



# Sociodemographic and Toxicological Characteristics of Patients with Opioid/Stimulant Poisoning

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## Abstract

**Background:** This study aimed to examine the toxicological and sociodemographic characteristics of patients who have experienced poisoning from common illicit drugs, such as opioids and stimulants.

**Methods:** This retrospective chart review study was conducted on cases of opioid and stimulant poisoning who were admitted to the referral poisoning emergency center in the central part of Iran, Isfahan, from January 2019 to January 2020. The toxicological and sociodemographic characteristics of patients were evaluated.

**Findings:** Data obtained from 496 patients were analyzed. Poisoning with opioids and stimulants accounted for 67.13% and 7.86% of cases, respectively. Most of the patients in both the opioid and stimulant groups were male. The most common route of poisoning was ingestion (82%) for opioids and inhalation (43.6%) for stimulants. Suicide (40.2%) was common in patients with opioid poisoning, whereas abuse (28.2%) was more commonly observed in stimulant poisoning. There were no significant differences regarding marital status, occupation, education, criminal convictions, history of somatic diseases, and psychiatric diseases between patients with opioid and stimulant poisoning. The mortality rate in opioid poisoning was 0.9%, whereas no deaths were reported in patients with stimulant poisoning. Binary regression analysis showed that age, coma/stupor, abnormal respiratory manifestations, previous cardiovascular disease, incomplete response to naloxone, and endotracheal intubation were predictive factors for worse outcomes (complications/death) in opioid poisoning.

**Conclusion:** Opioid poisoning was more common than stimulant poisoning. Except for the type and route of exposure, there were no significant differences between patients poisoned with opioid or stimulant drugs. This highlights the necessity for targeted interventions based on specific clinical characteristics to improve patient outcomes.

**Keywords:** Poisoning, Opioids, Stimulants, Outcome

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## Introduction

Poisoning with illicit drugs has a significant impact on our communities. The number of poisoning or overdose cases admitted to emergency rooms is likely to increase due to the increase in substance abuse. Many studies have assessed poisoning with drugs of abuse, which include alcohol, nicotine, cannabinoids, opioids, sedatives, volatile solvents, stimulants, and hallucinogens.<sup>1,2</sup> In the United States, opioids accounted for two-thirds of drug overdose deaths in 2018 and 70% of drug overdose deaths in 2019.<sup>3</sup> Additionally, drug overdose deaths, involving stimulants, cocaine, or psychostimulants with abuse potential, have significantly increased among all ages since 2015 from 12 122 to 57 497 in 2022 in the United States.<sup>2</sup> There has been a significant increase in deaths caused by opioids mixed with stimulants, as well as deaths

related to stimulant use.<sup>4</sup> In 2020, 92 000 people in the US died from drug-involved overdoses, including illicit drugs and prescription opioids.<sup>2</sup> Moreover, among all stimulant toxicity deaths in Canada in 2021, nearly 90% were also related to an opioid.<sup>5</sup> There is a growing trend in the concurrent use of opioids and stimulants. Individuals who use opioids have three times the likelihood of concurrently using methamphetamine compared to those who do not report using opioids.<sup>6</sup> This concurrent use has been associated with an increased burden of chronic health conditions,<sup>7</sup> necessitating access to care to prevent premature morbidity and mortality from causes including illicit drug toxicity. In Iran, some studies have specifically focused on opioid poisoning.<sup>8,9</sup> Mehrpour et al reported that 26.2% of opioid poisoning cases were due to suicide, which was more common among male patients, especially



those who were residents of urban areas.<sup>10</sup> Additionally, in a study by Rastegari et al, the prevalence of stimulant use in Iran was 0.84%. There is evidence of an increase in stimulant use from 2013 to 2016.<sup>11</sup>

