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ORIGINAL ARTICLE

Prognostic Value of Routine Biochemical Markers in Acute Aluminum Phosphide Poisoning: A Prospective Cohort Study

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Abstract

***Background*:** Aluminum phosphide (AlP) is a highly toxic pesticide widely used in agricultural settings. Due to its low cost and lack of regulatory control, it has become a common cause of poisoning in Egypt, often with fatal outcomes. Early identification of prognostic markers using routine laboratory investigations may aid in improving patient outcomes.
***Methods*:** This prospective cohort study was conducted at the Poison Control Center of Zagazig University Hospitals from January to June 2021. A total of 42 patients with confirmed AlP poisoning were enrolled. Routine laboratory parameters, including total leukocyte count (TLC), liver enzymes (AST, ALT), renal function markers (creatinine, BUN), and serum electrolytes (Na^+, K^+), were collected within 24 hours of admission. Patients were followed until discharge or in-hospital death. Survivors and non-survivors were compared to identify significant predictors.
***Results*:** Serum sodium levels were significantly higher in non-survivors (P = 0.04). Potassium levels were lower overall but did not differ significantly between groups. The Total leukocyte count showed an increasing trend in non-survivors, although this trend was not statistically significant. Liver enzymes and renal function markers showed mild elevations in some cases but were not significantly associated with mortality.
***Conclusion*:** In this prospective cohort of acute AlP poisoning, elevated serum sodium was significantly associated with in-hospital mortality, as ROC analysis for serum sodium yielded an AUC of 0.67 (0.5-0.83), while total leukocyte count showed a non-significant upward trend. These findings suggest that routine markers may offer early prognostic insight but require further validation.

Keywords: Aluminum Phosphide, Acute Toxicity, Serum Sodium, Total leukocyte count, Mortality

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INTRODUCTION

Aluminum phosphide (AlP), commonly referred to as the "wheat pill," is a widely used fumigant in developing countries for grain preservation, particularly in Egypt. It is inexpensive, accessible, and lacks adequate regulatory control, making it a frequent agent in both accidental and intentional poisonings [1]. AlP toxicity is associated with high mortality, largely due to rapid release of phosphine gas upon contact with moisture, which disrupts mitochondrial respiration by inhibiting cytochrome oxidase and altering haemoglobin function [2, 3].

As previously reviewed, aluminum phosphide poisoning leads to widespread cellular toxicity involving multiple organs, most notably the heart, lungs, liver, and kidneys, often manifesting as severe acid-base imbalance, oxidative stress, and circulatory collapse [4]. Despite its clinical severity, no specific antidote exists for AlP poisoning. Treatment remains primarily supportive and symptomatic. Several adjunctive therapies have been tried, including paraffin oil, magnesium sulfate, corticosteroids, and antioxidants such as N-acetylcysteine, but no standardized protocol has demonstrated consistent efficacy [5-8]. Outcomes often depend on the dose ingested, delay to presentation, and early clinical status, but remain difficult to predict.

Efforts to identify reliable prognostic markers have included both physiological parameters and laboratory indices such as pH, serum bicarbonate, liver and kidney function tests, blood glucose, and serum electrolytes [9]. While some studies have examined individual markers [10, 11], few have assessed routine biochemical panels in a

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structured cohort. Moreover, despite multiple retrospective studies on ALP, prospective assessments of routine markers within the first 24 hours of ingestion remain scarce, especially in resource-limited settings.

Therefore, this study aims to evaluate the early prognostic significance of routine parameters—including total leukocyte count (TLC), liver enzymes (AST, ALT), renal markers (creatinine, BUN), and serum electrolytes (Na^+, K^+)—in patients with acute AlP poisoning.

METHODS

Study design

This was a prospective observational cohort study conducted at the Poison Control Center of Zagazig University Hospitals over a 6-month period from January 2021 to June 2021. Patients aged 15–45 years with confirmed acute aluminum phosphide ingestion were enrolled following clinical assessment and supportive history. Patients were enrolled consecutively upon presentation to the Poison Control Center. Cases with incomplete biochemical data were excluded from analysis..

Inclusion criteria

Patients were eligible for inclusion if they had:

- ✓ A clear history of acute AlP ingestion,
- ✓ Clinical signs consistent with AlP poisoning (e.g., vomiting, hypotension, acidosis),
- ✓ Age between 15 and 45 years.

