

Aluminum phosphide poisoning in Saudi Arabia over a nine-year period

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BACKGROUND: Aluminum phosphide (AIP) is an insecticide and rodenticide used to protect stored grains from rodents and other household pests. This substance is highly toxic to humans and has been the cause of many accidental and intentional deaths due in part to poor regulation of sales and distribution in many countries.

OBJECTIVES: Describe poisonings reported to the Ministry of Health in Saudi Arabia in terms of demographic variables and by time and geographic distribution.

DESIGN: Retrospective medical record review.

SETTING: Ministry of Health hospitals nationwide.

PATIENTS AND METHODS: Using a semi-structured checklist, data was collected from patient records that contained sociodemographic variables and the outcome (died or discharged).

MAIN OUTCOME MEASURES: Aggregated data, summary statistics and statistical comparisons.

SAMPLE SIZE: 68 patients.

RESULTS: Thirty-eight (56%) were female and the mean (SD) age of patients was 18.6 (1.86) years. Eighteen of 22 (82%) patients who died were younger than 20 years old. Mortality in patients younger than 20 years of age was greater than in adults ($P=.043$). Mortality was highest in patients younger than 7 years of age ($P=.006$). The cases were reported by the Islamic years 1427-1435, corresponding approximately to Gregorian years 2006 to 2017. Fifty-six cases (83%) were reported from Jeddah. Most cases were due to accidental exposure to phosphine gas during fumigation.

CONCLUSION: Mortality due to AIP poisoning was highest in children and most commonly occurred during fumigation of households. Delays in medical attention and diagnosis may have contributed to mortality.

LIMITATIONS: Retrospective data collection and relatively small sample size. Data on exact amount and route of phosphide ingestion or exposure not available.

CONFLICT OF INTEREST: None.

Poisoning is a shared medicosocial problem that represents a major health challenge the world over and consumes valuable health service resources with considerable morbidity and mortality. Aluminum phosphide (AIP) is a well known, highly efficient insecticide and rodenticide,¹ and is one of the most commonly used pesticides readily available in local markets though its sale is illegal.^{2,3} It does not alter seed viability and leaves no residue on protected grains, yet elicits extreme toxic effects to humans for which no suitable antidote is available. Mortality from AIP poisoning ranges from 37% to 100%.⁴ Exposure is either accidental, occupational or by suicidal intent.^{4,5}

When exposed to moisture, phosphides emit phosphine gas (PH₃), which is the active form of the agent. The gas is colorless, flammable and toxic with a distinct odor of garlic or decaying fish.^{5,6} The released phosphine can disrupt myocardial contractility and cause fluid loss leading to pulmonary edema. As a result, metabolic acidosis and acute renal failure may ensue. Other reported toxic symptoms are disseminated intravascular coagulation, hepatic necrosis and altered magnesemia.⁷ AIP-induced death can occur between 1 to 48 hours with almost 95% of the deaths within 24 hours.⁸

AIP is synthesized as dark gray or dark yellow crystals and formulated as tablets, pellets, granules, or dust. In Saudi Arabia, it is marketed as dark grey 3-gram tablets containing AIP (56%) and carbamate (44%). It is sold under brand names as Celphos, Alphos, Quickphos, Phosfume, Phostoxin, Talunex, Degesch, Synfume, Chemfume, Phostek, and Delicia.⁹ In Saudi Arabia, the easy accessibility to this fumigant insecticide was an important public health concern as its fatal dose ranges from 0.15-0.5 grams and ingestion of three or more tablets invariably results in death. Creating awareness among healthcare professionals and the general public may help reduce the risk of poisoning.¹⁰

The tragic deaths of two young Danish children in Jeddah from AIP poisoning in 2009 led to a major reshuffle in the health organization and the introduction of numerous legal and legislative changes. A new Chemical Safety Program (CSP) division was established under the General Department of Environmental and Occupational Health in the Ministry of Health (MOH). The MOH mandated that all hospitals and health centers under the ministry report all cases of chemical and drug poisoning in a prescribed format on a monthly basis to the CSP, which in turn reviewed and forwarded data to other relevant health authorities. To regularize the sale, use, distribution and disposal of agricultural and industrial chemicals, CSP conducted various

training and awareness programs at the national and regional levels for stakeholders. It continues to liaison with the World Health Organization in all matters of policy implementation and recommendations. The CSP, in collaboration with other governmental organizations, made several recommendations to monitor the safe use, sale and distribution of chemical pesticides in Saudi Arabia.¹¹

This first review of aluminum phosphide poisonings reported to the MOH in Saudi Arabia should provide valuable feedback for poison information centers and health policymakers. We expect the data and analysis to contribute significantly in strengthening preventive measures against aluminum phosphide poisoning-induced mortality and morbidity. The goal of the study was to report the numbers of cases during the approximate period of 2006 to 2017 by demographic and geographic variables, gain some idea of trends and some perspective on the complex issues of the problem (e.g., increased controls from policymakers, public awareness and education).

