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Systematic Review and Meta-Analysis

Aspartate Aminotransferase and Lactate Dehydrogenase in Evaluating the Risk of Rhabdomyolysis-Induced Acute Kidney Injury: A Systematic Review and Meta-analysis

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Abstract

Objective: This study aimed to investigate the diagnostic accuracy of serum levels of lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) in evaluating the risk of Acute Kidney Injury (AKI) following traumatic rhabdomyolysis.

Methods: A systematic review and meta-analysis were conducted by searching Medline, Embase, Scopus, and Web of Science for relevant studies up to June 2025, considering terms such as "Crush Syndrome," "Crush Injury," "Rhabdomyolysis," AND "Serum Glutamic Oxaloacetic Transaminase," "SGOT," or "Aspartate Transaminase." Studies that compared LDH or AST levels in traumatic rhabdomyolysis patients with and without AKI were included. The pooled effect size was evaluated using the standardized mean difference (SMD), and a 95% confidence interval (CI) was calculated. A random-effects model was employed to handle the heterogeneity. Subgroup analyses were conducted based on age group (adults and pediatrics). All analyses were performed using the statistical program STATA 17.0.

Results: For AST, the initial database search identified a total of 5,120 articles (2362 duplicates). Initially, 2,758 studies were screened by title and abstract, 52 articles were selected for full-text assessment, and finally, six articles were included in the quantitative analysis. In the case of LDH, the initial database search identified 4,044 articles (1471 duplicates). The initial 2,573 articles were screened by title and abstract, 49 articles were selected for full-text review, and finally, five studies were included in the quantitative analysis.

A total of seven studies involving 277 AKI and 2592 non-AKI patients were included in the meta-analysis. The pooled SMD for AST was 1.46 (95% CI: 0.79–2.13, I^2 = 88.02%) in adults and 0.80 (95% CI: 0.23–1.37, I^2 = 65.49%) in children. Similarly, the SMD for LDH was 2.16 (95% CI: 0.20–4.11, I^2 = 97.37%) in adults and 1.18 (95% CI: 0.70–1.67, I^2 = 32.94%) in children.

Conclusion: Current evidence suggests a significant association between elevated levels of AST and LDH and the incidence of AKI following traumatic rhabdomyolysis, with moderate and low levels of evidence, respectively. However, due to the limited number of studies, it was not possible to assess their effectiveness as a screening test.

Keywords: Meta-analysis, Aspartate aminotransferase, Lactate dehydrogenase, Rhabdomyolysis, Acute kidney injury

Introduction

Rhabdomyolysis is a pathological condition marked by the breakdown of skeletal muscle. It can result from various factors, including metabolic disorders, immobilization, genetic predisposition, trauma, burns, exercise, drug use, sepsis, surgical procedures, poisoning, and animal bites (1, 2). Earthquakes are among the most common causes of traumatic rhabdomyolysis. Being trapped under the rubble has been estimated to cause crush syndrome in 3% to 20% of all victims (3, 4). Rhabdomyolysis presentations range from asymptomatic states and isolated elevations in laboratory values to life-threatening electrolyte disturbances and multiple organ failure (5).

Acute kidney injury (AKI) is the most important complication of rhabdomyolysis (6-8). AKI is the second leading cause of death following a disaster, after direct trauma, and the most common cause of death in patients with rhabdomyolysis (9). The incidence of AKI has been reported to range from 15% to 81.4% in patients with rhabdomyolysis (10-12) and is independently associated with 19.2% to 59.0% increased mortality (11, 13). However, AKI can be prevented by early and consistent initiation of prophylactic intravenous hydration therapy (14-16).

In the aftermath of disasters like earthquakes, a large number of rhabdomyolysis cases may be encountered, and equipment shortages may exacerbate the situation (17). Given the challenging circumstances following disasters, administering extensive prophylactic hydration to all patients may not be feasible. Thus, prioritizing the identification of potentially effective factors of rhabdomyolysis-induced AKI and determining which patients require appropriate intravenous fluid therapy seems crucial. To prevent and detect AKI early on, only a small number of clinical prediction rules have been developed by analyzing clinical and laboratory factors across multiple studies.

While creatine phosphokinase (CK) has been shown to contribute to the development of AKI in most predictive models (18-20), there is scarce evidence regarding the predictive capacity of aspartate transaminase (AST) and lactate dehydrogenase (LDH). Some studies have identified a relationship between LDH or AST and the incidence of AKI (19), while other investigations have not found such an association (21).

This study focused on evaluating the levels of AST and LDH in the context of rhabdomyolysis. Typically, CPK, AST, and LDH are measured in cases of rhabdomyolysis. However, during mass disasters, access to comprehensive laboratory resources may be limited. Therefore, the objective of this study is to determine whether AST and LDH can be used as reliable alternatives to CPK. The study aims to assess the value of AST and LDH independently, without relying on CPK if feasible, or to omit their assessment if they prove to be inadequate substitutes.

Methods

The current systematic review and meta-analysis were conducted following the guidelines of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) statement (22). The protocol of the present study was not previously registered by the authors. The study selection process was summarized in a flow diagram according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses PRISMA 2020 guidelines.

The present study was designed to evaluate the predictive value of serum AST and LDH levels for the incidence of AKI in patients with traumatic rhabdomyolysis. The PICO framework for this study was defined as follows: The population (P) consisted of patients with traumatic rhabdomyolysis, the index test (I) was serum LDH or AST levels in the AKI patients, the comparison (C) was serum LDH or AST levels in the non-AKI group, and the outcome (O) of interest was the occurrence of AKI. The search strategy was designed to include only the population (P) and index test (I) in the search terms to reduce the possibility of missing relevant articles.

