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Paper

Shock and modified shock indices in predicting poisoning severity and outcomes in acute aluminum phosphide poisoned patients

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Background: Severe refractory hypotension and cardiogenic shock are the main contributors to death in acute aluminum phosphide (ALP) poisoning. Shock index (SI) and modified shock index (MSI) are easily obtained parameters that reflect shock at an early stage.
Aim: This study aimed to evaluate the role of SI and MSI in the prediction of the severity and outcomes of acute ALP poisoned patients.
Patients and methods: This cross sectional study was conducted on patients admitted to Tanta University Poison Control Centre with acute ALP poisoning from April 2022 to March 2023. Socio-demographics and toxicological data were taken, findings of clinical examination and laboratory investigations were recoded, SI was calculated by dividing heart rate over systolic blood pressure, and MSI was obtained by dividing heart rate over mean arterial pressure. Poisoning severity was assessed using poisoning severity score (PSS). Patients were divided into groups according to intensive care unit (ICU) admission and mortality.
Results: The study enrolled 94 patients. The median values of SI and MSI were significantly higher in ICU-admitted patients and non-survivors rather than their comparable groups. Significant positive correlations were observed between each of SI and MSI and PSS. At cut-off >1.14, SI conveyed fair performance to predict ICU admission and mortality (AUC = 0.710 and 0.739, respectively). Similarly, MSI had fair performance to predict ICU admission (AUC = 0.731) and mortality (AUC = 0.744) at cut-off >1.47 and >1.5, respectively.
Conclusion: Both SI and MSI could be considered simple bedside adjuncts to predict ICU admission and mortality in acute ALP poisoning.

Key words: aluminum phosphide poisoning; intensive care unit; mortality; prediction; shock index; modified shock index.

Introduction

Aluminum phosphide (ALP) is a well-known pesticide that is used as a cheap fumigant in many countries to protect crops during transportation or storage.[1] Regrettably, ALP poisoning is associated with high mortality and has been identified as the most lethal pesticide poisoning.[2]

Toxicity is mediated through the release of phosphine gas when ALP tablets come in contact with the gastric acidity or exposed to the moisture in the surrounding environment. Phosphine is cytotoxic and causes oxidative stress. In addition, it inhibits cytochrome c oxidase enzyme and oxidative phosphorylation with adenosine triphosphate depletion and subsequently cellular death occurs.[3,4]

Among different body organs, heart is highly susceptible to mitochondrial dysfunction and oxidative stress caused by ALP toxicity because it is rich in mitochondria and has low antioxidant capacity. Cardiotoxicity is a critical event related to acute ALP poisoning that nearly 70% of fatalities were attributable to cardiovascular disorders with severe and refractory hypotension is the dominant clinical manifestation.[5,6] Accordingly, previous studies investigated the role of cardiac markers like troponin, electrocardiographic changes, and echocardiographic findings to predict the outcome of acute ALP poisoning.[7–9] However, to the best of the authors' knowledge, shock index (SI) and modified shock index (MSI) were not previously investigated with regard to ALP poisoning.

Shock index is a simple bedside assessment parameter determined easily by dividing the heart rate (HR) over the systolic blood pressure (SBP). Modified shock index is defined as the ratio between HR and mean arterial pressure (MAP).[10] Shock index can evaluate acute hypovolemia and bleeding, as well as, acute circulatory failure and was found as an independent predictor of microvascular damage and extent of myocardial injury. Moreover, it may reflect the worsening of stroke volume, cardiac index, and left ventricular stroke work.[11] Remarkably, MAP is thought to be the best evaluator for organs perfusion compared with SBP and diastolic blood pressure (DBP) alone and is considered the recommended indicator for deciding fluid resuscitation and vasopressors titration.[10]

Both SI and MSI were previously investigated in patients with different clinical conditions including trauma,[12] sepsis,[13,14] COVID-19 infection,[15] and acute myocardial infarction.[16] However, after meticulous search through the literature, only one study has investigated SI in the field of clinical toxicology. Lau and Wong[17] conducted a study on calcium channel blockers poisoned patients and found that, using univariate and multivariate regression analysis, SI was significantly associated with life-threatening manifestations, mortality, and ICU admission. They

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also concluded that higher SI is associated with more serious patient outcome.

Hence, the current study aimed to evaluate the role of SI and MSI in predicting the poisoning severity and outcomes (intensive care unit [ICU] admission and mortality) in patients with acute ALP poisoning.

