breakdown results from direct sarcolemmal injury or ATP depletion, which leads to increased intracellular calcium, activation of proteases and phospholipases, and eventual myocyte necrosis [4, 7]. Myoglobin, which is freely filtered by the glomerulus, can precipitate in renal tubules and exert direct cytotoxic effects, contributing to AKI. Additional risk factors for kidney injury include hypovolemia, renal ischemia, and uric acid crystallization, particularly in exertional or heat-induced rhabdomyolysis [6, 8-10].

The etiology of rhabdomyolysis is diverse. Traumatic causes include crush injuries, prolonged immobilization, heavy exertion, and events such as earthquakes [11-13]. Non-traumatic causes encompass medications (e.g., statins), illicit drugs, infections, and metabolic or genetic disorders [3, 4, 8]. Certain populations, including men, African Americans, pediatric patients, and individuals with underlying medical conditions, are at higher risk [3, 8]. Common complications include electrolyte imbalances such as hyperkalemia, hyponatremia, hypocalcemia, and hyperphosphatemia, which are particularly prevalent in traumatic rhabdomyolysis [13].

Diagnosis is primarily laboratory-based, with key markers including elevated serum CK (>5× the upper limit of normal), myoglobin, LDH, aspartate aminotransferase (AST), and potassium; while urinary myoglobin may provide additional evidence [1, 2]. Early recognition and prompt treatment are critical to prevent AKI and other complications. The cornerstone of management is aggressive intravenous fluid resuscitation with isotonic crystalloids to maintain adequate urine output [1, 2, 10]. Although sodium bicarbonate and mannitol have been proposed to prevent kidney injury, evidence supporting their routine use remains limited and controversial [1, 2, 10].

Overall, rhabdomyolysis has a favorable prognosis with early recognition and treatment. However, the development of AKI significantly worsens outcomes, highlighting the importance of timely intervention and careful monitoring [1, 4].

To date, no study has provided definitive evidence that adding sodium bicarbonate to fluid therapy is superior to fluid therapy alone. Given the inconclusive nature of existing literature and the lack of comprehensive analyses, this systematic review and meta-analysis was conducted to determine the role of urine alkalinization in preventing rhabdomyolysis-induced AKI and the need for dialysis.

Materials and Methods

This systematic review and meta-analysis was conducted in accordance with the PRISMA guidelines [14]. The study protocol was registered in PROSPERO (registration number CRD42024502360).

A comprehensive literature search was performed on January 21, 2024, across four databases, including MEDLINE/Pubmed, Scopus, Web of Science, and Embase, to ensure the inclusion of all available relevant research. Key search terms included “rhabdomyolysis”, “crush injury”, “urine alkalization”, “sodium bicarbonate”, and “management”. The complete search strategy for each database is provided in the supplementary data. No time or language restrictions were applied to maximize the scope of the results.

After the search, duplicates were removed using EndNote software (version 20). Two reviewers (AJK and MAS) conducted an initial screening of titles and abstracts against the study eligibility criteria. Irrelevant records were excluded, and any conflicts were resolved through discussion. The same two reviewers then independently performed a full-text assessment of the remaining articles. Studies that did not meet the inclusion criteria were excluded, and any discrepancies were resolved via discussion. Forward and backward citation tracking was performed during the full-text screening; however, no additional relevant articles were identified.

The risk of bias for each included study was independently assessed by the reviewers using the ROBINS-I tool [15]. Any differences in opinion were resolved through discussion. Studies with a critical risk of bias were excluded from the final meta-analysis.

Inclusion and Exclusion Criteria

All relevant cohort studies, clinical trials, and case-control studies with appropriate populations, interventions, controls, and outcomes were included. Case reports, case series, animal studies, and review studies were excluded.

The specific characteristics of the population, intervention group, control group, and outcomes are detailed in the following section.

-Population: Adult patients (over 18 years of age) with rhabdomyolysis, irrespective of the cause.

-Intervention: Patients who received urine-alkalizing agents (e.g., sodium bicarbonate or acetazolamide) in addition to fluid therapy. The dosage and mode of administration were not restricted.

