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Gender differences in opioid and stimulant poisoning in the central region of iran: a cross-sectional study

Nastaran Eizadi-Mood[1], Elnaz Barzam[2], Zahra Pirali[2], Awat Feizi[3,4], Melika Namvar[5], Elahe Abdi[5], Parisa Mirmoghtadaee[6], Omid Mehrpour[7,9]✉ & Rokhsareh Meamar[8]✉

Despite the importance of sex differences in substance-related issues, regional studies have paid little attention to their impact on opioid poisoning. This study aimed to assess this disparity in patients with opioid and stimulant poisoning. The cross-sectional study was conducted at a referral poisoning center in Isfahan, Iran. Medical records of patients admitted between December 2014 and October 2016 with opioid and stimulant poisoning were retrospectively reviewed. A total of 1243 patients with opioid poisoning and 94 with stimulant poisoning were evaluated, with a majority being male (70.9% and 79.8%, respectively). Methadone poisoning was the most common opioid substance (49.7%), followed by tramadol (18.4%), and methamphetamine was the most common cause of stimulant poisoning(52.1%). Among both sexes, methadone from the opioid class and methamphetamine from the stimulant class were the most frequent causes of intoxication. Males were more likely to have a history of addiction and a criminal record compared to females in both types of poisoning. No significant differences in outcomes were observed between the sexes. Males were about 3.92 times more likely to experience multiple opioid poisonings compared to females (OR: 3.92, 95% CI 1.39–11.09). Sex disparities in opioid and stimulant poisoning were identified, highlighting the importance of considering sex-specific educational programs when developing strategies for opioid and stimulant use prevention.

Keywords Opioids, Poisoning, Sex, Stimulants

Acute drug poisoning is a major global health concern, with rising mortality rates worldwide. Some studies have shown a surge in stimulant and fentanyl overdoses, as well as a rise in stimulant-only cases[1–4]. The COVID-19 pandemic has accelerated this trend, particularly for substances like fentanyl and methamphetamine[5–9].

Developing countries, including Iran, have also faced challenges related to opioid and stimulant poisoning. In Iran, the use of opioids and stimulants is illegal, except for medical purposes[10]. Iran has a high rate of illicit and prescribed opioid use, leading to high rates of opioid use disorder (OUD) and its associated burden[11].

Opioid poisoning has been a long-standing concern[10]. In Iran, opioids are the leading cause of acute poisoning[10,12–14]. Methadone, a synthetic opioid, is recommended as the treatment of choice for OUD. In a systematic review published in 2022, methadone was responsible for 10.4% of adult acute poisoning cases and 16.0% in children[11]. Iran's strategic location on the southern drug trafficking route from Afghanistan to global markets makes it a key transit point for smuggling[15].

[1]Department of Clinical Toxicology, Isfahan Clinical Toxicology Research Center, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. [2]Isfahan University of Medical Sciences, Isfahan, Iran. [3]Department of Epidemiology & Biostatistics, School of Public Health, Isfahan University of Medical Sciences, Isfahan, Iran. [4]School of Medicine, Isfahan Clinical Toxicology Research Center, Khorshid Hospital, Isfahan University of Medical Sciences, Isfahan, Iran. [5]School of Medicine, Isfahan Clinical Toxicology Research Center, Khorshid Hospital, Isfahan University of Medical Sciences, Isfahan, Iran. [6]Deputy of research and Technology, Isfahan University of Medical Sciences, Isfahan, Iran. [7]Medical Toxicology LLC, Tucson, AZ, Iran. [8]Department of Clinical Toxicology, School of Medicine, Isfahan Clinical Toxicology Research Center, Khorshid Hospital, Isfahan University of Medical Sciences, Isfahan, Iran. [9]Michigan Poison & Drug Information Center, School of Medicine, Wayne State University, Detroit, MI, United States of America. ✉email: omid.mehrpour@yahoo.com.au; meamar@med.mui.ac.ir

Stimulant poisoning in Iran, primarily caused by methamphetamine, has risen significantly, affecting both adults and children[16–20]. The combined lifetime prevalence in Iran of methamphetamine, ecstasy, and non-prescribed methylphenidate use was 6.7%, 5.9%, and 16.4%, respectively[21]. Cocaine use appears to be rare in Iran[22]. According to the 2019 World Drug Report, Iran ranked ninth globally in methamphetamine seizures[23]. Despite strict regulations on stimulant control in Iran, methamphetamine has been produced on a large scale due to high demand. These factors provide strong evidence for the prevalence of its abuse and dependence[24].

Substance intoxication affects all demographics, with certain groups being more vulnerable[25]. Factors such as sex and age, concurrent use of sedative-hypnotics, comorbid substance use and mental health disorders, the method of ingestion, and the purity of the substance play a role in overdose risk[7,26–28].

Moreover, the role of gender in the opioid epidemic is increasingly being addressed by researchers[29]. Evidence suggests that sex, as a biological variable, exerts differential effects on the outcomes of substance use. Epidemiological studies show that males tend to have greater overdose mortality compared to females[30], and the number of female victims has been steadily rising[31]. Although men are less likely to receive opioid prescriptions than women, this disparity does not appear to reduce their overdose risk[29].

The causes of these sex differences may vary. In a clinical trial involving 162 individuals with non-medical opioid use and chronic pain, the demographic profile was similar between sexes; however, women reported more psychiatric comorbidity and greater pain-related impairment, whereas men reported more aberrant behaviors[32]. Some human cohort studies reported that women may progress to addiction sooner, be more likely to relapse, be more sensitive to the effects of drug use due to sex hormones, and be more likely to experience a fatal overdose[33]. There is a lack of comprehensive data on sex-based differences among patients with opioid and stimulant poisoning in Iran. Mesgarpour et al. conducted a cross-sectional study on 29,083 patients with acute poisoning caused by agents affecting the nervous system, focusing on sex differences[25]. However, this study did not provide a detailed analysis of different opioid and stimulant subtypes separately[25]. In another study based on a registry system in Mazandaran, Iran, from 2020 to 2021, the majority of the patients, 70.9% ($n = 158$), were male[34].

The rates of drug-related mortality are higher among Iranian men compared to women[35–38]. In Iranian culture, women are perceived as the cornerstone of the family. Therefore, substance use by women may be seen as a violation of this moral value[22,36]. Additionally, illicit drug use among women is often under-reported or misclassified due to pressures stemming from the sociocultural context[35,39]. Furthermore, barriers to accessing addiction care and treatment for women, such as the high stigma of drug use and a limited number of women-only substance use services, increase the likelihood of drug-related mortality[35,36,40].

