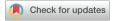
Original Research

Obstetrical and perinatal outcomes of patients with methamphetamine-positive drug screen on labor and delivery



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BACKGROUND: The incidence of methamphetamine use in reproductive-age women across the United States is increasing. The existing literature on methamphetamine use in pregnancy has indicated an elevated risk of adverse maternal and neonatal health outcomes.

OBJECTIVE: This study aimed to investigate pregnancy outcomes in patients with recent methamphetamine use compared with patients who received negative test results for methamphetamine at the time of delivery. **STUDY DESIGN:** A single-site retrospective cohort study from January to December 2015 was performed. Patients with a documented urine drug screen during the delivery encounter were identified from the electronic medical records. The outcomes of patients with methamphetamine-positive urine drug screens were compared with controls with urine drug screens negative for methamphetamine. Maternal outcomes of interest included placental abruption, hypertensive disorders, premature preterm rupture of membranes, postpartum hemorrhage, and preterm birth. Utilization of prenatal care, social work consults, and child protective services referrals were also recorded. Neonatal outcomes included birthweight, neonatal intensive care unit length of stay, Apgar scores, and perinatal mortality.

RESULTS: The 2 groups had similar demographic characteristics (age, multiparity, ethnicity), with the methamphetamine-positive group more likely to have no or limited prenatal care. Both groups engaged in polysubstance use. A methamphetamine-positive urine drug screen at the time of delivery carries an increased risk of abruption (odds ratio, 5.63; confidence interval, 1.21—26.21) but indicated no increased risk of maternal hypertensive disorders. Additional associated risks include preterm birth (odds ratio, 3.10; confidence interval, 1.44—6.68), lower Apgar scores at 1 and 5 minutes (*P*=.012 and *P*=.02, respectively), and increased perinatal mortality (odds ratio, 6.9; confidence interval, 1.01—47.4).

CONCLUSION: Positive urine drug testing for methamphetamines during labor admission confers considerable maternal and perinatal morbidity and mortality including an increased risk of placental abruption, preterm birth, and perinatal demise. Given the limited treatments for methamphetamine addiction, further research is urgently needed.

Key words: abruption, high-risk pregnancy, maternal morbidity, methamphetamine use, neonatal demise, stillbirth, stimulant, substance use disorder

Introduction

Methamphetamine (MA) has been recognized as a global public health threat. Within the United States, the market for MA is expanding, most notably in the West.² The Central Valley of California is a primary production area for MA in the state, and one of the largest suppliers in the United States.³ MA is a neurotoxic stimulant with both alpha- and beta-adrenergic effects and a half-life of 12 hours.⁴ It is inexpensive, widely available, and highly addictive.1 From 2008 to 2017, the prevalence of MA use in the United States doubled to 0.6%. Despite these findings, MA resources and treatment programs are

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2589-9333/\$36.00 © 2020 Elsevier Inc. All rights reserved. https://doi.org/10.1016/j.ajogmf.2020.100195 underwhelming in comparison with resources for opioid use.

The opioid epidemic has captured the attention of the US government and public, resulting in a large-scale mobilization of resources and treatment programs.⁵ Unlike the long-standing and well-accepted pharmacologic treatments for opioid addiction, there is a notable absence of useful pharmacotherapies for MA addiction.⁶ In marginalized communities that are affected by MA abuse, limited research and treatment programs perpetuate the problem. In 2015, 0.7% of reproductive-age women used MA in the previous month.^{7,8} MA use is associated with poverty,9 psychiatric comorbidities, 10 history of trauma, 11 and coexisting polysubstance use. MA is one of the most reported drugs used during pregnancy behind marijuana and opioids¹² and leads to adverse perinatal outcomes. 13-18

The consensus regarding MA use during pregnancy is that it is highly problematic. The existing literature on MA use in pregnancy indicates an elevated risk of preterm birth, low birthweight, and fetal or neonatal demise. 8,13,14,17,18 The findings on maternal outcomes are mixed regarding increased risk of hypertension and placental abruption. 13,15,18 Given the vasoconstrictive effects of MA, 4 there is likely a correlation. Confounding factors such as tobacco and polysubstance use, poverty, unstable housing, poor prenatal care, and nutrition complicate this research.

