INTRODUCTION

Plant and mushroom poisoning is a less investigated area of clinical toxicology. Many plant species are capable of producing toxicity; however, relatively few cases cause severe intoxication. Solanaceae is among the herbal families that contain the highest number of poisonous plant species. Datura is a genus of about nine species of poisonous flowering plants in this family. Datura stramonium (also known as jimsonweed or thorn apple), the most common species within the Datura family, is a weed that may be found along roadsides or meadows. Traditionally, Datura leaves are rolled into cigarettes or smoked in a pipe for narcotic effects or asthma relieving properties. Usually, low doses of alkaloids are absorbed by smoking Datura species; otherwise, it is considered extremely dangerous. Intentional abuse for hallucinogenic and stimulating effects is also reported by eating seeds, drinking tea, or smoking cigarettes.

Poisonous Datura compounds include tropane alkaloids: hyoscine, atropine (D, L-hyoscyamine), and scopolamine (L-hyoscine). The toxicity mechanism is due to the competitive blockade of acetylcholine at peripheral and central muscarinic receptors. Poisoning symptoms include mydriasis, cycloplegia, dry skin, dry mouth, urinary retention, tachycardia, delirium, and respiratory arrest. Symptoms usually begin within 30 to 60 min of consuming the plants. Effects can last from 24 to 48 h but have been reported to persist for up to 2 weeks. Toxicity management depends on the severity of the symptoms and includes monitoring, supportive care, decontamination, agitation and seizure control, and antidote administration.
Here, we present a case series of *Datura* intoxication in a family after consuming refreshing herbal tea at a family gathering.

## 2 | CASE PRESENTATION

In June 2020, six members of a family were admitted to the poisoning ward of a teaching hospital affiliated with Tehran University of Medical Sciences in Tehran, Iran. About an hour before admission to the hospital, six members of this family developed symptoms of hallucinations, agitation, and disinhibited behavior (playing with imaginary objects, trying to pick imaginary things off the carpets, trying to throw things out of the closed window). Two of the family members were out for work, and the mother did not take the herbal tea due to illness and concern about drug–herb interactions. These members of the family were asymptomatic and had called the emergency services.

They denied the use of any hallucinogenic substances or recreational drug use. They stated consumption of a decoction that was prepared at home after buying a herbal product from an apothecary (a shop selling medicinal plants). They did not know the name of the product. The seller of this herb had suggested this as an invigorating and refreshing product. The leaves that they brought to the hospital were identified as *Datura*. Four commonly occurring *Datura* species include *D. stramonium*, *D. metel*, *D. innoxia*, and *D. ferox*, of which *D. stramonium* is predominant in Iran. It is not easy to determine the exact species, as they brought product was crushed leaves and stems. So, it has been reported as *D. spp*.

Based on history and physical examination, anticholinergic poisoning was suspected. Acute hypoglycemia, neuroleptic malignant syndrome, hallucinogen toxicity, serotonin syndrome, meningitis, sepsis, and lithium toxicity are among the possible differential diagnosis of the present cases. All were ruled out by appropriate laboratory tests (blood sugar, urine screen, and blood culture tests) and complete medication history.

The clinical information of each case and the treatment measures taken for them are discussed here. Laboratory data at the admission of all patients are summarized in Table 1. A summary of the patients’ signs and symptoms and the management are presented in Table 2.

### 2.1 | Case 1

A 67-year-old male, with no significant medical and drug history, presented with severe agitation that required restraints. On physical examination, symptoms of anticholinergic toxicity were evident. The level of consciousness was slightly depressed. Because of his elevated creatine phosphokinase (CPK) and lactate dehydrogenase (LDH), there were some concerns about rhabdomyolysis. Myoglobinuria or any indicative symptoms or signs of rhabdomyolysis were not detected. Intravenous fluids and midazolam (0.2 mg/kg) were administered for him. A gradual improvement in his symptoms was observed. He was fully recovered and discharged home after 2 days of hospitalization. His elevated LDH and CPK returned to normal at the time of discharge.

### 2.2 | Case 2

A 32-year-old female presented with agitation, hallucination, and nausea. She had been diagnosed with depression, but she did not receive any medication for it. On physical examination, her pupils were widely dilated, and her mucous membranes were dry. Supportive treatment, including hydration, ondansetron, and midazolam (0.2 mg/kg), was administered. She received four doses of midazolam, but her agitation did not resolve. She was sedated with intravenous diazepam (5 mg). She was fully recovered and discharged home after 1 day.