There is an urgent need to understand more about opioid and stimulant poisoning, as well as particular risks, in order to offer effective, tailored preventive interventions to reduce the harmful effects of drug use. In 2023, 0.89% of all deaths in Iran, 6.72% of all Years of Life Lost, and 4.17% of all Years Lost Due to Disability were related to drug abuse[41]. In 2016, drug abuse mortality in Iran was nearly 38.23 per million, with the greatest deaths stated in the western provinces, although drug abuse mortality rates vary throughout Iran[42,43].

Given the impact of biological, social, and psychological differences between men and women on all aspects of substance abuse, evaluating sex-based differences among individuals with opioid and stimulant overdose will help in implementing sex-specific intervention measures for risk reduction programs. A cross-sectional study was conducted to assess sex-based differences in opioid and stimulant poisoning cases among patients admitted to a referral poisoning center in the central part of Iran, Isfahan. This study assessed demographic characteristics, toxicological patterns, and clinical outcomes.

Method

Study Design and Setting

This cross-sectional study was conducted at the referral poisoning center of Khorshid Educational Hospital, a teaching center specializing in poisoning cases affiliated with Isfahan University of Medical Sciences in Isfahan, Iran. The poisoning center of Khorshid Educational Hospital is a major referral poisoning center in Isfahan province, Iran. It serves both urban and rural populations, receiving cases primarily from Isfahan city, nearby cities, and sometimes neighboring provinces. The hospital admits patients of diverse socioeconomic backgrounds, including individuals covered by public (government-supported), private, and uninsured insurance. Given that it is a public teaching hospital, a significant proportion of patients belong to lower- to middle socioeconomic groups. However, it also provides care to individuals from various financial backgrounds.

Participants

We reviewed patient records in the hospital archive from December 2014 to October 2016. Patients hospitalized with all types of opioid poisoning (such as heroin, opium, methadone, tramadol, opium syrup [tincture], and buprenorphine) and stimulant poisoning, whether intentional or unintentional, with discharge diagnosis codes according to the tenth revision of ICD-10 (T40.0–T40.4, T43.6, T40.5–T40.7) were included in our study. Patients who co-ingested other substances or did not provide informed consent upon hospital admission were excluded.

Data collection

Trained health professionals collected data on toxicoepidemiological characteristics, including age, sex, marital status, education level, place of residence, route of exposure, history of addiction, psychiatric disease, suicide, criminal records, self-harm, past medical history, and clinical outcomes (mortality, survival with complications, or full recovery). Sex is determined by the identification card information individuals provide during admission.

Patients' addiction history was determined based on documented clinical records during hospital admission, which was based on patient or companion self-report or physician documentation of substance use disorder diagnosis. Addiction was defined as a self-reported lifetime history of problematic substance use (opioids,

stimulants, alcohol, cigarettes, or other illicit substances) or a previously documented diagnosis of substance dependence from patient medical records. The history of psychiatric disease was defined based on patient or companion reports of previous psychiatric disorders (such as depression, bipolar disorder, anxiety disorder, schizophrenia, or other DSM-5-diagnosed psychiatric disorders), regardless of their severity. Past medical history was defined as a self-reported history or documented medical diagnosis of chronic conditions such as cardiovascular, respiratory, renal, hepatic, neurological, endocrine, or other medical conditions requiring ongoing medical management regardless of severity. The history of suicide and self-harm was recorded based on the patient's self-report, indicating any previous intentional suicide attempt or act of self-harm during the patient's lifetime.

This study examined seven categories of opioids[1]: methadone[2], tramadol[3], heroin[4], opium[5], buprenorphine[6], other opioids (including diphenoxylate, fentanyl, dextromethorphan), and[7] multiple opioids.

We also classified patients with stimulant poisoning into two groups: Group 1 included patients with amphetamine, methamphetamine, cocaine, or Ritalin poisoning; Group 2 included patients with cannabis, hashish, or marijuana poisoning.

Statistical analysis

Results were presented as frequency (percent) for qualitative variables and mean ± standard deviation (SD) for quantitative variables. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test and the Q-Q plot. We compared categorical variables across both sexes using the chi-square test or Fisher's exact test. Independent samples t-test or Mann–Whitney U test were used to compare normally and non-normally distributed continuous variables, respectively. A P-value < 0.05 was considered statistically significant. A P-value from 0.05 to 0.1 was considered borderline significance (marginal significance). Data analyses were conducted using the Statistical Package for the Social Sciences (SPSS) software for Windows, version 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). The association between sex and type of opioid poisoning was analyzed using cross-tabulation analysis reported as odds ratios (ORs) with 95% confidence intervals (95% CIs). The association between sex and type of stimulant poisoning was analyzed using binary logistic regression, which was reported as the odds ratio (OR) and 95% confidence interval (95%CI) for OR.

Ethics declarations

This study was approved by the ethics committee of Isfahan University of Medical Sciences under the code IR.MUI.MED.REC.1397.314 and was conducted in accordance with the principles of the Helsinki Declaration. Informed consent had been obtained from all participants (or their surrogates) upon hospital admission. The following criteria were considered for informed consent[1]: disclosure of information[2], competency of the patient (or surrogate), and[3] voluntary consent. To maintain the confidentiality of our patients' identities, we used password-protected files to keep their records securely.

Results

During the study period, a total of 1243 patients with opioid poisoning and 94 patients with stimulant poisoning were included.

Opioid-related poisoning cases

The mean (SD) age of patients with opioid poisoning was 40.34 (16.16) years, with the majority being male ($N = 881$, 70.9%; male/female ratio: 2.43). Methadone poisoning accounted for the largest proportion of opioid cases ($N = 619$, 49.7%), followed by tramadol ($N = 229$, 18.4%) and opium ($N = 217$, 17.5%).

Table 1 presents the baseline and toxicological characteristics of patients according to the type of opioid consumed. The majority of poisoning cases occurred in the 30–40 age range. The most frequent route of exposure was oral ingestion (94.1%). A high level of comorbidity was observed (35.2%), with approximately two-thirds of these patients having a history of past medical disease. A significant sex difference was observed, with males outnumbering females across all opioid types ($P < 0.05$).