-Control: Patients who received fluid therapy alone, without any urine-alkalizing agents.

-***Outcomes:*** Acute renal failure (ARF), AKI, and the need for dialysis.

The ROBINS-I tool was used to assess the risk of bias (ROB) in the included studies. Two reviewers (AJK and MAS) conducted the assessment independently, and any conflicts were resolved through discussion. Studies with a critical risk of bias were excluded. This tool assessed the risk of bias in non-randomized studies of interventions (NRSI) across seven domains. The first three domains differ between NRSI and randomized trials, as randomization protects against biases that occur before the intervention begins. The last four domains had considerable overlap in bias assessment for both NRSI and randomized trials.

The meta-analysis was performed using Stata software (version 17), applying a random-effects model with the DerSimonian–Laird method. Three outcomes were investigated, and a meta-analysis was conducted for any outcome reported by at least two studies. Heterogeneity was assessed using the Chi squared test and was reported as I^2 statistic. According to the Cochrane Handbook, there was no need to evaluate publication bias due to the small number of included studies [16].

A sensitivity analysis was performed using the leave-one-out method.

Results

The systematic search initially identified 9,230 articles. After the removal of 1,858 duplicates, 7372 records underwent initial screening based on their titles and abstracts. Following the primary screening, 12 articles were deemed eligible for a full-text review. During the secondary screening, six studies were excluded for the following reasons: one study measured different outcomes, four had significant study design errors, and the full text of one study could not be retrieved. This process resulted in six studies being considered for inclusion (Table 1). Following a risk of bias assessment, one study with a critical risk of bias was excluded, leaving five studies to be included in the final meta-analysis (Figure 1).

Table 1. Characteristics of excluded studies during secondary screening and risk of bias assessment

Title	Authors	Publication year	Exclusion reason
Bicarbonate and Mannitol Treatment for Traumatic Rhabdomyolysis Revisited [23]	Nielsen et al.,	2015	Design: The study lacked an appropriate control group, and two drugs were administered simultaneously in the intervention group.
Rhabdomyolysis-associated Acute Kidney Injury [27]	Subashri et al.,	2023	Outcome: Study reports prevalence of rhabdomyolysis types, not its treatment
Bicarbonate may not be the best treatment for rhabdomyolysis: A retrospective cohort study [28]	Kim et al.,	2020	Non retrieval
LPIN1 rhabdomyolysis: A single site cohort description and treatment recommendations [29]	Kanderi et al.,	2022	Design: This study did not investigate the effectiveness of urine alkalinization.
Safety and effectiveness of the combination acetazolamide and bicarbonates to induce alkaline diuresis in patients with rhabdomyolysis [30]	Ioannidis et al.,	2014	Design: In this study, the effectiveness of various alkalizing agents in alkalizing urine was investigated, and the desired results of our study were not reported. The two study groups received urine alkalizing agents.
Multivariate Regression Analysis of Risk Factors for Acute Kidney Injury after Traumatic Rhabdomyolysis [31]	Garcia et al.,	2016	Design: The control and intervention groups are not precisely defined, and the association of several factors with acute renal failure in traumatic rhabdomyolysis has been investigated.
The Effect of Infusion of Mannitol-Sodium Bicarbonate on the Clinical Course of Myoglobinuria [32]	Eneas et al.,	1979	Critical risk of bias

Table 2. The results of the risk of bias assessment of the studies in each of the investigated domains.

