Original Article

PGI Score as a Predictor of Cardiotoxicity and Mortality in Patients with Acute Aluminum Phosphide Poisoning

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ABSTRACT

Background: Aluminum phosphide (ALP) is a major cause of suicidal poisoning in Egypt, with a high mortality rate owing to cardiac toxicity. Aim of the work: To explore the value of PGI score [stands for blood pH, Glasgow Coma Scale (GCS), and Impaired systolic blood pressure (SBP)] as a predictor of cardiotoxicity and mortality in acute ALP-poisoned patients. Methods: A prospective study was conducted on acute ALP-poisoned patients presented to Zagazig University Hospital from October 2021 to March 2022. Patients who met the inclusion criteria were assessed at presentation by PGI score. Electrocardiogram (ECG) was done immediately and repeated as needed. On admission, serum troponin T and creatine phosphokinase-MB (CPK-MB) levels were measured. According to the outcome, patients were categorized into survivors and non-survivors. Results: 73 patients were classified based on the PGI score as follow; 4 patients had score 0, 6 patients had score 1, 27 patients had score 2, and 36 patients had score 3. PGI score 3-patients displayed the highest mortality incidence contrary to those with score 0 (100% VS 25%). All PGI 3-patients ingested one tablet or more of ALP, exhibited ECG changes, and required vasopressors and mechanical ventilation, unlike to score 0 and 1-patients. Troponin T levels significantly elevated in the non-survivors, while CPK-MB levels showed no significant difference among the two groups. The PGI score negatively correlated with the survivability, while positively correlated with ALP ingested amount, ECG changes, serum troponin T levels, vasopressors need, and ventilation requirement. In ALP-poisoned patients, the best cutoff point of PGI score for cardiotoxicity prediction was ≥1, with 93.9% sensitivity and 85.7% specificity. Meanwhile, the best cutoff point of PGI score for mortality prediction was ≥2, with 95.4% sensitivity and 87.5% specificity. Conclusion: The PGI score is a recommended predictor of cardiotoxicity and mortality in ALP-poisoned patients.

Key words: Poisoning, ALP, Cardiotoxicity, PGI, Troponin T, Outcome.

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INTRODUCTION

Aluminum phosphide (ALP) is a metal phosphide commonly used as a rodenticide and grain preservative in developing countries, where it represents a typical 'suicide poison' due to cheap price, uncontrolled accessibility, rapid onset of severe toxidrome, and lack of effective antidotes (Karimani et al., 2018; Anbalagan et al., 2021).

In humans, oral ingestion is the most common route of exposure to ALP poisoning, although inhalation and skin penetration can also contribute to some cases (Gurjar et al., 2011). In stomach, ALP reacts with the moisture, yielding phosphine gas (PH3) which is rapidly absorbed to the circulation. At the cellular level, PH3 targets the mitochondrial respiratory mechanisms resulting in ATP depletion, cytochrome C oxidase inhibition, reduction in the mitochondrial membrane potential, and electron leakage (Anand et al., 2011).

Inhibition of cytochrome C oxidase shifts cell metabolism from aerobic to anaerobic condition and permits hypoxia and lactate accumulation. Meanwhile, the electron leakage enhances formation of free radicals and depletes cellular stores of endogenous antioxidants like glutathione, superoxide dismutase, and catalase. Consequently, lipid peroxidation, DNA damage, and even cell death can supervene (Anbalagan et al., 2021).

In the clinical course of oral ALP poisoning, nausea and vomiting are the earliest manifestations (Sahoo et al., 2020). Mild cases present usually with nausea, vomiting, diarrhea, headache, abdominal pain, and tachycardia (Goel and Aggarwal, 2007). Meanwhile, moderate to severe cases develop early cardiovascular (CVS) toxicity, respiratory and nervous systems manifestations, in addition to the possible hepatic and renal failure (Proudfoot et al., 2009). As a fact, the CVS system is the prime target of PH3-related hypoxia and oxidative stress. Thus, it is not surprising that the circulatory failure is the core of toxidrome in most poisoned patients (Anbalagan et al., 2021). Cardiac toxicity is usually reflected by hypotension, tachycardia or bradycardia, arrhythmia, ECG changes, congestive heart failure, toxic myocarditis, and shock (Gurjar et al., 2011). The cardiac toxicity has been attributed to the myocardial damage secondary to cytochrome C oxidase inhibition and hypoxia (Mogal et al., 2018).

Among the manifestations of cardiac toxicity, hypotension and arrhythmias are the commonest in patients with ALP poisoning (Mathai and Bhanu, 2010). Meanwhile, deaths within the first 12–24 hours are mostly ascribed to cardiogenic shock (Hakimoğlu et al., 2015). Therefore, a reliable, simple, and accurate scoring tool is warranted to guide the prediction, clinical intervention, and prognosis of cardiotoxicity in patients with ALP poisoning.