### 2.3 | Case 3

A 38-year-old female presented with agitation, restlessness, and nausea. She had been diagnosed with depression and treated with various antidepressants, which ameliorated but did not cure her condition. On physical examination, her pupils were widely dilated. Arterial blood gas analysis revealed respiratory acidosis. An oxygen mask was applied (4 L/min), and midazolam was administered. Supportive treatment, including hydration and midazolam (0.2 mg/kg), also was administered. She received four doses of midazolam, which did not control her agitation. She was sedated with intravenous diazepam (5 mg). She was fully recovered and discharged home after 1.5 days.

### 2.4 | Case 4

A 22-year-old female presented with severe agitation, hallucination, and drowsiness. She had been diagnosed with bipolar mood disorder that was controlled with antipsychotics. Her agitation was controlled with intravenous midazolam and haloperidol. She was fully recovered and discharged home after 1.5 days.

### 2.5 | Case 5

A 15-year-old male presented with severe agitation, dizziness, and hallucination. His previous medical and drug
history was insignificant. The patient’s mucus and skin were hot and dry. The abdominal sounds were decreased. Arterial blood gas analysis revealed respiratory acidosis. Intravenous hydration was started for him. Midazolam was administered at the maximum allowable dose. He was in the intensive care unit for 2 days, and after another day of observation in the general ward, he was fully recovered and discharged.

2.6 | Case 6

A 50-year-old male with no known comorbidities presented with restlessness, dizziness, and drowsiness. Intravenous hydration was administered. He was fully recovered and discharged home after 9 h of observation.

3 | DISCUSSION, AND REVIEW OF THE LITERATURE

Various compounds have anticholinergic effects, including prescription drugs, over-the-counter medications, illicit street drugs, and plants. Among these, plants that cause anticholinergic toxicity are less investigated.6 Poisonous plant exposures have increased in recent years and caused health concerns. There are case reports of

| Table 1 | Laboratory data of each patient at admission |
|---------|---------------------------------------------|
| Test (unit) | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | Reference range |
| SBP/DBP | 165/95 | 140/90 | 130/85 | 140/90 | 130/95 | 140/80 | 90–130/65–85 |
| PR (beats/min) | 132 | 135 | 130 | 142 | 134 | 114 | 60–100 |
| RR (breaths/min) | 18 | 16 | 19 | 16 | 18 | 16 | 12–16 |
| Temperature (°C) | 38 | 37.3 | 37.1 | 37.3 | 38.5 | 37.8 | 36.1–37.2 |
| BS (mg/dl) | 124 | 102 | 93 | 105 | 121 | 115 | 80–200 |
| WBC (10^3/μl) | 4.5 | 8.5 | 8.7 | 8.6 | 10.4 | 7.4 | 4.5–11 |
| Hemoglobin (g/dl) | 16.3 | 13.5 | 14 | 12.8 | 12.9 | 16.3 | 12–15 (F) 14–17 (M) |
| Platelet (10^3/μl) | 169 | 213 | 279 | 247 | 216 | 220 | 150–450 |
| AST (U/L) | 46 | 25 | 16 | 23 | 24 | NA | 10–40 |
| ALT (U/L) | 39 | 25 | 12 | 15 | 15 | NA | 7–56 |
| ALP (U/L) | 140 | 124 | 154 | 139 | NA | NA | 45–145 |
| Urea (mg/dl) | 34 | 33 | 31 | 24 | 21 | 37 | 15–40 |
| Creatinine (mg/dl) | 0.9 | 0.9 | 1 | 0.8 | 0.8 | 0.9 | 0.5–1.4 |
| Sodium (mEq/L) | 137 | 140 | 141 | 161 | 136 | 145 | 135–145 |
| Potassium (mEq/L) | 4.1 | 4.2 | 4.2 | 4 | 3.9 | 4.2 | 3.5–5.5 |
| CPK | 313 | 119 | 95 | 158 | 95 | 177 | 39–300 (M) 26–195 (F) |
| LDH (U/L) | 650 | 417 | 356 | 324 | 436 | 531 | <480 |
| INR | 0.95 | 0.94 | 0.89 | 1.02 | 1.13 | 0.85 | 0.8–1.2 |
| O₂ saturation (%) | 96 | 98 | 93 | 98 | 92 | 97 | 94–100 |
| pH | 7.43 | 7.39 | 7.32 | 7.34 | 7.33 | 7.39 | 7.35–7.45 |
| PaCO₂ | 43 | 39 | 50 | 42 | 60 | 27 | 35–45 |
| HCO₃⁻ | 25 | 24 | 27 | 22 | 31 | 21 | 22–28 |
| Urine screen test for amphetamines, methamphetamine, benzodiazepines, barbiturates, marijuana, PCP, methadone, opioids | Neg. | Neg. | Neg. | Neg. | Neg. | Neg. | - |
| Blood culture | Neg. | Neg. | Neg. | Neg. | Neg. | Neg. | - |
| Pregnancy test | - | Neg. | Neg. | Neg. | - | - | - |

