ORIGINAL ARTICLE

Acute Iron Poisoning in Tehran-Iran: A Five-Year Retrospective Study in a Referral Poison Center

MITRA RAHIMI[1], RASTIN RADFAR[1], SHAHIN SHADNIA[1], KAMBIZ SOLTANINEJAD[2*]

[1]Toxicological Research Center, Excellence Center of Clinical Toxicology, Department of Clinical Toxicology, Loghman Hakim Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[2]Department of Forensic Toxicology, Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran.

Abstract

Background: The present study was conducted to determine the prevalence of acute iron poisoning among patients in a referral poison control center located in Tehran. It also studied their clinical profile, treatment, and outcome.
Methods: This retrospective cross-sectional study was conducted on acute iron poisoned patients, who were admitted to the poison center from March 21, 2015 to March 19, 2020. Some background variables such as age, gender, ingested dose, time interval between onset of poisoning to hospital admission, the need for antidote, clinical presentations, paraclinical findings and outcome of poisoning were extracted from patients' medical records. Data analysis was carried out using SPSS software.
Results: A total of 74 patients with acute iron poisoning with a mean age of 16.85 ± 11.97 years included in this study. Sixty-one (82.4%) patients were female and the most affected age group was 19-30 years (35.1%). The ingestion dose median in patients under 18 years old was 2450 (IQR=5600, Min= 120, Max= 30000) mg and in the group over 18 years old it was 9000 (IQR= 11125, Min= 600, Max= 30000) mg. Vomiting (66.2%) and lethargy (24.3%) were the most common clinical presentations on admission.
Metabolic acidosis was the most common abnormality in blood gas analysis (43.2%). Positive findings in abdominal radiography have been observed in 4 (5.4%) cases. The serum iron concentration in the patients were 259.54 ± 153.96 µg/dL. Moreover, mortality was reported in one case (1.3%). There was a significant difference between the age of the patients whom received deferoxamine and more patients under 18 years of age received the antidotal therapy (p=0.003).
Conclusion: The present study showed a low mortality rate among the acute iron poisoning patients. From this view, it can be concluded that adults have lower mortality rates than children.

Keywords: Iron, Poisoning, Epidemiology

How to cite this article: Rahimi M, Radfar R, Shadnia S, Soltaninejad K. Acute Iron Poisoning in Tehran-Iran: A Five-Year Retrospective Study in a Referral Poison Center**. Asia Pac J Med Toxicol 2022; 12(1):20-24.**

INTRODUCTION

Iron is an essential transition metal for living organisms. It has a critical role in erythropoietic function, the mitochondrial respiratory chain, oxidative metabolism and cellular immune system [1,2]. Also, it is a component or cofactor of many vital proteins and enzymes including hemoglobin, myoglobin, catalase, xanthine oxidase, peroxidases, and cytochrome oxidase [2, 3].

Iron in doses less than 20 mg/kg is not toxic. Ingestion of 20-60 mg/kg induces a moderate toxicity and more than 60 mg/kg leads to severe toxicity [3, 4]. Iron toxicity related to the production of free radicals may result in lipid peroxidation. Therefore, tissues, which are exposed to high concentrations of iron and high metabolic activity such as gastrointestinal (GI) and cardiovascular systems are more affected as target organs in the poisoning [3,5].

The clinical presentations of iron acute poisoning are based on five distinct stages, including GI symptoms (nausea, vomiting, abdominal pain, GI bleeding, hematemesis), a short period of relative stability with apparent clinical improvement, then systemic toxicity with associated signs of hypoperfusion and cardiogenic shock (pallor, cold extremities, tachycardia, tachypnea, metabolic acidosis and hypotension). In some cases, liver failure and scarring of the gastrointestinal tract have been reported [3,5]. The treatment of iron poisoning is based on symptomatic and supportive measures including whole bowel irrigation (WBI) with polyethylene glycol (PEG), gastric lavage, fluid and metabolic resuscitation and chelating therapy with deferoxamine [3,5].

Although accidental iron acute poisoning is a common cause of morbidity and fatality in children due to the ingestion of pharmaceutical iron-containing formulations, over the decades, suitable legislation and manufacturing measures, family education, and healthcare modalities have led to a dramatic decrease in pediatric iron acute poisoning has been observed [6]. Despite this change, iron acute poisoning remains as a threat among intentional poisoning in adults [7]. However, there are scant reports on acute iron poisoning with intentional intent in adults [8-10].