Patients and methods

Study design and setting

The current cross-sectional study was conducted on patients with acute ALP poisoning who were admitted to Tanta University Poison Control Centre, Tanta Emergency Hospitals, Egypt during the period from April 2022 to March 2023.

Ethical consideration

The study followed the World Medical Association Declaration of Helsinki and was conducted after the agreement of our institution ethics committee (Approval code: 35329/2/22). A written informed consent was obtained from each patients or his/her guardian in case of incompetency. To maintain patients' confidentiality, a code number was assigned for each patient for anonymous analysis of the collected data.

Inclusion criteria

All male and female patients with the age of 18 years or more and presented with symptomatic acute ALP poisoning were enrolled in the study. Diagnosis depended upon the history of exposure, requesting the container if available, presence of suggestive clinical manifestations (such as: metabolic acidosis, hypotension, and typical garlic odor of breath), and performing silver nitrate test on the gastric aspirate to detect phosphine gas.[18,19]

Exclusion criteria

The current study excluded patients with co-exposure of other pharmaceutical or non-pharmaceutical preparations and patients with comorbidities such as cardiovascular, hepatic, or renal disorders. Patients who gave a history of acute ALP exposure, but remained asymptomatic during the in-hospital follow-up and those who received any medical intervention before admission to our center were also excluded.

Data collection

Patients who fulfilled the eligibility criteria were subjected to history taking including socio-demographics (age, sex, and residence), toxicological history (route of exposure, alleged mode of poisoning, and time interval between exposure and hospital admission). Findings of initial clinical assessment including HR, SBP, DBP, MAP, and respiratory rate (RR) were recorded, as well as, the level of consciousness as assessed by Glasgow Coma Scale (GCS), and oxygen saturation (O_2 saturation).

The following laboratory investigations were performed at admission and before the start of the treatment. Arterial blood gas (ABG) analysis (pH, HCO_3; serum bicarbonate, and $PaCO_2$; partial arterial carbon dioxide pressure) using pHOx plus L Stat profile calibrator cartridge C from Nova Biomedical GmbH, Germany (catalog number: 34086). Serum sodium (Na) and potassium (K) levels done using diestro electrolyte analyzer using ISE calibrating pack from Diestro, Argentina (catalog number: IN0100). Kidney function tests (urea and creatinine) and liver enzymes (AST; aspartate aminotransferase and ALT; alanine aminotransferase) were measured by Konelab Prime 60i apparatus using kits obtained from Thermo Fisher Scientifc-Finland (catalog numbers:, 981,820, 981,811, 981,769, and 981,771, respectively).

Grading the severity of the poisoning

To grade the severity of the poisoning condition of each patients, poisoning severity score (PSS) was applied according to the International Programme on Chemical Safety (IPCS). The grading was based on the patient's most severe symptoms or signs including five grades: grade 0 (no symptoms), grade 1 (mild transient with spontaneously resolving symptoms), grade 2 (pronounced or prolonged symptoms), grade 3 (severe or life-threatening symptoms), and grade 4 (death).[20]

Calculation of shock index and modified shock index

The following formulae were used to calculate SI and MSI[14]:

$$SI = HR/SBP$$
$$MSI = HR/MAP$$
$$MAP = [(DBP \times 2) + SBP]/3$$

Treatment

The included patients received the standard and routine treatment in the form of emergency treatment care to maintain patent airway, breathing, and circulation. Intravenous fluids and vasopressors (norepinephrine) were given for hypotensive patients. Gastric lavage was done using paraffin oil. Additionally, treatment of metabolic acidosis and any other expected manifestations was considered.

Outcome

According to the requirement of ICU admission, the enrolled patients were divided into ICU-admitted and non-ICU-admitted groups. Patients were also grouped according to mortality into survivors and non-survivors.

Criteria for ICU admission included hemodynamic instability, severe metabolic acidosis, respiratory distress, severe central nervous system depression, and the requirement for mechanical ventilation or vasopressor administration.[21]

Statistical analysis

Statistical analysis was carried out using the Statistical Package for Social Sciences (IBM SPSS Statistics), version 26 for Windows (IBM Corp., Armonk, N.Y., USA). Numerical variables were assessed for normality of distribution using the Shapiro-Wilk test. Variables following the normal distribution were summarized as the mean and standard deviation (SD), and the comparisons between the groups were done using the independent samples T-test. Variables not following the normal distribution were summarized as the median and interquartile range (IQR; expressed as the 25th–75th percentiles), and the comparisons were done using the Mann-Whitney test. Correlations between numerical variables were tested using Spearman's rank-order correlation. Categorical data were summarized as frequencies (count and percentage), and associations between categorical variables were done using Pearson's Chi-square test or Fisher's exact test. To assess the diagnostic performance of the studied scores, receiver operating characteristics (ROC) curve analysis was performed with identification of the optimal cut-off point and its associated sensitivity, specificity, positive and negative predictive values (PPV, NPV), and overall accuracy. A P-value <0.05 was chosen to define the significance of the statistical test results.

