RESEARCH PAPER

Efficacy of N-Acetylcysteine as an Adjuvant Therapy in Acute Hydrogen Cyanamide (Dormex^{R}) Toxicity Cases: A Prospective Observational Study

Morid Malak Hanna[1], Eman Ismail Hasan[1], Mohamed Ismail Hafez[1], Alaa Mohammed Abd Elmoez Ibrahim[1], Omima Mohammed Mohammed[2]

[1]Forensic Medicine and Toxicology Department, Faculty of Medicine, Minia University
[2]Clinical Pathology Department, Faculty of Medicine, Minia University

Received 15 July 2026, Revised 28 July 2026, Accepted 11 August 2026, Available Online 14 August 2026

Abstract

Background: Acute hydrogen cyanamide poisoning lacks a specific antidote, and management relies on supportive care. N-acetylcysteine (NAC) offers a theoretical mechanism-driven approach to counteract cyanamide-induced catalase inhibition. This study aimed to evaluate the clinical and biochemical efficacy of adjunctive IV NAC.

Methods: Thirty-three patients were divided into two groups: Standard supportive care (n=18) versus Supportive care plus IV NAC at 150mg/kg for 3 to 5 days (n=15). Clinical parameters, organ dysfunction scores (SOFA and GCS), and laboratory markers were tracked longitudinally. ROC curves were generated to determine the prognostic accuracy of CBC-derived ratios for predicting mortality.

Results: NAC therapy did not yield statistically significant improvements in hemodynamics, renal function, or metabolic acidosis. However, the NAC cohort demonstrated significantly lower Malondialdehyde (MDA) levels at discharge ($p=0.04$), indicating superior mitigation of lipid peroxidation. Clinically, NAC recipients exhibited significantly faster neurological recovery (higher GCS on days 2-4, $p<0.05$), better preservation of platelet counts, and lower SOFA scores during early follow-up. Beside these transient benefits, mortality in NAC group was half the mortality in the non- NAC group (13.3% vs 22.2%, respectively, $p=0.66$) despite the mortality and hospital length of stay changes were statistically unsignificant. ROC analysis identified that the platelet-to-lymphocyte ratio (PLR) failed to predict mortality (AUC 0.48).

Conclusion: Adjunctive NAC provides measurable biological efficacy by accelerating the resolution of oxidative stress, facilitating early neurological recovery, and reducing the hard mortality outcomes but insignificantly in this cohort.

How to cite this article: Morid Malak Hanna, Eman Ismail Hasan, Mohamed Ismail Hafez, Alaa Mohammed Abd Elmoez Ibrahim, Omima Mohammed Mohammed. Efficacy of N-Acetylcysteine as an Adjuvant Therapy in Acute Hydrogen Cyanamide (DormexR) Toxicity Cases: A Prospective Observational Study. Int J Drug Deliv Technol. 2026;16(78s):462-470. DOI: 10.25258/ijddt.16.78s.55.

Introduction

Hydrogen cyanamide (Dormex) is a liquid plant growth regulator extensively utilized in warmer agricultural climates to overcome insufficient chilling hours and promote uniform bud break in perennial crops such as grapes and kiwifruit **(Chervin & Fennell, 2019).**

Hydrogen cyanamide toxicity is more common to be due to un-intentional exposure as an occupational risk in workplaces or wrongly by children through ingestion, dermal exposure, and inhalation while reports of intentional exposure (suicidal attempts) are less common **(Bernasconi et al., 2023).**

Regardless of the route of administration, patients frequently experience a variety of symptoms, including nausea, vomiting, headache, fatigue, unsteady gait, hypotension, palpitations, bradycardia, tachypnea, vertigo, and tremors. They develop later after cutaneous exposure and earlier after intake **(Sharif & Fayed, 2021).**

Current management protocols rely entirely on symptomatic resuscitation including metabolic correction, renal replacement therapy, vasopressors, and mechanical ventilation as no specific antidote exists to neutralize the toxin or reverse its primary mechanism of action **(Ye et al., 2024).**

Consequently, many patients frequently progress to toxic encephalopathy or refractory shock and death due to uncontrolled systemic inflammation and oxidative cellular destruction **(Rezk et al., 2023).**

Acute hydrogen cyanamide poisoning represents a critical therapeutic challenge in clinical toxicology, It frequently progresses to fatal multi-organ failure despite aggressive, maximal supportive care, highlighting an urgent therapeutic gap **(Gamaluddin et al., 2012; Ye et al., 2024).**

