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RESEARCH

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ABSTRACT

Objective: To describe birth outcomes following intentional acute poisoning during pregnancy.

Setting: California Linked Vital Statistics-Patient Discharge Database, 2000 to 2004.

Participants: Pregnant women age 15 to 44, who had a singleton live birth or fetal death that occurred between gestational ages 20 and 42 weeks who were discharged from the hospital for an intentional poisoning were compared to pregnant women discharged from the hospital for any nonpoisoning diagnosis. Intentional acute poisoning hospital discharges were identifed by the presence of an ICD-9-CM E-Codes E950-E952 (suicide, attempted suicide and self-inflicted injuries specified as intentional.)

Methods: Through a retrospective cohort design, birth outcomes including low birth weight; preterm birth; fetal, neonatal, and infant death; and congenital anomalies were identified by the presence of ICD-9-CM diagnosis codes or by notation in the dataset.

Results: There were 430 hospital discharges for an intentional poisoning during pregnancy documented in the dataset (rate = 25.87/100,000 person years). The rate of intentional poisoning was greatest in the first weeks of gestation and declined with increasing gestational age. Analgesics, antipyretics, and antirheumatics were most commonly implicated. Adverse birth outcomes associated with intentional poisoning included preterm birth (odds ratio [OR] = 1.34; 95% Confidence Interval [CI] [1.01, 1.77]), low birth weight (OR = 1.49; 95% CI [1.04, 2.12]), and circulatory system congenital anomalies (OR = 2.17; 95% CI [1.02, 4.59]).

Conclusion: Intentional acute poisoning during pregnancy was associated with several adverse birth outcomes; however, these relationships may be confounded by concomitant maternal substance abuse.

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Approximately 6% to 7% of women experience an injury requiring medical treatment during pregnancy. The leading causes of injury hospitalizations during pregnancy are motor vehicle occupant–related injuries (27.1%), falls (21.2%) and poisonings (16.4%; Weiss, 1999). Several population-based studies have examined the risks of adverse birth outcomes secondary to injuries sustained by the mother during pregnancy. Research in this area has focused primarily on traumatic mechanisms of injury during pregnancy, with the majority of publications investigating the risks and outcomes of motor vehicle crashes (Hyde, Cook, Olson, Weiss, & Dean, 2003; Schiff & Holt, 2005; Sirin, Weiss, Sauber-Schatz, & Dunning, 2007; Weiss, Lawrence, & Miller, 2002b) and assaults (El Kady, Gilbert, Xing, & Smith, 2005; Rachana, Suraiya, Hisham, Abdulaziz, & Hai, 2002; Weiss, Lawrence, & Miller, 2002a). Despite the relative proportion of injuries that are attributable to poisonings, there is a dearth of population-based data regarding the effects of poisoning on birth outcomes among women hospitalized for a poisoning during pregnancy.

The 2004 Toxic Exposure Surveillance System annual report indicated that of all 2,438,644 poison exposures called into Poison Control Centers (PCC), 8,431 occurred in pregnant women: 32.0% of the 8,431 occurred in the first, 37.6% in the second, and 30.5% in the third trimesters, respectively (Watson et al., 2005). Approximately 0.07% of all telephone inquiries about drug overdose at a Michigan metropolitan PCC were related to drug overdose during pregnancy (Rayburn, Aronow, DeLancey, & Hogan, 1984).

The majority of poisonings occurring during pregnancy are self-inflicted (McClure, Katz, Patrick, Kelsey, & Weiss, 2010). In a population-based prospective examination of the timing of self-poisoning in pregnant women for the years 1985 to 1993 in Budapest, Hungary, Czeizel, Timar, and Susanszky (1999) reported a striking inverse relationship between the number of suicide attempts by poisoning across postconceptional months. Sixty-one percent of all attempts occurred before the third month postconception, with a significantly lower proportion attempting suicide parallel with fetal development (Czeizel et al., 1999).

