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TOXICOLOGY INVESTIGATION

# Acute Poisoning During Pregnancy: Observations from the Toxicology Investigators Consortium

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**Abstract** Acute poisonings during pregnancy pose a particular challenge to health care providers because of the potential for an immediate life threat or possible life-long implications for both the mother and fetus, including teratogenicity of the poison or its antidote. We describe recent consequential exposures among pregnant women in the USA. We identified all poisoning cases involving pregnant women that were catalogued by the medical toxicology services across the 37 sites of the Toxicology Investigators Consortium (ToxIC) Registry of the American College of Medical Toxicology between January 2010 and December 2012. Of 17,529 exposure cases reported in the ToxIC Registry, 103 (0.6 %) involved pregnant women, 80 % of whom were symptomatic and about a quarter displayed a specific toxidrome. The majority of cases (*n*=53; 51.5 %) involved intentional exposures, most commonly to pharmaceutical agents, followed by unintentional pharmaceutical exposures (10 %) and withdrawal syndromes (9 %). Non-opioid analgesics were the most common class of agents encountered (31 %), followed by sedative-hypnotics/muscle relaxants (18 %), opioids (17 %), anti-convulsants (10 %), and anti-depressants (10 %). Over a third of cases involved exposure to multiple substances, and 32 % involved exposure to more than one drug class. The most commonly administered antidotes were *N*-acetylcysteine (23 %), sodium bicarbonate (10 %), flumazenil (4 %), and physostigmine (4 %). About half of acute poisoning cases among pregnant women presenting for emergency care involved intentional exposures, mostly with over-the-counter analgesics and psychoactive medications. Clinicians should be cognizant of the unique circumstances, maternal and fetal risks, and management principles of the acutely poisoned pregnant woman.

**Keywords** Poisoning · Pregnancy · Emergency medicine · Registry

Drs. Brent and Finkelstein have made an equal contribution and are, therefore, co-senior authors.

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**Abbreviations**

| | |
|---|---|
| ADE | Adverse drug event |
| ADR | Adverse drug reaction |
| AAPCC | American Association of Poison Control Centers |
| ACMT | American College of Medical Toxicology |
| ASA | Acetylsalicylic acid |
| AST | Aspartate aminotransferase |
| CNS | Central nervous system |
| CroFab | Crotalidae Polyvalent Immune Fab |
| ED | Emergency department |
| HBO | Hyperbaric oxygen |
| NAC | *N*-acetylcysteine |

| | |
|---|---|
| NPDS | National Poison Data System |
| NSAID | Non-steroidal anti-inflammatory drugs |
| ToxIC | Toxicology Investigators Consortium |
| TCA | Tricyclic anti-depressants |

## Introduction

Poisoning is the third leading cause of injury-related hospitalization during pregnancy after traffic accidents and falls [1]. According to the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS), approximately 7500–8000 poisoning cases in pregnancy are phoned-in to poison control centers in the USA each year [2–4]. Such cases present a unique challenge to health care providers because toxicological exposures may not only be harmful to the mother, but also lead to fetal distress, teratogenicity, or even fetal demise. To complicate the issue further, there is limited evidence-based knowledge on the safety and efficacy of antidotes and on how to best manage the poisoned pregnant woman.

Beyond the general estimates of exposures in AAPCC's NPDS reports and teratogen information centers, data on exposure patterns and management of confirmed, consequential poisonings in pregnant women are limited. A relatively new source of data about potentially serious poisonings in pregnancy is the American College of Medical Toxicology's (ACMT) Toxicology Investigators' Consortium (ToxIC), which maintains a prospective case registry of poisoned patients managed by medical toxicologists at the bedside. We sought to describe recent consequential exposures among pregnant women in the USA.