N-acetylcysteine (NAC), a potent glutathione (GSH) precursor and free-radical scavenger, presents a highly rational, theoretically sound, mechanism-driven approach to counteracting cyanamide-induced redox collapse. However, its clinical efficacy in human subjects with this specific toxidrome remains unproven **(Elbastawesy et al., 2022).**

Because cyanamide's primary method of cellular destruction is the inhibition of catalase and the subsequent catastrophic depletion of endogenous antioxidant defenses, exogenous replenishment of the intracellular thiol pools via NAC presents a logical therapeutic strategy **(Bernasconi et al., 2023).**

While experimental models suggest NAC can reduce MDA levels, its true clinical efficacy in human subjects specifically its ability to accelerate neurological recovery, preserve organ function, and ultimately reduce mortality in this specific toxidrome has not been prospectively validated **(Tenório et al., 2021).**

Furthermore, early and accurate prognostication is vital for ICU resource allocation, yet the predictive accuracy of routine biomarkers and dynamic clinical scoring in cyanamide toxicity is poorly defined **(Ebrahimi et al., 2018).**

Equally important to the pursuit of a therapeutic intervention is the ability to utilize cheap, rapidly calculated Complete Blood Count (CBC)-derived ratios, such as the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR), which remains unexplored in cyanamide toxicity **(Abdelwahab et al., 2022).**

Aim of the Work:

The current study aimed to evaluate the clinical and biochemical efficacy of adjunctive intravenous N-acetylcysteine (NAC) in acute hydrogen cyanamide poisoning through comparing the longitudinal clinical outcomes (neurological recovery using GCS, organ dysfunction using SOFA, hemodynamic stability, and mortality rates) between patients receiving standard supportive care versus those who received the standard supportive care plus adjunctive NAC therapy.

In addition to validate the clinical utility of CBC-derived inflammatory ratios (NLR and PLR) as rapid, cost-effective prognostic tools in this specific toxidrome, and to explain the pathophysiological limitations of these ratios in the context of cyanamide-induced thrombocytopenia.

Patients & Methods:

Study Design and Setting

This prospective, observational comparative study was conducted at the Minia Poison Control Center (MPCC), affiliated with Minia University Hospital. The study evaluated patients admitted with acute hydrogen cyanamide (Dormex) toxicity over a 24-month period, from June 2023 to June 2025. The research protocol was designed to evaluate the adjunctive biochemical and clinical efficacy of N-acetylcysteine (NAC).

Ethical Considerations

The study protocol was reviewed and approved by the Scientific Committee for Research Ethics at the Faculty of Medicine, Minia University (Approval No. 580/2023). Written informed consent was obtained from all enrolled patients or their legal guardians prior to data collection, ensuring compliance with the Declaration of Helsinki.

Patient Population and Selection Criteria

During the study period, 45 patients with acute Dormex toxicity were admitted to the MPCC. Following strict inclusion and exclusion criteria, 33 patients were enrolled in the final analysis. Twelve patients were excluded based on the following criteria: five patients fell outside the designated age parameters (<16 or >60 years), four patients had uncontrolled pre-existing comorbidities (specifically diabetes mellitus), and three patients refused to participate in the research.

The inclusion criteria mandated adult patients of both sexes with a confirmed history of Dormex exposure, accompanied by characteristic clinical manifestations such as altered mental status, chemical burns at dermal contact sites, or hemodynamic instability. While the exclusion criteria were the age limits less than 16 years, more than 60 years, presentation with history and clinical picture of co ingestion of other drugs, history of chronic illness, malignancy, autoimmune diseases or refusal to participate in the study.

Study Groups and NAC Administration

The enrolled 33 patients were divided into two observational cohorts:

Group I (Control, non-NAC group, n=18): Received standard, guideline-directed supportive and symptomatic care. This included comprehensive decontamination, fluid resuscitation, vasopressors for shock, sodium bicarbonate for metabolic acidosis, seizure control, and mechanical ventilation if required.

Group II (NAC group, n=15): Received the exact standard supportive care as Group I, plus adjunctive intravenous N-acetylcysteine (NAC). The NAC protocol consisted of a dose of 150 mg/kg, administered as an intravenous infusion over 1 hour. This was administered once daily for a minimum of 3 days up to 5 days.

