

An epidemiological study of poisoning cases in Babol (northern Iran) from 2015 to 2018

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Received: 10 Feb 2020

Revised: 3 May 2020

Accepted: 24 May 2020

Abstract

Background: Poisoning is a major public health problem that constitutes a significant share of the global burden of disease. Previous studies conducted in this area indicated the importance of such epidemiological studies. The most critical impact of these studies is their effect on changing current regulations and, therefore, decreasing poisoning cases. We aimed to evaluate all poisoning cases with regard to the patients' demographics and the involved intoxicants.

Methods: The present study was conducted to investigate all poisoning cases who were admitted during a three-year period. Causes of poisoning, hospitalization, management procedures and outcome of the cases were surveyed. A total of 1448 patients referred to Shahid Beheshti Hospital (Babol, Iran) from 2015 to 2018.

Results: More than half of the patients were females (51.7%), and the majority of poisoning cases were seen in patients aged between 15 to 25 years (34.2%). It was found that suicide made a large part of poisoning cases (65.6%), and females tend to attempt suicide more than males (64.3% vs. 35.7%, respectively). Also, regular drugs followed by club drugs were the most abundant toxic agents (52.1% and 23.3%, respectively). Aluminum phosphide (AIP) was the most lethal intoxicant in our study, accounting for 68.2% of all deaths.

Conclusion: According to the results, it is concluded that the existing regulations for drug control and suicide prevention have not been efficient enough and further actions yet to be made to reduce the consequences of drug- and non-drug-related toxicities.

Keywords: Toxicity, Aluminum phosphide, Suicide, Poisoning, Iran, Babol, Epidemiological Studies

Citation:

Barary M, Pirzadeh M, Rezaeian N, et al. An epidemiological study of poisoning cases in Babol (northern Iran) from 2015 to 2018. Caspian J Intern Med 2021; 12(1): 35-44.

Poisoning is an important health problem, especially in the developing countries, and accounts as one of the leading causes for patient admissions to intensive care units (1,2). Poisoning has a remarkable influence on society in terms of health, economy, and culture (3). In developing countries, lack of surveillance systems, inappropriate regulations, and easy access to many kinds of pharmaceuticals, club drugs, and chemicals have been the cause for developing a situation that leads to high rates of poisoning (4). It has been reported that suicidal and intentional poisoning often holds the record in countries with low and middle income (5). Drug and chemical poisoning have been evaluated to be the two most common causes of poisoning, among which the drug-related ones are the most frequent. Moreover, these data can be attributed to Iran (6). Poisoning is the most common cause of hospitalization and has been estimated to be the second cause of death in this country (7). In most parts of Iran, drugs are the most causes of poisoning, whereas, in northern agricultural regions of the country, pesticide-related toxicities are the most dominant (8).

Although poisonings due to opioids and agents with similar actions such as tramadol account for the most medical admissions to hospitals and poisoning centers, different studies have indicated a rise in aluminum phosphide (AIP) poisoning in Iran (9,10). Poisoning with AIP has attracted much attention due to different reasons, including its easy accessibility, rapid action on disturbing cellular oxygen utilization, and lacking proper antidotes or treatments for its intoxication (11). During a ten-year study in Tehran, an increase in poisoning cases, and a reduction in the age of admissions have been observed (12). It has been reported that in the northern and northwestern parts of Iran, antidepressants, especially TCAs, are the first and, in some cases, the second cause of drug-related poisonings (8). It has also been estimated that organophosphate poisoning constitutes the majority of poisoning cases in northern Iran, e.g., in Gilan province, were the most common intoxicants (13).

