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Original Article

A Retrospective Cross-Sectional Study on Methadone Poisoning: A Decade of Insights from Kerman, Iran

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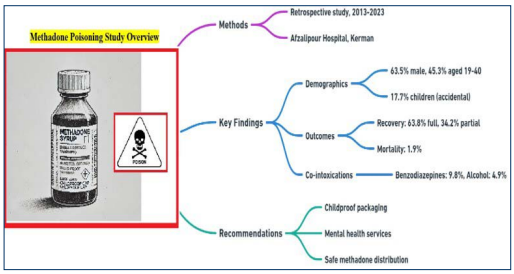
Abstract



Introduction: Methadone poisoning, involving both syrup and tablet formulations, represents a significant public health concern, particularly in regions where methadone is widely utilized for opioid substitution therapy. Methadone accounted for approximately 16% of pediatric acute poisonings and was the leading cause of drug-related deaths in 2023. This study provides a decade-long retrospective analysis of methadone poisoning cases in Kerman, Iran, with a focus on demographic patterns, clinical outcomes, and risk factors to guide prevention and treatment strategies.

Methods: This retrospective cross-sectional study reviewed medical records of 5,826 methadone poisoning cases, primarily acute but including some chronic cases, admitted to Afzalipour Hospital between 2013 and 2023. Data on demographics, clinical presentations, comorbidities, and outcomes were analyzed using SPSS version 22, with statistical significance set at $P<0.05$.

Results: The majority of patients were male (63.5%), with the highest prevalence among individuals aged 19–40 years (45.3%). Notably, 17.7% of cases involved children under six years old, primarily due to accidental ingestion linked to unsafe storage practices. Intentional poisoning accounted for 80.2% of cases, underscoring the role of mental health and socio-economic factors. Co-intoxication with benzodiazepines (9.8%) and alcohol (4.9%) exacerbated toxicity, while 8.8% of cases coincided with COVID-19 infection, compounding respiratory complications. The mortality rate was low at 1.9% (95% CI: 1.6–2.2%), with 63.8% of cases achieving full recovery; and notably, 17.7% of cases involved were children aged under six years old.

Conclusion: The findings, including high co-intoxication risks with benzodiazepines (9.8%) and alcohol (4.9%), highlight the urgent need for targeted interventions, including stricter regulation of methadone distribution, childproof packaging, and public education campaigns to reduce accidental pediatric poisonings. Integrated mental health services are critical to addressing intentional poisoning cases (80.2%), while healthcare providers should remain vigilant about polysubstance use. These strategies can significantly reduce methadone-related morbidity and mortality, especially among vulnerable populations such as children and young adults.

Keywords: Methadone, Poisoning, Child, Opiate substitution treatment

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Introduction

Methadone, a synthetic long-acting opioid agonist, targets mu-opioid receptors, providing analgesia and suppressing withdrawal in opioid use disorder (OUD) and pain management.[1,2] Its 24–36-hour half-life allows once-daily dosing but increases overdose risk, particularly respiratory depression. Widespread use in Iran highlights the need to study its poisoning risks.[1,3] Poisoning accounts for a significant proportion of global mortality and disability rates. As addiction rates rise, poisoning from harmful

drugs poses a considerable challenge to communities.[4] Opioid use disorder (OUD), a type of substance misuse associated with drug consumption, impacts approximately 40.5 million individuals globally as of recent estimates.[5] It is estimated that over 80% of individuals who inject drugs utilize opioids, making them the most prevalent category of injectable substance globally.[5] Opium usage, either by smoking or ingestion, remains one of the most common types of opioids in Iran.[6,7] The main drugs used to treat OUD are methadone, buprenorphine, and naltrexone, administered in outpatient settings with varying levels of supervision.[8] Iran implemented methadone maintenance therapy (MMT) in 2002, and it has since expanded nationwide. Despite its prescribed use, numerous reports highlight its misuse.[2,9] Concerns persist about non-prescribed methadone use, despite positive MMT outcomes in Iran.[10,11] Multiple incidents of accidental poisoning in children have emerged, raising alarms due to widespread addiction and methadone accessibility in Iran.[2,7,12,13] Consequently, methadone poisoning has become the leading cause of poisoning in Iran, accounting for over 50% of opioid-related deaths in 2023, with approximately 370 fatalities reported in Tehran Province during 2020–2021.[14] Globally, similar trends are observed; in the United States, methadone-related overdoses increased by 48.1% in 2020 relative to 2019, driven by disrupted treatment access and polysubstance use during the COVID-19 pandemic.[15]