Poisoning is the leading mechanism of suicide among pregnant women in California; however, there is little research on the effects of poisoning on birth outcomes.

Teratogenesis

Teratogens are xenobiotics (a chemical or substance that is foreign to an organism or biological system) to which the mother is exposed that induce structural and/or functional changes in offspring before or during pregnancy (Bresloe et al., 2002). In humans the only major teratogens identified before 1950 were rubella and radiation. Nonetheless, throughout the 1950s, teratologists assumed that the human fetus was protected from chemical insults. However, in the late 1950s approximately 8,000 infants were born with severe thalidomide-induced phocomelia. The immediate result of the thalidomide disaster was heightened awareness of the human fetus's susceptibility to environmental insults, engendering a new emphasis on reproductive testing of drugs, pesticides, and other chemicals. Currently, a nimiety of substances has been identified to cause malformations in humans, including antiepileptic drugs, anticoagulants, alcohol, cigarettes, Accutane, methadone, and Diethylstilbestrol (DES; Ostrer, 2006). Ten percent of all fetal malformations are now believed the result of exposures to drugs, maternal conditions or disease states, physical agents, chemicals, and infections (Hogge & Prosen, 2006).

The time during gestation at which the fetus is exposed to a teratogen can determine fetal development and outcome. During the first weeks of gestation from the time of conception to implantation there appears to be an "all-or-nothing" principle. If the embryo is exposed to a teratogen at this time it is either (a) highly toxic resulting in fetal demise or (b) innocuous causing no harmful effects (Foster et al., 2001; Kenner, Dreyer, & Amlung, 2000). During weeks 2 through 10 organogenesis begins, and the germ layers appear that will lead to the development of all of the fetus' physiologic systems (Hogge & Prosen, 2006; Kenner et al.).

The fetal period of development extends from week 10 until birth. During this time the fetus grows in weight and length, and the organs mature. At any time during this period the most vulnerable organ system is the one that is growing most rapidly (Hogge & Prosen, 2006; Kenner et al., 2000).

Teratogenic mechanisms have mainly been studied in laboratory animals. Previously, there have been two approaches to study poisonings as reproductive hazards in humans: case studies examining exposures and epidemiological studies of self-poisoning. Several case studies have been published regarding poisonings during pregnancy, encompassing a broad array of legal and illicit drugs as well as environmental poisons. Reported birth outcomes range from preterm delivery, low birth weight and length, and congenital anomalies, to spontaneous abortion and infant death. In some instances the exposures resulted in the aforementioned outcomes, whereas in others the poisonings were not associated with any apparent adverse effects.

It is difficult to make generalizations using case reports/series. Fetal toxicity varied depending on dose and apparent timing of exposure during the pregnancy. In some instances fetal toxicity was reported even despite seemingly low toxin concentrations compared with the mother.

Several studies have shown no effect of self-poisoning on the prevalence of congenital anomalies, prematurity or low birth weight (Gunnarskog & Kallen, 1993; McElhatton, Sullivan, & Volans, 1997). Gunnarskog and Kallen reported no increased risk of congenital anomalies in a register-based study of 424 infants exposed to chemicals in utero, of which 70 were exposed during the period of organogenesis. In a population-based prospective study of 559 self-poisoned pregnant women admitted to the toxicology inpatient clinic the overall prevalence of congenital anomalies and proportion of multimalformed babies was significantly higher in the 178 infants in the study group than comparable controls. However, after excluding eight infants with fetal alcohol syndrome, the rate of congenital anomalies in the remaining infants (9%) was not significantly different than that in the control group (6.1%). Therefore, no teratogenic effects were identified, even though in 27 cases large doses of drugs were ingested between the 3rd and 8th weeks of fetal development (Czeizel & Mosonyi, 1997).

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Infants born to pregnant women hospitalized for intentional acute poisoning exhibited higher rates of preterm birth, low birth weight, and circulatory system congenital anomalies.

