

Impact of MOUD in Pregnancy on Fetal Growth and Biometry: A Case-Control Study

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Background

- As many as 6.6% of pregnant patients use prescription opioids, with 21.2% of those reporting misuse. [1]
- Medications for opioid use disorder (MOUD), including methadone and buprenorphine, improve maternal outcomes by reducing maternal mortality. [2]
- However, exposure to any opioids including MOUD can lead to neonatal opioid withdrawal syndrome (NOWS). [2]
- Buprenorphine is preferred over methadone and associated with a lower rate of NOWS and higher birth weights. [3]
- Better understanding of the effect of MOUD on fetal biometry is necessary to understand the biological impact on fetal development, placental function, and nutrient transfer.
- Furthermore, results could guide better dosing and medication management guidelines in pregnancy.

Hypothesis

MOUD exposure in pregnancy will result in a smaller increase in fetal growth over time and reduced fetal biometric measurements in the third trimester compared to unexposed controls.

Methods

Study Design:

- Secondary analysis of a prospective case-control, multi-site study of pregnant patients with opioid use disorder (OUD) on MOUD vs controls (no exposure).

Data Collection:

- Maternal and neonatal characteristics, along with ultrasound data from 2nd and 3rd trimester ultrasounds, were abstracted from electronic medical records.

Statistical Analysis:

- Fisher's exact tests and t-tests for between group comparisons
- Repeated measures ANOVA analyzed growth differences between groups over pregnancy.
- Significance was set at $p < 0.05$.

Table 1: Maternal and Neonatal Characteristics

Maternal Characteristics		Control (n=27)	Opioid-exposed (n=42)	p-value
Maternal Age (years)		33 ±4	32 ±5	0.51
Maternal Race	White	24 (89%)	39 (93%)	0.57
	Black	2 (7%)	5 (12%)	0.55
Hispanic		1 (4%)	0	0.21
BMI		30.4 ±5.1	31.2 ±7.7	0.63
Smoker		0	32 (76%)	<0.001*
Pregestational Diabetes		1 (4%)	2 (5%)	0.83
Gestational Diabetes		1 (4%)	2 (5%)	0.83
Chronic Hypertension		2 (7%)	4 (10%)	0.76
Hypertension of Pregnancy		5 (19%)	6 (14%)	0.64
Fetal Growth restriction		3 (11%)	7 (17%)	0.50
Gestational age at delivery (weeks)		39 ±1	38 ±2	0.05
Neonatal characteristics				
Head circumference (cm)		34.2 ±4.5	33.5 ±1.7	0.35
Neonatal length (cm)		50.7 ±2.4	48.0 ±3.2	<0.001*
Birth weight (grams)		3519 ±538	2993 ±552	<0.001*

Results: Preliminary Analysis of Fetal Biometry Differences between MOUD-Exposed and Control Pregnancies

Biometric Variables	S.E.	Wald	Significance
Head circumference	0.162	0.098	0.099
Abdominal Circumference	-0.149	0.134	0.267
Femur Length	-0.342	0.332	0.304
Biparietal Diameter	-0.693	0.321	0.031
Estimated Fetal Weight	0.014	0.011	0.211

Results

- Baseline demographics were similar between groups aside from high rates of smoking in the opioid-exposed group.
- There were no differences in second trimester fetal biometry measurements between groups ($p > 0.05$).
- Unadjusted analysis of third trimester biometry revealed significantly smaller head circumference, abdominal circumference, femur length, biparietal diameter (BPD) and estimated fetal weight in the opioid-exposed group compared to the control group ($p < 0.001$).
- After controlling for smoking, regression models show a **statistically significant difference in third trimester biparietal diameter ($p = 0.031$) only.**

Conclusions

- Our data analysis **highlights a significant third trimester BPD difference in controls versus MOUD-exposed pregnancies, while other third trimester metrics and all second trimester ultrasound measurements show no significant differences after accounting for smoking.**
- These preliminary results may suggest that **later fetal development, specifically BPD, is more sensitive to methadone or buprenorphine exposure.**
- Inadequate brain development causes smaller BPD, which may lead to **neurological sequelae, low resistance to diseases of blood pressure, and an underdeveloped brain** after birth.
- Further analysis will focus on additional confounders, comparing methadone and buprenorphine outcomes, and considering MOUD dosing. **Clinical implications could include closer monitoring of fetal biometry, specifically BPD, in MOUD pregnancies and possible adjustments in prenatal care.**

References

- [1]: Ko JY, D'Angelo DV, Haight SC, et al. *Vital Signs: Prescription Opioid Pain Reliever Use During Pregnancy* — 34 U.S. Jurisdictions, 2019. *MMWR Morb Mortal Wkly Rep* 2020;69:897–90
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- [3]: Mother To Baby | Fact Sheets [Internet]. Brentwood (TN): Organization of Teratology Information Specialists (OTIS); 1994-. Buprenorphine. 2023 Aug. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK582609/>