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PROGNOSTIC FACTORS IN ACUTE ALUMINIUM PHOSPHIDE POISONING: A PROSPECTIVE STUDY AT TERTIARY CARE HOSPITAL FROM NORTH INDIA

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ABSTRACT

Aluminum phosphide (ALP), an inexpensive solid fumigant, is frequently used for grain conservation despite its alleged high toxicity. Increased utilization of ALP for agricultural and non-agricultural purposes during the last four decades has resulted in increment of ALP-attributed poisoning numbers. Moreover, due to its limitless accessibility in developing countries, ALP has been increasingly used for suicide. Moisture-exposed ALP undergoes a chemical reaction producing phosphine gas, which in turn inhibits cytochrome oxidase and impedes cellular oxygen consumption. Lethality remains elevated reaching rates of >50% and no effective antidote is available. Nevertheless, experimental and clinical studies suggested that magnesium sulfate, melatonin, *N*-acetylcysteine, glutathione, sodium selenite, vitamin C and E, triiodothyronine, liothyronine, vasopressin, milrinone, *Laurusnobilis* L., 6-aminonicotinamide, boric acid, acetyl-L-carnitine and coconut oil, may serve as antidotes by reducing the deleterious oxidative properties of ALP. Commercial formulations, which usually contain 55 to 75% active ingredient, are sold in the form of tablets. Aluminum phosphide is available without restriction in some countries. In India, for example, ALP poisoning, which was almost nonexistent a three decade ago, has now reached epidemic proportions, and many reports of high mortality (> 50%) have recently been published . Pellets of solid aluminum phosphide react rapidly with water Aluminium phosphide (AlP) is a toxic agent associated with a high mortality rate following acute exposure from various routes. The aim of this study was to determine the clinical and laboratory findings useful for predicting the medical outcome of ALP-poisoned patients using established scoring systems. This is a prospective study of ALP-poisoned patients from 2008 to 2017 at UP University of Medical Sciences from North India. All patients that presented with a confirmed diagnosis of acute ALP poisoning in the study interval were included in the study. Clinical and laboratory data, using Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA) and Simplified Acute Physiology Score II (SAPS II) scoring systems, were compared for their predictive value in determining differences between survived and non-survived patients. Univariate analysis (t-test), multiple logistic regression analysis, receiver operating characteristic (ROC), curve analysis and the Pearson correlation test were performed using STATA/SE 13.0 and the Nomolog Software**.** A total of 38 ALP-poisoned patients with confirmed acute ALP poisoning were included for evaluation. Of these, 18 were non-survived. Multiple logistic regression analysis was performed using parameters and values derived from patient clinical and laboratory data, and revealed that four factors were significant for predicting mortality: Glasgow coma score (GCS); systolic blood pressure (SBP); urinary output (UOP); and serum HCO_3. A four-variable, risk-prediction nomogram was developed for identifying high-risk patients and predicting the risk of mortality. Study results showed that SBP of <92.5 mmHg (p = 0.006); HCO_3^- < 12.9 mEq/L (p = 0.01), UOP < 1725 mL/day (p = 0.04); and GCS < 14.5 (p = 0.003) were significant predictors of ALP mortality. Scoring systems analysis showed SAPS II score >24.5, APACHE II score >8.5 and SOFA score >7.5 were predictive of non-survival patients. The results of our study showed that SBP, GCS, UOP and serum HCO_3 levels are the best prognostic factors for predicting mortality in ALP-poisoned patients.

INRODUCTION

Aluminum phosphide (AlP) has been extensively used on account of its ideal properties like leaving little residue on food grains and exterminating insects with no impact on seed viability.[1,2,3] However, its widespread use has contributed to a marked increase in the related suicidal.[3,4,5] and accidental poisonings.[6,7,8] with high-risk mortality.[10,11,12] Due to unlimited and uncontrolled accessibility, ALP poisoning is one of the most common causes of poisoning in the developing countries such as India.[12,13,14,15,16,17,18] ALP-poisoned cases have been also reported from developed countries.[19,20,21,22]

Following ALP ingestion, reaction with hydrochloric acid in the stomach produces a lethal gas called "phosphine" (PH_3) (Fig. 1). Interestingly, prompt liberation of this gas following exposure to atmospheric moisture, has also made AlP a potential chemical terrorism agent.[23,24,25] Phosphine induces cellular hypoxia by affecting the mitochondria.[26,27,28,29] inhibits cytochrome c oxidase,[30] and leads to formation of highly reactive hydroxyl radicals,[29.30] The signs and symptoms of ALP intoxication are nonspecific and appear instantaneously,[26,29] ALP-related fatality is attributed to cardiac failure caused by inhibition of cytochrome c oxidase, decrement of adenosine triphosphate (ATP) production and cardiomyocyte impairment,[25,31] Oxidative stress has been shown to play a major role in ALP toxicity,[31,32] Nevertheless, AlP-induced inhibition of cytochrome c oxidase as the underlying cause of AlP toxicity, has raised controversies.[32.33] No definitive antidote has been proven clinically efficient ALP toxicity is mainly treated by supportive approaches including intra-aortic balloon pump and extracorporeal membrane oxygenation (ECMO), a recent promising technique that provides temporary cardiorespiratory support.[30,31,32] Here, we discuss the pros and cons of different agents suggested as potential antidotes for ALP.