Individuals with substance use disorder may face life-threatening side effects due to methadone poisoning. Symptoms related to methadone poisoning include lack of awareness, psychosis, myosis, vomiting, reduced respiratory function, cyanosis, convulsions, and ataxia.[16,17] One of the primary and potentially fatal effects of methadone is cardiotoxicity, evidenced by QT interval prolongation and torsade de pointes.[18] Methadone, widely used for pain management and opioid dependence, poses a significant overdose risk. Studies show high drug-related mortality within four weeks post-treatment cessation in Dublin [19], with women aged 45–54 years in Clark County, Nevada, at the highest risk for unintentional poisoning.[20] In Mazandaran, Iran, deliberate methadone poisonings commonly caused respiratory depression and reduced consciousness.[21] In France, 41% of methadone exposures were suicide attempts, highlighting the need for preventive measures, ongoing therapy, and identifying at-risk individuals.[22]

The significance of retrospective studies, particularly in the context of methadone poisoning, underscores the necessity of this cross-sectional investigation, which scrutinized the medical records of patients admitted to Afzalipour Hospital. Although similar studies have been conducted in Tehran and Hamadan, there is a lack of decade-long data specific to Kerman, a region with unique socio-economic and cultural factors influencing opioid use.[23] This analysis aimed to delineate the trends associated with methadone poisoning in Kerman County over the decade spanning from 2013 to 2023. The findings derived from this research are anticipated to facilitate the identification of vulnerable populations, guide the development of preventive measures, and enhance treatment protocols, ultimately contributing to a reduction in methadone-related poisoning incidents within the region.

Methods

Study Design and Setting

This cross-sectional, retrospective study analyzed the patterns and trends of methadone poisoning among patients admitted to Afzalipour Hospital, Kerman, over a decade (2013–2023). The study included all patients admitted during this period, with trained personnel using a purpose-made questionnaire designed by toxicology experts to comprehensively review medical records and ensure eligibility.

Inclusion and Exclusion Criteria

Inclusion Criteria

Hospitalized patients diagnosed with methadone poisoning using ICD-10 code T40.3, based on clinical symptoms (e.g., miosis, respiratory depression), patient history, and toxicology screens where available.

Exclusion Criteria

Cases with incomplete medical records (approximately 5%, n = 308, lacking key diagnostic or outcome data), those not requiring hospitalization (e.g., mild cases managed outpatient), or those with background diseases (e.g., chronic liver disease, severe renal failure) or multi-drug toxicity where methadone was not the primary toxic agent (confirmed via toxicology screens or clinical assessment).

Data Collection

Data collection commenced following ethical approval from the Ethics Committee of Kerman University of Medical Sciences (Ethical Code: IR.KMU.REC.1402.413). Patient confidentiality was rigorously maintained. A structured questionnaire was used to extract relevant information from medical records, including demographic and clinical data such as:

Demographic Variables

Age, gender, occupation, residence, history of substance abuse, psychiatric disorders.

Clinical Data

Symptoms, duration of hospitalization, comorbidities, patient outcomes (discharge or death), and co-intoxicants (verified via toxicology screens where available; inter-rater reliability assessed).

Sample Size

All 5,826 hospitalized cases of methadone poisoning from 2013 to 2023 were included, eliminating the need for separate sample size calculations due to the comprehensive inclusion of all eligible cases.

Data Analysis

Data were analyzed using SPSS software (version 22). Descriptive statistics were used to summarize demographic and clinical characteristics, including frequency distributions and percentages for categorical variables and means for continuous variables. Chi-square tests and t-tests were used to assess the statistical significance of the associations between variables. A p-value of less than 0.05 was considered statistically significant.

Results

Demographic Patterns, Outcomes, and Age-Specific Differences in Methadone Poisoning

The demographic analysis indicated (Table 1) that a significant proportion of poisoning cases (63.5%) were observed in males. The predominant age group affected was between 19 and 40 years, representing 45.3% of cases. Regarding marital status, single individuals comprised the largest segment at 53.4%, followed by married individuals at 40.9%. Most cases involved Iranian nationals, accounting for 79.4%, while Afghan individuals represented a smaller fraction at 2.9%, along with other nationalities. Intentional poisoning was identified as the most common type, comprising 80.2% of cases, in contrast to accidental poisoning, which accounted for 19.8%. Regarding patient outcomes, 34.2% of individuals experienced partial recovery, while 63.8% of cases resulted in full recovery. The mortality rate was relatively low at 1.9%.

