Original Article
http://mjiri.iums.ac.ir
Medical Journal of the Islamic Republic of Iran (MJIRI)

Med J Islam Repub Iran. 2026 (5 Aug);40.84. https://doi.org/10.47176/mjiri.40.84

Predictive Factors of Abnormal Brain CT Scan in Patients with Opioid Poisoning: A Single-Center Study

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Received: 11 Mar 2026 Revised: 25 Jul 2026 Accepted: 1 Aug 2026 Published: 5 Aug 2026

Abstract

Background: Opioid poisoning is a major cause of morbidity and mortality, particularly in Iran; however, no clear guidelines exist regarding the appropriate timing for non-contrast BCTS in these patients. This study aims to identify clinical and laboratory factors that predict abnormal BCTS findings in individuals with opioid poisoning. We conducted the study among patients presenting to the emergency department of Shiraz Namazi Hospital with opioid poisoning.

Methods: This retrospective cross-sectional study was performed on 208 patients with opioid poisoning who were referred to the emergency department of Namazi Hospital between March 2019 and March 2021. Data collection involved accessing the archives of Namazi Hospital to gather the necessary information for this study.

Results: Among 208 patients with opioid poisoning who underwent brain CT, 57 (27.4%) exhibited abnormal BCTS findings within this selected subgroup. Multivariable logistic regression identified two independent predictive factors for abnormal BCTS: advanced age (OR 1.041 per year; 95% CI 1.01–1.07; P=0.008) and lower serum bicarbonate (OR 0.908 per mEq/L; 95% CI 0.83–0.99; P=0.025). The most prevalent abnormal findings included microvascular ischemic damage, followed by ischemic infarctions.

Conclusion: Advanced age and lower serum bicarbonate levels are independent predictors of abnormal BCTS findings in patients with acute opioid poisoning. Clinicians should consider urgent BCTS in older patients or those with metabolic acidosis, as these groups are at higher risk and may derive the greatest benefit from emergent neuroimaging.

Keywords: Poisoning, Opioid, Brain CT scan, Opium, methadone, heroin, Pethidine, Tramadol, ischemia, infarction

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Cite this article as: Abbasi A, Farhadi M, Sadegh R, Kavari K, Rastaghi F, Parvizi F, Azadian Z, Rajabi AH, Nasr A. Predictive Factors of Abnormal Brain CT Scan in Patients with Opioid Poisoning: A Single-Center Study. *Med J Islam Repub Iran.* 2026 (5 Aug);40:84. https://doi.org/10.47176/mjiri.40.84

Introduction

Opioid poisoning continues to present a significant global public health challenge. In Iran, opium and its residues are consistently reported as leading agents in toxic exposures and emergency department (ED) presentations. National reports indicate that opioids are predominant causes of poisoning across various provinces and age groups, influenced by proximity to major opium-producing regions and local availability (1, 2). Opium is derived from the dried latex of Papaver somniferum, containing natural alkaloids such as morphine, codeine, and thebaine, and is utilized either in its crude form or as refined extracts. The use of opium is deeply rooted in the sociocultural fabric of Iran, with estimates suggesting over 2 million users and a prevalence several-fold higher than the global average (3, 4). Opioids may induce structural changes in the white or gray matter of the central nervous system (CNS). For

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Key Messages:

↑What is "already known" in this topic:

Brain computed tomography (CT) scans are frequently performed in patients with opioid poisoning to identify intracranial pathology. However, the routine application of brain CT in all poisoned patients may be unwarranted, exposes patients to radiation, and contributes to increased healthcare costs.

→What this article adds:

This study identifies clinical predictors associated with abnormal brain CT findings in patients with opioid poisoning. Recognizing these factors can assist clinicians in selecting patients who will genuinely benefit from brain CT imaging, thereby avoiding unnecessary investigations.

instance, heroin can cause acute or chronic ischemia, leukoencephalopathy, and atrophy, and may precipitate infections. Acute effects are typically associated with intravenous use of heroin, resulting from angiospasm, vasculitis, or emboli (5). In addition to the primary effects of opioids on the brain, several secondary complications may arise. These complications include toxic effects from impurities such as lipophilic adulterants, exposure to lead-adulterated opium (a particular issue reported in Iran), and the presence of insoluble crystalline particles. Further complications may also stem from associated conditions, including infections and seizure disorders (5, 6).