This study aimed to contribute to the existing literature regarding perinatal MA use and outcomes. For this study, we chose to investigate a cohort of women who received positive test results for MA on urine drug screen (UDS) at the time of admission to labor and delivery (L&D) compared with women who received negative test results for MA at the time of admission to L&D. The objective is to compare the maternal and neonatal outcomes in patients with MA-positive UDS during their L&D

AJOG MFM at a Glance

Why was this study conducted?

There are few studies on methamphetamine use in pregnancy. This study focuses on outcomes at a single-site safety-net hospital in central California.

Key findings

Positive urine drug screens for methamphetamine during admission for labor and delivery are associated with poor maternal and perinatal outcomes such as placental abruption, preterm birth, low birthweight, low Apgar scores, and perinatal demise.

What does this add to what is known?

The study findings support previous research regarding the risks of methamphetamine use in pregnancy and highlight the need for future research and treatments.

admission with the outcomes of patients with MA-negative UDS.

Methods

This was a single-site retrospective cohort study performed from January to December 2015 at Community Regional Medical Center (CRMC) in Fresno, California, which is a safety-net hospital with approximately 5000 to 6000 deliveries per year. This study was approved by the institutional review board at the University of California, San Francisco-Fresno, and CRMC. An Epic (Epic Systems, Verona, WI) query was performed by the CRMC data services to obtain the medical record number (MRN) of patients admitted to L&D in 2015 who also had a UDS present in their chart. Patient admissions without a documented UDS during the delivery encounter were excluded. Patients with multiple gestations were also excluded. No additional UDS was performed later during the hospital stay, and neonatal meconium testing information was not collected.

Maternal outcomes of interest were placental abruption, hypertensive disorders, premature preterm rupture of membranes, chorioamnionitis, postpartum hemorrhage, and preterm birth. Hypertensive disorders included gestational hypertension, preeclampsia with and without severe features, and chronic hypertension with superimposed preeclampsia. Neonatal outcomes assessed included gestational age, birthweight, Apgar scores, and perinatal demise.

Intrauterine and neonatal demise are categorized within perinatal demise. Of note, neonatal demise was not tracked after discharge from the hospital. Both maternal and neonatal outcomes were determined based on the review of provider documentation and the electronic medical record.

The following patient characteristics were collected: age, marital status, race or ethnicity, gravida and para, selfreported history of MA use, other substance use, extent of prenatal care, social work involvement, child protective services (CPS) involvement, and mode of delivery. Prenatal care was coded as no prenatal care, limited prenatal care (<3 visits), or routine prenatal care (≥ 3 visits), which was determined by the documentation in the history and physical or progress notes. Social work and CPS involvement was determined by the presence of a social work note and freetext documentation of communication with CPS. Other substance abuse was defined as the presence of barbiturates, benzodiazepine, cocaine, opiates, marijuana, or phencyclidine detected on UDS during the delivery encounter. Selfreported use of tobacco and alcohol was determined by the documentation in the history and physical or social work notes. History of MA use was defined as a patient reporting history of MA use during their lifetime in the admission note or social work notes or a previous positive UDS for MA in the chart.