Table 1. Demographic distribution, poisoning type, and outcomes in methadone poisoning patients

Characteristics	Subcategories	Frequency (N)	Percentage (%)
Gender	Male	3700	63.5
	Female	2126	36.5
Age Groups	0-6 years	1029	17.7
	7-12 years	220	3.8
	13-18 years	838	14.4
	19-40 years	2640	45.3
	41-60 years	882	15.1
	61 + years	217	3.7
Marital Status	Single	3110	53.4
	Married	2380	40.9
	Unknown	264	4.5
	Divorced	67	1.2
	Widowed	5	0.1
Nationality	Iranian	4628	79.4
	Afghan	168	2.9
	Unknown	1000	17.2
	Others (Iraqi, Pakistani)	30	0.5
Type of Poisoning	Intentional	4675	80.2
	Accidental	1151	19.8
Final Outcome	Partial recovery	1995	34.2
	Full recovery	3718	63.8
	Death	113	1.9

Figure 1 demonstrates the annual gender distribution of methadone poisoning cases over 10 years. The data reveals a consistent upward trend in the number of male and female cases throughout the years. However, the rate of increase is more pronounced among males, who constitute the majority of cases. These findings underscore the growing prevalence of methadone poisoning across both genders.

Figure 2 shows the distribution of methadone poisoning cases across various age groups over a decade (2013–2023). The highest number of cases was observed in the 19–40 age range, indicating that young and middle-aged individuals are disproportionately affected. The second most affected group was 41–60 years, followed by children aged 0–6 years. The data highlights the need for age-specific strategies to address methadone poisoning, particularly in younger populations who are more vulnerable due to behavioral and social factors.

Table 2 summarizes the significant differences in methadone poisoning cases across various age groups for males and females. Among males, younger age groups (e.g., 0–6 years and 7–12 years) show significant differences compared to older groups, such as 19–40, 41–60, and 61 + years. Similarly, for females, significant differences were observed between the youngest age groups (0–6 years and 7–12 years) and older groups. The middle-aged group (19–40 years) also differs significantly from other age groups, particularly for males. These findings highlight a clear disparity in methadone poisoning prevalence across different age groups, suggesting age-specific patterns that may inform targeted prevention strategies.

Co-Intoxications and Related Conditions in Methadone Poisoning Cases

In this study, we examined the prevalence of co-intoxications and related conditions in cases of methadone poisoning (Table 3). The results reveal significant insights into the concurrent presence of other substances or conditions that may exacerbate or complicate the effects of methadone toxicity. Out of the total cases, 573 (9.8%) involved co-intoxication with benzodiazepines, while 90.2% (5253 cases) did not show concurrent use. This indicates a notable association between methadone poisoning and benzodiazepine co-intoxication. This combination may increase the risk of respiratory depression and central nervous system depression, which can be fatal. A smaller proportion of methadone poisoning cases (513, or 8.8%) was also found to be associated with COVID-19 infection. The remaining 91.2% (5313 cases) were not diagnosed with COVID-19 at the time of the methadone poisoning. While COVID-19 may not be directly linked to methadone toxicity, respiratory complications associated with the virus could compound the dangers of opioid overdose. Alcohol was involved in 287 (4.9%) of methadone poisoning cases, with the remaining 95.1% (5539 cases) was free of alcohol intoxication.

