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Outcomes of Prenatal Marijuana Use

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Scholarly Project Paper

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Introduction

Holistic therapy is becoming a national trend and a lot of people are turning to marijuana for its potential benefits. Even pregnant women are using marijuana to manage nausea and vomiting. [1] Currently, medical marijuana is legal in 33 states and the District of Columbia, with 10 states also legalizing its recreational use. [1] In the US, between 16.2% of pregnant women are using marijuana daily.[2] In a study surveying 785 pregnant women, 79% reported perceiving little to no harm in prenatal marijuana use.[3] Due to the increase in its use and the common perception of being harmless, it is important that we determine whether there is an association between adverse fetal outcomes and marijuana use during pregnancy.

Studies have shown a correlation between neurodevelopment disruption, decreased birth weight, and increased NICU admissions with prenatal marijuana use. [1,4] However other recent studies have shown no significant impact on fetal growth, rates of stillbirth and preterm delivery, or congenital malformations.[5,6] One study concluded that there is a significantly lower proportion of infants admitted to the NICU compared to nonusers.[6] In a recently reported California study comparing 2,890,555 mothers who used opioid, cocaine, cannabis, amphetamine, other, or polysubstance showed that mothers with reported drug abuse/dependence during pregnancy were at an increased risk of having a preterm birth and all groups except those using cannabis were at risk of having an early term birth. [7]

It is apparent that studies on the effects of prenatal exposure to marijuana have conflicting results and conclusions.[4] However, the American College of Obstetricians and Gynecologists(ACOG) released guidelines in 2017 advising physicians to inquire about marijuana use in pregnant and breastfeeding mothers and encourage them to discontinue use.[8] It is difficult to know whether marijuana is independently responsible for negative birth outcomes considering tobacco, nutrition, stress and other factors also have an effect on birth outcome and are heavily associated with prenatal marijuana use.[9]

With prenatal marijuana use being on the rise, physicians could benefit from well designed studies assessing the effects of prenatal exposure to marijuana in humans. This retrospective study aims to investigate the birth outcomes of neonates born to mothers who used marijuana during their pregnancy and compare to those women who used other prenatal illicit drugs with and without marijuana as well as women who did not use illicit drugs at all. The results of this study may be useful for future research on the benefits and harms associated with prenatal marijuana use.

Methods

This is a retrospective cohort study comparing outcomes of prenatal marijuana use. We looked at two groups of mothers: mothers using marijuana alone and mothers using nothing (our control group). This investigation will also attempt to discover any trends or correlations between birth outcomes and biological factors like sex, race, and maternal comorbidities. The study will include extraction of medical records from EPIC, the Premier Health electronic medical record, for all mothers ages 18 to 40 years old who delivered at Miami Valley hospital between 2012 and 2017.

The data were analyzed with SPSS version 25. We used a chi square test for categorical data such as respiratory distress, jaundice, sepsis, necrotizing enterocolitis, NICU admission, sex, race, still birth, congenital birth defects, breastfeeding issues, maternal race, maternal diabetes or preeclampsia, and drugs used by mom. We t-test for birth weight, gestation age at delivery, NICU length of stay, preterm delivery age, NAS score, APGAR score at 1 minute and 5 minutes, maternal age, and maternal gravida and parity.

Since prenatal marijuana use is illegal, it is best to approach this topic by reviewing the healthcare system database rather than addressing mothers directly. Data were stored on a Premier drive which requires unique usernames and passwords. PHI such as admission dates and discharge dates were converted to length of stay, and birth date was converted to age, so actual dates could be removed from the dataset prior to analysis. Only members of the study team had access to the electronic research records. MRN and patient name were needed to match records, but once matched, they were removed from the dataset and replaced with a patient research ID number. Only the PI had access to the Key connecting the patient research ID and MRN.

Miami Valley Hospital delivers about 4,000 babies per year. If the US prenatal marijuana use has an 11% prevalence, this will provide us with an experimental group of at least 2,200 mothers over a 5 year time span. This will provide enough information to conduct an exploratory analysis.

