Pediatric RESEARCH

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CLINICAL RESEARCH ARTICLE

Cannabis use and measurement of cannabinoids in plasma and breast milk of breastfeeding mothers

Michael J. Moss[1,2], Ittai Bushlin[3], Steven Kazmierczak[4], Dennis Koop[5], Robert G. Hendrickson[6], Katharine E. Zuckerman[7] and Tamara M. Grigsby[7]

BACKGROUND: Information on cannabinoids in breast milk and maternal cannabis use is limited. We quantified cannabinoids in plasma and breast milk of breastfeeding mothers and assessed cannabis use patterns.

METHODS: This is a prospective study at a university hospital in a state with legal medical and recreational cannabis. Breast milk and plasma samples along with survey data were collected from volunteers using cannabis in the last 48 h at 2 weeks and 2 months postpartum.

RESULTS: Twenty subjects were enrolled. Median age (IQR) was 27 (24–34) years. Median (IQR) instances of cannabis use in the last 7 days were visit 1: 17 (6–29) and visit 2: 23 (15–45). Median (IQR) tetrahydrocannabinol (THC) concentrations were: plasma 3.7 ng/ml (0.8–56.8) and breast milk 27.5 ng/ml (0.8–190.5). Median (IQR) cannabidiol (CBD) concentrations were: plasma 0.6 ng/ml (0.5–6.4) and breast milk 1.2 ng/ml (0.5–17.0). Median (IQR) THC M/P: 7.0 (1.8–34.6) and CBD M/P: 2.6. Median breast milk THC concentration increased from visit 1 to visit 2 by 30.2 ng/ml (95% CI 3.05–69.3 ng/ml).

CONCLUSIONS: THC and CBD accumulate in breast milk. Breastfeeding mothers used cannabis frequently and increased use in the early postpartum period. Research on the effects of infant exposure to cannabinoids in breast milk is urgently needed.

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IMPACT:

- Cannabis use is increasing in the general population and many nursing mothers use cannabis.
- THC has been previously detected in breast milk but little is known on how it concentrates relative to plasma. Data on cannabinoids other than THC, reasons for cannabis use, and patterns of use in breastfeeding women are also limited.
- We detected THC and CBD in breast milk. Both concentrate in breast milk relative to plasma.
- We showed that breastfeeding mothers increased cannabis use in the weeks after childbirth.
- Further research is needed to evaluate infant exposure to cannabinoids via breast milk and effects on infant health.

INTRODUCTION

Breast milk provides ideal nutrition for infants and is encouraged until at least 1–2 years of age.[1,2] While public health efforts are underway to increase breastfeeding rates, cannabis use continues to rise among pregnant and breastfeeding women in the U.S.[3,4]

Healthcare agencies recommend that mothers abstain from cannabis use or not breastfeed when using cannabis.[5–7] However, acceptance of cannabis is growing among the general population and is now used by 15% of women of childbearing age and 4–6% of pregnant and breastfeeding women.[4,8,9] Online media articles commonly mention treatment of nausea and vomiting in pregnancy as a potential benefit of cannabis use.[10] Nearly 70% of pregnant women report that they perceive slight to no harm associated with occasional cannabis use.[11]

Few studies have evaluated the magnitude of infant exposure to cannabis in breastfeeding mothers. Breast milk tetrahydrocannbinol (THC) and metabolites have been reported in anonymous breast milk donors,[12] in samples at a research breast milk bank,[13] and in case reports.[14–16] Simultaneous maternal plasma and breast milk concentrations have only been documented in a single case report.[14] Cannabidiol (CBD) M/Ps have not previously been reported.

These studies are lacking in their description of maternal cannabis usage patterns, evaluation of edible cannabis and CBD products, and the assessment of THC and metabolites in breast milk. We sought to expand the current literature by (1) simultaneously measuring the concentration of cannabinoids in maternal plasma and breast milk; (2) comparing cannabinoid concentrations in breast milk 2 weeks and 2 months postpartum; (3) quantifying cannabinoid concentrations in plasma and breast milk after edible use; and (4) describing the demographics and cannabis usage patterns in new breastfeeding mothers.

[1]Utah Poison Control Center, College of Pharmacy, University of Utah, Salt Lake City, UT, USA; [2]Division of Emergency Medicine, University of Utah, Salt Lake City, UT, USA; [3]Department of Pediatrics, Division of Pediatric Neurology, Oregon Health & Science University, Portland, OR, USA; [4]Department of Pathology, Oregon Health & Science University, Portland, OR, USA; [5]Department of Physiology & Pharmacology, Oregon Health & Science University, Portland, OR, USA; [6]Oregon Poison Center & Department of Emergency Medicine, Oregon Health & Science University, Portland, OR, USA and [7]Department of Pediatrics, Oregon Health & Science University, Portland, OR, USA
Correspondence: Michael J. Moss (michael.moss@utah.edu)