The study design was chosen based on 3 factors. First, it has clinical relevance to the population of interest. Anecdotally, we noted sporadic triage or emergency room visits in pregnancy for MA-positive women who were often subsequently lost to prenatal care until delivery. Our main opportunity for identifying these women was at the time of admission to L&D with a positive UDS. Second, previous studies used similar approaches, such as recruiting subjects based on self-report data, using retrospective birth certificate data, or screening for a positive drug screen at any point during the pregnancy. Finally, serum drug screening is not used in routine clinical care, making UDS a pragmatic choice for identification of recent drug usage. At this institution, a UDS is selectively ordered by providers based on risk factors such as history of drug use, no prenatal care, or concerning clinical presentation such as placental abruption or hypertensive disorders. The UDS used by the institution was the Beckman Coulter Emit Amphetamine Assay (Beckman Coulter, Brea, CA), which was reported to have a sensitivity of 95% for detecting MA.¹⁹ Statistical analysis was performed with the chisquare test for categorical data and the Student's t test or analysis of variance (ANOVA) for continuous variables. Two-tailed *P*<.05 was considered statistically significant. Mann-Whitney U test was performed on demographic metrics with a skewness value of >0.9. Odds ratios (ORs) were calculated for primary outcomes with 95% confidence intervals (CIs). Multivariate analysis was conducted using generalized linear models as follows: binomial logistic regression using a logit link function for categorical data or Gaussian multiple regression using an identity link function for numerical data. ORs were calculated from the coefficients of logistic regression. Adjusted *P* values as reported were taken from the likelihood ratio test of the generalized model coefficients. Overall model performance was evaluated using ANOVA and was found to be a good fit for all reported outcomes. Independent variables accounted for the effects of marijuana on UDS, self-reported alcohol or tobacco use, and prenatal care utilization (no, limited, or routine care). All statistics were calculated using the software R version 3.6.3 (R Foundation, Vienna, Austria).

Results

The electronic medical record query obtained from the CRMC yielded 121 patients who received documented UDS during an L&D encounter (n=121). Of the 121 patients, 38.8% had a MApositive UDS (n=47) compared with the control group of 61.2% MA-negative UDS patients (n=74).

The demographics and characteristics of both groups are presented in Table 1. Both groups were similar in their demographics but differed with respect to patterns of polysubstance use. The groups consisted of predominantly single, multiparous Hispanic females with a mean age of 29 years. Patients who received positive test results for MA had an increased trend of concurrent use of opiates (12.8%) and marijuana (25.5%). Meanwhile, the MA-negative group had higher self-reported incidences of tobacco and alcohol use. Self-reported history of previous MA use was 93.6% in the MA-positive group and 83.8% in the MA-negative group. Only the differences in marijuana use reached statistical significance (P=.004).

Differences in social factors were markedly different between the 2 cohorts. The MA-positive group had a substantially higher rate of no prenatal care than the MA-negative group (42.6% vs 8.1%). In addition, the MA-positive group had higher utilization of both social work consults (100% vs 79.7%) and CPS involvement (89.4% vs 43.2%). Spontaneous vaginal delivery was similar for both the MA-positive and MAnegative groups. In the MA-positive group, there was a higher rate of operative vaginal deliveries (10.6% vs 4.1%) and vaginal birth after cesarean delivery (10.6% vs 5.4%), with a lower cesarean delivery rate (27.7% vs 40.5%) (Table 2).

The 2 statistically significant maternal outcomes identified were placental abruption and preterm birth (<37 weeks' gestation). The MA-positive group experienced greater risk of placental abruption (OR, 5.63; 95% CI, 1.21–26.21) and greater risk of preterm birth (OR, 3.10; 95% CI, 1.44-6.68) than the MA-negative group. There was a slight trend toward increased risk of hypertensive disorders in the MA-positive