Inclusion criteria are: women, minimum of 18 years old, maximum of 40 years old, delivered at Miami Valley Hospital between 2012 and 2017.

Results

Demographics

In all, 499 patients from Miami Valley Hospitals records were reviewed. Less than one fourth of the mothers tested positive for THC at delivery. **Table 1** shows the base characteristics of the two study groups, control and THC. The control group(n=386) included more mothers than the THC group(n=113). The median ages for the control group and THC group were 24 and 25 years old, respectively. Most of the patients included in the study were African American, 95%. Interestingly, only 4% of the THC self-reported drug use and 4% of the control group also self-

reported drug use. Gravida(p=.01), para(p=.01), race(.03), and tobacco use(p<.01) showed statistically significant differences.

Table 1: Demographics

	Control	THC	p value
Mother's age	24.94±4.89	25.7±5.12	0.15
Gravida	2.98±1.98	3.55±2.26	0.01
Para	1.26±1.40	1.65±1.35	0.01
African American	59.1%(295)	19.0%(95)	0.03
Caucasian	18.0%(90)	3.4%(17)	0.03
Bi-racial	.2%(1)	0%	0.03
Unreported Race	0%	.2%(1)	0.03
Male Neonate	39.7%(198)	11.8%(59)	0.85
Female Neonate	37.5%(187)	10.8%(54)	0.85
Neonate Gender Unknown	.2%(1)	0%	0.85
Medicaid/Medicare	70.1%(350)	20.6%(103)	0.87
Private Insurance	6.8%(34)	1.8%(9)	0.87
Uninsured	.4%(2)	.2%(1)	0.87
Reported alcohol use	.4%(2)	.2%(1)	0.55
Reported drug use	3%(15)	1%(5)	0.79
Reported tobacco use	17.4%(87)	9.8%(49)	<.001

Neonatal Outcomes

When comparing the groups' neonatal outcomes, living, fetal demise, meconium, polyhydramnios, and decreased variability cases were higher in the control group but were not statistically significant. **Table 2** shows data for all neonatal outcomes. The BMI and average NAS score were significantly different between the two groups(p=.03 and p=.04 respectively). NICU admissions, jaundice, necrotizing enterocolitis, respiratory distress syndrome, feeding

problems, sepsis, and acidosis were included in the original data set but showed no cases for either groups.

Maternal Outcomes

There was more hypertension, preeclampsia (severe and mild), gestational diabetes, and complicated diabetes amongst the control group and more placental abruption in the THC group (**Table 3**). The increase in cases of hypertension in the control group was the only outstanding maternal outcome that showed statistical significance (p = <.001). More than 85% of the hypertension cases were in the control group while the THC group made up less than 15% of the cases. Eclampsia, embolus, hemorrhage, placenta previa, prolonged labor, prolonged 2nd stage, uterine tachysystole, and HELLP were included in the original data set but showed no cases for either groups.

Table 2: Neonatal Outcomes

	Control	THC	p value
Fetal Demise	16.3% (8)	.4% (2)	0.77
Neonatal Demise	.4% (2)	0%	0.77
Living	74.5% (372)	22.2% (111)	0.77
BMI (latest)	33.951±8.2195	31.838±7.5467	0.03
Meconium	2.4% (12)	.2% (1)	0.1
Oligohydramnios	.2% (1)	.4% (2)	0.19
Polyhydramnios	.6% (3)	0%	0.56
Multiple Late Decels	1% (5)	.4% (2)	1
Extended Fetal Bradycardia	.2% (1)	.2% (1)	0.49
Decreased Variability	1.2% (6)	0%	0.18
APGAR at 1 minute*	7.44±1.977	7.58±1.674	0.5
APGAR at 5 minutes*	8.64±1.504	8.77±1.044	0.42
Length of Stay	3±3.576	2.7±1.117	0.38
NAS (highest score)**	4.82±3.621	6.33±1.528	0.49
NAS (average score)**	3.1418±2.34139	6.1667±1.75594	0.04
Chorioamnionitis	1.4% (7)	.8%(4)	0.5