Authors	Domain							Overall
	1	2	3	4	5	6	7	
Sitzwohl et al., [17]	S	L	L	L	L	M	L	S
Kim et al., [21]	M	L	L	L	L	M	L	M
Homsi et al., [20]	S	L	L	M	L	M	L	S
Eneas et al., [32]	S	C	S	L	L	M	L	C
Chendrasekhar et al., [18]	S	L	L	L	L	M	L	S
Brown et al., [19]	M	L	M	L	L	M	L	M

Domain 1: Bias due to confounding; Domain 2: Bias in the selection of participants into the study; Domain 3: bias in the classification of interventions; Domain 4: bias due to deviations from intended interventions; Domain 5: Bias due to missing data; Domain 6: bias in the measurement of outcomes; Domain 7: Bias in the selection of the reported result; M: moderate; S: serious: L: Low; C: Critical

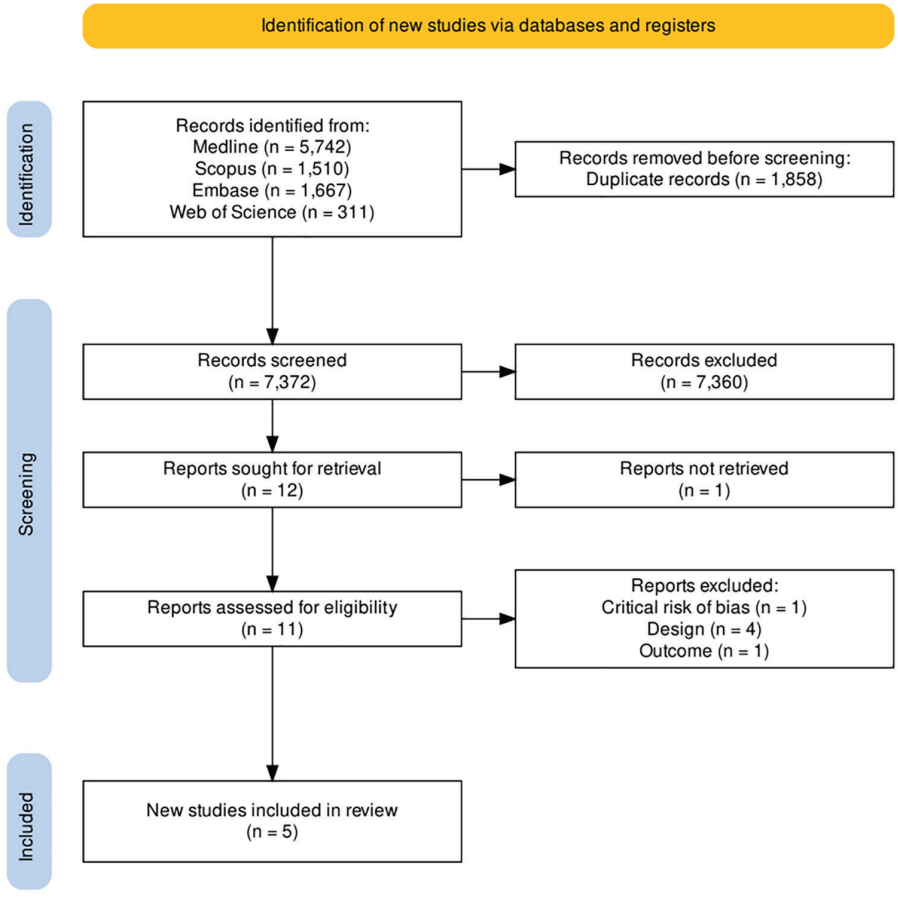

Fig. 1. PRISMA flowchart of the included studies

Risk of Bias Assessment

The risk of bias for the six shortlisted studies was assessed using the ROBINS-I tool. The assessment revealed that three studies had a serious risk of bias, and two studies had a moderate risk. One study was judged to have a critical risk of bias and was consequently excluded from the final analysis (Table 2).

Sensitivity Analysis

A sensitivity analysis was conducted using the leave-one-out method across the various outcomes (Figure 2). The results for the dialysis outcome were sensitive to the exclusion of either the Brown or Kim studies. In contrast, no discernible sensitivity was observed for the other two outcomes. This pattern was anticipated, given the limited number of studies, as a small pool of included research increased the susceptibility of the overall results to the influence of individual studies.