PATIENTS AND METHODS

This was a retrospective, nationwide observational study of all cases of patients with AIP poisoning reported by hospitals to the CSP Division, General Department of Environmental and Occupational Health, Ministry of Health, Riyadh, Saudi Arabia for the period from March 2006 to December 2017 (data collection recorded by Islamic years 1427-1435).

Data was collected using a semi-structured checklist from patient records that contained sociodemographic variables and the outcome (died or discharged alive). Counts and percentages were tabulated to assess the characteristics of patients with AIP poisoning. The proportions of demographic characteristics and outcomes were compared using the Pearson chi-squared test for associations. The statistical analysis was done using the IBM SPSS software for Windows, version 20.0, Armonk, NY: IBM Corp.

RESULTS

Between March 2006 to December 2017 (Islamic years 1427 to 1439) there were 68 cases of AIP poisoning reports as documented by the CSP. Of the 68 patients admitted, 53 had phosphine gas inhalation, 5 had topical exposure and the route of exposure was unknown in 10. In the majority of the cases, AIP tablets were being used as a rodenticide in households or in the neighborhood or there was accidental exposure to the tablets, with the number of tablets in the range of 1 to 8 (no cases were reported as intentional). Thirty-eight (56%)

of the 68 AIP patients were female with a female/male ratio of 1.26:1. The mean (SD) age of patients was 18.6 (15.3) with a range of 1 to 60 years. Forty-two patients (62%) were 1-20 years of age (**Figure 1**) and 50 (74%) were non-Saudis (**Table 1**). Of the 68 cases admitted, 22 (32%) died. The majority of deaths occurred during the first 36 hours, mostly due to delayed identification of the cause or type of poisoning. Forty-six (68%) survived and were discharged without any major complications. Differences between age groups in the number of deaths were statistically significant: 82% of dead patients (18/22) were younger than 19 years of age. Among children, deaths were more frequent among the youngest (**Figure 2**). Three were infants and 17 were children of <6 years of age. Sixteen (73%) out of the 22 dead were 1-14 years of age with a mean age of 2.8 (2.5) years. Of the patients who died, 19 of the 22 were non-Saudi (**Table 2**). The difference in the number of cases between men and women was greatest in the 20- to 40-year old age group, but the differences were not statistically significant (**Figure 3**).

All cases had common signs and symptoms of nausea and vomiting, metabolic acidosis (82%), hemodynamic instability (82%) and abdominal pain (64%) with 7 cases being asymptomatic (**Table 3**). The majority of the cases were due to accidental use of AIP as rodenticide in the household and a few due to occupational

exposure to phosphine gas in agricultural settings. As no specific antidote is available, treatment was only supportive. Compared to patients who survived, those who died were either not diagnosed early and hence were not given specific supportive treatment or were later found to have been exposed to high doses (4.2

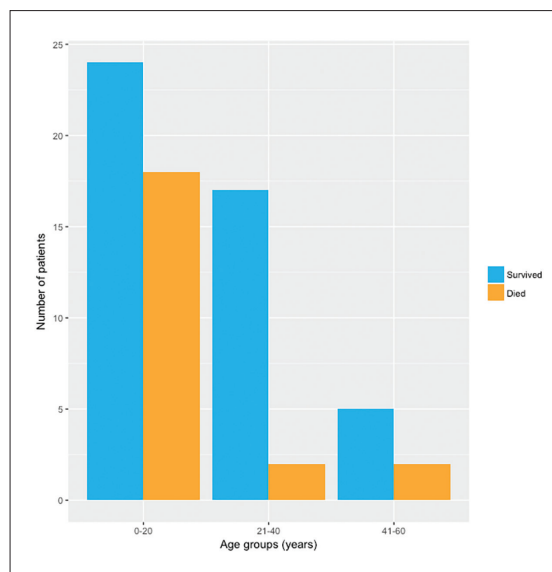


Figure 1. Number of aluminum phosphide poisoning cases by age group and outcome (chi-squared=6.299, df=2, $P<.043$).

Table 1. Number of aluminum phosphate poisoning cases by nationality, outcome and sex for each Gregorian year.