Clinical Evaluation and Scoring Systems

Detailed clinical and physiological data were documented upon admission and tracked longitudinally for five days. Neurological Assessment: The Glasgow Coma Scale (GCS) was calculated daily to monitor the trajectory of neurotoxicity **(Olsen, 2014).**

Domain	Response	Score
Eye opening	Spontaneous	4
	To speech	3
	To pain	2
	None	1
Best verbal response	Oriented	5
	Confused	4
	Inappropriate	3
	Incomprehensible	2
	None	1
Best motor response	Obeying	6
	Localizing	5
	Withdrawal	4
	Flexing	5
	Extending	3
	None	1
Total score	Deep coma or death	3
	Fully alert and oriented	15

Severity Scoring: the Sequential Organ Failure Assessment (SOFA) scores were calculated daily. To ensure accuracy and capture peak daily illness severity, the worst physiological and laboratory values recorded during each 24-hour period were utilized for these calculations **(Vincent et al., 1996).**

Variables	0	1	2	3	4
Respiratory PaO2/FiO2 mm hg	>400	<=400	<=300	<=200	<=100
Coagulation Platelets X10*3/ul	>150	<=150	<=100	<=50	<=20
Liver Bilirubin Mg/dl	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12
Cardiovascular Hypotension	No hypotension	Mean arterial pressure<70 mm hg	Dopamine<=5 or Dobutamine any dose(microgm/kg)	Dopamine>5 or Epinephrine<=0.1 or Norepinephrine<=0.1(microgm/kg)	Dopamine>15 or Epinephrine>0.1 or Norepinephrine >0.1 (microgm/kg)
Central nervous system Glasgow coma scale	15	13-14	10-12	6-9	<6
Renal Creatinine (mg/dl) Urine output (ml/dl)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or <500	>5.0 or <200

Laboratory Investigations and Biomarker Analysis

Sample Collection: Venous blood samples were drawn upon admission (prior to the administration of any therapeutic interventions) and repeated daily for follow-up. Additionally, heparinized arterial blood samples were collected for arterial blood gases analysis (ABG).

Routine Panels: Complete blood counts (CBC) with differentials were performed to calculate the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). Standard biochemical panels assessed renal function (creatinine, urea), hepatic function (ALT, AST, bilirubin, albumin, INR), and metabolic status (random blood glucose, arterial PH, and bicarbonate). Serum ammonia levels were also evaluated to assess hepatocerebral dysfunction.

Oxidative Stress Markers: Specific assays were utilized to quantify the redox state: Malondialdehyde (MDA) and Catalase (CAT) Enzyme activity were estimated colorimetrically. Both MDA and Catalase were measured on Day 1 (baseline) and at discharge (or Day 5) to evaluate the longitudinal impact of the poisoning and the NAC intervention.

Statistical Analysis

Data were coded, entered, and analyzed using an appropriate statistical software package (SPSS version 26) Continuous variables were checked for normality using the Shapiro-Wilk test and presented as mean ± standard deviation (SD). Categorical variables (e.g., mortality rates) were presented as frequencies and percentages **(Lang & Secic, 2006).**

Comparative Analysis: To compare continuous variables (e.g., GCS, platelets, glucose) between the NAC and non-NAC groups at specific time points, the Independent-Samples t-test was utilized or the Mann-Whitney U test if assumptions of normality were violated) **(Glantz, 2012).**

Longitudinal Analysis: To evaluate changes within each group over the 5-day follow-up period, Repeated-Measures Analysis of Variance (RM-ANOVA) was applied. Post-hoc tests with baseline comparisons were used to identify specific days where significant deviations occurred **(Glantz, 2012).**

Prognostic Accuracy (ROC Analysis): Receiver Operating Characteristic (ROC) curves were generated to determine the predictive power of various biomarkers for in-hospital mortality. The Area Under the Curve (AUC) was calculated, with values interpreted as poor (0.50), fair (0.50–0.70), good (0.70–0.80), excellent (0.80–0.90), or outstanding (0.90–1.00). The Youden Index was applied to determine optimal cut-off values, alongside their corresponding sensitivity and specificity. A p-value of < 0.05 was considered statistically significant **(Akobeng, 2007).**

Results:

The analyzed cohort consisted of 31 males and 2 females adults patients who were diagnosed with acute dormex poisoning and admitted to Minia Poison Control Center (MPCC), during the period from June 2023 till June 2025. Patients were stratified into two groups: 18 receiving standard supportive care and 15 receiving adjunctive intravenous NAC.