Abnormal findings can be observed in both CT scans and MRIs of the brain in patients with opioid poisoning. These modalities play a critical role in the timely diagnosis and management of the adverse neurologic effects of opioids on the brain (7). Acknowledging that the management of a patient with opioid overdose is multifactorial, there is currently no established guideline to determine whether a brain CT scan (BCTS) is indicated. Furthermore, no formal guideline exists specifically for BCTS in cases of opium poisoning, and a similar lack of clear guidance is evident for patients presenting with altered mental status in general (8). Additionally, based on certain Appropriateness Criteria (not validated as guidelines), BCTS in patients with altered mental status due to known medical or toxic-metabolic causes generally has a low diagnostic yield (9). This imaging modality is readily available and can provide invaluable information in a relatively short period. However, its cost-effectiveness and diagnostic yield are questioned in patients with drug overdose, necessitating a consideration of the risks versus benefits of performing this procedure. As discussed, there is a need for further research to assist in the development of such guidelines (8, 10, 11). We conducted the present study to determine the predictive factors of abnormal BCTS findings in patients with opioid poisoning admitted to the Namazi Hospital emergency room, a tertiary care center in Shiraz, Iran.

Methods

This retrospective cross-sectional study reviewed the medical records of adults with opium or opioid poisoning who were admitted to the ED of Namazi Hospital in Shiraz, Iran, between March 2019 and March 2021. Cases were identified through the electronic discharge diagnosis system based on the ICD-10. Inclusion criteria included age ≥18 years, presentation within 24 hours of exposure, and a non-contrast BCTS performed within 24 hours of admission for altered mental status with minimal response to naloxone, or for patients who were intubated prehospital or upon arrival at the ED (including those who received naloxone without improvement). The study specifically targeted a high-risk subgroup of patients with a clinical indication for brain CT scanning, such as persistent altered mental status. Cases with incomplete records or documented co-ingestion of non-narcotic substances were excluded; for example, cases with urine toxicology positive for non-narcotic co-ingestants were excluded.

- Incomplete patient records
- The documented co-ingestion of non-narcotic substances in urine toxicology included seven patients who also tested positive for methamphetamine. These patients were retained in the analysis because opioid ingestion was deemed the primary exposure responsible for their clinical presentation, and the methamphetamine levels were not toxicologically significant.

After obtaining the history from the patient (if conscious after treatment) or relatives regarding the type and route of the consumed opioid, the diagnosis of opioid poisoning was based on clinical presentation, specifically the presence of the opioid toxidrome or a positive clinical response to Naloxone. The decision to obtain BCTS was at the discretion of the treating physician, based on the clinical status of the patient. Urine toxicology was performed to support the diagnosis and document the suspected opioid type, while acknowledging the known limitations of immunoassays (12). We extracted demographics, time from exposure to admission, clinical manifestations, initial ED vital signs (systolic blood pressure, diastolic blood pressure, respiratory rate, heart rate, SpO_2, temperature), first available laboratory values (pH, PCO_2, HCO_3^-, sodium, glucose, calcium, magnesium, BUN, creatinine, potassium, CPK, LDH, hemoglobin, WBC, platelet count), GCS, disposition and in-hospital outcome, and BCTS findings.

BCTS interpretations were based on reports provided by the senior radiology attendant at Namazi Hospital. Any discrepancies were resolved by reviewing the original BCTS.

Abnormal BCTS was defined as any intracranial finding that was either acute (hemorrhage, acute infarct, edema, mass effect, or hypoxic-ischemic encephalopathy pattern) or chronic (microvascular ischemic change, old infarct, atrophy) as reported by radiology. If both types of findings were present, the scan was classified as abnormal BCTS.