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METHODS

We conducted a prospective observational study of mothers who both used cannabis products and were breastfeeding. Our research protocol, STUDY00017114, was approved by The Oregon Health & Science University Institutional Review Board. Postpartum mothers admitted to our facility and indicating ongoing cannabis use with intention to breastfeed were screened for interest and eligibility. Inclusion criteria were age between 21 and 44 years, current cannabis use, and establishment of the infant's primary care at a university clinic. Subjects were excluded who did not have custody of the infant, had not used cannabis within 48 h of sample collection, or did not speak English. At the time of enrollment, subjects were counseled and discouraged from using cannabis during lactation as recommended by experts in the fields of breastfeeding, family medicine, obstetrics, and pediatrics[5–7] and resources were provided upon request.

Samples were collected from the mother during the child's 2-week and 2-month newborn appointments. At each visit, study participants were remunerated with a gift card for a local coffee shop and a $35.00 debit card following breast milk and blood donations. Upon clinic arrival, subjects were greeted by a research assistant who facilitated study tasks during the clinic encounter including: confirming continued breastfeeding and cannabis use within 48 h; administering a questionnaire regarding cannabis and other substance use, demographics, and medications; and collecting subject's donation of at least 5 ml of expressed breast milk and 3 ml of blood obtained by venipuncture. Mothers' expression of breast milk was not standardized; breast milk samples presumably included varying amounts of foremilk and hindmilk.

Preparation of plasma samples was performed following protein precipitation as described by Zhang et al.[17] Samples were thawed and 100 µl of standards, quality control, or samples were pipetted into a Protein Impact PPT plate, followed by the addition of 5 µl of IS mix (1 ng) followed by 300 µl of 0.1% formic acid in acetonitrile. The internal standard (IS) mix was prepared using deuterated d_3-CBD, d_3-THC, d_3-11-OH-THC, d_3-THC-COOH, and d_3-THC-COOH-glucuronide. Each sample was pipetted up and down 2–3 times to mix using an 8-channel pipettor. The cleaned extract was then eluted into a 2-ml collection plate on a Biotage 96-well positive pressure device. The capture plate was removed from the device, 650 µl of water was added to each well and mixed and then a partial aliquot was transferred to an Oasis HLB prime 2 mg µ-elution plate, following the initial transfer, the remainder was transferred and pushed through the plate. The plate was then washed with 2 × 250 µl of 25:75 methanol:water. The plate was then placed onto a mass spectrometry (MS)-compatible 1 ml collection plate and the compounds were eluted using 2 × 25 µl of 90:10 acetonitrile:methanol. Fifty µl per well of water was added and the plate was analyzed.

The preparation of breast milk samples was performed using a modification of Marchei et al's method.[15] Samples were thawed on ice and 600 µl of 1% formic acid was added into a Captiva EMR lipid 1 ml cartridge, followed by 200 µl of breast milk that had been thawed on ice and vortexed well prior to pipetting. IS mix containing 1 ng of each of the following d_3-CBD, d_3-THC, d_3-OH-THC, d_3-COOH-THC, and finally d_3-COOH-THC-glucuronide was added. Passive mixing and protein precipitation was allowed to occur for 5 min followed by the application of positive pressure at 2–4 psi such that a drop occurred every 3–5 seconds, finished by higher positive pressure to drive out the remainder of the samples from the cartridge bed. The samples were then dried in a speed vacuum concentrator for 3 h at 40 °C, brought up in 100 µl of acetonitrile:water (55:45) with 0.1% formic acid, filtered through a 0.22-µm centrifugal sample filter, placed into sample vials with inserts, and analyzed by liquid chromatography tandem MS (LC-MS/MS. The injection volume was 5 µl. A spiked standard curve in naive breast milk was used for these studies.