Exclusion criteria

- ✓ Patients were excluded if they had:
- ✓ Uncertain history of ingestion
- ✓ Co-ingestion of other substances,
- ✓ Pre-existing chronic liver, kidney, or hematologic diseases that could confound lab values.

Ethical Considerations: Approval was obtained from the Zagazig University Institutional Review Board (IRB No. ZU-IRB #6665/13-1-2021). Verbal consent was obtained from patients or their legal representatives.

Clinical Assessment and Management

All enrolled patients were subjected to history taking and Clinical assessment and were managed according to the local toxicology protocol. Data was collected by using a standardized case report form. Initial stabilization included airway protection, oxygen therapy, fluid resuscitation, and vasopressors as needed. Gastrointestinal decontamination was performed using repeated doses of coconut, almond, or paraffin oil. Adjunct therapies included corticosteroids, sodium bicarbonate, N-acetylcysteine, magnesium sulfate, and mechanical ventilation when indicated. Each case received the appropriate management from the mentioned protocol according to their own situation.

Laboratory Investigations

Blood samples were collected within the first 24 hours of admission. All tests were performed in a central laboratory using instruments under regular internal and external quality control.

The following routine biochemical parameters were analyzed:

- ✓ Complete blood count including total leukocyte count (TLC), using the Dyn 1700 hematology analyzer.
- ✓ Liver function tests: Aspartate transaminase (AST) and alanine transaminase (ALT), using the Spinreact biochemistry kit.
- ✓ Renal function tests: Serum creatinine and blood urea nitrogen (BUN), using Jaffé and urease-colorimetric methods, respectively.
- ✓ Serum electrolytes: Sodium (Na^+) and potassium (K^+), measured via ion-selective electrodes.

Reference ranges were as follows:

- ✓ TLC: 4,000 – 11,000 cells/µL
- ✓ ALT: ≤ 22 U/L (male), ≤ 18 U/L (female)
- ✓ AST: ≤ 38 U/L (male), ≤ 31 U/L (female)
- ✓ Creatinine: 0.7–1.4 mg/dL (male), 0.6 – 1.1 mg/dL (female)
- ✓ BUN: 32.9 – 65.7 mg/dL
- ✓ Sodium: 135 – 145 mEq/L
- ✓ Potassium: 3.5 – 5.5 mEq/L

Outcome and Statistical Analysis

Patients were monitored in high-dependency or intensive care settings. Symptomatic patients were discharged only after at least 48 hours of clinical stability, with normalization of vital signs and key laboratory parameters, and following clearance by a cardiologist.

At the end of hospitalization, patients were categorized into the following:

- ✓ Survivors: Those who achieved full clinical recovery
- ✓ Non-survivors: Those who died during admission

Data were analysed using IBM SPSS version 27.0. Quantitative variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Comparisons between survivors and non-survivors were performed using the independent t-test or Mann–Whitney U test. Categorical variables were compared using the chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

Study Population

The prospective cohort included 42 AlP-poisoned patients admitted to PCC-ZUH. Patients were classified into survivors (n = 17) and non-survivors (n = 25).

All of the included cases were suicidal. The average amount ingested by almost all poisoned patients was approximately one tablet, and the average lag time till the arrival to the ER was around three hours for all evaluated patients. Table 1 illustrates that both the number of ingested tablets and the average time lapse had no significant relation to the outcome of the case.

Table 1. Statistical comparison between survivors and non-survivors in poisoning data by Mann-Whitney test

Variable	Survivors (n = 17)	Non-survivors (n = 25)	MW/χ2	P
Amount (tablet) Median (IQR)	1 (0.5-1)	1(0.5-1)	1	0.32 (NS)
Lag time (h) Median (IQR)	3 (2-3)	3(2-4)	0.55	0.58 (NS)

NS: non-significant (P > 0.05)

Electrolytes and Haematological Findings

Potassium (K^+) & Sodium (Na^+):

There was no significant difference in sodium (Na^+) level, while potassium (K^+) was significantly lower in the studied cases in comparison with the reference range values (P = 0.01). However, Na+ was significantly higher among the non-survivors compared with the survivors. Receiver Operating Characteristic (ROC) analysis revealed that serum sodium had the best predictive performance for in-hospital mortality, with an AUC of 0.67, indicating acceptable discrimination while potassium showed poor discriminatory ability (Figure 1 and Table 2).

