TPM Vol. 32, No. S1, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

ROLE OF N-ACETYL CYSTEINE IN RODENTICIDE POISONING - A SYSTEMATIC REVIEW AND META-ANALYSIS

SORNAVALLI VALLIAPPAN[1], PONAMBALAGANAPATHI NADAR[2], SAI SINDHURI MARUVADA[3], SUBASH MOHAN THULASI[4], GAUTHAM PALLAMPARTHY[5], SHRUTHI MANOHARAN[6], DR. S. RAGHAVENDRA JAYESH[7]

[1]DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU, INDIA
[2]DEPARTMENT OF GENERAL MEDICINE, MADHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU, INDIA
[3]DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU, INDIA
[4]DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU, INDIA
[5]DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU, INDIA
[6]DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU, INDIA
[7]PROFESSOR & DIRECTOR OF PG STUDIES, DEPARTMENT OF PROSTHODONTICS AND CROWN & BRIDGE, SREE BALAJI DENTAL COLLEGE & HOSPITAL, CHENNAI, INDIA
CORRESPONDING AUTHOR: SORNAVALLI VALLIAPPAN
DEPARTMENT OF GENERAL MEDICINE, SAVEETHA MEDICAL COLLEGE AND HOSPITAL, CHENNAI, TAMILNADU, INDIA

Abstract

Background: Rodenticide poisoning poses significant health risks, often requiring effective and timely intervention. N-Acetyl cysteine (NAC), known for its antioxidant and detoxifying properties, has been widely used as an antidote for various poisonings, but its efficacy and safety in the context of rodenticide exposure have not been comprehensively analyzed.

Objectives: To evaluate the efficacy and safety of NAC in the treatment of rodenticide poisoning.

Materials and Methods: Relevant studies were identified through a systematic search of databases including PubMed, Web of Science, and Scopus up to December 2023. This systematic review was conducted from January to June 2024. Studies that met the inclusion criteria provided data on mortality, recovery rates, and adverse events, which were analyzed to calculate pooled effect sizes and confidence intervals.

Results: The pooled meta-analysis indicated that NAC administration resulted in an overall 49% reduction in mortality odds (OR: 0.51, 95% CI: 0.45–0.57), reinforcing the therapeutic benefit of NAC. This beneficial effect was observed across various rodenticides, including aluminum phosphide, zinc phosphide, and other unspecified rodenticides.

Conclusions: N-Acetyl cysteine is effective and safe in treating rodenticide poisoning, significantly reducing mortality and improving recovery outcomes. These findings support the broader use of NAC in clinical settings where rodenticide exposure is confirmed.

Keywords: N-Acetyl cysteine, Rodenticide poisoning, Rat killer

INTRODUCTION

Rodenticide poisoning represents a significant and often underestimated public health concern globally. Among the various management strategies for this condition, the use of N-Acetyl cysteine (NAC) has garnered attention due to its potential role in counteracting the toxic effects of rodenticides, especially those that disrupt oxidative balance within the body [1]. Rodenticides are chemicals designed to kill rodents, primarily rats and mice, which pose risks to agriculture, food storage, and public health. There are several types of rodenticides, but the most common can be categorized into anticoagulants and non-anticoagulant rodenticides [2]. Anticoagulant rodenticides inhibit vitamin K epoxide reductase, a critical enzyme in the synthesis of clotting factors, leading to uncontrolled bleeding and eventually death in rodents. Conversely, non-anticoagulant rodenticides, which include metal phosphides (releasing phosphine gas) and bromethalin (a neurotoxin), act through different mechanisms, such as causing oxidative stress and bioenergetic disruptions in cells [3].

The incidence of rodenticide poisoning in humans varies geographically, with higher rates often reported in areas where these substances are used extensively in agricultural or urban settings [4]. Accidental ingestions, suicidal attempts, and occupational exposures are common routes of human poisoning. The clinical manifestations of rodenticide poisoning depend on the type of rodenticide involved but can range from acute bleeding and coagulopathy (in cases of anticoagulant rodenticides) to severe metabolic acidosis and neurological symptoms (as seen with phosphides and bromethalin) [5].