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences and the Directorate of Health, Rescue and Treatment of Police Headquarters (ethics code: IR.SBMU.TEB.POLICE.REC.1402.015).

In order to design a comprehensive search strategy, the keywords were derived from expert recommendations and from reviewing the titles and abstracts of relevant papers. Additionally, synonyms and equivalent terms were identified from the MeSH and Emtree databases.

Two independent search strategies were conducted to ensure comprehensive coverage of the literature. The first strategy utilized keywords related to traumatic rhabdomyolysis and aspartate aminotransferase (AST), including terms such as "Crush Syndrome," "Crush Injury," "Rhabdomyolysis," and "Serum Glutamic Oxaloacetic Transaminase," "SGOT," or "Aspartate Transaminase." The second search strategy focused on keywords related to rhabdomyolysis and Lactate Dehydrogenase (LDH), including terms such as "Crush Syndrome," "Crush Injury," "Rhabdomyolysis," and "Lactate Dehydrogenases" or "LDH." Detailed queries for each search strategy are presented in Supplementary Table 1 for the AST-related search and Supplementary Table 2 for the LDH-related search.

Using a combination of appropriate keywords, two separate authors searched four major electronic databases (Medline, EMBASE, Scopus, and Web of Science) from their inception until June 2025. There were no restrictions on publication date, geographic location, or language. A manual search of relevant studies' bibliographies and citation lists, as well as Google and Google Scholar, was conducted to identify additional appropriate publications and unpublished data. In cases where essential data could not be extracted from the published articles, the authors were approached to provide the necessary information. The process of article inclusion was continued until the final stage, where articles that were suitable for quantitative analysis were selected. Then, the results of the selection processes for both LDH and AST were combined, and the final set of studies was chosen from this merged list.

Table 1. Characteristics of the studies that have evaluated the predictive value of aspartate aminotransferase (AST) and lactate dehydrogenase (LDH)

First author, year	Location	Laboratory test assessed	Patients (*N*)		Age (years)	Male (%)	RM etiology	AKI definition	Timing* (days)	Study Design
			AKI +	AKI -						
Divine, 2020 (32)	United States	LDH	10	13	≥20	100	Exertional	RIFLE	1st to 5th	PCS
Hu, 2012 (20)	China	AST	42	59	23 [13.5–42]	47.5	Crush and trauma	Cr≥2 K>6 Oliguria	1st to 7th	RCS
Lim, 2018 (29)	South Korea	AST	14	25	14 (3 to 18)	71.8	Trauma and exertional	KDIGO	1st	RCS
Najafi, 2008 (19)	Iran	LDH & AST	94	1347	≥15	52	Crush and trauma	Cr≥1.6	1st to 3rd	RCS
Omrani, 2020 (30)	Iran	LDH & AST	10	360	39.24 ±20.3	41.4	Crush and trauma	Cr≥1.6	1st	RCS
Sanadgol, 2009 (21)	Iran	LDH & AST	8	7	<15	33.3	Crush and trauma	GFR<75% Oliguria	1st	PCS
Yoo, 2021 (31)	South Korea	LDH & AST	99	781	8.0 [4.0–14.0]	72	Trauma and exertional	KDIGO	1st	RCS

AKI: acute kidney injury, RM: rhabdomyolysis, Cr: serum creatinine (mg/dl), K: serum potassium (mEq/L), GFR: glomerular filtration rate, RIFLE: risk, injury, failure, loss of kidney function, and end-stage kidney disease; KDIGO: kidney disease improving global outcomes, PCS: prospective cohort study, RCS: retrospective cohort study. *: Timing refers to the time from the admission to the measurement of the AST or LDH

Table 2. Risk of bias assessment of the included studies based on QUADAS-2 tool

Study	Lab test	Risk of bias				Applicability			Overall
		Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard	
Najafi, 2008 (19)	AST	Low	Low	Low	Low	Low	Low	Low	Low
Najafi, 2008 (19)	LDH	Low	Low	Low	Low	Low	Low	Low	Low
Hu, 2012 (20)	AST	Low	Low	Low	Low	Low	Low	Unclear	Some concern
Sanadgol, 2009 (21)	AST	Low	Low	Low	Low	Low	Low	Low	Low
Sanadgol, 2009 (21)	LDH	Low	Low	Low	Low	Low	Low	Low	Low
Lim, 2018 (29)	AST	Low	Low	Low	Low	Low	Low	Low	Low
Omrani, 2020 (30)	AST	Low	Low	Low	Low	Low	Low	Low	Low
Omrani, 2020 (30)	LDH	Low	Low	Low	Low	Low	Low	Low	Low
Yoo, 2021 (31)	AST	Low	Low	Low	Low	High	Low	Low	Some concern
Yoo, 2021 (31)	LDH	Low	Low	Low	Low	High	Low	Low	Some concern
Divine, 2020 (32)	LDH	Low	Low	Low	Low	High	Low	Low	Some concern

The present study included studies that met the following inclusion criteria: a clear definition of rhabdomyolysis and AKI according to known diagnostic criteria, assessment of a variable or scoring framework for detecting rhabdomyolysis, studies primarily focused on patients with rhabdomyolysis caused by traumatic or exertional factors, measurement of serum AST or LDH levels until 7 days post-event or hospitalization but before the onset of AKI, comparison based on AST or LDH levels, Estimating occurrence of AKI based on creatinine (serum) level, glomerular filtration rate (GFR), and RIFLE criteria, and inclusion of a comparison group without AKI. All observational studies that examined the association between LDH or AST serum levels and the occurrence of AKI in patients with rhabdomyolysis were included.