Generally, different scoring tools have been developed to help decision-making in poisoned patients, including Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) Score, Rapid Acute Physiology Score (RAPS), the Sequential Organ Failure Assessment Score (SOFA), and the Simplified Acute Physiology Score (SAPS) (El-Sarnagawy and Hafez, 2017; Sheta et al., 2019; Shahin and Hafez, 2020). However, the difficulty of application and the time needed to perform such calculations restrict their usage in the toxicological emergencies (Pannu et al., 2022).

Recently, a new simple prognostic tool called 'PGI' score which stands for blood pH, Glasgow Coma Scale (GCS), and Impaired systolic blood pressure (SBP); has been suggested as a simplified three-points clinical score for severity scoring and prediction of prognosis in acute ALP poisoning (Pannu et al., 2020).

In this study we aimed to explore the value of using PGI score as a predictor of cardiotoxicity and mortality in patients

with acute ALP Poisoning in Zagazig University Hospital, Egypt.

I. SUBJECTS and METHODS

II.1. Study population:

This prospective cohort study was conducted on the consecutive ALP-poisoned patients, who were admitted to Zagazig University Hospitals from October 2021 to March 2022.

The sample size was calculated using open epi based on the positive predictive value of PGI score (78%) in prediction of mortality in patients with acute ALP poisoning (Pannu et al., 2020). The number of ALP-patients presenting to Zagazig University Hospitals over the duration of 6 months was expected to be 100 patients. So, at confidence interval 95%, the sample size was calculated to be 73 cases.

This prospective cohort study was approved by the Institutional Review Board "IRB" of Faculty of Medicine, Zagazig University (No. ZU-IRB# 9614/5-9-2021). Also, informed consents were obtained for all the included patients and personal data were kept anonymous to ensure confidentiality of records.

II.2. Inclusion criteria:

Patients presented to the emergency department during the first 24 hours of acute oral ALP poisoning, based on the accurate history and clinical examination.

II.3. Exclusion criteria:

Patients who were presented later than 24 hours of poisoning, patients who received pre-hospital treatment, patients with co-ingestion of other drugs or toxins, pregnant women, and those having chronic diseases (cardiac diseases, pulmonary diseases, diabetes mellitus, thyroid disease, hepatic diseases, and renal dysfunction), in addition to patients exceeding 60 years.

All patients were assessed immediately for the hemodynamic parameters (systolic & diastolic blood pressure, heart rate, central venous pressure, and GCS) in addition to the ECG. Also, routine investigations (blood sugar, blood gas analysis, kidney and liver functions) were undertaken.

On admission, all patients received emergency stabilization, gastric decontamination using paraffin oil, corticosteroids, Mg sulphate, and Rotacysteine according to the standard protocol of Zagazig university hospital. Administration of vasopressors (adrenaline, noradrenaline, and dobutamine) and Na bicarbonate, as well as the need for the mechanical ventilation were guided by the clinical presentations and the laboratory investigations.

The socio-demographic data (sex, age, occupation, residence) and intoxication data (mode of exposure, amount of ingested ALP (number of tablets), and delay time between intoxication and arrival to emergency department) were recorded. The diagnosis of cardiotoxicity was based on the presence of one or more of the clinical manifestations reflecting hemodynamic instability, heart failure, conduction deficits, dysrhythmias, and/or ECG changes.

II.4. Parameters:

II.4.1. PGI score:

All patients were assessed 'at the time of presentation' to the emergency department according to the PGI scoring system (Pannu et al., 2020). Each of the three points of PGI score (the blood pH <7.25, GCS <13, and SBP <87 mm Hg) was given a score of 1 with a total score of 3.

II.4.2. Electrocardiogram (ECG):

Electrocardiogram was done for the study participants at time of presentation to the emergency department and repeated based on clinical presentations using FuKuda denstti Cardimex (model Fx-2111, Japan). Analysis of ECG included the rate, rhythm, ST/T abnormalities, conduction defects, and measurement of PR and QT intervals

II.4.3. Biochemistry:

The laboratory work for the included patients was undertaken at the laboratory of Zagazig university hospital as follow: 1mL arterial blood was freshly drawn from radial artery or femoral artery for immediate analysis of blood gas using Rapid lab 855 of Bayer Company. Also, 5 mL venous blood sample was collected, centrifuged at 3000 rpm for 10 min, and serum was collected for the determination of: 1) troponin T using Enzyme Immunoassay test kit (RayBiotech, Parkway Lane, Georgia, USA). 2) Serum creatine phosphokinase-MB (CPK-MB) using Creatine kinase-MB (CK-MB) Activity Assay Kits of Biovision incoporated, USA).

II.5. PATIENTS' OUTCOME:

According to the final outcome, patients were categorized into:

(A) Survivors and (B) Non-survivors.

