ACUTE ALUMINIUM PHOSPHIDE POISONING IN EAST DELTA, EGYPT: A GROWING PUBLIC HEALTH PROBLEM OVER THE LAST FIVE YEARS

BY

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ABSTRACT

Background: Aluminium phosphide (AlP) is a pesticide used to preserve grains from rodents and household bugs. It's one of the most common causes of poisoning in developing countries as it's cheap, easy to use, and instantly fatal. **Aim of the study:** Assessment of the magnitude of acute AlP poisoning, characters of prevalent cases, and the general outcome of poisoning in the Eastern Delta of Egypt over the last five years. **Patient and Method**: We surveyed all patient records of AlP-poisoned cases admitted to local poisoning centers; Poison Control Center-Zagazig University Hospitals (PCC-ZUH) and Zagazig General Hospital, from Jan. 2017 to Jan. 2022, we calculated poisoning incidence over the studied years and extracted patient demographic data and poisoning sequelae to create detailed statistical patterns, then we evaluated all available case data to relate them to the patient outcome. **Results:** AlP poisoning is an increasing public health problem with the most frequent age group being 18 to 45 years (66%). Females represented the majority (62.5%), and 79.3% of the cases were from rural areas. Most of the cases were suicidal (70.6%), and the overall mortality rate of AIP over the last 5 years was 72.5%. **Conclusions and Recommendations:** The rising incidence of AlP poisoning is a threatening public health problem that mandates the government intervention to enact restrictive legislation on the purchase and use of wheat pills and raise public awareness through community education programs or campaigns.

Keywords: *Aluminum Phosphide, Poison Control Centre, Wheat pill, Rice tablet, poisoning pattern.*

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INTRODUCTION

Pesticides are an effective way to increase crop output and defend against vector-borne diseases for a fast-growing population. Nonetheless, they pose several human and environmental health risks ***(Kumar and Kalita, 2017).***

The incidence of pesticide poisoning is estimated between one and five million among agricultural workers worldwide with 300,000 lethal cases annually (***Burgess et al., 2000).*** The incidence is likely to be high in developing countries as there is inadequate regulation, lack of training, poor surveillance or information systems, and no personal protective equipment ***(Thundiyil et al., 2008).***

Aluminum phosphide (AlP) comes in the form of tablets or pellets. It has practically ideal pesticide properties: it is poisonous to all stages of insects; highly potent; retains seed viability, and leaves only a small amount of non-toxic Al (OH)3 residue on food grains ***(Moghadamnia, 2012).***

Furthermore, its low cost and widespread availability in the market facilitate its usage as a suicide mean especially in developing agricultural countries ***(Singh et al., 2014).*** In Egypt, AlP tablets **(Figure 1)** became lately a common way to commit suicide and, consequently, a common reason for admission to poison control centers ***(El-Sarnagawy et al., 2022).***

Figure (1): Aluminum phosphide wheat pills with the trade name "Celphos" in Egypt.

Following AlP ingestion, it reacts with water and hydrochloric acid in the stomach liberating phosphine (PH3) gas which is absorbed through the gastric mucosa ***(Hashemi-Domeneh et al., 2016).*** It causes widespread organ damage ***(Farahani et al., 2016).*** Its toxicity mechanism is not fully understood. Some authors attributed it to cytochrome C oxidase suppression or oxidative stress ***(Anand et al., 2013),*** heart failure, a lack of arterial wall integrity ***(Changal et al., 2017),*** reduction of cholinesterase activity, hemolysis, and corrosive effects on the alimentary mucosa ***(Moghadamnia, 2012).***

The released phosphine disrupts mitochondrial activity at the cellular level, it primarily inhibits cytochrome c oxidase activity (Complex IV) and ATP production is significantly reduced ***(Anand et al., 2013).*** Additionally, PH3 has been shown to increase the generation of reactive oxygen species (ROS) and promote oxidative stress by inhibiting enzymatic antioxidants such as catalase (CAT), glutathione, glutathione reductase (GR), and superoxide dismutase (SOD). These changes hasten lipid peroxidation, resulting in cell membrane damage, ionic barrier disruption, nucleic acid damage, and cell death ***(Agarwal et al., 2014; Asghari et al., 2017; Baghaei et al., 2016).***

Cardiovascular collapse, refractory shock, severe acidemia, fulminant hepatic failure, and/or adult respiratory distress syndrome are the most common causes of death ***(Navabi et al., 2018).*** Laboratory abnormalities include leucopenia, leukocytosis, elevated creatinine, and blood urea nitrogen (BUN), raised serum alanine transaminase (ALT), and aspartate transaminase (AST), metabolic acidosis, and electrolyte disturbance ***(Bogale et al., 2021; Sharma et al., 2018).***

Aluminum phosphide poisoning usually progresses so quickly that a large proportion of deaths occur during the first 24 hours of significant exposure, and in severe situations, death can occur as early as three hours ***(Farahani et al., 2016).***