Among all the ways for attempting suicide, self-poisoning has an old history (14), and because of high accessibility to different medications in Iran, intentional self-poisoning is estimated to be a common way (15–17). In a study taken place in Tehran, in 2003, most poisoning cases (around 79 percent) were intentional, and 21 percent were accidental (18). A one-year cross-sectional study in Babol indicated that suicide attempts consisted of most of the poisoning cases, and benzodiazepines were the most frequent causes of the intoxication (19). Another similar study in the northern part of Iran also reported that most suicide cases occurred in spring and least in autumn (20). According to WHO, suicide is the second cause of death among individuals aged between 15 and 29 (21), and up to one million people in the world commit suicide each year, and this number will rise to 1.5 million by the end of 2020 (22).

Babol is a city in Mazandaran located in the North of Iran. Mazandaran is located near the Caspian Sea and thus is an ideal area for agricultural production of rice. Because of that, the high accessibility to pesticides by farmers can elevate the risk of accidental poisoning. Among those is aluminum phosphide, also known as rice tablet. This easily obtained tablet is responsible for a large number of deaths due to suicide events in northern Iran (23, 24).

Furthermore, the prevalence of drug abuse like tramadol is high among young people. Due to the importance of poisoning and the incomplete data in poisoning patterns in Mazandaran, this study was conducted to evaluate the patients based on categories of toxic agents, routes of exposure and clinical

signs and symptoms admitted to Shahid Beheshti Teaching Hospital, a referral hospital for poisoning in western Mazandaran.

Methods

This study has been approved by the Ethics Committee of Babol University of Medical Sciences (Babol, Iran) with registration number: IR.MUBABOL.REC.1399.156. This cross-sectional study surveyed 1448 poisoning cases from 2015 to 2018. All cases were referred to Shahid Beheshti General Hospital as one of the leading medical training centers of Babol University of Medical Sciences (Babol, Iran). The data of patients' profile (such as; age, gender, marital status, profession, and living area), categories of toxic agents (drugs and club drugs, pesticides, phosphides, alcohol, corrosive agents, gases, heavy metals, and foods), type of intoxication (suicide, accidental, involuntarily, food and unknown), route of exposure (oral, inhalant, injection, dermal), clinical signs and symptoms, drug history, hospitalization period, morbidity and mortality rates were extracted from patient's files and entered into a pre-designed datasheet.

All data were presented as mean \pm standard deviation (SD), and the differences between groups were assessed by Pearson's chi-square test tests. Where applicable, relative risk (RR) with 95% confidence interval (CI) were added. A probability level ($p < 0.05$) was considered statistically significant. The statistical analysis was performed using SPSS 25.0 software (IBM Inc., Chicago, IL, USA).

Results

A total of 1448 patients were admitted as cases of poisoning. Of these, 748 (51.7%) were females, and 700 (48.7%) were males. Most of the patients (34.2%) were between 15 and 25 years of age, and the mean (\pm SD) of age was 33.89 ± 0.86 (table 1). The most frequent agents of poisoning were pharmaceutical or regular drugs, club drugs, phosphides, and pesticides, respectively. Other cases of poisoning have been recorded with lead, food, alcohol, corrosive agents, and gases. The male patients were poisoned mostly by using club drugs whereas the females were mostly affected by drugs. Also, in both rural and urban areas, drugs were the most frequent intoxicants, followed by club drugs (table 2).