Statistical analysis was performed using SPSS version 16.0. Descriptive statistics were reported as frequencies and percentages for categorical variables, and as means with standard deviations (SD) for continuous variables. To compare variables between patients with normal and abnormal BCTS, an independent t-test was used for continuous data. Categorical variables were compared using the Chi-square test or Fisher's exact test (two-sided) when the expected cell count was less than 5. The effect sizes in these bivariate analyses were presented as Odds Ratios (OR) with Confidence Intervals (CI). Statistical significance was defined as a p-value of less than 0.05.

To develop a multivariable predictive model for abnormal BCTS findings, candidate variables were selected based on bivariate statistical significance ($P<0.20$) or prespecified clinical relevance (e.g., vital signs and initial clinical manifestations). Composite variables (such as 'any underlying condition') were excluded to prevent collinearity with specific comorbidities evaluated independently. Variables with missing values (e.g., poisoning-to-admission time) were excluded from the multivariable model to preserve the total sample size (n=208). Multicollinearity was evaluated using the Variance Inflation Factor (VIF), retaining only candidate predictors with VIF < 5. The selected

variables were then entered into a multivariable logistic regression model to identify independent predictors, reporting adjusted odds ratios (aOR) and 95% confidence intervals (CI).

This study was reviewed and approved by the institutional review board of Shiraz University of Medical Sciences and the ethics committee (IR.SUMS.MED.REC.1400.326).

Results

A total of 208 patients comprised the study population, of which 32 (15.4%) were female. Methadone was the most prevalent concomitant substance, documented in 34 cases (16.3%) (Table 1). A small number of patients also tested positive for methamphetamine; however, in all such instances, opium was identified as the primary exposure based on clinical assessment. Given that stimulant co-ingestion could potentially influence neuroimaging findings independently, a sensitivity analysis was performed

Table 1. Demographic, clinical, and laboratory findings of the patients with/without abnormal brain CT scan findings