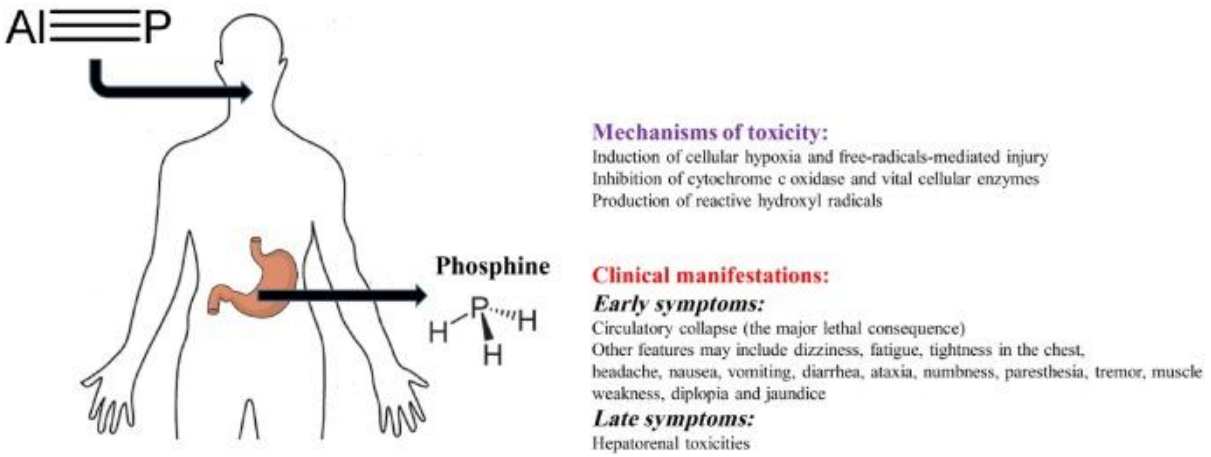

Fig. 1: Pathophysiology of aluminum phosphide (AlP) intoxication. After ingestion, AlP reacts with stomach acid and releases phosphine (PH_3) gas. PH_3 reaches the heart through the systemic circulation and causes myocardial cell death and arrhythmias.

Aluminium phosphide (AlP) is a type of fumigant that is applied to protect stored grains.[25,33] ALP is available in 3-g tablets, each tablet containing 56% (total 1680 mg) aluminium phosphide and 44% ammonium carbonate When ALP is exposed to moisture and an acid environment, a highly toxic phosphine gas is generated It is an important cause of suicidal poisoning, resulting in a high mortality rate in Asian countries such as Iran and India. ALP is highly toxic, cheap and easily accessible, which is the reason for its being one of the leading factors for severe poisoning in developing countries. Ready accessibility to this fumigant insecticide and its consequent use as a suicidal agent in Asian countries has led to it being considered a major public health issue, particularly because no definitive treatment or antidote is available for treating acutely poisoned patients Current medical management is to provide supportive care for almost all cases, until the toxicant has been cleared through the lungs and kidney There is an extremely high ratio of death in ALP poisoning, even when patients are in the intensive care unit. This ratio may equal 30 to 100% and potentially amount to more than 60%, even in high-level specialized hospitals with advanced life-support equipment. Many ALP-poisoned patients deteriorate despite proper supportive treatment, and a known antidote does not exist. In fact, it is one of the most significant causes of fatal poisoning worldwide.

Simplified Acute Physiology Score II (SAPS II), Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scoring systems are widely used in intensive care units (ICUs) to predict patient survival outcome. In the speciality of medical toxicology,[22,25,33] the performance of these systems in the prediction of ALP-poisoned patient outcome has been evaluated in only a few published studies.