TABLE 1 Demographic and other characteristics of study patients				
	MA-positive (n=47)	MA-negative (n=74)	<i>P</i> value	
Patient demographics				
Age (mean, SD)	29.2 (5.6)	29.800 (5.1)	.59	
Marital status, n (%)				
Single	40 (85.1)	60 (81.1)	.85	
Married	3 (6.4)	8 (10.8)		
Divorced	3 (6.4)	5 (6.8)		
Unknown	1 (2.1)	1 (1.4)		
Race or ethnicity, n (%)				
White non-Hispanic	14 (29.8)	21 (28.4)	.84	
Black	3 (6.4)	4 (5.4)		
Asian	1 (2.1)	1 (1.4)		
Hispanic or Latino	29 (61.7)	46 (62.2)		
Native American	0 (0)	2 (2.7)		
Obstetrical history				
Gravida (median, 25th-75th percentile)	5 (3-7)	5 (4-9)	.19 ^a	
Para-living (median, 25th—75th percentile)	3 (2-4)	3 (2-5)	.56ª	
Preterm (median, 25th—75th percentile	0 (0-1)	0 (0-0.25)	.91ª	
Self-report or documented MA history, n (%)			
Yes	44 (93.6)	62 (83.8)	.19	
No	3 (6.4)	12 (16.2)		
Unknown	0 (0)	0 (0)		
Other substance use, n (%)				
Barbiturates, UDS	0 (0)	1 (1.4)	N/A	
Benzodiazepine, UDS	1 (2.1)	2 (2.7)	1	
Cocaine, UDS	0 (0)	0 (0)	N/A	
Opiates, UDS	6 (12.8)	7 (9.5)	.79	
Marijuana, UDS	12 (25.5)	4 (5.4)	.004 ^b	
Phencyclidine, UDS	0 (0)	1 (1.4)	N/A	
Self-reported tobacco	11 (23.4)	21 (28.3)	.69	
Self-reported alcohol	2 (4.3)	9 (12.2)	.25	
Prenatal care visits, n (%)				
No	20 (42.6)	6 (8.1)	<.005 ^b	
Limited (<3 visits)	19 (40.4)	23 (31.1)		
Routine (≥3 visits)	8 (17.0)	45 (60.8)		
Unknown	0 (0)	0		
CPS involvement, n (%)	·			
Yes	42 (89.4)	32 (43.2)	<.005 ^b	
No	3 (6.4)	39 (52.7)		
Unknown	2 (4.3)	3 (4.1)		
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TABLE 1 Demographic and other characteristics of study patients (continued)

	MA-positive (n=47)	MA-negative (n=74)	<i>P</i> value
Social work involvement, n (%)	_	_	
Yes	47 (100)	79.7	.004 ^b
No	0	20.3	

CPS, child protective services; MA, methamphetamine; N/A, not available; SD, standard deviation; UDS, urine drug screen.

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group with an OR of 1.19 (95% CI, 0.55-2.58). A summary of the maternal outcomes assessed is presented in Table 2. Concomitant MA-positive screening and marijuana-positive screening on UDS were associated with increased risk of fetal mortality over MA alone with a relative risk ratio of 3.88 (95% CI, 2.54-5.23; P<0.038 [chisquare test]).

A summary of the perinatal outcomes assessed in MA-positive and MAnegative cohorts is presented in Table 3. gestational mean age MA-positive births was 35.9 weeks vs 36.9 weeks for the MA-negative group. Apgar scores at both 1 and 5 minutes were lower in the MA-positive group (1 minute, P=.012; 5 minutes, P=.02) than the MA-negative group. Perinatal demise was significantly higher in the MApositive group (OR, 6.9; 95% CI, 1.01-47.4) than the MA-negative group. Of interest, in the MA-positive group, 2 of 7 perinatal deaths were associated with a clinically suspected placental abruption on chart review, and the others were unexplained. Only 1 neonatal death in the MA-positive group occurred in the setting of regular prenatal care.

Comment **Principal findings**

This single-site, retrospective cohort study found substantial maternal and neonatal adverse outcomes in patients with an MA-positive UDS at the time of delivery. There was an increased risk of placental abruption, preterm birth, and lower 1- and 5-minute Appar scores in the MA-positive women on UDS. Moreover, the risk of perinatal mortality increased nearly 7-fold.

Results

Our findings indicated an elevated maternal risk consistent with the results of previous studies for most outcomes. A California-based study conducted by Gorman et al¹³ found that MA use during pregnancy was associated with greater odds of placental abruption (OR, 2.7; 95% CI, 4.9–6.3) and preterm birth (OR, 2.9; 95% CI, 2.7-3.1). Gorman et al¹³ also found an increased risk of hypertensive disorders of pregnancy with MA use which was not consistent with the hypertensive disorder results of our study. Similarly, a retrospective cross-sectional analysis of the National Inpatient Sample from 2004 to 2015 conducted by Admon et al15 reported greater odds of placental abruption (OR, 4.3; 95% CI, 3.6-5.0) and preterm birth (<37 weeks' gestation) (OR, 16.7; 95% CI, 15.3-18.0), along with an increased risk of preeclampsia (OR, 9.3; 95% CI, 8.2-10.4), the latter of which was not consistent with our study.