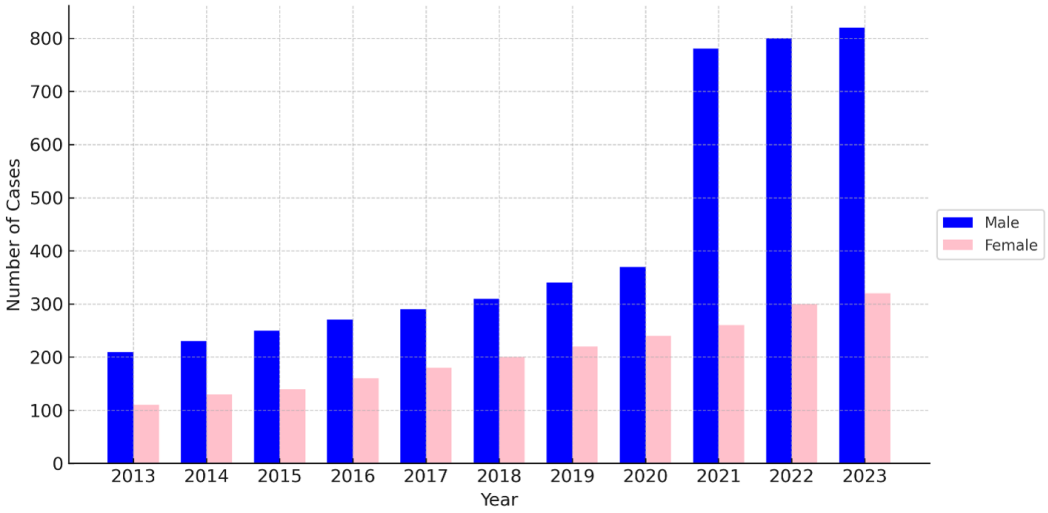

Figure 1. Annual gender distribution of methadone poisoning cases (2013–2023), showing a significant male predominance (63.5%, n = 3,700) over females (36.5%, n = 2,126), with a consistent increase in cases for both genders ($\chi^2 = 45.6$, $P < 0.001$)

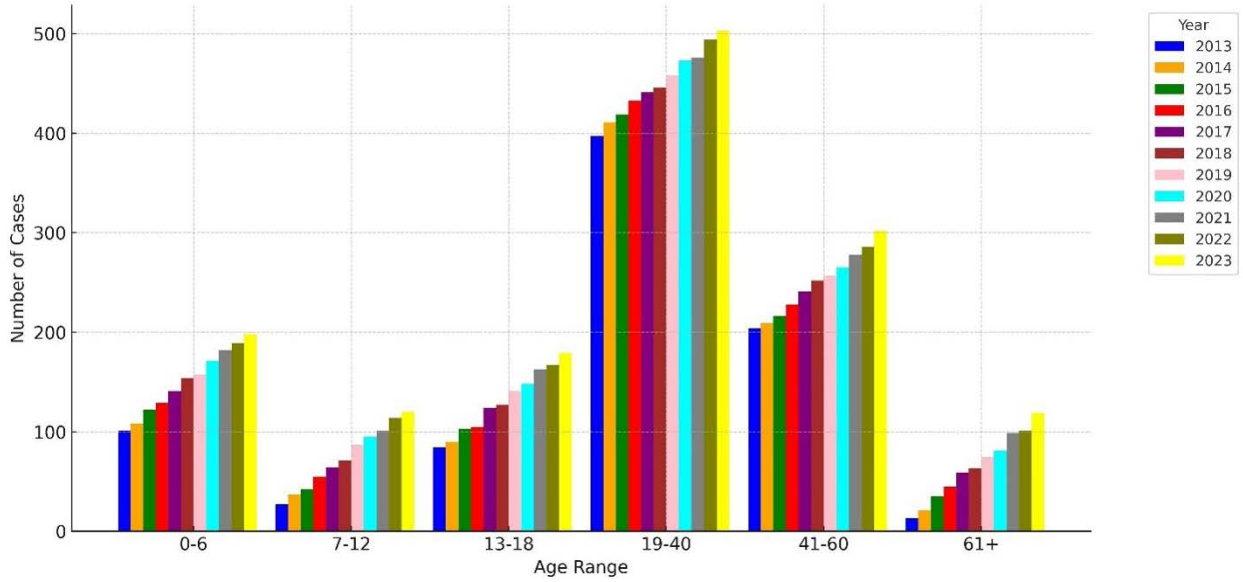

Figure 2. Age distribution of methadone poisoning cases (2013–2023), with the 19–40 age group most affected (45.3%, n = 2,639), followed by 41–60 years (28.1%, n = 1,637) and 0–6 years (17.7%, n = 1,031), showing significant age-group differences ($\chi^2 = 132.4$, $P < 0.001$)

Table 2. Summary of Significant Differences Across Age Groups

Gender	Age Group	Significant Differences
Male	0–6	13–18, 19–40, 41–60, 61 +
	7–12	19–40, 41–60, 61 +
	13–18	0–6, 19–40, 41–60, 61 +
	19–40	0–6, 7–12, 13–18
	41–60	0–6, 7–12, 13–18, 19–40
	61 +	0–6, 7–12, 13–18
Female	0–6	19–40, 41–60, 61 +
	7–12	19–40, 41–60, 61 +
	13–18	0–6, 19–40, 41–60, 61 +
	19–40	41–60
	41–60	0–6, 7–12, 13–18, 19–40