Table 1. Socio-demographics and toxicological data of patients with acute aluminum phosphide poisoning (n = 94).

	ICU admitted (n = 84)	Non-ICU admitted (n = 10)	P-value	Non-survivors (n = 68)	Survivors (n = 26)	P-value	Total (n = 94)
Age Mean ± SD (Min–Max)	27.5 ± 11.0 (18.0–57.0)	22.6 ± 6.9 (18.0–35.0)	0.178 t	28.8 ± 11.4 (18.0–57.0)	22.1 ± 6.7 (18.0–35.0)	<0.001* t	26.9 ± 10.7 (18.0–57.0)
Gender Male n (%) Female n (%)	36 (42.9%) 48 (57.1%)	5 (50.0%) 5 (50.0%)	0.743 X^2	33 (48.5%) 35 (51.5%)	8 (30.8%) 18 (69.2%)	<0.001* Z	41 (43.6%) 53 (56.4%)
Residence Rural n (%) Urban	77 (91.7%) 7 (8.3%)	6 (60.0%) 4 (40.0%)	0.015* X^2	61 (89.7%) 7 (10.3%)	22 (84.6%) 4 (15.4%)	0.490 X^2	83 (88.3%) 11 (11.7%)
Mode Suicidal n (%) Accidental n (%)	84 (100.0%) 0 (0.0%)	10 (100.0%) 0 (0.0%)	NA	68 (100.0%) 0 (0.0%)	26 (100.0%) 0 (0.0%)	NA	94 (100.0%) 0 (0.0%)
Route Oral Inhalation	84 (100.0%) 0 (0.0%)	10 (100.0%) 0 (0.0%)	NA	68 (100.0%) 0 (0.0%)	26 (100.0%) 0 (0.0%)	NA	94 (100.0%) 0 (0.0%)
Delay (hours) Median [IQR] (Min–Max)	2.0 [1.5–4.0] (0.5–6.0)	2.0 [1.0–2.5] (1.0–4.0)	0.195 Z	2.0 [1.3–4.0] (0.5–6.0)	2.0 [2.0–3.0] (1.0–6.0)	0.952 Z	2.0 [1.5–3.5] (0.5–6.0)

n: number, ICU: intensive care unit, SD: standard deviation, Min: minimum, Max: maximum, IQR: interquartile range (25^{th}–75^{th} percentiles), t: Independent samples T-test, Z: Mann–Whitney test, X^2: Pearson's Chi-square test/ Fisher's exact test, *significant at $P < 0.05$

Results

The current study included 94 acute ALP poisoned patients; of them 84 patients (89.4%) required ICU admission and non-survivors were 68 patients (72.3%). The age of the enrolled patients ranged from 18–57 years (mean ± SD: 26.9 ± 10.7 years) with female predominance (56.4%). Patients from rural areas constituted the major counterpart 88.3%. All patients alleged suicidal ingestion of ALP tablets. The delay time ranged from 0.5 to 6 h with median and [IQR] of 2.0 [1.5–3.5] hours. Table 1 shows socio-demographics and toxicological characteristics of the studied patients.

The initial clinical assessment and laboratory investigations results of the studied patients are illustrated in (Table 2). Pulse rate did not show significant difference between ICU-admitted and non-ICU-admitted patients, while it was significantly lower in non-survivors rather than the survivors ($P = 0.012$). The adverse outcome groups had significantly lower SBP, DBP, and MAP rather than their comparable groups. Conversely, ICU-admitted patients and non-survivors had significantly higher RR in comparison with non-ICU admitted and survived patients ($P < 0.001$ for each). Regarding GCS, a significant difference was observed between survivors and non-survivors ($P = 0.023$), while it did not show significant difference between ICU-admitted and non-ICU admitted groups. Oxygen saturation and HCO_3 were significantly lower in ICU-admitted patients compared with non-ICU admitted patients ($P < 0.001$ and 0.033, respectively). However, pH and $PaCO_2$ did not exhibit significant difference between ICU admitted and non-ICU admitted patients. Non-survivors had significantly lower O_2 saturation, pH, and HCO_3 rather than survivors ($P < 0.001$ for each) with no significant difference as regard to $PaCO_2$. The mean value of serum K level was significantly lower and median value of serum creatinine was significantly higher in non-survivors in comparison with the survivors ($P = 0.034$ and 0.006, respectively), however they did not show significant difference between ICU-admitted and non-ICU admitted patients. No significant difference was observed regarding serum Na level, blood urea, and liver enzymes (AST and ALT) between adverse outcome groups and their respective groups.