Similarly, our cohort of MA-positive patients indicated a trend toward an elevated incidence of hypertensive disorders. The lack of statistical significance was likely because of the overall elevated incidence of hypertensive disorders of >30% in both MA-positive and control groups. This is likely attributable to selection bias of the patients, because a UDS is often ordered in L&D in the setting of hypertension.

Clinical implications

The most alarming finding within our study was the significant increase in perinatal demise with an OR of 6.9 (P<.02). A previous study conducted by Gorman et al¹³ identified an elevated risk of intrauterine fetal demise (OR, 5.1; 95% CI, 3.7-7.2) and neonatal demise (OR, 3.1; 95% CI, 2.3–4.2). Good et al¹⁴ also noted an increase in neonatal mortality (4% vs 1.0%). A previous study using birth certificate data by Mischkot et al¹⁶ estimated a 1.4% risk of intrauterine demise in MA-affected pregnancies compared with a 0.4% risk in controls.

The higher OR reported in our study than in previous research may be because of health behaviors of the MApositive and MA-negative cohorts. MApositive patients were more likely to have no prenatal care and engaged in polysubstance use with marijuana. In the MA-negative cohort, despite high rates of self-reported use of tobacco, alcohol, and even MA, these patients were more likely to have prenatal care. We speculate that the behaviors of these 2 groups were different and perhaps the MA-negative group had different substance use patterns, along with more housing stability or social support, facilitating greater engagement in prenatal care and outcomes like affecting perinatal survival.

It is possible that MA exposure leads to physiological changes that can trigger preterm delivery or fetal demise and that long-term, repeated exposures or differing patterns of substance use may confer greater risk. Alternatively, hypertensive disorders and placental abruption caused by stimulant use are potentially the underlying explanation for the association with fetal demise. MA has known effects as a vasoconstrictor on the cardiovascular system.

Research implications

Additional studies are necessary to better characterize the dose- and timedependent effects of MA exposure on the mother and fetus. The safety profile of different routes of MA administration during pregnancy is unknown. One unanswered question, for example, is whether smoking MA is less likely to result in a fetal demise than intravenous use. Although this kind of question may seem at odds with the goal of MA abstinence in pregnancy, from a public health perspective, it would be relevant

^a Mann-Whitney U test; ^b P<.05 was considered statistically significant.

	MA-positive (n=47)	MA-negative (n=74)	OR (95% CI)	<i>P</i> value	Adjusted OR
Maternal hypertensive disorders	23 (48.9)	21 (28.4)	1.28 (0.6 -2.8)	.33	1.19 (0.55—2.58)
Placental abruption	8 (17.0)	2 (2.7)	7.4 (1.5 -36.5)	.01 ^a	5.63 (1.21 -26.21)
Premature preterm rupture of membranes	5 (10.6)	4 (5.4)	2.1 (0.5-8.1)	.48	1.77 (0.44-7.09)
Chorioamnionitis	4 (8.5)	4(5.4)	1.6 (0.39 6.80)	.77	2.28 (0.51 -10.18)
Postpartum hemorrhage	1 (2.1)	3 (4.1)	0.5 (0.05 -5.00)	.96	0.11 (0.01—1.30)
Preterm birth (<37 wk gestation)	19 (40.4)	11 (14.9)	3.9 (1.6-9.2)	.003 ^a	3.10 (1.44-6.68)
Mode of delivery				.23	
Spontaneous vaginal delivery	24 (51.1)	37 (50.0)			
Operative vaginal delivery	5 (10.6)	3 (4.1)			
Vaginal birth after cesarean delivery	5 (10.6)	4 (5.4)			
Cesarean delivery	13 (27.7)	30 (40.5)			

Categorical data are reported as n (percentage). Hypertensive disorders include pregnancy-induced hypertension and preeclampsia. Adjusted OR and 95% CI estimated with logistic regression with adjustments for tobacco, alcohol, marijuana, and prenatal care utilization. Data are presented as n (%).

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and potentially helpful during patient counseling, given the realities of addiction. Future research utilizing the principles of harm reduction, a public health approach that focuses on attenuating the harmful effects of addiction, might be particularly needed for MA use in pregnancy, given the current lack of effective interventions.