In Denmark, researchers reported that among 122 women exposed to drug overdose during pregnancy (paracetamol, salicylates, benzodiazepines, and psychotropics) 44 underwent elective abortions, 17 experienced spontaneous abortion, and 61 gave birth. The proportion of spontaneous abortion was nearly double that of the background population with a rate ratio of 1.7; the background population corresponds to crude figures from the surrounding population during the study period. There was no increased risk of major malformation or premature birth when compared to the background population. The authors do, however, cite lack of power to detect congenital anomalies that usually depend upon a short time window of drug exposure (Flint, Larsen, Nielsen, Olsen, & Sorensen, 2002). They concluded that a drug overdose shortly before or during pregnancy was associated with a substantially increased risk of miscarriage, but no increase in fetal birth defects among survivors.

In addition to these studies, ingestion of a drug or corrosive substance was recently reported as the leading mechanism of attempted suicide among pregnant women in California (Gandhi et al., 2006). Outcomes associated with attempted suicide during pregnancy included preterm labor, Cesarean delivery, low birth weight, and respiratory distress syndrome. Although the majority of suicide attempts were by poisoning, attempts by firearms, jumping, cutting, ingestion of a gaseous substance, and hanging were also included in the outcome analyses; therefore these results do not accurately represent birth outcomes associated specifically with intentional poisoning during pregnancy (Gandhi et al.). Consequently, this study aims to describe the patterns of birth outcomes following intentional acute poisoning during pregnancy, including preterm delivery, low birth weight, congenital anomalies, and fetal, neonatal, and infant death.

Methods

Materials

Through a retrospective cohort design, data from the Vital Statistics-Patient Discharge Database (VSPDD), maintained by the California Office Statewide Health Planning and Development, for the years 2000 to 2004, were analyzed. All California-licensed hospitals are mandated to semiannually submit specific data on every discharged patient. These data include patient demographic information, diagnostic and treatment information, total hospital charges, and payer source. The linked VSPDD includes data from several sources including California patient discharge data, vital statistics birth certificate data, vital statistics death certificate data, the vital statistics fetal death file, and the vital statistics birth cohort file. It also includes maternal antepartum and postpartum hospital records for the 9 months prior to and 1 year postdelivery. The database also includes birth records and all infant readmissions occurring in the first year of life. The data were linked by variables common between the data sets, and linkage was successful in 98% of the cases. Detailed linkage procedures have been described previously (Herrchen, Gould, & Nesbitt, 1997). Permission to use this data was granted by the California Office of Statewide Health Planning and Development.

This study was approved by the University of Pittsburgh Institutional Review Board, the California Department for the Protection of Human Subjects, and the California Office of Statewide Health Planning and Development. No unique patient identifiers were included in the database.

Inclusion/Exclusion Criteria

Intentional acute poisoning hospital discharges were identifed by the presence of an International Classification of Diseases, Ninth Revision, Clinical Modification External Cause of Injury Codes (ICD-9-CM E-Code) E950-E952 (suicide, attempted suicide and self-inflicted injuries specified as intentional; *Online ICD9/ICD9CM codes*, 2007).

Irrespective of maternal outcome, all hospital discharges for intentional acute poisonings in pregnant women age between 15 and 44, who had a a singleton live birth or fetal death that occurred between gestational ages 20 to 42 weeks, were identified and compared to all other nonpoisoning hospital discharges in pregnant women age between 15 and 44 who had a pregnancy outcome consisting of live birth or fetal death that occurred within gestational ages 20 to 42 weeks, during the 5-year period from 2000 to 2004. Reported last menstrual period (LMP) was used to estimate gestational age. Data on deliveries prior to 20 weeks gestation are not captured by the state and thus are excluded from the data set. Clinical Classifications Software (CCS), developed at the Agency for Healthcare Research and Quality (AHRQ), was used to define *concomitant mental illness* and *substance*

abuse. Specifically, mental illness was defined using CCS categories 657 (mood disorders), 658 (personality disorders), and 659 (schizophrenia and other psychotic disorders). Substance abuse was defined using CCS categories 660 (alcohol-related disorders) and 661 (substance-related disorders; Clinical Classification Software for ICD-9-CM, 2007).