II.6. STATISTICAL ANALYSIS:

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA 2011). Qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage). Percentages of categorical variables were compared using Chi-square test or Fisher's exact test when appropriate. Spearman correlation coefficient was tested to assess relationship between study variables, (+) sign indicated direct correlation & (-) sign indicated inverse correlation. Receiver operating characteristic curve (ROC) was used to assess prognostic performance of PGI score in the prediction of cardiotoxicity and mortality in ALP-poisoned patients on admission, using the Area under the Curve (AUC), cut off points, sensitivity, specificity, positive predictive value and negative predictive value. The significance level was considered at p value < 0.05.

III. RESULTS:

As per the demographic and toxicological data analysis, most patients were females (91.8%), 15 to 20 years old (43.8%), and from rural areas (69.9%). Suicidal ingestion of ALP was indicated in almost all poisoned patients (97.2%). Moreover, the majority of included patients reported one tablet ingestion (68.5%), while only 17.8% of the patients ingested less than one tablet and 13.7% ingested more than one tablet. In response to ALP poisoning, more than half of cases (57.5%) sought medical advice within the first 6 hours following ingestion. Regarding survivability, out of the 73 enrolled patients, 65 didn't survive the ALP poisoning (89%). Based on PGI scoring system, 4 patients had score 0, 6 patients had score 1, 27 patients had score 2, and 36 patients had score 3 (Table 1).

As per findings, there was a highly ($P<0.001$) significant difference among survivor and non-survivor groups regarding the ingested amount of ALP (number of tablets), the presence of ECG changes, vasoactive drugs need, and ventilation requirement. As regards to the biochemical parameters, a significant ($p<0.05$) difference was detected between the survivors and non-survivors in serum troponin T levels. Whereas, the time elapsed between toxicity and seeking medical advice and serum CPK-MB levels were not found to be significantly ($p>0.05$) different among the two groups (Table 2).

On a different note, the negative correlation between PGI score and patient survivability was well established. The highest incidence of mortality (100%) was registered among PGI score 3- patients, followed by score 2-patients (96.3%). On the contrary to PGI score 0 and 1-patients demonstrated lower mortality rate (25% and 33.3% respectively) (Tables 3 & 4). In other words, the lower the PGI score, the higher the survivability likelihood.

Besides, the severity of PGI score positively correlated with the number of ALP ingested tablets as all PGI score 3-patients ingested one tablet or more, while most of PGI score-0 patients ingested less than one tablet. Likewise, the severity of PGI score was positively correlated with

the development of ECG changes as indicated in all the PGI score 3-patients who developed ECG changes while most PGI score-0 patients showed normal ECG. Also, a significant ($p<0.05$) relation was noticed between the severity of PGI score and serum troponin T elevation. Likewise, results indicated the pressing need for the vasopressors support and mechanical ventilation in patients with high PGI score (Tables 3 & 4).

Concerning the ECG analysis, dysrhythmias represented 69.9% of the total ECG changes with the tachyarrhythmias prevalence. The other ECG changes detected in this study entailed ST segment elevation (11%), prolonged QT interval (6.8%), and wide QRS complex (2.7%) (Table 5).

The present results showed that the best cutoff point of PGI score for prediction of cardiotoxicity in ALP-poisoned patients was ≥1, with sensitivity 93.9%, specificity 85.7% and accuracy 93.2% (Table 6; Figure1). While, the best cutoff point of PGI score for prediction of mortality in ALP-poisoned patients was ≥2, with sensitivity 95.4%, specificity 87.5% and accuracy 94.5%. The area under the curve was statistically highly significant (Table7; Figure 2).

Table (1): Demographic data, toxicological features, outcome, and PGI score of acute aluminum phosphide poisoned patients included in this study (n=73).

Demographic and toxicological data	N	%
Sex		
Male	6	8.2
Female	67	91.8
Age		
15-20	32	43.8
20-25	15	20.5
25-30	12	16.4
30-35	8	11.0
35-40	6	8.2
Residence		
Urban	22	30.1
Rural	51	69.9
Mode of poisoning		
Suicidal	71	97.2
Accidental	2	2.8
Amount (number of tablets)		
Less than one tablet	13	17.8
One tablet	50	68.5
More than one tablet	10	13.7
Time between toxicity and seeking medical advice		
1-6 h	42	57.5
6-12 h	18	24.7
12-24 h	13	17.8
Outcome (survivability)		
Survivors	8	11.0
Non-survivors	65	89.0
PGI score		
0	4	5.5
1	6	8.2
2	27	37.0
3	36	49.3

n: number of patients, %: percentage.

