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RESEARCH ARTICLE

Limited Utility of Toxicology Testing at Delivery for Perinatal Cannabis Use

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ABSTRACT

OBJECTIVES: To describe the characteristics of individuals undergoing toxicology testing at delivery for a sole indication of cannabis use and to evaluate the rate of unexpected positive toxicology testing results among this cohort.

METHODS: This retrospective cohort study included dyads with a maternal history of cannabis use who underwent peripartum toxicology testing between 2016 and 2020 at 5 birthing hospitals in Massachusetts. We collected information on maternal demographic characteristics and toxicology test results and reviewed records of dyads with unexpected positive results to identify additional social risk factors and clinical outcomes.

RESULTS: Of 60 608 live births reviewed, 1924 dyads underwent toxicology testing, including 614 (31.9%) for a sole indication of cannabis use. Significantly greater percentages of patients in the cannabis cohort were <25 years old (32.4% vs 6.1% of the birthing population, $P < .001$), non-Hispanic Black (32.4% vs 8.1%, $P < .001$), Hispanic or Latino (30.5% vs 15.5%), American Indian/Alaskan (0.7% vs 0.1%), and publicly insured (39.9% vs 15.6%, $P < .001$). Eight of the 614 dyads (1.3%) had an unexpected positive toxicology test result, including 2 (0.3%) unexpectedly positive for opioids. Seven dyads (1.1%) had false positive test results for unexpected substances. Only 1 test result changed clinical management; a urine test positive for opioids prompted monitoring (but not medication) for neonatal opioid withdrawal syndrome.

CONCLUSIONS: Toxicology testing of patients for a sole indication of cannabis use, without other risk factors, may be of limited utility in elucidating other substance use and may exacerbate existing disparities in perinatal outcomes.

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Drs Sarathy and Schiff conceptualized and designed the study, participated in data collection, conducted initial data analysis, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Chou conceptualized and designed the study, participated in data analysis, and reviewed and revised the manuscript for important intellectual content; Drs Lerou, Terplan, and Mark participated in data analysis and reviewed and revised the manuscript for important intellectual content;

Cannabis is the most frequently used nonprescribed substance during pregnancy after alcohol and tobacco, with increasing prevalence over the past 15 years coinciding with widespread legalization across the United States.[1,2] In 2020, 8% of pregnant individuals and 16.1% of people with childbearing potential reported cannabis use to the National Survey on Drug Use and Health,[1] and other studies have revealed prevalence ranging from 3% to 35% depending on location and method for assessing use.[3–6] Because of concerns for adverse outcomes, including preterm delivery, small for gestational age, need for NICU admission, and long-term neurodevelopmental effects of in utero and postnatal cannabis exposure,[7–12] the American Academy of Pediatrics and American College of Obstetrics and Gynecology discourage cannabis use during pregnancy and while breastfeeding.[13,14] Despite these recommendations, prenatal counseling is inconsistent,[2,15,16] and up to two-thirds of individuals who use cannabis continue after becoming pregnant.[4,17]

Although the American College of Obstetrics and Gynecology recommends universal verbal screening with a standardized tool for substance use in pregnancy over routine toxicology testing,[18] historical cooccurrence of cannabis use with other nonprescribed substances[19,20] may compel clinicians to obtain toxicology testing on patients endorsing prenatal cannabis use, and in some cases may be recommended by hospital guidelines.[21] However, in the setting of increasing cannabis legalization and use, the extent to which individuals who disclose prenatal cannabis use are still more likely to use other nonprescribed substances remains uncertain. Toxicology testing can help identify individuals with recent substance use and may help guide clinical management of exposed newborns, but it also has significant consequences for pregnant individuals given mandating reporting laws in many states for nonprescribed substance use at delivery.[22] The increased prevalence of prenatal cannabis use among younger, less-educated, unmarried, and lower socioeconomic status individuals[3,23–25] also raises the concern that testing in this population may exacerbate existing health and social disparities. Given these potentially major consequences, a reexamination of the utility of toxicology testing in this group is needed.