Birth outcomes were identified by the presence of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes or by notation in the data set (*Online ICD9/ICD9CM codes*, 2007). *Preterm delivery* was defined as birth at fewer than 37 weeks gestation. *Low birth weight* was defined as a birth weight fewer than 2,500 g and extremely low birth weight as less than 1,500 g. *Fetal death* was defined as an intrauterine death identified by a fetal death certificate. Nonchromosomal congenital anomalies were determined utilizing ICD-9-CM codes.

We also separately examined the effects of poisonings occurring during and after the period of organogenesis (prior to the fetal period of development which occurs from week 10 until birth). Time of poisoning was calculated using the following formula: gestational age at delivery—date of poisoning admission. Specifically, women who were discharged during the first 9 weeks of pregnancy and those discharged between 10 weeks gestation and delivery were assessed separately.

Statistical Methods

Incidence rates were calcuated per 100,000 person years, following the methodology used by Greenblatt, Dannenberg, and Johnson (1997). Denominators were adjusted downward to account for the 9 of 12 months of the year a pregnant woman is gravid.

Data were summarized as means plus or minus the standard deviation or median interquartile range for continuous variables and frequencies for categorical variables. To determine statistical signficance, *t* tests or Wilcoxon rank-sum tests were computed for continuous variables and the chi-square test was computed for categorical variables. Odd ratios (OR) and 95% Confidence Intervals (CI) were calculated for risk factors using logistic regression analyses.

Odds ratios and 95% CIs were calculated to determine if intentional acute poisoning hospital discharge was associated with the selected birth outcomes. Reported ORs are adjusted for potential confounders, identified a priori, including age, race, ethnicity, maternal education, and insurance payer. Additional models were adjusted for gestational age and substance abuse. All analyses were calculated using SAS 8.2 software (SAS Institute, Cary, NC). All *p* values less than .05 were considered statistically significant.

Results

There were 2,215,920 deliveries that fulfilled the inclusion criteria identified in the VSPDD between 2000 and 2004. Four hundred and thirty women with hospital discharges for an intentional acute poisoning during pregnancy (population-based rate 25.87/100,000 person years) were documented. These women made up the exposed group, and 2,215,490 women with nonpoisoning hospital discharge made up the control group. Further analysis of the study group revealed that 178 (41%) of the intentional poisonings occurred within the first 9 weeks of gestation.

Demographic characteristics of women with an intentional acute poisoning hospital discharge during pregnancy are shown in Table 1. In addition, the table illustrates the associations between demographic characteristics and incidence of poisoning. This analysis determined that compared to women in other age groups, women between the ages of 15 and 19 years were more likely to be hospitalized for an intentional poisoning during pregnancy. African American women were more likely to be hospitalized for an intentional poisoning than White women. In addition, women with less than a high school education had the greatest odds of intentional poisoning hospitalization during pregnancy when compared to women with additional schooling. Time of initiation of prenatal care was not associated with intentional acute poisoning hospital discharge. The presence of concomitant substance abuse and mental illness were each associated with higher odds of intentional poisoning during pregnancy.

Of all intentional acute poisoning hospital discharges during pregnancy, 45% occurred in the first trimester, 31% in the second, and 24% in the third. The rate of acute poisoning hospital discharges in the first trimester was significantly greater than that in the second and the third trimesters (both $p < .05$; 11.67, 8.00, and 6.20 per 100,000 person years, respectively); the rate of poisonings in the second trimester did not differ significantly from that in the third.