Abbreviations: ALT = alanine aminotransferase; ALP = alkaline phosphatase; AST = aspartate aminotransferase; BS = blood sugar; CPK = creatine phosphokinase; DBP = diastolic blood pressure; INR = international normalized ratio; LDH = lactate dehydrogenase; PR = pulse rate; PTT = partial thromboplastin time; RR = respiratory rate; SBP = systolic blood pressure; WBC = white blood cell.
| NO. | Year, country | Plant species | Amount symptom onset | Symptoms | Management | LOS | Outcome |
|-----|---------------|---------------|----------------------|----------|------------|-----|---------|
| 1-6 | 2020, Iran (current cases) 67, M | *Datura spp.* | The whole family brewed about 4 tablespoons and each person consumed about a glass of decoction. 5 min | Severe agitation, hallucination, tachycardia, hyperthermia, flushing, mucous and skin dryness, dilated pupils | Hydration, BZD | 2 days | Fully recovered |
| 32, F | 2020, France | *Datura stramonium* | Unintentionally drank herbal tea that was prepared for refreshing effects. | Agitation, hallucination, nausea, tachycardia, hyperthermia, mucous and skin dryness, dilated pupils | Hydration, ondansetron, BZD | 1 day | Fully recovered |
| 38, F | 2020, France | *Datura stramonium* | Eating a meal (spinach inadvertently mixed with *Datura*) | Agitation, restlessness, nausea, tachycardia, mucous and skin dryness, dilated pupils | Oxygen, Hydration, BZD | 1.5 days | Fully recovered |
| 22, F | 2020, Iran | *Datura stramonium* | Unintentional, mistook them for edible opium poppy seeds (*Papaver somniferum*) | Agitation, hallucination, dizziness, tachycardia | Hydration, BZD, haloperidol | 1.5 days | Fully recovered |
| 15, M | 2020, Armenia | *Datura wrightii* | Inadvertently ingested some kind of plant | Severe agitation, dizziness, hallucination, tachycardia | Hydration, BZD | 3 days | Fully recovered |
| 50, M | 2020, Iran | *Datura stramonium* | *Datura stramonium* | Restlessness, dizziness, drowsiness, tachycardia | Observation | 9 h | Fully recovered |
| 7-13 | 2020, France | 1 adult and two children | NR | Mild neurological signs (moderate agitation, headache, and mydriasis) | Observation | Rapid discharge | None |
| F, 41 M, 3 M, 11 | 2020, France | 1 adult and two children | NR | Severe restlessness, balance disturbances, hallucinations, mydriasis, tachycardia | Observation | Several hours | Recovered |
| 14 | 2020, Iran | *Datura stramonium* | Ingested 1 teaspoon of seeds, vomited a substantial amount | Agitation, headache, nausea, ataxia, visual hallucinations | Sedative (diazepam and haloperidol), rehydration, cardiac monitoring | NR | Recovered |
| 15 | 2020, Armenia | *Datura wrightii* | Inadvertently ingested some kind of plant | NR | Visual hallucination and irritability, ataxia, inappropriate behavior | Intramuscular prozerin, symptomatic treatment | 3 days | Fully recovered |
| NO. | Year, country | Plant species | Amount | Symptoms | Management | LOS | Outcome |
|-----|--------------|---------------|--------|----------|------------|-----|---------|