No Specific antidote described so far for AlP poisoning. Management is mainly supportive and aims to control developed toxic manifestations and prevent the expected complications. One of the major preventive measures is avoiding water-based solutions in gastric decontamination (lavage) due to the rapid dissolution of rice tablets in aqueous solutions. This is why oils are used for lavage as alternatives to water-based solutions ***(Darwish et al., 2020; Farahani et al., 2016; Shadnia et al., 2005).*** General supportive and symptomatic treatment is the cornerstone ***(Agrawal et al., 2015).***

AlP poisoning is known for having a high mortality rate. In some poison control centers, it may reach 100%. The amount taken, whether the tablet is fresh or expired, and the duration between exposure and the beginning of supportive treatment all influence the outcome ***(Hashemi-Domeneh et al., 2016).***

However, several modalities have been introduced to save patients' lives and improve the outcome, like the use of intravenous lipid emulsion for phosphine elimination ***(Baruah et al., 2015),*** the introduction of antioxidants to replenish the cellular antioxidant capacity against the aggressive oxidant stress induced by phosphine gas ***(Agarwal et al., 2014; Asghari et al., 2017; Bhalla et al., 2017),*** the myocardial support by digoxin (***Changal et al., 2017; Mehrpour et al., 2011),*** and recently trimetazidine ***(El Shehaby et al., 2022)*** to compat phosphine-induced toxic myocarditis, and the hemodynamic support by intra-aortic balloon pump ***(Mehrpour et al., 2014)***, or the extracorporeal membrane oxygenation ***(Hassanian-Moghaddam et al., 2016; Mohan et al., 2019)*** in cases of intractable shock.

Aim of the work: This study aimed at evaluating the magnitude of acute AIP poisoning, characters of prevalent cases, the general outcome of poisoning, and the most related parameters to patient mortality by a comprehensive retrospective analysis of patient records in the Poison Control Center-Zagazig

University Hospitals (PCC-ZUH) and the poison center of Zagazig General Hospital serving the region of Eastern Delta of Egypt during the period from January 2017 to January 2022. The current research also posed a question of whether AlP poisoning is a true public health problem that urges the reinforcement of proper preventive and control measures to limit its rising morbidity and mortality.

PATIENTS AND METHODS

- **Study Design and Setting:**

This work is a retrospectively cross-sectional study performed in Zagazig University Hospitals and Zagazig General Hospital during the period from the 1st of February to the 30th of April 2022.

- **Study population (patients):**

All cases of Aluminium Phosphide poisoning referred to the Poison Control Center-Zagazig University Hospitals (PCC-ZUH) during the period from January 2017 to January 2022 and to the Poison Center of Zagazig General Hospital during the period from January 2020 to January 2022 (as it was opened during the last quarter of 2019). Both PCC-ZUH and the Poison Center of Zagazig General Hospital serve the residents of the East Delta, the Suez Canal, and the Sinai Peninsula.

I. Inclusion criteria:

All patients with a sure history of absolute exposure to AlP only without any other toxic exposures, of all ages, both sexes, and from all areas served by the poison control centers in the study.

II. Exclusion criteria:

Patients with uncertain history of exposure, those with a history of co-ingestion of other poisons, drugs, or insecticides, and those with unknown poisoning outcomes e.g. those who left the hospital against medical advice.

- **Methods:**

I.Tools of the study and technical design:

We examined all patient records of both poison control centers during the last five years and, using a checklist, we extracted data about patients' age, gender, residence, occupation, mode of exposure, the lag time between exposure and hospital presentation, and the amount ingested besides the routine laboratory investigations performed for all cases including liver function tests especially alanine transaminase level (ALT) and aspartate transaminase level (AST), kidney function tests especially serum creatinine and blood urea nitrogen (BUN), complete blood count (CBC) especially total leukocyte count (TLC), electrolyte levels especially potassium (K) and sodium level (Na), and Arterial blood gases. All patients were divided according to their poisoning outcome into survived and dead (non-survived) and all the above-mentioned data were statistically evaluated among different years and compared in both survived and dead patients to detect their impact on patient outcomes.

II.Administrative and Ethical design:

The design of the study was approved by the Ethical Committee of the Faculty of Medicine, Zagazig University with the number ZU-IRB:#9569-2-1-2022. All patient data were kept confidential and used only for research purposes.

STATISTICAL ANALYSIS

The collected data were computerized and statistically analyzed using Statistical Package for Social Science program (SPSS) (IBM crop. Released 2020. IBM SPSS statistics for windows, Version 27.0. Armonk, NY: IBM crop). Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean ± SD (Standard deviation) and median. The Chi-square test was used to calculate the difference between qualitative variables. The Independent T-test was used to calculate the difference between quantitative variables in two groups in normally distributed data. Mann Whitney (MW) test was used to calculate the difference between quantitative variables in two groups in not normally distributed data. The threshold of significance is fixed at 5% level (P-value) where a P-value of <0.05 indicates significant results and the P-value of <0.001 indicates highly significant results.