Substances implicated in intentional acute poisoning hospital discharges during pregnancy are presented

Table 1: Relationships Between Demographic Characteristics of Women With Intentional Acute Poisoning Hospital Discharge and Nonpoisoning Hospital Discharge, During Pregnancy, California, 2000 to 2004

		Nonpoisoning Hospitalizations During Pregnancy, *N* = 2,215,490	Intentional Poisoning Hospitalizations During Pregnancy, *N* = 430				
Characteristic	Category	*N*	*n*	%	OR	95% CI	*p*
Maternal age	15–19	211,458	103	0.05	3.28	2.47, 4.37	< .0001
	20–24	499,769	139	0.03	1.89	1.88, 2.45	< .0001
	25–29	579,672	86	0.01	1.00	1.00 ref.	
	30–34	554,635	69	0.01	0.84	0.84, 1.15	.28
	35–39	299,906	20	0.01	0.45	0.45, 0.73	.001
	40–44	70,050	13	0.02	1.25	0.70, 2.24	.45
Race	White	1,769,223	324	0.02	1.00	1.00 ref.	
	Black	130,531	51	0.04	2.13	1.59, 2.87	< .0001
	Asian	272,143	41	0.02	1.02	0.70, 1.49	.91
	Other	36,644	14	0.04	0.92	0.61, 1.38	.68
Ethnicity	Hispanic	1,021,208	193	0.02	1.00	1.00 ref.	
	non-Hispanic	1,150,066	234	0.02	0.93	0.77,1.13	.46
Maternal education	Less than high school	627,022	175	0.03	1.00	1.00 ref.	
	Completed high school	612,110	125	0.02	0.73	0.58, 0.92	.008
	Some college, no degree	421,636	78	0.02	0.66	0.51, 0.87	.003
	College	514,835	40	0.01	0.28	0.20, 0.39	< .0001
Insurance	Medicare/other government	21,440	18	0.08	3.97	2.45, 6.42	< .0001
	Medi-Cal	958,375	203	0.02	1.00	1.00 ref.	
	Private	1,170,391	133	0.01	0.54	0.43, 0.67	< .0001
	Indigent	48,737	47	0.10	4.56	3.32, 6.26	< .0001
	Self-pay	3,072	24	0.78	36.89	24.13, 56.40	< .0001
	Other	13,151	5	0.04	1.80	0.74, 4.36	.20
Parity	Nulliparous	3,980	0	0	—	—	—
	1	872,506	192	0.02	1.00	1.00 ref.	
	2	704,959	104	0.01	0.67	0.53, 0.85	.001
	≥ 3	633,402	134	0.02	0.96	0.77, 1.20	.73
Initiation of prenatal care	First trimester	1,914,651	352	0.02	1.00	1.00 ref.	
	Second trimester	231,225	62	0.03	1.61	0.23, 11.48	.63
	Third trimester	45,965	10	0.02	2.35	0.33, 16.96	.40
	None	8,768	[a]	[a]	1.91	0.24, 14.90	.54
Substance abuse	Yes	23,714	289	0.60	46.05	37.67, 56.31	< .0001
	No	2,191,776	143	0.01	1.00	1.00 ref.	
Mental illness	Yes	14,304	283	1.94	296.28	242.59, 361.86	< .0001
	No	2,201,186	147	0.01	1.00	1.00 ref.	

Note. CI = confidence interval; OR = odds ratio.
[a] Cell frequency < 5: data not reported.

Table 2: Substances Implicated in Intentional Acute Poisoning Hospital Discharge During Pregnancy and Substance Specific Population-Based Rates by E-Code and by Diagnosis Code

	Rate (Per 100,000 Person Years)
Intentional (E-code)	
Suicide and self-inflicted poisoning by analgesics, antipyretics, and antirheumatics	12.94
Suicide and self-inflicted poisoning by other specified drugs and medicinal substances	8.85
Suicide and self-inflicted poisoning by tranquilizers and other psychotropic agents	6.32
Suicide and self-inflicted poisoning by other and unspecified solid and liquid substances	1.38
Suicide and self-inflicted poisoning by other sedatives and hypnotics	0.54
Intentional (diagnosis code)	
Poisoning by aromatic analgesics, NEC	
Acetanilid; Paracetamol [acetaminophen]; Phenacetin [acetphenetidin]	8.18
Poisoning by antidepressants	
Amitriptyline; Imipramine; Monoamine Oxidase [MAO] Inhibitors	2.89
Poisoning by antirheumatics (antiphlogistics)	
Propionic acid derivatives	
Fenoproten; Fluriprofen; Ibruprofen; Ketoprofen; Naproxen; Oxaprozin	2.35
Poisoning by benzodiazepine-based tranquilizers	
Chlordiazepoxide; Diazepam; Flurazepam; Lorazepam; Medazepam; Nitrazepam	2.11
Poisoning by salicylates	
Acetylsalicylic acid [aspirin]; Salicylic acid salts	2.11