The following were considered exclusion criteria in the present study: absence of a non-AKI comparison group, absence of AKI as an outcome, absence of reported data for LDH or AST, absence of rhabdomyolysis as the cause of AKI, absence of original data, absence of any valuable data, publication of study protocols, animal studies, editorials, letters to the editor, case reports, duplicate studies, and reviews.

Using EndNote version 20.0 software, initial search results were consolidated, and duplicates were deleted. The initial assessment of titles and abstracts of potentially relevant articles was carried out by two separate assessors (A.A. and M.Y.). The entire texts of the retrieved papers were reviewed, and studies that met the criteria were included. Data from the included studies were retrieved and entered into an Excel spreadsheet checklist. Any discrepancies in the selection process were resolved by a third reviewer (S.S.).

The data collected contained study features (such as the name of the first author, date, and country), methodology, patient demographics (age, sex, and rhabdomyolysis etiology), sample size, mean and standard deviation (SD) of LDH or AST serum levels, screening efficiency of LDH or AST in detecting AKI, including true positive (TP), true negative (TN), false positive (FP), and false negative (FN), odds ratio (OR), 95% confidence interval (95% CI), and the number of AKI and non-AKI patients.

If multiple studies were reporting the same data, the study with the largest sample size was included. To identify studies that used the same registry, the name, date, location, and sample characteristics were compared. In cases where data extraction from an article was not possible, the corresponding author was contacted for additional information. If the mean and standard deviation of AST or LDH were not reported, the corresponding author was asked to provide other measures such as median, inter-percentile range, and range. Whenever the contributors did not answer, the mean, standard deviation, and the number of participants (TP, TN, FP, and FN) were estimated using appropriate statistical approaches (23, 24). If the results were presented graphically, the PlotDigitizer online tool was used to extract the necessary data.

The quality of the selected papers' methods was evaluated using the Quality Assessment of Diagnostic Accuracy Studies Version 2 (QUADAS-2) technique (25). This instrument includes the risk of bias and applicability, which were independently assessed and reported by two researchers for each article. The QUADAS-2 instructions categorize the results into three levels: low risk, high risk, and unclear.

The two reviewers exhibited a desirable level of inter-rater reliability in their qualitative assessment of the studies, achieving a 95% agreement rate. A third reviewer was consulted in case of disagreement.

The grading of the Recommendations, Assessment, Development, and Evaluations (GRADE) framework was used to determine the level of evidence for our primary outcome of interest in the included articles (26). The GRADE framework consists of a subjective assessment of five domains: risk of bias, imprecision, inconsistency, indirectness, and publication bias. To identify publication bias, the Egger's test was employed (27).

All analyses were performed using the statistical program STATA 17.0. I^2 was used to quantitatively assess heterogeneity between results based on the Higgins classification (28). Hedges' *g* was utilized to compute only the standardized mean difference, and a pooled effect size with a 95% confidence interval was presented due to the inadequacy of the data, although the data were reported in three different forms: mean and standard deviation, odds ratio with 95% confidence intervals, and diagnostic accuracy. Forest plots were used to visualize the results.

To minimize heterogeneity in the current study, subgroups were formed, and subsequent subgroup analyses were conducted based on age, with the groups being divided into adults and children. Because of the small number of included studies, it was not possible to further stratify based on the etiology of rhabdomyolysis, study methodology, the duration between the occurrence of the event (or admission) and sample collection, and how AKI was defined. As a result of considerable heterogeneity between the included studies, the meta-analysis was performed based on the random effect model. Finally, all of the articles were combined into a single meta-analysis (*p*-values less than 0.05 were deemed significant).

Results

For the AST component of the review, the initial database search identified a total of 5120 articles. After removing duplicates, 2758 studies were screened by title and abstract for potential inclusion. Among these, 52 articles were selected for full-text assessment, with 26 articles fulfilling the inclusion criteria. However, 20 studies were subsequently excluded according to the exclusion criteria. Ultimately, six studies (19-21, 29-31) were included in the quantitative analysis for AST.

In the case of LDH, the initial database search identified 4044 articles, which were then reduced to 2573 studies after duplicate removal. Subsequently, 49 articles were selected for full-text review, of which 21 studies met the inclusion criteria. However, 16 studies were subsequently excluded due to the exclusion criteria. Finally, five studies (19, 21, 30-32) were included in the quantitative analysis for LDH.

The study selection process is summarized in a flow diagram according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses PRISMA guidelines, as shown in Figure 1.

Table 1 summarizes the characteristics of the articles included in this systematic review and meta-analysis. Out of the seven unique studies included, four studies have reported both mean AST and mean LDH levels in participants with AKI and without AKI (19, 21, 30, 31). One study only reported LDH levels, and two studies only reported AST levels. One study presented its findings as odds ratios (OR), and two studies presented sensitivity, specificity, and receiver operating characteristic (ROC) curves. As meta-analyses on the odds ratios and diagnostic accuracy were not applicable, the meta-analyses were only performed on the standardized mean difference.