	All patients (n = 208)	Abnormal brain CT scan (n = 57)	Normal brain CT scan (n = 151)	*P*-value
Age *	54.72 ± 19.29	66.23 ± 16.78	50.37 ± 18.41	<0.001
Sex (male) +	176 (84.6%)	50 (87.7%)	126 (83.4%)	0.44
Poisoning-to-admission time†				0.002
Less than one hour	1 (0.6%)	1 (1.9%)	0	
One to six hours	40 (24.0%)	4 (7.7%)	36 (31.3%)	
More than six hours	126 (75.4%)	47 (90.4%)	79 (68.7%)	
Substance				
Opium	154 (74%)	49 (85.9%)	105 (69.5%)	0.02
Methadone	34 (16.3%)	6 (10.5%)	28 (18.5%)	0.16
Heroin	10 (4.8%)	1 (1.8%)	9 (6.0%)	0.20
Methamphetamine	7 (3.4%)	0	7 (4.6%)	0.09
Tramadol	2 (1%)	1 (1.8%)	1 (0.7%)	0.47
Pethidine	1 (0.5%)	0	1 (0.7%)	0.53
Underlying Condition				
Any	100 (48.1%)	40 (70.2%)	60 (39.7%)	<0.001
Diabetes	20 (9.6%)	5 (8.8%)	15 (9.9%)	0.80
Renal failure	11 (5.2%)	6 (10.5%)	5 (3.3%)	0.03
Hepatic failure	3 (1.4%)	1 (1.8%)	2 (1.3%)	0.81
Heart failure	47 (22.5%)	19 (33.3%)	28 (18.5%)	0.02
Pulmonary diseases	28 (13.4%)	10 (17.5%)	18 (11.9%)	0.28
Diseases of central nervous system	3 (1.4%)	2 (3.5%)	1 (0.7%)	0.12
Epilepsy	6 (2.8%)	2 (3.5%)	4 (2.6%)	0.74
Hypertension	20 (9.6%)	10 (17.5%)	10 (6.6%)	0.01
Blood gasses				
Serum pH	7.32 ± 0.11	7.32 ± 0.11	7.32 ± 0.11	0.91
Serum Bicarbonate (mEq/L)	25.67 ± 6.13	24.13 ± 5.72	26.26 ± 6.21	0.03
Serum CO2 partial pressure (mmHg)	47.24 ± 31.12	44.67 ± 15.59	48.22 ± 35.27	0.48
Laboratory data on admission				
Sodium (mEq/L)	139.31 ± 9.61	139.67 ± 17.10	139.18 ± 4.39	0.78
Blood Sugar (mg/dL)	121.69 ± 56.84	125.14 ± 56.12	120.50 ± 57.38	0.70
Calcium (mg/dL)	9.19 ± 0.76	9.37 ± 0.70	9.13 ± 0.77	0.21
Magnesium (mg/dL)	2.14 ± 0.41	2.04 ± 0.40	2.18 ± 0.41	0.25
Blood Urea Nitrogen (mg/dL)	20.81 ± 15.66	25.95 ± 21.06	18.87 ± 12.65	0.04
Creatinine (mg/dL)	1.38 ± 0.87	1.70 ± 1.13	1.26 ± 0.71	0.01
Potassium (mEq/L)	4.27 ± 0.73	4.48 ± 0.88	4.20 ± 0.66	0.02
Creatine phosphokinase (units/liter)	1116.49 ± 3075.15	1395.28 ± 5015.37	1016.12 ± 2040.76	0.65
Lactate dehydrogenase (units/liter)	531.93 ± 475.60	521.15 ± 585.95	536.00 ± 434.37	0.91
Hemoglobin (gr/dL)	13.46 ± 2.49	13.61 ± 2.94	13.41 ±2.30	0.63
White blood cell (per microliter)	10.04 ± 7.83	9.80 ± 5.63	10.13 ± 8.52	0.81
Platelet (per microliter)	186.98 ± 80.47	188.20 ± 91.23	186.52 ± 76.49	0.90
Glasgow Coma Scale	12 ± 3	11 ± 4	12 ± 3	0.08
Systolic blood pressure (mmHg)	119 ± 22	118 ± 29	120 ± 19	0.63
Diastolic blood pressure (mmHg)	74 ± 15	74 ± 20	74 ± 13	0.97
Respiratory rate (per minute)	18 ± 4	18 ± 4	17 ± 4	0.42
Heart rate (per minute)	90 ± 18	88 ± 19	91 ± 17	0.32
Oxygen saturation (%)	87 ± 14	88 ± 11	87 ± 15	0.45
Body Temperature (Celsius)	36.9 ± 0.6	36.9 ± 0.7	36.9 ± 0.5	0.86
Intubated	34 (16.3%)	15 (26.3%)	19 (12.6%)	0.01
ICU admission	9 (4.3%)	3 (5.3%)	6 (4.0%)	0.68
Outcome				0.001
Expired	18 (8.7%)	11 (19.3%)	7 (4.6%)	
Discharged	190 (91.3%)	46 (80.7%)	144 (95.4%)	

All stated p-values refer to the comparison of patients with normal Vs abnormal brain CT scan. * Data are presented as mean ± standard deviation, + Data are presented as frequency (prevalence%), †Percentages for poisoning-to-admission time were calculated based on available cases (n=167 overall: n=52 in the abnormal BCTS group and n=115 in the normal BCTS group). Data were missing for 41 patients.

Table 2. Multivariate logistic regression analysis of the relevant factors in abnormal BCTS findings in patients with opium overdose

Variable	β	Adjusted Odds Ratio (aOR)	95 % Confidence Interval	*P*-value
Age	0.041	1.041	1.01 – 1.07	0.008
Methadone	1.007	2.736	0.49 – 15.15	0.249
Renal Failure	-0.299	0.741	0.12 – 4.45	0.743
Heart Failure	0.409	1.506	0.50 – 4.52	0.466
Diseases of central nervous system	-2.008	0.134	0.01 – 2.60	0.184
Intubated	-0.707	0.493	0.05 – 4.59	0.534
Glasgow Coma Scale	0.038	1.039	0.83 – 1.30	0.736
Vomiting	-0.933	0.394	0.03 – 4.68	0.460
Apnea	-0.767	0.465	0.05 – 4.15	0.492
High blood pressure on arrival	-0.764	0.063	0.01 – 1.80	0.106
Low blood pressure on arrival	1.883	6.573	0.08 – 556.97	0.406
Bicarbonate	-0.097	0.908	0.83 – 0.99	0.025
Blood Urea Nitrogen	0.005	1.005	0.97 – 1.05	0.818
Creatinine	0.065	1.068	0.50 – 2.27	0.865
Potassium	0.441	1.555	0.69 – 3.51	0.288