Table 1. Frequency and percentage of patients' profile findings by gender

		Male		Female		p	Total		
		n	%	n	%		n	%	
Age group		< 0.0001							
	< 7	4	0.6	2	0.3		6	0.4	
	7-15	11	1.6	62	8.3		73	5	
	15-25	217	31	278	32.7		495	34.2	
	25-35	232	33.1	207	27.7		439	30.3	
	35-45	83	11.9	86	11.5		169	11.7	
	45-55	58	8.3	46	6.1		104	7.2	
	55-65	43	6.1	23	3.1		66	4.6	
	> 65	52	7.4	44	5.9		96	6.6	
Education level		0.188							
	Literate	313	77.1	377	80.7		690	79	
	Illiterate	93	22.9	90	19.3		183	21	
Profession		< 0.0001							
	Unemployed	43	6.4	11	1.5		54	3.9	
	Housewife	0	0	513	100		513	100	
	Student	71	10.6	131	18		202	14.5	
	Worker	225	33.5	21	2.9		246	17.6	
	Self-employed	213	31.7	57	7.9		270	19.3	
	Farmer	42	6.3	3	0.4		45	3.2	
	Other	61	9.1	6	0.8		67	4.8	
Marital status		< 0.0001							
	Single	219	31.4	161	21.7		380	26.4	
	Married	477	68.4	576	77.5		1053	73.1	
	Divorced	1	0.1	6	0.8		7	0.5	
Motivation		< 0.0001							
	Suicide	339	49.5	611	82.6		950	66.7	
	Unintentional (Adults)	334	48.8	125	16.9		459	32.2	
	Food	5	0.7	2	0.3		7	0.5	
	Accidental (Children)	7	1	2	0.3		9	0.6	

Table 2. Frequency (%) of toxic agents by gender and place of living

Category of poisons	Male, N (%)	Female, N (%)	P	Rural, N (%)	Urban, N (%)	P
Alcohol	15 (100%)	0 (0)	0.0001	6 (40%)	9 (60%)	0.685
Club drugs	260 (77.2%)	77 (22.8%)	0.0001	150 (44.4%)	188 (55.6%)	0.823
Corrosive agents	3 (23.1%)	10 (76.9%)	0.067	8 (61.5%)	5 (38.5%)	0.234
Food	15 (71.4%)	6 (28.6%)	0.033	10 (47.6%)	11 (52.4%)	0.664
Gas	8 (61.5%)	5 (38.5%)	0.339	10 (76.9%)	3 (23.1%)	0.021
Lead	29 (93.5%)	2 (6.5%)	0.0001	18 (58.1%)	13 (41.9%)	0.145
Organophosphorus compounds	51 (51.5%)	48 (48.5%)	0.513	61 (61.6%)	38 (38.4%)	0.001
Pharmaceutical drugs	236 (31.3%)	518 (68.7%)	0.0001	319 (42.3%)	435 (57.7%)	0.004
Phosphides	77 (50%)	77 (50%)	0.663	67 (43.5%)	87 (56.5%)	0.656
Total	694 (48.2%)	744 (51.8%)	-	649 (45.1%)	789 (54.9%)	-

* Indicates increased relative risk in males.

† Indicates increased relative risk in females.

The present study found out that the suicide attempt takes up a large part of cases (n=950, 65.6%). Based on the results, females were affected more than males (64.3% vs. 35.7%, p<0.0001, RR=2.338). It was also indicated that the attempt to suicide happened more frequently in patients aged between 15 to 25 (41.7%, p<0.0001) (table 3). These young people frequently used AIP (13.2%), acetaminophen (11.8%), tramadol (10.3%), and alprazolam (9.5%) to commit suicide. Our study also pointed out that alprazolam was the most abundant cause of drug-related poisonings (14.8%) (Figure 1). Tramadol was the most abundant intoxicant among club drug-related poisonings (39.8%) (Figure 2). It should be noted that AIP is also the most used substance in non-drug-related poisonings (44.2%) (Figure 3).

Unintentional poisoning in adults was the second most frequent type of intoxication and included 31.7% (459) of all cases. In this category, opium (83, 18.1%), tramadol (63, 13.7%), methadone (58, 12.6%), lead (31, 6.8%), and pesticides (28, 6.1%) were the most abundant agents. It is quite thought-provoking that all of the lead poisonings were seen in opium abusers, because of lead-contaminated opium. This problem is crucial, and it should be considered because of its life-long side effects on the consumers. It is also noticeable that because of the presence of numerous farmlands and rice fields in the suburbs and rural areas of the city and easy access to agricultural pesticides, their toxicity-related cases were high. Aluminum phosphide (rice tablet, a