Previous studies have examined the association between drug poisoning and various social vulnerability factors, including ethnicity, age, and employment. An individual's socioeconomic status, such as their geographic location, is correlated with the likelihood of experiencing drug use disorder and poisoning.<sup>12,13</sup> A study conducted from 2013 to 2016 found that fentanyl and heroin overdose was more common among younger age groups, non-Hispanic Blacks, and individuals with education higher than high school.<sup>14</sup> Other studies have analyzed different vulnerability factors and their association with drug overdose.<sup>12,15,16</sup> Among individuals who reported ever using illicit drugs, those in the lowest income group were more likely to report problems related to substance abuse compared to those in the highest income group.<sup>17</sup> On the other hand, over the past few decades, research has shed light on the short- and long-term effects of drug abuse. These effects include changes in brain structure and function, physical health problems, and possible genetic susceptibility to various addictions.<sup>18</sup>

The trend of co-use of opioids and stimulants is emerging as a new and concerning challenge. The increase in co-use of opioids and stimulants necessitates a deeper understanding of the associated poisoning risks. Comparing the characteristics of opioid and stimulant poisoning can help identify factors that contribute to more severe outcomes, enabling better risk stratification of patients. Poisoning with illicit drugs, including opioids and stimulants, is one of the most common types of poisoning in our provincial poisoning referral center. Since poisoning with illicit drugs may differ concerning toxico-clinical and sociodemographic characteristics in various societies as vulnerable factors, these variables were compared in patients with common illicit drug poisoning, including opioids and stimulants. Also, the risk factors for worse outcomes (complications/death) in patients with illicit drug poisoning were determined.

## Methods

### *Study design and setting*

This retrospective study was conducted at the Poisoning Referral Center of Khorshid Hospital, affiliated with Isfahan University of Medical Sciences, in Isfahan, Iran. The study protocol was approved by the Research Ethics Committee of Isfahan University of Medical Sciences (ethical code: IR.MUI.MED.REC.1399.918).

### *Participants*

The study included patients with acute poisoning involving opioids and/or stimulants who were hospitalized in the poisoning referral emergency center of Khorshid

Hospital from January 2019 to January 2020. Patients who were discharged against medical advice or had more than 20% missing data in their medical files were excluded from the study. Written informed consent was obtained from all patients or their legal guardian(s). The patients were managed in the hospital under the supervision of medical toxicologists. Poisoning was diagnosed by a medical toxicologist based on the history reported by the patients/relatives or emergency medical service, clinical manifestations upon admission, urine toxicology analysis, serological toxicology tests if necessary, and response to naloxone in patients with opioid poisoning.

We categorized patients based on the type of drug poisoning into five groups: 1- Opioids (opium, codeine, morphine, heroin, methadone, pethidine, buprenorphine, tramadol) 2- Stimulants (amphetamine/methamphetamines, cocaine, methylphenidate, ephedrine, pseudoephedrine, caffeine, ethanol)<sup>19</sup> 3- Combined use of opioids and pharmaceutical drugs, 4- Combined use of stimulants and pharmaceutical drugs, 5- combined use of opioids, stimulants, and pharmaceutical drugs.

### *Data collection*

The medical records of all patients who met the inclusion criteria were evaluated. Patients' medical records for opioid and stimulant poisoning were extracted from the hospital's archive using the ICD-10 classification. A general physician recorded the data in the data gathering form. The demographic information collected included age, gender, occupation, marital status, and education level. The toxin-related variables collected included the route of poisoning, type of poisoning (suicide, accidental, abuse), length of hospital stay (days), and the time interval between poisoning and admission. Furthermore, information related to the history of problems was recorded, including history of addiction, type of addiction (alcohol, cigarettes, opium, heroin, and others), history of psychiatric diseases, history of suicide, number of previous suicides, and history of self-harm as well as past medical history such as chronic renal failure, hypertension, respiratory diseases, cardiovascular disease, diabetes, and liver failure. The recorded clinical manifestations included skin, pupil size, heart, lung, abdomen, and central nervous system (CNS) examination upon admission. Abnormal heart and lung examinations were defined as heart rate ( $\leq 60$  or  $\geq 100$ ) and respiratory rate ( $\leq 12$  or  $\geq 20$ ), respectively. The abdominal examination included abdominal inspection, auscultation for bowel sounds, percussion, and palpation. Furthermore, the treatment approach, including the administration of naloxone, response to naloxone, charcoal therapy, and intubation, was also recorded.