RESULTS

The total number of acutely AIP poisoned cases fulfilling inclusion criteria was 309 cases out of total 6788 poisoned cases admitted to PCC-ZUH and Zagazig General Hospital Poison Center in the period from Jan. 2017 to Jan. 2022. **Table (1)** shows the basic characteristics of the AlP poisoned cases. The most frequent age group was 18 to 45 years (66%) followed by adolescents from 12 to 18 years (20.1%). Regarding sex and residence, females represented the majority (62.5%), and 79.3% of the cases were from rural areas. Occupation of the poisoned cases varies among unemployed (30.4%), students (26.9%), farmers (17.8%), and others (24.9%). The majority of poisoned cases were suicidal (70.6%). The overall frequency of AIP poisoning over the last 5 years was 4.55% of total poisoning cases. **Table (2)** and **figure (2)** show a highly statistically significant increase (P<0.001) in AlP frequency in the last two years compared to previous years (7.12% in 2021 and 5.97% in 2020 versus 3.11% in 2019, 2.23% in 2018, and 1.66 in 2017). **Table (2)** and **figure (3)** show that the overall mortality rate of AIP over the last 5 years was 72.5% (224 cases from 309 cases) with no statistically significant difference between the studied years.

Table (1): The basic character of the AIP poisoning cases during the last 5 years (total =309 cases).

Variable	(n=309) N (%)
Age group:	
<12 years	26 (8.4%)
12-18 years	62 (20.1%)
>18-45 years	204 (66%)
>45 years	17 (5.5%)
Sex:	
Male	116(37.5%)
Female	193(62.5%)
Residence:	
Rural	245(79.3%)
Urban	64(20.7%)
Occupation:	
Unemployed	94(30.4%)
Student	83(26.9%)
Farmer	55(17.8%)
Other	77(24.9%)
Mode:	
Accidental	45(14.6%)
Occupational	46(14.9%)
Suicidal	218 (70.6%)

Table (2): Frequency of AlP poisoning and Mortality rate of AlP poisoning in different years (total =6788 cases).

Year	Total poisoned cases (n=6788)	AlP poisoned cases		χ^2 P	AlP poisoned cases		χ^2 P
		N (n=309)	%		Dead N(%) (n=224)	Survived N(%) (n=85)	
2017	1085	18	1.66	**77.61 <0.001 ****	12 (66.7%)	6 (33.3%)	**7.53** 0.11 NS
2018	1212	27	2.23		15 (55.6%)	12 (44.4%)	
2019	933	29	3.11		18 (62.1%)	11 (37.9%)	
2020	1591	95	5.97		71 (74.7%)	24 (25.3%)	
2021-Jan 2022	1967	140	7.12		108 (77.1%)	32 (22.9%)	
Total	6788	309	4.55		224 (72.5%)	85 (27.5%)	

*χ^2: Chi-square test NS: Non-significant (P>0.05) **: highly significant (P<0.001)*

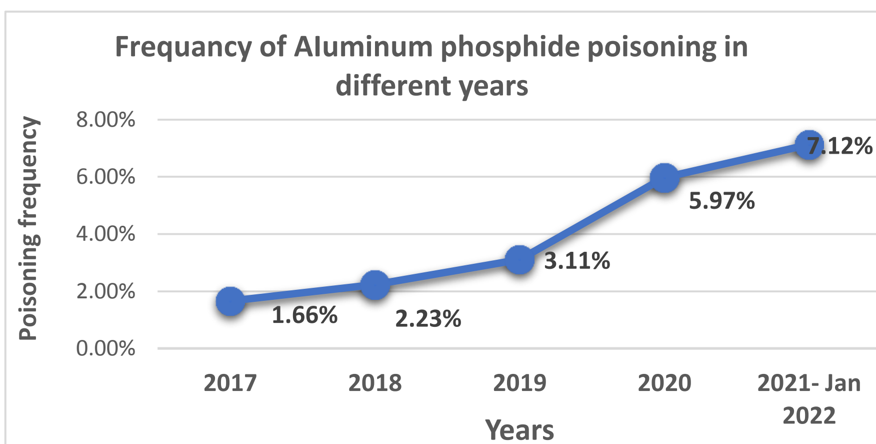

Figure (2): Frequency of Aluminum Phosphide poisoning in different years with rising incidence (total =6788 cases).

Table (3) shows a comparison between different years regarding the demographic data of age and sex reflecting no difference between different years. Regarding residence, as shown in **figure 4**, there was a statistically significant increase (P<0.05) in AlP poisoning among urban residents in the last two years compared with the previous three years (23.2% in 2020 and 25.7% in 2021 versus 5.6% in 2017,7.4% in 2018 and 10.3% in 2019).

Figure (5) shows a statistically significant decrease in farmers (being 14.7% and 14.3% in 2020 and 2021 versus 16.7%, 33.3%, and 31% in 2017, 2019, and 2019 respectively) and an increase in the frequency of unemployed patients (35.8% and 33.6% in 2020 and 2021 versus 16.7%, 18.5%, and 17.2% in 2017, 2018, 2019 respectively) in the last two years compared with the first three years of the study (P<0.05).

Table (3): Change in age and sex of the cases in different years (total =309 cases).