The management of rodenticide poisoning is challenging and depends on the specific type involved. For anticoagulant rodenticides, treatment typically involves the administration of vitamin K1. However, there is no specific antidote for many non-anticoagulant rodenticides, which is where N-Acetyl cysteine might play a role. NAC is primarily known as a precursor to glutathione, the body's most abundant antioxidant, and has been used effectively in conditions characterized by oxidative stress and acute liver toxicity, such as acetaminophen overdose [6]. The potential therapeutic effects of NAC in rodenticide poisoning stem from its ability to replenish intracellular glutathione levels, thereby helping to mitigate oxidative damage to cells and tissues [7]. This mechanism suggests that NAC could be particularly useful in cases of poisoning with phosphine and bromethalin, where oxidative stress is a significant pathophysiological component. However, the evidence supporting the use of NAC in rodenticide poisoning is varied and derives from a mix of animal studies, small clinical trials, and anecdotal reports [8-10]. Thus, the aim of this study was to evaluate the efficacy and safety of N-Acetyl cysteine in the management of rodenticide poisoning through a systematic review and meta-analysis. The objectives were to systematically review the literature on the use of N-Acetyl cysteine in rodenticide poisoning and to perform a meta-analysis of the outcomes related to efficacy and safety of N-Acetyl cysteine in treating rodenticide poisoning.

MATERIAL AND METHODOLOGY

Protocol:

This systematic review was conducted following a pre-established protocol and is reported according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta Analyses) guidelines.

The PICOS criteria used for this systematic review were as follows:

- The Population included patients of any age or gender diagnosed with rodenticide poisoning, encompassing exposures to aluminum phosphide, zinc phosphide, bromethalin, or unspecified rodenticides.
- The Intervention was the administration of N-Acetyl cysteine (NAC) as part of the therapeutic regimen.
- The Comparison group, where available, consisted of patients who received standard care without NAC. However, it is important to note that several included studies were observational and lacked prospective control groups, relying instead on retrospective or historical comparisons, which may introduce selection bias.
- The Outcomes assessed included mortality reduction as the primary outcome, and secondary outcomes such as recovery rates, duration of hospital stay, and the incidence of adverse events attributed to NAC.

Eligibility criteria

Articles that reported on the usage of N-Acetyl cysteine in rodenticide poisoning were considered for inclusion. Eligible study designs included peer-reviewed research articles, conference papers, and case reports. Editorials, viewpoints, and animal or in vitro studies were excluded, unless they contributed significantly to the research question.

Search Strategy
Relevant studies were identified through electronic searches of PubMed, Scopus, Web of Science and Google Scholar. A snowballing method, searching the bibliographies of retrieved articles, was also applied to identify potentially relevant studies. Search terms included specific keywords and MeSH terms such as "N-Acetyl cysteine" and "rodenticide poisoning". A Boolean search strategy was utilized to combine these terms effectively across selected databases. The search was conducted for articles published till December 2023, with no language restrictions. Grey literature and unpublished studies were excluded to maintain the quality and verifiability of data. There was no focus on a specific geographic location and included research conducted globally.

Study Duration
The review process and meta-analysis were conducted over a period of six months, from January to June 2024.

Study selection
Two reviewersinitially screened the titles and abstracts of all retrieved records to identify duplicates. Full-text versions of potentially relevant studies were then reviewed independently to determine their eligibility for inclusion. Any discrepancies between the reviewers were resolved through discussion and consensus. In cases of duplicate data from the same patient population, the information was consolidated to ensure complete and accurate data.

Data extraction
The following data were extracted from the selected studies: study details (title, authors, publication date, publication type, study location, and sample size), characteristics of the population, and any correlations with N-Acetyl Cysteine usage in Rodenticide poisoning. Two authors independently extracted the data, and any discrepancies were resolved by a third author, who also checked for data duplication. Two authors assessed the quality of the studies, along with efficacy and outcomes.
Risk of Bias and overall quality were assessed using tools appropriate to study design.
Systematic reviews were evaluated with AMSTAR 2 (A Measurement Tool to Assess systematic Reviews), which rates methodological quality as high, moderate, low, or critically low [17]. Observational studies were assessed using the Newcastle–Ottawa Scale (NOS) based on selection, comparability, and outcome; scores of 7–9 indicated high quality, 5–6 moderate, and <5 low quality [18]. Case report was appraised with the Joanna Briggs Institute (JBI) checklist, rating risk of bias as low, moderate, or high [19]. Two reviewers independently assessed quality of all studies, resolving discrepancies by consensus, findings have been given in Table 1.
The final manuscript was checked by three authors.