To better understand current outcomes of toxicology testing in patients with prenatal cannabis use, the objectives of this study were to (1) describe the characteristics of individuals selected for toxicology testing at delivery for a sole indication of cannabis use and to (2) evaluate the rate of unexpected positive maternal and infant toxicology test results among this cohort.

METHODS

Study Design and Sample

We conducted a retrospective cohort study of all deliveries that resulted in a live birth between 2016 and 2020 at 5 birthing hospitals across a linked network in Massachusetts. This network included both community and university hospital settings, level I–IV newborn nurseries, and an annual delivery volume ranging from 500 to 6000. All 5 hospitals employed a risk-based approach to toxicology testing; none had a policy for universal toxicology testing during the prenatal period. Hospitals in the network varied with respect to specific testing guidelines; 1 hospital defined "any cannabis misuse" during pregnancy as an indication for testing, whereas others simply recommended testing for "a history of illicit or licit substance use." In the absence of a clear guideline, maternal and newborn providers made individual decisions on who to test. When testing was determined to be indicated, hospital policy at the time of data collection was to obtain a maternal urine sample and both infant urine and meconium as soon as possible after birth.

The network's Enterprise Data Warehouse was used to identify any birthing person or their newborn who underwent peripartum toxicology testing, defined as any maternal urine, infant urine, or infant meconium toxicology test within 96 hours of delivery. The indication for testing was determined by a manual review of the medical record by a clinical research team; 5% of charts were then reviewed by a second team member to ensure the accuracy of the chart review. Dyads with a maternal history of cannabis use within 2 years before delivery (determined by clinician documentation of self-report or previous positive toxicology test result for cannabis) with no other known indication for testing were included in our cohort. To identify patients with a sole risk factor of cannabis use, we excluded those with any of the following indications: a history of nonprescribed substance use (excluding cannabis), monitoring of prescribed controlled substances, inadequate prenatal care (defined by clinician documenting indication for testing), a perinatal event of uncertain etiology (eg, placental abruption, preterm labor, preterm rupture of membranes, gestational hypertension), or newborn clinical concern (eg, withdrawal signs, abnormal neurologic examination, or other clinical concerns). Multiple gestations and multiple deliveries to the same birthing person were included. Study data were collected and managed by using REDCap (Research Electronic Data Capture) tools hosted at our institution.[26,27] This study was reviewed by our institutional review board and approved as exempt health/medical record research.

Study Context

In Massachusetts, where this study was conducted, cannabis became legal for medical use in 2012. Additional changes in legalization occurred during the study period; penalties for limited possession and cultivation for adult use were eliminated in 2016, nonmedical sales became legal in 2017, and dispensaries for recreational use first opened in 2018.[28]

Toxicology Testing Results

Our primary study outcome was the presence of an unexpected positive toxicology test result on either maternal or infant testing. There were variations in

the type of testing, including the substances that were measured at each of the 5 hospitals, but we extracted results for metabolites of amphetamines, barbiturates, benzodiazepines, cocaine, opiates, fentanyl, methadone, buprenorphine, and tetrahydrocannabinol (THC, the main psychoactive component in cannabis). Test results were categorized as negative for all substances, positive for THC only, or unexpectedly positive for other substances. Given our exclusion criteria of patients with known prescribed or nonprescribed substance use, there was no category for expected noncannabis substances. Maternal and infant urine testing was performed locally at each institution by using an immunoassay, with the exception of fentanyl, which was analyzed by immunoassay or liquid chromatography-mass spectrometry depending on the institution. Infant meconium testing was performed at an outside facility for analysis.

False Positive Results

Definitive or confirmatory testing was performed automatically on all positive meconium samples and on urine samples only on clinician request. A false positive test result was defined as the presence of a positive or presumptive positive test result listed in the medical record followed by a negative definitive test result. Our urine cocaine immunoassay has no known cross reactants and, as such, was not considered to yield false positives.