Variable	Total (n=309) N(%)	Years					χ^2 P
		2107 (n=18) N(%)	2018 (n=27) N(%)	2019 (n=29) N (%)	2020 (n=95) N (%)	2021 to Jan 2022 (n=140) N (%)	
Age group: **<12 years** **12-18 years** **>18-45 years** **>45 years**	26(8.4%) 62(20.1%) 204(66%) 17(5.5%)	2(11.1%) 4(22.2%) 11(61.1%) 1(5.6%)	3(11.1%) 7(25.9%) 14(51.9%) 3(11.1%)	2(6.9%) 10(34.5%) 15(51.7%) 2(6.9%)	7(7.4%) 14(14.7%) 70(73.7%) 4(4.2%)	12(8.6%) 27(19.3%) 94(67.1%) 7(5%)	10.15 0.60 NS
Sex: **Male** **Female**	116(37.5%) 193(62.5%)	6(33.3%) 12(66.7%)	6(22.2%) 21(77.8%)	10(34.5%) 19(65.55)	34(35.8%) 61(64.2%)	60(42.9%) 80(57.1%)	4.77 0.31 NS

χ^2: Chi square test NS: Non-significant (P>0.05)

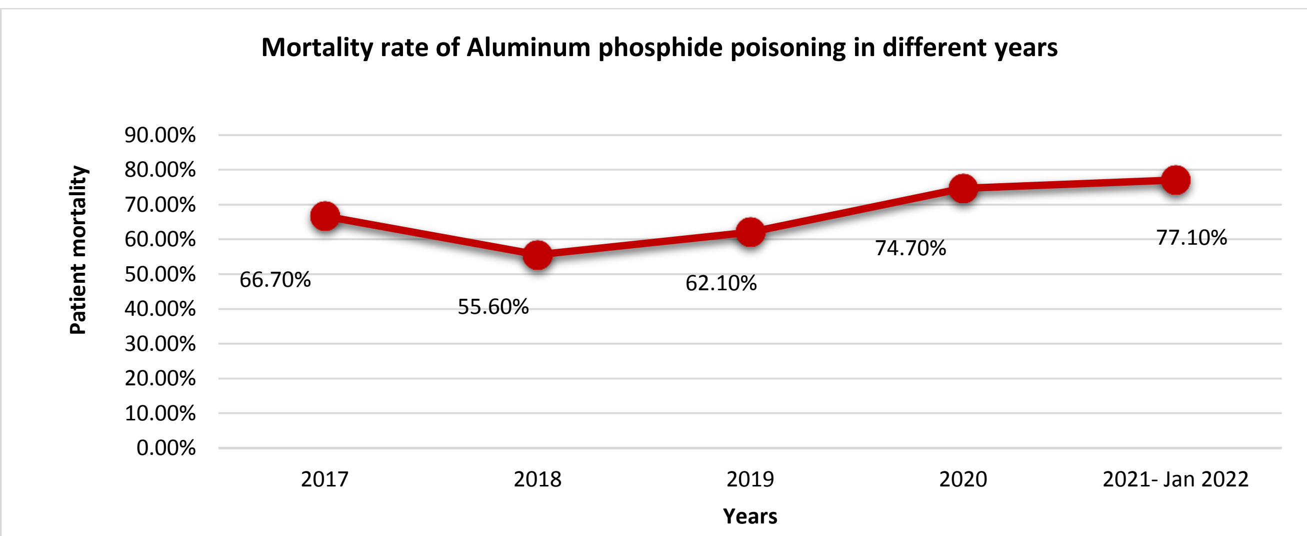

Figure (3): Mortality rate of Aluminum Phosphide poisoning in different years (total =309 cases)

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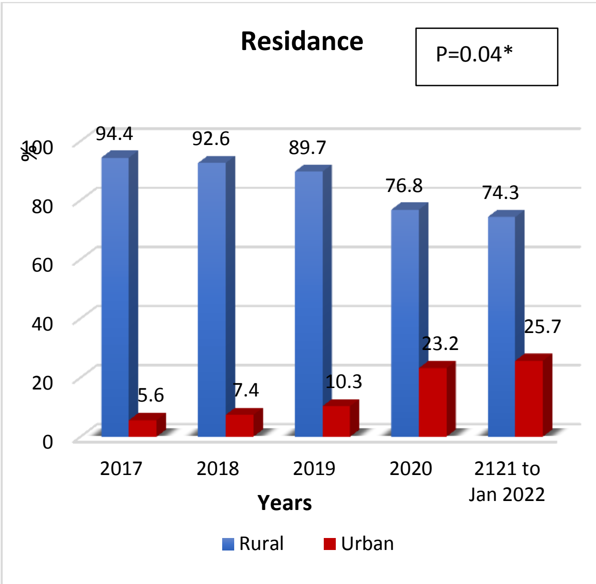

Figure (4): Residence of AlP poisoned cases in different years showing a significant increase in patients from urban localities during the last two years (total =309 cases).