aOR = Adjusted Odds Ratio; CI = Confidence Interval. The multivariable regression model was performed on n=208 complete cases.

excluding these cases. The exclusion did not alter the main outcomes of the regression analysis, thereby confirming the robustness of our primary predictors. Overall, 151 patients (72.6%) exhibited normal BCTS results, while 57 (27.4%) had at least one abnormal finding. When considering all patients as the denominator, the most frequent abnormalities included microvascular ischemic changes in 36 patients (17.3%) and acute ischemic infarction in 13 (6.3%). Hydrocephalus was observed in 3 patients (1.4%), subarachnoid hemorrhage and vasogenic edema each in two patients (1.0%), and each of the following was noted in one patient (0.5%): intracerebral hemorrhage, calcified meningioma, isolated cerebral edema, and posterior reversible encephalopathy syndrome.

Patients with abnormal BCTS were older (66.23 ± 16.78 vs 50.37 ± 18.41 years, *P*<0.001) and were more likely to present >6 h after exposure (90.4% vs 68.7%, *P*=0.002). Intubation occurred more frequently among those with abnormal BCTS (26.3% vs 12.6%, *P*=0.01) (Table 1). Among patients with available times (n=167), admission >6 h after exposure was more frequent in the abnormal BCTS group (90.4% vs 68.7% overall; χ^2 *P*=0.002). In a binary contrast, >6 h was associated with higher odds of abnormal BCTS (OR 4.28; 95% CI 1.57–11.68; *P*=0.003).

Univariate analyses demonstrated a higher OR of abnormal BCTS for hypertension (OR 3.00; 95% CI 1.18–7.65; *P*=0.031), heart failure (OR 2.20; 95% CI 1.11–4.37; *P*=0.027), and intubation (OR 2.48; 95% CI 1.16–5.31; *P*=0.021), as well as for 'any underlying condition' (OR 3.57; 95% CI 1.85–6.87; *P*<0.001). Furthermore, abnormal BCTS was associated with increased mortality (19.3% vs 4.6%; OR 4.92; 95% CI 1.80–13.43; *P*=0.0018).

Drowsiness was the most common presenting manifestation, occurring in 196 cases (94.2%). Dyspnea was reported in 51 cases (24.5%), seizures in 15 cases (7.2%), apnea in 13 cases (6.3%), and vomiting in 9 cases (4.3%). There was no statistically significant association between presenting manifestations and abnormal BCTS. For vomiting, the proportion of patients with abnormal BCTS was 55.6% compared to 26.1% in those without vomiting (Fisher exact *P*=0.066; OR 3.53; 95% CI 0.91–13.66), although this estimate was imprecise.

The presence of any underlying medical condition was significantly associated with abnormal BCTS findings (*P*<0.001). Renal failure (10.5% vs 3.3%, *P*=0.03), heart failure (33.3% vs 18.5%, *P*=0.02), and hypertension (17.5% vs 6.6%, *P*=0.01) were each individually linked to abnormal BCTS (Table 1). Furthermore, in-hospital mortality was higher in the abnormal BCTS group (19.3% vs 4.6%, *P*=0.001).