Characteristics of the Included Studies

Table 3 provides a comprehensive summary of the characteristics and data from the five studies included in the meta-analysis. Sitzwohl *et al.,* investigated the incidence of AKI and renal failure in 60 patients with a serum myoglobin above 2000 mol/L within 24 hours after trauma [17]. Chendrasekhar *et al.,* performed a retrospective analysis of 23 patients who were entrapped for more than 30 minutes in motor vehicle accidents and had myoglobinuria [18]. Brown *et al.,* reported the incidence of renal failure and the need for dialysis in 382 patients admitted to a trauma intensive care unit (ICU) with serum CK levels above 5000 U/L [19]. Homsi *et al.,* reported acute renal failure in 24 ICU patients with serum CK levels above 5000 U/L [20]. Kim *et al.,* investigated the incidence of AKI and the need for dialysis in 4,077 patients with serum CK levels above 1000 U/L [21].

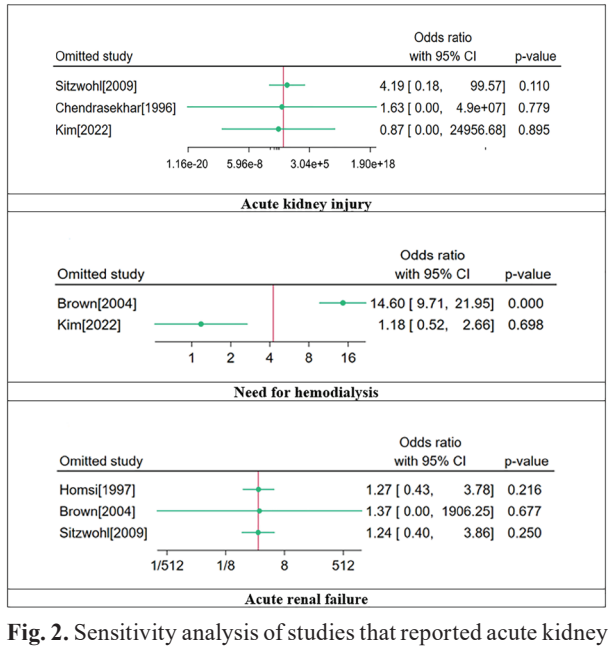

Fig. 2. Sensitivity analysis of studies that reported acute kidney injury, need for hemodialysis, and acute renal failure.

Table 3. Characteristics of the studies included in the final meta-analysis

Authors, Country	Year	Cases (n)		Male [c]	Age[d]	Reported outcomes (n)					
		Case[a]	Control[b]			AKI[e]		Dialysis		ARF[f]	
						Case	Control	Case	Control	Case	Control
Sitzwohl et al., Austria [17]	2009	20	40	NM[g]	NM	0	3	NR[h]	NR	1	1
Kim et al., South Korea [21]	2022	2493	1584	NM	60.7	1974	730	473	25	NR	NR
Homsi et al., Brazil [20]	1997	15	9	83.3	31.0	NR	NR	NR	NR	0	0
Chendrasekhar et al., USA [18]	1996	12	11	NM	NM	3	2	NR	NR	NR	NR
Brown et al., USA [19]	2004	154	228	88.4	34.4	NR	NR	11	14	34	42

a: Patients who received bicarbonate; b: Patients who did not receive bicarbonate; c: Sex is reported as the percentage of males; d: age is reported as the mean (year); e: Acute kidney injury; f: Acute renal failure; g: Not mentioned; h: Not reported