Maternal Characteristics

Maternal characteristics extracted using the Enterprise Data Warehouse included age at delivery, insurance type (Medicaid, Medicare, private/commercial, other), and race/ethnicity (Black non-Hispanic, white non-Hispanic, Hispanic or Latino, Asian, American Indian or Alaskan, other/multiple, or unavailable). Race and ethnicity determination relied on documentation in the electronic medical record using a preset list of options.

Analysis

The characteristics of dyads undergoing toxicology testing because of a history of cannabis use were compared with all other dyads with a live birth during the study period by using Pearson's χ^2 tests and Fisher's exact tests. Next, the proportion of toxicology test results that were positive for THC, unexpectedly positive, and negative were computed. Next, the proportion of false positive findings was computed. Finally, for each dyad with an unexpected positive, the medical record was reviewed a second time to identify any additional social concerns, including previous involvement with child protective services, loss of previous custody, mental health concerns, and the presence or history of intimate partner violence or other safety concerns; the clinical outcome of each dyad, including breastfeeding recommendations; and whether definitive testing was performed or whether any patients disclosed use after learning of these results. Analyses were performed by using SAS 9.4 statistical software (SAS Institute, Cary, NC) and R (Foundation for Statistical Computing, Vienna, Australia).

RESULTS

Demographics

A total of 60 608 live births were reviewed. Of these, 1924 dyads underwent toxicology testing, 614 (31.9%) of which were for a sole indication of cannabis use. Demographics for the overall birthing population and cohort population are listed in Table 1. In the cohort of patients tested solely for a history of cannabis use, there were significantly greater percentages of patients <25 years old, (32.4% of the cannabis cohort vs 6.4% of the birthing population), identifying as Non-Hispanic Black (19.4% vs 8.2%), Hispanic or Latino (30.5% vs 15.7%), and American Indian/Alaskan (0.7% vs 0.1%), and with public insurance (39.9% vs 15.9% with Medicaid).

Toxicology results

Of the 614 dyads tested solely for a history of cannabis use, 245 (40.0%) had a positive toxicology test result. Two hundred thirty-seven of the 614 dyads (38.6%) were positive for THC only and 8 (1.3%) were positive for a substance previously unknown to the patient's care team, including 2 (0.3%) opioids (Fig 1). Of the unexpected positive results, 5 were identified by maternal urine testing (2 were positive for amphetamines, 1 for barbiturates, 1 for cocaine, and 1 for buprenorphine, fentanyl, and cocaine; this mother's infant was also positive for fentanyl and cocaine). The remaining 3 dyads consisted of 2 mothers who had negative urine toxicology test results and 1 who declined testing but whose infants had positive toxicology test results (1 for cocaine in urine, 1 for cocaine in meconium, and 1 for opiates in meconium; Table 2). Only 1 maternal urine sample was sent for confirmation and no additional patients disclosed use after learning of positive test results.

Of note, despite hospital policy, not all dyads underwent all types of toxicology testing because of missed collection of first void or meconium passage, participants declining testing, and additional patient-level factors. A total of 459 of the 614 mothers (74.8%) were tested, 418 infants underwent urine toxicology testing (68.1%), and 464 infants underwent meconium toxicology testing (75.6%; Supplemental Figure 2).

A manual chart review of the 8 dyads with unexpected positive results revealed that 1 birthing individual had other children not in their custody and 3 more had a history of involvement with child protective services (CPS). One had a history of intimate partner violence. One birthing individual had a partner with active substance use disorder. Seven individuals had a history of mood disorders, including depression and anxiety, not receiving medication at the time of birth hospitalization, including 1 subject with a history of suicide attempt. Six of the 8 dyads with unexpected positive results had a report of suspected child abuse or neglect filed; the remaining dyads had a social work consult only. One infant required an extended hospitalization for monitoring for Neonatal Opioid Withdrawal