There were significant differences among the opioid groups in terms of age, marital status, place of poisoning, addiction history, suicide history, criminal record history, self-harm history, and past medical history ($P < 0.05$). Patients with tramadol poisoning were younger compared to other groups, whereas those with opium poisoning were older. Except for tramadol poisoning, other types of opioid poisonings were more common among married patients. More than half of the patients had a history of addiction, with the highest proportions observed among the heroin (92.2%) and multiple-opioid groups (90.2%). Individuals with heroin poisoning had the highest proportion of suicide history (29.7%) and self-harm history (23.5%). Criminal records were more common among individuals with heroin (39.0%) and multiple-opioid ingestion (15.6%).

There were 12 deaths among patients with opioid poisoning, half of which were attributed to opium. Most patients (92.0%) achieved complete recovery. No significant differences in outcomes were observed across the different types of opioid poisoning ($P > 0.05$).

Stimulant-related poisoning cases

The mean (SD) age of the study population with stimulant poisoning was 34.35 (12.69) years, with the majority of them being male ($n = 75$, 79.8%, male/female ratio: 3.95) (Table 2).

Methamphetamine poisoning was responsible for the majority of stimulant poisoning ($N = 49$, 52.1%), followed by Ritalin ($N = 19$, 20.2%), hashish ($N = 11$, 11.7%), marijuana ($N = 6$, 6.4%), cannabis ($N = 3$, 3.2%), crystal ($N = 3$, 3.2%) and cocaine ($N = 2$, 2.1%). There was a significant difference in terms of sex, addiction

			Total N = 1243	Methadone N = 619	Tramadol N = 229	Heroin N = 51	Opium N = 217	Others* N = 8	Buprenorphine N = 78	Multiple opioid ingestion N = 41	P-value
Demographics	Age	Mean (SD)	40.34 (16.16)	40.13 (16.22)	30.41 (8.46)	39.53 (9.51)	50.39 (17.69)	45.25 (27.41)	43.18 (15.07)	40.37 (11.32)	< 0.001
		<=20	44 (3.5%)	30 (4.8%)	6 (2.6%)	0 (0.0%)	4 (1.8%)	1 (12.5%)	3 (3.8%)	0 (0.0%)	< 0.001
		20–30	342 (27.5%)	150 (24.2%)	133 (58.1%)	8 (15.7%)	31 (14.3%)	1 (12.5%)	14 (17.9%)	5 (12.2%)	
		30–40	386 (31.1%)	208 (33.6%)	77 (33.6%)	21 (41.2%)	35 (16.1%)	3 (37.5%)	22 (28.2%)	20 (48.8%)	
		40–50	192 (15.4%)	92 (14.9%)	4 (1.7%)	17 (33.3%)	49 (22.6%)	1 (12.5%)	18 (23.1%)	11 (26.8%)	
		50–60	120 (9.7%)	62 (10.0%)	6 (2.6%)	3 (5.9%)	36 (16.6%)	0 (0.0%)	11 (14.1%)	2 (4.9%)	
		> 60	159 (12.8%)	77 (12.4%)	3 (1.3%)	2 (3.9%)	62 (39.0%)	2 (25.0%)	10 (12.8%)	3 (7.3%)	
	Sex	Male	881 (70.9%)	423 (68.3%)	158 (69.0%)	44 (86.3%)	164 (75.6%)	5 (62.5%)	50 (64.1%)	37 (90.2%)	0.003
		Female	362 (29.1%)	196 (31.7%)	71 (31.0%)	7 (13.7%)	53 (24.4%)	3 (37.5%)	28 (35.9%)	4 (9.8%)	
	Marital status	Single	519 (41.8%)	262 (42.3%)	133 (58.1%)	25 (49.0%)	51 (23.5%)	2 (25.0%)	31 (39.7%)	15 (36.6%)	< 0.001
		Married	724 (58.2%)	357 (57.7%)	96 (41.9%)	26 (51.0%)	166 (76.5%)	6 (75.0%)	47 (60.3%)	26 (63.4%)	
	Education level	Illiterate	2 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	-	1 (16.7%)	0 (0.0%)	0.30
		Middle school	24 (30.4%)	14 (33.3%)	2 (14.3%)	3 (42.9%)	3 (33.3%)		2 (33.3%)	0 (0.0%)	
		Diploma	35 (44.3%)	18 (42.9%)	10 (71.4%)	3 (42.9%)	3 (33.3%)		0 (0.0%)	1 (100.0%)	
		Associate degree	3 (3.8%)	2 (4.8%)	1 (7.1%)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
		Bachelor's degree and higher	15 (19.0%)	8 (19.0%)	1 (7.1%)	1 (14.3%)	2 (22.2%)		3 (50.0%)	0 (0.0%)	
	Place of poisoning	Home	736 (82.9%)	379 (83.8%)	124 (78.5%)	24 (66.7%)	122 (84.7%)	6 (100.0%)	55 (84.6%)	26 (96.3%)	0.001
		At work	59 (6.6%)	27 (6.0%)	14 (8.9%)	0 (0.0%)	11 (7.6%)	0 (0.0%)	6 (9.2%)	1 (3.7%)	
		Other	93 (10.5%)	46 (10.2%)	20 (12.7%)	12 (33.3%)	11 (7.6%)	0 (0.0%)	4 (6.2%)	0 (0.0%)	
	Route of exposure	Oral	1147 (94.1%)	611 (99.5%)	227 (100.0%)	24 (50.0%)	168 (82.4%)	6 (75.0%)	78 (100.0%)	33 (82.5%)	0.77
		Inhalation	39 (3.2%)	0 (0.0%)	0 (0.0%)	10 (20.8%)	28 (13.7%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	
		Injection	20 (1.6%)	2 (0.3%)	0 (0.0%)	12 (25.0%)	3 (1.5%)	2 (25.0%)	0 (0.0%)	1 (2.5%)	
		Both	13 (1.1%)	1 (0.2%)	0 (0.0%)	2 (4.2%)	5 (2.5%)	0 (0.0%)	0 (0.0%)	5 (12.5%)	
Past medical and social history	Addiction history	Yes	690 (57.5%)	324 (54.3%)	89 (40.3%)	47 (92.2%)	143 (69.1%)	3 (37.5%)	47 (61.8%)	37 (90.2%)	< 0.001
		No	511 (42.5%)	273 (45.7%)	132 (59.7%)	4 (7.8%)	64 (30.9%)	5 (62.5%)	29 (38.2%)	4 (9.8%)	
	History of psychiatric disease	Yes	171 (15.3%)	91 (16.4%)	31 (14.8%)	13 (29.5%)	21 (11.0%)	1 (12.5%)	9 (12.7%)	5 (12.8%)	0.09
		No	946 (84.7%)	463 (83.6%)	179 (85.2%)	31 (70.5%)	170 (89.0%)	7 (87.5%)	62 (87.3%)	34 (87.2%)	
	Suicide history	Yes	152 (16.5%)	75 (16.3%)	40 (22.9%)	11 (29.7%)	18 (11.4%)	0 (0.0%)	4 (6.9%)	4 (12.9%)	0.007
		No	772 (83.5%)	386 (83.7%)	135 (77.1%)	26 (70.3%)	140 (88.6%)	4 (100.0%)	54 (93.1%)	27 (87.1%)	
	Criminal record history	Yes	91 (8.9%)	54 (10.5%)	4 (2.2%)	16 (39.0%)	8 (4.6%)	0 (0.0%)	4 (5.9%)	5 (15.6%)	< 0.001
		No	930 (91.1%)	181 (97.8%)	181 (97.8%)	25 (61.0%)	165 (95.4%)	7 (100.0%)	64 (94.1%)	27 (84.4%)	
	Self-harm history	Yes	73 (10.0%)	35 (9.6%)	19 (14.6%)	8 (23.5%)	9 (7.0%)	0 (0.0%)	0 (0.0%)	2 (8.7%)	0.010
		No	656 (90.0%)	330 (90.4%)	111 (85.4%)	26 (76.5%)	120 (93.0%)	2 (100.0%)	46 (100.0%)	21 (91.3%)	
	Past medical history	Yes	343 (35.2%)	163 (34.1%)	54 (29.2%)	10 (25.6%)	90 (51.7%)	3 (42.9%)	15 (24.2%)	8 (27.6%)	< 0.001
		No	631 (64.8%)	315 (65.9%)	131 (70.8%)	29 (74.4%)	84 (48.3%)	4 (57.1%)	47 (75.8%)	21 (72.4%)	
Clinical outcome	Outcome	Survived without complication	1133 (92.0%)	568 (92.7%)	206 (90.7%)	48 (94.1%)	191 (88.8%)	7 (87.5%)	74 (96.1%)	39 (97.5%)	0.29
		Survived with complications	86 (7.0%)	41 (6.7%)	19 (8.4%)	3 (5.9%)	18 (8.4%)	1 (12.5%)	3 (3.9%)	1 (2.5%)	
		Death	12 (1.0%)	4 (0.7%)	2 (0.9%)	0 (0.0%)	6 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