METHOD

This was a prospective study of all acute ALP-poisoned patients from 2008 to 2017 admitted to the ICU of UP University of medical Sciences,India, Inclusion in the study of ALP-poisoned patients was based on a history of taking an ALP tablet, clinical findings and a confirmed positive silver nitrate test (SNT), which was performed at the time of admission . As it is a relatively low-sensitivity test and may yield false-negative results for certain patients, the patients were also assigned as ALP-poisoned if they had a history of previous ALP ingestion (according to the remarks of the patient or their closest relative) and presented with relevant clinical manifestations (SBP <80mm Hg/; serum HCO_3 < 15meq/L; pH < 7.2) despite a negative SNT. Exclusion criteria were being <15 years of age, dissolving the tablet(s) in water before ingestion, ingestion of air-exposed ALP tablets, diagnosis of an underlying chronic disease (e.g. diabetes mellitus and renal failure), co-ingestion of other drugs or having concomitant acute pathology with ALP intoxication (such as burns and trauma).Acute ALP poisoning was managed by supportive approaches because no specific antidote exists for this type of poisoning. The patients were treated and managed according to a single protocol that included calcium gluconate 10% (1 g for the initial dose, then 1 g every 6 hr, intravenously), magnesium sulphate (1 g initially, and then 1 g every 6 hr, intravenously), hydrocortisone (initially 200 mg and then 200 mg every 6 hr, intravenously), vitamin E (400 units, intramuscular injection), vitamin C (1000 mg every 12 hr, intravenous injection) and sodium bicarbonate ($NaHCO_3$, intravenously) administration for treatment of acidosis. Other standard therapies included the administration of inotropic medications, intravenous fluids and electrolyte resuscitation, intubation and mechanical ventilation and, if indicated, anti-arrhythmic agents.

Patient history included demographic data, time between ALP consumption and hospital admission, biochemical laboratory value results, ICU length of stay, hospital length of stay, APACHE II, SAPS II and SOFA scores, and a clinical outcome assessment. Patients were compared and categorized into two groups considering the outcome: survived and non-survived. The Simplified Acute Physiology Score II (SAPS II) calculator yields an integer point score from 0 to 163. This system consists of the following 15 items: age, type of admission, body temperature, heart rate, systolic blood pressure (SBP), Glasgow coma score (GCS), partial pressure of oxygen (PaO_2), urine output (UOP), serum urea or blood urea nitrogen (BUN), sodium(Na), potassium (K), bicarbonate(HCO_3), bilirubin, white blood cell count (WBC) and chronic disease history.Data analysis was performed using SPSS Statistics Software (version 19) and R 3.3.1 with the Package ‘pROC’ statistical software. Data were reported as mean (±SD). t-test was used to test normal distribution of numerical variables. Student's t-test was used for two-group comparisons of continuous variables. Variables that were significant (<0.1 in the univariate analysis and t- test) were evaluated using multiple logistic regression models. Multiple logistic regressions were then applied on variable clusters for the different parameters of APACHE II, SAPS II and SOFA. Significant variables from each cluster were included in the final model. Odds ratios (ORs) with confidence intervals (CIs) were calculated. The goodness-of-fit of the multiple regression models was evaluated using the Hosmer and Lemeshow test, and the results were used to generate a nomogram. STATA/SE 13.0 and the Nomolog program were used to generate a Kattan-style nomogram, a nomogram used for binary logistic regression predictive models. To investigate relationships between variables, the Pearson Correlation or Spearman Correlation was used. Because the APACHE II, SAPS II and SOFA systems had collinearity with each other in analysing mortality, they were not included in the multiple logistic regression models. Also, there was a collinearity between the HCO_3 and pH variables so that the HCO_3 was included in the final model.

RESULTS

A total of 62 cases with suspected ALP ingestion were referred; however, 28 were excluded because of having dissolved the tablet(s) in water before ingestion, ingesting air-exposed ALP tablets or had a confirmed negative SNT result. These cases may have involved the ingestion of non-toxic tablets, or they may have been mild cases of acute ALP poisoning whose diagnoses could not be confirmed.

Thirty four ALP-poisoned patients met the inclusion criteria and were studied, and of these, 18(52.9%) died (not survived) while the remaining 16 (47.1%) survived. The mean age was 25.0 ± 7.3 years (range, 16–49 years). The mean number of tablets ingested was 1.6 ± 1.1(range, 0.25–4) with 40% of patients having been poisoned with only one tablet. The median time for hospital admission after ingestion was 3.0 hr (range, 1.0–5.0) (table-1). Greater than half of the patients (59.1%) exhibited an abnormal electrocardiographic (ECG) record.

Table 1: Comparison of different variables in the survived and non-survived groups according to outcome.