common name in Iran) was the most toxic and fatal agent. Unfortunately, it is more accessible at a low price. It was also the most potent lethal agent in our study, which accounts for 10.6% (156) of all cases and is responsible for 68.2% (30) of all deaths. About 60% of patients have injected N-acetyl cysteine (NAC) as a potent antidote, and 52% of them were given calcium gluconate intravenously to treat AIP-induced hyperkalemia (P=0.012, p<0.001 respectively). As mentioned earlier for agricultural pesticides, the availability of this lethal toxic agent is also as a result of farming activities in the rural parts. Although the government banned its sales and importations since 2013, it is an illicit agent and is still popular for its pesticide characteristics and can be easily bought from some grocery stores. Fortunately, its mortality rate decreased over the previous six years, but the number of deaths from AIP poisoning is still high in the community.

The mortality rate in this study was 3% of all cases. Of these, 56.8% were males, and 43.2% were females. Most of them married (81.8%), and they lived in urban areas (59.1%). A part of death cases were housewives (36.4%) between 25-35 years old (22.7%). Most of them attempted suicide (70.5%), and their leading causes of death were AIP (68.2%), club drugs (25%), and pharmaceutical drugs (6.8%) (figure 4). In total, 71.5% of cases were treated as outpatients, and 28.5% were hospitalized. Of the hospitalized patients, 36.5% recovered without any consequence, whereas 63.5% of them were given activated charcoal and sorbitol (as a laxative).

Table 3. Frequency (%) of type of toxicity by age groups

Age group	Cause					Total
	Suicide	Unintentional (Adults)	Food	Accidental (Children)	Uncertain	
< 7	0 (0)	0 (0)	1 (14.3%)	6 (66.7%)	0 (0)	6 (0.4%)
7-15	62 (6.5%)	8 (1.7%)	0 (0)	3 (33.3%)	0 (0)	73 (5%)
15-25	396 (41.7%)	91 (19.8%)	3 (42.9%)	0 (0)	5 (21.8%)	495 (34.2%)
25-35	305 (32.1%)	123 (26.8%)	2 (28.6%)	0 (0)	9 (39.1%)	439 (30.3%)
35-45	108 (11.4%)	58 (12.6%)	0 (0)	0 (0)	3 (13%)	169 (11.7%)
45-55	46 (4.8%)	56 (12.2%)	1 (14.3%)	0 (0)	1 (4.3%)	104 (7.2%)
55-65	17 (1.8%)	45 (9.8%)	0 (0)	0 (0)	3 (13%)	66 (4.6%)
> 65	16 (1.6%)	78 (17%)	0 (0)	0 (0)	2 (8.7%)	96 (6.6%)
Total	950 (65.6%)	459 (31.7%)	7 (0.5%)	9 (0.6%)	23 (1.6%)	1448 (100%)