| 16  | 2019, India  | *Datura stramonium* | • 50–70 seeds | Drowsiness, slurred speech, hyperpyrexia, hypertension, tachycardia, pupillary dilatation, impaired concentration | Maintaining hydration, propranolol, paracetamol, diazepam | 1 week | Relatively recovered with anisocoria, loss of eyesight, and cataract |
| 17  | 2019, Italy  | *Datura stramonium* | • NR | Acute dysarthria, dysphagia, impaired consciousness | r-TPA because of stroke suspicious | 3 days | Recovered |
| 18  | 2019, Turkey | *Datura stramonium* | • NR | Incoherent talks, visual hallucination, irrational behavior, dry mouth, bilateral dilated pupils, agitation, sinus tachycardia | Gastric decontamination (nasogastric lavage and activated charcoal) I.V fluid, midazolam, physostigmine | 2 days | Fully recovered |
| 19–35 | 2018, Hungary | *Datura stramonium* | • 30 min | 11 patients: Pronounced hallucinations, agitation, tachycardia, mydriasis, and dry, warm skin Seven patients: dry mouth, dizziness, blurred vision | Sedatives, physostigmine, parenteral fluid, and supportive therapy | 1 day | Completely recovered |
| 36–37 | 2018, Malaysia | *Datura stramonium* | • Five to six well-cooked fruits | Restlessness and abnormal behavior, flushing, dilated pupils, sinus tachycardia | Activated charcoal, midazolam | 24 h | Completely recovered |
| 38  | 2018, Australia | *Datura innoxia* | • NR | Delirium, visual hallucinations, disinhibited behavior, tachycardia, dilated pupils, blurred vision | Observation | 24 h | |
| NO. | Age (years), sex | Plant species | Amount | Symptoms | Management | LOS | Outcome |
|-----|-----------------|---------------|--------|---------|------------|-----|---------|
| 39–40 | 2018, Algeria | *Datura stramonium* | NR | Agitation, impaired balance, tachycardia, bilateral mydriasis | Gastric lavage | 26 h | Fully recovered |
| 4, M |  | Unintentional, swallowing seeds from a plant that he picked near his home | NR | Restlessness, agitation, tachycardia, bilateral mydriasis, tachypnea, erythema in the chest and upper limbs | BZD | 3 days | |
| 41–42 | 2017, Turkey | *Datura innoxia* | NR | Excitation, delirium, impaired general condition, tachycardia, bilateral mydriasis | Gastric lavage, activated charcoal. Intravenous fluids and midazolam | 3 days | Unresolved mydriasis (fully recovered after 7 days) |
|  | 41, M | Drunk a beverage containing *Datura* for asthma | 2 h | | | | |
| 21, F | *Datura innoxia* | Eaten contaminated food | NR | Vomiting, disorientation, hallucinations, impaired general condition, tachycardia, bilateral mydriasis | Gastric lavage, activated charcoal. Intravenous fluids and diazepam | 3 days | Unresolved mydriasis (fully recovered after 5 days) |
| 43–44 | 2017, Turkey | *Datura stramonium* | NR | Agitation, exhaustion, nausea, dryness in the mouth, tachycardia, urinary retention | I.V fluid, proton pump inhibitor | 2 days | Fully recovered |
| 67, M | Unintentional, used for relieving urinary symptoms | NR | | | | | |