Furthermore, additional research is needed to clarify maternal cardiovascular risks. Although no cases were identified in this chart review, one of the long-term complications of MA use, that is, drug-induced cardiomyopathy, was encountered during obstetrical care in this population. The true incidence in reproductive-age women remains unknown. Finally, the robust evidence regarding treatments for opioid addiction is not mirrored in the MA literature. More work is needed in evaluating outcomes of wraparound services and behavioral and pharmacotherapy treatments for MA addiction.

Strengths and limitations

Apart from the normal limitations within a retrospective design, there are several other limitations within this study. The data gathering for the study relied on data managers within the hospital to identify patients with both an admission to L&D and a UDS. It is possible that some patients were missed during the MRN gathering phase. Of the estimated 5000 deliveries per year at CRMC, nearly 1% of pregnancies were affected by MA use—which is consistent with but on the lower end of the national average of MA use estimated to be between 0.7% and 5.2%.

Moreover, it is likely that some women who were using MA during pregnancy did not receive a UDS and were not included in the study. In addition, MA assays can give false positive results from over-the-counter substances such as pseudoephedrine or ranitidine, so there may be false positive results in the MA-positive cohort. The

72-hour half-life of MA in a UDS gives a single view into substance use patterns. We did not obtain longitudinal data on daily or intermittent use throughout pregnancy, the preferred route of administration, or meconium drug screens of neonates at delivery.

With respect to patient characteristics, the study controlled for dissimilarities in the use of marijuana, tobacco, and alcohol—all of which are confounding variables which can affect perinatal outcomes. The increased relative risk of fetal death seen in patients with positive UDS for both MA and marijuana is suggestive of possible increased risk with polysubstance use. We did not report on psychiatric medications in this study. Finally, there are socioeconomic confounders, such as poverty and homelessness, which were not assessed, but could explain the discrepancies within our study in comparison with other studies.

There are several strengths within this study. Patients were selected based on the

CI, confidence interval; MA, methamphetamine; OR, odds ratio.

^a P<.05 was considered statistically significant.

TABLE 3 Perinatal outcomes in MA-positive and MA-negative cohorts

	MA-positive (n=47)	MA-negative (n=74)	OR (95% CI)	<i>P</i> value	Adjusted OR	Adjusted <i>P</i> values
Gestational age in wk	35.9	36.9		.15		.95
Birthweight in g	2826±585	3112±917		.04 ^a		.06
Apgar at 1 min	6.2±2.9	7.5±1.6		.008 ^a		.012 ^a
Apgar at 5 min	7.5±3.0	8.6±1.2		.001 ^a		.02 ^a
Perinatal demise	7 (14.9)	1 (1.4)	12.8 (1.5—17.6)	.01 ^a	6.9 (1.01-47.40)	.02 ^a

Categorical data are reported as n (percentage). Continuous data are reported as mean ±SD. Adjusted OR and 95% CI estimated with logistic regression with adjustments for tobacco, alcohol, marijuana, and prenatal care utilization. Adjusted P values controlling for tobacco, alcohol, marijuana, and prenatal care utilization.

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documented UDS at the time of delivery, which provides a snapshot at the time of the delivery encounter for high-risk women. The chart review allowed for the evaluation of some characteristics that are not often found in large database studies, such as involvement of social work and CPS consults. Finally, the study population (60% Hispanic or Latina) is underrepresented in medical research.

Conclusions

The ethnically diverse and vulnerable population described in our cohort study and the alarming maternal and perinatal complications associated with MA use indicate an urgent need for the development of resources in endemic areas. Emphasizing the perinatal risks, including the risk of fetal demise, could be used when advocating for funding for social services and MA treatment options. Providers should strive to provide nonjudgmental and nonpunitive care for pregnant women with MA addiction to encourage engagement in prenatal care and hopefully improve L&D outcomes. We call for further efforts to study effective interventions for MA addiction in pregnancy.

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CI, confidence interval; MA, methamphetamine; OR, odds ratio; SD, standard deviation.

^a P<.05 was considered statistically significant.

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