Variable	Total (*n* = 34)	Survived	Non-survived	*p*-value
SAPS II score	30.50 ± 9.42	25.31 ± 6.23	35.11 ± 8.93	<0.001
APACHE II score	8.41 ± 4.61	4.81 ± 2.96	11.61 ± 3.24	<0.001
SOFA score	7.0 [6.0–8.75]	6.0 [6.0–7.0]	8.0 [8.0–9.0]	<0.001
Age (years)	23.0 [20.0–28.0]	21.0 [19.5–27.0]	24.0 [20.0–31.0]	0.14
ICU (days) length of stay	3.0 [1.0–4.0]	4.0 [3.0–5.0]	1.0 [1.0–2.0]	<0.001
Hospital (days) length of stay	3.0 [1.0–5.0]	5.0 [4.0–5.0]	1.0 [1.0–1.0]	<0.001
SBP (mmHg)	87.56 ± 18.49	97.96 ± 15.36	78.34 ± 16.10	<0.001
DBP (mmHg)	60.34 ± 11.27	62.15 ± 11.16	58.75 ± 11.29	0.22
UOP (mL/day)	2090.44 ± 1742.19	2717.19 ± 2258.66	1533.33 ± 783.22	0.004
Na (mEq/l)	141.06 ± 4.73	140.38 ± 4.41	141.65 ± 4.98	0.28
GCS	15.0 [12.0–15.0]	15.0 [15.0–15.0]	12.0 [12.0–15.0]	<0.001
K (mEq/l)	4.10 ± 0.81	4.21 ± 1.04	4.01 ± 0.54	0.32
Creatinine (mg/dL)	1.01 ± 0.39	0.90 ± 0.19	1.10 ± 0.49	0.04
PO_2 (mmHg)	83.84 ± 43.04	90.48 ± 43.86	77.76 ± 41.96	0.23
WBC ($10^3/\mu L$)	11.84 ± 5.73	11.33 ± 5.71	12.30 ± 5.78	0.49
pH	7.27 ± 0.13	7.35 ± 0.08	7.19 ± 0.13	<0.001
HCO_3 (mEq/L)	14.2 [10.25–17.2]	16.0 [13.7–17.2]	10.9 [8.6–17.2]	0.001
HCT (%)	39.68 ± 6.07	38.92 ± 7.16	40.36 ± 4.97	0.34
BS (mg/dL)	120.58 ± 59.46	112.45 ± 47.98	127.33 ± 67.47	0.32
HGB (g/dL)	13.31 ± 2.34	13.69 ± 2.31	12.96 ± 2.35	0.29
BUN (mg/dL)	13.69 ± 4.05	13.03 ± 4.72	14.27 ± 3.31	0.23
$PaCO_2$ (mmHg)	30.53 ± 9.49	29.81 ± 7.97	31.18 ± 10.77	0.56
ECG record				
Abnormal	37 (66.1%)	13 (48.1%)	24 (82.8%)	0.006
Normal	19 (33.9%)	14 (51.9%)	6(17.2%)	

SAPS, Simplified Acute Physiology Score; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; SBP, systolic blood pressure; DBP, diastolic blood pressure; Na, sodium; K, potassium; WBC, white blood cell; GCS, Glasgow coma score; HCO_3, serum bicarbonate; UOP, urine output; HCT, haematocrit; BUN, blood urea nitrogen; ECG, electrocardiography.

Values are the mean ± the standard deviation.

Significant differences were observed between survived and non-survived groups according to the SAPS II score, APACHE II score and SOFA score ($p < 0.001$) (table 1).

Using the multiple logistic regression analysis model, it was determined that four factors were significant for predicting mortality ($p < 0.05$) including GCS, SBP, UOP and HCO_3. Moreover, the death rate rose 0.91 times per unit of SBP increase (table-2). Based on the results of this study, the sensitivity, specificity and area under the curve for this multiple logistic regression model were 89.7%, 87.9% and 95.2%, respectively.

Table 2: Prognostic factors in predicting mortality using multiple logistic regression analysis.

Variable	Coefficient	SE	OR	95%CI	*p*-value
GCS	−1.40	0.48	0.24	0.09–0.63	0.003
SBP	−0.10	0.04	0.91	0.84–0.97	0.006
UOP (mL/day)	−0.001	0.001	0.99	0.98–0.99	0.04
HCO_3 (mEq/L)	−0.31	0.14	0.70	0.53–0.93	0.01
Cr (mg/dL)	1.81	1.76	6.16	0.19–19.4	0.30

GCS, Glasgow coma score; SBP, systolic blood pressure; UOP, urine output; HCO_3, serum bicarbonate; Cr, creatinine.