Abnormal BCTS was associated with lower serum bicarbonate (24.13 ± 5.72 vs 26.26 ± 6.21 mEq/L, *P*=0.03) and higher levels of BUN (25.95 ± 21.06 vs 18.87 ± 12.65 mg/dL, *P*=0.04), creatinine (1.70 ± 1.13 vs 1.26 ± 0.71 mg/dL, *P*=0.01), and potassium (4.48 ± 0.88 vs 4.20 ± 0.66 mEq/L, *P*=0.02). A multivariate logistic regression analysis identified two independent variables with *P*-values<0.05. The first was age (β 0.041; OR 1.041 per year; 95% CI 1.01–1.07; *P*=0.008) and the second was serum bicarbonate (β −0.097; OR 0.908 per mEq/L; 95% CI 0.83–0.99; *P*=0.025) (Table 2). For interpretability, this corresponds approximately to a 1.5-fold increase in odds per 10 years of age and a 38% decrease in odds per 5 mEq/L higher bicarbonate.

For interpretability, each 1-year increase in age was associated with a 4.1% increase in the odds of an abnormal BCTS (aOR 1.041 per year; 95% CI 1.01–1.07; *P*=0.008), which translates to an approximately 1.5-fold increase in odds per 10-year increase in age (aOR 1.49 per 10 years). Similarly, serum bicarbonate was inversely associated with abnormal BCTS (aOR 0.908 per mEq/L; 95% CI 0.83–0.99; *P*=0.025), corresponding to an approximate 38% decrease in odds per 5 mEq/L increase (aOR 0.62 per 5 mEq/L).

Discussion

This cross-sectional study evaluated the factors associated with abnormal BCTS findings in patients with opium poisoning. Patients exhibiting abnormal BCTS results were intubated more frequently and demonstrated lower in-hospital survival rates. In the multivariable analysis, only age and serum bicarbonate levels independently predicted abnormal BCTS findings.

Prevalence of poisoning

There is a higher prevalence of opium poisoning compared to other narcotic substances in Iran (12). In our study,

poisoning cases were primarily attributed to opium, with smaller proportions involving other opioids such as methadone, heroin, tramadol, or pethidine, reflecting the regional epidemiology in which opium remains the predominant agent of poisoning. A study conducted in eastern Iran between 2010 and 2017 indicated that all acute poisoning manifestations were predominantly comprised of opioids (26.2%), followed by pesticides (13.9%) (13). Additionally, another study in Tehran corroborated the relatively high rate of opioid poisoning in this region (57.1%) (14). Although opium and opioid use are less prevalent in Western countries compared to Iran, their increasing rates may pose significant concerns in the near future (4, 15).

Abnormal BCTS findings

In the present study, abnormal BCTS findings were observed in 27.4% of cases. Variations in the types of substances involved, BCTS indications, characteristics of the study population, radiologists' expertise, and the volume of imaging requests may account for differences in abnormal BCTS findings. Jamshidi et al. reported a 19.7% prevalence of abnormal findings in BCTS, noting generalized cerebral edema as the most common finding, followed by infarction/ischemia (16). Taheri et al. studied 229 unconscious patients and reported that, among 92 (40.2%) with isolated opium poisoning, 14 cases (15.2%) exhibited abnormal BCTS. In contrast to the prior study, abnormal findings included infarction (7.6%), cerebral edema (3.3%), and hemorrhage (2.2%) (17).

There are three major categories of abnormal findings in BCTS for cases involving opioid poisoning. The first category includes ischemic changes (18), which may result from the activation of μ-opioid receptors leading to reversible vasospasm, potentially causing ischemia or infarction (5). Additionally, the concurrent dose-dependent respiratory suppression caused by opioids distorts blood oxygenation and consequently precipitates ischemia (19). Ischemia/infarction is typically the most commonly reported abnormal finding in BCTS across all cases of poisoning. Taghadosi et al. studied 1,571 patients admitted to the toxicology ICU, of whom 56 were included in their analysis due to having at least one focal neurological complication at early admission or during the course of hospitalization, or significant abnormal findings on BCTS. Hypoxia was identified as the most common cause of neurological sequelae identified on BCTS in the studied patients (n=36, 64.3%). Among these BCTS, ischemic infarction was observed in 29 cases (51.8%), followed by cerebral edema in 15 cases (26.8%) (14). According to most studies, cerebral edema was the second most frequent finding in BCTS (16, 20). However, we identified chronic ischemic change as the most common finding (17.3%), followed by ischemic infarcts (6.3%). It is crucial to differentiate between acute pathological changes directly resulting from the current poisoning episode and chronic, potentially incidental findings. In our cohort, acute ischemic infarctions (6.3%) and cerebral edema represent true acute complications likely triggered by opioid-induced hypoxia and vasospasm. Conversely, microvascular ischemic changes (17.3%) are chronic in nature. While these changes are strongly correlated with normal aging, it is also well-documented that chronic opioid use can accelerate such microvascular changes and leukoencephalopathy. Thus, while not an acute complication of the single poisoning event, these chronic findings reflect a diminished neurological reserve in older opioid users, rendering them more vulnerable to severe acute outcomes.