We analyzed the data from 496 opioid- and stimulant-poisoned patients who had data on outcome variables.

Outcomes were categorized as survived without complications, survived with complications (pulmonary, renal, cardiovascular, and hepatic), and death. Consensus meetings were held to ensure uniform data collection methods.

### Statistical analysis

Data were analyzed using SPSS version 15 software (SPSS Inc., Chicago, USA). The results were reported as frequency (percent) or mean (standard deviation) for categorical and continuous data, respectively. The outcomes of the patients were categorized as surviving without complications, surviving with complications, or death. Categorical data were compared using Fisher's exact test or chi-square test. The means of variables were compared using the independent samples *t*-test or one-way analysis of variance (ANOVA). To address multiple testing and inflation of the type one error rate, we adjusted the obtained *P* values from independently conducted tests on study variables using the Benjamini-Hochberg procedure.<sup>20</sup> Stepwise binary logistic regression analysis was performed to calculate the odds ratio (OR) as an estimate of the association of potential risk factors with outcomes. Complications and death were combined into a single category; therefore, we modeled a binary outcome in logistic regression comprising two possible categories: (i) survived without complication and (ii) complication/death. A *P* value less than 0.05 was considered statistically significant.

### Results

In the present study, 6731 poisoning cases were assessed. Five hundred patients were included in the study. Four patients met the exclusion criteria; therefore, data from 496 (7%) patients poisoned with stimulants and opioids, accounting for 333 (67.13%) and 39 (7.86%) cases, respectively, were analyzed. The most common route of poisoning was ingestion for opioids (82%), and inhalation for stimulants (43.6%). The study population consisted of 395 males (79.6%) with a mean age of  $33.58 \pm 15.65$  years. Most patients in both the opioid and stimulant groups were male, with ingestion as the most common route of poisoning (75.4%). Suicide was responsible for 39.9% of the poisonings, and a history of addiction and psychiatric diseases were prevalent in 63.9% and 87% of cases, respectively.

Opioid and stimulant poisoning were more common in male patients with suicide, as the most common type of poisoning in patients with opioid poisoning (40.2%), and abuse was more commonly observed in stimulant poisoning (28.2%). The frequency of demographic and toxico-clinical variables is presented in Table 1. Significant differences were found between sex, route of exposure, type of poisoning, and history of psychiatric diseases in the five defined groups. There were no significant

differences in terms of age among the subgroups. In addition, there were no significant differences among the five groups concerning other variables (marital status, occupation, education level, history of addiction and suicide, number of previous suicides, history of criminal conviction and self-harming, history of past medical history, and length of hospital stay). Clinical manifestations at admission showed that most patients were alert. Significant differences were found in the level of consciousness, pupil size, cardiovascular examinations, naloxone, and response to naloxone among the five groups. In addition, there were significant differences between the groups in the use of charcoal. Specifically, charcoal therapy was more common in cases of opioid poisoning compared to cases of stimulant poisoning. However, the other variables, including skin, lung, and abdomen examinations, intubation, and outcomes, were not different between the groups (Table 1).

The mortality rate in opioid poisoning was 0.9%, while no deaths were reported in patients with stimulant poisoning. All variables were compared in patients who survived versus those who experienced complications/death. Patients with complications tended to be older, have a lower level of consciousness and a lower level of education, and exhibited abnormal respiratory and cardiovascular manifestations upon admission, requiring endotracheal intubation (Table 2).

We also analyzed the predictive factors in patients with opioid and stimulant poisoning separately (Table 3). As there were no deaths in patients with stimulant poisoning and due to the small sample size in the stimulant group, no statistically significant predictive factors were determined for the outcome in patients with stimulant poisoning. Stepwise binary logistic regression analysis revealed that age, low level of consciousness (stupor/coma), abnormal respiratory manifestations, a history of previous cardiovascular disease, need for endotracheal intubation, and incomplete response to naloxone administration were predictive factors for the outcome (complications/death) in patients with opioid poisoning.

