Risk of Fetal Death Associated With Maternal Drug Dependence and Placental Abruption: A Population-Based Study

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Abstract

Objective: Substance use in pregnancy is associated with placental abruption, but the risk of fetal death independent of abruption remains undetermined. Our objective was to examine the effect of maternal drug dependence on placental abruption and on fetal death in association with abruption and independent of it.

Methods: To examine placental abruption and fetal death, we performed a retrospective population-based study of 1 854 463 consecutive deliveries of liveborn and stillborn infants occurring between January 1, 1995 and March 31, 2001, using the Canadian Institute for Health Information Discharge Abstract Database.

Results: Maternal drug dependence was associated with a tripling of the risk of placental abruption in singleton pregnancies (adjusted odds ratio [OR] 3.1; 95% confidence intervals [CI] 2.6–3.7), but not in multiple gestations (adjusted OR 0.88; 95% CI 0.12–6.4). Maternal drug dependence was associated with an increased risk of fetal death independent of abruption (adjusted OR 1.6: 95% CI 1.1–2.2) in singleton pregnancies, but not in multiples. Risk of fetal death was increased with placental abruption in both singleton and multiple gestations, even after controlling for drug dependence (adjusted OR 11.4 in singleton pregnancy; 95% CI 10.6–12.2, and 3.4 in multiple pregnancy; 95% CI 2.4–4.9).

Conclusion: Maternal drug use is associated with an increased risk of intrauterine fetal death independent of placental abruption. In singleton pregnancies, maternal drug dependence is associated with an increased risk of placental abruption.

Key Words: Fetal death, drug dependence, placental abruption, substance use, perinatal mortality

Competing Interests: None declared.

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Résumé

Objectif : Bien que la consommation d'alcool et de drogues au cours de la grossesse soit associée au décollement placentaire, le risque de mort fœtale n'étant pas associé à ce dernier demeure indéterminé. Notre objectif était d'examiner l'effet de la dépendance de la mère aux drogues sur le décollement placentaire, ainsi que sur la mort fœtale attribuable à ce dernier et sur la mort fœtale n'y étant pas attribuable.

Méthodes : Pour examiner le décollement placentaire et la mort fœtale, nous avons mené une étude rétrospective en population générale portant sur 1 854 463 accouchements consécutifs de nourrissons vivants et mort-nés, survenus entre le 1er janvier 1995 et le 31 mars 2001, au moyen de la Base de données sur les congés des patients de l'Institut canadien d'information sur la santé.

Résultats : La dépendance de la mère aux drogues a été associée à un risque triplé de décollement placentaire dans le cas des grossesses monofœtales (rapport de cotes [RC] corrigé, 3,1; intervalle de confiance [IC] à 95 %, 2,6–3,7), mais non pas dans celui des grossesses multiples (RC corrigé, 0,88; IC à 95 %, 0,12–6,4). La dépendance de la mère aux drogues a été associée à une hausse du risque de mort fœtale n'étant pas attribuable au décollement (RC corrigé, 1,6; IC à 95 %, 1,1–2,2) dans le cas des grossesses monofœtales, mais non pas dans celui des grossesses multiples. Le risque de mort fœtale connaissait une hausse en présence d'un décollement placentaire, tant dans le cas des grossesses monofœtales que dans celui des grossesses multiples, et ce, même à la suite de la neutralisation de l'effet de la dépendance aux drogues (dans le cas des grossesses monofœtales : RC corrigé, 11,4; IC à 95 %, 10,6–12,2; dans celui des grossesses multiples : RC corrigé, 3,4; IC à 95 %, 2,4–4,9).

Conclusion : La consommation de drogues par la mère est associée à une hausse du risque de mort fœtale intra-utérine, peu importe la présence ou non d'un décollement placentaire. Dans le cas des grossesses monofœtales, la dépendance de la mère aux drogues est associée à une hausse du risque de décollement placentaire.