RESULTS

Identification of Relevant Study Data
A total of 6 full-text publications were assessed for eligible content. They consistedof 2 systematic reviews, 2 retrospective observational studies, 1 prospective observational study and 1 case reportwas included. The PRISMA flow diagram for the review has been elaborated in Figure 1.

Statistical Methods
For the meta-analysis, Comprehensive Meta-Analysis software was utilized. This software facilitated the calculation of pooled effect sizes, which were expressed as odds ratios for dichotomous outcomes and mean differences for continuous outcomes, each with 95% confidence intervals. Heterogeneity was quantitatively assessed using the I^2 and was found to be greater than 50% indicated substantial heterogeneity, necessitating a random-effects model.
Publication bias was evaluated through visual inspection of funnel plots, which helped detect asymmetry in meta-analysis results potentially caused by unpublished negative studies.

Observation and Results:
The summarized studies presented in Table 1 collectively evaluate the effectiveness and safety of N-Acetyl Cysteine (NAC) in treating patients with various forms of rodenticide and related poisonings.
The evidence consistently supports the clinical benefit of NAC administration, highlighting its significant impact in reducing mortality rates across diverse clinical settings. Notably, systematic reviews and meta-analyses by Rashid et al. [14] and Sobh et al. [12] demonstrate statistically significant reductions in mortality (OR=0.53 and RR=0.70,

respectively), reinforcing the therapeutic efficacy of NAC. Prospective observational evidence from Bhat et al. [11] reports an impressive survival rate improvement to 91%. Retrospective observational studies by Mark et al. [15] and Padmavathi et al. [16] further corroborate these findings, demonstrating significant mortality reductions of approximately 52% and 20%, respectively, albeit with limitations due to their retrospective nature. Additionally, case reports by Oghabian et al. [13] provide supportive anecdotal evidence of hepatoprotective benefits without reported adverse effects. Collectively, safety outcomes were consistently favorable, with minimal reported adverse reactions, primarily mild gastrointestinal disturbances. Despite inherent methodological limitations such as small sample sizes, heterogeneity, and observational study designs, the collective evidence strongly indicates NAC as a safe and effective intervention in rodenticide poisoning scenarios.

Risk of bias analysis:
The included observational studies have been evaluated with the Newcastle-Ottawa scale and the results are tabulated in table 2.Systematic Reviews were assessed using AMSTAR2 tool with the results tabulated in Table 3.Case report was assessed using the Johanna-Briggs Institute checklist and the results have been tabulated in Table 4.

Meta-Analysis:
Five studies were included for meta analysis [11-12, 14-16]. Oghabian et al has been excluded as it consists of case reports [13].
The funnel plot in Figure 2 visually assesses potential publication bias and precision among the included studies evaluating N-Acetyl Cysteine (NAC) for rodenticide poisoning.No significant evidence of publication bias was noted. The distribution of studies is relatively symmetrical around the pooled log odds ratio, and studies with smaller standard errors (greater precision) cluster closely around the overall effect estimate. Although a few studies with higher standard errors appear dispersed, namely Padmavathi et al [16] and Sobh et al [12], overall symmetry suggests that the observed beneficial effects of NAC are likely robust and not influenced by significant publication bias.

The forest plot in Figure 3 clearly illustrates the efficacy of N-Acetyl Cysteine (NAC) in reducing mortality associated with rodenticide and related poisonings.

Individual study results, represented by log odds ratios and their respective confidence intervals, consistently favour NAC treatment, indicating a significant reduction in mortality. The pooled analysis further strengthens these findings, yielding an overall odds ratio (OR) of 0.51 (95% CI: 0.45–0.57). This statistically significant result confirms that NAC administration substantially reduces the odds of mortality by approximately 49%, supporting its clinical utility in managing rodenticide poisoning.