Table 1: Baseline and Demographic Data

	Descriptive (N=33)
Age (years)	
Mean ±SD	32.52 ± 13.52
Range	(17–58)
Gender	
Males	31 (93.9%)
Females	2 (6.1%)
Time of delay (hours)	
Mean ±SD	13.97 ± 9.88
Range	(3–32)
Length of stay (days)	
Mean ±SD	6.82 ± 3.43
Range	(3–15)
Route of exposure	
Ingestion	10 (30.3%)
Dermal	23 (69.7%)
Seasonal variation	
Winter (mostly January 19 & Feb. 7)	29 (87.9%)
Spring	1 (3.0%)
Summer	2 (6.1%)
Autumn / Fall	1 (3.0%)
Treatment	
Symptomatic & supportive	33 (100%)
NAC Therapy	15 (45.5%)
Mortality	6 (18.2%)

This table shows the classic occupational character of Dormex toxicity. The stark male predominance (93.9%) and the clustering of cases in winter months (87.9%) directly reflect the demographic reality of agricultural workers applying dormex to break winter dormancy in fruit crops. The mean delay of nearly 14 hours highlights a critical "latent period" where the toxin continues to absorb and cause systemic damage before the patient reaches the hospital.

Furthermore, the route of exposure (nearly 70% dermal) highlights a critical gap in occupational safety protocols, indicating widespread failure to utilize appropriate personal protective equipment (PPE). The 18.2% mortality rate, despite 100% receiving standard care, confirms that current supportive measures are often insufficient to halt the secondary oxidative cascade once systemic toxicity is established.

Comparison of Mean Arterial Pressure (MAP)

The hemodynamic trajectory in both groups demonstrated a significant, progressive increase in MAP over the first five days, crossing into hypertensive ranges ($p<0.005$ in the non-NAC group). This delayed hypertension is likely mediated by the vasodilatory effects of nitroxyl radicals generated during cyanamide oxidation, which initially drops blood pressure, followed by a massive sympathetic compensatory response as the body attempts to maintain cerebral perfusion.

NAC provided non statistically significant hemodynamic advantage. This aligns with NAC's mechanism of action as it restores the redox state but does not possess acute inotropic or vasopressor properties. This demonstrates that NAC cannot be viewed as a hemodynamic rescue agent.

Comparison of Heart Rate (HR)

A transient finding emerged regarding heart rate. While baseline HR was similar, the NAC group exhibited significantly lower heart rates on days 2 and 3 compared to the non-NAC group ($p<0.05$). This transient bradycardic effect likely reflects NAC's ability to mitigate oxidative stress within the myocardium and potentially stabilize autonomic regulation. However, by days 4 and 5, this difference dissipated. This suggests that while NAC may offer a brief window of cardiac protection, it cannot override the profound autonomic instability caused by severe cyanamide toxicity.

Comparison of Respiratory Rate (RR)

Respiratory dynamics further illustrate the specific, targeted benefits of NAC. While the non-NAC group experienced a significant, paradoxical spike in respiratory rate on day 3 ($p=0.04$), the NAC group remained stable. Tachypnea in the control group likely reflects the body's compensatory mechanism to clear the severe lactic acidosis induced by mitochondrial uncoupling. NAC's ability to blunt this respiratory drive suggests it may mitigate the depth of metabolic acidosis or protect against early pulmonary complications, keeping the patients breathing at a normal rate while standard bicarbonate therapy takes effect.

Comparison of Bicarbonate (HCO_3)

Both groups presented with significant metabolic acidosis on admission (HCO3 ~17 mEq/L) which progressively and significantly normalized over the 5-day period ($p<0.001$). However, NAC offered no accelerated correction of acidosis compared to standard care ($p=0.88$). This clearly demonstrates that the metabolic acidosis of cyanamide is driven by acute cellular hypoxia and lactic acid accumulation. Because NAC does not reverse mitochondrial uncoupling, it cannot accelerate the clearance of lactic acid. The improvement seen in both groups is entirely attributable to standard ICU resuscitation, fluid administration, and systemic clearance.

Comparison of Platelet Count

This table shows the significant protective effects of NAC. Both groups exhibited progressive, significant thrombocytopenia, which is a well-documented, direct toxic effect of cyanamide on bone marrow and thrombopoiesis. However, the rate of platelet drop was significantly blunted in the NAC group on days 2, 3, and 4 ($p<0.05$). This indicates that NAC exerts a cytoprotective effect on the bone marrow, likely by preserving thrombopoietin production in the liver and kidneys, thereby mitigating the severity of toxin-induced bone marrow suppression.

Comparison of Serum Creatinine

This table shows that NAC did not confer any renal protection. Serum creatinine remained stable

and statistically identical between the two groups across all time points. This indicates that while NAC is an effective antioxidant, it cannot reverse acute tubular necrosis or protect the kidneys from ischemic injury once profound shock and hypoperfusion have occurred. It reinforces the concept that NAC is highly specific to redox modulation rather than a universal organ protectant.

Comparison of Serum Urea

This data shows urea levels equalized by Day 2 and normalized in both groups, reflecting the efficacy of standard fluid resuscitation rather than a specific NAC-driven renal clearance.