Table 2. Statistical comparison electrolytes, and total leucocytic count (TLC) between survivors and non-survivors by T-test

Variable	Survivors (n = 17)	Non-survivors (n = 25)	t/MW	P
K (mmol/L) Mean ± SD	3.31 ± 0.5	2.96 ± 0.97	1.22	0.23 (NS)
Na (mEq/L) Mean ± SD	139.77 ± 6.51	148.81 ± 17.07	2.08	0.04*
TLC (x103 /mm) Median (IQR)	8.8 (7.6-10.5)	10.5 (7.9-14.3)	1.6	0.11 (NS)

SD: Standard deviation, IQR: Interquartile range, MW: Mann-Whitney test, t: Independent t-test, *: Significant (P < 0.05), **: highly significant (P < 0.001), PH: the potential of hydrogen, NS: non-significant (P > 0.05)

Total Leucocytic Count (TLC):

The total leucocytic count (TLC) was neither significantly different from the normal population average range nor correlated to the outcome of the poisoned cases (Figure 2 and Table 1).

Liver and Kidney Function Tests

Despite the significant increase in ALT and creatinine among enrolled AlP-poisoned cases compared with the known reference range values, there was no significant difference in the values of AST and BUN compared with normal values. There was no statistically significant impact of AST, ALT, Creatinine, or BUN on the case outcome. Creatinine and ALT showed poor discriminatory ability (AUC < 0.6) as illustrated in Figure 3 and Table 3.

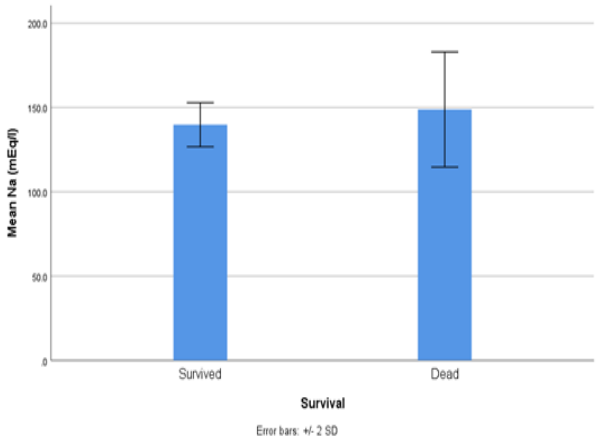

Figure 1. Comparison of sodium (Na) levels between acutely poisoned aluminium phosphide survivors and non-survivors

Table 3. Statistical comparison of liver and kidney function tests between acute aluminum phosphide poisoned cases and reference range

Variable	Cases (n = 42) Mean ± SD	Reference range	P
ALT (IU/L)	63.96 ± 83.53	Up to 22	0.001
AST (IU/L)	39.39 ± 53.6	Up to 38	0.56 NS
Creatinine (mg/dl)	1.51 ± 0.56	Up to 1.4	0.005*
BUN (mg/dl)	30.38 ± 17.28	≤ 32.9-65.7	0.35 NS

SD: Standard deviation, NS: Non-significant (P > 0.05), *: Significant (P < 0.05), ALT: alanine transferase enzyme, AST: aspartate aminotransferase, BUN: blood

DISCUSSION

Aluminum phosphide (AlP) is an important pesticide that is widely used in several developing agricultural countries, like Egypt, to prevent wheat and rice infestation. The rate of AlP poisoning is increasing in Egypt, as it is a cheap and available poison without legal legislation controlling its purchasing. AlP is highly toxic and causes severe symptoms with a high mortality rate (40-80%).The cause of death is shock resistant to fluid therapy and inotropes accompanied by complications such as disseminated intravascular coagulation (D.I.C.) and multi-organ failure. Unfortunately, there is no specific antidote for AlP poisoning, and most of the treatment is supportive treatment only [12].

This prospective study aimed to assess whether routine biochemical parameters could serve as early prognostic markers of mortality in acute aluminum phosphide (AlP) poisoning. While numerous prognostic tools have been studied in the context of AlP toxicity, few have comprehensively evaluated commonly available biochemical markers on admission.