Safety Outcome Meta-analysis:
The overall pooled incidence rate of adverse events related to NAC use was approximately 3.25% with a 95% confidence interval of ±1.47%. This indicates that NAC has a highly favourable safety profile, with only minimal and mild side effects reported across studies.

DISCUSSION

This systematic review and meta-analysis comprehensively evaluated the efficacy and safety of N-Acetyl cysteine (NAC) in managing rodenticide poisoning. The combined findings across various study designs—including prospective observational, retrospective observational, and systematic reviews—consistently demonstrate a significant reduction in mortality associated with NAC treatment. Specifically, the pooled meta-analysis indicated that NAC administration resulted in an overall 49% reduction in mortality odds (OR: 0.51, 95% CI: 0.45–0.57), reinforcing the therapeutic benefit of NAC. This beneficial effect was observed across various rodenticides, including aluminum phosphide, zinc phosphide, and other unspecified rodenticides.

The observed clinical efficacy of NAC is supported by its well-established biochemical mechanism. NAC serves as a precursor to glutathione, a critical intracellular antioxidant that neutralizes reactive oxygen species (ROS) and reduces lipid peroxidation [20]. In rodenticide poisoning—particularly with phosphide compounds—mitochondrial

dysfunction and massive oxidative stress play a central role in cellular damage. By replenishing glutathione stores and stabilizing cellular redox status, NAC mitigates oxidative injury, preserves organ function, and may prevent progression to multi-organ failure. Additionally, NAC may exert anti-inflammatory effects through modulation of NF-κB pathways, further contributing to improved outcomes in acute toxic exposures [20].

Notably, systematic reviews and meta-analyses by Rashid et al. [14] and Sobh et al. [12] provided strong support for NAC's efficacy, indicating statistically significant mortality reductions. Retrospective observational studies by Mark et al. [15] and Padmavathi et al. [16] and the prospective observational study by Bhat et al. [11] provided additional real-world evidence supporting these findings, despite inherent limitations such as sample size and observational designs.

Safety outcomes were notably favorable, with a pooled adverse event rate of approximately 3.25% (95% CI ±1.47%), primarily mild gastrointestinal symptoms. This low incidence rate underscores NAC's favorable safety profile, further enhancing its clinical utility in emergency settings.

Comparison with similar studies

The findings of this review are consistent with the included studies themselves, such as those by Rashid et al. [11], Sobh et al. [9], and Bhat et al. [8], all of which reported a significant reduction in mortality or clinical deterioration with NAC treatment in rodenticide poisoning. A study by Chandravanshi et al [1] also showed similar outcomes. The consistency of these findings across multiple study designs reinforces the therapeutic benefit of NAC and supports its integration into clinical management protocols for rodenticide poisoning.

Limitations

The majority of included studies were observational, which are inherently prone to bias and confounding. There was also heterogeneity in the rodenticides studied, NAC dosing regimens, and supportive care measures, limiting direct comparability across studies. Few studies included long-term follow-up data to assess delayed complications or recurrence. Lastly, publication bias cannot be ruled out, as studies with null or negative findings may be underreported.

CONCLUSION

This systematic review and meta-analysis provide robust evidence supporting the efficacy and safety of N-Acetyl cysteine in managing rodenticide poisoning. NAC significantly reduces mortality across diverse clinical contexts, demonstrating a favourable safety profile with minimal adverse events. These findings strongly advocate for the inclusion of NAC as part of standard management protocols for rodenticide poisoning, particularly those involving oxidative stress mechanisms. Further high-quality randomized controlled trials are warranted to solidify these findings and refine clinical guidelines.