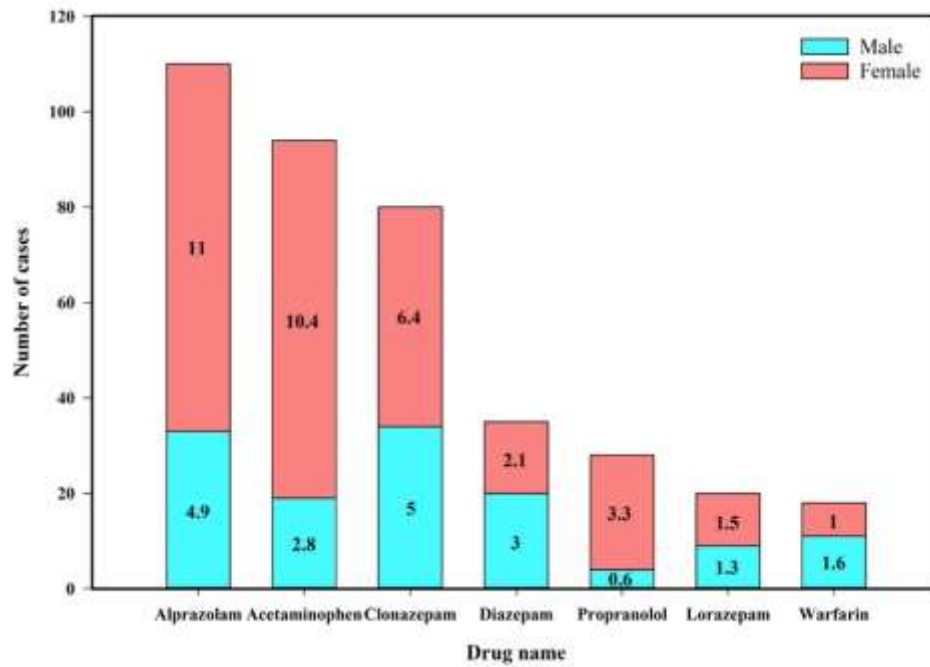


Figure 1. Total cases of the poisoning incidences based on drug-related events. The numbers regarding each gender presented in the figure are in percentage.

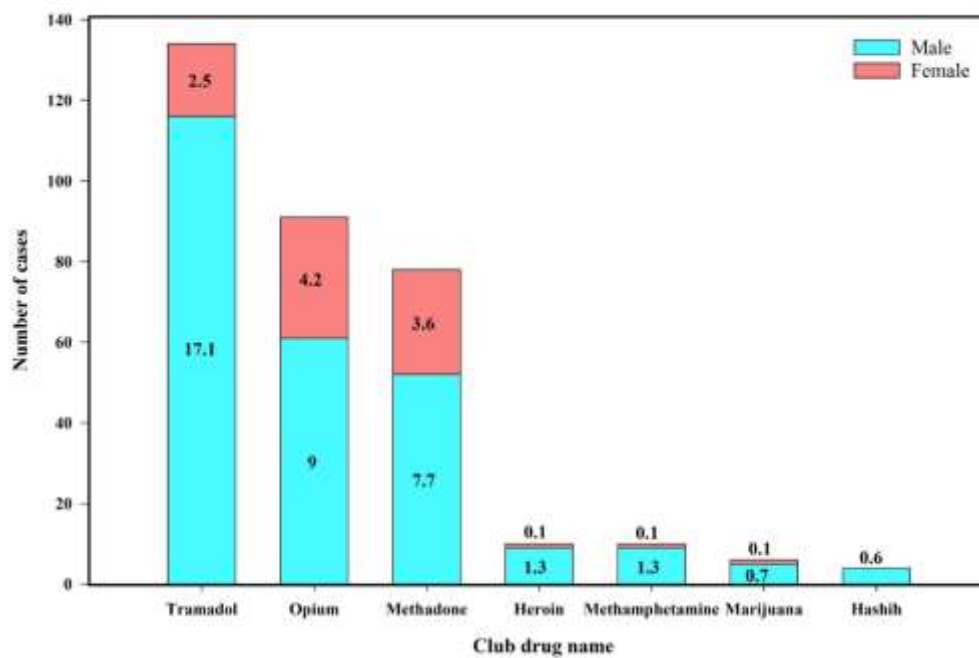


Figure 2. Total cases of the poisoning incidences based on club drug-related events. The numbers regarding each gender presented in the figure are in percentage.