Following preparation of standards and samples, cannabinoids were analyzed using LC-MS/MS. THC and metabolites were analyzed using a 5500 Q-TRAP hybrid/triple quadrupole linear ion trap mass spectrometer (SCIEX, Framingham, MA) with electrospray ionization in positive mode. The mass spectrometer was interfaced to a Shimadzu (Columbia, MD) SIL-20AC XR autosampler followed by two LC-20AD XR LC pumps. The instrument was operated with the following settings: source voltage 5000 kV, GS1 40, GS2 50, CUR 15, TEM 700, and CAD gas HIGH. The gradient mobile phase consisted of two solvents, A: 0.1% formic acid in water, B: 0.1% formic acid in acetonitrile. The column used was a Phenomenex Kinetex 2.6µ XB-C18 (100 × 3 mm) column, with a flow rate of 0.35 ml/min. The gradient consisted of an initial concentration of 55% B. Start conditions were held for 1 min, followed by an increase to 95% B over 4 min, held at 95% B for 3 min, decreased to start condition of 55% B over 0.1 min, and re-equilibration for 1.9 min. The standard curves ranged from 0.1 to 200 ng/ml and the lower limit of quantitation (LLOQ) was as follows: For plasma samples: 0.5 ng/ml for 11-nor-tetrahydrocannabinol carboxylic acid (THC-COOH; accuracy 102% and precision as the relative standard deviation (RSD) 6.8%), 0.1 ng/ml for THC-COOH-glucuronide (accuracy 94%, RSD 5.7%), 5 ng/ml for 11-hydroxy-tetrahydrocannabinol (11-OH-THC) due co-eluting high background interference (accuracy 100%, RSD 16.3%), 1 ng/ml for CBD (accuracy 88%, RSD 2.8%), and 1 ng/ml for THC (accuracy 102%, 10.6% RSD). For plasma samples: 5 ng/ml for THC-COOH (accuracy 89%, RSD 12%, 0.5 ng/ml for THC-COOH-glucuronide (accuracy 89%, RSD 7%), 1 ng/ml for 11-OH-THC (accuracy 100%, RSD 7%), 0.5 ng/ml for CBD (accuracy 95%, RSD 3%), and 0.5 ng/ml for THC (accuracy 93%, 15% RSD). The LLOQs for breast milk were: 0.5 ng/ml for THC-COOH, 5 ng/ml for 11-OH-THC 1 ng/ml for CBD, and 1 ng/ml for THC.

One breast milk sample was an outlier from the rest of the samples and is not included in any of the analyses. The sample was noted to be highly viscous and analyzed twice to verify results. This sample contained: THC 2024 ng/ml, 11-OH-THC 58.4 ng/ml, CBD 1.7 ng/ml, and THC-COOH 171.8 ng/ml. The plasma results from this subject fell into expected ranges.

Descriptive statistics were used to summarize the data. M/Ps were calculated for sample pairs that were collected within 1 h of each other. An estimated infant dose of THC from breast milk was calculated using an average 1-month infant weight of 4.3 kg ingesting 150 ml/kg/day of breast milk. Means of non-normal continuous variables were compared using Wilcoxon rank-sum test and normal continuous variables were compared using *t* test. Associations between cannabinoid concentrations and reported use were analyzed by Spearman's rank correlation.

RESULTS

Enrollment, survey, and sample collection

Twenty-two subjects completed demographic and cannabis use surveys; two did not provide sufficient blood or breast milk samples. Twenty subjects provided at least one set of plasma and breast milk samples. Eighteen subjects completed both surveys at visit 1 (approximately 2 weeks) and visit 2 (approximately 2 months).

A total of 38 plasma samples were collected at visits 1 and 2. Eighteen subjects provided plasma samples at both visits; two provided a sample at only one visit. A total of 35 breast milk samples were collected at visits 1 and 2. Fifteen subjects provided samples at both visits; five provided samples at one visit. One subject was enrolled in the study <48 h from last cannabis use, but sample collection was delayed (51 h for plasma and 53 h for breast milk). However, THC was detected in breast milk and THC-COOH was detected in plasma and thus the samples were included in the analysis. A summary of subject demographics are shown in Table 1. Subjects used cannabis almost daily. Alcohol and nicotine use were reported by 33% of subjects. Opioids were used by 19%.

Table 1. Demographics and cannabis use ($n = 21$).

Characteristic	Median (IQR) or *n* (%)
Age—median (IQR)	27 (24–34)
Race	$n = 20$
White	18 (90)
Black/African-American	3 (15)
American Indian/Alaska Native	2 (10)
Pacific Islander	—
Other	—
Ethnicity	($n = 21$)
Hispanic or Latino	3 (14)
Educational attainment	
8th grade or less	2 (10)
9–12th grade	0 (0)
High school graduated or GED	5 (24)
Some college	8 (38)
Associate's degree	4 (19)
Bachelor's degree or higher	2 (10)
Cannabis use	
First cannabis use—median age (IQR)	16 years (14–19)
Recreational use	4 (19)
Medical use	17 (81)
Reasons for medical use	($n = 17$)
Pain	12 (70)
Nausea	8 (47)
PTSD	7 (41)
Anxiety/depression/mental health	5 (29)
Appetite	2 (12)
Headache	2 (12)
Insomnia	1 (6)
Typical method of cannabis use	
Inhaled (all methods)	21 (100)
Edible	4 (19)
Topical	2 (10)
Cannabis use frequency—median (IQR)	
Number of days used in prior 30—visit 1	28 (19–30)
Number of days used in prior 30—visit 2	30 (28–30)
Total times used in prior 7 days—visit 1	17 (6–29)
Total times used in prior 7 days—visit 2	23 (15–45)
Alcohol use	7 (33)
Nicotine use	7 (33)
Medications—prescription	17 (81)[a]
Antidepressant use	6 (29)
Opioid use	4 (19)
Medications—over the counter/supplements	12 (57)[b]

Subjects may select multiple options for race, reasons for medical use, and method of cannabis use, thus totals do not sum to 100%.
GED General Educational Development, *PTSD* post-traumatic stress disorder.
[a]Vitamin (7), antidepressant (6), opioid (4), NSAID (2), histamine-2 blocker or proton pump inhibitor (3), stool softener/laxative (3), asthma inhaler (2), antiemetic (2), prednisone (1), nifedipine (1), bactrim (1).
[b]Acetaminophen (5), vitamin (9), NSAID (3), iron (2), calcium carbonate (1), fish oil (1), probiotic (1).