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Table 1. Participant characteristics*

Maternal characteristic in the index pregnancy	Singleton deliveries (n = 1 828 319)	Multiple deliveries (n = 26 164)	All deliveries (n = 1 854 463)
Mean age in years (SD)	28.3 (5.7)	29.6 (5.4)	28.3 (5.7)
Preeclampsia	60 721 (3.3)	2 273 (8.7)	62 994 (3.4)
Hypertension	52 868 (2.9)	1 248 (4.8)	54 116 (2.9)
Diabetes mellitus	11 637 (0.64)	144 (0.55)	11 781 (0.64)
Thrombophilia	1 813 (0.10)	51 (0.19)	1 864 (0.10)
Drug dependence	3 255 (0.18)	45 (0.17)	3 300 (0.18)
Antepartum hemorrhage	21 095 (1.2)	581 (2.2)	21 676 (1.2)
Placenta previa	12 790 (0.70)	276 (1.1)	13 066 (0.70)
Placental abruption	23 903 (1.3)	586 (2.2)	24 492 (1.3)
Mode of delivery			
Vaginal	1 315 597 (72.0)	14 623 (55.9)	1 330 220 (71.7)
Instrumental (forceps and/ or vacuum)	214 152 (11.7)	3116 (11.9)	217 268 (11.7)
Caesarean section	298 570 (16.3)	8 425 (32.2)	306 995 (16.6)
Poor fetal growth	37 178 (2.0)	2 317 (8.9)	39 495 (2.1)
Intrauterine fetal death	8 318 (0.45)	495 (1.9)	8 813 (0.48)

*Data are presented as number (%), unless otherwise specified

SD: Standard deviation

INTRODUCTION

Placental abruption, the premature separation of the placenta from the uterus, accounts for about 12% of all perinatal deaths.[1] Although maternal substance use in pregnancy is believed to be a precipitant of placental abruption, this observation has been limited to studies that were of insufficient size to measure perinatal mortality.[2] However, previous epidemiological studies of the burden of placental abruption on the fetus did not evaluate the influence of maternal substance use.[1,3] We sought to determine the effect of maternal drug dependence on placental abruption and on fetal death in association with abruption and independent of it.

METHODS

We performed a retrospective population-based study. Data were obtained from the Canadian Institute for Health Information Discharge Abstract Database, an administrative database that contains up to 16 discharge diagnoses, coded according to the International Classification of Diseases (9th revision: ICD-9).

We included all consecutive deliveries of a liveborn or stillborn infant in a Canadian hospital from January 1, 1995, to March 31, 2001. Deliveries in the province of Quebec, the Northwest Territories, Yukon, and Nunavut were not included because these regions do not contribute a complete data set to the Canadian Institute for Health Information Discharge Abstract Database.

We assessed the risk of placental abruption and fetal death in association with maternal drug dependence. We used ICD-9 codes to define a delivery, study exposures, covariates, and outcomes (Appendix). We have previously reported the effect of folic acid fortification on the rate of placental abruption from this data set.[4]

Statistical Analysis

The main analysis was the association between non-tobacco maternal drug dependence in pregnancy and the risk of placental abruption. In a second analysis, we explored the risk of intrauterine fetal death in the presence of either placental abruption or maternal drug dependence.

Logistic regression analysis was used to generate crude and adjusted odds ratios (OR) and 95% confidence intervals (CI). Adjustment variables were based on those from other studies.[1,3] (Tables 2 and 3). Statistical analyses were performed using SAS, Version 8.02 (SAS Institute, Cary, NC), with a 2-sided *P*-value set at less than 0.05. All patient identifiers were removed prior to database extraction, and permission to conduct this study was granted by the Research Ethics Board of Mount Sinai Hospital, Toronto.

Table 2. Risk of placental abruption in association with maternal drug dependence

Measure	Singleton deliveries (n = 1 828 319)	Multiple deliveries (n = 26 164)	All deliveries (n = 1 854 463)
Number of placental abruptions	23 903	586	24 492
Crude OR (95% CI)	3.4 (2.9–4.0)	0.99 (0.14–7.2)	3.3 (2.8–4.0)
Adjusted OR (95% CI)*	3.1 (2.6–3.7)	0.88 (0.12–6.4)	3.1 (2.6–3.6)

*Adjusted for maternal age > 35 years, preeclampsia or hypertension, intrauterine fetal death, poor fetal growth, antenatal hemorrhage, and placenta previa

OR: odds ratio; CI: confidence interval.