*APGAR: Appearance, Pulse, Grimace, Activity, and Respiration

**NAS: Neonatal Abstinence Score

Table 3: Maternal Outcomes			
	Control	THC	p value
Gestational Diabetes	2.2%(11)	.2%(1)	0.19
Complicated Diabetes	.6%(3)	0%	1
Placental Abruption	0%	.6%(3)	0.02
Precipitous Labor	.2%(1)	0%	1
Preeclampsia	1%(5)	.8%(4)	0.27
Mild Preeclampsia	2.2%(11)	.6%(3)	1
Severe Preeclampsia	8.4%(42)	1.6%(8)	0.2
Premature Rupture of Membrane	.6%(3)	1%(5)	0.04
Uterine Rupture	.2%(1)	0%	1
Hypertension	26.7%(133)	4.2%(21)	<.001

Discussion

We carried out a retrospective cohort study comparing the outcomes of prenatal marijuana use. Previous studies have shown conflicting results and lack of well-designed studies making it difficult to reach a finite conclusion about the effects of prenatal marijuana use. The only statistically significant difference between the two groups in neonatal outcomes was average NAS score which was higher in the THC group. Literature states that a large portion of marijuana users go on to use other illegal drugs. [10] This could explain why the THC group has a higher average NAS score in comparison to the control group. Although our study did not include mothers who tested positive at delivery for any other drug in addition to marijuana in the THC group, this does not mean that the mothers studied were not using opiates or other illegal drugs during the duration of their pregnancy and contribute to birth outcomes. Feeding complications, HELLP, jaundice, necrotizing enterocolitis (NEC), neonatal intensive care unit (NICU) admissions, and respiratory distress syndrome(RDS), sepsis, and acidosis were reviewed in addition to neonatal outcomes listed in Table 2 but there were no cases for either groups thus removed from the final data set. However, the results of this exploratory study did show notably more cases of hypertension, mild and severe preeclampsia, and gestational diabetes in the control group compared to the THC group, with a statistical significance in regards to hypertension. The finding that the control group had more hypertension cases is intriguing and unexpected. A

possible explanation is that THC has vasodilatory effects resulting in protection from common cardiovascular and peripheral vasculature pathologies in pregnancy. Available literature shows that THC increases peripheral vasculature resistance, heart rate, and cardiac output in humans while causing bradycardia and hypotension in animals which is inconsistent with our findings.[11,12] There is little data speaking to the effects of marijuana on metabolic processes but available data states that THC decreases fasting plasma glucose and improves pancreatic β cell function.[13] Our findings of higher BMI and more cases of gestational diabetes in the control group are consistent with this conclusion. A major strength of this study is that the THC group was created by positive urine drug screen at delivery rather than self-reported use like in most available studies. This study also has several limitations. Selection bias was likely as we limited the sample size to 500, meaning all patients who had the appropriate inclusion criteria were not included in the study. The sample size was limited to 500 due to purpose of this study being an exploratory study which limited generalizability. Most of the mothers studied were African American which also limits generalizability across races. There were also more patients in the control group(n=386) than the THC group(n=113) which makes it confusing to know whether the results that were significantly higher in the control group (hypertension, gestational diabetes, and mild and severe preeclampsia) were truly because of the lack of THC or because of higher number of participants. Due to the retrospective nature of the study, we were not able to adjust data for confounding factors. Mothers in the control group did not test positive for any illicit drug use at delivery but this does not mean that the mothers did not participate in illicit drug use at any point in time during the duration of the pregnancy. To effectively measure the neonatal outcomes of prenatal marijuana, future research needs to include a prospective study with a larger, diverse sample in mothers with similar demographics and equal number of mothers in each group while eliminating confounding factors. This was a pilot study conducted to help understand the prenatal marijuana use at Miami Valley Hospital and respective neonatal outcomes as well as to assist with generating a hypothesis for future studies. In conclusion, this study showed significantly higher average NAS scores in neonates born to mothers who tested positive for marijuana use at delivery and significantly higher rates of hypertension in mothers who did not.

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This paper has been read and approved by Dr. Rose Maxwell.