### Discussion

We investigated the toxico-clinical and sociodemographic features of patients with poisoning from commonly used opioids and stimulants. The results showed that poisoning with opioids accounted for 67.13% of cases while poisoning with stimulants accounted for 7.86%. The prevalence of drug use has been increasing in Iran.<sup>21</sup> Statistics indicate that approximately 2 million people in Iran, or about 2.7% of the population, use illicit drugs daily.<sup>22</sup> The results also showed that the mortality rate in opioid poisoning was 0.9%, while no deaths were reported in patients with stimulant poisoning. The present study aligns with previous reports highlighting the predominance of opioid poisoning compared to

**Table 1.** Comparison of demographic and toxico-clinical variables among poisoning cases with opioids and/or stimulant drugs

| Variables                                       |                                       | Opioids<br>(n=333) | Stimulants<br>(n=39) | Opioids with<br>pharmaceutical<br>drugs (n=79) | Simulants with<br>pharmaceutical<br>drugs (n=3) | Combination<br>of opioids/<br>stimulants with<br>pharmaceutical<br>drugs (n=42) | Total<br>(N=496) | P value* |
|-------------------------------------------------|---------------------------------------|--------------------|----------------------|------------------------------------------------|-------------------------------------------------|---------------------------------------------------------------------------------|------------------|----------|
| Gender, No. (%)                                 | Female                                | 80 (24)            | 0 (0.0)              | 19 (24.1)                                      | 0 (0.0)                                         | 2 (4.8)                                                                         | 101 (20.4)       | <0.0001  |
|                                                 | Male                                  | 253 (76)           | 39 (100)             | 60 (75.9)                                      | 3 (100)                                         | 40 (95.2)                                                                       | 395 (79.6)       |          |
| Route of poisoning,<br>No. (%)                  | Ingestion                             | 273 (82.0)         | 11 (28.2)            | 70 (88.6)                                      | 2 (66.7)                                        | 18 (42.9)                                                                       | 374 (75.4)       | <0.0001  |
|                                                 | Inhalation                            | 23 (6.9)           | 17 (43.6)            | 2 (2.5)                                        | 0 (0.0)                                         | 4 (9.5)                                                                         | 46 (9.3)         |          |
|                                                 | Injection                             | 8 (2.4)            | 0 (0.0)              | 0 (0.0)                                        | 0 (0.0)                                         | 0 (0.0)                                                                         | 8 (1.5)          |          |
|                                                 | More than one<br>route of poisoning   | 5 (1.5)            | 6 (15.4)             | 4 (5.1)                                        | 1 (3.3)                                         | 15 (35.7)                                                                       | 31 (6.3)         |          |
|                                                 | Unknown                               | 24 (7.2)           | 5 (12.8)             | 3 (3.8)                                        | 0 (0.0)                                         | 5 (11.9)                                                                        | 37 (7.5)         |          |
|                                                 |                                       |                    |                      |                                                |                                                 |                                                                                 |                  |          |
| Type of poisoning,<br>No. (%)                   | Suicide                               | 134 (40.2)         | 10 (25.6)            | 35 (44.3)                                      | 1 (33.3)                                        | 18 (42.9)                                                                       | 198 (39.9)       | 0.02     |
|                                                 | Accidental                            | 57 (17.1)          | 5 (12.8)             | 5 (6.3)                                        | 0 (0.0)                                         | 1 (2.4)                                                                         | 68 (13.7)        |          |
|                                                 | Abuse                                 | 47 (14.1)          | 11 (28.2)            | 4 (5.1)                                        | 0 (0.0)                                         | 5 (11.9)                                                                        | 67 (13.5)        |          |
|                                                 | Unaware                               | 0 (0.0)            | 0 (0.0)              | 1 (1.3)                                        | 0 (0.0)                                         | 1 (2.4)                                                                         | 2 (0.4)          |          |
|                                                 | Unknown                               | 95 (28.5)          | 13 (33.3)            | 34 (43)                                        | 2 (66.7)                                        | 17 (40.4)                                                                       | 161 (32.5)       |          |
| History of<br>psychiatric diseases,<br>No. (%)  |                                       |                    |                      |                                                |                                                 |                                                                                 |                  |          |
|                                                 | Yes                                   | 48 (15.2)          | 6 (16.7)             | 22 (31.4)                                      | 3 (100)                                         | 8 (25)                                                                          | 87 (19.7)        | <0.0001  |