Table 3. Co-intoxications and related conditions in methadone poisoning cases

Variable	Yes (N)	Yes (%)	No (N)	No (%)
Benzodiazepine Co-intoxication	573	9.8	5253	90.2
COVID-19 Infection	513	8.8	5313	91.2
Alcohol Co-intoxication	287	4.9	5539	95.1

Frequency of Respiratory Conditions (COPD and Dyspnea) in Methadone Poisoning Cases

Table 4 indicates that Chronic Obstructive Pulmonary Disease (COPD) was reported in only 2.1% of cases, while the majority of patients (97.9%) did not have COPD. Similarly, dyspnea was observed in 2% of cases, with 98% of patients not exhibiting this condition. These findings suggest that respiratory symptoms, such as COPD and dyspnea, are relatively uncommon among methadone-poisoning patients in this study population. The low reported rates of respiratory symptoms may be attributable to under-documentation in medical records,

Table 4. Frequency of respiratory disorders (COPD and dyspnea) among methadone poisoning cases

Condition	Condition Status	Frequency (N)	Percentage (%)
	No	5705	97.9
COPD	Yes	121	2.1
	Total	5826	100
	No	5709	98
Dyspnea	Yes	117	2
	Total	5826	100

*Chronic Obstructive Pulmonary Disease.

the inclusion of milder cases not requiring detailed symptom logging, or early intervention preventing progression to severe respiratory depression.

Frequency of Nausea and Vomiting in Methadone Poisoning Cases

Nausea and vomiting occurred in 2.3% of methadone poisoning cases (n = 135, 95% CI: 1.9–2.7%), with 97.7% (n = 5,691) reporting no such symptoms.

Frequency Of Mental and Behavioral Disorders In Methadone Poisoning Cases

Mental and behavioral disorders were reported in 2.8% of methadone poisoning cases (n = 166, 95% CI: 2.4–3.2%), with 97.2% (n = 5,660), indicating no such disorders.

Frequency Of Withdrawal Syndrome In Methadone Poisoning Cases

In this study, Withdrawal syndrome was observed in 2.3% of methadone poisoning cases (n = 136, 95% CI: 1.9–2.7%), primarily among chronic users, with 97.7% (n = 5,690), showing no withdrawal symptoms.

Frequency of Seizures and Coma in Methadone Poisoning Cases

In a study of 5,826 methadone poisoning cases, seizures occurred in 90 individuals (1.5%), while 5,736 (98.5%) reported none, indicating seizures are uncommon and typically linked to prolonged hypoxia from delayed treatment. Coma was more frequent, affecting 1,991 individuals (34.2%), with 3,835 (65.8%) experiencing no coma.

Discussion

This study presents a decade-long analysis of methadone poisoning patterns among patients admitted to Afzalipour Hospital in Kerman, Iran. The findings underscore significant demographic trends, co-intoxication risks, and the alarming prevalence of poisoning in young children, alongside implications for public health interventions and clinical care.

The predominance of methadone poisoning among males (63.5%) and individuals aged 19–40 years (45.3%) aligns with global patterns—similar studies, such as Mehrpour *et al.* [24] and several studies, have highlighted the disproportionate vulnerability of young and middle-aged men to opioid-related toxicities, driven by factors such as substance abuse and risky behaviors.[25-27] This pediatric rate of 17.7% is consistent with national data in Iran, which indicates a significant proportion of acute poisonings in children are due to opioids, often linked to accidental ingestion from household access.[6] The slightly higher rate in our study may reflect regional factors in Kerman, such as increased methadone availability or inadequate storage practices. Several studies [28-31] corroborate our findings regarding the susceptibility of children to methadone poisoning due to accidental ingestion. These studies emphasize that methadone's long half-life and delayed toxicity significantly increase the risk of severe health complications in pediatric cases. Furthermore, they highlight the critical importance of secure storage practices, public education, and early medical intervention in preventing fatalities and reducing the burden of methadone poisoning in children, consistent with the trends identified in our research. Public health strategies should prioritize childproof packaging for methadone and raise awareness among caregivers about the dangers of leaving medications within reach of children.