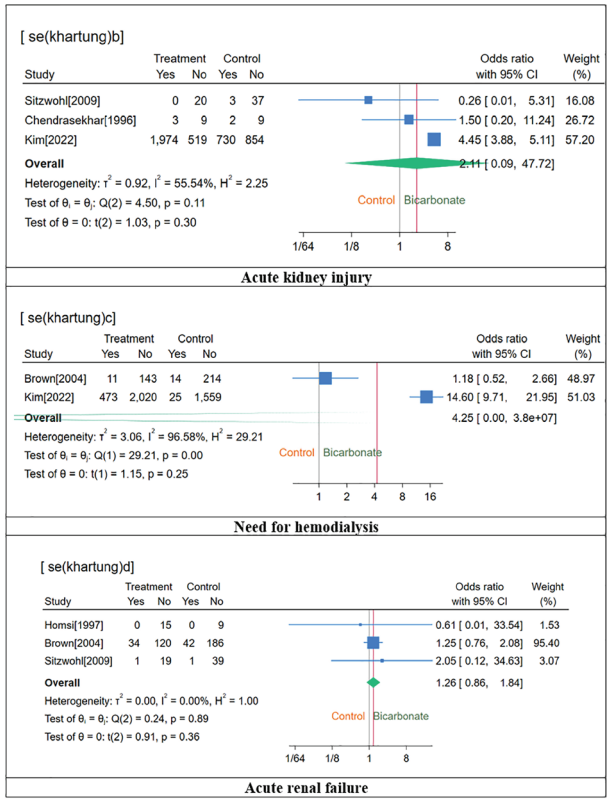

Fig. 3. Odds ratio and heterogeneity in comparing the effect of urine alkalinization with fluid therapy alone on the prevention of acute kidney injury, the need for hemodialysis, and acute renal failure in patients with rhabdomyolysis

Meta-Analysis

Odds ratios were used to assess the efficacy of adding urine alkalizing agents to fluid therapy for rhabdomyolysis by comparing the intervention and control groups (Figure 3). The results revealed that the intervention group did not exhibit a significant improvement in any of the measured outcomes compared to the control group. Specifically, statistical analysis indicated no significant differences between the groups for the need for dialysis (OR: 4.25; 95% CI: 0-3.8e^{+07}; p=0.25) or the occurrence of AKI (OR: 1.26; 95% CI: 0.86-1.84, p=0.36).

Heterogeneity Analysis

Heterogeneity was examined using the Chi squared test, and the results are reported as the I^2 statistic (Figure 3). For the outcome of AKI, the I^2 value of 55.54% indicated moderate heterogeneity, which may stem from differences in population age, diverse underlying causes of rhabdomyolysis, various comorbidities, and an undisclosed duration of treatment initiation. For the need for dialysis, a substantial I^2 of 95.58% suggested significant heterogeneity, likely due to causes similar to those for AKI. In contrast, acute renal failure (ARF) exhibited an I^2 of 0%, indicating no notable heterogeneity. Due to the observed heterogeneity and the limited number of included studies (fewer than 10), a subgroup analysis was not performed, in accordance with the Cochrane Handbook recommendations [16].

Discussion

This study is the first systematic review and meta-analysis to specifically investigate the effect of urine alkalinization on preventing AKI in patients with rhabdomyolysis. To ensure a comprehensive review of the available literature, we developed an inclusive search strategy that did not apply time or language filters.

The utility of urine alkalinization for preventing AKI in rhabdomyolysis patients has remained uncertain in previous research. Some studies suggested a potential benefit. For instance, an animal study by Özgüç *et al.,* indicated that a hypertonic saline-dextran solution could effectively prevent oxidant damage and restore tissue blood flow in experimental rhabdomyolysis. However, the same study noted that a combination of 0.9% saline, sodium bicarbonate, and mannitol seemed to be superior to hypertonic saline and dextran in reducing oxidant injury. They concluded that further investigation is required to understand the effects of solute overload and metabolic acidosis resulting from hypertonic saline-dextran resuscitation on renal function in this context [22]. Supporting a potential role in humans, a study

by Nielsen *et al.,* involving 77 patients with CK levels exceeding 10,000 U/L, concluded that supplementing fluid therapy with bicarbonate and mannitol helped to prevent acute renal dysfunction [23].

In contrast, other evidence disputed the benefit of urine alkalinization. One study concluded that there was no significant difference between urine alkalinization and fluid therapy for treating patients with rhabdomyolysis. In their case series, Tazmini *et al.,* reported that urinary alkalization did not yield significantly different outcomes from fluid therapy alone in individuals with exercise-induced rhabdomyolysis [24].