Table 1. Comparison of demographics and history of patients according to the type of opioid consumed. **Other opioids including diphenoxylate, fentanyl, and dextromethorphan; Group 1 including amphetamine, methamphetamine, cocaine, and Ritalin; Group 2 including cannabis, hashish, and marijuana; Results are presented as number (percent) or mean ± SD; Categorical variables were compared between groups with Fisher's exact or Chi-square tests or Mann–Whitney U test for non-normal continuous data, where appropriate.*

			Total	Group1	Group2	*P*-value
Demographics	Age	Mean (SD)	34.35 (12.69)	33.66 (11.4)	36.90 (17.39)	
		<=20	9 (9.6%)	9 (12.2%)	0 (0.0%)	0.009
		20–30	30 (31.9%)	20 (27.0%)	10 (50.0%)	
		30–40	31 (33.0%)	25 (33.8%)	6 (30.0%)	
		40–50	17 (18.1%)	16 (21.6%)	1 (5.0%)	
		50–60	3 (3.2%)	3 (4.1%)	0 (0.0%)	
		> 60	4 (4.3%)	1 (1.4%)	3 (15.0%)	
	Sex	Male	75 (79.8%)	56 (75.7%)	19 (95.0%)	0.046
		Female	19 (20.2%)	18 (24.3%)	1 (5.0%)	
	Place of poisoning	Home	32 (57.1%)	25 (58.1%)	7 (53.8%)	0.65
		At work	5 (8.9%)	3 (7.0%)	2 (15.4%)	
		Other	19 (33.9%)	15 (34.9%)	4 (30.8%)	
	Route of exposure	Oral	65 (74.7%)	57 (80.3%)	8 (50.0%)	0.009
		Inhalation	19 (21.8%)	11 (15.5%)	8 (50.0%)	
		Injection	-			
		Both	3 (3.4%)	3 (4.2%)	0 (0.0%)	
Past medical and social history	Addiction history	Yes	57 (64.8%)	44 (63.8%)	13 (68.4%)	0.70
		No	31 (35.2%)	25 (36.2%)	6 (31.6%)	
	History of psychiatric disease	Yes	18 (23.4%)	16 (27.6%)	42 (72.4%)	0.13
		No	59 (76.6%)	2 (10.5%)	17 (89.5%)	
	Suicide history	Yes	9 (13.0%)	8 (15.4%)	44 (84.6%)	0.31
		No	60 (87.0%)	1 (5.9%)	16 (94.1%)	
	Criminal record history	Yes	14 (19.4%)	14 (25.9%)	0 (0.0%)	0.011
		No	58 (80.6%)	40 (74.1%)	18 (100.0%)	
	Self-harm history	Yes	7 (13.0%)	6 (15.0%)	1 (7.1%)	0.45
		No	47 (87.0%)	34 (85.0%)	13 (92.9%)	
	Past medical history	Yes	20 (31.3%)	17 (34.7%)	3 (20.0%)	0.28
		No	44 (68.8%)	32 (65.3%)	12 (80.0%)	
Clinical outcome	Outcome	Outcome without complication	85 (91.4%)	67 (91.8%)	18 (90.0%)	0.97
		survived with complications	4 (4.3%)	3 (4.1%)	1 (5.0%)	
		Death	4 (4.3%)	3 (4.1%)	1 (5.0%)	

Table 2. Comparison of demographics and history of patients according to the type of stimulant consumed. *Group 1 includes amphetamine, methamphetamine, cocaine, and Ritalin; Group 2 includes cannabis, hashish. and marijuana; Results are presented as number (percent) or mean ± SD; Categorical variables were compared. Where appropriate, between groups with Fisher's exact or Chi-square tests or the Mann-Whitney U test for non-normal continuous data.*

history, and criminal record between groups 1 and 2 ($P < 0.05$) (Table 2). We found that 4 (4.3%) of the studied cases had expired, with 3 of them consuming methamphetamine and 1 of them consuming cannabis.