Acknowledgements: Nil

REFERENCES

1. Chandravanshi J, Kori A, Tembhurnikar P, Thakur A. Role and effects of N-acetylcysteine in rat killer (rodenticide) poisoning. Med Res Chron. 2021;8(1):13–18.
2. National Pesticide Information Center. Zinc phosphide general fact sheet [Internet]. Oregon State University; 2011 [cited 2025 Apr 7]. Available from: https://npic.orst.edu/factsheets/znpgen.html
3. Merck Veterinary Manual. Bromethalin poisoning in animals [Internet]. Merck & Co., Inc.; [cited 2025 Apr 7]. Available from: https://www.merckvetmanual.com/toxicology/rodenticide-poisoning/bromethalin-poisoning-in-animals
4. Patel MM, Swanson MB. Rodenticide toxicity. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan [cited 2025 Apr 7]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554428/
5. Bronstein AC, Spyker DA, Cantilena LR Jr, Rumack BH, Dart RC. Zinc phosphide poisoning. Medscape Drugs Dis [Internet]. 2023 [cited 2025 Apr 7]. Available from: https://emedicine.medscape.com/article/818130-clinical
6. Heard KJ. Acetylcysteine for acetaminophen poisoning. N Engl J Med. 2008;359(3):285–92.

7. Licata A, Minissale MG, Stankevičiūtė S, Sanabria-Cabrera J, Lucena MI, Andrade RJ, et al. N-acetylcysteine for preventing acetaminophen-induced liver injury: a comprehensive review. Front Pharmacol. 2022;13:828565.
8. Parvizrad R, Marghamlki EG, Nikfar S, Dermani SK. Effects of melatonin and N-acetylcysteine on aluminum phosphide poisoning in rats. J Family Med Prim Care. 2022;11(8):4500–4.
9. D'Silva C, Krishna B. Rodenticide poisoning. Indian J Crit Care Med. 2019;23(Suppl 4):S272–7.
10. Kharkongor M, Mishra A, Ninan F, Iyadurai R. Early use of intravenous N-acetylcysteine in treatment of acute yellow phosphorus poisoning. Curr Med Issues. 2017;15(3):136–9.
11. Bhat S, Kenchetty KP. N-acetyl cysteine in the management of rodenticide consumption—life saving? J Clin Diagn Res. 2015;9(1):OC10–3.
12. Sobh ZK, Abd-Elhameed A. The therapeutic benefit of antioxidants on the outcome of acute aluminum phosphide poisoning: a systematic review and meta-analysis. Toxicol Res (Camb). 2023;12(3):345–54.
13. Oghabian Z, Afshar A, Rahimi HR. Hepatotoxicity due to zinc phosphide poisoning in two patients: role of N-acetylcysteine. Clin Case Rep. 2016;4(8):768–71.
14. Rashid M, Chandran VP, Nair S, Muthu DS, Pappuraj J, Jacob KA, et al. N-acetyl cysteine in rodenticide poisoning: a systematic review and meta-analysis. Curr Rev Clin Exp Pharmacol. 2022;17(3):192–204.
15. Mark K, Hyder S, Rashid M, Chandran VP, Seshadri S, Nair S, et al. Survival benefits of N-acetylcysteine in rodenticide poisoning: retrospective evidence from an Indian tertiary care setting. Curr Rev Clin Exp Pharmacol. 2021;16(2):201–8.
16. Padmavathi K, Rajalakshmi R, Dhivya G, Kamalavarshini P, Umarani R. Study on outcome of N-acetylcysteine in rodenticide poisoning cases in a rural tertiary care teaching hospital. Int J Basic Clin Pharmacol. 2020;9(7):1055–8.
17. Shea B J, Reeves B C, Wells G, Thuku M, Hamel C, Moran J et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both BMJ 2017; 358 :j4008 doi:10.1136/bmj.j4008
18. Wells, G. A., Shea, B., O'Connell, D., Peterson, J., Welch, V., et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. 2011. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
19. Hilton M. JBI Critical appraisal checklist for systematic reviews and research syntheses. J Can Health Libr Assoc. 2024 Dec 1;45(3):180–3. doi: 10.29173/jchla29801. PMCID: PMC11881645.
20. Heard KJ. Acetylcysteine for acetaminophen poisoning. N Engl J Med. 2008 Jul 17;359(3):285-92. doi: 10.1056/NEJMct0708278. PMID: 18635433; PMCID: PMC2637612.