Comparison of Liver Function and Random Blood Glucose

This table illustrates that in the non-NAC group, ALT and AST experienced a highly significant spike on Day 2 (p=0.04), reflecting acute hepatocellular necrosis. The NAC group, however, did not experience this spike, suggesting NAC successfully stabilized hepatocyte membranes against lipid peroxidation.

Furthermore, the Random Blood Glucose in non-NAC group experienced a severe stress-induced hyperglycemic spike on Day 2 (187 mg/dL), whereas the NAC group was significantly blunted (146 mg/dL, p=0.03). This strongly validates NAC's recognized anti-inflammatory properties, effectively dampening the systemic stress response and potentially protecting pancreatic beta-cells from acute oxidative injury.

Comparison of Ammonia

Hyperammonemia is a known consequence of acute liver failure and shutting down the urea cycle. Both groups showed a highly significant reduction in ammonia by discharge (p<0.001). However, NAC did not accelerate this clearance (p=0.21). This proves that while NAC can reduce oxidative stress, it cannot act as a direct ammonia scavenger or restart the urea cycle in severely necrotic livers.

Table 2 Comparison of Catalase and MDA

This table represents that on admission, both groups had low Catalase and high MDA, confirming severe catalase inhibition and lipid peroxidation. By discharge, both groups naturally improved. However, the MDA at discharge was significantly lower in the NAC group (1.91 vs 2.60, p=0.04).

This is the definitive proof of biological efficacy: NAC successfully acted as a direct free-radical scavenger, halting lipid peroxidation much more effectively than the body's natural recovery.

Table (2) Comparison of catalase and MDA on admission and discharge between cases who received N-acetyl cysteine (NAC) and cases who didn't

	NAC therapy		**P value**
	Group (I)	**Group (II)**	
	Non-NAC group (N=18)	**NAC group (N=15)**	
Catalase 1st day Mean ±SD Range	1.23 ± 0.30 (0.97–1.98)	1.18 ± 0.17 (0.96–1.41)	0.53
Catalase on discharge Mean ±SD Range	1.93 ± 0.5 (0.56–2.72)	2.09 ± 0.10 (1.94–2.23)	0.28
P value	<0.001*	<0.001*	
MDA 1st day Mean ±SD Range	3.45 ± 0.44 (2.68–4.17)	3.14 ± 0.63 (2.52–4.22)	0.10
MDA discharge Mean ±SD Range	2.60 ± 1.32 (1.49–6.16)	1.91 ± 0.30 (1.62–2.41)	0.04*
P value	0.01*	<0.001*	

*** Significant at p value <0.05**

Normal range of serum catalase is 1.5–4.0 unit per milliliter (U/mL), and of serum malondialdehyde (MDA) is 0.5–2 nanomole per milliliter (nmol/mL).

Comparison of Glasgow Coma Scale (GCS)

The GCS data represents that the non-NAC group showed non-significant neurological improvement over the 5 days (p=0.20). In contrast, the NAC group demonstrated a highly significant improvement from days 2 through 4 (p=0.01). Because GCS is highly sensitive to neuronal function, this confirms that by stopping lipid peroxidation, NAC actively facilitates neurological recovery and protects the blood-brain barrier from secondary inflammatory injury.

Table 5: Comparison of SOFA Score

The SOFA scores essentially group organ dysfunction. Because NAC showed benefits in GCS and platelet count, it is entirely logical that the SOFA scores were significantly lower in the NAC group from days 2 to 4 (p<0.05). This validates SOFA as a sensitive composite tool that accurately reflects the targeted cytoprotective benefits of NAC across multiple organ systems simultaneously.

Comparison of Outcomes

Numerically, the NAC group had a shorter hospital stay (6.0 vs 7.5 days) and a lower mortality rate (13.3% vs 22.2%). However, the p-values (0.21 and 0.66) indicate these differences are not statistically significant. This lack of statistical significance is almost due to the sample size. However, It serves as the primary justification for larger, multicenter Randomized Controlled Trials (RCTs) needed.