Furthermore, some guidelines explicitly recommend against the practice. Kodadek *et al.,* recommended against the use of bicarbonate and urine alkalinization. They concluded that, due to limitations in the available clinical studies—such as inadequate control groups, inconsistent outcome definitions, retrospective designs, and low statistical power—the use of sodium bicarbonate or diuretics for preventing AKI in patients with rhabdomyolysis is not recommended [2].

Previous systematic reviews concluded that the effectiveness of urine alkalinization remained uncertain. For instance, Manspeaker *et al.,* highlighted that the efficacy of treating exertional rhabdomyolysis (ER) was unclear due to variations in study types and methodologies. They noted that intravenous fluid replacement, predominantly with normal saline, is the common practice to reduce CK levels and myoglobinuria, with sodium bicarbonate or chloride sometimes added as an adjunct [25]. Additionally, in another study, Somagutta *et al.,* concluded that aggressive early volume resuscitation using normal saline was the cornerstone of rhabdomyolysis management. Based on their findings, they questioned the practical utility of sodium bicarbonate and mannitol and emphasized the need for more robust future research to inform definitive recommendations [26].

The risk of bias was assessed using the ROBINS-I tool, which is specifically designed for non-randomized studies. This was appropriate as none of the identified articles were large randomized clinical trials. Given the limited number of studies available, those with a moderate or serious risk of bias were included in the meta-analysis. However, any study with a critical risk of bias was excluded. It is important to note that a low risk of bias was not anticipated, given the non-randomized nature of all included studies. To enhance the generalizability of our findings, a random-effects meta-analysis model was employed. While the minimum recommended number of studies for such an analysis is five, it is crucial to acknowledge the limitations of this research. The most significant limitation is the small number of articles included. Consequently, the results of this meta-analysis should be interpreted with caution.

Several limitations must be considered when interpreting our findings. For each outcome that was investigated, a maximum of three studies were included in the meta-analysis, which restricted the statistical power and generalizability of the findings. Furthermore, the methodological rigor of the included studies varied. Only one study measured urine pH to confirm the effect of the intervention, while most others prescribed medication to alkalize the urine without verifying its efficacy. It is also important to note that the evidence is confined to intravenous sodium bicarbonate; other alkalinizing agents, such as acetazolamide, or other forms of administration, such as oral administration, were not examined.

Significant clinical heterogeneity was also present. The treatment protocols in the reviewed studies differed considerably in the volume and type of fluid therapy administered. Although the target urine output was relatively consistent, typically aiming for between 1 mL/Kg/min and 3 mg/Kg/h, the methods to achieve it varied. While fluid therapy was the cornerstone, some protocols included diuretics, such as mannitol or furosemide. The types of diuretics used were not uniform across studies, and crucially, most studies differentiated between those who received sodium bicarbonate alone and those who received it simultaneously with a diuretic. Additionally, the diagnostic methods for rhabdomyolysis itself were inconsistent. Given these limitations, further randomized clinical trials with well-defined populations and standardized protocols are necessary to definitively explore the impact of urine alkalinization on preventing renal failure in patients with rhabdomyolysis.

The interpretation of these findings must be approached with caution due to the limited number of studies available for the meta-analysis. Each outcome was investigated in a maximum of three studies, which restricted the generalizability of the results. A significant methodological limitation was the lack of consistent verification of the intervention's effect; while one study assessed urine pH, it provided no details, and the other studies did not explore this aspect at all. Furthermore, the scope of this review was confined to intravenous sodium bicarbonate, leaving the effects of alternative alkalinizing agents, such as acetazolamide, or other routes of administration, such as the oral route, unexamined. Clinical heterogeneity was also substantial, as the studies employed varying criteria to define rhabdomyolysis, AKI, and ARF. Treatment protocols exhibited significant disparities in the volume and type of fluid therapy, and the diuretics used alongside bicarbonate were not consistent. Critically, most studies did not distinguish between patients who received sodium bicarbonate concurrently with diuretics and those who received bicarbonate alone.