The included studies had varying designs, with five retrospective cohort studies and two prospective cohort studies. The total number of participants in the AKI group was 277, while in the non-AKI group, it was 2592. All studies measured the levels of AST or LDH before the occurrence of AKI, with the timing ranging from the first day to the 7th day after the rhabdomyolysis. Subgroup analyses were performed based on the age group of participants. Four studies included only adult participants (19, 20, 30, 32), while three studies included only pediatric participants (21, 29, 31). Furthermore, the etiology of

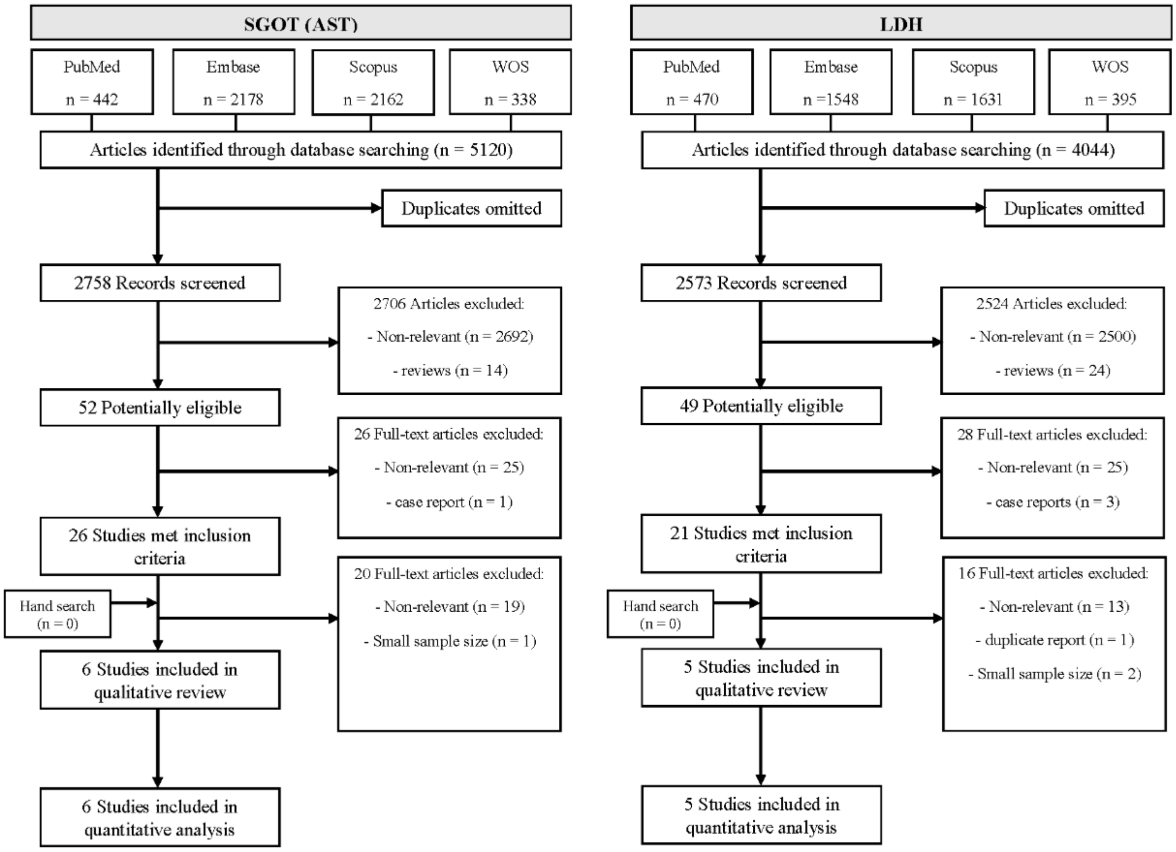

Figure 1. PRISMA flowchart of study selection for aspartate aminotransferase (AST) and lactate dehydrogenase (LDH).

rhabdomyolysis in each study and the definition of AKI are shown in Table 1.

Six studies comparing mean serum AST levels in AKI and non-AKI patients were found. In total, these studies included 267 AKI and 2579 non-AKI cases. On average, 56.8% of the patients were male. A substantial relationship was found between serum AST levels and AKI incidence in rhabdomyolysis based on pooled standardized mean differences (SMD = 1.13, 95% CI: 0.64–1.63, p-value < 0.001), as depicted in Figure 2. Subgroup analysis based on age groups was also conducted, as illustrated in Figure 2. The difference in AST levels between adults (SMD = 1.46, 95% CI: 0.79–2.13, p-value < 0.001) was higher compared to pediatric patients (SMD = 0.80, 95% CI: 0.23–1.37, p-value = 0.005), which were both statistically significant.

Five studies comparing mean serum LDH levels in AKI and non-AKI patients were found, with a total of 221 AKI and 2508 non-AKI cases included. On average, 57.3% of the patients were male. A strong association was found between LDH levels and AKI incidence in rhabdomyolysis based on pooled standardized mean differences (SMD = 1.71, 95% CI: 0.48–2.94, p-value = 0.006), as shown in Figure 3. Age-based subgroup analysis was performed, as demonstrated in Figure 3. The standardized mean difference in LDH levels was higher in adults (SMD = 2.16, 95% CI: 0.20–4.11, p-value = 0.030) compared to pediatric patients (SMD = 1.18, 95% CI: 0.70–1.67, p-value < 0.001). Both differences were statistically significant.

All studies in both AST and LDH components were judged to have a low risk of bias in all four domains: patient selection, index test, reference standard, and flow and timing. This suggests that the included studies were of good quality and provide reliable evidence for the analysis. The results of the risk of bias assessment are summarized in Table 2, which presents the QUADAS-2 ratings for each included study. Based on the applicability assessment using the same tool, two studies were rated as having high concerns for applicability in the patient selection domain. Additionally, one study was rated as unclear in the reference standard domain. Due to the small number of included studies, we could not afford to conduct subgroup analysis based on the risk of the studies. However, based on the authors' judgment, the overall risk of bias in the included articles was low.