Nomogram development

A nomogram was developed using the four independent variables (GCS, SBP, UOP and HCO_3) that predicted in-hospital mortality. The nomogram was characterized by one scale corresponding to each variable; a total score scale, individual variable score scale and a probability scale (fig.2). The use of the nomogram involves three steps: 1) on the scale of each variable, the value corresponding to a specific patient is read, and then, the score scale is used to determine the scores of all variable values; 2) the total score is calculated by aggregating all the scores derived in the previous step, and its value is identified on the total score scale; 3) the probability of an

event corresponding to the total score in question is read on the probability scale (fig.3).

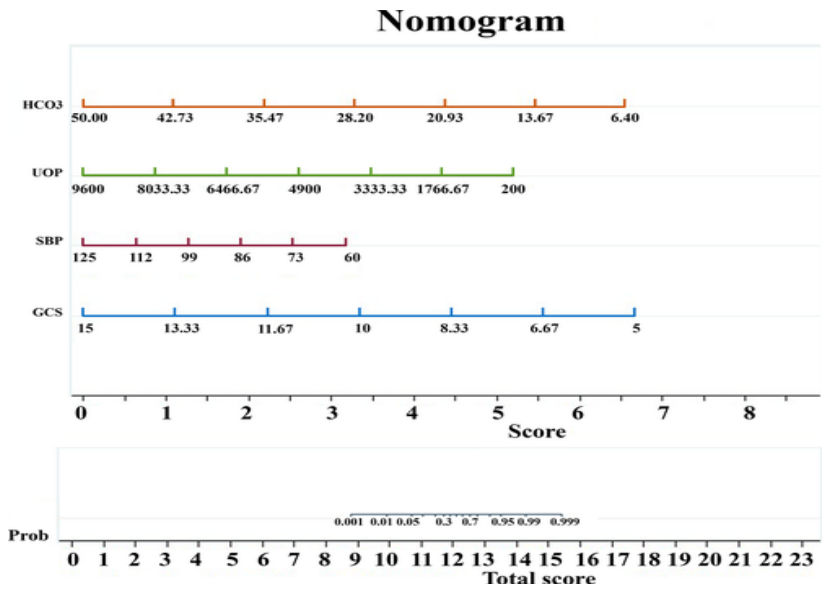

Figure 2: Risk-prediction nomogram for mortality in aluminium phosphide-poisoned patients admitted to the intensive care unit (ICU), incorporating GCS, SBP (mmHg), UOP (mL/day) and HCO3(mEq/L). GCS, Glasgow coma score; SBP, systolic blood pressure; UOP, urine output; HCO3, bicarbonate.

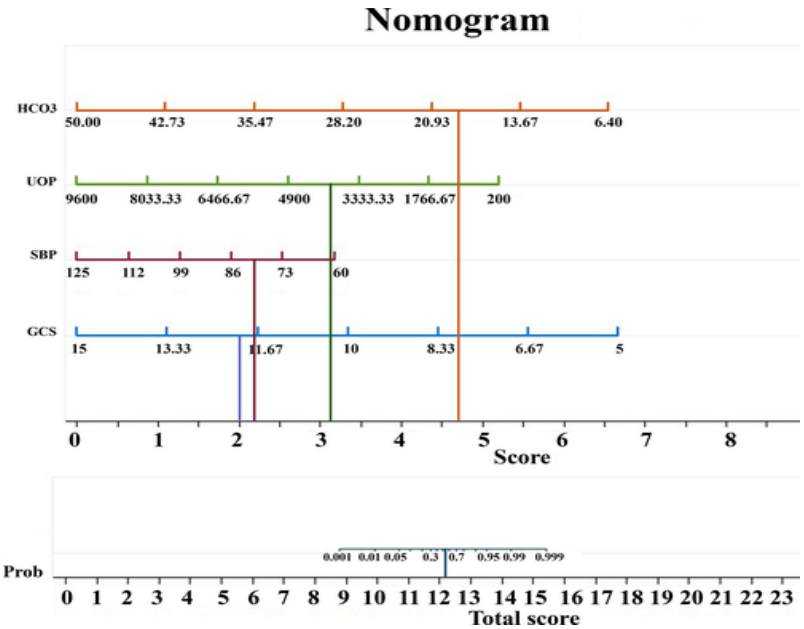

Figure 3: An example using the risk-prediction nomogram in a patient with aluminium phosphide poisoning. A line is drawn downward from the value of each category to the score line. The points are then added to determine the total score, and a line is drawn upward to find the risk of mortality. Death probability estimation: GCS: 12 _ score =1.98, SBP (mmHg):80 _ score = 2.3, UOP (mL/day):4000 _ score =3.2, and HCO3 (mEq/L):19 _ score = 4.7. Total score = 12.2, with a death probability of 0.63.