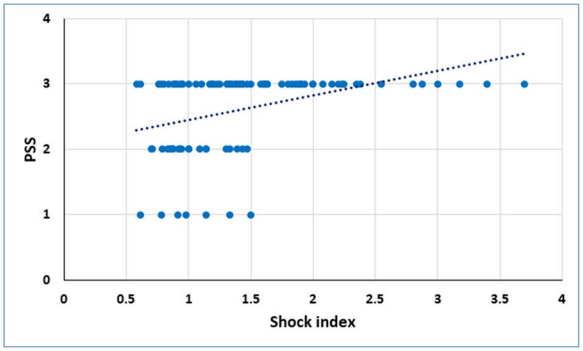

Fig. 1. Correlation between shock index and poisoning severity score (PSS) in acute aluminum phosphide poisoned patients.

As demonstrated in (Table 3), ICU-admitted patients and non-survivors had significantly higher median values of PSS ($P < 0.001$ for each). The median values of SI were significantly higher in ICU-admitted patients rather than non-ICU admitted patients (1.33 versus 0.97, $P = 0.031$) and in non-survivors compared with survivors (1.41 versus 0.95, $P < 0.001$). Similarly, MSI median value in ICU-admitted patients was significantly higher than non-ICU admitted patients (1.86 versus 1.27, $P = 0.017$) and it was also significantly higher in non-survivors (1.99) compared with the survivors (1.33) ($P < 0.001$).

A significant positive correlation was observed between SI and PSS ($r = 0.454$, $P < 0.001$). Similarly, MSI had significant positive correlation with PSS ($r = 0.482$, $P < 0.001$) (Figs 1 and 2).

Table 4 depicts the results of ROC curve analysis. Both SI and MSI were significantly valid to predict the need for ICU admission and mortality among ALP poisoned patients. At cut-off >1.14, SI conveyed fair performance to predict ICU admission (AUC = 0.710)

Table 2. Comparison between acute aluminum phosphide poisoned groups regarding initial clinical assessment and laboratory investigations (n = 94).