As shown in Figure 4, the funnel plot analysis revealed an asymmetrical distribution of the included studies, indicating that studies reporting no significant difference in the mean difference between the AKI and non-AKI groups were overrepresented in this meta-analysis compared to studies reporting a significant difference. However, the Egger's test did not detect any significant publication bias in either of the analyses for both AST and LDH components (AST: p-value = 0.436; LDH:

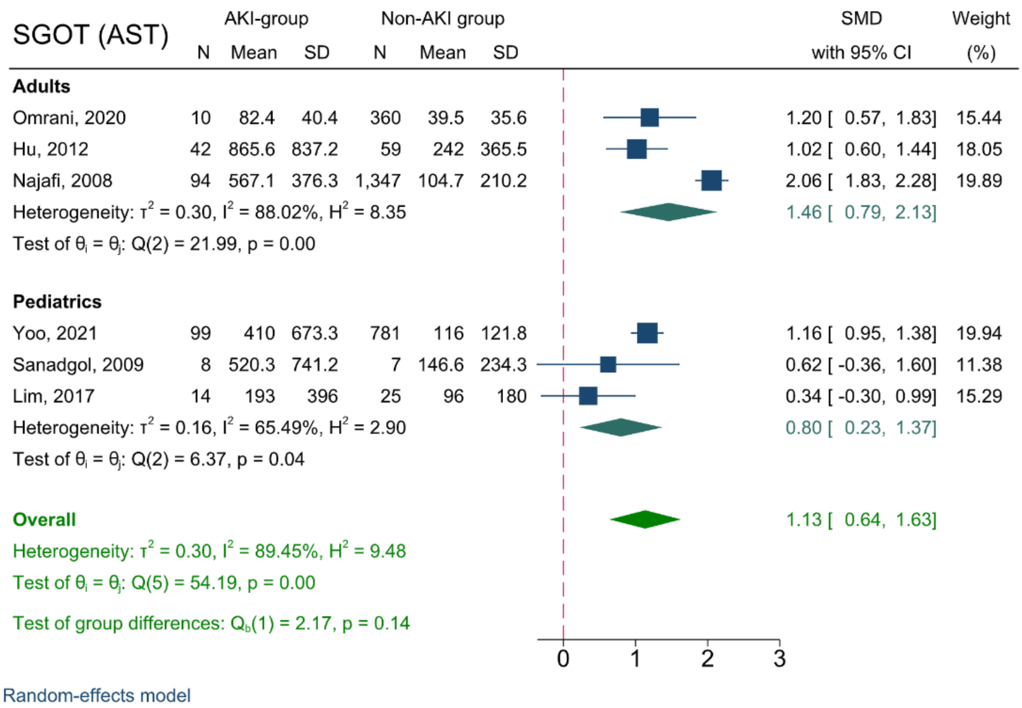

Figure 2. Forest plot showing the standardized mean difference of aspartate aminotransferase (AST) in the rhabdomyolysis patients with and without acute kidney injury

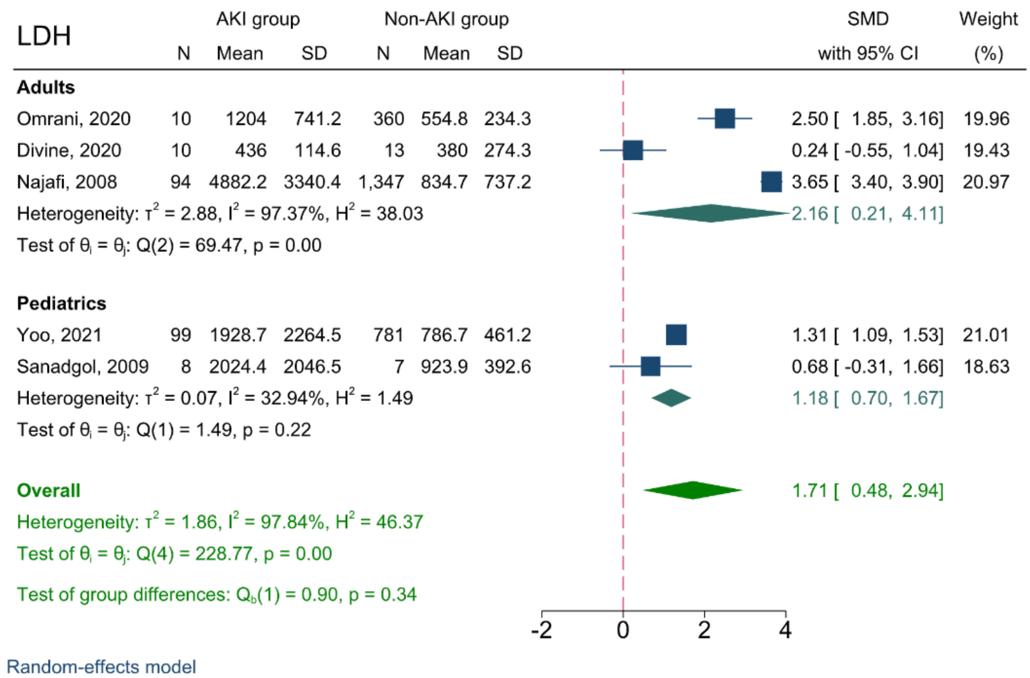

Figure 3. Forest plot showing the standardized mean difference of lactate dehydrogenase (LDH) in the rhabdomyolysis patients with and without acute kidney injury

p-value = 0.660).