Based on the ROC curve analyses, a HCO_3 <12.9 mEq/L, UOP <1725 mL/day, SBP <92.5 mmHg and GCS <14.5 are able to predict mortality (fig.4). The APACHE II score best cut-off point between survived and non-survived patients was determined to be 8.5 with a sensitivity of 90.6% and specificity of 91.7%. Additionally, the SAPS II score and SOFA score best cut-off points between survived and non-survived patients were found to be 24.5 and 7.5, considering a sensitivity and specificity of 56.2% and 100.0%, 93.8% and 77.8%, respectively. Based on the AUC measures (93.3%), APACHE II demonstrated a better discriminatory power compared with SAPS II and SOFA (fig. **5**).

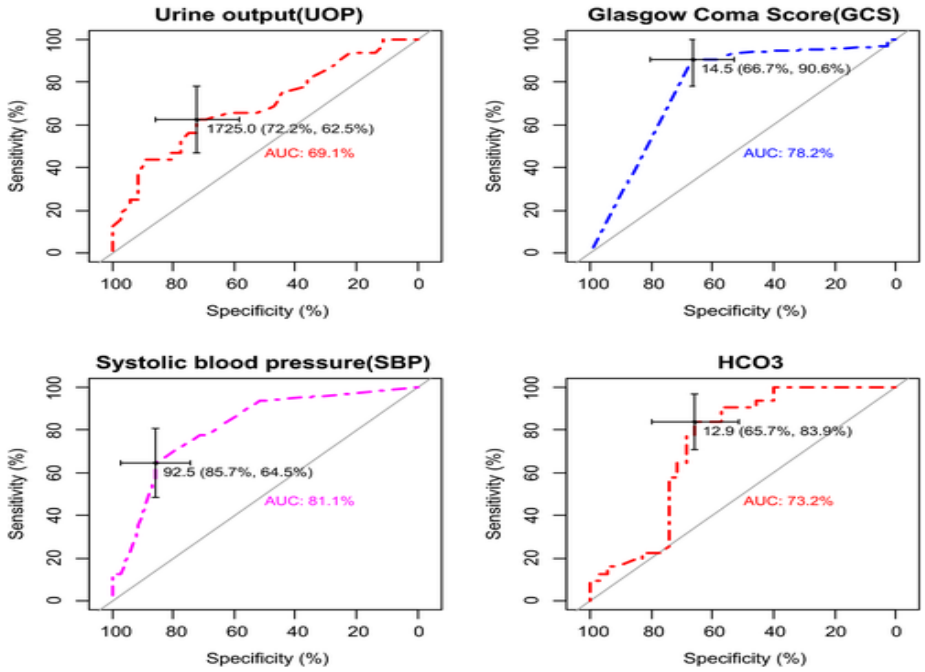

Figure 4: Receiver operating characteristic curve analysis to evaluate the best cut-off point for SBP, GCS, UOP and serum HCO_3 levels, with its specificity and sensitivity of risk-prediction for AlP-poisoned patient survival.

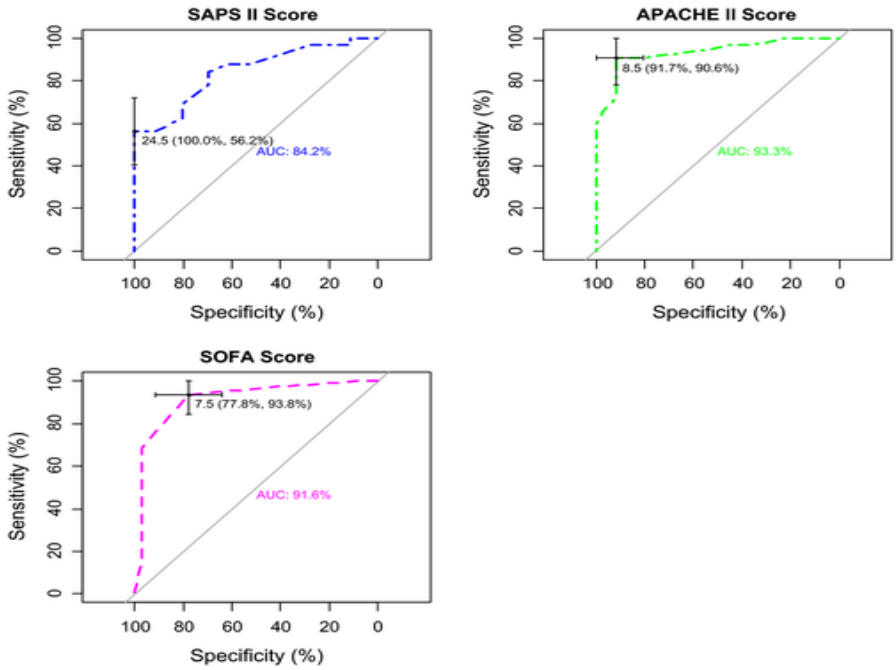

Figure 5: Receiver operating characteristic (ROC) curve analysis to evaluate the best cut-off point with its specificity and sensitivity for SAPS II, APACHE II and SOFA scores in assessing difference between survived and non-survived patients. APACHE II demonstrated a better discriminatory power between survivors and non-survivors compared with SAPS II and SOFA.