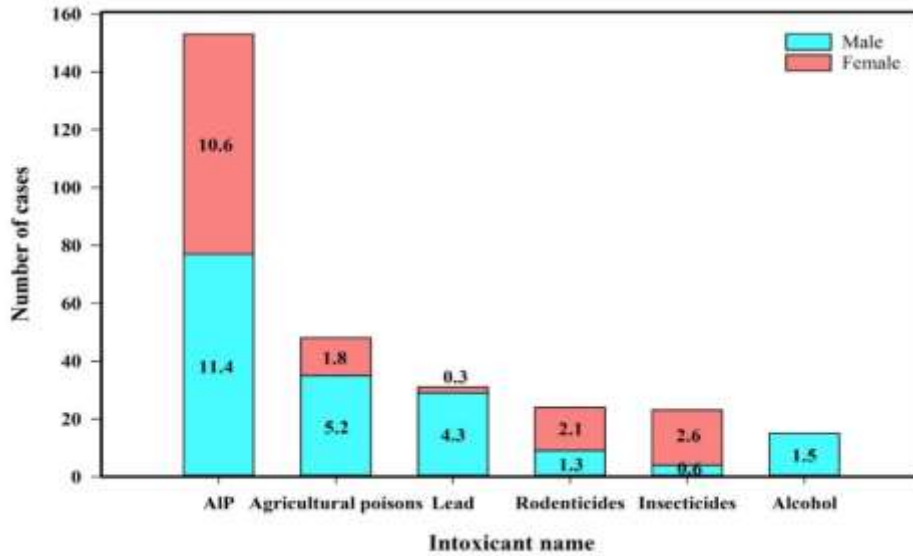


Figure 3. Total cases of the poisoning incidences based on non-drug-related events. The numbers regarding each gender presented in the figure are in percentage.

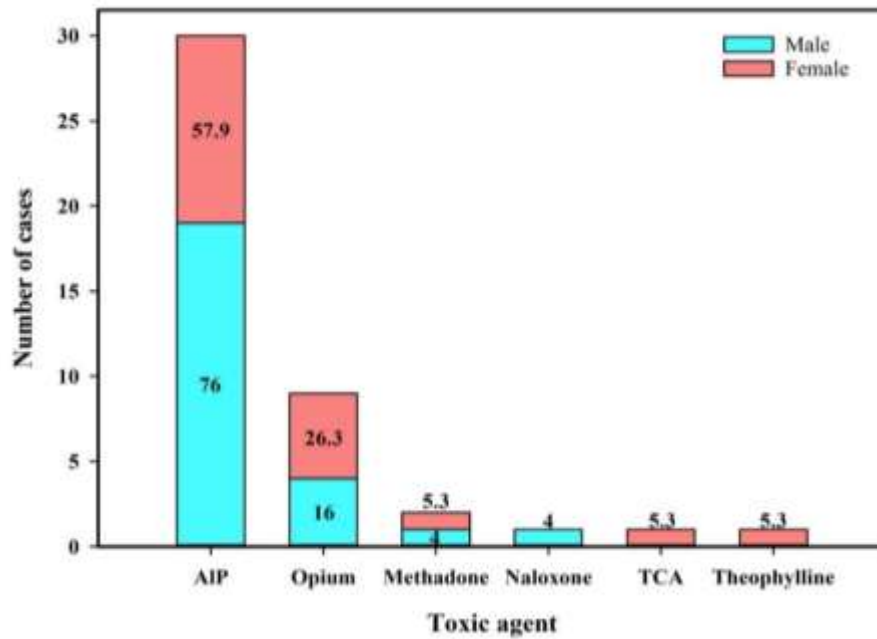


Figure 4. Frequency of toxic agents responsible for mortalities. The numbers regarding each gender presented in the figure are in percentage.

Discussion

The results of our study indicate that among children, most cases were accidental, whereas, in adults, most were suicide attempts.

Of these attempted suicide cases, young people between 15 to 25 years of age constitute the majority of them. Suicide attempts consisted a significant number of cases in our

study (65.5%). Similarly, suicide cases comprised more than 50 percent of poisoning cases in similar studies in Babol (19,20,27). Our study revealed a reduction in suicide cases in the past decade (19). However, when compared to a study in Babol in 2002, an increase in suicide cases could be observed (25,27). It has been reported in similar studies in Babol that

the age range of 16-25 consisted the majority of poisoning cases (19,27) (table 4). Also, we found that females commit suicide more frequently than males, which may be due to social or marital problems (28,29), whereas completed suicide is observed most common in men (30). Moreover, antipsychotics are among the most common drugs involved in a suicide attempt (31). The mortality rate has been observed to be higher in those who attempt suicide (32).