Acute opioid poisoning and sex

Table 3 shows a detailed descriptive analysis of opioid poisoning categorized by sex. Male patients were significantly older than female patients ($p = 0.01$). The 30–40 age group also represented the highest proportion for both sexes. Poisoning was more prevalent among younger females, but after age 20, the prevalence shifted, with males experiencing more cases. Differences between sexes were also apparent in previous addiction and criminal record history ($P < 0.001$). While 70.2% of males had a previous history of addiction, only 26.1% of females reported a similar history. The history of psychiatric disease showed a marginally significant association with sex ($P = 0.075$). No significant sex differences were observed in clinical outcomes between males and females ($P > 0.05$). Comparing different variables in the six study groups, age, marital status, addiction history, suicide history, past medical history, and criminal record history showed significant differences between males and females separately($P < 0.001$).

The study population was subsequently stratified into five distinct categories, each further divided into two groups: those who experienced opioid intoxication from one of the specified medications (methadone, tramadol, heroin, buprenorphine, or multiple opioid ingestion) and those who did not experience intoxication from the specified opioids within that category. We then evaluated the relationship between sex and each of these categories. Our findings indicated that males are 3.92 times more likely to experience multiple opioid poisoning compared to females (OR: 3.92, 95% CI 1.39–11.09; $P = 0.002$). However, no statistically significant association between sex and the odds of poisoning from tramadol, heroin, opium, or buprenorphine was observed.

			Male	Female		Male								Female							
			Total N = 881	**Total N = 362**	***p*-value**	**Methadone N = 423**	**Tramadol N = 158**	**Heroin N = 44**	**Opium N = 164**	**Others N = 5**	**Buprenorphine N = 50**	**Multi opioid N = 37**	***P*-value**	**Methadone N = 196**	**Tramadol N = 71**	**Heroin N = 7**	**Opium N = 53**	**Others N = 3**	**Buprenorphine N = 28**	**Multi opioid N = 4**	***P*-value**
Demographics	**Age**	Mean (SD)	41.35 (16.02)	37.87 (16.24)	0.01	41.91 (16.39)	30.20 (7.01)	38.95 (9.96)	50.49 (17.47)	38.20 (27.16)	45.00 (12.96)	40.49 (11.86)	< 0.001	36.31 (15.18)	30.87 (11.05)	43.14 (5.05)	50.08 (18.53)	57.00 (28.69)	39.93 (18.06)	39.25 (4.27)	< 0.001
		<=20	21 (2.4%)	23 (6.4%)	0.011	16 (3.8%)	1 (0.6%)	0 (0.0%)	3 (1.8%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	< 0.001	14 (7.1%)	5 (7.0%)	0 (0.0%)	1 (1.9%)	0 (0.0%)	3 (10.7%)	0 (0.0%)	< 0.001
		20–30	230 (26.1%)	112 (30.9%)		88 (20.8%)	97 (61.4%)	8 (18.2%)	25 (15.2%)	1 (20.0%)	6 (12.0%)	5 (13.5%)		62 (31.6%)	36 (50.7%)	0 (0.0%)	6 (11.3%)	0 (0.0%)	8 (28.6%)	0 (0.0%)	
		30–40	272 (30.9%)	114 (31.5%)		141 (33.3%)	53 (33.5%)	20 (45.5%)	24 (14.6%)	2 (40.0%)	15 (30.0%)	17 (45.9%)		67 (34.2%)	24 (33.8%)	1 (14.3%)	11 (20.8%)	1 (33.3%)	7 (25.0%)	3 (75.0%)	
		40–50	144 (16.3%)	48 (13.3%)		68 (16.1%)	3 (1.9%)	11 (25.0%)	36 (22.0%)	0 (0.0%)	16 (32.0%)	10 (27.0%)		24 (12.2%)	1 (1.4%)	6 (85.7%)	13 (24.5%)	1 (33.3%)	2 (7.1%)	1 (25.0%)	
		50–60	92 (10.4%)	28 (7.7%)		48 (11.3%)	3 (1.9%)	3 (6.8%)	28 (17.1%)	0 (0.0%)	8 (16.0%)	2 (5.4%)		14 (7.1%)	3 (4.2%)	0 (0.0%)	8 (15.1%)	0 (0.0%)	3 (10.7%)	0 (0.0%)	
		>60	122 (13.8%)	37 (10.2%)		62 (14.7%)	1 (0.6%)	2 (4.5%)	48 (29.3%)	1 (20.0%)	5 (10.0%)	3 (8.1%)		15 (7.7%)	2 (2.8%)	0 (0.0%)	14 (26.4%)	1 (33.3%)	5 (17.9%)	0 (0.0%)	
	Marital status	Single	371 (42.1%)	148 (40.9%)	0.91	178 (42.1%)	99 (62.7%)	22 (50.0%)	40 (24.4%)	2 (40.0%)	16 (32.0%)	14 (37.8%)	< 0.001	84 (42.9%)	34 (47.9%)	3 (42.9%)	11 (20.8%)	0 (0.0%)	15 (53.6%)	1 (25.0%)	0.020
		Married	510 (57.9%)	214 (59.1%)		245 (57.9%)	59 (37.3%)	22 (50.0%)	124 (75.6%)	3 (60.0%)	34 (68.0%)	23 (62.2%)		112 (57.1%)	37 (52.1%)	4 (57.1%)	42 (79.2%)	3 (100.0%)	13 (46.4%)	3 (75.0%)	
	Education level	Illiterate	1 (2.1%)	1 (3.1%)	0.94	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (25.0%)	-	0 (0.0%)	-	0.11	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	1 (33.3%)	0 (0.0%)	0.52
		Middle school	14 (29.8%)	10 (31.3%)		10 (35.7%)	1 (12.5%)	1 (25.0%)	1 (25.0%)		1 (33.3%)			4 (28.6%)	1 (16.7%)	2 (66.7%)	2 (40.0%)		1 (33.3%)	0 (0.0%)	
		Diploma	22 (46.8%)	13 (40.6%)		11 (39.3%)	7 (87.5%(	2 (50.0%)	2 (50.0%)		0 (0.0%)			7 (50.0%)	3 (50.0%)	1 (33.3%)	1 (20.0%)		0 (0.0%)	1 (100.0%)	
		Associate degree	1 (2.1%)	2 (6.3%)		1 (3.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)			1 (7.1%)	1 (16.7%)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
		Bachelor's degree and higher	9 (19.1%)	6 (18.8%)		6 (21.4%)	0 (0.0%)	1 (25.0%)	0 (0.0%)		2 (66.7%)			2 (14.3%)	1 (16.7%)	0 (0.0%)	2 (40.0%)		1 (33.3%)	0 (0.0%)	