DISCUSSION

ALP is a fumigant with a high rate of mortality in cases of acute poisoning, estimated to be from 30 to 100%.[1,3,5] For a subject weighing 70 kg, the lethal dose is 150–500 mg.[26,27,34] The most prevalent clinical symptoms are due to cardiovascular toxicity that may result in cardiogenic shock and severe acidosis[2]

In the current study, the mean APACHE II, SAPS II and SOFA scores were 8.40 ± 4.60, 30.49 ± 9.42 and 7.34 ± 1.5, respectively. Ahuja *et al.*[14,35] found in their study of acute poisonings that among the cases of ALP poisoning, the mean APACHE II and SOFA scores at admission time were 10.6 ± 6.5 and 4.6 ± 4.0, respectively, which were in line with those of our study. Masson *et al.*[29,35] assessed SAPS II and SOFA scores in patients suffering from severe poisoning which resulted in

persistent shock or cardiac arrest and reported higher scores than those in the current study for SAPS II (66 ± 18) and SOFA (median: 11 [interquartile range (IQR), 9–13]). Very few studies have been conducted on the use of SOFA in AlP poisoning. The results of our study showed that the APACHE II score compared with SOFA and SAPS II can better discriminate between survivors and non-survivors. To the best of our knowledge, few studies have compared APACHE II, SOFA and SAPS II scores with respect to AlP poisoning. Results of our previous study using SAPS II also showed reasonable predictive outcome in patients suffering from acute AlP poisoning.[29,36] APACHE II, SOFA and SAPS II are three useful scoring systems previously used in predicting the necessity for intubation and ventilation in other types of poisonings, such as organophosphate and parquet poisoning.[33,34,36] Banderas-Bravo *et al*.[31] concluded APACHEII and APACHEIII provide proper predictions about mortality, while SAPS III overestimated mortality in poisoned patients admitted to the ICU. Additionally, the results obtained by Alizadeh *et al*.[31] and Ratanarat *et al*.[31,34] showed APACHE II had a greater power than SAPS II in determining the final outcome.[36,37] However, results of the current study revealed that a SAPS II score >24.5, APACHE II score >8.5 and a SOFA score >7.5 were able to predict acute AlP-poisoning mortality with acceptable sensitivity and specificity. Cut-off values are different between AlP-poisoned cases and those obtained involving other types of intoxication. For instance, APACHE II scores higher than 11 and 16.5 and SAPS II scores higher than 28 and 29.5 were determined to provide more accurate predictions for the mortality in organophosphate-poisoned patients.

According to our results, systolic blood pressure of <92.5 mmHg, HCO_3 <12.9 mEq/L, UOP <1725 mL/day and GCS <14.5 predicted acute AlP poisoning mortality with good sensitivity and specificity. Very few studies have shown the best cut-off point in laboratory tests to predict acute AlP-poisoning mortality.[15,37] Rehab *et al*. concluded that the best cut-off points for pH and HCO_3 that can predict mortality of poisoned patients were pH <7.27 and HCO_3 <13.3.

According to the results determined using multiple logistic regressions, serum HCO_3, SBP and UOP were predictive prognostic factors of mortality in AlP poisoning.[38,39,40]

Louriz *et al*. found that in AlP poisoning, the prognostic factors included in determining the APACHE II score were a lower GCS, acute kidney injury, shock, abnormalities in the electrocardiogram, low prothrombin time, hyper-leucocytosis, use of vasopressors drugs and the use of mechanical ventilation. Their study, which used a multivariate analysis, indicated a correlation between mortality in acute AlP poisoning and shock and altered consciousness.[38,40]

In another study by Shadnia *et al*. variables such as SBP, GCS, HCT, WBC, blood sugar level, BUN, SAPS II score, blood pH, ECG and the number of AlP tablets ingested were also effective for predicting patient outcome.

Sulaj reported that the dose of AlP ingested, the interval between ingestion and the beginning of treatment, and the depth of coma were the predictors of mortality in patients poisoned with AlP tablets. Erfantalab demonstrated that certain factors such as blood pressure, heart rate, blood pH and serum bicarbonate levels were significantly different between people who died due to acute AlP poisoning and those who survived after AlP tablet ingestion.