Table (3) Comparison of SOFA score and outcome over the first 5 days between cases who

received N-acetyl cysteine (NAC) and cases who didn't

	NAC therapy		P value
	Group (I) Non-NAC group (N=18)	**Group (II) NAC group (N=15)**	
SOFA 1st day Mean ±SD Range	3.22 ± 1.22 (0–5)	2.50 ± 1.08 (0–3)	0.08
SOFA 2nd day Mean ±SD Range	3.33 ± 2.28 (0–7)	2.00 ± 1.73 (0–5)	0.05*
SOFA 3rd day Mean ±SD Range	3.50 ± 2.71 (0–8)	1.93 ± 2.05 (0–5)	0.05*
SOFA 4th day Mean ±SD Range	**N=15** 4.60 ± 3.94 (0–11)	**N=13** 2.00 ± 2.27 (0–5)	0.04*
SOFA 5th day Mean ±SD Range	**N=13** 5.69 ± 5.30 (0–14)	**N=9** 3.22 ± 3.03 (0–8)	0.23
P value	0.22	0.80	
Hospital stay/ day Mean ±SD Range	7.5±3.7 (3-15)	6±2.9 (3-12)	0.21
Mortality	4 (22.2%)	2 (13.3%)	0.66

Table 6, 7: the inflammatory Markers (NLR/PLR) and Prognostic ROC Curves

Regarding the NLR: Both groups experienced a highly significant drop in NLR by Day 2 ($p<0.001$), indicating that the acute stress response subsides once exposure ceases and supportive care begins. NAC did not provide any additional benefit in reducing this inflammatory ratio, confirming that NAC's primary mechanism is redox modulation, not broad anti-inflammatory cytokine suppression.

The NLR on Day 2 proved to be a "good" mortality predictor (AUC 0.77), meaning a score >11 has 93% specificity. However, the PLR completely failed to predict mortality (AUC 0.48).

Table (4) Comparison of NLR on admission and 2nd day between cases who received N-acetyl cysteine (NAC) and cases who didn't

	NAC therapy		P value
	Group (I) Non-NAC group (N=18)	**Group (II) NAC group (N=15)**	
NLR 1st day Mean ±SD Range	7.33 ± 3.55 (3–17)	6.87 ± 4.12 (1–14)	0.47
NLR 2nd day Mean ±SD Range	6.72 ± 5.99 (1–19)	5.87 ± 5.08 (2–17)	0.66
P value	0.001*	0.004*	
PLR 1st day Mean ±SD Range	116.41 ± 54.86 (29.13–218.1)	122.47 ± 84.85 (31.6–303.6)	0.80
PLR 2nd day Mean ±SD Range	100.26 ± 72.66 (12.38–296)	155.21 ± 186.19 (40.1–310)	0.25
P value	0.44	0.52	

*** Significant at p value <0.05**

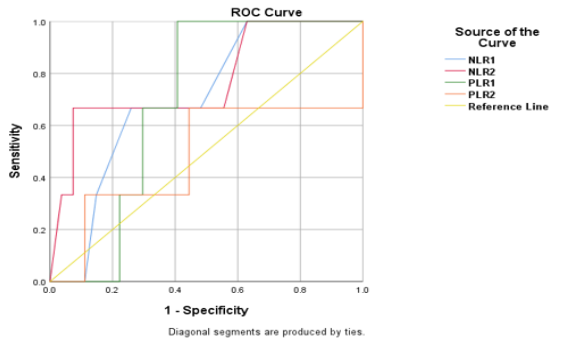
Neutrophil to lymphocyte ratio is measured by dividing Neutrophils over lymphocytes count or percentage. A normal NLR is roughly 1-3, NLR of 6-9 suggests mild stress, and higher than 9 NLR is mostly in critically ill patients.

Platelet-to-lymphocyte ratio (PLR) is measured by dividing Platelets over lymphocytes count or percentage. Normal PLR ranges roughly between 36.63 to 172.68.

Table (5) ROC curve for different variables for prediction of mortality on 1st and 2nd days of admission

	NLR 1st day	**NLR 2nd day**	**PLR 1st day**	**PLR 2nd day**
AUC	0.70	0.77	0.69	0.48
95% CI	0.50-0.90	0.54-0.99	0.52-0.86	0.17-0.79
P value	0.12	0.04*	0.14	0.88
Cut off value	>8.5	>11	>130	102.6
Sensitivity	66.7%	66.7%	66.7%	66.7%
Specificity	75%	93%	70.4%	55.4%

*** Significant at p value <0.05**



Discussion

The evaluation of adjunctive use of NAC therapy in this cohort reveals a complex dichotomy between biochemical efficacy and ultimate clinical survival and outcomes. NAC did not exert a statistically significant effect on mean arterial pressure, heart rate, or the rate of bicarbonate correction. This suggests that NAC's primary mechanism, which is modulation of the redox state, does not immediately reverse the hemodynamic or metabolic shock induced by mitochondrial uncoupling **(Sheshadri et al., 2011).**