	ICU admitted (n = 84)	Non-ICU admitted (n = 10)	*P*-value	Non-survivors (n = 68)	Survivors (n = 26)	*P*-value	Total (n = 94)
Pulse rate (b/min)	90.1 ± 22.0	93.4 ± 18.3	0.648 t	87.0 ± 21.2	99.4 ± 20.1	0.012* t	90.4 ± 21.5
Mean ± SD	(36.0–148.0)	(63.0–120.0)		(36.0–136.0)	(63.0–148.0)		(36.0–148.0)
(Min–Max)							
SBP (mmHg)	70.0	85.0	0.021* Z	70.0	90.0	<0.001* Z	80.0
Median [IQR]	[40.0–90.0]	[80.0–90.0]		[40.0–80.0]	[80.0–110.0]		[40.0–90.0]
(Min–Max)	(40.0–150.0)	(70.0–160.0)		(40.0–150.0)	(40.0–160.0)		(40.0–160.0)
DBP (mmHg)	40.0	55.0	0.014* Z	35.0	55.0	<0.001* Z	40.0
Median [IQR]	[20.0–50.0]	[50.0–60.0]		[20.0–50.0]	[50.0–60.0]		[20.0–50.0]
(Min–Max)	(20.0–100.0)	(30.0–90.0)		(20.0–100.0)	(20.0–100.0)		(20.0–100.0)
MAP (mmHg)	53.3	65.0	0.019* Z	48.3	70.0	<0.001* Z	53.3
Median [IQR]	[26.7–63.3]	[60.0–70.0]		[26.7–56.7]	[60.0–76.7]		[26.7–70.0]
(Min–Max)	(26.7–116.7)	(46.7–113.3)		(26.7–116.7)	(26.7–116.7)		(26.7–116.7)
RR (cycle/minute)	27.1 ± 6.7	19.2 ± 4.4	<0.001* t	28.5 ± 6.1	20.4 ± 5.3	<0.001* t	26.3 ± 6.9
Mean ± SD	(16.0–48.0)	(15.0–30.0)		(16.0–48.0)	(15.0–40.0)		(15.0–48.0)
(Min–Max)							
GCS	15 [15–15]	15 [15–15]	0.204 Z	15 [15–15]	15 [15–15]	0.023* Z	15 [15–15]
Median [IQR]	(3–15)	(15–15)		(3–15)	(15–15)		(3–15)
(Min–Max)							
O_2 saturation (%)	88.6 ± 11.3	97.2 ± 2.0	<0.001* t	87.0 ± 11.8	96.2 ± 3.4	<0.001* t	89.6 ± 11.0
Mean ± SD	(35.0–100.0)	(93.0–99.0)		(35.0–100.0)	(86.0–100.0)		(35.0–100.0)
(Min–Max)							
pH	7.34	7.38	0.100	7.31	7.40	<0.001 * Z	7.35
Median [IQR]	[7.27–7.40]	[7.33–7.45]	Z	[7.25–7.37]	[7.35–7.45]		[7.28–7.40]
(Min–Max)	(7.03–7.55)	(7.30–7.48)		(7.03–7.55)	(7.12–7.52)		(7.03–7.55)
HCO_3 (mmol/L)	13.1	16.6	0.033* Z	12.8	17.5	<0.001* Z	13.8
Median [IQR]	[10.5–16.6]	[14.2–18.0]		[10.3–15.5]	[14.2–19.9]		[10.6–17.4]
(Min–Max)	(6.5–26.0)	(12.0–19.9)		(6.5–26.0)	(9.2–23.0)		(6.5–26.0)
$PaCO_2$ (mmHg)	24.3	23.9	0.516	23.6	27.0	0.147	24.3
Median [IQR]	[19.1–32.9]	[21.5–38.0]	Z	[18.7–31.9]	[22.0–34.6]	Z	[19.4–33.7]
(Min–Max)	(11.0–49.0)	(14.3–42.1)		(11.0–49.0)	(14.2–42.1)		(11.0–49.0)
K level (mmol/L)	3.57 ± 0.50	3.82 ± 0.48	0.130	3.53 ± 0.44	3.77 ± 0.61	0.034* t	3.60 ± 0.50
Mean ± SD	(2.10–5.20)	(3.08–4.59)	t	(2.80–4.40)	(2.10–5.20)		(2.10–5.20)
(Min–Max)							
Na level (mmol/L)	141.2 ± 5.4	141.6 ± 4.2	0.814 t	141.0 ± 5.3	141.7 ± 5.5	0.610 t	141.2 ± 5.3
Mean ± SD	(130.0–165.5)	(135.6–150.0)		(130.0–165.5)	(133.0–155.5)		(130.0–165.5)
(Min–Max)							
Serum creatinine (mg/dL)	1.10	1.00	0.303	1.15	1.00	0.006* Z	1.10
Median [IQR]	[1.00–1.30]	[1.00–1.20]	Z	[1.00–1.35]	[0.90–1.20]		[1.00–1.30]
(Min–Max)	(0.60–2.10)	(0.90–1.20)		(0.60–2.10)	(0.60–1.60)		(0.60–2.10)
Blood urea (mg/dL)	36.9 ± 11.5	33.6 ± 7.3	0.376	37.6 ± 11.8	34.0 ± 9.2	0.162	36.6 ± 11.2
Mean ± SD	(16.0–85.0)	(20.0–47.0)	t	(16.0–85.0)	(20.0–51.0)	t	(16.0–85.0)
(Min–Max)							
AST (U/L)	29.0	25.0	0.801 Z	30.0	25.0	0.337	29.0
Median [IQR]	[15.0–35.5]	[16.0–36.0]		[15.0–39.5]	[16.0–32.0]	Z	[15.0–36.0]
(Min–Max)	(7.0–150.0)	(15.0–74.0)		(7.0–150.0)	(10.0–74.0)		(7.0–150.0)
ALT (U/L)	24.0	19.5	0.717	26.5	18.0	0.196	23.0
Median [IQR]	[15.5–33.0]	[16.0–35.0]	Z	[15.5–34.5]	[16.0–27.0]	Z	[16.0–33.0]
(Min–Max)	(7.0–161.0)	(12.0–54.0)		(8.0–161.0)	(7.0–54.0)		(7.0–161.0)