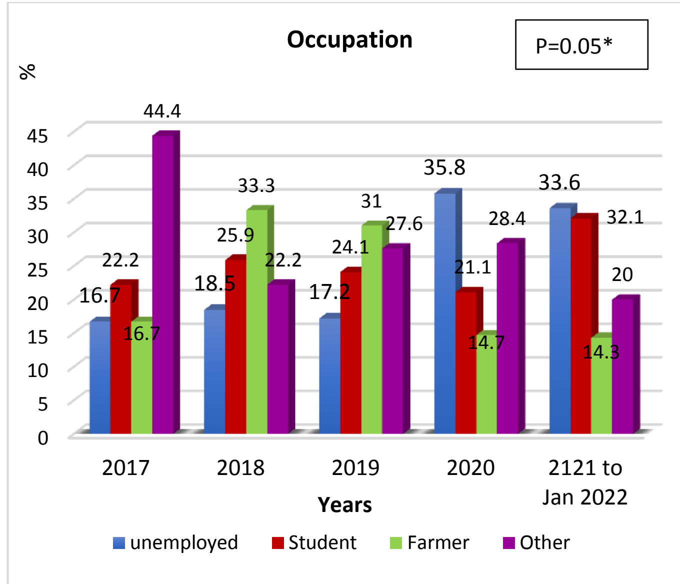

Figure (5): Occupation of Aluminum Phosphide poisoned cases in different years showing a significant rise in unemployed patients during the last two years (total =309 cases).

Suicidal mode of exposure was the predominant over years, but interestingly, it showed a statistically significant increase (P<0.05) in the last 2 years compared with the previous three years (77.9% in 2021, 72.6% in 2020 versus 62.1% in 2019, 44.4% in 2018 and 55.5% in 2017) **(Figure 6).**

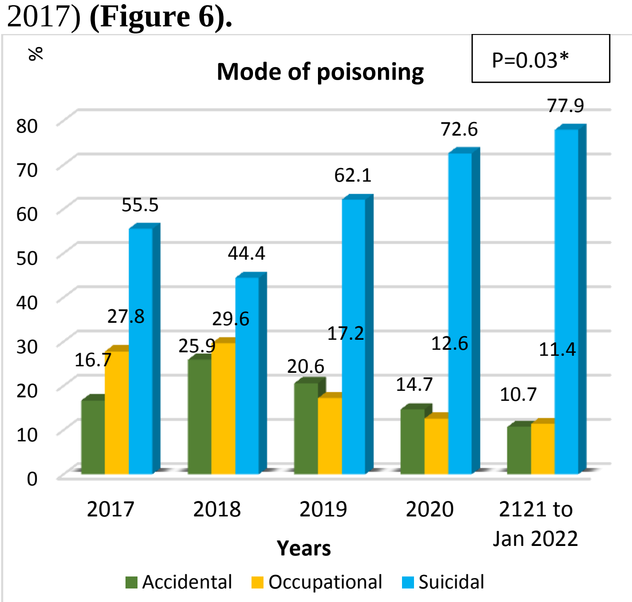

Figure (6): Mode of Aluminum Phosphide poisoning among the studied cases in different years. Suicidal poisoning is predominant with a significant rise over the last two years (total =309 cases).

Statistical analysis of factors related to patient mortality over the studied years showed that neither demographic data variation (age, sex, residence, and occupation) nor the mode of poisoning shows a statistically significant impact on the patient mortality over the years **(Table 4).**

Table (4): Relation between patient mortality and demographic data and mode of AlP poisoning (total =309 cases).

Variable	Total (n=309)	Dead (n=85) N(%)	Survived (n=224) N(%)	χ^2 P
Age group:				
<12 years	26(8.4%)	7(26.9%)	19(73.1%)	
12-18 years	62(20.1%)	18(29%)	44(71%)	0.70
>18-45 years	204(66%)	54(26.5%)	150(73.5%)	0.87
>45 years	17(5.5%)	6(35.3%)	11(64.7%)	NS
Sex:				0.06
Male	116(37.5%)	31(26.7%)	85(73.3%)	0.81
Female	193(62.5%)	54(28%)	139(72%)	NS
Residence:				2.88
Rural	245(79.3%)	62(25.3%)	183(74.7%)	0.09
Urban	64(20.7%)	23(35.9%)	41(64.1%)	NS
Occupation:				
Not working	94(30.4%)	24(25.5%)	70(74.5%)	
Student	83(26.9%)	20(24.1%)	63(75.9%)	2.08
Farmer	55(17.8%)	19(34.5%)	36(65.5%)	0.56
Other	77(24.9%)	22(28.6%)	55(71.4%)	NS
Mode:				
Accidental	45(14.6%)	11(24.4%)	34(75.6%)	0.35
Occupational	46 (14.9%)	12(26.1%)	34(73.9%)	0.84
Suicidal	218(70.5%)	62(28.4%)	156(71.6%)	NS

χ2: Chi-square test NS: Non-significant (P>0.05)

However, **table (5)** shows the important data on the poisoning history and routine laboratory findings that were significantly related to patient outcomes. The amount of AlP ingested and serum ALT, AST, and creatinine levels were significantly higher in dead patients over the studied years (P<0.05). Moreover, a highly significant decrease (P<0.001) in TLC, serum Na^+, PH, bicarbonate (HCO3), and base excess (BE), and a significant decrease in serum K^+ (P<0.05) were found in dead cases compared with the survived. On the other hand, no significant difference was found between the dead and survived cases regarding lag time or BUN among different years.

Table (5): Relation between Aluminum phosphide poisoned patient mortality and the poisoning history with the routine laboratory data (total =309 cases).