## Methods

### Registry and Study Sites

The ToxIC Registry is a nationwide, prospective toxicosurveillance system established in 2010 by the ACMT. By the end of 2012, 35 medical toxicology practices operating in 65 institutions across the USA were contributing data on medical toxicology consults to the registry. A complete list of all institutions that contribute cases to the registry can be found in previous ToxIC reports [5]. Most participating sites are university-affiliated institutions, which collectively constitute the majority (63 %) of medical toxicology fellowship training programs in the USA. Generally, cases that are recorded in the registry tend to be of more serious nature, as they require consultation by medical toxicologists and, frequently, hospitalization [5]. Case entries are uploaded online using a password-protected database maintained centrally by ACMT, allowing for the pooling of toxicological exposures across all participating centers. Basic demographics and detailed medical information for each case recorded in the registry are obtained through review of patient history, physical examination performed at the bedside by medical toxicologists, and, when appropriate, additional diagnostic tests (e.g., urine toxic screens, serum drug concentrations, organ function tests). Pregnancy status was determined from patient records, physical examination, and through pregnancy screening that is routinely conducted in medical toxicology practice on all consults that involve women of childbearing age. The ToxIC Drug Dictionary records individual substances and medications. The study investigators analyzed them per drug class. The ToxIC Registry functions under the Western Institutional Review Board approval, and sites contribute cases following the approval of their respective Institutional Review Board and in accordance with their policies and procedures. Detailed description of the ToxIC Registry has previously been published [5, 6].

### Data Collection and Analysis

Using data from the ToxIC Registry, we identified all medical toxicology consultations involving pregnant women over a 3-year period between Jan. 1, 2010, through Dec. 31, 2012. Eligible cases were identified by searching for female exposures and then sorting the database by pregnancy status. All available relevant data pertaining to each case were extracted into a standardized form that sought information on the substances involved in the exposure, circumstances and reasons for exposure, source of referral, presence of clinical signs and symptoms, and case management. Age was coded as a categorical variable (two age ranges 13–18 and 19–64 years). Descriptive statistics were used to report proportions among groups. The lower and upper limits of the 95 % confidence interval for reported proportions were calculated using the Wilson procedure with correction for continuity [7]. Missing data was recorded as "unknown." In this report, poisoning was defined as any drug overdose or substance exposure (intentional or unintentional) which required bedside consultation by the medical toxicology service, initiated at the discretion of the frontline physician.

## Results

### Toxicological Consultations During Pregnancy

Of the 17,529 medical toxicology consultations recorded in ToxIC Registry during the study period, 103 involved pregnant women (0.6 %, 95 % confidence interval (CI) 0.5–0.7 %). In this group, 12.6 % (13/103) of consultations involved women aged 13–18 and 85.4 % (88/103) involved

women aged 19–64, and in two cases, the age range was not reported.

## Drug Exposures

The most common reasons for medical toxicology consultation of pregnant patients were intentional exposures (53/103 of all cases or 51.5 %; 95 % CI 41.5–61.4 %; Fig. 1), and the majority of them (47/53, 88.7 %) involved pharmaceutical agents. Thirty-eight women (37 %, 95 % CI 27.8–47.0 %) ingested multiple (≥2) agents, 33 (86.8 %) of whom were exposed to more than one class of drugs (only one agent/agent class was reported in 66/103 cases). The most frequently reported drug classes and agents (i.e., with five or more cases) are presented in Table 1. Non-opioid analgesics were the most common drug class encountered, with acetaminophen being involved in 81.2 % (26/32) of all exposures in this category and in 25.2 % (26/103) of all poisoning cases. Sedative-hypnotics/muscle relaxants were the second most frequently encountered drug class (18.4 % of all consultations), followed by opioids (16.5 % of all consultations).

## Clinical Presentation

Eighty of 103 pregnant women requiring a medical toxicology consultation (77.7 %) had signs of toxicity. Twenty patients (19.4 %) were not symptomatic at the time of the examination, and signs were not detailed in three (2.9 %) cases. Thus, signs of toxicity were observed in 80 out of 100 women (80.0 %, 95 % CI 70.6–87.1 %; Table 2). The most commonly observed signs and symptoms were vomiting, tachycardia, and central nervous system (CNS) depression. A defined toxidrome was recorded in 25 cases (31.2 % of symptomatic women), with sedative-hypnotic being the most common (observed in 15.0 % [12/80] of all symptomatic women and constituting 48.0 % [12/25] of all toxidromes noted).