Table 2. Plasma and breast milk cannabinoid concentrations.

	Samples detectable *n* (%)	Median (IQR), ng/ml
Plasma samples ($n = 38$)		
THC	34 (89)	3.7 (0.8–56.8)
11-OH-THC	36 (95)	3.1 (0.4–47.8)
THC-COOH	38 (100)	58.0 (2.2–390.3)
CBD	3 (8)	0.6 (0.5–6.4)
Breast milk samples ($n = 35$)		
THC	33 (94)	27.5 (0.8–190.5)
11-OH-THC	5 (14)	1.4 (0.7–5.2)
THC-COOH	18 (51)	1.9 (0.5–16.6)
CBD	13 (37)	1.2 (0.5–17.0)

THC tetrahydrocannabinol, *11-OH-THC* 11-hydroxy-tetrahydrocannabinol, *THC-COOH* 11-nor-tetrahydrocannabinol carboxylic acid, *CBD* cannabidiol.

The subjects using topical cannabis products also reported using inhaled cannabis prior to sample collection. Of the four subjects reporting edible cannabis use, three provided breast milk and plasma samples after using edible products alone. The other subject had used both edible and inhaled cannabis.

Plasma and breast milk samples

At least one cannabinoid or metabolite was detected in all plasma samples. THC and CBD were detected in 89 and 8% of samples, respectively.

All but a single breast milk sample had at least one cannabinoid or metabolite detected. The sample with no detectable cannabinoids was collected 40 h after last cannabis use. Plasma and breast milk cannabinoid concentrations from both visits combined are summarized in Table 2. There was a moderate positive correlation between plasma THC concentration and breast milk THC concentration ($\rho = 0.6$ and 0.92, respectively) at both visits (Fig. 1a, b).

Milk/plasma ratios

M/Ps for THC, 11-OH-THC, and CBD from both visits combined are shown in Table 3. Eight THC sample pairs and one 11-OH-THC sample pair were not collected within 1 h of each other and were not included in the analysis. THC M/Ps did not correlate with the difference in collection time of milk and plasma when samples were obtained <1 h apart ($r^2 = 0.028$). Additionally, M/P did not correlate with time from last cannabis use ($r^2 = 0.0661$).

Infant dose of THC

Based on the THC concentrations that we found in breast milk, an infant dose in an 8-ounce sample is 6.6 mcg (0.83 mcg/oz) with a range of 0.19–45.7 mcg (0.024–5.7 mcg/oz) yielding an estimated daily infant dose of 17.7 mcg/day (or 4.12 mcg/kg/day) with a range of 0.52–123 mcg/day.

Change between 2-week and 2-month visits

During the second visit, four subjects indicated a decrease or no change in their weekly pattern of cannabis use and 14 subjects reported an increase in weekly frequency and methods of cannabis use. Subjects reported a median increase of 4 (95% confidence interval (CI) −8.3 to 16.3; $p = 0.34$) in the number of occasions of cannabis use per week between the first and second visit; and four subjects increased their use by >20 occasions per week. There was a moderate non-significant correlation between the increase in weekly cannabis usage and the difference in breast milk THC concentrations between visits ($\rho = 0.45$; Fig. 2).

