The Association between Prenatal Marijuana Use and Stillbirth

Janelle Berridge, BSN, RN and Jessica Schmidt, BSN, RN
Columbia University School of Nursing, New York, NY

(Johnson, 2019)

BACKGROUND

- Cannabis is the most used recreational drug during pregnancy, particularly in women aged 15-24 (Young-Wolff, 2019)
- Prevalence of prenatal marijuana use has increased by nearly 30% from 2012-2017 (Young-Wolff, 2019)
- Cannabinoids cross the human placenta and increase the permeability of the placenta to other toxins (Petrangelo, 2018)
- It is believed that cannabinoids affect placental vasculature and decrease blood flow to the fetus (Luke, 2019)
- It is unclear how prenatal marijuana use affects maternal and birth outcomes, though it is thought to cause adverse effects such as low birth weight, preterm birth and stillbirth.

OBJECTIVES

1. Determine the association between prenatal marijuana use and stillbirth.
2. Identify limitations in current research in order to guide future studies.

METHODS

- A priori protocol
- 2 databases searched: PubMed, Embase
- Inclusion criteria:
  - Human studies
  - Full text articles in English
  - Studies that included prenatal marijuana use as an exposure and stillbirth as a birth outcome
  - Articles within the last 10 years

RESULTS

- Four retrospective cohorts and one case control studies
- Four studies relied on maternal self report of marijuana use
- One study used maternal blood and umbilical cord testing to detect prenatal cannabis use
- **One study did not find any statistically significant association with stillbirth (Warshak, 2015); one study found a positive association with intrapartum stillbirth, but not overall stillbirth (Luke et al., 2018)**
- **The three remaining studies found statistically significant positive associations between prenatal marijuana use and stillbirth**
  - Odds ratios ranged 1.25 – 2.83.

Author (Year)	Study Characteristics	Cannabis Testing	Controlled variables	Study Findings
Corsi et al. (2019)	Matched retrospective cohort study consisting of 661,617 pregnancies across Ontario	Maternal self-report in medical records	Matched cohort to account for following confounders: age, parity, area-income quintiles, prepregnancy BMI, gestational weight gain, self-reported substance use during current pregnancy (including tobacco smoking), mental health conditions, antenatal care, and year of birth.	Statistically significant increased risk of stillbirth among cannabis users compared to non-users. • Adjusted relative risk: **1.25; 95% CI 1.05-1.48**
Luke et al. (2018)	Retrospective cohort study consisting of 243,140 pregnancies across British Columbia	Maternal self-report in medical records	• Maternal age • Pre-pregnancy BMI • Tobacco use • Alcohol use • Other substance use • Socioeconomic status • Race/ethnicity	After adjustment, the association between cannabis use in pregnancy and overall stillbirth and antepartum stillbirth *did not* reach statistical significance: • Overall stillbirth aOR: **1.38; 95% CI 0.95-1.99** • Antepartum stillbirth aOR: **1.34; 95% CI 0.88-2.06** After adjustment, there was a statistically significant increased odds of intrapartum stillbirth in cannabis users: • Intrapartum stillbirth aOR: **2.84; 95% CI 1.18-6.82**
Petrangelo et al. (2018)	Retrospective cohort study consisting of 12,578,557 pregnancies across 44 US states	Maternal self-report in medical records	• Maternal age • Race • Hospital location • Teaching hospital • Income • Insurance • Multiple pregnancy • Pre-existing diabetes mellitus • Smoking • Hypertension • Alcohol use • Other illicit drug use	Statistically significant increased odds of stillbirth among cannabis users compared to non-users. • Adjusted odds ratio **1.50; 95% CI 1.39-1.62**
Varner et al. (2014)	Case control study consisting of 663 stillbirth deliveries and 1932 live birth deliveries from five geographically diverse regions in the US	Maternal blood and umbilical cord testing	• Unable to control for confounders due to small sample size	Positive cord homogenate THC was associated with an increased odds of stillbirth. • All pregnancies OR: **2.34; 95% CI 1.13-4.81** • Nonanomalous, singleton pregnancies excluding intrapartum stillbirth OR: **2.83; 95% CI 1.34-5.99**
Warshak et al. (2015)	Retrospective cohort study consisting of 6,468 pregnancies at the University of Cincinnati Medical Center	Maternal self-report in medical records and toxicology screens on high risk mothers only	• Maternal age • Race • Parity • BMI class • Prenatal care	After adjustment, the association between cannabis use in pregnancy and overall stillbirth and antepartum stillbirth *did not* reach statistical significance: • All pregnancies aOR: **1.03; 95% CI 0.62-1.72** • Amongst tobacco nonusers aOR: **1.16; 95% CI 0.57-2.38** • Amongst tobacco users aOR: **1.0; 95% CI 0.47-2.12**