Table (2): Statistical comparison between survivors and non-survivors of acute aluminum phosphide poisoned patients regarding amount, time between toxicity and seeking medical advice, ECG changes, troponin T, CPK-MB, vasoactive drugs need, and ventilation requirement (n=73)

Parameters		Survivors (n=8)		Non-survivors (n=65)		^{FET}p-value
		n	%	n	%	
Amount (number of tablets)	Less than one tablet	7	87.5	6	9.2	χ^2=29.848 p-value= 0 .001**
	One tablet	1	12.5	49	75.4	
	More than one tablet	0	0.0	10	15.4	
Time between toxicity and seeking medical advice	1-6 h	4	50.0	38	58.5	χ^2=2.584 p-value=0.275
	6-12 h	1	12.5	17	26.2	
	12-24 h	3	37.5	10	15.4	
ECG changes	Absent	7	87.5	0	0.0	**0.001****
	Present	1	12.5	65	100.0	
Troponin T	Normal	7	87.5	27	41.5	**0.022***
	Elevated	1	12.5	38	58.5	
CPK-MB	Normal	6	75.0	36	55.4	0.454
	Elevated	2	25.0	29	44.6	
Vasoactive drugs	Not needed	6	75.0	0	0.0	**0.001****
	Needed	2	25.0	65	100.0	
Ventilation	Not required	8	100.0	0	0.0	**0.001****
	Required	0	0.0	65	100.0	

Data expressed as number (n) and percentage (%).
FET: Fisher exact test, χ^2: Chi square test, non-significant (p>0.05), *: statistically significant (p<0.05), **: statistically highly significant (p<0.001), CPK -MB: creatine phosphokinase-MB

Table (3): Relation between PGI score and clinical and biochemical data of acute aluminum phosphide poisoned patients (Outcome, amount, time between toxicity and seeking medical advice, ECG changes, troponin T, CPK-MB, vasoactive drugs need and ventilation) (n=73).

Parameters		**PGI score**								χ^2 **p-value**
		0 (n=4)		**1 (n=6)**		**2 (n=27)**		**3 (n=36)**		
		n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	
Outcome (survivability)	Survivors	3	75.0	4	66.7	1	3.7	0	0.0	**41.781 (0.001**)**
	Non-survivors	1	25.0	2	33.3	26	96.3	36	100.0	
Amount (number of tablets)	Less than one tablet	3	75.0	4	66.7	6	22.2	0	0.0	**34.974 (0.001**)**
	One tablet	1	25.0	2	33.3	21	77.8	26	72.2	
	More than one tablet	0	0.0	0	0.0	0	0.0	10	27.8	
Time between toxicity and seeking medical advice	1-6 h	4	100.0	1	16.7	17	63.0	20	55.6	**9.77 (0.135)**
	6-12 h	0	0.0	2	33.3	5	18.5	11	30.6	
	12-24 h	0	0.0	3	50.0	5	18.5	5	13.9	
ECG changes	Absent	3	75.0	3	50.0	1	3.7	0	0.0	**35.94 (0.001**)**
	Present	1	25.0	3	50.0	26	96.3	36	100.0	
Troponin T	Normal	4	100.0	4	66.7	15	55.6	11	30.6	**10.150 (0.017*)**
	Elevated	0	0.0	2	33.3	12	44.4	25	69.4	
CPK-MB	Normal	4	100.0	5	83.3	17	63.0	16	44.4	**7.437 (0.059)**
	Elevated	0	0.0	1	16.7	10	37.0	20	55.6	
Vasoactive drugs	Not needed	3	75.0	2	33.3	1	3.7	0	0.0	**32.618 (0.001**)**
	Needed	1	25.0	4	66.7	26	96.3	36	100.0	
Ventilation	Not required	3	75.0	4	66.7	1	3.7	0	0.0	**41.781 (0.001**)**
	Required	1	25.0	2	33.3	26	96.3	36	100.0	

Data expressed as number (n) and percentage (%).

χ^2: Chi square test, non-significant ($p>0.05$), *: statistically significant ($p<0.05$), **: statistically highly significant ($p<0.001$).

Table (4): Distribution of ECG changes in acute aluminum phosphide poisoned patients included in this study (n=73).

ECG Changes	n	%
Dysrhymias -Tachyrythmia -Bradyrythmia	**51** 43 8	**69.9** 84.3 15.7
Elevated ST segment	**8**	**11.0**
Prolonged QTc interval	**5**	**6.8**
Wide QRS	**2**	**2.7**
No changes	**7**	**9.6**

ECG: electrocardiogram, n: number of patients, %: percentage

Table (5): Correlation matrix between PGI Score, and clinical and biochemical data of acute aluminum phosphide poisoned patients (Outcome, amount, time between toxicity and seeking medical advice, ECG changes, troponin T, CPK-MB, vasoactive drugs need, and ventilation requirement).

	Survivability (Outcome)	Amount (number of tablets)	Time between toxicity and seeking medical advice	ECG changes	Troponin T	CPK-MB	Vasoactive drugs need	Ventilation requirement
	(r)							
PGI Score	-0.536**	0.610**	0.006 NS	0.497**	0.263*	0.032 NS	0.523**	0.599**

r: correlation coefficient, NS: non-significant (p>0.05), *: statistically significant (p<0.05), **: statistically highly significant (p<0.001), ECG: electrocardiogram, CPK-MB: creatine phosphokinase-MB.

Table (6): Prognostic performance of PGI score in the prediction of cardiotoxicity of acute aluminum phosphide poisoned patients on admission.