TABLE 1 Demographics

	Tested for Cannabis Indication		Birthing Population		
	n	%	*n*	%	*P*
Total	614		60 608		
Age					
<25	199	32.4	3858	6.4	<.001
25–35	366	59.6	38 861	64.1	
>35	49	8.0	17 889	29.5	
Race/ethnicity					
Non-Hispanic white	260	42.4	36 764	60.7	<.001
Hispanic or Latino	187	30.5	9483	15.7	
American Indian or Alaska	4	0.7	62	0.1	
Non-Hispanic Black	119	19.4	4999	8.2	
Asian	13	2.1	6680	11.0	
Other	18	2.9	1666	2.7	
Unavailable	13	2.1	954	1.6	
Insurance					
Medicaid	245	39.9	9625	15.9	<.001
Medicare	22	3.6	300	0.5	
Private pay/ commercial	345	56.2	50 411	83.2	
Other	2	0.3	272	0.4	

Syndrome after fentanyl was discovered in maternal and infant urine. This resulted in a transfer to a level II nursery after the birthing person was discharged per hospital protocol; the infant remained asymptomatic (Table 2). None of the unexpected positive results changed the breastfeeding recommendations provided by the care team.

Seven additional dyads (1.1%) were found to have preliminarily positive results (other than THC) on initial toxicology testing, which were later found to be negative on definitive testing. Substances initially identified included amphetamines (3), cocaine (1), methadone (1), opiates (1), and fentanyl (1; Table 3).

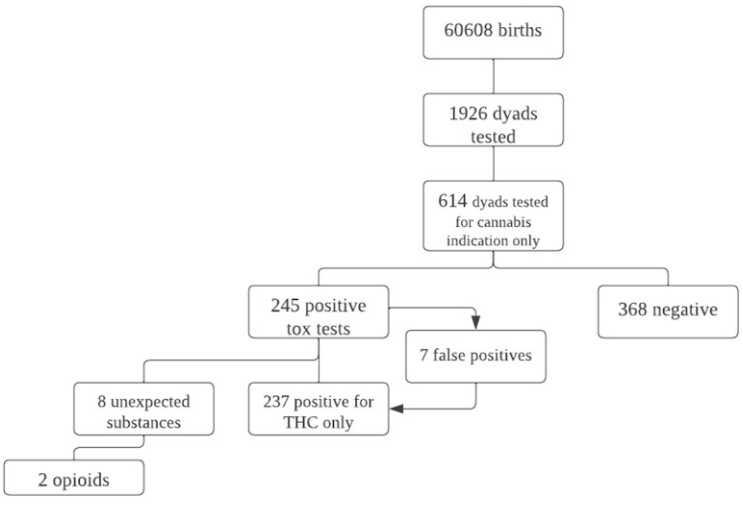

FIGURE 1 Toxicology testing schematic among live births between 2016 and 2020 in a Massachusetts birthing hospital network.

DISCUSSION

The objective of our study was to assess the rate of unexpectedly positive maternal and infant toxicology test results among dyads who were tested solely because of a history of cannabis use. We found that one-third of all toxicology tests were sent only because of cannabis use, of which 1.3% (potentially as low as 0.8%, given 3 unconfirmed tests) were found to have unexpectedly positive results for other nonprescribed substances and with a similar rate of false positive results (1.1%, potentially up to 1.6%). To our knowledge, this is the first study to specifically examine the results of perinatal toxicology testing for a sole indication of cannabis use.

Although new information was discovered through toxicology testing for 0.8% to 1.3% of the dyads in this cohort, clinical management was impacted for only 1 dyad (0.2%). Given that a number needed to treat of 222 male neonates requiring phototherapy to avoid exchange transfusion[29] was considered sufficiently high to raise phototherapy thresholds to avoid overtreatment,[30] our number needed