According to this systematic review and meta-analysis, the co-administration of sodium bicarbonate with fluid therapy did not confer

significant protection against AKI, ARF, or the need for dialysis in patients with rhabdomyolysis when compared to fluid therapy alone. Thus, we do not recommend the routine administration of sodium bicarbonate to these patients in the absence of a separate indication, such as metabolic acidosis. To establish more definitive evidence, future research should prioritize conducting large randomized clinical trials with well-defined patient populations.

Declaration

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Conflict of Interest: None declared.

Funding and support: None.

Authors' Contribution: SS: Conceptualization, study design, searched the databases, screened the records for eligibility, assessed the quality of the studies, and data extraction; IN: Study design; MAS: Searched the databases, screened the records for eligibility, assessed the quality of the studies, and data extraction; AJK: Provided the primary draft, study design, searched the databases, screened the records for eligibility, assessed the quality of the studies, data extraction, data analyses, and supervision; MAS: Provided the primary draft; AS: Data analyses; SHA: Provided the primary draft. All the authors have read and approved the final version of the manuscript.

Acknowledgment: Not applicable.

Data availability: The data underlying this article are available in the article and its online supplementary material.

References

1. Cabral BMI, Edding SN, Portocarrero JP, Lerma EV. Rhabdomyolysis. *Dis Mon*. 2020;**66**(8):101015.
2. Kodadek L, Carmichael SP, Seshadri A, Pathak A, Hoth J, Appelbaum R, et al. Rhabdomyolysis: an American association for the surgery of trauma critical care committee clinical consensus document. *Trauma Surg Acute Care Open*. 2022;**7**(1):e000836.
3. Long B, Koyfman A, Gottlieb M. An evidence-based narrative review of the emergency department evaluation and management of rhabdomyolysis. *Am J Emerg Med*. 2019;**37**(3):518-23.
4. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med*. 2009;**361**(1):62–72.
5. Chavez LO, Leon M, Einav S, Varon J. Beyond muscle destruction: a systematic review of rhabdomyolysis for clinical practice. *Crit Care*. 2016;**20**(1):135.
6. Polderman K. Acute renal failure and rhabdomyolysis. *Int J Artif Organs*. 2004;**27**(12):1030-3.
7. Holt S, Moore K. Pathogenesis and treatment of renal dysfunction in rhabdomyolysis. Intensive care medicine. 2001;**27**(5):803-11.
8. Bagley W, Yang H, Shah K. Rhabdomyolysis. *Intensive Care Med*. 2007;**2**(3):210-8.
9. Sanchez-Lozada L-G, García-Arroyo FE, Gonzaga G, Silverio O, Blas-Marron MG, Muñoz-Jimenez I, et al. Kidney injury from recurrent heat stress and rhabdomyolysis: protective role of allopurinol and sodium bicarbonate. *Am J Nephrol*. 2018;**48**(5):339-48.
10. Scharman EJ, Troutman WG. Prevention of kidney injury following rhabdomyolysis: a systematic review. *Ann Pharmacother*. 2013;**47**(1):90-105.
11. Cervellin G, Comelli I, Benatti M, Sanchis-Gomar F, Bassi A, Lippi G. Non-traumatic rhabdomyolysis: background, laboratory features, and acute clinical management. *Clin Biochem*. 2017;**50**(12):656-62.
12. Omrani H, Najafi I, Bahrami K, Najafi F, Safari S. Acute kidney injury following traumatic rhabdomyolysis in Kermanshah earthquake victims; a cross-sectional study. *Am J Emerg Med*. 2021;**40**:127-32.
13. Safari S, Aghili SH, Shahlaee MA, Kerachi AJ, Ranjbar MF, hadi Aghili S. Incidence of Electrolyte Imbalances Following Traumatic Rhabdomyolysis: A Systematic Review and Meta-Analysis. *Cureus*. 2024;**16**(4):e59333.
14. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *International journal of surgery*. 2010;**8**(5):336-41.
15. Jonathan ACS, Miguel AH, Barnaby CR, Jelena S, Nancy DB, Meera V, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
16. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions*. 2nd Edition. Chichester (UK): John Wiley & Sons, 2019. p. 299-304.
17. Sitzwohl C, Hoerner E, Huepfl M, Chiari A, Weinstabl C, Kettner S, editors. Renal protection after traumatic rhabdomyolysis - is alkalinization of the urine better than forced diuresis alone? [abstract]. *Crit Care Med*. 2009;**37**(12 Suppl):A472.
18. Chendrasekhar A, Colli J, Timberlake GA. Myoglobinuria incidence and the efficacy of bicarbonate after entrapment in motor vehicle accidents. [abstract]. *Chest*. 1996;**110**(4 Suppl):145S.
19. Brown CV, Rhee P, Chan L, Evans K, Demetriades D, Velmahos GC. Preventing renal failure in patients with rhabdomyolysis: do bicarbonate and mannitol make a difference? *J Trauma*. 2004;**56**(6):1191-6.
20. Homsi E, Barreiro MFFL, Orlando JMC, Higa EM. Prophylaxis of acute renal failure in patients with rhabdomyolysis. *Ren Fail*. 1997;**19**(2):283-8.
21. Kim HW, Kim S, Ohn JH, Kim N-H, Lee J, Kim ES, et al. Role of bicarbonate and volume therapy in the prevention of acute kidney injury in rhabdomyolysis: a retrospective propensity score-matched cohort study. *Kidney Res Clin Pract*. 2022;**41**(3):310.
22. Özgüç H, Kahveci N, Akköse S, Serdar Z, Balci V, Ocak Ö. Effects of different resuscitation fluids on tissue blood flow and oxidant injury in experimental rhabdomyolysis. *Crit Care Med*. 2005;**33**(11):2579-86.
23. Nielsen JS, Sally M, Mullins RJ, Slater M, Groat T, Gao X, et al. Bicarbonate