Area under curve (AUC)	0.994
Cutoff point	1
Sensitivity	93.9%
Specificity	85.7%
Positive predictive value	98.4%
Negative predictive value	60%
Accuracy	93.2%
P -value	0.001**

**: highly significant (p<0.001), %: percentage.

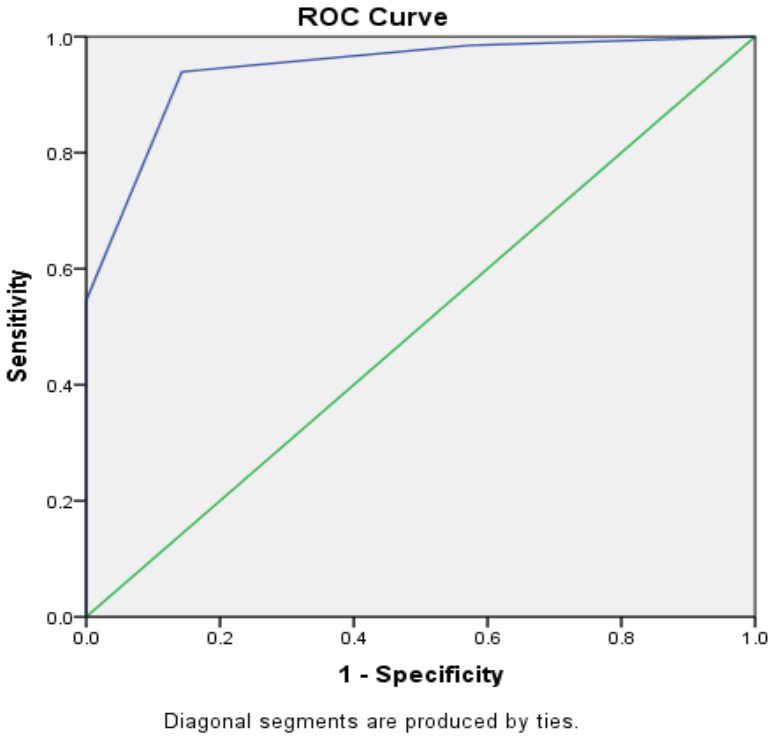

Figure (1): ROC curve showing prognostic performance of PGI score in the prediction of cardiotoxicity of acute aluminum phosphide poisoned patients on admission.

Table (7): Prognostic performance of PGI score in the prediction of mortality of acute aluminum phosphide poisoned patients on admission.

Area under curve (AUC)	0.951
Cutoff point	2
Sensitivity	95.4%
Specificity	87.5%
Positive predictive value	98.4%
Negative predictive value	70%
Accuracy	94.5%
P-value	0.001**

**: highly significant ($p<0.001$), %: percentage.

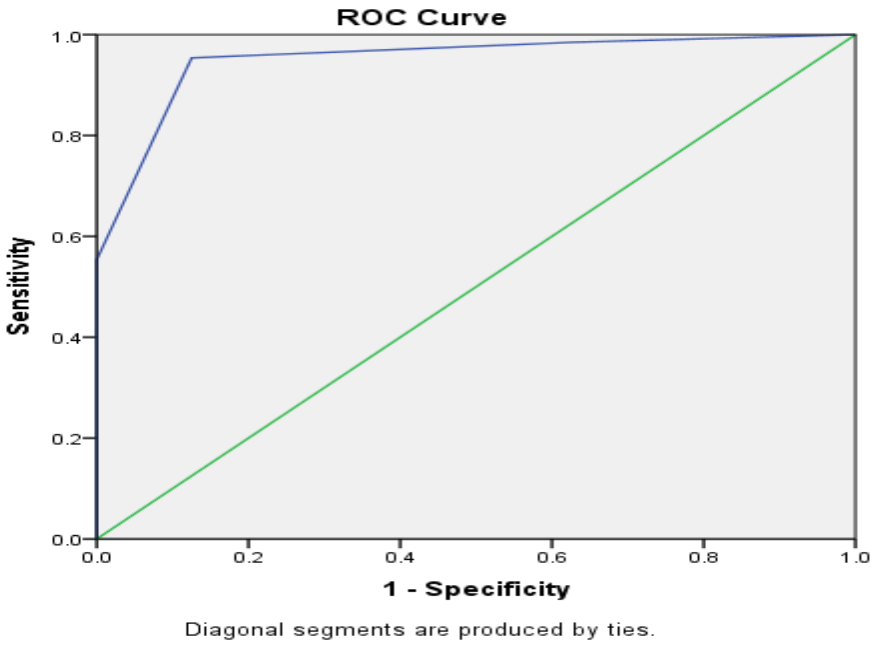

Figure (2): ROC curve showing prognostic performance of PGI score in the prediction of mortality of acute aluminum phosphide poisoned patients on admission.

IV. DISCUSSION:

Aluminum phosphide poisoning has been widely used as a grain preservative for the extermination of insects with little residues and negligible impact on the viability of seeds (Sankhla et al., 2017). The unlimited and uncontrolled accessibility renders ALP as one of the most commonly used suicidal poisons in the developing countries (Nosrati et al., 2013; Kordrostami et al., 2017).