| Central nervous<br>system, No. (%)              | Alert                                 | 185 (55.6)         | 22 (56.4)            | 28 (36.7)                                      | 1 (33.3)                                        | 19 (45.2)                                                                       | 256 (51.6)       | 0.04     |
|                                                 | Drowsiness                            | 104 (31.2)         | 9 (23.1)             | 32 (40.5)                                      | 1 (33.3)                                        | 13 (31)                                                                         | 159 (32.1)       |          |
|                                                 | Obtundation                           | 16 (4.8)           | 5 (12.8)             | 8 (10.1)                                       | 0 (0.0)                                         | 2 (4.8)                                                                         | 31 (6.3)         |          |
|                                                 | Stupor                                | 17 (5.1)           | 0 (0.0)              | 6 (7.6)                                        | 0 (0.0)                                         | 2 (4.8)                                                                         | 25 (5)           |          |
|                                                 | Coma                                  | 4 (1.2)            | 0 (0.0)              | 2 (2.5)                                        | 0 (0.0)                                         | 1 (2.4)                                                                         | 7 (1.4)          |          |
|                                                 | Restlessness                          | 7 (2.1)            | 3 (7.7)              | 2 (2.5)                                        | 1 (33.3)                                        | 5 (11.8)                                                                        | 18 (3.6)         |          |
| Pupil size, No. (%)                             | Normal                                | 162 (48.6)         | 19 (48.7)            | 38 (48.1)                                      | 1 (33.3)                                        | 18 (42.9)                                                                       | 238 (48)         | <0.0001  |
|                                                 | Mydriasis                             | 15 (4.5)           | 12 (30.8)            | 10 (12.7)                                      | 0 (0.0)                                         | 5 (11.9)                                                                        | 42 (8.5)         |          |
|                                                 | Miosis                                | 134 (40.2)         | 5 (12.8)             | 28 (35.4)                                      | 0 (0.0)                                         | 15 (35.7)                                                                       | 182 (36.6)       |          |
|                                                 | Undetermined                          | 22 (6.6)           | 3 (7.7)              | 3 (3.8)                                        | 2 (66.7)                                        | 4 (9.5)                                                                         | 34 (6.9)         |          |
| Cardiovascular<br>system examination<br>(N (%)) |                                       |                    |                      |                                                |                                                 |                                                                                 |                  |          |
|                                                 | Abnormal                              | 47(14.2)           | 13 (33.3)            | 8 (10.1)                                       | 1 (33.3)                                        | 9 (21.4)                                                                        | 78 (15.8)        | 0.04     |
| Naloxone<br>administration, No.<br>(%)          | Not administered                      | 170 (51.1)         | 36 (92.3)            | 53 (67.1)                                      | 3 (100)                                         | 28 (66.7)                                                                       | 290(58.5)        | 0.008    |
|                                                 | Administered in<br>the primary center | 23 (6.9)           | 0 (0.0)              | 6 (7.6)                                        | 0 (0.0)                                         | 3 (7.1)                                                                         | 32 (6.5)         |          |
|                                                 | Administered in<br>emergency service  | 84 (25.2)          | 2 (5.1)              | 15 (19)                                        | 0 (0.0)                                         | 7 (16.7)                                                                        | 108 (21.8)       |          |
|                                                 | Administered in<br>the ward           | 56 (16.8)          | 1 (2.6)              | 5 (6.3)                                        | 0 (0.0)                                         | 4 (9.5)                                                                         | 66 (13.3)        |          |
| Response to<br>naloxone, No. (%)                | Complete                              | 108 (67.5)         | 0 (0.0)              | 14 (53.8)                                      | 0 (0.0)                                         | 10 (71.4)                                                                       | 135 (66.5)       | 0.008    |
|                                                 | Partial                               | 44 (27.5)          | 0 (0.0)              | 9 (34.6)                                       | 0 (0.0)                                         | 4 (28.6)                                                                        | 57 (28.1)        |          |
|                                                 | No response                           | 8 (5)              | 3 (100)              | 3 (11.5)                                       | 0 (0.0)                                         | 0 (0.0)                                                                         | 11 (5.4)         |          |