Continued

			Male	Female		Male								Female							
			Total *N* = 881	Total *N* = 362	*p*-value	Methadone *N* = 423	Tramadol *N* = 158	Heroin *N* = 44	Opium *N* = 164	Others *N* = 5	Buprenorphine *N* = 50	Multi opioid *N* = 37	*P*-value	Methadone *N* = 196	Tramadol *N* = 71	Heroin *N* = 7	Opium *N* = 53	Others *N* = 3	Buprenorphine *N* = 28	Multi opioid *N* = 4	*P*-value
Past medical and social history	Addiction history	Yes	599 (70.2%)	91 (26.1%)	< 0.001	281 (69.0%)	74 (48.1%)	41 (93.2%)	128 (82.1%)	2 (40.0%)	38 (76.0%)	35 (94.6%)	<0.001	43 (22.6%)	15 (22.4%)	6 (85.7%)	15 (29.4%)	1 (33.3%)	9 (34.6%)	2 (50.0%)	0.009
		No	254 (29.8%)	257 (73.9%)		147 (77.4%)	52 (77.6%)	1 (14.3%)	36 (70.6%)	2 (66.7%)	17 (65.4%)	2 (50.0%)		147 (77.4%)	52 (77.6%)	1 (14.3%)	36 (70.6%)	2 (66.7%)	17 (65.4%)	2 (50.0%)	
	Mental illness history	Yes	131 (16.6%)	40 (12.2%)	0.075	72 (19.3%)	22 (15.0%)	11 (29.7%)	14 (9.6%)	0 (0.0%)	7 (15.6%)	5 (14.3%)	0.041	19 (10.6%)	9 (14.3%)	2 (28.6%)	7 (15.6%)	1 (33.3%)	2 (7.7%)	0 (0.0%)	0.51
		No	658 (83.4%)	288 (87.8%)		161 (89.4%)	54 (85.7%)	5 (71.4%)	38 (84.4%)	2 (66.7%)	24 (92.3%)	4 (100.0%)		161 (89.4%)	54 (85.7%)	5 (71.4%)	38 (84.4%)	2 (66.7%)	24 (92.3%)	4 (100.0%)	
	Suicide history	Yes	98 (15.0%)	54 (20.1%)	0.11	54 (16.9%)	25 (20.3%)	8 (25.8%)	6 (5.2%)	0 (0.0%)	2 (5.9%)	3 (10.3%)	0.005	21 (14.8%)	15 (28.8%)	3 (50.0%)	12 (28.6%)	0 (0.0%)	2 (8.3%)	1 (50.0%)	0.034
		No	557 (85.0%)	215 (79.9%)		265 (83.1%)	98 (79.7%)	23 (74.2%)	110 (94.8%)	3 (100.0%)	32 (94.1%)	26 (89.7%)		121 (85.2%)	37 (71.2%)	3 (50.0%)	30 (71.4%)	1 (100.0%)	22 (91.7%)	1 (50.0%)	
	Criminal record history	Yes	83 (11.6%)	8 (2.6%)	< 0.001	46 (13.1%)	4 (3.2%)	16 (44.4%)	8 (6.3%)	0 (0.0%)	4 (9.3%)	5 (17.2%)	<0.001	8 (4.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.32
		No	634 (88.4%)	296 (97.4%)		305 (86.9%)	121 (96.8%)	20 (55.6%)	120 (93.8%)	5 (100.0%)	39 (90.7%)	24 (82.8%)		156 (95.1%)	60 (100.0%)	5 (100.0%)	45 (100.0%)	2 (100.0%)	25 (100.0%)	3 (100.0%)	
	Self-harm history	Yes	52 (10.2%)	21 (9.6%)	0.25	26 (10.6%)	10 (11.2%)	8 (27.6%)	6 (6.3%)	0 (0.0%)	0 (0.0%)	2 (9.5%)	0.023	9 (7.6%)	9 (22.0%)	0 (0.0%)	3 (8.8%)	-	0 (0.0%)	0 (0.0%)	0.063
		No	458 (89.8%)	198 (90.4%)		220 (89.4%)	79 (88.8%)	21 (72.4%)	89 (93.7%)	2 (100.0%)	28 (100.0%)	19 (90.5%)		110 (92.4%)	32 (78.0%)	5 (100.0%)	31 (91.2%)		18 (100.0%)	2 (100.0%)	
	Past medical history	Yes	253 (36.8%)	90 (31.4%)	0,1	123 (37.8%)	37 (28.7%)	7 (21.2%)	66 (50.8%)	3 (60.0%)	10 (25.6%)	7 (26.9%)	0.001	40 (26.1%)	17 (30.4%)	3 (50.0%)	24 (54.5%)	0 (0.0%)	5 (21.7%)	1 (33.3%)	0.015
		No	434 (63.2%)	197 (68.6%)		202 (62.2%)	92 (71.3%)	26 (78.8%)	64 (49.2%)	2 (40.0%)	29 (74.4%)	19 (73.1%)		113 (73.9%)	39 (69.6%)	3 (50.0%)	20 (45.5%)	2 (100.0%)	18 (78.3%)	2 (66.7%)	
Clinical outcome	Outcome	Outcome without complication	804 (92.1%)	329 (91.9%)	0.73	385 (91.7%)	146 (93.6%)	42 (95.5%)	145 (89.0%)	5 (100.0%)	46 (93.9%)	35 (97.2%)	0.64	183 (94.8%)	60 (84.5%)	6 (85.7%)	46 (88.5%)	2 (66.7%)	28 (100.0%)	4 (100.0%)	0.088
		Death	8 (0.9%)	4 (1.1%)		31 (7.4%)	10 (6.4%)	2 (4.5%)	14 (8.6%)	0 (0.0%)	3 (6.1%)	1 (2.8%)		0 (0.0%)	2 (2.8%)	0 (0.0%)	2 (2.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
		Pneumonia aspiration	61 (7.0%)	25 (7.0%)		4 (1.0%)	0 (0.0%)	0 (0.0%)	4 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		10 (5.2%)	9 (12.7%)	1 (14.3%)	4 (7.7%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	