In evaluating the heterogeneity between the studies, a high degree of diversity was observed. For the AST component, I^2 ranged from 65.49% in the pediatric subgroup to 88.02% in the adults (all *p*-values < 0.05). Similarly, for the LDH component, I^2 ranged from 32.94% in the pediatric subgroup to 97.37% in the adults (all *p*-values < 0.05). As the number of included studies was limited, subgroup analysis was not feasible to identify the sources of heterogeneity.

The initial GRADE rating for the included studies was "low" due to their observational nature. Regarding AST, the score was downgraded by one level due to the high degree of heterogeneity among the included studies.

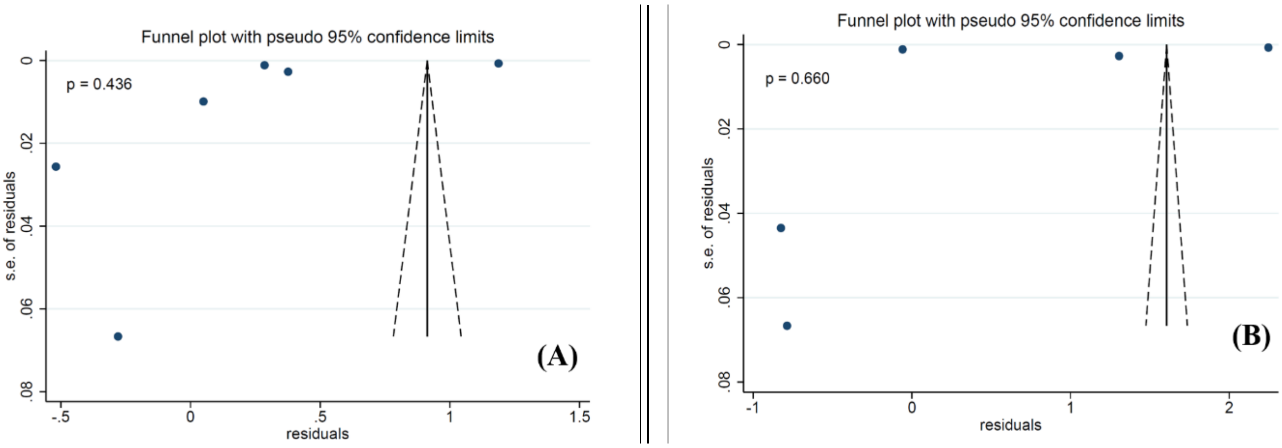

Figure 4. **(A)** funnel plot of studies evaluating the predictive value of AST in the rhabdomyolysis-induced acute kidney injury. **(B)** funnel plot of studies evaluating the predictive value of LDH in the rhabdomyolysis-induced acute kidney injury

However, due to the presence of publication bias in favor of non-significant results (as shown by the funnel plots) and the large effect size, the quality of evidence was upgraded by two levels, resulting in a final rating of "moderate."

As for LDH, the score was downgraded by two levels due to the high degree of heterogeneity among the included studies and imprecision in the results. Nonetheless, due to the presence of publication bias in favor of non-significant results and the large effect size, the quality of evidence was upgraded by two levels. Thus, the final certainty of evidence for LDH is considered "low" (Supplementary Table 1).

Discussion

This meta-analysis was the first study to explore the predictive value of AST and LDH for the risk of acute kidney injury following rhabdomyolysis. The results of this study showed a significant association between higher levels of both AST and LDH and the development of AKI in rhabdomyolysis patients. The Standardized Mean Differences (SMD) observed in the study were greater in adult patients compared to pediatric patients, suggesting a stronger association between elevated levels of AST and LDH and the risk of AKI in adults.

Prior research on rhabdomyolysis has focused on identifying biomarkers that can help predict the likelihood of developing AKI. Some of the most commonly studied biomarkers in this context include creatine phosphokinase (16), urine dipstick test (33), blood myoglobin (34), and urine myoglobin (35). In a previous systematic review and meta-analysis, we examined the potential of CPK as a prognostic biomarker for rhabdomyolysis-induced AKI. The study's findings revealed a strong association between the mean CPK level and the risk of developing AKI (SMD = 1.34, 95% CI: 1.25–1.42; p-value < 0.001), an association more pronounced in cases of crush injury (18).

Despite the investigation of biomarkers for predicting AKI in patients with rhabdomyolysis, the predictive capacity of AST and LDH has remained a controversial topic. Notably, these biomarkers have been assessed as adjunct factors to primary markers such as CPK or myoglobin, rather than being evaluated as the main biomarkers. Rhabdomyolysis is a condition that can arise from a range of causes, such as trauma, exertion, infections, drugs, and neurologic disorders (1). In the case of rhabdomyolysis triggered by infections or drugs, levels of AST and LDH may be affected by reasons other than muscle injury, such as liver injury. Thus, for this study, we only included research that focused solely on traumatic or exertional rhabdomyolysis, where these biomarkers were less likely to be influenced by non-muscular factors. Specifically, we included studies where all or the majority of participants had traumatic or exertional rhabdomyolysis.

One of the strengths of this study is that we focused exclusively on traumatic or exertional rhabdomyolysis, which minimized the potential sources of heterogeneity that can arise from including cases with diverse etiologies. This approach contrasts with our previous study, where the inclusion of patients with non-traumatic etiologies contributed to the observed heterogeneity (18). Another strength of this study was the inclusion of patients with rhabdomyolysis resulting from earthquakes, who experienced both high and low-intensity traumatic injuries. As a result, the findings of this study hold greater generalizability to mass disaster scenarios compared to previous studies. Additionally, this study only included confirmed cases of AKI.