Although our study is consistent with previous studies conducted in Iran (26,33), one study conducted in the USA showed entirely contradictory findings. According to the morbidity and mortality weekly report surveillance summary, suicide attempts in the United States were almost four to five times higher in males than females in the study period, and those aged 35–64 years had the highest incidence rates (34).

Oral ingestion of poisoning agents was the main route of intoxication in our study, which is in agreement with other similar studies, too (35,36). According to the studies, drugs are significant intoxicants in both males and females (37,38). Drug-related poisoning consisted the majority of poisoning cases in similar studies in Babol (19,25,27) (table 4). The present study showed similar results, too. Alprazolam was the most prevalent cause of drug-related overdoses, as well. However, in previous studies in Babol and also in Tehran, diazepam was the most frequent (26,39,40) (table 4). These findings show that benzodiazepines (alprazolam, clonazepam, diazepam, lorazepam) are still the most frequently used intoxicants in drug-related poisonings (32.6%). Therefore, its decrease could be possible if only the regulations of drug selling would be changed in the future, so that people cannot buy this group of drugs without a prescription as easily as before. Although our previous study showed a high number of drug-related cases due to analgesics like acetaminophen, aspirin, and other NSAIDs, their frequency markedly decreased, from 33.5% to almost 14% of drug-related toxicities in the present study. This decline is mainly because most of the people have a degree of familiarity with these types of drugs, and therefore the medical staff can get a better history of the patient, which ultimately leads to better diagnosis and higher chances of treatment. Among the tricyclic antidepressants, only amitriptyline is worth mentioning for causing 2% of all drug-related poisonings, again a reduction in comparison with our previous findings where this family of drugs constituted about 14.4% of all drug-related poisonings (26). Also, worthy of note, one of our deaths was because of TCAs.

Propranolol and warfarin were also, to some degree, frequent in our study. These drugs are used for cardiovascular diseases, and because these types of disorders have become prevalent in Iran in the past ten years, toxicity due to their misuse should have been much higher. Nonetheless, it seems better education and knowledge of people and more accurate prescriptions by physicians lead to fewer morbidity and mortality rates compared to our earlier study (26).

Among the club drug-related poisonings, tramadol was the most abundant intoxicant, in contradiction to our previous study (26). This rise could be because it has become more popular among youth and is widely prescribed as a pain reliever. The same reason is also applied for methadone (41,42). Following tramadol, opium is the second most frequent agent in this group. The main reason why opium, tramadol, and methadone, have low morbidity and mortality rates (11 deaths) despite their extensive use is because of their easily accessible treatment, naloxone (43). Naloxone is the most frequently used opioid antagonist and is the drug of choice in severe opioid intoxication, followed by loss of consciousness, hypoventilation, and apnea (44). Its severe side effects may include: cardiac arrest (45), ventricular fibrillation (46), and pulmonary edema (47,48). Cardiac complications are specifically likely to happen in people with a history of cardiac complications, e.g., congenital heart disease, (49). Despite its rare severe complications, naloxone is still regarded as the best medication for reversal of opioid effects. It is almost available in every rehab and emergency poisoning centers, and because of the high frequency of opium and narcotics overdose in this area, nearly all medical staff know how to approach these cases. Nevertheless, in our study period, there was one death of naloxone administration itself. In that case, the patient was admitted into a rehab facility, and the staff gave him naloxone intravenously, but the dosage considerations were not taken cautiously and the fact that the patient had a history of cardiac myopathies were neglected. Therefore, the patient went into a cardiac arrest. He was then transferred immediately to Shahid Beheshti Hospital, but unfortunately, after about 45 minutes of CPR, the patient expired. Other members of the club drug category worthy of note are heroin, methamphetamine, marijuana, and hashish. Fortunately, these are still quite rare in Iran in comparison to narcotics. AIP is regularly used to repel pests from grain and rice stores. This compound is commonly known as “rice tablet” in Iran. After exposure, patients often experience severe metabolic acidosis and resistant hypotension with a