Table 3. Comparison of demographics, toxicological, and history of patients with opioid poisoning according to sex. **Other opioids, including diphenoxylate, fentanyl, and dextromethorphan; Results are presented as number (percent) or mean ± SD; Categorical variables were compared between groups with Fisher's exact or Chi-square tests or Mann–Whitney U test for non-normal continuous data, where appropriate.*

		Male	Female	*P*-value	Male			Female		
					Group 1	Group 2	P-value	Group 1	Group 2	P-value
Age	< 30	28 (37.3%)	11 (57.9%)	0.16	18 (32.1%)	52.6%	0.19	11 (61.1%)	0 (0.0%)	< 0.001
	30–50	41 (54.7%)	7 (36.8%)		34 (60.7%)	7 (36.8%)		7 (38.9%)	0 (0.0%)	
	> 50	6 (8.0%)	1 (5.3%)		4 (7.1%)	2 (10.5%)		0 (0.0%)	1 (100.0%)	
Marital status	Single	43 (57.3%)	10 (52.6%)	0.71	30 (53.6%)	13 (68.4%)	0.26	9 (50.0%)	0 (0.0%)	0.33
	Married	32 (42.7%)	9 (47.4%)		26 (46.4%)	6 (31.6%)		9 (50.0%)	0 (0.0%)	
Route of exposure	Oral	48 (69.6%)	17 (94.4%)	0.009	41 (75.9%)	7 (46.7%)	0.021	16 (94.1%)	1 (100.0%)	0.80
	Inhalation	18 (26.1%)	1 (5.6%)		10 (18.5%)	8 (53.3%)		1 (5.9%)	0 (0.0%)	
	Both	3 (4.3%)	0 (0.0%)		3 (5.6%)	0 (0.0%)		-	-	
Place of poisoning	Home	20 (46.5%)	12 (92.3%)	0.64	13 (43.3%)	7 (53.8%)	0.61	12 (92.3%)	12 (92.3%)	-
	At work	5 (11.6%)	0 (0.0%)		3 (10.0%)	2 (15.4%)		-	-	
	Other	18 (41.9%)	1 (7.7%)		14 (46.7%)	4 (30.8%)		1 (7.7%)	1 (7.7%)	
Type of poisoning	Intentional	37 (60.7%)	12 (75.0%)	0.18	30 (65.2%)	7 (46.7%)	-	12 (80.0%)	0 (0.0%)	0.074
	Unintentional	37 (60.7%)	4 (25.0%)		4 (8.7%)	3 (20.0%)		3 (20.0%)	1 (100.0%)	
	Overdose	15 (24.6%)	0 (0.0%)		10 (21.7%)	5 (33.3%)		-	-	
	Other	2 (3.3%)	0 (0.0%)		2 (4.3%)	0 (0.0%)		-	-	
Addiction history	Yes	52 (75.4%)	5 (26.3%)	< 0.001	39 (76.5%)	13 (72.2%)	0.53	5 (27.8%)	0 (0.0%)	0.71
	No	17 (24.6%)	14 (73.7%)		12 (23.5%)	5 (27.8%)		13 (72.2%)	0 (0.0%)	
Mental illness history	Yes	12 (20.3%)	6 (33.3%)	0.20	10 (24.4%)	2 (11.1%)	0.24	6 (35.3%)	0 (0.0%)	0.46
	No	47 (79.7%)	12 (66.7%)		31 (75.6%)	16 (88.9%)		11 (64.7%)	1 (100.0%)	
Suicide history	Yes	6 (11.8%)	3 (16.7%)	0.43	5 (14.3%)	1 (6.3%)	0.40	3 (17.6%)	0 (0.0%)	0.64
	No	45 (88.2%)	15 (83.3%)		30 (85.7%)	15 (93.8%)		14 (82.4%)	1 (100.0%)	
Criminal record history	Yes	14 (25.5%)	0 (0.0%)	0.020	14 (36.8%)	0 (0.0%)	0.004	-	-	-
	No	41 (74.5%)	17 (100.0%)		24 (63.2%)	17 (100.0%)		16 (100.0%)	1 (100.0%)	
Self-harm history	Yes	6 (15.0%)	1 (7.1%)	0.45	5 (18.5%)	1 (7.7%)	0.36	1 (7.7%)	0 (0.0%)	0.77
	No	34 (85.0%)	13 (92.9%)		22 (81.5%)	12 (92.3%)		12 (92.3%)	1 (100.0%)	
Past medical history	Yes	13 (27.1%)	7 (43.8%)	0.21	10 (29.4%)	3 (21.4%)	0.57	7 (46.7%)	0 (0.0%)	0.36
	No	35 (72.9%)	9 (56.3%)		24 (70.6%)	11 (78.6%)		8 (53.3%)	1 (100.0%)	
Outcome	Survived without complication	66 (89.2%)	19 (100.0%)	0.33	18 (94.7%)	1 (5.3%)	-	49 (74.2%)	17 (25.8%)	> 1
	Survived with complications	4 (5.4%)	0 (0.0%)		-			3 (75.0%)	1 (25.0%)	
	Death	4 (5.4%)	0 (0.0%)		-			3 (75.0%)	1 (25.0%)	

Table 4. Demographics, toxicological, and past history of patients with stimulant poisoning according to sex. *Group 1 includes amphetamine, methamphetamine, cocaine, and Ritalin; Group 2 includes cannabis, hashish, and marijuana. Results are presented as. number (percent); Categorical variables were compared between groups with Fisher's exact or Chi-square tests or the Mann–Whitney U test for. non-normal continuous data, where appropriate.*

Acute stimulant poisoning and sex

The sex distribution in stimulant poisoning is shown in Table 4. The predominant age range was 30–50 years in males and < 30 years in females (54.7% and 57.9% respectively). Oral ingestion was the main route of exposure in both sexes, but was significantly more common among females (94.4% vs. 69.9%, $P < 0.05$). Moreover, intentional poisoning was more frequent among women, whereas accidental poisoning and overdose were more common among men, although these differences were not statistically significant. Significant sex differences were observed in addiction history and criminal record history, with higher proportions among men. No statistical difference was found in the history of psychiatric disease between sexes; however, psychiatric history was more prevalent among women compared to men (33.3% vs. 20.3%, $P > 0.05$).