Variable	Patient prognosis	N	Mean	SD	Median	Test	P
Lag time (h)	Survived	85	2.76	1.33	3.00	MW=1.44	0.15 NS
	Dead	224	3.12	1.59	3.00		
Amount	Survived	85	0.81	0.38	1.00	**MW=2.54**	**0.01***
	Dead	224	0.90	0.45	1.00		
ALT (IU/L)	Survived	85	44.82	26.42	35.25	**MW=3.26**	**0.001 ***
	Dead	224	73.73	34.18	48.82		
AST (IU/L)	Survived	85	33.12	17.97	26.19	MW=3.16	**0.002***
	Dead	224	52.00	33.76	42.67		
Creatinine (mg/dl)	Survived	85	1.37	0.48	1.51	**t=2.76**	**0.006***
	Dead	224	1.61	0.57	1.52		
BUN (mg/dl)	Survived	85	28.88	15.96	25.11	MW=0.96	0.34 NS
	Dead	224	31.51	17.61	32.16		
TLC (x1000/mm3)	Survived	85	11.06	3.82	10.50	**t=4.92**	**<0.001****
	Dead	224	8.81	2.91	8.80		
K (mEq/l)	Survived	85	3.31	0.51	3.35	**MW=3.23**	**0.001***
	Dead	224	2.91	1.11	3.12		
Na (mEq/l)	Survived	85	148.11	16.23	144	**t=4.60**	**<0.001****
	Dead	224	139.77	6.36	140		
PH	Survived	85	7.36	0.11	7.39	**t=6.13**	**<0.001****
	Dead	224	7.21	0.21	7.27		
HCO3 (%)	Survived	85	17.74	4.01	17.60	**t=14.06**	**<0.001****
	Dead	224	11.04	3.63	10.20		
Base Excess (mEq/l)	Survived	85	-7.12	3.70	-5.90	**MW=9.77**	**<0.001****
	Dead	224	-13.70	4.40	-12.40		

SD: Standard deviation *t: Independent t-test* *MW: Mann Whitney test*
NS: Non-significant (P>0.05) **: Significant (P<0.05)* ***: Highly significant (P<0.001)*
ALT: Alanine transaminase, *AST: Aspartate transaminase, BUN: Blood urea nitrogen,*
TLC: Total leucocyte count, *K: Potassium, Na: Sodium, HCO3: Bicarbonate*

DISCUSSION

Because of being cheap, widely available, and lacking an effective antidote, aluminum phosphide (AlP) poisoning, particularly self-poisoning, is a prevalent and rising public health problem. The first published Indian report of AlP poisoning was in the 1980s, since then it's become a leading cause of poisoning and death, especially in agricultural countries like India, Iran, and African countries, with some case reports from many developed countries ***(Burgess et al., 2000; Gurjar et al., 2011).*** In the Egyptian market, AlP is available with the name Celphos and the general public refers to it as the wheat pills, it accounts for a considerable proportion of patient admissions to poison control centers. Several studies evaluated the magnitude of AlP poisoning in their communities both in Egypt ***(Badawi et al., 2018; El-Sarnagawy, 2017; Mwaheb and Hassan, 2021; Saleh and Makhlof, 2018)*** and in several African and Asian countries ***(Bogale et al., 2021; Navabi et al., 2018; Sharma et al., 2018; Singh et al., 2014).***

This study, to our knowledge, was the first to evaluate the magnitude of absolute AlP poisoning in the East Delta of Egypt, including Sharkia governorate, governorates of Suez Canal, and those of the Sinai Peninsula, showing its rising frequency and increasing spread among different socioeconomic and demographic classes. As well, the current study compared different poisoning conditions and laboratory findings of all patients with their poisoning outcome; which was either recovery and survival or deterioration and death.

The overall frequency of AlP poisoning over the last 5 years in the area of East Delta of Egypt was 4.55% which was a considerable percentage of one agent poisoning. A lower incidence of 1.17% was reported before in Tanta Poison Control Center in the period between 2012 and 2016 ***(El-Sarnagawy, 2017)***

The percentage of AlP poisoned patients has been increasing over the studied years to be significantly higher during the last two years. This increasing trend of AlP poisoned cases was detected in several studies ***(Gargi et al., 2006; Soltaninejad et al., 2012b).*** This uprising number of poisoned cases reflects the AlP increased use for both agricultural and non-agricultural purposes. The availability and laxity in the implementation of its sale has eventually led to misuse in addition to abuse as a means of committing suicide especially with more public recognition of its instant fatality ***(Soltaninejad et al., 2012b)***

The present study showed that the AlP poisoning among the age group of 18-45 years was predominant over the studied years (66%) and it's the most common age group encountered in previous AlP poisoning studies ***(Abdel-Hady et al., 2019; Darwish et al., 2020; Kalawat et al., 2016; Mathai and Bhanu, 2010; Mwaheb and Hassan, 2021).*** However, AlP tablets were found to be frequently used to commit suicide among teenagers by El-***Sarnagawy (2017), Badawi et al. (2018), and Bogale et al.(2021)*** while this age group, from 12 to 18 years (20.1%), comes the second in the current work, ***Sharma et al. (2014)*** in Northern India informed younger age (8.5 years); which may be attributed to the alteration in the mode of poisoning; either accidental or homicidal, whereas, the main poisoning situation in the current study was suicidal.