Cyanamide-induced mitochondrial uncoupling and vasodilatory shock are primarily hemodynamic crises. NAC's mechanism of replenishing glutathione does not address these acute mechanical failures, explaining its lack of effect on mean arterial pressure or lactate clearance **(Ershad et al., 2024).**

However, NAC demonstrated targeted biochemical mechanism-driven cyto-protection efficacy. While both groups naturally restored Catalase levels over time, the NAC group achieved a significantly greater reduction in serum MDA by discharge compared to standard care ($p=0.04$). This confirms that exogenous glutathione precursors actively enhance the clearance of lipid peroxidation byproducts in this toxidrome **(Tenório et al., 2021).**

This biochemical advantage translated into transient, yet statistically significant, clinical improvements. The NAC group exhibited a steeper and more sustained resolution of neurotoxicity and improvement in Glasgow Coma Scale scores from days 2 through 4 ($p<0.05$) **(El Mahdy and Kharoub, 2020; Rezk et al. 2023; Fouad et al., 2025).**

In agreement with **Gamaluddin et al. (2012) and El Mahdy & Kharoub (2020)** studies, NAC attenuated the characteristic thrombocytopenia of Dormex poisoning. Furthermore, SOFA scores which gather respiration, coagulation, liver, and neurological metrics were significantly lower in the NAC group during the same period. Notably, this SOFA improvement was largely mathematically driven by the concurrent preservation of platelet counts (which dropped significantly less in the NAC group) and the improved GCS **(Vincent et al., 1996; Lambden et al., 2019).**

NAC also appeared to blunt the stress-induced hyperglycemic spike observed on day two in the control group. Ultimately, while NAC showed favorable trends in reducing mortality (13.3% vs 22.2%) and shortening hospital stays, the lack of a statistically significant reduction in mortality suggests that while NAC mitigates secondary oxidative injury, it cannot reverse the primary neuronal or hepatic damage inflicted prior to hospital admission, this limitation almost exacerbated by the study's sample size.

Due to the absence of a specific diagnostic test for Dormex, identifying reliable early mortality predictors is critical. The current study evaluated the utility of CBC-derived ratios, the second-day NLR proved to be a good predictor (AUC 0.77) with exceptionally high specificity (93%), making it a reliable rule-in test for mortality accurately reflecting the peak of the systemic inflammatory cascade. Conversely, the PLR completely failed to predict outcomes (AUC 0.48) **(Zahorec, 2021).**

This null finding attributed to the unique pathophysiology of Dormex, unlike sepsis, where reactive thrombocytosis elevates the PLR, dormex toxicity induces profound thrombocytopenia via bone marrow suppression and hepato-renal injury. Because both the numerator (platelets) and denominator (lymphocytes) drop simultaneously due to different mechanisms (toxicity vs. stress), the ratio becomes mathematically skewed by the unique thrombocytopenic nature of the poison, destroying its prognostic validity.

Conclusion

The current study concludes that while standard care gradually restored catalase and MDA levels to normal, adjunctive treatment with NAC showed clear biological efficacy in accelerating the reduction of lipid peroxidation. This biological improvement translated into clinical benefits such as a significant improvement in neurological outcomes (GCS), platelet preservation, attenuation of hyperglycemia, and improvement in organ dysfunction scores.

However, its effect on liver function, ammonia, coagulation parameters, and inflammatory markers such as NLR and PLR appeared to be limited. In addition, a significant reduction in mortality was not demonstrated.

Therefore, further studies are recommended to elucidate the exact mechanism of hydrogen cyanamide toxicity, identify the causes of rapid deterioration, and adopt better measures to save patients. Furthermore, more scientific researches with larger sample size are needed to investigate the optimal

dose and route of administration of NAC to obtain maximum anti-inflammatory and antioxidant benefits, and to evaluate and confirm its effect on mortality to avoid lack of statistical power.