Table 3. Risk of intrauterine fetal death in association with placental abruption and maternal drug dependence

Antenatal risk factor	Measure	Singleton deliveries (n = 1 828 319)	Multiple deliveries (n = 26 164)	All deliveries (n = 1 854 463)
	Number of fetal deaths	8318	495	8813
Drug dependence	Crude OR (95% CI)	2.3 (1.7–3.3)	2.4 (0.6–10.0)	2.3 (1.7–3.3)
	Adjusted OR (95% CI)*	1.6 (1.1–2.2)	0.75 (0.73–1.1)	1.6 (1.1–2.2)
Placental abruption	Crude OR (95% CI)	10.7 (10.0–11.4)	3.4 (2.4–4.9)	10.3 (9.7–11.0)
	Adjusted OR (95% CI)†	11.4 (10.6–12.2)	3.4 (2.4–4.9)	11.4 (10.6–12.2)

*Adjusted for maternal age > 35 years, preeclampsia or hypertension, diabetes mellitus, thrombophilia, poor fetal growth, antenatal hemorrhage, placenta previa, instrumental delivery or Caesarean section, and placental abruption.

†Adjusted for maternal age > 35 years, preeclampsia or hypertension, diabetes mellitus, thrombophilia, poor fetal growth, antenatal hemorrhage, placenta previa, instrumental delivery or Caesarean section, and drug dependence.

OR: odds ratio, CI: confidence interval.

RESULTS

Of the 1 854 463 deliveries included, 98.6% were singleton pregnancies (Table 1). Placental abruption occurred in 13.1 per 1000 singleton deliveries (95% CI 12.9–13.2) and 22.5 per 1000 multifetal deliveries (95% CI 20.7–24.4).

Maternal drug dependence was diagnosed in approximately 0.18% of all gestations (Table 1). Maternal drug dependence was associated with a tripling of the risk of placental abruption in singleton pregnancies (adjusted OR 3.1; 95% CI 2.6–3.7) but not in multiple gestations (adjusted OR 0.88; 95% CI 0.12–6.4) (Table 2).

After adjusting for several covariates, including placental abruption, we found maternal drug dependence in singleton pregnancies to be independently associated with a 1.6 times higher risk of fetal death (95% CI 1.1–2.2) (Table 3). The risk of fetal death was increased with placental abruption in both singleton and multiple gestations, even after we adjusted for several covariates (adjusted OR 11.4; 95% CI 10.6–12.2, and 3.4; 95% CI 2.4–4.9, respectively) (Table 3).

DISCUSSION

We found an elevated risk of placental abruption and intrauterine fetal death associated with maternal drug dependence in singleton pregnancies. To our knowledge, this is the first study to demonstrate an increased risk of intrauterine fetal death associated with maternal drug use that may be independent of a placental abruption. Nonetheless, placental abruption was also strongly associated with a higher risk of fetal death in both singleton and multiple pregnancies.

We did not possess specific information about other sociodemographic characteristics such as ethnicity, the type of drug dependence, or cigarette smoking (a known risk factor for placental abruption[3]), or about chromosomal abnormalities or structural anomalies, nor could we quantify the degree of placental separation. Our findings may have been biased by the possibility that women found to have a placental abruption were more likely to be screened for illicit substances.[5] However, the size of this study allowed us to estimate with confidence the risk of intrauterine fetal death that is associated with maternal substance use during pregnancy.

The rate of placental abruption in our study parallels the findings in a recent study in the United States, which identified rates of 0.94% to 1.43% in the years 1999–2001.[3] Furthermore, in a retrospective cohort study of 53 000 singleton births in the United States, placental abruption was found to be associated with a nearly nine fold increase in the risk of stillbirth,[1] approximately the same as our estimate. Although the reported rate of cocaine and other substance use in pregnancy may vary according to the population studied,[2] the prevalence of drug dependence of 0.18% that we found may be an underestimate of the true rate. For example, in one multicentre study, 1.2% of pregnant women tested serologically positive for cocaine, although only 9% of these women had disclosed its use.[6] Hence, the association between fetal death and drug dependence may be stronger.