\*Resulted from one-way ANOVA for continuous and chi-square for categorical variables. The reported *P* values are adjusted by the Benjamini-Hochberg procedure for multiple testing. Patients were divided into five subgroups: 1- Opioids (opium, codeine, morphine; heroin, methadone, pethidine, buprenorphine, and tramadol) 2- Stimulants (amphetamine/methamphetamines, cocaine, methylphenidate, ephedrine, pseudoephedrine, caffeine, and ethanol), 3- Combined use of opioids and pharmaceutical drugs, 4- Stimulants with pharmaceutical drugs, 5- Combined use of opioids, stimulants, and pharmaceutical drugs.

stimulant poisoning in Iran.<sup>23</sup> Opioids primarily act on the CNS, with the risk of respiratory depression leading to potential death from hypoxia.

Stimulants primarily affect the CNS and cardiovascular system, and while potentially life-threatening complications like arrhythmias can occur, respiratory

depression is less common. This inherent difference in physiological effects may contribute to the observed mortality disparity. Additionally, variations in drug purity could influence the severity of poisoning and the associated mortality risk. Our study included a relatively small number of patients with stimulant poisoning (*n* = 39)

**Table 2.** Comparison of different variables concerning outcome in poisoning cases with opioids and/or stimulant drugs\*

| Variables                                        | Survived without complication (n=486) | Complication/death (n=10) | P value* |
|--------------------------------------------------|---------------------------------------|---------------------------|----------|
| Age (years), mean $\pm$ SD, median               | 33.28 $\pm$ 15.54 (31)                | 46.25 $\pm$ 22.98 (43)    | 0.04     |
| Education level (high school diploma and higher) | 304 (60.6%)                           | 3 (30%)                   | 0.03     |
| Low level of consciousness                       | 256 (50.6%)                           | 7 (66.7%)                 | 0.05     |
| Abnormal cardiovascular manifestations           | 75 (21.4%)                            | 4 (57.1%)                 | 0.05     |
| Abnormal respiratory manifestations              | 9 (2.2%)                              | 2 (25%)                   | 0.03     |
| No response to naloxone                          | 8 (4%)                                | 3 (75%)                   | <0.0001  |
| Need for endotracheal intubation                 | 19 (3.9%)                             | 6 (60%)                   | <0.0001  |

The reported *P* values are adjusted by the Benjamini-Hochberg procedure for multiple testing.

\*Patients were divided into five subgroups: 1- Opioids (opium, codeine, morphine; heroin, methadone, pethidine, buprenorphine, and tramadol) 2- Stimulants (amphetamine/methamphetamines, cocaine, methylphenidate, ephedrine, pseudoephedrine, caffeine, and ethanol), 3- Combined use of opioids and pharmaceutical drugs, 4- Stimulants with pharmaceutical drugs, 5- Combined use of opioids, stimulants, and pharmaceutical drugs.

**Table 3.** Prediction of outcome (complications/mortality) based on all studied variables in patients with opioid poisoning

| Variables                             | P value* | OR (95% CI)         |
|---------------------------------------|----------|---------------------|
| No response to naloxone               | 0.007    | 45.37 (4.22–487.13) |
| Endotracheal intubation               | 0.000    | 32.41 (6.68–157.10) |
| Coma                                  | 0.03     | 18.9 (1.46–244.35)  |
| Past medical history (cardiovascular) | 0.007    | 16.5 (2.57–165.61)  |
| Abnormal respiratory manifestations   | 0.04     | 10.65 (1.06–106.36) |
| Stupor                                | 0.03     | 9 (1.20–67.24)      |
| Age (years)                           | 0.01     | 1.05 (1.01–1.09)    |

The reported *P* values are adjusted by the Benjamini-Hochberg procedure for multiple testing.

compared to the opioid group ( $n=333$ ). This limits the generalizability of the findings regarding mortality in stimulant poisoning. Future studies investigating the specific types and quantities of drugs involved could provide further insights.