*Correspondence to: Kambiz Soltaninejad, PharmD, PhD, Department of Forensic Toxicology, Legal Medicine Research Center, Legal Medicine Organization, Behesht Street, Tehran-1114795113, Iran
E-mail: kamsoltaninejad@gmail.com, Tel: +98-21-55613731

The epidemiological pattern of acute iron poisoning in Tehran is not clear. Therefore, the current study aimed to determine the prevalence of acute iron poisoning among patients attending poison control center of a teaching hospital in Tehran, and studied their clinical profile, treatment and outcome during a five-year period.

METHODS

Study Design and Population

The present study is a retrospective cross-sectional study, based on hospital information that was conducted among patients with acute iron poisoning admitted to the Loghman Hakim Hospital Poison Center (LHHPC) (as an academic referral hospital) in Tehran- Iran, during March 21, 2015 - March 19, 2020. We evaluated the baseline demographics, clinical features, paraclinical findings, clinical management, and outcomes of acute iron poisoning.

Data Collection

We reviewed the records of all iron-poisoned patients referring to the LHHPC (both outpatients and inpatients) with available data on Hospital Information System (HIS). Patients with missing data and co-ingestion with other drugs and substances were excluded from the study. The diagnosis of acute iron poisoning has been done according to patient's history, clinical presentations and paraclinical findings.

Demographic information including age, gender, ingested dose, time interval between onset of poisoning to hospital admission, the need for antidote, clinical presentations, paraclinical findings and outcome of poisoning were extracted from the patients' medical records.

Statistical Analysis

Statistical analyses were performed with Statistical Package for Social Science (SPSS) software version 23. Descriptive findings were presented as frequency and percentage or mean ± standard deviation. In addition, the data were analyzed using Mann-Whitney U test, Fisher's exact test, Pearson's Chi-square and Kruskal-wallis for analytical statistics. A p-value of less than 0.05 was considered statistically significant.

RESULTS

From a total of 74 acute iron-poisoned cases were included in this study, 61 (82.4%) patients were female. The mean (± SD) age of patients was 16.85 ± 11.97 years (age range: 1-48 years) and the most affected age group was 19-30 years (35.1%). In patients with age over 18 years old, there was a significant difference according to gender (p=0.002) (Table 1).

Table 1. Baseline characteristics and on admission clinical presentations of the cases with acute iron poisoning

Variable		Patients Groups			P-value
		Under 18 years old (n=39)	Over 18 years' old (n=35)	Total (n= 74)	
Gender/ Number (%)	Male	12 (30.8%)	1 (2.9%)	13 (17.6%)	0.002
	Female	27 (69.2%)	34 (97.1%)	61 (82.4)	
Type of ingested pharmaceutical iron formulation/ Number (%)	Tablet or Capsule	28 (71.8%)	35 (100%)	63 (85.1)	0.003
	Syrup	6 (15.4%)	0	6 (8.1)	
	Drop	5 (12.8%)	0	5 (6.8)	
Ingested dose (mg) / median (IQR, Min, Max)		2450 (5600, 120,30000)	9000 (11125, 600, 30000)	11.450	0.001
Clinical presentations / Frequency (%)	Vomiting	23 (89.7%)	26 (74.3%)	49 (66.2)	0.033
	Abdominal pain	8 (20.5%)	4 (11.4%)	12 (16.2)	
	Diarrhea	1 (2.6%)	3 (8.6%)	4 (5.4)	
	Headache	2 (5.1%)	4 (11.4%)	6 (8.1)	
	Vertigo	3 (7.7%)	3 (8.6%)	6 (8.1)	
	Lethargy	14 (35.9%)	4 (11.4%)	18 (24.3)	
	Tachycardia	14 (35.9%)	1 (2.8%)	15 (20.3)	
	Bradypnea	0	0	0	
	Hypertension	2 (5.1%)	2 (5.7%)	4 (5.4)	
Treatment/ Number (%)	Supportive care	20 (51.3%)	15 (42.9%)	35 (47.3)	0.003
	Whole Bowel Irrigation (PEG administration)	8 (20.5%)	17 (48.6%)	25 (33.8)	
	Antidotal therapy with deferoxamine	9 (23.1%)	0	9 (12.2)	
	Deferoxamine and PEG	2 (5.1%)	3 (8.6%)	5 (6.8)	

Tachycardia: defined as the sinus rhythm with a rate greater than 100 beats per minute. *Hypertension:* defines as an elevated blood pressure, with a systolic pressure (SBP) between 120 and 129 mmHg and diastolic pressure (DBP) less than 80 mm Hg, and stage 1 hypertension, with an SBP of 130 to 139 mmHg or a DBP of 80 to 89 mmHg. *Bradypnea:* defined as a respiration rate below 12 breaths per minute. PEG: Polyethylene glycol

Regarding pharmaceutical dosage forms, all patients ingested ferrous sulfate and 63 (85.1%) patients ingested iron tablet or capsule. All adults over 18 years of age had taken tablet or capsule formulation (Table 1).