Only a minority of all placental abruptions (2.4%) and fetal deaths (5.6%) in our study occurred in multiple pregnancies. This likely reduced our ability to evaluate, with adequate statistical power, maternal drug dependence as a related risk factor for either abruption or fetal death in women with a multiple pregnancy. We could not distinguish between twin and triplet pregnancies, or determine whether they were monochorionic or dichorionic; however, the relative risk of fetal death related to placental abruption was less pronounced in all multiple pregnancies in our study group (OR 3.4) than in singleton pregnancies (OR 11.4). This may be partly explained by the greater use of fetal surveillance among multiple pregnancies and the higher rate of Caesarean section before term,[7] leading to earlier delivery.

We found that drug dependence in pregnancy was modestly associated with fetal death, even after adjusting for a diagnosis of preeclampsia and both placental abruption and placenta previa. Placenta previa is associated with maternal cocaine use in pregnancy.[2,8] The unrecorded presence of maternal poverty, domestic violence, or HIV or other sexually transmitted diseases may partly explain the association between fetal death and drug use,[9] but these findings clearly warrant further study. A strategy that is aimed at reducing substance use in pregnancy could reduce the risk of placental abruption and fetal death.

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REFERENCES

1. Ananth CV, Berkowitz GS, Savitz DA, Lapinski RH. Placental abruption and adverse perinatal outcomes. JAMA 1999;282:1646–51.
2. Addis A, Moretti ME, Ahmed SF, Einarson TR, Koren G. Fetal effects of cocaine: an updated meta-analysis. Reprod Toxicol 2001;15:341–69.
3. Ananth CV, Oyelese Y, Yeo L, Pradhan A, Vintzileos AM. Placental abruption in the United States, 1979 through 2001: temporal trends and potential determinants. Am J Obstet Gynecol 2005;192:191–8.
4. McDonald SD, Vermeulen M, Ray JG. Placental abruption and infarction in association with folic acid food fortification. Epidemiology 2005;16:419–20.
5. Birchfield M, Scully J, Handler A. Perinatal screening for illicit drugs: policies in hospitals in a large metropolitan area. J Perinatol 1995;15:208–14.
6. Shiono PH, Klebanoff MA, Nugent RP, Cotch MF, Wilkins DG, Rollins DE, et al. The impact of cocaine and marijuana use on low birth weight and preterm birth: a multicenter study. Am J Obstet Gynecol 1995;172:19–27.
7. Smith-Levitin M, Skupski DW, Chervenak FA. Multifetal pregnancies. Curr Opin Obstet Gynecol 1995;7:465–71.
8. Macones GA, Sehdev HM, Parry S, Morgan MA, Berlin JA. The association between maternal cocaine use and placenta previa. Am J Obstet Gynecol 1997;177:1097–100.
9. Stein JA, Lu MC, Gelberg L. Severity of homelessness and adverse birth outcomes. Health Psychol 2000;19:524–34

APPENDIX.

International Classification of Diseases, 9th revision (ICD-9) codes used for the current study

A. Obstetrical delivery: 640–676 and ending with a fifth-digit subclassification of 1, any V27, or a patient service code 51.

B. Drug dependence in pregnancy: 648.3

C. Placental abruption: 641.2

D. Intrauterine fetal death: 656.4

E. Other variables:

- Multiple pregnancy: 651.0–651.9
- Poor fetal growth: 656.5
- Antepartum hemorrhage: 641.8, 641.9
- Placenta previa : 641.0, 641.1
- Preeclampsia: 642.4–642.7
- Hypertension: 642.0–642.3, 642.9
- Diabetes mellitus: 250.0–250.9, 648.0
- Thrombophilia: 671.3–671.5, 451.1, 451.2, 451.8, 451.9, 415.1