	2006	2007	2008	2009	2014	2015	Total
Nationality							
Saudi	0	0	8	0	1	9	18
Non Saudi	1	9	5	18	6	11	50
Total	1	9	13	18	7	20	68
	Chi-squared=22.35, df=5, $P<.001$						
Outcome							
Survived	0	5	7	12	4	18	46
Dead	1	4	6	6	3	2	22
Total	1	9	13	18	7	20	68
	Chi-squared=8.75, df=5, $P=.12$						
Sex							
Male	1	1	4	10	4	10	30
Female	0	8	9	8	3	10	38
Total	1	9	13	18	7	20	68
	Chi-squared=7.90, df=5, $P=.16$						

grams vs 1.5 grams), or developed severe metabolic acidosis and hemodynamic instability. Jeddah had the highest number of cases (83%) followed by Riyadh (7%) and Madinah (6%) (Figure 4). Sixteen of the 22 deaths occurred in Jeddah.

The number of reported cases increased in the first 4 years, followed by no reported cases for three years (Figure 5). However, in 2014 and 2015 there was an upsurge in reported cases followed again with no reported cases in subsequent years.

DISCUSSION

Aluminum phosphide (AIP) is highly toxic with serious and fatal detrimental effects.¹⁰ There is a great risk of a fatal outcome with ingestion of 'unexposed' (fresh) tablets. Severe poisoning can lead to death in about 3 hours, ranging between 1-48 hours. Clinical presentation depends upon the time elapsed from the time of ingestion or exposure. A qualitative silver nitrate paper

test (turns black on reaction) or liquid gas chromatography can confirm presence of phosphine in gastric fluids and exhaled breath. Hence, utmost care must be taken to avoid poisoning episodes.¹² In Saudi Arabia, pesticide use has increased rapidly with increased development of agriculture. Such pesticides must be used by skilled professionals at crop transport, storage or processing facilities.^{13,14} Even though there is a ban in the country on use of AIP, products containing AIP can still be purchased or brought into the country fairly easily. These particular products are not intended for personal or home use and are frequently sold to untrained civilians who use it improperly inside homes with often deadly results, and all too often small children are the victims.^{15,16} Preventive strategies therefore need to be adopted at a national level to spread awareness among the population. A series of tragic accidents involving AIP that were widely reported by the media, such as

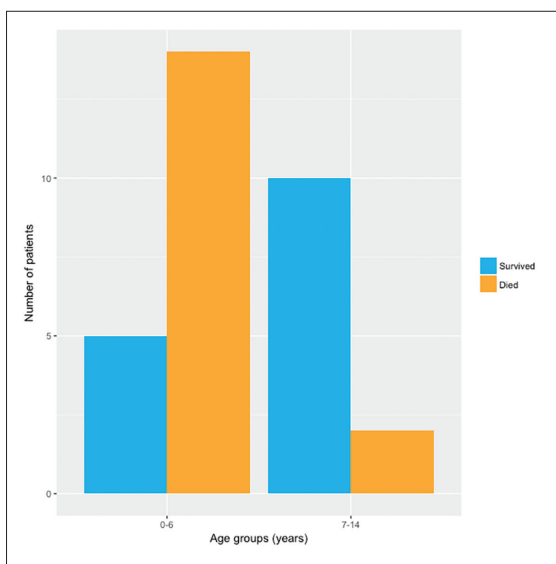


Figure 2. Number of aluminum phosphide poisoning cases in children by outcome (chi-squared=7.4272, df=1, P=.006).

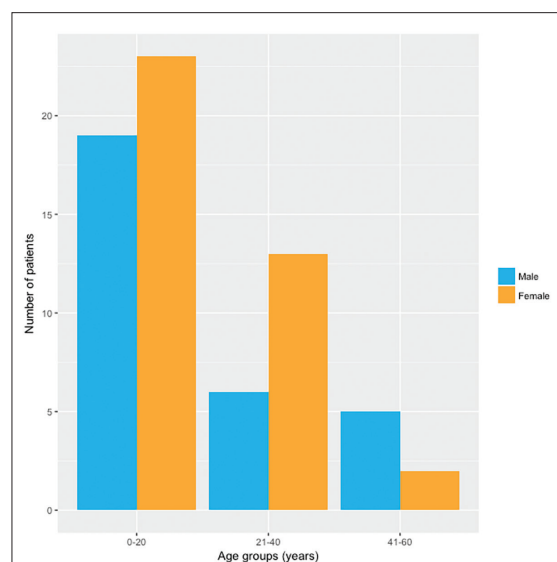


Figure 3. Number of aluminum phosphide poisoning cases by age group and sex (chi-squared = 3.3508, df=2, P value=.1872).