and mannitol treatment for traumatic rhabdomyolysis revisited. *Am J Surg*. 2017;**213**(1):73–9.
24. Tazmini K, Schreiner C, Bruserud S, Raastad T, Solberg EE. Exercise-induced rhabdomyolysis–a patient series. *Tidsskr Nor Laegeforen*. 2017;**137**(21).
25. Manspeaker S, Henderson K, Riddle D. Treatment of exertional rhabdomyolysis in athletes: a systematic review. *JBI Database System Rev Implement Rep*. 2016;**14**(6):117–47.
26. Somagutta MR, Pagad S, Sridharan S, Nanthakumaran S, Arnold AA, May V, et al. Role of bicarbonates and mannitol in rhabdomyolysis: a comprehensive review. *Cureus*. 2020;**12**(8): e9742.
27. Subashri M, Sujit S, Thirumalvalavan K, Poongodi A, Srinivasaprasad N, Fernando ME. Rhabdomyolysis-associated acute kidney injury. *Indian J Nephrol*. 2023;**33**(2):114–8.
28. Kim HW, Lee Y, Kim S. Bicarbonate May Not Be the Best Treatment for Rhabdomyolysis: A Retrospective Cohort Study: PO0072. *Journal of the American Society of Nephrology*. 2020;**31**(10S):81.
29. Kanderi N, Kirmse B, Regier DS, Chapman KA. LPIN1 rhabdomyolysis: a single site cohort description and treatment recommendations. *Mol Genet Metab Rep*. 2022;**30**:100844.
30. Ioannidis K, Papachristos A, Athanassa Z, Katsouda E, Skarlatinis I, Paskalis H. Safety and effectiveness of the combination acetazolamide and bicarbonates to induce alkaline diuresis in patients with rhabdomyolysis. *European Journal of Hospital Pharmacy*. 2015;**22**(6):328–32.
31. Garcia AF, Bayona JG, Puyana JC, Villa D, Ossa S, Martinez N, et al. Multivariate regression analysis of risk factors for acute kidney injury after traumatic rhabdomiolysis. *Journal of the American College of Surgeons*. 2016;**223**(4):e201.
32. Eneas JF, Schoenfeld PY, Humphreys MH. The effect of infusion of mannitol-sodium bicarbonate on the clinical course of myoglobinuria. *Arch Intern Med*. 1979;**139**(7):801–5.