In this study, most of the patients were young men, which is consistent with the findings of some studies.<sup>24–26</sup> There are sex differences in the propensity for the development of substance-use disorders. Men, compared to women, have a higher inclination towards risky behaviors, which are associated with higher rates of morbidity and mortality. For instance, at a biological level, the X-chromosome contains numerous genes and microRNA that play a role in neuronal and glial functions, and the regulation of these may vary between males and females.<sup>27</sup> Additionally, at the behavioral and social levels, the patterns of initial opioid exposure may differ between men and women, potentially influencing the course of opioid use and the risk of overdose.<sup>28</sup> In a study published in 2019, 1731 patients with acute poisoning were evaluated, and opioids were reported as the cause in 34% of cases, the majority of whom were male.<sup>29</sup> Furthermore, men were found to be at a higher risk of fatal opioid overdoses compared to women.<sup>30</sup> However, other studies have found significant epidemiological patterns of substance abuse poisoning with higher frequencies among females at younger ages.<sup>31</sup> Also, Georgieva et al presented the gender-specific illicit

substance use. They have discussed the faster rate of increase in opioid and cocaine consumption and addiction in women and provided specific reasons for drug use and higher levels of major depression diagnosis in women.<sup>32</sup> These different results may justify the development of gender-specific prevention.

Most of our patients had a history of addiction, which aligns with previous studies.<sup>24,25</sup> There was no significant difference in education level among patients using different types of drugs. In addition, another study found that lower education levels were linked to higher rates of comorbid mental health and drug use problems,<sup>33</sup> which aligns with previous studies.<sup>34,35</sup> However, individuals with a high school diploma had a lower risk of drug use problems up to the age of 30 years in another study.<sup>36</sup> It appears that educational campaigns aimed at raising public awareness could be beneficial in preventing suicidal overdoses.<sup>37</sup>

The present study showed that the prevalence of worse outcomes increased with age. The mean ages of patients with complications were higher than those without complications. Substance Abuse and Mental Health Services Administration data show that the early to late 20s are the most common age range for reporting prescription opioid misuse.<sup>38</sup> Moreover, consistent with the results of the present study, middle-age is presented as a risk factor for overdose death related to opioid users.<sup>39</sup> However, the findings of a previous study indicate a higher rate of cumulative incidence of death from illicit drugs at younger ages in Iran.<sup>9</sup> The long-term shift in the age distribution of opioid-related mortality towards younger individuals likely corresponds to changes in regional prescribing practices and the most common substances in the unregulated drug supply. Lower marriage rates in this age range, unemployment, and lack of financial security and housing have been suggested as the most important risk factors for drug-related deaths.<sup>9</sup>

Our results showed that age, cardiovascular history, low levels of consciousness, abnormal respiratory manifestations, the need for endotracheal intubation, and incomplete response to naloxone administration