According to this study, the majority of patients were females, 15 to 20 years old, and from the rural areas. Similarly, Abdel Wahab et al. (2020) indicated the female predominance (63.3%) among phosphide intoxicated patients in poison control center, Ain Shams University Hospitals. Another study conducted in Tehran by Etemadi-Aleagha et al. (2015) over the period from 2006 to 2013, showed that 51.8% of patients were females at age of 10 to 40 years old. Instead, in India, Kapoor et al. (2006) reported the predominance of males over females (2:1 ratio), and that most of patients were at age of 11–30 years (65.1%), and belonged to rural areas.These results were ascribed to the easy availability of ALP in the rural areas of India especially for males working in farming. In addition, the increased susceptibility of this age group was linked to the excessive exposure to social and psychological stresses (Kapoor et al., 2006). In the same line, suicidal ingestion was the commonest mode of intoxication by ALP in the current study. Similarly, Kalawat et al. (2016), Saleh and makhlof (2018), and Bogale et al. (2021) noted that most patients administered ALP intentionally for self-destructive purposes.

Toxicological data of the present study revealed a significant difference among survivors and non-survivors regarding the amount of ALP ingested by the patients. Yet, a non-significant difference was detected for the time elapsed between ALP ingestion and seeking medical advice. Consistently, a recent study conducted in Ethiopia by Bogale et al. (2021) had indicated a significant difference among survivors and non-survivors in the number of ingested tablets, while the average time between the toxicity and hospitalization was not found to be significantly different among the two groups. Also, in India, Pannu et al. (2020)

denoted a non-statistical significance in the seeking medical advice among survivors and non-survivors.

Unlikely, a significant relation ($P<0.05$) was reported by Saleh and makhlof (2018) between the outcome of toxicity and the delay time, while no significant difference was noted regarding the number of ingested tablets in ALP-poisoned patients admitted to Fayoum General Hospital. According to Pannu et al. (2020), the dose ingested by patients of acute ALP poisoning may not be accurately reported which impairs its accuracy in predicting the severity and outcomes of patients. Thus, more accurate and reproducible predictors are required to guide prognosis in ALP-poisoned patients.

The PGI score has been suggested as a toxidrome-specific and simplified risk-stratification tool by Pannu et al. (2022). This scoring system comprises two easily identifiable and reproducible clinical parameters (SBP and GCS), and one laboratory parameter (pH) readily available at a reasonable cost in most tertiary care centers (Mohan et al., 2019; Pannu et al., 2020).

The toxicity of ALP particularly affects the cardiovascular tissues via causing direct myocardial damage, hypoperfusion, myocarditis, pericarditis, and arrhythmias (Abdel Wahab et al., 2020). Cardiotoxicity primarily manifests by profound and refractory hypotension and/or ECG changes (Gurjar et al., 2011).

Also, metabolic acidosis is commonly observed in patients with ALP toxicity due to lactic acid accumulation secondary to oxidative phosphorylation block and poor tissue perfusion. The severity of metabolic acidosis escalates with the increased severity of ALP toxicity (Jaiswal et al., 2009).

In addition, patient with ALP poisoning may eventually develop signs of central nervous system disorders that can persist in the presence of shock leading to coma (Ghodsi et al. 2020). The GCS is used to objectively describe the extent of time elapsed between ingestion and impaired consciousness. This scale assesses patients according to three aspects of responsiveness namely, the eye-opening, the motor response, and the verbal response. Reporting each of these aspects can separately provide a clear picture of the patients of different medical illness (Teasdale et al., 2014; Borgialli et al., 2016).

In current study, patients with PGI score 0 revealed the least incidence of mortality, whereas patients with PGI score 3 had the highest incidence of mortality followed by patients with PGI score 2. Correspondingly, Pannu et al. (2020) stated that PGI score could provide essential predictor of case-fatality in acute ALP poisoning where score 0 was associated with no mortality, score 1 with the least incidence of mortality (15%), followed by score 2 (39%). Meanwhile, score 3 demonstrated the highest incidence of mortality (96.4%).

Most of patients with ALP poisoning develop cardiac arrhythmias and ECG changes within the first 24 hours (Anbalagan et al., 2021; Ataei et al., 2021). Inhibition of the mitochondrial respiration by ALP results in energy depletion with ischemia like effect on ECG. In addition, oxidative stress impairs myocardial proteins and alters transmembrane trading of Na+, Ka+, Ca++, and Mg++particles causing arrhythmia (Soltaninejad et al., 2012).

Gupta et al. (1995) indicated that 80% of ALP-poisoned patients showed variable ECG changes with prevalent ST-segment and T wave abnormalities in 40% of patients. Also, Eshraghi et al. (2019) reported lethal ECG changes in the non-survivors in the first 6 to 24 hours, and non-lethal changes in survivors within the first 12 to 24 hours. The ECG changes last usually in survivors for up to three weeks before being normalized (Ataei et al., 2021).