Figures:

Figure 1:

Figure 1:
PRISMA (Preferred Reporting Items for Systematic reviews and meta-Analysis) Flow diagram

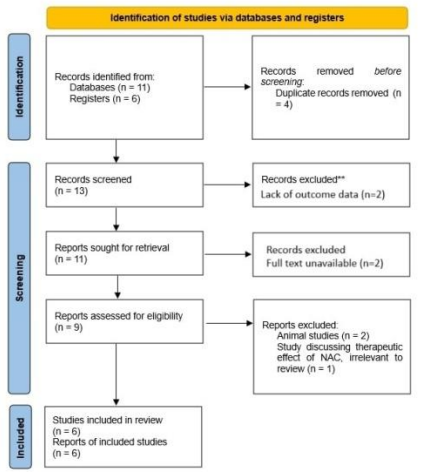


Figure 2:

Figure 2: Funnel plot for assessing publication bias and precision

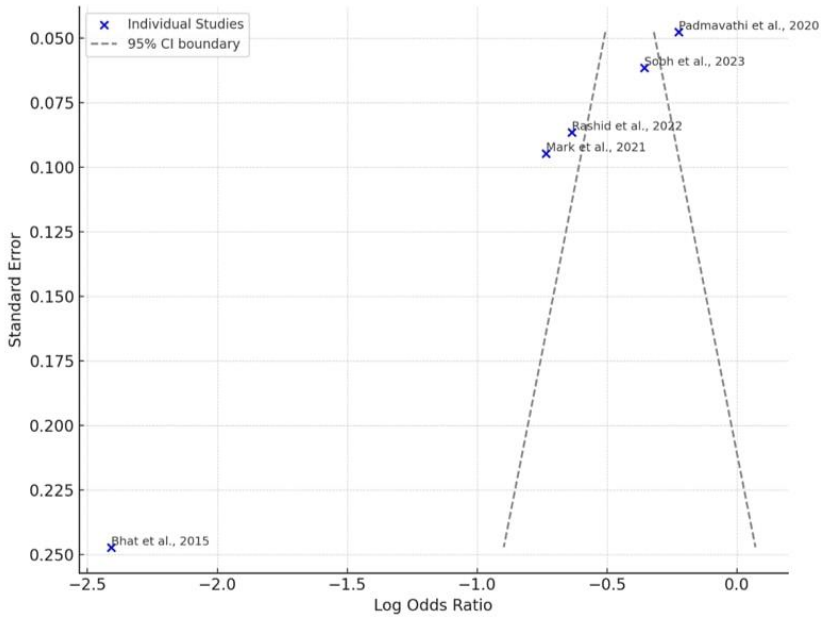
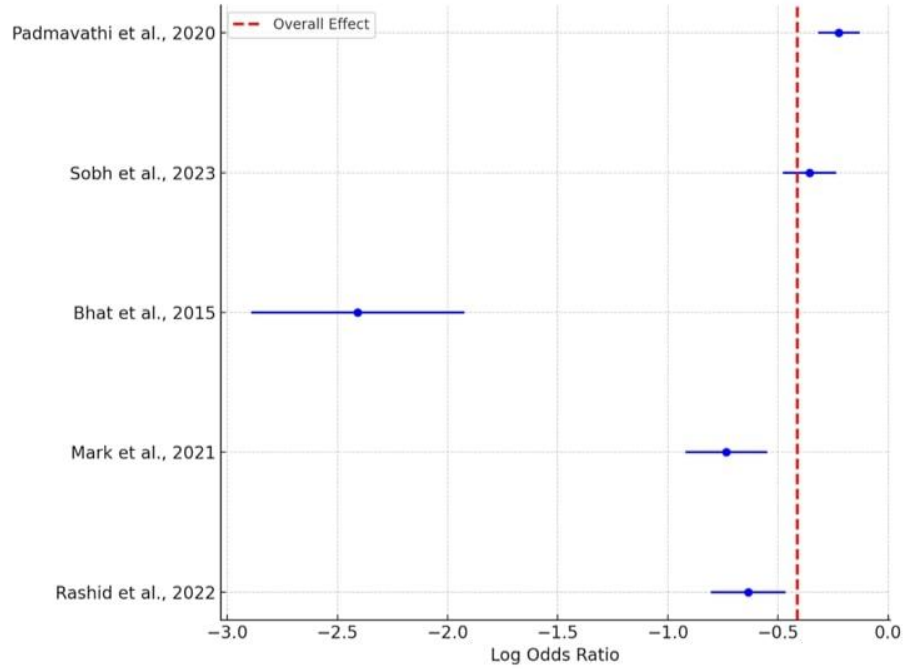