According to Table 1, most patients were admitted to the hospital with a chief complaint of vomiting (66.2%) and lethargy (24.3%). Lethargy and tachycardia were more frequent clinical presentations in patients under 18 years old (p=0.033) (Table 1).

The mean (±SD) time of the interval between the onset of symptoms and arrival to the hospital were 3.44± 2.95 hours. The minimum and maximum intervals between the onset of symptoms and arrival to the hospital were 0.5 and 20 hours, respectively. The ingested dose median in patients under 18 years old was 2450 (IQR=5600, Min= 120, Max= 30000) mg and in the patients over 18 years old it was 9000 (IQR= 11125, Min= 600, Max= 30000) mg. It was significantly difference between the groups (p=0.001) (Table 1). Whole Bowel Irrigation (PEG administration) has been performed significantly (p-value= 0.003) more in people over 18 years old and Deferoxamine alone has been administered mostly in patients under 18 years of age (Table 1).

Table 2 summarizes the laboratory findings in the iron-poisoned cases. The anemia was observed in 38 (51.35%) patients and polycythemia was detected in one case (1.3%). Hyponatremia and hypokalemia were observed in 9 (12.2%) and 5 (6.8%) cases, respectively. Furthermore, acidosis was the most common abnormality in blood gas analysis of these patients (43.2%). From 57 (77%) abdominal radiography which has done in the patients, positive findings have been observed in 4 (5.4%) cases (Table 2). Serum iron concentrations was determined in 52 (70.3%) patients. The serum iron concentration in the patients were 259.54 ± 153.96 µg/dL (range: 10- 651 µg/mL).

Deferoxamine was administered as an antidote in 14 (19%) patients. In addition, 5 cases among them, received PEG for WBI. In our cases, one patient was admitted to ICU. GI bleeding occurred in a patient. Moreover, mortality was reported in one case (1.3%). There was not any sequel in the discharged patients.

There was a significant difference between the age of the patients, who received deferoxamine and those under 18 years of age (p=0.003). In addition, no significant correlation has been shown between ingested iron dose and serum iron concentrations with deferoxamine administration (p=0.27). Also, there were no statistical significant differences between age (p=0.06), serum iron concentration (p=0.40), and the onset of symptoms in patients on admission time (p=0.08). Furthermore, there was a significant correlation between ingested dose of iron and serum concentrations in the patients

Table 2. Common laboratory and paraclinical findings in the acute iron poisoning patients on admission time

Laboratory testing (definition and normal range)/ finding			Patients Groups: Under 18 years old Frequency (%) (n=39)	Over 18 years old Frequency (%) (n=35)	Total (n=74)	p-value
Hematologic	Anemia (hemoglobin < 13-14g/dL in men and less than12-13g/L in women)		24 (61.5)	14 (40)	38 (51.3)	0.015
	Polycythemia (hematocrit is greater than 48% in women and 52% in men)		0	1 (1.3)	1 (1.3)	0.574
	International Normalized Ratio (INR) (<1.1)	Increased	5 (12.8)	11 (31.4)	16 (21.7)	0.282
	Blood Glucose (70-110 mg/dL)	Hyperglycemia	5 (12.8)	9 (25.7)	14 (18.9)	0.259
		Hypoglycemia	0	1 (2.8)	1 (1.3)	
	Blood pH (7.36-7.44)	Acidosis	16 (41.02)	16 (45.7)	32 (43.2)	0.638
		Alkalosis	1 (2.6)	3 (8.6)	4 (5.4)	
	Hyponatremia (serum sodium level of less than 135 mEq/L)		8 (20.5)	1 (2.8)	9 (12.2)	0.009
	Hypokalemia (serum potassium level of less than 3.5 mEq/L)		3 (7.7)	2 (5.70)	5 (6.8)	0.590
Renal	Creatinine (0.7-1.2 mg/dL)	Increased	1 (2.6)	2 (5.7)	3 (4.05)	0.592
Hepatic	ALT (29 to 33 IU/L for males and 19 to 25 IU/L for females)	Increased	9 (23.1)	3 (8.6)	12 (16.2)	0.121
	AST (10-40 IU/L)	Increased	1 (2.6)	3 (8.6)	4 (5.4)	0.409
	Bilirubin (0.3-1.2 mg/dL)	Increased	0	0	0	0
Abdominal Radiography	No		5 (12.8)	12 (34.3)	17 (23)	0.001
	Yes	Positive	4 (10.3)	0	4 (5.4)	
		Negative	30 (76.9)	23 (65.7)	53 (71.6)	

ALT: Alanine aminotransferase
AST: Aspartate aminotransferase

(p= 0.021).