Table 2. Outcome of aluminum phosphate poisoning cases by nationality and sex.

	Survived	Died	Chi-squared results
Saudi	15 (22)	3 (4)	2.75, df=1, P=.097
Non-Saudi	31 (45)	19 (28)	
Male	20 (66.7)	10 (33.3)	0.024, df=1, P=.878
Female	26 (68.7)	12 (31.4)	

Values are n (%).

Table 3. Symptoms and clinical presentations among patients reported as having aluminum phosphide poisoning (n=68).

Variable	n (%)
Nausea and vomiting	68 (100)
Metabolic acidosis	61 (90)
Hemodynamic disorders	34 (50)
Epigastric pain	30 (45)
Loss of consciousness	20 (30)

the deaths of two young Danish children in Jeddah from pesticide gas poisoning in 2009, are wake-up calls for authorities. Prior to that event, several news outlets reported cases like the death of two Ethiopian boys during home fumigation with AIP, which also led to the deaths of two neighboring Saudi children. In 2007, three Pakistani children in Madinah and two Egyptian girls in Riyadh died after their homes were fumigated. A month before an entire Pakistani family of six died when their apartment was fumigated.¹⁴ All these events exerted political pressure on the authorities to act to control the menace of AIP poisoning.

The symptoms of the patients in our study were similar to those in other studies.^{4,6,17} The fatal dose of AIP ranges from 150-500 mg/70 kg⁴ and in our study the deceased patients had been allegedly exposed to 1-8 tablets of AIP when compared to those survived. Suicidal or accidental poisoning with AIP has become rather notorious in many Asian countries over the past few decades and exposure to AIP is a relatively common cause of poisoning from agricultural chemical exposures in many countries, including Saudi Arabia. In the present study, however, all cases of AIP poisoning were reported to be accidental without any suicidal intent. Loose application of the regulations controlling the use of AIP, together with their availability and ignorance of its danger by users, might put exposed people at risk of poisoning.¹⁷

Despite the well-documented literature about the

risks associated with exposure to AIP, intoxication from phosphine inhalation can be difficult to confirm and is frequently a diagnosis of exclusion when reliable biomarkers of exposure and environmental measurements are not available. Treatment should be started as soon as history and clinical examination support AIP poisoning, and should not be delayed for the confirmatory diagnosis. In the present study, most of the deaths reported were due to inability in diagnosing AIP poisoning in time or uncertainty in the prediction of symptoms that delayed or resulted in wrong supportive care.

Mortality due to AIP principally depends on the amount consumed. Fatal accidental cases have been reported when AIP was used as a grain fumigant for bulk shipment of food. The mortality rate in our study was 32%, and 62% of the patients were younger than 20 years. In similar studies, 28 cases with mean (SD) age of 24 (11) years of AIP poisoning admitted in Morocco between January 1992 and December 2002.^{8,9} Another study in Iran reported an overall mortality of 31%, with 50% being male with a mean age of age of 27.1 years.² Most of the patients were between 20 and 40 years old. However, in contrast to our study, the Iranian study reported that 93% of cases were self-poisoning with a suicidal intent.¹⁸ In our study, 16 of 22 dead (73%) were 0-14 years of age. In other studies, mortality reported was 47% and 58.6%.¹⁹⁻²¹ The higher mortality in children in our study may be because cases were due to accidental exposure when AIP was used for house

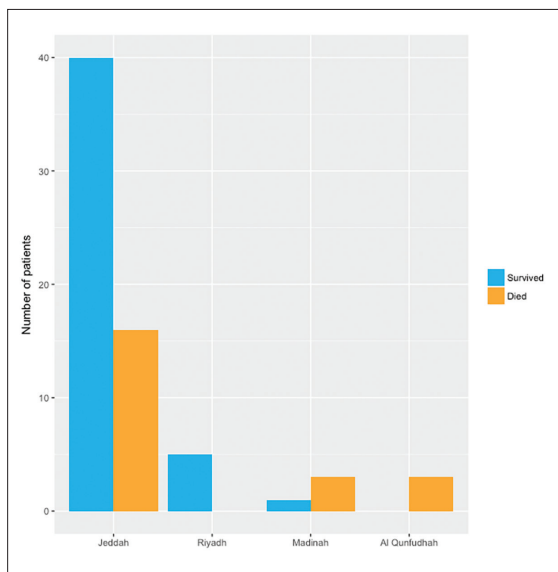


Figure 4. Number of aluminum phosphide poisoning cases by region and outcome (chi-squared=12.354, df=3, P=.006).