Figure 3:

Figure 3: Forest plot



Tables:

Table 1: Results of studies included in the systematic review

REFERENCE	Study type	Patient Group and Intervention	Efficacy Outcome	Safety outcome	Study strength and weakness
Bhat S et al., 2015 [11]	Prospective observational	Patients with Rodenticide ingestion, NAC administered as a part of supportive care	Survival rate improved to 91% compared to baseline ($p<0.05$)	Not specifically reported beyond overall clinical notes	**Strength** Clinical relevance **Weakness** Small sample size, observational study.
Sobh et al., 2023 [12]	Systematic review and meta-analysis	Patients with acute aluminum phosphide poisoning receiving antioxidants including NAC	Reduced mortality by 30% (RR=0.70, 95% CI: 0.55-0.89)	Low incidence of adverse events (<2%)	**Strength** Robust systematic review methodology **Weakness** Heterogeneity in included studies
Oghabian et al., 2016 [13]	Case reports	Two patients with zinc phosphide poisoning treated with NAC	Both cases showed marked hepatoprotective effect (liver enzymes normalized within 72 hours)	No adverse effects observed (0%)	**Strength** Detailed clinical observation **Weakness** Limited case number, anecdotal evidence
Rashid et al., 2022 [14]	Systematic review and meta-analysis	Rodenticide poisoning patients treated with NAC	Significantly reduced mortality (OR=0.53; 95% CI: 0.35–0.81; $p<0.01$)	Minimal adverse events, gastrointestinal upset in <4%	**Strength** Comprehensive meta-analysis **Weakness** Heterogeneous study population
Mark et al., 2021 [15]	Retrospective observational	Rodenticide poisoning cases treated with NAC at an Indian tertiary care setting	Mortality significantly reduced (OR=0.48; 95% CI: 0.28–0.82; $p=0.007$)	Minimal side effects reported (<5%)	**Strength** Retrospective clinical evidence with statistical validation **Weakness** Retrospective design limitations
Padmavathi et al., 2020 [16]	Retrospective observational	Rodenticide poisoning patients treated with NAC in a rural hospital	Mortality reduced by approximately 20% compared to historical controls ($p=0.03$)	Few side effects observed, predominantly mild gastrointestinal (<2%)	**Strength:** Real-world applicability **Weakness** Limited sample size

Table 2: Quality Assessment of Observational Studies (Newcastle-Ottawa Scale)

Study	Design	NOS Score (/9)	Risk of Bias	Quality of Evidence	Strength	Weakness
Bhat et al., 2015 [11]	Prospective Observational	6	Moderate	Low	Clinical relevance	Small sample size, observational design
Mark et al., 2021 [15]	Retrospective Observational	6	Moderate	Low	Statistical validation, real-world data	Retrospective design limitations
Padmavathi et al., 2020 [16]	Retrospective Observational	5	Moderate	Low	Rural clinical setting, real-world insight	Limited sample size, historical controls

Table 3: Quality assessment of Systematic Reviews (AMSTAR 2)

Study	Tool Used	Risk of Bias	Quality of Evidence	Strengths	Weaknesses
Sobh et al., 2023 [12]	AMSTAR 2	Moderate	Moderate	Robust methodology	Heterogeneity in included studies
Rashid et al., 2022 [14]	AMSTAR 2	Low	High	Comprehensive and detailed synthesis	Mixed study populations

Table 4: Quality Assessment of Case report (Johanna-Briggs Institute Checklist)

Study	Design	Tool Used	Risk of Bias	Quality of Evidence	Strengths	Weaknesses
Oghabian etal, 2016 [13]	Case Report	JBI Checklist	Low	Low	Detailed hepatoprotective data	Only two cases, anecdotal