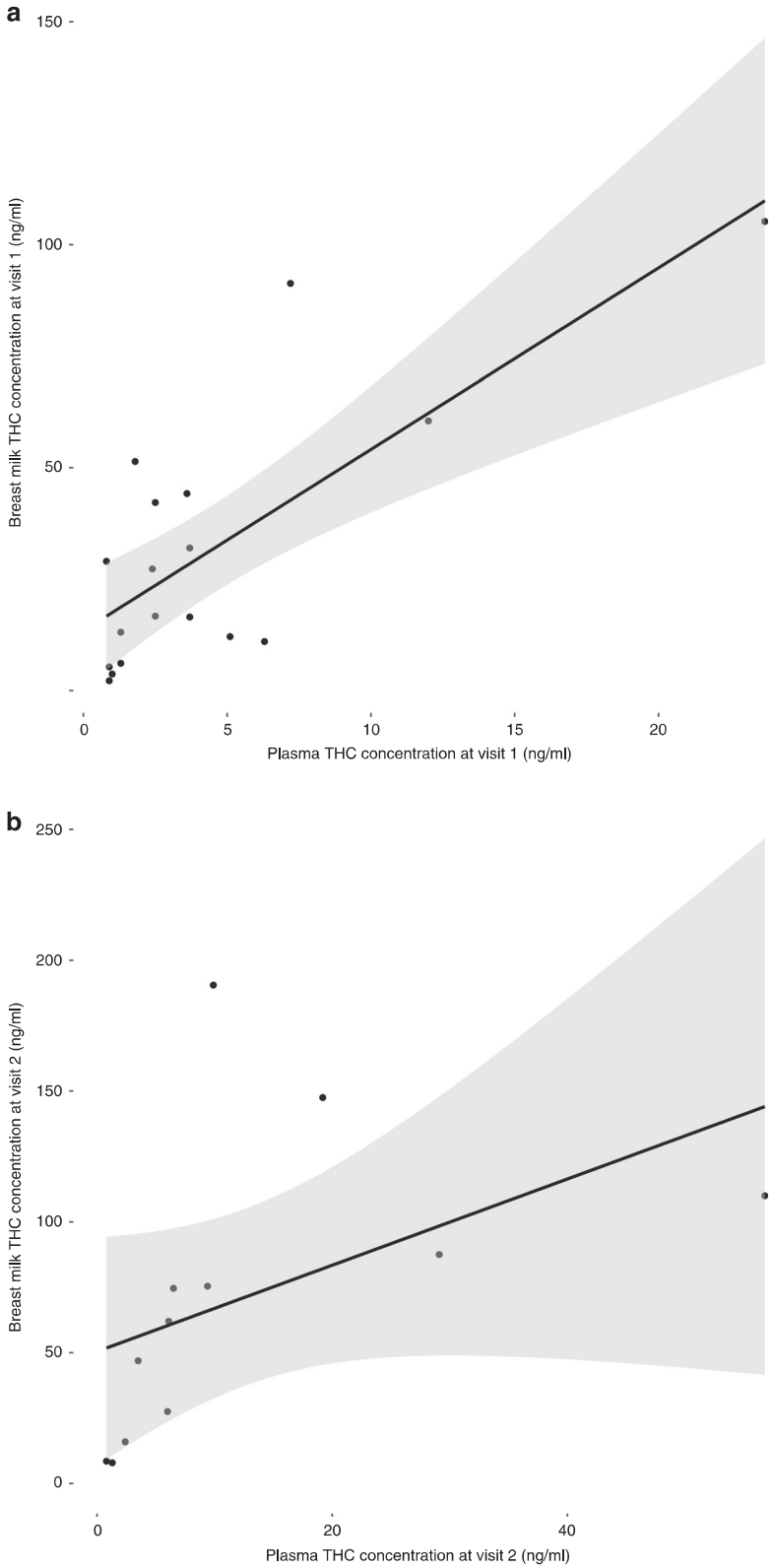

Fig. 1 Association between plasma THC concentration and breast milk THC concentration. a Visit 1, Spearman rank correlation = 0.60 (95% CI: 0.18–0.83). **b** Visit 2, Spearman rank correlation = 0.92 (95% CI: 0.74–0.98).

Plasma THC concentrations significantly increased from first to second sample in 88% (15/17) of subjects. Median plasma THC concentrations were 2.5 ng/ml at visit 1 and 6.05 at visit 2 with a median increase of 3.6 ng/ml (95% CI −3.2 to 10.6 ng/ml; $p = 0.02$). Breast milk THC concentrations increased from first to second sample in 77% (10/13) of subjects. Median breast milk THC concentrations were 16.7 ng/ml at visit 1 and 54.5 ng/ml at visit 2 with a median increase of 37.8 ng/ml (95% CI 3.05–69.3 ng/ml; $p = 0.02$).

Time from use to detectable THC samples in plasma and breast milk

THC concentrations in plasma and breast milk compared to the time sample was collected after last cannabis use are shown in Fig. 3. The longest interval between collection and cannabis use with detectable THC was 53 h for breast milk and 36 h for plasma.

Edible use

Three subjects provided milk and plasma samples after ingestion of edibles. The profile of cannabinoid concentrations in these subjects is shown in Table 4. THC M/P was 1.9 in one subject. Another subject had a THC M/P of 2.4 and CBD M/P of 2.7 after ingesting an edible containing 20 mg THC (hybrid sativa/indica strain).

Cannabidiol

No subjects reported using CBD-only products. CBD was detected in 37% (13/35) of breast milk samples. The 13 subjects with detectable breast milk CBD concentrations had higher THC concentrations in breast milk (median 75.4 ng/ml; 95% CI 46–105 ng/ml vs. 12.1 ng/ml; 95% CI 2.4–21.8 ng/ml; $p =$ 0.000366) compared to subjects without detectable CBD in breast milk. The median THC:CBD ratio in breast milk was 48.0 (interquartile range 28.25, 122.45) and ranged from 13.2 to 191, with one outlier at 0.712.