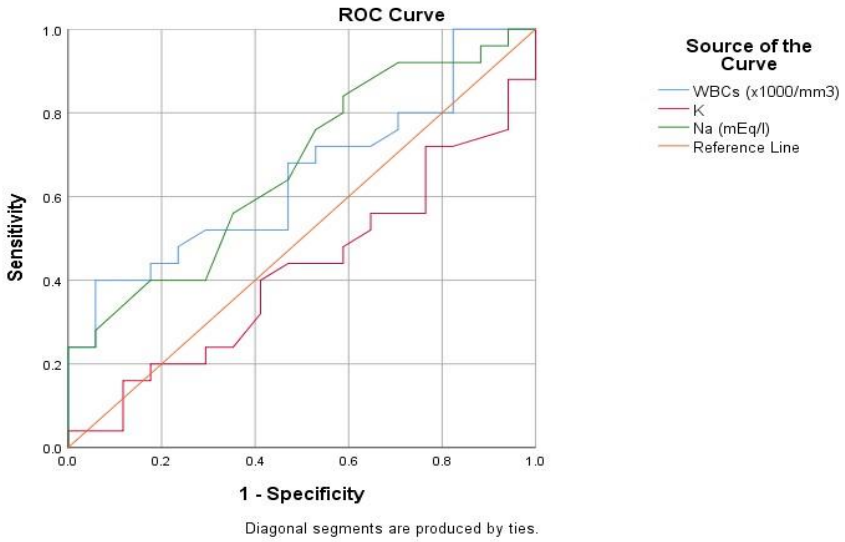

Figure 2. Receiver operator characteristic curve (Roc) curve for Validity for total leucocytic count and electrolytes

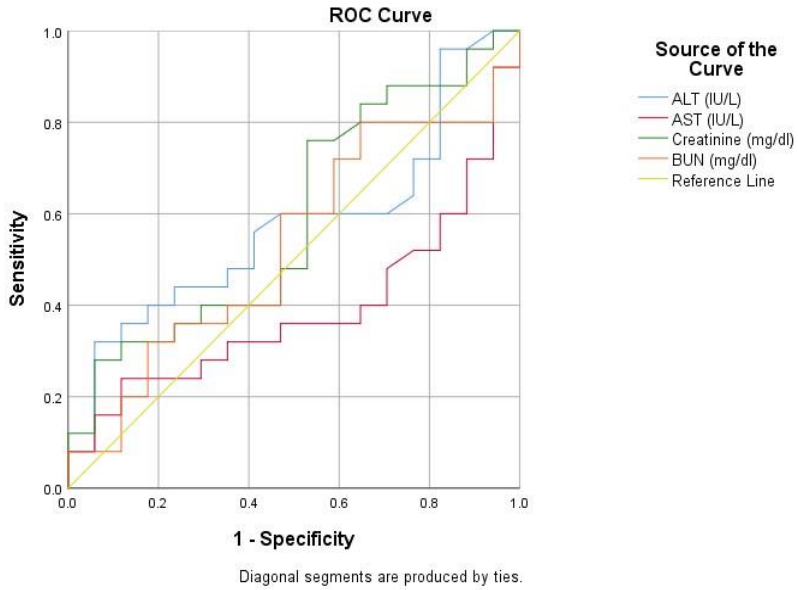

Figure 3. Receiver operator characteristic curve (Roc) curve for Validity of liver and kidney functions

Total Leukocyte count was notably elevated in most cases, in agreement with Hosseinian et al. (2011) and Masoud and Barghash [1], who reported leukocytosis as a frequent finding in AlP toxicity. Our data showed that total leukocyte count (TLC) was significantly higher in non-survivors, suggesting a potential role as a simple, early prognostic indicator reflecting systemic stress or inflammation [12].

Liver transaminases, particularly AST, were mildly elevated across both groups, while ALT largely remained within reference ranges. However, the lack of statistical correlation with outcome aligns with the findings of Taramsari et al. (2013), who attributed the absence of predictive value to delayed hepatic enzyme elevation in comparison to short hospitalization time and high mortality rates. Early sampling in our cohort may have similarly

preceded hepatocellular injury manifestation, which could be delayed for up to 72 hours [13].