Abbreviations: BZD = benzodiazepine, F = female, I.V = intravenous, LOS = length of hospital stay, M = male, NR = not reported.

Case reports published in French and English between 2017 and March 2021 are summarized.
intentional and unintentional poisonings following the use of jimsonweed and other related species. Toxic plants are better perceived by the rural residents, whereas urban inhabitants have had fewer opportunities to explore nature and identify plants. Thus, the risk of poisoning is generally higher among uninformed urban users. Kerchner and Farkas studied Datura poisoning cases from 2005 to 2017. We searched Embase and PubMed in English and French to find relevant cases that had been reported from 2017 to 2021. A total of 38 cases were identified. Table 2 summarizes their data, along with our six reported cases (shown in the first gray row). Among these total 44 cases, eight patients were female, 18 were male, and gender information of the other 18 cases was not available. A 3-year-old boy and a 67-year-old male were the youngest and oldest cases, respectively.

Common causes of toxicity include food confusion, accidental ingestion (usually by children), and overdoses when used as a traditional remedy. It is also used for recreational purposes for its hallucinogenic properties. Its low cost and easy access are the factors for an increase in consumption as a psychoactive substance. Lastly, in some countries in South East Asia and South America, Datura is used for criminal purposes, as chemical submission, to steal or abuse tourists. e reported a novel cause of toxicity.

Regarding our cases, poisoning occurred following the preparation of aerial parts of the plant, including crushed and dried leaves and stems. This family had prepared a product obtained from an apothecary to have a refreshing drink. It is an example of unintentional poisoning that emphasizes careful monitoring of the sale of herbal products. While it is commonly believed that herbal products are safer than prescribed drugs, it is worrying that the specific effects and harmful interactions are not well understood. We recommend that all herbal products should be labeled with plant information and its effects. For this purpose, the supervision of the relevant legislative authorities is necessary.

Three members of this family have a history of psychiatric problems without proper treatment. Severe agitation of some members of this family may have been due to their underlying problem, as the severity of these symptoms did not match other signs. Physicians and the general public should be more aware of the dangers of using herbal products without the advice of a complementary medicine specialist.

The extent of toxicity varies depending on the season, stage of maturation and hydration, and the plant part. Although seeds and stems are the most toxic plant part of Datura, the leaves also have significant toxicity. The onset of poisoning symptoms was from 5 min to 3 h. This family drank herbal tea brewed from aerial parts of Datura, and poisoning symptoms appeared after about 5 min of consumption. Consumption of herbal products in decoction form may cause rapid release and absorption of alkaloids.

The most dominant symptoms of Datura poisoning are because of the anticholinergic effects and blockade of peripheral muscarinic receptors that innervate various organs. The anticholinergic toxicity could be peripheral, central, or both. The peripheral toxicity is less concerning. Mydriasis, dry skin and mucosa, tachycardia, and fever and flushing (because of vasodilation) are considered as the peripheral toxic manifestations. Central involvement, alone or in combination with peripheral signs, is considered more severe. Most of the reported cases presented both toxicities. Specific manifestations of CNS anticholinergic toxicity in these cases include anxiety, agitation, dysarthria, confusion, disorientation, visual hallucinations, bizarre behavior, impaired balance, and delirium. None of these patients experienced seizures or coma (Table 2).

There were no specific changes in laboratory values in most cases. Thus, proper history taking was the most crucial step for appropriate diagnosis. The botanical toxicology training of health care staff is often limited, so making a proper diagnosis and appropriate treatment can be complicated.

Most patients can be managed with supportive treatment and monitoring for a few days (Table 2). Cases of rhabdomyolysis, liver dysfunction, seizure, coma, and death are also reported. Most of the cases described in the literature had a good prognosis after supportive treatment (Table 2). Our cases were managed with benzodiazepines and supportive care, and none of them received physostigmine. The administration of physostigmine, as an antidote is controversial and is limited to severe cases; its side effects including, cardiac, cholinergic effects, hypersensitivity, and seizures must be considered.

4 CONCLUSION

Many people consume herbal medicines and preparations for their presumed therapeutic or other health benefits. People often think that herbs are harmless, but consuming some of these herbs can be life-threatening. Here, we reported cases of family poisoning caused by the preparation of the herbal tea with refreshing effects. It is necessary to inform society about the rational use of herbal products. We recommend that all herbal products should be labeled with plant information and its presumed effects.

AUTHOR CONTRIBUTIONS

Study conception and design: Kheirrollah Gholami, Niloofar Khoshnam-Rad. Patients’ data collection: Marzieh Heydari, Zahra Sahraei. Literature review: Niloofar Khoshnam-Rad. Analysis and interpretation of results: Niloofar Khoshnam-Rad, Mojgan Mashayekhi. Draft manuscript preparation: Niloofar Khoshnam-Rad, Marzieh Heydari, Kheirrollah Gholami, Keyhan
Mohammadi. Revising the manuscript: Kheirollah Gholami, Keyhan Mohammadi, Niloofar Khosham-Rad. All authors reviewed the results and approved the final version of the manuscript.

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CONSENT
Written informed consent was obtained from the family for the publication of any potentially identifiable images or data contained in this article.

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