References

1. **Abdelwahab, H. M., Nafea, O. E., Elsherif, R., Gharib, A. F., Alrehaili, A. A., & Abdelhamid, W. G. (2022).** Neutrophil-to-lymphocyte ratio versus platelet-to-lymphocyte ratio in predicting clinical outcomes in acute methanol poisoning. Human & Experimental Toxicology, 41, 09603271221102504.
2. **Akobeng, A. K. (2007).** Understanding diagnostic tests 3: receiver operating characteristic curves. Acta paediatrica, 96(5), 644-647.
3. **Bernasconi, L., Carnovale, M., Lonati, D., Petrolini, V. M., Schicchi, A., et al. (2023).** Hydrogen cyanamide exposure: A case series from Pavia Poison Control Centre. Occupational Medicine, 73(8), 500–506.
4. **Chervin, C., & Fennell, A. (2019).** Ethanol sprays to release grapevine bud dormancy: a potential alternative to cyanamides. OENO One, 53(4).
5. **Ebrahimi, K., Vaisi Raigani A.A., Jalali R., & Rezaei M. (2018).** Determining and Comparing Predictive and Intensity Value of Severity Scores – "Sequential Organ Failure Assessment Score," "Acute Physiology and Chronic Health Evaluation 4," and "Poisoning Severity Score" – in Short-Term Clinical Outcome of Patients with Poisoning in an ICU. Indian Journal of Critical Care Medicine, 22(6),415-421.
6. **El Mahdy, N.M. and Kharoub, H.S. (2020).** Acute Toxicity Due to Occupational Exposure to The Plant Growth Regulator Hydrogen Cyanamide (Case Report). Egyptian Journal of Occupational Medicine, 44(1), 471-484.
7. **Elbastawesy, S., Ibrahim, F., Abo Safia, H., El Shamy, A., Ibrahim, H., Helal, N. (2022).** Nephrotoxic effect of Hydrogen Cyanamide (Dormex) and possible protective role of N-acetyl cysteine in male albino rats. Ain Shams Journal of Forensic Medicine and Clinical Toxicology, 39(2), 21-29.
8. **Ershad, M., Naji, A., Patel, P., & Vearrier, D. (2024).** N-acetylcysteine. In StatPearls [Internet]. StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/sites/books/NBK537183/
9. **Fouad, M. M., Zawilla, N. H., & Ali, A. M. (2025).** Occupational exposure to hydrogen cyanamide in a young farmer: Case report of acute toxicity. Toxicologie Analytique et Clinique.
10. **Gamaluddin, H., Mahmmoud, S., Mosa, M., Halawa, H., Khalifa, E. (2012).** A Clinical Study of Acute Hydrogen Cyanamide Toxicity in the Period between 2006-2009 in the Poison Control Center, Ain Shams University. Ain Shams Journal of Forensic Medicine and Clinical Toxicology, 19(2), 97-103.
11. **Glantz, S. A. (2012).** Primer of biostatistics (7th ed.). McGraw-Hill Education.
12. **Lambden, S., Laterre, P.F., Levy, M.M. et al. (2019).** The SOFA score—development, utility and challenges of accurate assessment in clinical trials. Crit Care. 23, 374.
13. **Lang, T. A., & Secic, M. (2006).** How to report statistics in medicine: annotated guidelines for authors, editors, and reviewers. ACP Press.
14. **Olsen, A. (2014).** Cognitive control function and moderate-to-severe traumatic brain injury: Functional and structural brain correlates (Doctoral dissertation, Norwegian University of Science and Technology). Circulation and Medical Imaging.
15. **Rezk, M.N.N., Beshreda, G.M., Meshref, D.A., Abdelzaher, W.Y., Batiha, G.E. et al., (2023).** Hypoxia inducible factor-1α (HIF-1α) as an early predictor of acute hydrogen cyanamide (Dormex) poisoning. Ecotoxicology and Environmental Safety, 256, 114847.
16. **Sharif, A.F. and Fayed, M.M. (2021)**: Evaluation of Multiple Organ Dysfunction Score (MODS) and the Sequential Organ Failure Assessment (SOFA) score as in hospital outcome predictors among cases of hydrogen cyanamide exposure: a cross-sectional study. Environmental science and pollution research international, 28(31):42161–42176**.**
17. **Sheshadri, S.H., Sudhir, U., Kumar, S., Kempegowda, P. (2011).** DORMEX®-hydrogen cyanamide poisoning. Journal of Emergencies, Trauma, and Shock, 4(3): 435-437.
18. **Tenório, M.C.d.S., Graciliano, N.G., Moura, F.A., Oliveira, A.C. M. d., & Goulart, M.O.F. (2021).** N-Acetylcysteine (NAC): Impacts on Human Health. Antioxidants, 10(6), 967.
19. **Vincent, J. L., Moreno, R., Takala, J., Willatts, S., De Mendonça, A., Bruining, H., Reinhart, C. K., Suter, P. M., & Thijs, L. G. (1996).** The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive care medicine, 22(7), 707–710.

20. **Ye, Y., Chen, L., Yang, B., Li, B., et al. (2024).** Unveiling the deadly effects of hydrogen cyanamide poisoning: A case report. Authorea.
21. **Zahorec, R. (2021).** Neutrophil-to-lymphocyte ratio, past, present and future perspectives. Bratisl Lek Listy, 122(7), 474-488.