in Table 2. The leading substances implicated were analgesics, antipyretics, and antirheumatics.

The median gestational age at delivery between cases and controls was not significantly different. In addition, the median gestational age at delivery of women with an intentional acute poisoning between conception through 9 weeks and of those 10 weeks through delivery was not significantly different.

The associations between intentional acute poisoning and birth outcomes are outlined in Table 3. Intentional poisoning was significantly associated with low birth weight (LBW) and preterm birth (PTB) even after controlling for age, race, ethnicity, insurance payer source, and maternal education. However, when gestational age was added into the multivariate logistic regression model, the association between intentional poisoning and LBW was no longer significant. When substance abuse was added to the multivariate model, neither LBW nor PTB was significantly associated with intentional poisoning hospital discharge during pregnancy.

Intentional poisoning occurring during the first 9 weeks of pregnancy was associated with a higher risk of delivery of a LBW infant (OR = 1.74, 95% CI [1.04, 2.91]). After controlling for gestational age, LBW no longer remained significantly associated with intentional poisoning hospitalization. Intentional poisoning occurring between 10 weeks gestation and delivery was associated with a higher rate of circulatory system congenital anomalies (OR = 2.17, 95% CI [1.02, 4.59]). These anomalies remained significantly associated with intentional poisoning after adjusting for gestational age. When substance abuse was added to the multivariate models, no outcomes remained significantly associated with intentional acute poisoning hospital discharge, regardless of timing of the poisoning during pregnancy.

Table 3: Birth Outcomes Following Intentional Acute Poisoning Hospital Discharge and Nonpoisoning Hospital Discharge During Pregnancy, California, 2000 to 2004

	Non-Poisoning Hospital Discharge, $N = 2,215,490$		Intentional Acute Poisoning Hospital Discharge, $N = 430$			
Birth Outcome	*n*	%	*N*	%	AOR	95% CI
Preterm delivery	225,820	10.19	58	13.49	1.34	1.01, 1.77
Low birth weight	118,062	5.33	34	7.91	1.49	1.04, 2.12
Fetal death	9,304	0.42	[a]	[a]	1.19	0.30, 4.77
Neonatal death	6,066	0.27	0	0		
Infant death	3,119	0.14	[a]	[a]	2.87	0.72, 11.49
Anancephalus and similar anomalies	107	0.00	0	0		
Bulbus cordis anomalies and anomalies of cardiac septal closure	22,001	0.99	5	1.16	1.27	0.53, 3.07
Certain congenital musculoskeletal deformities	9,658	0.44	0	0		
Cleft palate and cleft lip	3,826	0.17	[a]	[a]	1.41	0.20, 10.04
Congenital anomalies of genital organs	16,797	0.76	[a]	[a]	0.33	0.05, 2.33
Congenital anomalies of the ear, face, and neck	5,689	0.26	0	0		
Congenital anomalies of the eye	2,849	0.13	0	0		
Congenital anomalies of the integument	46,535	2.10	14	3.26	1.63	0.96, 2.78
Congenital anomalies of the respiratory system	5,842	0.26	[a]	[a]	0.94	0.13, 6.66
Congenital anomalies of the urinary system	8,582	0.39	[a]	[a]	0.67	0.10, 4.77
Other congenital anomalies of limbs	9,880	0.45	[a]	[a]	1.06	0.26, 4.25
Other congenital anomalies of nervous system	4,466	0.20	0	0		
Other congenital anomalies of the circulatory system	30,944	1.40	11	2.56	1.8	0.96, 3.36
Other congenital anomalies of the digestive system	5,202	0.23	[a]	[a]	1.03	0.15, 7.35
Other congenital anomalies of the heart	9,042	0.41	[a]	[a]	2.48	0.93, 6.61
Other congenital anomalies of upper alimentary tract	7,951	0.36	[a]	[a]	1.35	0.34, 5.43
Other congenital musculoskeletal anomalies	7,754	0.35	[a]	[a]	0.68	0.10, 4.81
Spina bifida	685	0.03	0	0		