Table 3. Milk/plasma ratios.

	Sample pairs (*n*)	Milk/plasma ratio
THC, median (IQR)	22	7.0 (1.8–34.6)
11-OH-THC, median (IQR)	4	0.07 (0.03–0.52)
CBD	1	2.6

DISCUSSION

We describe the demographics of cannabis users breastfeeding their children in real-world scenarios. Subjects were representative of chronic, daily cannabis users in Oregon.[18] They were well educated, first used cannabis in adolescence, and primarily inhaled botanical cannabis. The results reflect the amounts of cannabinoids that could be expected in women of childbearing age who use cannabis medicinally. We confirmed prior findings of THC accumulating in breast milk and added additional data on THC M/Ps as well as new data on M/Ps of CBD and after edible use.

While cannabinoid pharmacokinetics are well described with regard to metabolism and plasma concentration after inhalation, intravenous, and oral administration,[19] less is known about the distribution of cannabinoids to breast milk. THC is the primary psychoactive cannabinoid found in cannabis. THC is metabolized to the active metabolite 11-OH-THC and is further oxidized to the inactive metabolite THC-COOH. Following inhalation, THC reaches peak serum concentration within minutes and 11-OH-THC peaks shortly thereafter. Both compounds nearly disappear from serum in approximately 6 h. CBD, a non-psychoactive cannabinoid, reaches maximum plasma concentration 1–2 h after ingestion and remains detectable for 3–4 h.[20,21] CBD metabolism is similar to THC with alcohol and carboxylic acid metabolites.[20,22]

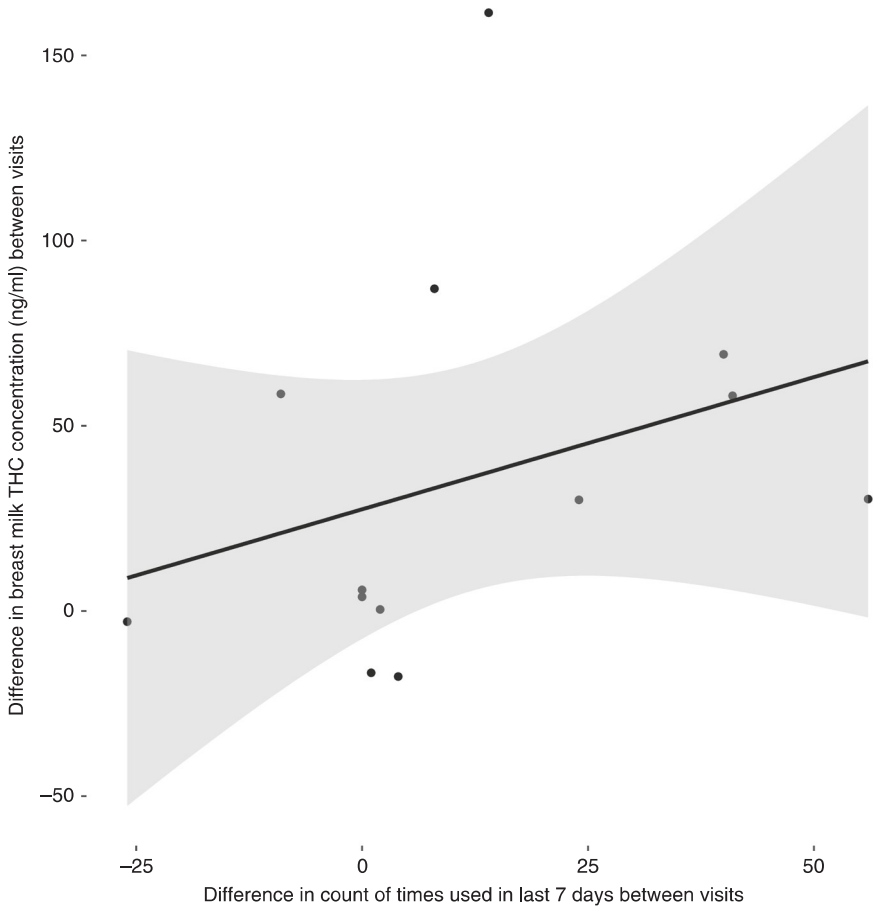

Fig. 2 Reported increase in cannabis use is associated with increase in breast milk THC concentration. Spearman rank correlation = 0.45 (95% CI: −0.14 to 0.80).