The present study had several limitations. Firstly, a high degree of heterogeneity was observed among the included studies, which made it challenging to draw definitive conclusions. Since the number of studies included in this analysis was limited, conducting subgroup analyses to identify the sources of heterogeneity was not possible. Despite attempts to standardize the methodology and control for confounding factors across studies, complete standardization is often not achievable even in ideal circumstances. However, the authors suggest that some potential sources of heterogeneity in the results are related to: 1) variations in the definition of AKI used across studies, 2) differences in study design, and 3) variability in the timing of serum AST and LDH measurements.

Additionally, while the current study only included articles with populations suffering from traumatic and exertional-induced rhabdomyolysis, differences in the severity of rhabdomyolysis among the etiologies included may also have contributed to the observed heterogeneity. Another important limitation of this study is related to the nature of meta-analyses in observational studies. Observational studies are inherently limited in their ability to control for all potential confounding factors and, therefore, cannot establish causal relationships. A further limitation of this study was the scarcity of studies that reported odds ratios and diagnostic accuracy measures. As a result, the meta-analyses were performed only on standardized mean differences. The limited number of relevant studies on this topic may have contributed to this limitation. Therefore, future research should address this issue by conducting more comprehensive studies in order to provide a more conclusive understanding of the prognostic value of AST and LDH in predicting rhabdomyolysis-induced AKI. Additionally, further research is needed to determine accurate cut-off values for these biomarkers.

In this study, the standardized mean differences of AST were 1.46 in adults and 0.80 in pediatrics, and for LDH were 2.16 in adults and 1.18 in pediatrics, indicating a strong association with the occurrence of AKI following rhabdomyolysis. However, given the limitations encountered in this study, relying solely on AST or LDH levels for triage and screening of patients may not be sufficiently accurate. It is recommended to interpret these measures in conjunction with other potential risk factors, including CPK, urine dipstick, and uric acid, to improve the accuracy of diagnosis (18, 35).

Conclusion

In conclusion, the present meta-analysis revealed a significant association between elevated levels of AST and LDH and the occurrence of AKI following rhabdomyolysis, with moderate and low levels of evidence, respectively. However, due to the limited number of studies available and the observed heterogeneity, the screening performance characteristics of AST and LDH could not be evaluated.

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Authors' Contribution

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Validation: Mahmoud Yousefifard, Saeed Safari.
Visualization: Mahmoud Yousefifard, Saeed Safari.
Writing–original draft: Mahmoud Yousefifard, Saeed Safari.

Competing Interests

None.

Ethical Approval

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences and the Directorate of Health, Rescue and Treatment of Police Headquarters (ethics code: IR.SBMU.TEB.POLICE.REC.1402.015).

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Supplementary Files

Supplementary file 1 contains Table S1.

References

1. Torres PA, Helmstetter JA, Kaye AM, Kaye AD. Rhabdomyolysis: pathogenesis, diagnosis, and treatment. Ochsner J. 2015;15(1):58-69.
2. McMahon GM, Zeng X, Waikar SS. A risk prediction score for kidney failure or mortality in rhabdomyolysis. JAMA Intern Med. 2013;173(19):1821-8. doi: 10.1001/jamainternmed.2013.9774.
3. Sever MS, Lameire N, Van Biesen W, Vanholder R. Disaster nephrology: a new concept for an old problem. Clin Kidney J. 2015;8(3):300-9. doi: 10.1093/ckj/sfv024.
4. Bartal C, Zeller L, Miskin I, Sebbag G, Karp E, Grossman A, et al. Crush syndrome: saving more lives in disasters: lessons learned from the early-response phase in Haiti. Arch Intern Med. 2011;171(7):694-6. doi: 10.1001/archinternmed.2011.122.
5. Chatzizisis YS, Misirli G, Hatzitolios AI, Giannoglou GD. The syndrome of rhabdomyolysis: complications and treatment. Eur J Intern Med. 2008;19(8):568-74. doi: 10.1016/j.ejim.2007.06.037.
6. Li PK, Burdmann EA, Mehta RL. Acute kidney injury: global health alert. Arab J Nephrol Transplant. 2013;6(2):75-81.
7. Najafi I, Safari S, Sharifi A, Sanadgol H, Hosseini M, Rashid-Farokhi F, et al. Practical strategies to reduce morbidity and mortality of natural catastrophes: a retrospective study based on Bam earthquake experience. Arch Iran Med. 2009;12(4):347-52.
8. Sever MS, Erek E, Vanholder R, Ozener C, Yavuz M, Kayacan SM, et al. Lessons learned from the Marmara disaster: time period under the rubble. Crit Care Med. 2002;30(11):2443-9. doi: 10.1097/00003246-200211000-00007.
9. Sever MS, Vanholder R, Lameire N. Management of crush-related injuries after disasters. N Engl J Med. 2006;354(10):1052-63. doi: 10.1056/NEJMra054329.
10. Grunau BE, Pourvali R, Wiens MO, Levin A, Li J, Grafstein E,