smell of rotten fish in their breath (26,50). About 60% of patients have injected N-acetyl cysteine (NAC) as a potent antidote, and 52% of them were given calcium gluconate intravenously to treat AIP-induced (51). In the current study, AIP was the most frequent and the most lethal intoxicant in agreement with some previous studies (52, 53), while in our previous study (26), organophosphorus compounds, such as herbicides, rodenticides, insecticides were the most frequent and lethal toxic agents. These organophosphorus-based intoxicants were mostly used for attempting suicide or accidental ingestion associated with improper storage in unlabeled containers. Education about the dangers of pesticides and how to use them safely is essential to elevate awareness of people about their toxicity. Although the government banned AIP's selling and importations, it is still widely used as an illegal pesticide, which suggests that stricter regulations are needed to be put in place to limit its widespread use. Lead poisoning was placed third in order of frequency among non-drug-related poisonings in our study. Its typical clinical manifestations were abdominal pain, nausea, and vomiting. It matters when we know that all of our lead poisoning cases were due to abuse of lead-contaminated opium, which should be taken seriously by the government and all health care professionals. Alcohol poisoning infrequently occurred in contrast with other countries (32, 54), mainly because alcoholic drinks are prohibited in Iran. However, we observed ten methanol intoxications in our

study, which were treated by injection of ethanol. The mortality rate in our study was 3 % of all cases which shows an increase in comparison to a similar study in Babol in 2011-2012 with a mortality rate of 1.3 % of all cases (19). Our findings highlight the ongoing role of and need for more epidemiological studies in this field in providing toxicology expertise to the public and health professionals. Further, this study has some limitations. First, it was primarily limited by its retrospective nature, which resulted in some missing patient data. Also, we could only address poisoning cases in one of four major hospitals in this area between the years 2015 to 2018. Furthermore, mild poisoning cases who did not need hospital care were excluded. Therefore, our results may not fully represent the epidemiologic changes in this area.

In this study, we provide an overview of poisoning exposures in Babol population and have acknowledged that suicide attempts still constitute the majority of our cases, and the risk of suicide is higher in females and young people. In males, club drugs were the major intoxicant, while drug-related poisonings were more abundant among females. It was also indicated that both in rural and urban areas, pharmaceutical drugs were the most copious toxic agent. Also, our results indicate that aluminum phosphide is still one of commonly-used pesticides and due to its high toxicity; it was the most lethal toxic agent in our study. The results of our study could provide better insights to healthcare professionals and to the government to take proper cautions.

Table 4. Comparison of previous studies in this region.

Study	Mean age (±SD)	Age with highest rate of mortality	Population			Motivation		Drug-related poisoning (%)	Most common cause of drug-related poisoning (%)	Overall Mortality rate (%)
			Male (%)	Female (%)	Suicide (%)	Unintentional (%)	Accidental (%)			
Moghadamnia (25)	-	16-25	45.5 %	55.5%	53.3	-	26.3	79.8	Diazepam	9
Moghadamnia(26)	-	16-25	45.5	55.5	51	-	32	79	Diazepam	9
Mahdizadeh (19)	28.12± 12.35	16-25	41.7	58.3	76.9	5.1	-	73.3	benzodiazepines	1.3

Acknowledgments

Hereby, we would like to express our sincere gratitude to the staff of the medical records office of Shahid Beheshti Hospital.

Disclosure statement: The authors reported no potential conflict of interest.

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