Creatinine levels showed a rising trend among non-survivors, but without statistical significance. This is consistent with findings from Majidi et al. [14], who reported elevated creatinine in fatal AlP cases, although not uniformly across cohorts. Blood urea nitrogen (BUN) did not significantly differ between groups. Notably, these discrepancies may be explained by the variability in timing of sample collection, renal perfusion states, and the early mortality common in AlP poisoning [1, 14].

In the study done by El-Sarnagawy [15], they reported elevation in AST, ALT, blood urea, and serum creatinine and that elevation had a direct relationship with mortality, attributing that to the fact that phosphine gas causes inhibition of cytochrome c and produces toxic free radicals, causing damage to the liver and kidney, which are more susceptible to hypoxic damage due to their high oxygen requirements.

Serum sodium levels were significantly higher in non-survivors (P = 0.04), and ROC analysis yielded an AUC of approximately 0.71, indicating acceptable discriminatory power. Hypernatremia in this context may reflect severe dehydration, shock, or cellular leakage —findings supported by Bogale et al. [16], who also noted electrolyte imbalances, particularly sodium and potassium derangements, in fatal AlP cases.

Hosseinian et al. [17] found similar results, and they correlated hypernatremia with poor outcomes and explained this by the dehydration associated with the severe vomiting in cases of severe AlP poisoning, in addition to the aggressive initial management of the shock by saline solution as a first aid tactic by the first medical caregivers.

Changes in serum sodium and TLC may be influenced by factors such as volume resuscitation, corticosteroid use, or stress leucocytosis, which were not controlled for in this study.

Serum potassium levels were lower in both groups, with non-survivors showing a greater degree of hypokalemia, although the difference did not reach statistical significance. Hypokalemia is a well-documented metabolic disturbance in AlP poisoning and is thought to result from a multitude of causes, the severe vomiting following the intake of the pill, which happened in most of the cases in this study; intracellular shifting due to metabolic acidosis; and phosphine-induced inhibition of oxidative phosphorylation. Madhumathi et al. [18] also reported a trend toward hypokalemia in non-survivors, while Bogale et al. (2021) highlighted potassium imbalance as a common feature in severe cases. Moreover, El-Sarnagawy [15] reported that a low potassium level was related to mortality in AlP acute intoxicated cases. However, as in our study, potassium alone was not found to be a reliable predictor of mortality. ROC analysis yielded an AUC of approximately 0.58, suggesting limited discriminatory ability [16, 18].

Importantly, our findings align with the literature suggesting that no single biochemical test is sufficient on its own to predict outcomes in AlP poisoning [18, 19]. However, simple markers like serum sodium and TLC, when used alongside clinical assessment and scoring systems, may provide early cues for risk stratification—particularly in low-resource settings where access to advanced diagnostics is limited [15, 16].

Taken together, TLC may offer early prognostic insight, while LFTs and KFTs appear less reliable in the acute phase. Future studies should consider serial measurements to capture delayed organ dysfunction. Our findings support the need for integrating simple markers into broader clinical scoring systems for improved prognostication in resource-limited settings.

This study's strengths include its prospective design and focus on accessible tests. Future research should aim to validate these findings across larger, multicenter cohorts and assess whether combining these parameters into composite scores improves prognostic accuracy

The main limitations of this study are the small sample size and short study duration, which reflects the emergency nature and high acuity of aluminum phosphide poisoning cases, often leading to early mortality or rapid deterioration before inclusion. In accordance with the clinical protocol, all laboratory samples were collected as early as possible after admission to guide urgent management decisions. While this approach aligns with real-world emergency care, it may not capture delayed biochemical changes, limiting the ability to assess the full trajectory of organ dysfunction. Finally, no multivariable adjustment (e.g., for initial severity or treatment) and no validation cohort or internal cross-validation were done.

CONCLUSION

Serum sodium showed a statistically significant association with in-hospital mortality in acute AlP poisoning and may serve as a candidate prognostic marker. Moreover, total leukocyte count also showed a non-significant trend toward poor outcome. However, given the small sample, further studies with larger sample sizes and serial testing are warranted to validate these observations and support their integration into standardized prognostic models.

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Conflict of interest: The authors declare that they have no competing interests.

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