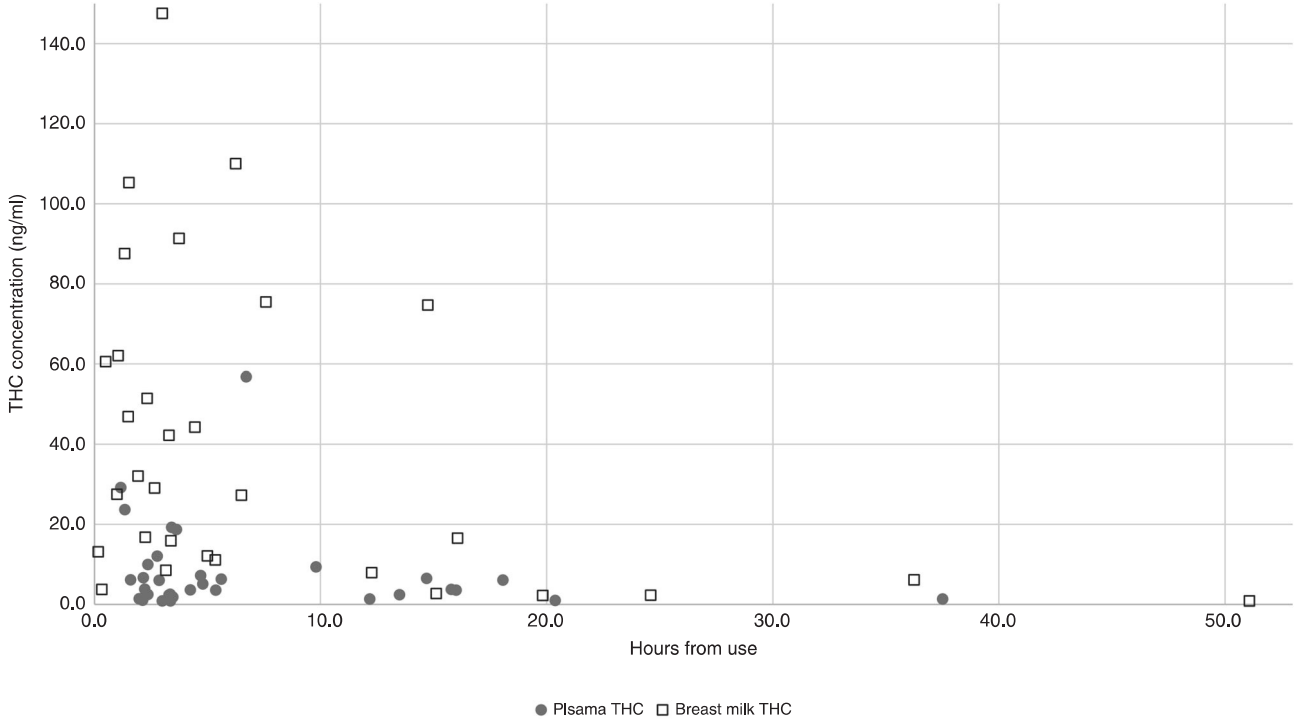

Fig. 3 Breast milk and plasma THC concentrations compared to time sample was collected after the last reported cannabis use.

Table 4. Cannabinoid concentrations after edible use.

	Source	Collection time after last use (h)	THC (ng/ml)	CBD (ng/ml)	11-OH-THC (ng/ml)	THC-COOH (ng/ml)
Patient 1	Milk	5.0	12.1	17.0	ND	0.8
	Plasma	4.8	5.1	6.4	10.7	190.0
Patient 2	Milk	6.2	110.0	2.1	1.4	11.2
	Plasma	6.7	56.8	ND	47.8	390.3
Patient 3	Milk	15.1	2.7	ND	ND	ND
	Plasma	15.0	ND	ND	0.8	24.5

ND not detected.

THC in plasma and breast milk samples

Plasma cannabinoid concentrations ranged widely (0.8–56.8 ng/ml) with a median of 3.7 ng/ml THC. These results are consistent with a previous study of male volunteers shortly after cannabis inhalation[23] and another report of similar concentrations in a breastfeeding woman 1 h after smoking cannabis.[14]

Breast milk samples contained a median of 27.5 ng/ml THC with a wide range of 0.8–190.5 ng/ml. This concentration range is consistent with a small previous study (median, 27.6 ng/ml),[12] analysis of breast milk bank samples (median, 9.47 ng/ml),[13] and one case report (60 ng/ml).[14]

Milk/plasma ratio

M/P refers to the concentration of a substance in breast milk divided by the concentration in maternal plasma and is used to quantify the amount of drug transferred to breast milk. Lipid soluble THC and CBD accumulate in breast milk (M/P ratios of 7.0 and 2.6, respectively) and the water-soluble active metabolite 11-OH-THC does not (M/P ratio of 0.07).

The single previously reported M/P of THC of 8.4[14] is quite close to our median of 7.0. However, we report a wide range of M/Ps (1.8–34.6). Thus an individual infant may be exposed to higher or lower amounts of THC depending on particular maternal pharmacokinetics. Though plasma and breast milk were not always obtained at the exact same time, M/P ratios were consistent in samples obtained within 60 min of each other.