Of the 32 cases that involved non-opioid analgesic exposure, six (five acetaminophen, one non-steroidal anti-inflammatory drug [NSAID]) developed hepatotoxicity (defined as AST >1000 IU/L) and six (two acetaminophen and four NSAID) had significant metabolic acidemia (defined as blood pH <7.20). Other serious manifestations, such as prolonged QRS and QTc, respiratory failure, and coagulopathy typically involved poly-substance ingestions. Acute renal injury (creatinine >2 mg/dL) was observed in two cases—one involving lithium and the second involving poly-substance exposure to ibuprofen, lamotrigine, acetaminophen, and clonazepam.

## Management

The majority of pregnant women in this report 68/103 (66.0 %) received interventional treatment, while in 24 cases (24/103 [23.3 %]), only observation and expectant management were necessary. Treatment details were missing in 11 cases (11/103 [10.7 %]). Thus, interventional treatment was given in 68 out of 92 cases with reported treatment details (73.9 %, 95 % CI 63.5–82.3 %) (Table 3). Of the 80 women showing clinical toxicity, 62 (77.5 %) received active treatment and 11 cases (13.8 %) were only monitored, and in 7 cases, treatments were not detailed.

The most commonly administered antidote was *N*-acetylcysteine (NAC), administered to 21/68 (30.9 %) of all cases that received a specific treatment and in 19/26 cases involving acetaminophen exposures (73.1 %). It was followed

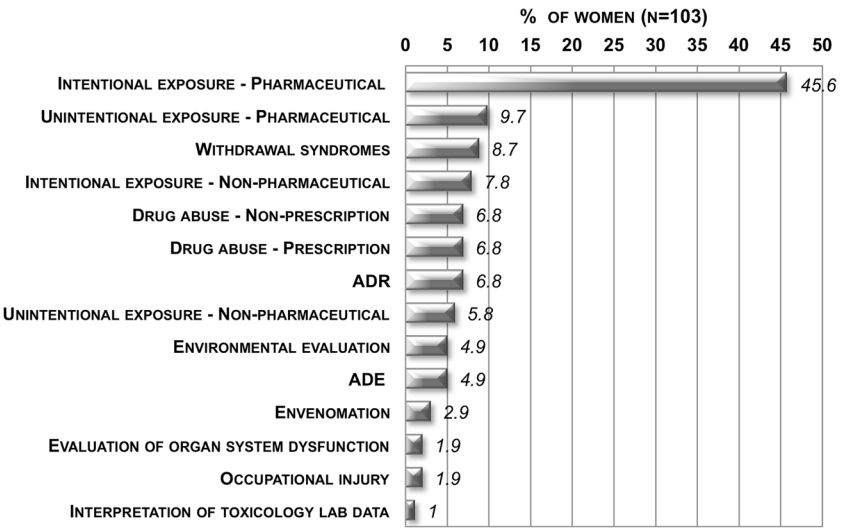


**Fig. 1** Reasons for medical toxicology consultation reported in cases involving pregnant women catalogued in the ToxIC Registry between January 2010 and December 2012. The percentage represents the proportion of the total number of cases ($n$=103) in which the specific reason for medical toxicology consultation was provided. Because some cases had multiple reasons for toxicology consultation, respondent could check off more than one reason for each case if others also applied; therefore, percentages add up to more than 100. *ADR* adverse drug reactions, *ADE* adverse drug event defined as medication error resulting in harm

**Table 1** Top drug classes and agents reported in exposures involving pregnant patients catalogued in the ToxIC Registry between January 2010 and December 2012