Females account for the majority of cases over the years representing 62.5% of all studied patients who were mainly from rural areas. This female and rural prevalence were reported before by several studies ***(Badawi et al., 2018; Bogale et al., 2021; Darwish et al., 2020; Mwaheb and Hassan, 2021; Sheta et al., 2019)*** where females face more stressful conditions, social burdens, marital conflict, and economic factors ***(El-Sarnagawy, 2017).*** On the contrary, ***Mathai and Bhanu (2010), Kalawat et al. (2016), Navabi et al. (2018), and Abdel-Hady et al. (2019)*** stated that males were more than females and that could be due to occupational accessibility and economic instability.

Most of the cases were from rural areas (79.3%), strongly associated with illiteracy, paucity of education and work facilities, disputes in the family, and easy availability of

AlP ***(Siwach et al., 1998).*** The Nile Delta is a known agricultural area, with few urban communities in big cities, where AlP is widely used in farming activity without restriction, and with lack of awareness ***(El-Sarnagawy, 2017).*** Nevertheless, the number of poisoned patients from urban communities was found to be significantly higher over the last two years. This could imply that the more the public becomes aware of AlP instant fatality, the more they use it in their suicidal attempts regardless of its availability in their surrounding environment.

Regarding the occupation, about a third of the cases were unemployed (30.4%), followed by students (26.9%), farmers (17.8%), and others (24.9%), and most of our patients were admitted due to suicidal attempts (70.6%) followed by the occupational exposure (14.9%). These findings were in agreement with ***El-Sarnagawy (2017), Badawi et al. (2018), Sheta et al (2019), and Mwaheb and Hassan (2021),*** interestingly, ***Navabi et al (2018)*** reported 100% suicidal poisoning. This contrasts with what was reported in ***2018*** by ***Badawi et al.,*** that most cases were civil employees.

Unemployed patients represented most of AlP poisoning during the last two years, in earlier years of the study farmers were more susceptible due to their occupational exposure and AlP availability in their vicinity, however, with deteriorated economic status and increased unemployment, suicidal incidence among the unemployed significantly rouse. The COVID-19 pandemic over the years 2020 and 2021 could be an accepted explanation for these trends. The COVID-19 pandemic has imposed restrictive measures with a substantial deteriorating effect on the worldwide economy, including the increase in the unemployment from 4·936% to 5·644%, which could be associated with a rise in suicidal attempts of about 2135-9570 suicides per year ***(Kawohl and Nordt, 2020).*** Indeed, a higher unemployment rate during the pandemic resulted in an increased number of suicides due to worsening living conditions with resultant psychological degeneration ***(Persaud, 2021).***

Case mortality has been always high with a mean of 67.24%, and overall mortality of 72.5% for the five years. Similar mortality was reported by previous authors ***(Mathai and Bhanu, 2010; Singh et al., 2014; Siwach et al., 1998),*** and case mortality has been reported to be higher up to 92% in other studies ***(Saleh and Makhlof, 2018),*** while ***Kalawat et al.(2016), Mwaheb and Hassan (2021) and Bogale et al. (2021)*** reported lower mortality of around 35%. The reported mortality rate of acute AlP poisoning varies widely in the literature, ranging from 40% up to 100% even in highly experienced and well-equipped centers either in Egypt or in other countries entangled in AlP poisoning ***(Abdel-Hady et al., 2019; El-Sarnagawy, 2017; Elgazzar et al., 2022; Farahani et al., 2016; Moghadamnia, 2012; Soltaninejad et al., 2012a).***

The reported causes of death in the current study were progressive cardiogenic and hypotensive shock, acute respiratory distress syndrome (ARDS), and late manifestation of hepatotoxicity and nephrotoxicity which are all defined causes of AlP poisoning mortality ***(Bogale et al., 2021; Gurjar et al., 2011; Moghadamnia, 2012).*** All received poisoned patients were admitted to ICU except one-third of survivors who were admitted to PCC-ZUH intermediated care. We found no impact of different demographic data or modes of poisoning on patients' mortality as reported before by ***Mathai and Bhanu (2010), and Kalawat et al. (2016).*** In contrast, ***El-Sarnagawy (2017)*** reported a statistically significant difference in age, residence, and mod of exposure between survivors and non-survivors.

Regarding the history of exposure, we found no significant differences between survived and non-survived patients in lag time from exposure to arrival being almost around three hours. This relatively short lag time could be explained by the fact that most patients in our communities, especially females, did not intend to end their lives but they just tried to gain the attention and compassion of their families, so, they rapidly sought medical intervention ***(El-Sarnagawy,***

2017). The lack of significance of patient lag time on the patient mortality was also reported before by ***Bogale et al. (2021).*** However, ***El-Sarnagawy (2017), Navabi et al. (2018), and Abdel-Hady et al., 2019)*** found it a significant factor.