n: number, IQR: interquartile range (25^{th}–75^{th} percentiles), Min: minimum, Max: maximum, SD: standard deviation, t: Independent samples T-test, Z: Mann–Whitney test, ICU: Intensive Care Unit, b/min: beats/minute, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial pressure, RR: respiratory rate, GCS: Glasgow Coma Scale, O_2 saturation: oxygen saturation, HCO_3: serum bicarbonate, $PaCO_2$: partial arterial carbon dioxide pressure, K: potassium, Na: Sodium, AST: aspartate aminotransferase, ALT: alanine aminotransferase, *significant at $P < 0.05$.

and mortality (AUC = 0.739). Similarly, MSI showed fair performance to predict ICU admission and mortality (AUC = 0.731 and 0.744, respectively) at cut-off >1.47 and >1.5, respectively.

Discussion

Over the last years, ALP has become a great challenge in many developing countries because of its wide availability and substantial toxicity that is associated with high morbidity and mortality.[22] In absence of specific antidote, intensive supportive care remains the backbone of ALP poisoning treatment. Therefore, early prognostic stratification of patients is critical to initiate appropriate interventions, including proactive ICU transfers and better allocation of limited resources.[19] Therefore, the current study aimed to evaluate the role of SI and MSI as simple parameters to predict the severity and outcomes of acute ALP poisoned patients.

Table 3. Comparison between acute aluminum phosphide poisoned groups regarding poisoning severity score, shock index, and modified shock index (n = 94).

Variables	ICU admitted (n = 84)	Non-ICU admitted (n = 10)	P-value	Non-survivors (n = 68)	Survivors (n = 26)	P-value	Total (n = 94)
PSS	3 [3–3]	2 [1–2]	<0.001* Z	3 [3–3]	2 [2–2]	<0.001* Z	3 [2–3]
Median [IQR]	(1–3)	(1–2)		(1–3)	(1–3)		(1–3)
(Min–Max)							
SI	1.33	0.97	0.031* Z	1.41	0.95	<0.001* Z	1.32
Median [IQR]	[0.94–1.84]	[0.86–1.14]		[1.07–1.90]	[0.86–1.20]		[0.93–1.75]
(Min–Max)	(0.58–3.70)	(0.61–1.50)		(0.58–3.40)	(0.61–3.70)		(0.58–3.70)
MSI	1.86	1.27	0.017* Z	1.99	1.33	<0.001* Z	1.83
Median [IQR]	[1.35–2.72]	[1.16–1.47]		[1.50–2.85]	[1.16–1.64]		[1.31–2.60]
(Min–Max)	(0.70–5.55)	(0.86–2.57)		(0.70–4.76)	(0.86–5.55)		(0.70–5.55)

n: number, IQR: interquartile range (25^{th}–75^{th} percentiles), Min: minimum, Max: maximum, Z: Mann-Whitney test, PSS: poisoning severity score, SI: shock index, MSI: modified shock index, *significant at $P < 0.05$.

Table 4. The receiver operating characteristic (ROC) curve analysis for shock index and modified shock index to predict the risk of ICU admission and mortality in acute aluminum phosphide poisoning.

Variables	AUC	95% CI	P-value	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
ICU admission									
SI	0.710	0.565 to 0.854	0.004*	>1.14	64.29	80.00	96.4	21.1	66.0
MSI	0.731	0.580 to 0.882	0.003*	>1.47	69.05	80.00	96.7	23.5	70.2
Mortality									
SI	0.739	0.629 to 0.849	<0.001	>1.14	72.06	73.08	87.5	50.0	72.3
MSI	0.744	0.634 to 0.854	<0.001*	>1.5	76.47	69.23	86.7	52.9	74.5

AUC: area under the curve, CI: confidence interval, PPP: positive predictive value, NPP: negative predictive value, PSS: poisoning severity score, SI: shock index, MSI: modified shock index, *significant at $P < 0.05$

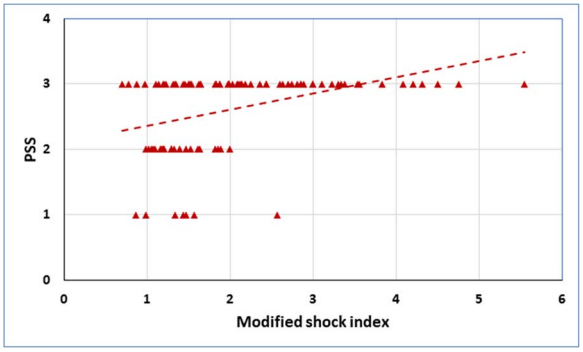

Fig. 2. Correlation between modified shock index and poisoning severity score (PSS) in acute aluminum phosphide poisoned patients.