TABLE 2 Unexpected Positive Toxicology Test Results

Dyad	Maternal Urine Toxicology Results	Infant Urine Toxicology Results	Infant Meconium Toxicology Results	Other Safety Concerns	Outcome
1	Buprenorphine, fentanyl, cocaine	Fentanyl,[a] cocaine	Cocaine	Mood disorder	NOWS monitoring CPS
2	Amphetamines[a]	—	—	Previous CPS	SW only
3	Amphetamines[a]	—	—	Mood disorder, previous CPS	CPS
4	Barbiturates[a]	—	—	Previous CPS, mood disorder, history of suicide attempt	CPS
5	—	Cocaine	—	Mood disorder	CPS
6	—	—	Cocaine	Previous custody loss, mood disorder	CPS
7	[Not tested]	—	Opiates	Mood disorder, IPV	CPS
8	Cocaine	—	—	Mood disorder	SW only

— signifies negative test result; CPS, referral to child protective services; IPV, intimate partner violence; NOWS, neonatal opioid withdrawal syndrome; SW, social work consultation.
[a] No definitive testing.

to test of 614 (and arguably higher given the infant remained asymptomatic) may prompt providers to reconsider the utility of testing in this cohort. In addition, our opioid unexpected positivity rate of 0.3% is lower than the previously reported rate of 0.6% found in prenatal patients without any known risk factors,[31] suggesting that a history of cannabis use alone may not increase the risk of perinatal opioid exposure. Beyond clinical utility, some providers may consider toxicology testing to be useful in determining the safety of a child's home environment (although neither the authors nor available evidence support this practice). However, we found that all dyads with an unexpected positive toxicology test result already had documentation in the prenatal record that would have prompted social work consultation or other interventions to ensure a newborn's safety before discharge. More importantly, all 8 newborns were discharged in parental custody, suggesting that immediate safety risks were not identified. Combining our low yield for unexpected opioid exposure with the minimal additional information elucidated by other unexpected positive findings, it could be argued that, for patients with a history of cannabis use but no other risk factors, targeted toxicology testing in this group may be of minimal benefit.

When weighing the risks and benefits of testing in this population, clinicians have a responsibility to acknowledge the potential harms and downstream consequences of toxicology testing.[32] Even presumptive positive findings that are later found to be inaccurate can result in parental distress and additional psychological trauma due to fear of an investigation for child abuse or neglect. The prospect of toxicology testing can also undermine the patient–caregiver relationship and motivate patients to disengage from prenatal care,[33–35] which can negatively affect perinatal outcomes[36] and disincentivize patients from disclosing cannabis use. Existing literature suggests that prenatal cannabis use is greatly underreported[37] and that fear of consequences is, in part, responsible for this phenomenon.[16,38] A lack of provider awareness of birthing persons' cannabis use represents a missed opportunity for counseling on the harms of perinatal cannabis exposure and harm reduction strategies and supporting patients in seeking treatment of potential substance use disorder or other unaddressed mental health issues if present. Finally, the presence of a true positive toxicology test result is not diagnostic of a substance use disorder; it only indicates that use occurred within the timeframe of the specific test, which for meconium testing can be as early as the second trimester.[39] Validated screening tools may be more effective in elucidating true substance use disorder[18,40,41] and may be less of a deterrent to patients seeking prenatal care.

TABLE 3 False Positive Results (Excluding THC)

Dyad	Maternal Urine Toxicology results	Infant Urine Toxicology Results	Infant Meconium Toxicology Results
1	—	—	Opiates
2	—	—	Amphetamines
3	Fentanyl	—	—
4	—	—	Methadone
5	—	—	Cocaine
6	Amphetamines	—	—
7	Amphetamines	[Not tested]	[Not tested]

— signifies negative test result.