| Agent class | *N* | % (*n*=103) | Agents (number of cases) |
|---|---|---|---|
| Analgesics (APAP, ASA, NSAIDs) | 32 | 31.1 | Acetaminophen (26) |
| | | | ASA (4) |
| | | | Ibuprofen (4) |
| Sedative-hypnotics/muscle relaxants | 19 | 18.4 | Clonazepam (5) |
| | | | Carisoprodol (4) |
| | | | Alprazolam (3) |
| | | | Zolpidem (2) |
| | | | Cyclobenzaprine (2) |
| | | | Diazepam (1) |
| | | | Phenobarbital (1) |
| | | | Unknown (1) |
| Opioids | 17 | 16.5 | Oxycodone (5) |
| | | | Hydrocodone (4) |
| | | | Unknown/withdrawal (3) |
| | | | Hydromorphone (1) |
| | | | Buprenorphine (1) |
| | | | Codeine (1) |
| | | | Methadone (1) |
| | | | Heroin (1) |
| Anti-convulsants | 10 | 9.7 | Lamotrigine (7) |
| | | | Gabapentin (1) |
| | | | Pregabalin (1) |
| | | | Carbamazepine (1) |
| | | | Topiramate (1) |
| Anti-depressants | 10 | 9.7 | Sertraline (4) |
| | | | Bupropion (2) |
| | | | Amitriptyline (2) |
| | | | Citalopram (1) |
| | | | Fluoxetine (1) |
| | | | Duloxetine (1) |
| | | | Venlafaxine (1) |
| Anti-cholinergics/anti-histamines | 9 | 8.7 | Diphenhydramine (5) |
| | | | Promethazine (2) |
| | | | Pyrilamine (1) |
| | | | Doxylamine (1) |
| | | | Chlorpheniramine (1) |
| | | | Pheniramine (1) |
| Ethanol | 8 | 7.8 | |
| Gas/vapors/irritants/dusts | 7 | 6.8 | Carbon monoxide (6) |
| | | | Flea bomb (1) |
| Anti-psychotics | 5 | 4.9 | Quetiapine (3) |
| | | | Aripiprazole (1) |
| | | | Trazodone (1) |
| | | | Ziprasidone (1) |
| Metals/metalloids/iron | 5 | 4.9 | Iron (2) |
| | | | Lead (1) |
| | | | Mercury (1) |
| | | | Magnesium (1) |
| Pesticides | 5 | 4.9 | Brodifacoum (1) |

**Table 1** (continued)

| Agent class | *N* | % (*n*=103) | Agents (number of cases) |
|---|---|---|---|
| | | | Imiprothrin/deltamethrin (1) |
| | | | Pyrethrins (1) |
| | | | Glyphosate (1) |
| | | | Unknown (1) |

The percentage represents the proportion of the total number of cases (*n*=103) in which the specific agent class and/or agent was reported. Respondents could report more than one agent and agent class for each case; therefore, percentages can add up to more than 100

*APAP N*-acetyl-*p*-aminophenol, *ASA* acetylsalicylic acid, *NSAIDs* non-steroidal anti-inflammatory drugs

by sodium bicarbonate (administered in 13.2 % of specifically treated cases, primarily for tricyclic anti-depressants (TCAs) and salicylate exposures), flumazenil (administered to 5.9 % of specifically treated cases, primarily for benzodiazepine overdose), and physostigmine (administered in 5.9 % of specifically treated cases, mainly for anti-cholinergic poisoning). Hemodialysis was used in one case of intentional ibuprofen overdose. Hyperbaric oxygen (HBO) therapy was administered to four of six women with carbon monoxide poisoning. All four were symptomatic and displayed some combination of headache, dizziness, syncope/pre-syncope, and nausea.

## Discussion

We identified all poisoning cases involving pregnant women recorded in the ToxIC registry over a 3-year period (*n*=103). They accounted for 0.6 % (95 % CI 0.5–0.7 %) of all exposures recorded in the registry as compared to 0.3 % of all human exposures reported to the AAPCC between 2010 and 2012 [2–4]. Importantly, about half of reported cases involved intentional exposures, primarily to pharmaceutical substances. Poly-pharmacy exposure was common, occurring in 37 % (95 % CI 27.8–47.0 %) of the cases, a proportion consistent with previous reports [8, 9]. These observations suggest that, when facing acute poisoning in a pregnant woman, consideration of volition and high index of suspicion regarding potential deliberate self-harm should take place, because unique psychiatric considerations and social interventions may be indicated.

Deliberate self-poisoning is the most common method of self-harm and attempted suicide in pregnancy [10]. Associated factors include young age (peak 18–20 years), first-time pregnancy, unmarried status, and lower socioeconomic status [11]. The majority of such episodes are impulsive and frequently precipitated by violent interpersonal disputes [12]. The peak time reported for self-harm attempts in pregnancy is the first trimester, after which, it declines with advanced gestational age [8, 9, 11, 13–15].