On the other hand, the amount ingested was significantly higher in dead patients as described before by several studies ***(Bogale et al., 2021; El-Sarnagawy, 2017; Navabi et al., 2018; Sharma et al., 2018).*** The lethal dose of ALP in an average human is between 150 and 500 mg depending on the exposure of the tablet, which is 3-gram weight, to moisture and the expiry date. ***Mathai and Bhanu (2010)*** reported that neither the amount ingested nor the lag time affects the patient outcome.

All patients were evaluated by certain routine investigations and the current study defined a significant difference in values of certain laboratory investigations between survived and non-survived. for example, although the liver enzymes ALT and AST whose values reflect a high variation (not normally distributed), both were significantly higher in non-survivors as reported before by several studies (***Abdel-Hady et al., 2019; El-Sarnagawy, 2017***). Conversely, ***Mathai and Bhanu (2010)*** found them with no significant relation to patient mortality.

Serum creatine, as well, was significantly higher in deceased patients which is in harmony with previous studies ***(Abdel-Hady et al., 2019; El-Sarnagawy, 2017; Ghonem et al., 2020; Mathai and Bhanu, 2010),*** while BUN wasn't significantly different among survivors and non-survivors and this is unlike what was described by other researchers such as ***El-Sarnagawy (2017) and Abdel-Hady et al.(2019).***

Impaired liver and kidney functions are part of the multiorgan failure induced by AlP secondary to cytochrome oxidase inhibition and failed cellular respiratory and metabolic activities, as well, the liver and kidney are one of the most sensitive organs to hypoxia secondary to shock ***(Gurjar et al., 2011; Hashemi-Domeneh et al., 2016).***

There was no absolute leucopenia reported in all enrolled patients, nevertheless, we detected a relative, but significant (P=0.001), reduction of TLC in deceased patients. Some case reports of developed leucopenia with AlP poisoning were reported ***(Ntelios et al., 2013) and Moghadamnia (2012)*** considered leucopenia as an indicator of severe AlP toxicity. However, severe leucopenia was an infrequent complication of AlP intoxication. Understanding the molecular targets of phosphine in white blood cells, especially neutrophils, made it difficult to explain the development of leucopenia due to neutrophil resistance to respiratory chain inhibitors, dependence on glycolysis for energy production, and being short-lived cells preprogrammed to undergo cellular death with the recognized role for ROS in regulating this process ***(Ntelios et al., 2013).*** On the contrary, ***Kalawat et al. (2016)*** found leucocytosis in the majority of patients and ***Ghonem et al. (2020)*** reported its predictor role in mortality and attributed it to the body's response to toxic stress.

Serum electrolytes, K^+ and Na^+, showed a significant decrease in expired cases. Significantly lower serum K^+ was reported before by ***Ghonem et al. (2020),*** meanwhile, other studies reported hypernatremia with hypokalemia ***(El-Sarnagawy, 2017)***.

Hypokalemia may be caused by vomiting after tablet ingestion or due to catecholamine release. Both hypo and hypernatremia could be found in AlP poisoned patients and are indicators of poor prognosis. Generally, serum electrolyte changes in acute AlP poisoning are variable and debatable ***(Hashemi-Domeneh et al., 2016).***

Arterial blood gases are considered an important evaluation tool for all AlP poisoned patients due to expected aggressive metabolic acidosis induced by phosphine gas with subsequent accumulation of lactic acid as a result of inhibition of oxidative phosphorylation and poor tissue perfusion resulting from the irreversible shock which is linked ultimately to poor patient prognosis ***(Anand et al., 2013; Gurjar et al., 2011).*** All of the PH, $HCO3^-$, and base excess values showed a highly significant decrease in the deceased patients and several studies have reported its association with mortality ***(Abdel-Hady et al., 2019; El-Sarnagawy, 2017; El-Sarnagawy et al., 2022; Elgazzar et al., 2022; Ghonem et al., 2020; Kalawat et al., 2016; Mathai and Bhanu, 2010; Navabi et al., 2018; Sheta et al., 2019).*** Metabolic acidosis increases the risk of mortality due to its depressive effect on the contractility of the myocardium resulting in cardiogenic shock ***(Hosseini et al., 2020).***

The limitation of the present study was the lack of records about the clinical or the electrocardiographic (ECG) evaluation for most cases which didn't allow us to incorporate them into the evaluation of important parameters related to patient mortality.

CONCLUSION

Assessment of the frequency of AlP poisoning over the last five years throws light on its growing public health threats especially by being an available means of committing suicide which was found to be more frequent in females and unemployed patients, not only in rural but also in urban communities. Moreover, thorough history taking and comprehensive routine workup, for example, the liver function tests, kidney function tests, complete blood count, serum electrolytes, and arterial blood gases, can evaluate the poisoning severity and be linked to patient mortality.

RECOMMENDATIONS

On the public health scale, it's recommended that the AlP users must be working under strict supervision and license from the Ministry of Agriculture in an attempt to limit its public availability, Restriction or forbid the open sales of AlP, and search for safer alternatives by official health care systems and raising the population's awareness about appropriate handling or storage through community education programs or campaigns, and on the patient assessment scale, further extensive and comprehensive clinical studies aiming to design a reliable prognostic system through more specific and sensitive parameters.

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