Soltaninejad *et al*.[41,42] reported that systolic blood pressure and ECG changes were the predictors of mortality among patients with acute AlP poisoning.[43] Shadnia *et al*. also found a statistically significant difference in blood pH and HCO_3 between people who died due to acute AlP poisoning and those who survived.

Association of these factors with mortality in patients with acute AlP poisoning can be attributed to the pathological effects of phosphine on different organs that lead to the production of free radicals and damage to various body tissues through inhibiting cytochrome oxidase. This damage is more severe in highly perfused organs that require high amounts of oxygen such as the brain, heart and kidneys. Factors derived to be the predictors of death in the current study can be associated with phosphine effects on such vital organs.

Neurotoxicity due to acute AlP poisoning is exhibited by clinical changes such as headache, restlessness, stupor, convulsion and finally CNS depression and coma.

Patients with low GCS are susceptible to different complications such as aspiration pneumonia because of lack of airway refluxes. As the GCS is a scoring system known to assess brain function and predict the results of nervous system integrity.[41,42,43] physicians should take into consideration the levels of poisoned patients' consciousness, in addition to careful documentation of their medical history. In our study, GCS was determined to be a useful prognostic factor.

AlP-induced toxic myocarditis causes severe haemodynamic changes that eventually lead to hypotension which is resistant to fluid therapy and inotropes, and is considered the main cause of death in patients with AlP poisoning.[44,45] The frequency of shock and hypotension in patients with acute AlP poisoning has been reported to vary from 76 to 100%. Shock and hypotension accompanied by certain factors such as disseminated intravascular coagulation and acute tubular necrosis can ultimately result in renal failure in such patients. Because phosphine gas is released through respiration and urination, inadequate renal perfusion and

inappropriate urinary output can affect outcome in cases of acute AlP poisoning.[43,45]

We have developed a specific nomogram using four independent variables to predict the risk of mortality among acute AlP-poisoned patients. To the best of our knowledge, few studies have yet been conducted to suggest a risk-prediction nomogram to investigate in-hospital mortality in patients with acute AlP poisoning. Lionte *et al*.[43] were the first to develop a seven-variable risk-prediction nomogram for patients with acute poisoning due to non-pharmaceutical agents and drugs at admission to the emergency department (ED).

Currently, there are nomograms available that are used to identify the benefits of antidote therapy in cases of acetaminophen poisoning and toxicity, and arrhythmia risk assessment and to guide the appropriate duration of haemodialysis in cases of acute methanol poisoning.[45] using a formula or algorithm involving several predictors modelled as continuous variables to predict an end-point, according to traditional statistical methods, such as multiple logistic regression and Cox proportional hazards analysis. Nomograms also offer optimal individualized disease-related risk estimations that simplify patient management-related decision-making.[45] Our developed risk-prediction nomogram may have a benefit over traditional tools, such as poisoning severity score (PSS), GCS or other clinical scores, because the association between predictors (GCS, HCO_3, SBP and UOP) and the predicted variable (death) can be readily determined.

According to our results, SBP, GCS, UOP and serum HCO_3 levels are the best prognostic factors of mortality in AlP-poisoned patients admitted to the ICU. We developed a four-variable risk-prediction nomogram that provides quick and simple analysis to identify high-risk patients and predict the risk of mortality. Physicians could apply this user-friendly instrument to detect cases of acute poisoning at risk of death during a patient's stay in the ICU, to enhance patient management to prevent mortality, and to detect those patients who appear well at first but may then progress towards a fatal outcome. For the patients at high risk, certain invasive procedures, including extracorporeal membrane oxygenation (ECMO) and intra-aortic balloon pump (IABP), could be considered. The earlier investigations had only provided the variables influencing the mortality rate in patients with AlP poisoning; however, according to the findings of the present study, the mortality risk may be estimated and calculated numerically. This developed tool is a basic chart which, through the use of four independent variables, is able to provide a numerical estimation of the rate of death in patients with AlP poisoning. In addition, the developed nomogram is easy to use as all its required factors are readily and routinely gathered in the medical care setting, requiring only five minutes for measuring and determining the risk of death in AlP-poisoned patients.

In summary, the APACHE II score >8.5, SAPS II score >24.5 and SOFA score >7.5 and SBP of <92.5 mmHg, HCO_3,-.<12.9 mEq/L, UOP <1725 mL/day and GCS <14.5 were shown to predict the ALP-poisoned patient mortality rate with good specificity and sensitivity. The APACHE II score was determined to be the best discriminator between non-survivors and those who survive. The results of the current study of patients suffering AlP poisoning demonstrate the potential value of prognostic scoring systems for prediction of patient outcome in AlP-poisoned patients.

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