The large proportion of intentional exposures that we observed (about half of all cases) contrasts with recent annual reports from the AAPCC's NPDS (from 2011 and 2012), which indicated that only about 20 % of exposures during pregnancy are intentional [3, 4]. This and other differences between our data and those reported by AAPCC likely stem from the fact that ToxIC exclusively records patients who present to hospitals across the country and are consulted by the medical toxicology service at the bedside. Therefore, the ToxIC Registry provides a distinctly unique profile of cases that tend to be more severe, because intentional poisonings tend to be, and thus complement the NPDS report. In contrast, AAPCC collects data from the public and health care providers who phone in for advice, frequently on mild or merely suspected exposures.

**Agents Encountered** Because the majority of cases in the registry were intentional exposures, the agent classes encountered are comparable to those found in studies on attempted suicide during pregnancy, which primarily involved non-opioid analgesics (mainly acetaminophen) and sedative-hypnotics/muscle relaxants [8, 9, 15–17]. The breakdown of agents ingested by pregnant women also mirrors that reported in the registry for the entire population [5]. Although analgesics were also the drug class most frequently involved in exposures during pregnancy reported to AAPCC in 2012, they were followed by cleaning substances and pesticides [2], which were involved in a minority of consultations in the ToxIC Registry.

**Presentation and Treatment** Eighty percent of pregnant women in our study manifested signs of toxicity, and 62 (77.5 %) of them received specific treatment. This is a reflection of the severity of cases recorded in the registry, which, once again, contrasts with the 2010 AAPCC's NPDS report, where moderate and major toxic effects (i.e., effects that typically require some type of treatment) were reported in 5.76 and 0.54 %, of pregnant women, respectively [2].

**Antidote Therapy** Management of the pregnant woman is similar to non-pregnant patients, but fetal health should be considered. A systematic review on the teratogenicity of antidotes concluded that despite the limited supporting evidence,

**Table 2** Most common clinical signs reported among pregnant patients catalogued in the ToxIC Registry between January 2010 and December 2012

| Symptom class | | *N* | % (of 100)[a] |
|---|---|---|---|
| Toxidrome | | 25 | 25.0 |
| | Sedative-hypnotic | 12 | 12.0 |
| | Withdrawal | 5 | 5.0 |
| | Opioid | 4 | 4.0 |
| | Anti-cholinergic | 2 | 2.0 |
| | Other[b] | 5 | 5.0 |
| Notable vital signs and symptoms | | 22 | 22.0 |
| | Tachycardia | 15 | 15.0 |
| | Hypotension | 6 | 6.0 |
| | Bradypnea | 2 | 2.0 |
| | Hypertension | 2 | 2.0 |
| | Other | 5 | 5.0 |
| Cardiovascular | | 9 | 9.0 |
| | Prolonged QTc[c] | 4 | 4.0 |
| | Prolonged QRS[d] | 4 | 4.0 |
| | Supraventricular tachycardia | 2 | 2.0 |
| | Other | 4 | 4.0 |
| Respiratory | | 6 | 6.0 |
| | Respiratory depression | 5 | 5.0 |
| | Other | 2 | 2.0 |
| Nervous system | | 42 | 42.0 |
| | Coma/CNS depression | 17 | 17.0 |
| | Hyperreflexia/myoclonus/clonus/tremor | 8 | 8.0 |
| | Delirium/toxic psychosis | 6 | 6.0 |
| | Headache | 4 | 4.0 |
| | Dizziness | 3 | 3.0 |
| | Seizure | 3 | 3.0 |
| | Blurred vision | 3 | 3.0 |
| | Agitation | 3 | 3.0 |
| | Ataxia | 2 | 2.0 |
| | Other | 14 | 14.0 |
| Metabolism | | 14 | 14.0 |
| | Significant metabolic acidosis[e] | 7 | 7.0 |
| | Significant electrolyte abnormalities | 5 | 5.0 |
| | Elevated anion gap[f] | 3 | 3.0 |
| | Hypoglycemia[g] | 3 | 3.0 |
| | Other | 2 | 2.0 |
| GI/Hepatic | | 25 | 25.0 |
| | Vomiting | 16 | 16.0 |
| | Nausea | 8 | 8.0 |
| | Hepatotoxicity[h] | 6 | 6.0 |
| | Abdominal pain | 4 | 4.0 |
| | Diarrhea | 3 | 3.0 |
| | Other | 4 | 4.0 |
| Hematology | | 7 | 7.0 |
| | Significant coagulopathy[i] | 3 | 3.0 |
| | Significant leukocytosis[j] | 3 | 3.0 |
| | Other | 1 | 1.0 |
| Dermatology | Rash/blisters/pruritus/other | 4 | 4.0 |
| Renal/muscle | Acute kidney injury[k] | 2 | 2.0 |

[a] Percentages are based on the total number of pregnant patients displaying the specific sign/symptom of interest. Percentages were calculated based on the 100 women (97.1 % of all consults) with documented symptomatology (80 women were symptomatic and 20 women were asymptomatic). Respondents could specify more than one sign/symptom for a patient in each category; therefore, the combined percentages of more than one category can add up to more than 100.