More broadly, unnecessary toxicology testing has the potential to exacerbate existing health disparities. In our study, dyads undergoing toxicology testing solely for a history of cannabis use were disproportionately younger, publicly insured, and identified as non-Hispanic Black, Hispanic or Latino, or American Indian/Alaskan. This echoes previous work by Perlman and colleagues, which revealed increased rates of toxicology testing among younger, unmarried, low-income, and non-white individuals.[42] However, Ko and colleagues found that cannabis use among pregnant individuals did not differ significantly by race/ethnicity among self-reports to the National Survey on Drug Use and Health,[3] suggesting that racial disparities may be introduced by prenatal toxicology testing, a phenomenon that echoes established racial disparities in legal prosecution but not in the prevalence of cannabis use.[43] Given abundant evidence on increased maternal morbidity among non-white individuals[44,45] and increased fetal and neonatal mortality among Black patients,[46,47] combined with potential negative effects of toxicology testing on the prenatal patient-provider relationship and, consequently, missed opportunities for education, support, and management of other medical issues; continuing to target prenatal patients with cannabis use may further exacerbate racial disparities in maternal and neonatal outcomes.

In 2011, Schroeder and colleagues coined the term "safely doing less," a concept that could and should apply to toxicology testing in the perinatal population. These authors acknowledged that "doing more feels safer, because it alleviates uncertainty … ordering fewer tests is not always easier; in fact, it often requires more vigilance and effort."[48] Indeed, pediatric providers may find reassurance that, by ordering a toxicology test, they are helping ensure a newborn's safety; however, toxicology testing did not achieve this goal for any of the dyads in our study. For pediatricians tasked with ensuring the safety of a newborn, investing time and resources in universal verbal screening of birthing individuals and new parents, to appropriately elucidate risk factors and offer treatment of substance use and mental health disorders, as well as screening for other safety risks in the home environment, may be more effective interventions than ordering a test.

Our study has several limitations. First, we only included subjects undergoing toxicology testing during the birth hospitalization; individuals with a history of cannabis use but no toxicology testing at delivery were not identified in this study. Our cohort was also identified on the basis of self-report or a positive toxicology test result for THC within 2 years of delivery; as such, findings may not be representative of all birthing individuals with a history of cannabis use. This may have resulted in an overrepresentation of individuals at risk for substance use for reasons not captured by our chart review and, as such, our rate of unexpected positive findings may be higher than the true rate among all patients with a sole risk factor of prenatal cannabis use. Conversely, recognizing that urine toxicology testing only captures use in the days leading up to delivery, and was the sole mode of testing in the portion of our study population that did not have meconium testing, our study likely underestimated the overall rate of nonprescribed substance use throughout pregnancy. We also were not able to characterize those with recent compared with more remote cannabis use nor the extent or frequency of use (only 40% of dyads were positive for THC at delivery); as such, our results may underestimate cooccurring nonprescribed substance use among individuals with ongoing cannabis use. Second, although recommendations exist for screening for substance use in the outpatient prenatal setting, hospitals in our study had varied approaches to screening on labor and delivery and, as such, may have incorrectly estimated patients with current or recent substance use. Third, as noted in our methods and results, given the lack of definitive testing on 3 urine toxicology tests, our true and false positive rates may be respectively lower and higher than initially reported. Finally, our study was limited to birthing hospitals within our network in a single state; as such, its generalizability may be limited, especially in states in which cannabis is not legal.

CONCLUSIONS

Our study findings suggest that toxicology testing of birthing individuals and their newborns for a sole indication of cannabis use, without other risk factors, may be of limited utility in elucidating other substance use and should be balanced with the harms of toxicology testing unique to pregnant and parenting individuals. Given the disproportionate rates of toxicology testing among younger, poorer, and Black/Hispanic birthing individuals, unnecessary toxicology testing may exacerbate existing disparities in perinatal outcomes by jeopardizing patient–provider relationships, obscuring opportunities for prenatal counseling on cannabis use, and triggering adverse downstream consequences of toxicology testing. Universal, validated screening tools are recommended as a more sensitive and equitable approach to risk assessment in the prenatal population.

Ms Dorfman participated in data analysis, participated in drafting of the initial manuscript, and reviewed the manuscript; Dr Wilens conceptualized and designed the study and reviewed and revised the manuscript for important intellectual content; Dr Bernstein conceptualized and designed the study, participated in data collection and analysis, and reviewed and revised the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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