Plasma THC concentrations peak and decline rapidly after inhalation.[20] M/P ratio may differ immediately after inhalation and before THC is distributed to tissues. We did not obtain samples until at least 2 h from last cannabis use. M/P ratio was not correlated with time to sample collection from last cannabis use.

Infant dose

Our estimate of a daily infant THC dose (4.1 mcg/kg/day) is identical to that found in a previous smaller study.[12]

Maternal usage pattern and change in breast milk THC concentration over time

We found that mothers had a statistically significant increase in THC concentration in breast milk between their first sample (2 weeks postpartum) and second sample (2 months postpartum). This may be driven by the non-significant trend toward increased cannabis use in over half of mothers. It is possible that mothers increased their cannabis use due to changes in sleep patterns and exacerbation of underlying conditions or that they increased their usage because they noted no acute effects in their child. Several mothers reported increased cannabis use as a method of treating increased anxiety in the postpartum period. Pediatricians should be aware that nursing mothers may increase cannabis use in the early postpartum period and this deserves further study.

CBD in breast milk

CBD M/Ps have not been previously described. The single subject with CBD detectable in both breast milk and plasma had an M/P of 2.6 suggesting that CBD may also accumulate in breast milk in a similar fashion to THC. CBD was present in one-third of breast milk samples but generally in a lower concentration relative to THC, suggesting that the CBD source is cannabis, as opposed to CBD-only products.

Edibles

M/Ps of THC in the two subjects who consumed edibles before sample collection were 2.4 and 1.9, within the same range as the rest of the study population, but somewhat lower than the median THC M/P. Thus both routes of administration produced similar breast milk cannabinoid concentrations. As edibles may be perceived as less harmful than smoked cannabis, breastfeeding mothers should be aware of the potential of THC to accumulate in breast milk after edible use.[24]

Although we set out to study the transfer of cannabis metabolites into human breast milk, we gained remarkable insight into the postpartum behavior and decision-making of mothers using cannabis. This is the first report of mothers describing an increase in cannabis consumption after giving birth. The perception of lack of harm to infants exposed to cannabis via breastfeeding may have been falsely reassuring to subjects, the majority of whom increased their consumption of cannabis postpartum, despite warnings from their infant's healthcare providers.

Limitations

Our results are subject to several limitations. Subjects were recruited on a volunteer basis and are not necessarily representative of all mothers using cannabis while breastfeeding. Excluding non-English speaking subjects narrowed demographics and survey responses and likely overlooked perspectives on the use of cannabis during pregnancy and lactation.

Ethically, we could not mandate mothers' cannabis use immediately prior to attending a well baby visit. Thus we recruited subjects who had recently used cannabis within the last 48 h. Even though cannabinoids may not be detectable at such a prolonged interval from last exposure, 89% of subjects had used cannabis within the last 24 h and 63% within the last 6 h. We did not assess prenatal cannabis use. However, THC concentrations were much higher shortly after cannabis use and much lower in samples collected many hours after use, likely reflecting the most recent cannabis use rather than prior accumulation of cannabinoids. An ideal measurement of THC M/P ratio would require a fixed dose of THC with multiple measurements of plasma and breast milk. Methods of cannabis use, dose, strain, and THC and CBD concentration were not mandated or controlled and presumably offer a glimpse into parenthood in the age of marijuana legalization. Though results on CBD, edibles, and resulting M/Ps are based on a very small number of patients, neither had previously been described. We relied on maternal recall for details and timing of cannabis use; nearly all subjects reported cannabis use within the last 24 h. THC and CBD concentrations may also have been influenced by the frequency and intensity of cannabis use preceding subjects' last reported use or concurrent medication use. Because breast milk samples were obtained and promptly transferred to the hospital laboratory for freezing and storage, it is unlikely that THC degradation affected results. Timing of breast milk expression (before or after nursing) was not standardized and samples likely contained varying amounts of foremilk and hindmilk.

CONCLUSIONS

The cannabinoids THC and CBD are present and accumulate in breast milk after maternal cannabis use, whether by inhalation or edible ingestion. They appear rapidly after exposure and may remain present for at least 1–2 days. Mothers using cannabis during breastfeeding were well educated and used cannabis daily for medical purposes. Their cannabis use increased significantly during the early postpartum period.

Further research is urgently needed to assess the neurodevelopmental impact of breast milk cannabinoid exposure in children with consideration of the beneficial effects of breastfeeding. Mothers using cannabis and breastfeeding should be informed of the potential for THC to accumulate in breast milk and advised of current public health and professional society recommendations on cannabis and breastfeeding.

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AUTHOR CONTRIBUTIONS

All authors contributed to study design and conception, data analysis and interpretation, manuscript drafting, and gave final approval to the manuscript.

ADDITIONAL INFORMATION

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