The ingested dose in patients with over 18 years old was significantly higher than those under 18 years old (p=0.001). Lethargy and tachycardia were significantly more common in patients under 18 years old (p=0.033). Hyponatremia was significantly observed in patients under 18 years of age (p=0.009). Positive abdominal radiography was significantly observed in patients under 18 years of age (p=0.001).

DISCUSSION

According to the results of the study, the most common gender in iron poisoning is female. This finding in line with the previous studies in Iran [10, 14]. Rahmani et al. showed that 94.2% of patients with acute iron poisoning in Ahvaz-Iran during 2014-2017 were female [7]. The most affected age group was between 19-30 years old. The result is similar to previous studies [7,12]. Although the accidental iron poisoning was a common health problem in the pre-school age group [6, 13,14], due to improvement to legislation, manufacturing measures, and public education, this poisoning has been decreased in the recent years [6]. This fact is in agreement with the results obtained in our study.

The most common clinical presentation in our study was vomiting and GI disturbances. The GI manifestations can be attributed to the direct local corrosive effects of iron on the GI mucosa and occur within several hours post ingestion [3]. The result is consistent with the previous study which the most common symptoms were GI symptoms (nausea, vomiting diarrhea, and abdominal pain) [7]. In addition, lethargy, headache, and dizziness in previous study on acute iron poisoning patients have been reported [7]. In previous study, 15.4% of cases with iron poisoning were lethargic [7]. The results of this study are consistent with the results of our study.

In present study, the coagulopathy and rise of liver enzymes were observed in one case with fatal iron poisoning. These findings have been reported in sever poisoning with iron [3]. In some cases, hepatic damage will be observed after 48-72 hours. Iron is concentrated within hepatic mitochondria and destroys mitochondrial membranes through the free radical production and lipid peroxidation and disrupts the electron transport of oxidative phosphorylation [3,5]. These effects contribute to both hepatic injury and metabolic acidosis [3]. Also, coagulopathy have been reported in some patients with severe iron poisoning because of direct inhibitory effect of iron on clotting factors including thrombin and reduced levels of clotting factors due to hepatic failure [3]. Metabolic acidosis was one of the most common laboratory findings in our patients. This abnormality has been reported by previous studies [3, 5, and 7]. Several mechanisms for the acidosis in iron poisoning have been proposed such as lactic acidosis due to free radical damage to mitochondrial membranes and inhibition of normal cellular respiration and electron transport, hypoperfusion and hypovolemia due to cardiogenic shock [3].

In the present study, 14(19%) patients received deferoxamine and major therapeutic measures were supportive and symptomatic. The results agree with the previous studies [10,13,14]. Gastric lavage should be done for gastric emptying [3, 13]. WBI using PEG was very effective in the patient with iron acute poisoning and it has been recommended with positive abdominal radiography [3,13]. In our study, only one patient was admitted to ICU. This result is different to previous studies [10, 14]. In a study conducted in India among 21 children, 18 patients were admitted to ICU [17]. It might be related to difference in poisoning severity and age group.

In this study, positive abdominal radiography findings were observed in 7% cases. In iron poisoning, an abdominal radiograph showing radiopaque tablets in the GI tract confirms the ingestion [3]. However, a normal radiograph does not exclude iron ingestion because not all iron formulations are equally visible on radiograph due to lower radiopacity [3]. The radiopacity of individual iron tablets was not uniform. The degree of radiopacity is affected by the many factors including the type and number of ingested pills, the number of pills removed by GI decontamination, the state, and the location of the tablets in the GI tract, the degree of absorption, and the formation of any bezoars [3].