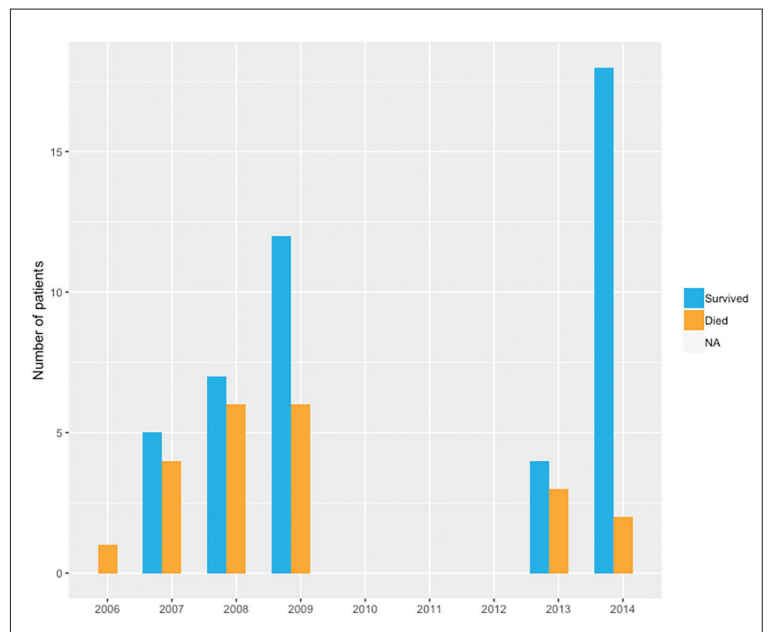


Figure 5. Number of aluminum phosphide poisoning cases by Gregorian year.

fumigation. In other retrospective studies in children the reported mean age of poisoning was 8.5 years. Increasing time lag, higher amount of AIP ingestion, and higher PRISM III score at admission were significant predictors of mortality among children, with AIP poisoning. In our study the toxic dose may not have been ascertained accurately as most poisonings were accidental during fumigation and occurred without the knowledge of the victims or family members. Also, the possibility of an inappropriate history on the amount of AIP ingested or exposed cannot be ruled out.^{22,23}

The mean time between AIP exposure and start of medical intervention in our study was not identical as the poisoning with AIP was not due to ingestion but due to exposure to released phosphine gas in an enclosed space in a residential or public buildings during fumigation and thus treatment was based on an evaluation of symptoms and signs. However, all patients admitted to the intensive care unit received gastric lavage with activated charcoal followed by supportive treatment. The cases reported during the years 2009 and 2014 saw 27% and 30% of total cases respectively. There was an increasing trend in the number of cases reported from 2006 to 2009 (1.5% to 27%) followed by no cases during 2010 to 2012. The years 2013 and 2014 witnessed an upsurge of about 30% followed by no reported cases from 2015 to 2017. Increases in the years 2007 and 2013 followed by a decrease in the immediate following years may indicate an initiation of control measures. However, no specific inference could be drawn from these data. The majority of cases in Jeddah probably reflects the fact that it is a commercial hub and densely populated with a sizeable expatriate population.

The limitations of the study are retrospective data collection and the relatively small sample size with lack of data on the definite amount of AIP and its route of exposure. Also, there is a lack of information on the

exact time lag between admission of the patients and initiation of treatment. This study is not exhaustive as the data were from hospitals under MOH, thereby leaving out many possible cases from non-governmental hospitals. In conclusion, mortality due to AIP poisoning affects children more than adults. Most cases are due to accidental exposure to phosphine gas during fumigation. Delays in medical evaluation and diagnosis are a factor in the high mortality. The rampant and illegal use of AIP for fumigation has been reported in the media.^{14,24}

The results of this study emphasize the need for legal and administrative organs of Saudi Arabia to strictly implement the adopted recommendations for the epidemiological surveillance of pesticide poisoning and agricultural pesticides training conducted by the Chemical Safety Program in the General Department of Environmental and Occupational Health during May of 2014 in Jeddah. Further, the authors would like to suggest the legal and legislative authorities to adopt the following:

- Overhauling the sale and distribution of AIP through a centralised single distributor for the whole of Saudi Arabia
- Authorising the redistribution only from the same single centralised distributor
- Use of bar coding or other identifying features to track logistical distribution and use
- Disseminating information on the safe and protective use of aluminum phosphide for the general public
- Promoting research for safe alternatives to AIP

In conclusion, mortality due to AIP poisoning affects children more than adults. The number of casualties among children reflects use of AIP during home fumigation. Awareness of its dangers must be created at the community levels and the agent must be regulated with utmost care.

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