Activation of calcium and sodium ion channels during opioid poisoning creates an osmotic gradient, resulting in the influx of water into the cells. Hypoxia impairs Na^+/K^+-ATPase function, leading to intracellular accumulation of sodium and water, which causes cellular swelling (cytotoxic edema). This process is accompanied by inflammatory responses that disrupt the blood-brain barrier and ultimately elevate intracranial pressure.

Hemorrhage has generally been reported to occur at lower rates compared to ischemic/infarction changes and cerebral edema (14, 17, 20). Incidental findings included hydrocephalus, calcified meningioma, and posterior reversible encephalopathy syndrome, all of which are unlikely to represent acute effects of opium poisoning.

Correlated factors

Through multivariate logistic regression analysis, we found that advanced age and lower serum bicarbonate levels are independently associated with an increased likelihood of abnormal findings in BCTS. Therefore, these factors should be considered in the diagnostic approach and management of such patients. Jamshidi et al. did not find this association statistically significant (age P=0.772, serum bicarbonate P=0.599) (16).

When to perform CT

Numerous studies suggest that BCTS has a low diagnostic yield in poisoned patients and similarly offers limited value for decision-making in management (10, 11, 21, 22). Furthermore, increased utilization of this modality may result in prolonged ED stays, higher costs, unnecessary radiation exposure, crowding, and potential adverse outcomes (22, 23). Consequently, it is crucial to determine whether BCTS is indicated in specific cases. To evaluate the effectiveness of performing BCTS, Tay et al. conducted a retrospective study on alcohol and drug overdose presentations. They measured the percentage of patients who underwent BCTS and whose management was altered as a result. Through this study, they developed a decision support tool named "HEAD," which comprises four groups of indications for performing BCTS. Their analysis revealed that age and a history of head injury were significantly associated with abnormal findings in BCTS (24). Our study also demonstrated a significant association between advanced age and an increased likelihood of abnormal BCTS findings. However, the proportion of cases involving alcohol poisoning in their cohort was substantially larger than in ours. It is important to emphasize that, because only patients who underwent BCTS were included in our analysis, the prevalence of observed abnormalities cannot be generalized to all opioid poisonings. Additionally, the HEAD tool relies solely on clinical characteristics derived from

history and physical examination; thus, serum bicarbonate levels are not incorporated.

We recommend that laboratory results, particularly serum bicarbonate levels, be incorporated as predictive factors in future studies, given the frequent occurrence of laboratory work-ups or blood gas analyses conducted prior to the decision to perform BCTS.

A reduced level of consciousness alone may not justify the performance of a BCTS; it is essential to consider the specific substance involved in the overdose when deciding to conduct a BCTS. For instance, Frenchi et al. (10) included 114 patients with drug overdoses and reduced GCS, of whom 55% underwent BCTS. Only four patients (6%) of the BCTS results were abnormal, two of which were due to trauma. This rate is significantly lower than that observed in our study, where approximately one fourth (27.4%) of the study population exhibited abnormal findings. The substances in Franchi's study included alcohol, amitriptyline, diazepam, paracetamol, tramadol, zopiclone, and several other substances. In comparison to our population, narcotics or opioids were much less frequent. The pathogenesis of these substances may account for the marked difference in abnormal findings from BCTS.