In the current study, ICU admission and mortality were reported in 89.4 and 72.3% of the enrolled patients, respectively. According to Ahmed et al.,[23] ICU admission was reported in 69.3% of ALP poisoned patients. Furthermore, non-survivors represented 77.4 and 89% of acute ALP poisoned patients according to Dorooshi et al.[24] and Sakr et al.,[25] respectively. High incidence of ICU admission and mortality among ALP poisoned patients can be justified by its potent toxic effects and progressive deteriorating clinical manifestations, as well as, the absence of specific antidote.[21]

In the present study, the value of the mean age and SD was 26.9 ± 10.7 years and suicidal ingestion was alleged by all patients. Stressful life conditions, associated anxiety, unemployment, and failure in education or love are common triggers for suicidal attempts especially in young adults.[26] Additionally, females represented 56.4% of the studied patients. Female predominance was previously indicated by Abdel Wahab et al.[7] and Bogale et al.[27] who reported that females constituted 57.6% and 63.3% of their enrolled patients, respectively. In contrast, males outnumbered females according to Navabi et al.[28] They contributed their results that men may access this poison easier than women through their occupational activities.

The risk of ALP exposure in rural areas is substantial because of its extensive use for different agricultural purposes without sufficient legal regulations.[29] Consequently, patients from rural areas constituted the major counterpart (88.3%) in this study. Near results (82%) were also reported by ELabdeen et al.[30]

Because of rapid onset of clinical manifestations and easy transportation, the median value of the duration between the exposure to the poison and the arrival to our treating center was 2 h. In agreement with our results, El-Sarnagawy et al.[31] and Elsharkawy et al.[32] reported that the median values of the delay time were 2 and 1 h, respectively.

In the current study, SBP, DBP, and MAP were significantly lower in all adverse outcome groups. These results are comparable to findings of Ghonem et al.,[4] Pannu et al.,[19] Ahmed et al.[23] Hypotension is one of the significant factors that contribute to poor outcome in ALP poisoning.[19] Myocardial and adrenal gland damage together with volume depletion are the main underlying causes of shock in ALP poisoning.[33]

It was detected that, pulse was significantly lower in non-survivors compared to the survivors while it did not show significant difference between ICU-admitted and non-ICU admitted groups. This was in line with Elhosary and Hodeib[26] and Erfantalab et al.[34] However, reference-wise, pulse rate had no significant difference between survivors and non-survivors according

to Sheta et al.,[29] El-Sarnagawy,[31] and Anbalagan et al.[35] While Elgazzar et al.[9] observed that pulse was significantly higher in non-survived acute ALP poisoned patient who were admitted to the ICU. Furthermore, pulse rate was significantly lower in patients who were admitted to the ICU according to Ahmed et al.[23] Different types of dysrhythmias are expected with ALP poisoning including both tachycardia and bradycardia.[24]

Respiratory system is vulnerable to acute ALP poisoning with different manifestations like tachypnea and dyspnea, as well as, the development of crepitation and pulmonary edema may occur.[36] In this regard, ICU-admitted patients and non-survivors had significantly higher RR and significantly lower O_2 saturation. These finding agreed with the results of Sheta et al.[29] and Abd Elghany et al.[37]

In the current study, GCS was significantly different between survivors and non-survivors. This was in agreement with Sheta et al.[29] and Sharma et al.[38] Brain cells hypoxia may occur with ALP poisoning as a result of oxygen free radicals formation and hypotension.[24] Moreover, with low GCS and lack of protective airway reflexes, patients are susceptible to some complications as aspiration pneumonia.[39]

In the current study, pH was significantly lower in non-survivors and HCO_3 was significantly lower in both ICU-admitted and non-survivors groups. Parallel with these results, Sagah and Elhawary[40] found that pH and HCO_3 were significantly lower in non-survivors. Moreover, they observed that pH was the best predictor of mortality among different ABG parameters. Low median values of pH and HCO_3 refers to metabolic acidosis which is known to be a significant contributor for death in acute ALP poisoning.[41] Inhibition of cytochrome c oxidase and massive hypoperfusion usually account for metabolic acidosis.[42]