Some patients with mild to moderately elevated serum iron levels (300-500 μg/dL) are asymptomatic, most have some symptoms, and a few experience serious toxicity [3]. In our study, the mean serum iron concentration in poisoned cases were 259.54 ± 153.96 μg/dL (range: 10- 651 μg/dL). In a related study, serum iron level in patients was determined between 95-300 μg/dL [7]. This difference can be due to different ingested dose and time of admission of a serum iron analysis. The results obtained from a study showed that the maximum serum iron concentration in adults ingested 20 mg/kg of elemental iron was 300 μg/dL (2-4 hours after the ingestion) [15]. However, if the patients referred early or late to hospital serum iron concentration may not be in toxic level in spite of clinical presentations. Therefore, ideal serum iron level should be available within 2-4 hours post ingestion, so an iron concentration measured many hours after an ingestion may be under the peak [3]. Although, we observed a significant correlation between ingested dose of iron and serum concentrations in the patients, serum iron level may not correlate with the severity of poisoning [3,15].

LIMITATIONS

Since the present study was retrospective, the data missing in some of the patients' medical record have been occurred as a limitation of this study. In addition, this research has been performed in a single center and the findings cannot be generalized to all centers.

CONCLUSION

In the present study, the prevalence of iron poisoning has been determined in the Tehran- Iran during a five-year period. Most studies have reported the morbidity and mortality in children and few case reports have been conducted on adult acute iron poisoning. The present study showed a low mortality rate among the patients. From this view, it can be concluded that adults have lower mortality rates than children. However, iron poisoning is more common in young adult groups. Further studies are needed for the determination of patterns of iron acute poisoning in the country.

Ethical Clearance

This article is prepared from data of MD thesis of Dr. Rastin Radfar (ID Code: 325M) and approval for the study was granted by the medical ethics committee of the School of Medicine, Shahid Beheshti University of Medical Sciences (Code: IR.SBMU.MSP.REC.1400.166), Tehran-Iran

ACKNOWLEDGEMENT

We appreciate staff of poisoning ward and medical records department of Loghman-Hakim Hospital for providing access to the database in research project.

Conflict of interest: None to be declared.
Funding and support: None

REFERENCES

1. Muñoz M, Villar I, García-Erce JA. An update on iron physiology. World J Gastroenterol. 2009;15(37):4617-26.
2. Valerio LG. Mammalian iron metabolism. Toxicol Mech Methods. 2007;17(9):497-517.
3. Fine JS. Iron poisoning. Curr Probl Pediatr. 2000;30(3):71-90.
4. Bhanot R, Jain NP, Midha V, Gupta S. Fatal iron toxicity in adults. Tropical Gastroenterology. 2019;38(4):250–2.
5. Tenenbein M. Toxicokinetics and toxicodynamics of iron poisoning. Toxicology Letters. 1998; 102–103: 653-56.
6. Crofton AC, Harris K, Wylie C, Isoardi KZ. Unintentional paediatric iron poisoning: A retrospective case series. Emerg Med Australas. 2021;33(6):1044-48.
7. Rahmani AH, Molavinia SH, Boustani F. Prevalence of symptoms in patients poisoned with iron in Ahvaz Razi Hospital in 2014-2017. Asia Pac J Med Toxicol. 2020; 9(3): 104-7.
8. Ramachandra Sane M, Malukani K, Kulkarni R, Varun A. Fatal iron toxicity in an adult: clinical profile and review. Indian J Crit Care Med. 2018;22(11):801-3.
9. Abhilash KPP, Arul JJ, Bala D. Fatal overdose of iron tablets in adults. Indian J Crit Care Med. 2013;17(5):311-3.
10. Skoczynska A, Kwiecinska D, Kielbinski M, Lukaszewski M. Acute iron poisoning in adult female. Hum Exp Toxicol. 2007;26(8):663-6.
11. Haghighat M, Moravej H, Moatamedi M. Epidemiology of pediatric acute poisoning in southern Iran: a hospital-based study. Bull Emerg Trauma. 2013; 1(1): 28–33.
12. Azizpour Y, Asadollahi K, Sayehmiri K, Kaikhavani S, Aba ngah G. Epidemiological survey of intentional poisoning suicide during 1993-2013 in Ilam Province, Iran. BMC Public Health. 2016;16(1):902.
13. Singhi SC, Baranwal AK, Jayashree M. Acute iron poisoning: Clinical picture, intensive care needs and outcome. Indian Pediatr. 2003;40(12):1177-82.
14. Valentine K, Mastropietro C, Sarnaik AP. Infantile iron poisoning: challenges in diagnosis and management. Pediatr Crit Care Med. 2009;10(3):e31-3.
15. Burkhart KK, Kulig KW, Hammond KB, Pearson JR, Ambruso D, Rumack B. The rise in the total iron-binding capacity after iron overdose. Ann Emergency Med. 1991;20(5):532–5.