As per results, the severity of PGI score positively correlated with the

presence of ECG changes (100% of ECG changes), while most of patients with PGI score 0 showed normal ECG. This positive correlation supports the value of PGI score in prediction of cardiotoxicity in ALP-poisoned patients.

In the present work, dysrhythmias were the most commonly detected ECG changes with particular respect to the tachyarrhythmias. In line with these results, tachyarrhythmias including ventricular tachycardia, ventricular fibrillation, supraventricular tachycardia, atrial fibrillation, and atrial flutter have been perceived as the most commonly detected arrythmias in patients with acute ALP poisoning (Anbalagan et al., 2021). Also, the observed ECG changes in this study including dysrhythmia, ST segment elevation, prolonged QT interval, and widened QRS complex were in accordance with the previous studies of Soltaninejad et al. (2012), Abdel Wahab et al. (2020), and Ataei et al. (2021).

The abnormalities of ST segment associated with ALP toxicity were attributed to the inferior wall myocardial ischemia (Mehrpour et al., 2012; Singh et al., 2014). Mohan et al. (2016) and Taghaddosinejad et al. (2016) attributed the ischemic changes to the oxidative stress injury and the direct toxicity on the myocardial membrane.

In agreement with the present work, several studies have reported prolonged QTc interval with either tachycardia or bradycardia in patients with metal phosphide poisoning (Taghaddosinejad et al., 2016; Asghari et al., 2017; Rahimi et al., 2018). Wide QRS complex observed by Moghadamnia (2012) and Hashemi-Domeneh et al. (2016) was indicative of either incomplete or complete right bundle branch block after ALP exposure.

Besides, the significant elevation in troponin levels acts as an indicator for severe myocardial injury, while small elevation reflects myocardial necrosis (microinfarction), tachyarrhythmias, or patients with score 3 developed variable myocarditis (Abdel Wahab et al., 2020). As regards CPK-MB, inconsistent reports of normal and abnormal levels could be found for patients with acute ALP poisoning (Kaushik et al., 2007; Soltaninejad et al., 2009).

In the present study, in spite of being elevated in some cases, no significant difference was detected in CPK-MB levels among survivors and non-survivors. Accordingly, the role of CPK-MB as a marker of cardiotoxicity seems to be limited in excluding severe toxicity and guiding prognosis in patients with ALP poisoning (Nayyar and Nair, 2009; Soltaninejad et al., 2012).

Regarding serum troponin T levels, a significant difference was detected among survivors and non-survivors denoting its value as a marker of cardiotoxicity in ALP-poisoned patients. The increased troponin T levels has been attributed to the liberation of phosphine gas which inhibits mitochondrial respiration and depletes myocardial energy like ischemia (Soltaninejad et al., 2012).

Likewise, Abdel Wahab et al. (2020) reported increased troponin I levels in ALP severely intoxicated group compared to the mild and moderate groups. Additionally, increased troponin I level was reported in 26% of patients with ALP toxicity and had positively correlated with the myocardial damage detected by the echocardiography (Kalawat et al., 2016). Meanwhile, Nayyar and Nair (2009) reported that normal levels of troponin T and CPK-MB can't contradict cardiotoxicity, though their elevation denotes myocardial damage.

Actually, the major challenge faced in ALP-poisoned patients is how to manage the refractory hypotension and profound shock (Changal et al., 2017). The presence of shock at time of presentation has been considered as a reliable predictor of mortality in ALP patients (Louriz M et al., 2009; Nadeem et al., 2015). Furthermore, Soltaninejad et al. (2012) has

perceived the reduced SBP as a key risk Consequently, the earlier the need for vasopressors support, the poorer the prognosis of ALP poisoning (Mathai and Bhanu 2010).

The circulatory failure and hypotension with ALP poisoning have different mechanisms including arrhythmias, conduction disturbances, reduced ejection fraction due to myocardial damage, peripheral vasodilatation due to small-vessel injury, hypovolemia secondary to vomiting, and decreased cortisol levels due to PH3-induced adrenal cortex injury (Bayazit et al., 2000; Bogle et al., 2006).

In the current study, almost all severe cases developed respiratory manifestations that necessitated mechanical ventilation. According to Anbalagan et al. (2021), mechanical ventilation requirement, shock requiring vasopressors, dysrhythmia, and low GCS are all features of high mortality risk in patients with ALP poisoning.

Finally, in order to validate these hypotheses regarding the predictor and prognostic value of PGI score in patients with acute ALP poisoning, the ROC curve was tested for PGI score. Results revealed that the best cutoff point of PGI score for prediction of cardiotoxicity in ALP-poisoned patients was ≥1, with sensitivity 93.9%, specificity 85.7% and accuracy 93.2%. While, the best cutoff point of PGI score for prediction of mortality in ALP-poisoned patients was ≥2, with sensitivity 95.4%, specificity 87.5% and accuracy 94.5%.