were predictive factors for poor outcomes in patients with opioid poisoning. Some of these factors have been mentioned in another study by Yeh et al. They showed that patients with illicit drug use who died were older, with deep coma, higher heart and respiratory rates, lower blood pressure and oxygen saturation, and more seizures, compared to the survivor patients.<sup>40</sup> These physiological factors likely reflect the severity of opioid intoxication and its impact on vital organ systems. For instance, respiratory depression caused by opioids can lead to hypoxia and subsequent cardiovascular complications, ultimately increasing the risk of death<sup>41</sup>. On the other hand, naloxone is an opioid antagonist that rapidly reverses opioid overdose by displacing opioids from receptor sites. A weak response to naloxone suggests a potentially larger opioid dose or co-ingestion with other substances, complicating the reversal process and increasing mortality risk.<sup>41</sup> To reduce overdose deaths, new strategies are necessary, such as greater access to naloxone.<sup>42</sup> One systematic review demonstrated a strong association between take-home naloxone programs and overdose survival.<sup>43</sup> Also, a study by Webster identified the risk factors for overdose deaths related to both medical and nonmedical opioid use, including age, comorbid mental and medical disorders, history of substance-use disorders, psychological and social stress, and heart or pulmonary complications. Heart failure and chronic pulmonary disease were particularly presented as strong predictors of opioid-induced respiratory depression. Some of these findings align with our results.<sup>39</sup> Regardless of the pattern of the illicit drug poisoning, the identified predictors assist in risk assessment and in determining the most appropriate treatment approach. Notably, underlying medical conditions, except for the history of cardiovascular disease, were not associated with increased mortality in the present study. This finding diverges from previous research highlighting chronic health conditions as risk factors for opioid overdose mortality.<sup>30</sup> Potential explanations for this discrepancy could be sample characteristics, and this study focused on the immediate effects of poisoning, while chronic health conditions might play a more significant role in long-term outcomes. Although we identified different risk factors for worse outcome prediction in patients with opioid poisoning, the large OR of these factors may weaken their significance in clinical practice. This large OR could also be attributed to the small sample size, which highlights the need for future studies to definitively establish the predictive role of these variables.

We were unable to analyze predictive factors in cases of stimulant toxicity due to the absence of mortality in this group and the low sample size. However, in a study by Paydar et al, age, history of suicide, route of poisoning, and pulmonary manifestations on admission were found to be highly associated with poor outcomes in cases of

methamphetamine overdose.<sup>25</sup> Rahimi et al<sup>24</sup> also showed a significant association between agitation, seizure, loss of consciousness, creatine phosphokinase level, and serum pH with mortality among amphetamine users.

### Limitations of the Study

1- The study was conducted at a single center. Although our referral poisoning center primarily serves adult patients, it is important to note that some children were also brought to the center by their families. Therefore, we included both adults and children in our evaluation. However, it is crucial to recognize that the outcomes and severity of poisoning may vary between these two age groups, and further research specifically focusing on children is recommended. Additionally, the number of patients in the stimulant groups was too low to effectively evaluate factors that predict outcomes.

2- Since this was a hospital-based sample, there may be some biases that may have resulted in the patient profile observed (e.g., poisoning with fentanyl is likely to be more fatal, and patients are likely to be dead before they reach the hospital). Hence, conclusions like "Opioid poisoning was more common than stimulant poisoning" should be cautiously framed, given the context. Stimulant poisoning may be more common in the community, but patients may be getting better with conservative management.

3- Although all toxico-clinical and sociodemographic factors were investigated among patients without complications and those with complications/death, only some of these variables were significantly different between the two groups, which may be due to the small number of patients in the complication/death group.

### Conclusion

Opioid poisoning was more common than stimulant poisoning in our referral poisoning center. Most of the patients were male in both opioid and stimulant poisoning cases. There were significant differences in the type and route of poisoning among patients with opioid and stimulant poisoning. However, there was no significant difference between patients poisoned with opioid or stimulant drugs regarding other toxico-clinical and sociodemographic factors. Age, coma/stupor, abnormal respiratory manifestations, previous cardiovascular disease, incomplete response to naloxone, and endotracheal intubation were predictive factors for poor outcomes in opioid poisoning. The findings of the present study emphasize the importance of early recognition and aggressive management of opioid poisoning, including early administration of naloxone. Based on the results of this study, we should research and plan new strategies to prevent and regulate the accessibility of illicit opioids in Iran.

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#### Competing Interests

The authors declare that they have no competing interests.

#### Ethical Approval

This research was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Isfahan University of Medical Sciences (ethical code: IR.MUI.MED.REC.1397.314). Written informed consent was obtained from all patients or their legal guardian(s).

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