The role of BCTS in opioid poisoning remains a subject of debate, as many abnormalities may reflect chronic or incidental findings. However, our results indicate that older age and lower serum bicarbonate levels are associated with a higher likelihood of abnormal scans. In clinical practice, particularly in resource-limited settings, these readily available factors may assist in prioritizing which patients should undergo emergent BCTS.

Limitations

This study has several limitations. First, substance identification relied on patient history, and confirmatory toxicology was not available, which raises the risk of misclassification. Second, as a single-center retrospective study, the generalizability of the findings is limited, and selection bias may be present since only patients who underwent BCTS were included. Consequently, the reported prevalence of abnormalities reflects this selected subgroup and cannot be generalized to all cases of opioid poisoning. Third, without prior baseline neuroimaging, it was not always possible to definitively distinguish chronic, pre-existing age-related changes (such as microvascular ischemia or atrophy) from changes explicitly induced by chronic opioid abuse. Similarly, incidental findings such as meningioma or hydrocephalus do not represent acute effects of poisoning. Our definition of 'abnormal BCTS' pragmatically encompassed both acute and chronic findings as encountered in real-world emergency settings, which may overestimate the rate of strictly acute toxicological complications. Fourth, the presence of stimulant co-ingestion (methamphetamine in 7 cases) may have contributed to abnormal imaging findings. Although our sensitivity analysis indicated that this did not alter the main findings, we acknowledge that amphetamines can independently affect cerebrovascular imaging. This limitation should be considered when interpreting the generalizability of our results. Fifth, while we successfully adjusted for recorded underlying comorbidities (such as heart failure and hypertension) and clinical indicators like GCS, the retrospective design inherently limits our ability to evaluate the precise duration or severity of these pre-existing conditions, which might still act as residual confounders. Additionally, our study focused on identifying individual associated factors rather than developing a formal clinical prediction tool; thus, overall model performance metrics such as the AUC were not evaluated, which should be addressed in future prospective studies aimed at building scoring systems. Finally, scans were interpreted in routine care rather than by blinded reviewers, and we did not assess how findings influenced management.

It should also be noted that, certain continuous laboratory parameters with right-skewed distributions (such as creatine phosphokinase and lactate dehydrogenase) were presented as mean ± standard deviation for uniform table formatting. Although non-parametric reporting (median with interquartile range) is methodologically preferred for skewed data, both CPK and LDH showed non-significant p-values in bivariate comparisons (P=0.65 and P=0.91, respectively) and were not selected as candidate predictors for the multivariable model, ensuring this had no bearing on the primary predictive conclusion.

Conclusion

In conclusion, abnormal brain CT findings were relatively common among patients with acute opioid poisoning who underwent neuroimaging in the emergency setting. Although several clinical and laboratory variables were associated with abnormal CT findings in the initial analyses, only advanced age and lower serum bicarbonate levels remained independent predictors after multivariable adjustment. The most frequent abnormalities observed were microvascular ischemic changes and acute ischemic infarction. These findings suggest that brain CT may be more appropriately prioritized for opioid-poisoned patients who are older or present with evidence of metabolic acidosis. A more selective imaging approach based on these predictors may improve clinical decision-making and optimize the use of emergency imaging resources. Further prospective multicenter studies are needed to validate these findings and clarify the impact of CT abnormalities on patient management and outcomes.

Acknowledgment

The authors would like to thank the Amir Oncology Hospital Clinical Research Development Center (ACRDC) for their scientific guidance and support throughout the study.

Conflict of Interests

The authors declare that they have no competing interests.

Authors' Contributions

RS and AA conceived and designed the study, developed the research framework, and drafted the initial version of the manuscript. AN and MF were responsible for data curation, statistical analysis, and interpretation of the results. All other authors contributed to patient recruitment, data collection, and the clinical management of participants

under the supervision of RS.

Ethical Considerations

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1400.326). This retrospective study used anonymized patient data; therefore, the requirement for informed consent was waived by the ethics committee.

Funding Support

This research received no external funding.

Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

AI Use Statement

The authors did not use artificial intelligence or AI-assisted technologies in the preparation of this manuscript.

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