Among males, oral ingestion was significantly more prevalent in Group 1, while inhalation was more commonly observed in Group 2 ($P = 0.021$). Moreover, criminal records were higher in group 1 ($P < 0.05$). Although all four patients who died were male, there was no significant difference between the sexes in terms of outcome.

Discussion

Despite the importance of sex differences in substance-related issues, there has been little attention in regional studies to how such sex differences impact opioid poisoning. Therefore, the present study aims to investigate the sex difference in demographic and toxicological characteristics in patients with opioid and stimulant poisoning referred to a hospital in Isfahan, Iran. A key strength of this study is its large sample size, which provides robust insight into a specific population of poisoning patients.

Our findings revealed a significantly higher prevalence of opioid and stimulant poisoning in males compared to females. This disparity may be attributed to men being more likely than women to use illicit drugs in general[44]. Men are more likely than women to use almost all types of illicit drugs[45].

Several studies have shown that in Iran, there are gender differences when it comes to acute drug poisoning, with males being more likely than females to be affected. Consistent with previous research, this study also found that men are more prone to acute poisoning and intentional poisoning compared to women[46,47]. Additionally, our recent report indicated that non-pharmaceutical poisoning cases were predominantly male[14]. A nation-level report on CDC data from 2017 to 2018 showed that males, compared to females, had greater overdose mortality for prescription opioids specifically and for all opioids combined[7]. Similarly, a nationwide study in the US showed a rise in overdoses involving synthetic opioids and psychostimulants from March 2018 to March 2021, with males having the highest mortality rates among users of these drugs[7].

However, mechanistic explanations cannot be obtained directly from epidemiological studies[48]. Nevertheless, some contributing factors can be considered. For instance, biological differences that could predispose an individual to the adverse effects of a substance cannot be disregarded[48]. Traditional masculinity norms that encourage men to take risks and emotional suppression, sometimes through substance-mediated escapism, may play pivotal roles in this disparity[49,50]. Additionally, men's increased tendency to use prescription opioids to feel good or to get high might make them vulnerable to adverse outcomes[29]. This pattern was also evident in our results, as most patients with criminal convictions were males. On the other hand, in a study by Ghaderi et al., 90% of women had no income and home[51]; we suggest that higher income and financial resources may have contributed to increased substance use among men.

Additionally, our results suggested that males were approximately four times more likely to experience multiple opioid poisonings compared to females.

The necessity of evaluating the availability of different opioids specifically for men warrants further investigation in future studies. The significantly higher prevalence of addiction history among males with opioids compared to females is a notable finding. Men were approximately twice as likely as women to experience complications or fatal outcomes from overdose; we could not find a significant difference in terms of outcomes between the two sexes. In our study, four patients who were male died due to opioid poisoning. However, previous studies showed opioid and stimulant-related deaths tend to be higher among males[52,53], which may be a particular result of riskier forms of substance use among males, including a higher risk of escalating their opioid medication doses[54] as well as obtaining from illegitimate source[55] and injecting alone compared to women. Our different results may have originated from a smaller sample size or may be due to the different severity of poisoning, which has not been evaluated in our study.

The high prevalence of opioid and stimulant poisoning among young adults of both sexes aligns with findings from previous studies[17,34,56,57]. It highlights the vulnerability of this demographic to opioid-related harms.

Similar to Bagley and colleagues[58], who reported that the first non-fatal opioid overdose in the 11–16 age group was more prevalent among girls, Poisoning prevalence was higher among younger females in opioid poisoning, with a shift towards males after the age of 20. It is worth noting that patients under 18 years old in our city are typically admitted to a pediatric unit in another hospital. Further research is needed to address these issues.

Methadone and methamphetamine were the most common causes of acute opioid and stimulant poisoning, respectively, in our study, with men accounting for the majority of cases. Notably, 70% of them exhibited a history of substance addiction. Studies in Iran and other countries showed the same sex pattern[59–61].

The widespread availability of methadone, together with the lack of standardized methadone maintenance treatment (MMT) programs in Iran, contributes significantly to the incidence of methadone poisoning[62]. People with a substance use disorder acquire methadone either from the MMT center or by purchasing it from the black market, thereby making it available to other family members[63]. Additionally, owing to unsafe storage of methadone syrup in Bottled water or other medicine containers, methadone syrup poisoning is very common[34].

This study had several limitations. Its retrospective nature, incomplete records, and lack of random sampling limited the generalizability of the findings. Excluding co-ingestion of other drugs may have masked any differential effects that those may have had on the outcome.

This manuscript suggests areas for future research studies to investigate the underlying causes of observed gender differences in intoxication patterns. Patterns and risk factors of poisoning vary from region to region and change over time within the same region. Regularly updating epidemiologic data is necessary to identify trends for specific risk factors, enabling global public health practitioners to develop preventive strategies and assist physicians in treating patients. Our study has provided an example of how to collect such data.

Conclusion

This cross-sectional study investigated sex disparities in opioid and stimulant poisoning cases at a referral poisoning center in Isfahan, Iran. Analysis of 1243 opioid poisoning cases and 93 stimulant poisoning cases revealed a significant male predominance in both groups. Males were also more likely to experience multiple opioid poisonings, and a higher proportion of men had a history of addiction and criminal records compared to women. These findings highlight the importance of incorporating sex-specific educational programs into strategies for opioid and stimulant use prevention.

Methadone and tramadol were the most common opioids involved in poisoning cases, likely reflecting their availability, widespread distribution, and non-prescription sales in the region. Among stimulants, methamphetamine was the most frequent cause of poisoning. Preventive measures targeting these substances are essential to reduce poisoning rates.

Data availability

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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Author contributions

NE: Conceptualization, Project administration, Funding acquisition, Data curation, Writing- Reviewing and EditingEB, ZP, MN: Investigation, Data gathering, Writing- Original draft preparationAF: Methodology, Software, Data Curation, Validation, Writing- Reviewing and EditingRM, OM: Conceptualization, Project administration, Data curation, Resources, Supervision. Visualization, Writing- Reviewing and Editing EA: Data collectionPM: Data curation, writing the manuscriptAll authors approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to O.M. or R.M.

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