Approximately 9.8% of methadone poisoning cases involved benzodiazepine co-intoxication. This combination is widely documented to amplify respiratory depression, leading to severe central nervous system (CNS) depression and increased mortality risk. Similar findings have been reported by Lee *et al.* [32] and White *et al.* [33], underscoring the dangers of combining methadone with sedative-hypnotic agents.

Alcohol co-intoxication was observed in 4.9% of cases. As alcohol potentiates methadone's sedative effects, even low levels of concurrent alcohol consumption significantly increase the risk of fatal respiratory failure.[34] Zhong *et al.* [34] similarly, reported heightened risks associated with alcohol use in opioid poisonings emphasize the need for greater awareness and preventive measures.

Interestingly, 8.8% of methadone poisoning cases coincided with COVID-19 infection, particularly during the pandemic's peak in 2020–2021. The respiratory complications of COVID-19 may exacerbate methadone's effects on ventilation, increasing the likelihood of adverse outcomes.[35-37]

Despite the potential severity of methadone poisoning, the mortality rate in our study was low (1.9%), with 63.8% of cases resulting in full recovery. This mortality rate is notably lower than global estimates of 5–10% for opioid-related poisonings, as reported in studies from regions with higher polysubstance use or delayed treatment.[17,20] Factors such as timely access to emergency care at Afzalipour Hospital, standardized naloxone protocols, and a lower prevalence of co-intoxicants (e.g., 9.8% benzodiazepines, 4.9% alcohol) likely contributed to this reduced mortality. This reflects the effectiveness of clinical interventions and emergency care at Afzalipour Hospital. However, the substantial proportion of partial recoveries (34.2%) indicates the need for enhanced post-discharge care

to address long-term sequelae and prevent recurrence. Similar outcomes have been documented in studies from the United States and Europe, where continuity of care plays a crucial role in reducing mortality rates.[38,39]

The findings of this study emphasize the urgent need for targeted interventions to reduce the prevalence and severity of methadone poisoning. Central to these efforts is the stricter regulation of methadone distribution, ensuring that access is limited to medical supervision and that clear guidelines for secure storage are enforced, particularly in households with children. Studies in Iran highlight the need for preventive measures like secure storage to reduce pediatric poisonings.[40] Evidence from the United States further demonstrates that childproof packaging significantly reduces accidental pediatric poisonings by limiting medication access.[41] Implementing such measures in Iran could mitigate the 17.7% pediatric poisoning rate observed in our study. Additionally, the high prevalence of intentional poisonings highlights the necessity of integrated mental health services, which can provide support and early intervention for at-risk individuals. Lastly, healthcare providers must remain vigilant about polysubstance use, particularly co-intoxicants such as benzodiazepines and alcohol, which can significantly amplify the risks associated with methadone toxicity. Collectively, these measures are critical to mitigating methadone poisoning and safeguarding public health.

Study Limitations and Future Directions

Additionally, not all cases had toxicology confirmation due to resource constraints, which may have affected the accuracy of methadone poisoning diagnoses in some instances. Unaccounted socioeconomic factors, such as poverty or low health literacy, prevalent in regions like Kerman, could also influence poisoning patterns, particularly accidental pediatric cases, but were not systematically captured in this retrospective design.[6,23] Future research should employ prospective designs to investigate the long-term outcomes of methadone poisoning and explore the genetic and environmental determinants of susceptibility. Additionally, the impact of public health policies on reducing pediatric poisonings warrants further evaluation. Future studies could stratify outcomes by comorbidities like COVID-19 to explore interactions more deeply.

Conclusion

In summary, this study highlights the critical public health challenge posed by methadone poisoning in Kerman, Iran, particularly among young adults and children under 6 years. The findings emphasize the need for robust preventive strategies, improved clinical management, and enhanced public awareness to mitigate the burden of methadone toxicity. The increasing incidence of methadone poisoning, driven by factors such as greater availability of methadone and the high prevalence of mental health issues such as depression, particularly among youth, underscores the urgency of addressing this issue. By implementing effective interventions, improving early detection, and providing targeted education to high-risk populations, healthcare systems can achieve better outcomes for vulnerable groups and reduce the societal impact of opioid misuse. Addressing these challenges not only helps in preventing poisonings but also in reducing long-term health and social consequences associated with opioid dependence and misuse.

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Writing–Review & Editing: Somayyeh Karami-Mohajeri, Zohreh Oghabian.

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval

This study was approved by the Ethics Committee of Kerman University of Medical Sciences (Ethical Approval Code: IR.KMU.REC.1402.413).

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