et al. Characteristics and thirty-day outcomes of emergency department patients with elevated creatine kinase. Acad Emerg Med. 2014;21(6):631-6. doi: 10.1111/acem.12385.
11. Rodríguez E, Soler MJ, Rap O, Barrios C, Orfila MA, Pascual J. Risk factors for acute kidney injury in severe rhabdomyolysis. PLoS One. 2013;8(12):e82992. doi: 10.1371/journal.pone.0082992.
12. Candela N, Silva S, Georges B, Cartery C, Robert T, Moussi-Frances J, et al. Short- and long-term renal outcomes following severe rhabdomyolysis: a French multicenter retrospective study of 387 patients. Ann Intensive Care. 2020;10(1):27. doi: 10.1186/s13613-020-0645-1.
13. Harrois A, Soyer B, Gauss T, Hamada S, Raux M, Duranteau J, et al. Prevalence and risk factors for acute kidney injury among trauma patients: a multicenter cohort study. Crit Care. 2018;22(1):344. doi: 10.1186/s13054-018-2265-9.
14. Gunal AI, Celiker H, Dogukan A, Ozalp G, Kirciman E, Simsekli H, et al. Early and vigorous fluid resuscitation prevents acute renal failure in the crush victims of catastrophic earthquakes. J Am Soc Nephrol. 2004;15(7):1862-7. doi: 10.1097/01.asn.0000129336.09976.73.
15. Better OS, Stein JH. Early management of shock and prophylaxis of acute renal failure in traumatic rhabdomyolysis. N Engl J Med. 1990;322(12):825-9. doi: 10.1056/nejm199003223221207.
16. Najafi I, Safari S, Hosseini M, Sanadgol H, Sharifi A, Rashid Farokhi F, et al. Prophylactic fluid therapy in crushed victims of Bam earthquake. Am J Emerg Med. 2011;29(7):738-42. doi: 10.1016/j.ajem.2010.02.018.
17. Asadi H, Bajoulvand R, Garavand A, Mohammadi R, Mirshekar-Jahangiri L. A review of studies conducted to evaluate the preparedness of medical centers against the potential risks of natural disasters in Iran. J Police Med. 2022;11(1):e18. doi: 10.30505/11.1.17.
18. Safari S, Yousefifard M, Hashemi B, Baratloo A, Forouzanfar MM, Rahmati F, et al. The value of serum creatine kinase in predicting the risk of rhabdomyolysis-induced acute kidney injury: a systematic review and meta-analysis. Clin Exp Nephrol. 2016;20(2):153-61. doi: 10.1007/s10157-015-1204-1.
19. Najafi I, Van Biesen W, Sharifi A, Hoseini M, Rashid Farokhi F, Sanadgol H, et al. Early detection of patients at high risk for acute kidney injury during disasters: development of a scoring system based on the Bam earthquake experience. J Nephrol. 2008;21(5):776-82.
20. Hu Z, Zeng X, Fu P, Luo Z, Tu Y, Liang J, et al. Predictive factors for acute renal failure in crush injuries in the Sichuan earthquake. Injury. 2012;43(5):613-8. doi: 10.1016/j.injury.2010.08.025.
21. Sanadgol H, Najafi I, Rajabi Vahid M, Hosseini M, Ghafari A. Fluid therapy in pediatric victims of the 2003 Bam, Iran earthquake. Prehosp Disaster Med. 2009;24(5):448-52. doi: 10.1017/s1049023x00007305.
22. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. JAMA. 2000;283(15):2008-12. doi: 10.1001/jama.283.15.2008.
23. Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0. The Cochrane Collaboration; 2011.
24. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005;5:13. doi: 10.1186/1471-2288-5-13.
25. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529-36. doi: 10.7326/0003-4819-155-8-201110180-00009.
26. Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011;64(4):380-2. doi: 10.1016/j.jclinepi.2010.09.011.
27. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629-34. doi: 10.1136/bmj.315.7109.629.
28. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-60. doi: 10.1136/bmj.327.7414.557.
29. Lim YS, Cho H, Lee ST, Lee Y. Acute kidney injury in pediatric patients with rhabdomyolysis. Korean J Pediatr. 2018;61(3):95-100. doi: 10.3345/kjp.2018.61.3.95.
30. 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. doi: 10.1016/j.ajem.2020.01.043.
31. Yoo S, Cho MH, Baek HS, Song JY, Lee HS, Yang EM, et al. Characteristics of pediatric rhabdomyolysis and the associated risk factors for acute kidney injury: a retrospective multicenter study in Korea. Kidney Res Clin Pract. 2021;40(4):673-86. doi: 10.23876/j.krcp.21.051.
32. Divine JG, Clark JF, Colosimo AJ, Detherage JP 3rd, Donaworth MA, Hasselfeld KA, et al. American football players in preseason training at risk of acute kidney injury without signs of rhabdomyolysis. Clin J Sport Med. 2020;30(6):556-61. doi: 10.1097/jsm.0000000000000652.
33. Alavi-Moghaddam M, Safari S, Najafi I, Hosseini M. Accuracy of urine dipstick in the detection of patients at risk for crush-induced rhabdomyolysis and acute kidney injury. Eur J Emerg Med. 2012;19(5):329-32. doi: 10.1097/MEJ.0b013e32834dd2ef.
34. Kasaoka S, Todani M, Kaneko T, Kawamura Y, Oda Y, Tsuruta R, et al. Peak value of blood myoglobin predicts acute renal failure induced by rhabdomyolysis. J Crit Care. 2010;25(4):601-4. doi: 10.1016/j.jcrc.2010.04.002.
35. Rodríguez-Capote K, Balion CM, Hill SA, Cleve R, Yang L, El Sharif A. Utility of urine myoglobin for the prediction of acute renal failure in patients with suspected rhabdomyolysis: a systematic review. Clin Chem. 2009;55(12):2190-7. doi: 10.1373/clinchem.2009.128546.