[b] Other reported toxidromes included anti-convulsant hypersensitivity, serotonin syndrome, excitatory/anti-cholinergic (mixed), envenomation, and salicylate

[c] Prolonged QTc defined as QTc interval >460 ms

[d] Prolonged QRS defined as duration >0.12 s

[e] Significant metabolic acidosis defined as arterial blood pH <7.20

[f] Anion gap >20 mEq/L

[g] Hypoglycemia defined as blood glucose <50 mg/dL

[h] Hepatotoxicity defined as aspartate aminotransferase (AST) >1000 IU/L

[i] Significant coagulopathy defined as prothrombin time >15 s

[j] Significant leukocytosis defined as >20,000 white blood cells per microliter

[k] Acute kidney injury defined as serum creatinine >2.0 mg/dL

antidotes should be used when indicated to decrease maternal morbidity and mortality associated with poisoning despite potential fetal risks [18, 19]. The majority of pregnant women in our cohort received active treatment (66 %). NAC was the most commonly used antidote, reflecting the relatively high number of cases of acetaminophen exposures. Acetaminophen crosses the placenta and is metabolized by fetal liver, where generation of the toxic metabolite (*N*-acetyl-*p*-benzoquinone imine) may occur [20]. Hepatic necrosis in the fetus has been reported if treatment is delayed [20], although at a lower rate than in adults because of immaturity of the cytochrome P450 enzymes. NAC, a glutathione precursor, is the accepted treatment for acetaminophen overdose in pregnancy because it crosses the placenta [21] and provides protection to the fetus [22–24]. NAC is not considered teratogenic when used therapeutically and is rated by the US Food and Drug Administration as pregnancy category B, meaning its risk has been studied and there is no demonstrated risk to pregnant women. Its administration should, therefore, not be delayed when indicated.

Sodium bicarbonate was administered primarily for tricyclic anti-depressants (TCAs) and salicylate exposures. For TCAs, bicarbonate is used to ameliorate sodium channel blockade when there is documented QRS prolongation [25]. For salicylates, blood and urinary alkalization with sodium

**Table 3** Most commonly administered treatments in pregnant patients catalogued in the ToxIC Registry between January 2010 and December 2012

| Treatment | | *N* | % (of 92)[a] |
|---|---|---|---|
| Antidotes | | 41 | 44.6 |
| | NAC | 21 | 22.8 |
| | Sodium bicarbonate | 9 | 9.8 |
| | Flumazenil | 4 | 4.3 |
| | Physostigmine | 4 | 4.3 |
| | Naloxone | 3 | 3.3 |
| | Other[b] | 8 | 8.7 |
| Anti-venom | CroFab | 1 | 1.1 |
| Pharmacologic treatments | | 20 | 21.7 |
| | Benzodiazepines | 7 | 7.6 |
| | Anti-emetics | 4 | 4.3 |
| | Opioids | 3 | 3.3 |
| | Glucose | 2 | 2.2 |
| | Anti-convulsants | 2 | 2.2 |
| | Other | 11 | 12.0 |
| Elimination | | 2 | 2.2 |
| | Hemodialysis | 1 | 1.1 |
| | Continuous renal replacement therapy | 1 | 1.1 |
| Non-pharmacological treatments | | 22 | 23.9 |
| | IV fluid resuscitation | 16 | 17.4 |
| | Hyperbaric oxygen | 4 | 4.3 |
| | Intubation/ventilatory management | 3 | 3.3 |
| | Other | 3 | 3.3 |