Note. AOR = adjusted odds ratio; odds ratio adjusted for age, race, ethnicity, maternal education, and insurance payer; CI = confidence interval.
[a]Cell frequency < 5: data not reported.

Discussion

Infants born to pregnant women hospitalized for intentional acute poisoning exhibited higher rates of LBW, PTB, and circulatory system congenital anomalies. These observations have been paradoxically supported and contradicted in the literature. Czeizel, Szentesi, and Molnar (1984) reported no association of poisoning with any of the following: mean birth weight, spontaneous abortion, major congenital anomalies, minor anomalies, infant mortality, or specific childhood diseases (Czeizel et al., 1984). However, lower mean birth weight has been reported to be significantly associated with poisoning during pregnancy in other studies (Czeizel et al., 1988; Lendvay & Czeizel, 1992). A recent analysis that utilized hospital discharge data from California reported that suicide attempt during pregnancy, the vast majority by poisoning, was associated with neonatal and infant death, preterm delivery, and respiratory distress syndrome (Gandhi et al., 2006). The results across studies are inconclusive, and outcomes are likely to vary based on severity, type and

timing of poisoning, as well as potential confounders such as substance abuse, illnesses, medication use, and other risk-taking behaviors. In addition, differences may also be attributed to variations in study design, operational definitions of poisoning, and study populations. Notable strengths of this study are that it is population based and utilizes a broad, yet clearly defined, definition of *intentional poisoning*.

We report that women hospitalized for an intentional acute poisoning within the first 9 weeks of pregnancy exhibited higher rates of LBW deliveries; however, after we adjusted for gestational age, this relationship was attenuated and no longer significant. In a study of 126 pregnant women self-poisoned in the first 4 weeks of fetal development, 114 pregnancies ended in very early fetal loss, and 12 fetuses survived until delivery (Czeizel & Mosonyi, 1997). The authors of that study suggested that though based on small numbers, these findings are consistent with an "all-or-nothing" effect of poisoning very early in human gestation (Czeizel & Mosonyi). Similar results were reported among 122 Danish women exposed to drug overdose during pregnancy; the proportion of spontaneous abortion was nearly double that of the background population with a rate ratio of 1.7 (Flint et al., 2002). However, associations between drug overdose and risk of major malformation or PTB were not observed. The authors concluded that a drug overdose shortly before or during pregnancy was associated with a substantially increased risk of miscarriage, but no increase in birth defects among survivors (Flint et al.).

In our study, intentional poisoning in early development was not associated with any adverse birth outcomes. However, the data set is limited to live births or fetal deaths greater than or equal to 20 weeks gestation. Therefore, a poisoning early in development that may have resulted in an early fetal death (prior to 20 weeks gestation) would not be captured.

Several studies have shown no effect of self-poisoning on the prevalence of congenital anomalies (Czeizel et al., 1984, 1988; Flint et al., 2002; Gunnarskog & Kallen, 1993; Timmermann, Acs, Banhidy, & Czeizel, 2008). In this study, we found that infants born to women who were hospitalized for an intentional poisoning during gestational weeks 10 and delivery were at an increased risk of circulatory system congenital anomalies. Nonetheless, it should be noted that observing an association between intentional acute poisoning in the weeks following organogenesis and congenital anomalies suggests the presence of other confounding variables (Timmerman et al.).