Potassium level was significantly lower and serum creatinine was significantly higher in non-survivors. However, Na, blood urea, and liver enzymes did not have significant difference between the comparable groups. Hypokalaemia in acute ALP poisoning may occur due to vomiting. Renal affection may be precipitated by either hypoperfusion or hypoxia. However, in this regard, literature revealed controversial results.[23,39,42,43]

Statistical analysis of the current study revealed that ICU-admitted patients and non-survivors had significantly higher median values of PSS rather than their comparable groups. In the same line, El-Sarnagawy et al.[21] documented that the median value of PSS in ALP poisoned patients who were admitted to the ICU was significantly higher than those who did not require ICU admission (3 versus 1, respectively).

Phosphine gas inhibits mitochondrial cytochrome c oxidase enzyme causing disruption of the cellular respiration and impairment of the energy production. Heart is the most vulnerable organ to ALP toxicity because of its high mitochondrial content, oxygen consumption, and metabolic activity. Moreover, heart is highly sensitive to oxidative stress caused by ALP. Consequently, most of fatalities are related to cardiovascular complications including refractory hypotension, serious dysrhythmias, and cardiogenic shock.[32,44,45] This definitely emphasizes the importance of HR and blood pressure to evaluate patients with acute ALP poisoning and predict their outcome.

However, vital signs are often initially within the normal ranges during the compensatory phase of shock. Accordingly, SI and MSI come to the fore; the elevation of SI has been correlated with reduced left ventricular end-diastolic pressure and circulatory volume, even when the values of HR and SBP are within the normal limits.[46] While SI includes only SBP, MSI incorporates also DBP owing to its undeniable importance in determining the clinical severity.[47]

In the current study, SI and MSI were calculated for each patient and statistical analysis showed that the median values of SI and MSI were significantly higher in ICU-admitted patients and non-survivors. Despite normal ranges were defined for both SI (0.5–0.7) and MSI (0.7–1.3),[14] it is appropriate to consider a risk value specific for each medical condition. The study herein demonstrated a value >1.14 as the best cut-off of SI to predict ICU admission and mortality. For MSI, the best cut-off to predict ICU admission was >1.47 and the best cut-off to predict mortality was >1.5.

According to the results of ROC analysis, SI, and MSI had fair performance to predict ICU admission and mortality among ALP poisoned patients. Furthermore, both SI and MSI showed significant positive correlations with PSS. In this regard, both SI and MSI could be introduced as simple, rapid, and applicable predictive and risk stratification adjuncts for patients presented with acute ALP poisoning. Additionally, MSI considers valuable information related to cardiovascular and hemodynamic stability by integrating HR, SBP, and DBP, which makes it a reasonable tool for assessment.[48]

Conclusion

In conclusion, acute ALP poisoning is a serious toxicological challenge with high rates of morbidity and mortality. Both SI and MSI have significant positive correlations with the severity of acute ALP poisoning. They have fair performance to predict the need for ICU admission and mortality. However, the simplicity of SI and MSI could support their utility as rapid bedside assessment tools for early evaluation of the patients with acute ALP poisoning and predicting their outcomes.

Strength and limitations

To the best of the authors' knowledge, this is the first study to investigate the role of SI and MSI in ALP poisoning. Although these parameters conveyed fair performance to predict the outcome, they are simple and easily obtained from vital signs that are initially measured at hospital admission. The main limitations of this study were small sample size and uni-centered nature of the study. Therefore, further studies are recommended for evaluation of the findings of our study.

Author contribution

Mona M. Ghonem and Aliaa A. Hodeib contributed to the study's conception and design. Material preparation and data collection were performed by Mona M. Ghonem, Aliaa A. Hodeib, and Amira A. Abdelnoor. The first draft of the manuscript was written by Mona M. Ghonem and Aliaa A. Hodeib. All authors read and approved the final manuscript.

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Conflict of interest statement

The authors have no relevant financial or non-financial interests to disclose.

Data availability

The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

Ethical approval

The study followed the World Medical Association Declaration of Helsinki and was conducted after the agreement of Faculty of Medicine – Tanta University ethics committee (Approval code: 35329/2/22).

Consent to participate

A written informed consent was obtained from each patients or his/her guardian in case of incompetency. To maintain patients' confidentiality, a code number was assigned for each patient for anonymous analysis of the collected data.

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