[a] Percentages are based on the total number of women who received the specific treatment of interest. Percentages were calculated based on the 92 patients (89.3 % of all consultations) for whom treatment details were documented (68 patients received specific treatment, 24 were not actively treated, treatment details were not reported for 11 cases). More than one treatment may have been given to a patient in each category; therefore, percentages in each category can add up to more than 100

[b] Other antidotes used include calcium, octreotide, vitamin K, dextrose, and tranexamic acid

*NAC N*-acetylcysteine, *CroFab* Crotalidae Polyvalent Immune Fab

bicarbonate is used to impede salicylate distribution to the CNS and other end organs and to enhance the drug's elimination in urine. Salicylate freely crosses the placenta and can lead to severe toxic effects, including fetal acidosis [26]. Because bicarbonate transfer across the placenta is slow, the correction of metabolic acidosis in the fetus is delayed, and thus, maternal hemodialysis or alkali therapy may not provide immediate benefit to the fetus [19]. However, the administration of bicarbonate is potentially advantageous to the fetus because preferential maternal blood alkalinization favors salicylate to partition into the mother by ion trapping. Thus, early and aggressive bicarbonate treatment is indicated in all but trivial cases, and delivery of the distressed fetus should be considered if it is potentially viable [19].

Flumazenil, a benzodiazepine receptor antagonist, was the third most commonly administered antidote. Little is known about its teratogenic risk [18]. It is classified by the FDA as a pregnancy category C drug [27]. While many cases of benzodiazepine toxicity may be treated supportively, in a case report of maternal diazepam overdose, cardiac rhythm abnormalities in the fetus were reversed by flumazenil and the infant was born healthy 2 weeks later [28].

The opioid antagonist naloxone was administered to three women in our study. Because opioids cross the placenta, naloxone administration should be used cautiously in opioid-dependent pregnant patients. Reports of adverse events, such as hypertensive crisis and precipitation of withdrawal, associated with naloxone use near delivery for reversal of opioid effects have been described in pregnant women [19, 29, 30], as well as induction of preterm labor and fetal distress [31]. Thus, naloxone should be used in pregnancy only if clearly indicated to save maternal life [31].

HBO therapy was administered to all symptomatic carbon monoxide poisoning cases. Although short hyperoxic exposure during HBO therapy is tolerated by the fetus and had been shown to reduce fetal risk of death in some reports [32], its efficacy in carbon monoxide poisoning is controversial and it is unknown if the elevated fetal carboxyhemoglobin fraction has a role in the toxicity of carbon monoxide to the fetus. Despite the uncertainty, many medical toxicologists tend to administer HBO therapy to treat pregnant patients with carbon monoxide poisoning. If deemed indicated, it has been suggested that the duration of HBO therapy should be longer for pregnant women than for non-pregnant women because of slower dissociation of carboxyhemoglobin in the fetus [33].

A few limitations of our study merit emphasis. The main one is the lack of access to patients' full medical records, which precluded a detailed exposition of the circumstances that led to poisoning in each case (e.g., suicide attempt vs. gesture, attempt to abort, etc.) beyond determining the general volition, as well as lack of more detailed demographic information such as gravidity, parity, and gestational age. Secondly, although it is routine practice in medical toxicology to conduct pregnancy tests in poisoning cases of women in the childbearing age, it is possible that few pregnancy cases were not recognized. Another limitation of our dataset is lack of follow-up to explore long-term pregnancy outcomes, especially fetal. Although the primary purpose of this study was to describe current consequential poisoning in pregnant women and their management, information on pregnancy outcomes would have been important.

In summary, the majority of poisoning cases during pregnancy that are consulted at the bedside by medical toxicologists are intentional drug exposures, with non-opioid analgesics and sedative-hypnotics/muscle relaxants being the most commonly ingested agents. Further research is indicated to explore the risk factors for poisoning in pregnancy, as well

as pregnancy and fetal outcomes after acute poisoning. Characterizing risk factors for poisoning among pregnant women will permit health care providers a potential opportunity for early intervention in this unique patient population, while exploring outcomes of such exposures is a unique opportunity to study the potential teratogenic effects of poisoning and safety of antidotes during early stages of pregnancy in a natural context.

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**Conflict of Interest** Authors IZ, JM, JRH, PW, GK, JB, and YF declare that they have no conflict of interest.

**Informed Consent** All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was waived for all patients by the respective IRBs.

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