Substance abuse or other risk-taking behaviors associated with intentional poisoning may confound the relationships between poisoning and congenital anomalies.

After substance abuse was added into the multivariate model, intentional poisoning during gestational weeks 10 through delivery was no longer associated with congenital anomalies. This is consistent with an earlier population-based prospective study of 559 self-poisoned pregnant women admitted to a toxicology inpatient clinic where the overall prevalence of congenital anomalies and proportion of multimalformed babies was significantly higher in the 178 infants in the study group than comparable controls (Czeizel, Tomcsik, & Timar, 1997). However, after excluding eight infants with fetal alcohol syndrome, the rate of congenital anomalies in the remaining infants (9%) was not significantly different than that in the control group (6.1%; Czeizel et al., 1997). Therefore, no teratogenic effects were identified, even though in 27 cases large amounts of drugs were ingested by the mother between the 3rd and 8th weeks of fetal development (Czeizel et al., 1997). It is important to note, however, that the drugs ingested by these women may have had variable degrees of teratogenicity.

We can only speculate the etiologies of the congenital anomalies observed. It is possible that substance abuse or other risk-taking behaviors characteristic of women hospitalized for an intentional poisoning may actually be responsible for the observed associations. It is difficult to quantify these potential confounding factors; however, future research should collect data on potential confounders such as substance abuse, stress, and medical, social, and behavioral factors that would influence birth outcomes.

Limitations

Limitations of this study, inherent in the utilization of retrospective, administrative data, are coding and reporting errors. This study may also have selection bias as the data set included only hospitalized patients, excluding deliveries prior to 20 weeks gestation and coroner's cases, which may lead to an underestimate of the true number of acute poisoning cases (including those that result in early fetal death). Additionally, although serum concentrations of toxins and/or the amount of poison

consumed are likely recorded in the medical record, they are not abstracted to administrative data sets. Thus, the use of administrative data restricted our knowledge of the severity of each poisoning. In addition, these results are specific to the state of California, and thus results may not be generalizable to populations with different sociodemographic and socioeconomic distributions. Furthermore, because LMP date was the only available data point to estimate gestational age from birth certificates in California prior to 2007, fetal age estimates may be biased. In addition, the majority of the significant results show ORs close to 1, therefore the clinical utility of this study is unknown.

Finally, although the results are reported after adjusting for the concomitant diagnosis of substance abuse, acute poisoning may in and of itself indicate substance abuse. In essence, because they may reflect the same issue, adjustment may not be appropriate or straightforward. Concomitant diagnoses of substance and/or mental illness may be a result of selection bias; women with intentional acute poisoning hospital discharge may be more likely to be simultaneously diagnosed with substance abuse or mental illness than women discharged with other diagnoses. However, substance abuse and mental health screening, and appropriate referral opportunities, by a treating health care professional may have the potential to prevent acute poisonings and their associated adverse effects in high-risk women.

Future Directions

Future research in the field of intentional acute poisoning should make an effort to distinguish poison severity. Currently, neither the Injury Severity Score System nor hospital administrative data provides indications of the dose of substance implicated in a poisoning. Birth outcomes are likely to differ based on the specific substance and amount of substance ingested, and the time of the poisoning in relation to fetal development. Studies with sufficient power to examine the effects of specific agents on birth outcomes are necessary. Additionally, further investigation into the concept of an "all-or-nothing" effect of acute poisoning during pregnancy resulting in early fetal loss is warranted.

Implications for Practice

The most salient findings of this study for nursing practice include the observation that the number of self-inflicted poisonings during pregnancy decrease with increasing gestational age and that women who suffer a self-inflicted poisoning during pregnancy are often plagued by concomitant mental illness and substance abuse. Substance abuse and mental health screening in women of reproductive age and during pregnancy may help prevent acute poisonings in high-risk women. In addition, education and screening should be implemented following delivery to women who suffered an overdose to prevent future poisonings and to improve the health and well-being of the infant and mother.

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