LIMITATIONS

Limitations of current research include:

- Maternal self report may have resulted in significant underreporting and recall bias
- Unclear how frequently marijuana screenings were done throughout pregnancy in each study
- Certain studies were not able to adjust for major confounders such as tobacco use, other substance and alcohol use, socioeconomic status, pre-pregnancy BMI and intrapartum infections
- Frequency, dosing, and timing of prenatal marijuana use were not studied
- Synthetic marijuana and route of use (ingestion, vaping, smoking) were not studied

CLINICAL IMPLICATIONS

- Marijuana is becoming increasingly legalized across the US
- More women of childbearing age are smoking marijuana
- Incidence of prenatal marijuana use is on the rise
- We recommend that providers conduct universal screenings via questionnaires and discuss marijuana use with every pregnant woman
- Providers should educate women on the risks that are associated with prenatal marijuana use, particularly stillbirth, and supply patients with appropriate resources including https://mothertobaby.org

CONCLUSION

- There is a positive association between prenatal marijuana use and stillbirth
- Further research that reduces recall bias and investigates frequency, dosing, timing and route of use is needed
- With the incidence of prenatal marijuana use continuing to rise, providers should be diligent in conducting universal screenings with questionnaires and in discussing marijuana use with every pregnant women
- Patient education can be provided through fact sheets and counseling

REFERENCES

Corsi, D.J. PhD, Walsh, L. MSc, Weiss, D. PhD,…, Walker, M. MD. (2019). Association Between Self-reported Prenatal Cannabis Use and Maternal, Perinatal, and Neonatal Outcomes. *Journal of American Medical Association, 322*(2), 145-152.

Luke, S., Hutcheon, J., & Kendal, T. (2019). Cannabis Use in Pregnancy in British Columbia and Selected Birth Outcomes. Journal of Obstetrics and Gynaecology Canada. Retrieved from https://www.jogc.com/article/S1701-2163(18)30909-5/pdf

Johnson, H., Lee, S. (2019). Marijuana and Pregnancy Stick [Image]. Retrieved from: https://www.insider.com/marijuana-pregnancy-breastfeeding-safe-risks-research-2019-2

Petrangelo, A., Czuzoj-Shulman, N., Balayla, J., & Abenhaim, H. (2018). Cannabis Abuse or Dependence During Pregnancy: A Population-Based Cohort Study on 12 Million Births. *Journal of Obstetrics and Gynaecology Canada*. doi: https://doi.org/10.1016/j.jogc.2018.09.009

Varner, M., Silver, R., Hogue, C., Willinger, M., Parker, C., Thorsten, V., …, Reddy, U. (2014). Association between Stillbirth and Illicit Drug Use and Smoking During Pregnancy. Obstetrics & Gynecology, 123(1), 113-125. https://doi.org/10.1097/AOG.0000000000000052

Warshak, C.R., Regan, J., Moore, B., Magner, K., Kritzer, S., Hook, J.V. (2015). Association between marijuana use and adverse obstetrical and neonatal outcomes. *Journal of Perinatology, 35*(12), 991-995.

Young-Wolff, K.C., Sarovar, V., Lue-Yen, T., …, Goler, N. Self-reported Daily, Weekly, and Monthly Cannabis Use Among Women Before and During Pregnancy. *JAMA Network Open*, 2019; 2 (7): e196471 DOI: 10.1001/jamanetworkopen.2019.6471

Berridge: jb4195@cumc.columbia.edu; Schmidt jms2425@cumc.columbia.edu