V. CONCLUSION:

In acute ALP-poisoned patients, PGI score demonstrated a negative correlation with the patients' survivability and a positive correlation with the ingested amount of ALP, development of ECG changes, serum troponin T levels, vasoactive drugs need, and the artificial ventilation requirement. These results strongly support the value of PGI score as factor for mortality at time of admission a simple and easy predictor of cardiotoxicity and mortality in patients with acute ALP poisoning.

VI. RECOMMENDATIONS:

The present study recommends the use of PGI score as a useful predictor of cardiotoxicity and mortality in patients with acute ALP poisoning.

VII. CONFLICT of INTEREST:

Authors declared no conflict of interest.

VIII. FUNDING:

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X. CONTRIBUTION:

Dr. Samar Sakr and Dr. Nashwa Shalaby contributed equally to the study conception, collection of data, and writing of first draft of manuscript. Dr. Mona Atef contributed to the data and results analyses. Dr. Samar Sakr was responsible for the edition of whole manuscript. All authors read and approved the final manuscript.

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الملخص العربى

مقياس البي جي اي كمتنبئ للسمية القلبية والوفيات في مرضى التسمم الحاد بفوسفيد الالمونيوم

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قسم الطب الشرعى و السموم الإكلينيكية - كلية الطب البشري-جامعة الزقازيق

يعد فوسفيد الألومنيوم سببا رئيسيا للتسمم الانتحاري في مصر لما ينجم عنه من معدل عال للوفيات نتيجة للتسمم القلبي. ولذلك اجريت هذه الدراسة لتقييم امكانية التنبؤ بالسمية القلبية والوفاة في مرضى التسمم الحاد بفوسفيد الألومنيوم باستخدام مقياس البي جي اي والذى يرمز إلى (درجة حموضة الدم ، ومقياس جلاسكو للغيبوبة ، وضغط الدم الانقباضي الضعيف) وعليه فقد أجريت دراسة جماعية مستقبلية على مرضى التسمم الحاد بفوسفيد الألومنيوم الذين تم استقبالهم في مستشفى جامعة الزقازيق من أكتوبر 2021 إلى مارس 2022 حيث تم تقييم المرضى الذين استوفوا معايير الانضمام للدراسة وقت وصولهم الى المستشفى باستخدام مقياس البي جي اي . أيضًا تم إجراء مخطط كهربية القلب على الفور وتكراره حسب الحاجة ، كما تم قياس مستويات التروبونين (تى) والكرياتين فوسفوكينيز الخاص بعضلة القلب فى مصل الدم. وفى النهاية تم تقسيم المرضى إلى ناجين وغير ناجين. وقد تم تصنيف 73 مريضًا بناءً على مقياس البي جي اي على النحو التالي ؛ 4 مرضى حصلوا على درجة 0 ، 6 مرضى حصلوا على درجة 1 ، 27 مريضًا حصلوا على درجة 2 ، فيما حصل 36 مريضًا على درجة 3. وقد أظهر المرضى الذين حصلوا على درجة 3 أعلى معدل للوفيات على عكس المرضى الذين حصلوا على درجة 0 والذين أظهروا أقل معدل للوفيات (100% مقابل 25%). كما وجد ان جميع المرضى الذين حصلوا على درجة 3 قد تناولوا قرصا او يزيد من فوسفيد الالمونيوم واظهروا تغييرات في مخطط كهربية القلب وكذلك احتاجوا الى قابضات الأوعية و للتنفس الاصطناعى على عكس المرضى الذين حصلوا على درجات 0 و 1. كما ارتفع مستوى التروبونين (تي) بشكل ملحوظ في غير الناجين ،بينما أظهرت مستويات إنزيم الكرياتين فوسفوكينيز فرقًا غير ملحوظ بين الناجين وغير الناجين. وقد اظهرت النتائج أن درجة مقياس البي جي اي ترتبط ارتباطًا سلبيًا بالبقاء على قيد الحياة وترتبط ارتباطًا إيجابيًا بعدد الاقراص التي تم تعاطيها وكذلك احتمالية مشاهدة تغيرات في مخطط كهربية القلب وارتفاع مستويات التروبونين (تى) في مصل الدم والاحتياج إلى قابضات الأوعية و التنفس الاصطناعى .وقد كانت أفضل نقطة فاصلة لدرجة مقياس البي جي اي للتنبؤ بالسمية القلبية لدى المرضى المصابين بتسمم فوسفيد الألومنيوم هي 1 ، مع حساسية 93.9% ونوعية 85.7%. بينما كانت أفضل نقطة فاصلة لمقياس البي جي اي للتنبؤ بالوفاة هي 2 مع حساسية 95.4% ونوعية 87.5%. واخيرا فيمكن استنتاج أن مقياس البي جي اي يمكن استخدامه كمؤشريعتد به للتنبؤ بالسمية القلبية والوفاة في المرضى المصابين بتسمم فوسفيد الألومنيوم الحاد.