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Association of Cannabis Use With Nausea and Vomiting of Pregnancy

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Abstract

Our objective was to evaluate whether cannabis use was associated with nausea and vomiting in early pregnancy. Participants from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be (nuMoM2b) study enrolled from October 2010 through September 2013 with a Pregnancy-Unique Quantification of Emesis (PUQE) questionnaire and available stored urine sample from the first study visit (median gestational age 12 weeks) were included. Cannabis exposure was ascertained by urine immunoassay for 11-nor-9-carboxy-delta-9-tetrahydrocannabinol (THC-COOH); positive results were confirmed with liquid chromatography tandem mass spectrometry. The primary outcome was moderate-to-severe nausea by the PUQE score. Overall, 9250 participants were included and 5.8% (95% CI 5.4-6.3%) had detectable urine THC-COOH. In adjusted analyses, higher THC-COOH levels were associated with greater odds of moderate-to-severe nausea (20.7% vs 15.5%, aOR 1.6, 95% CI 1.1-2.2 for a 500ng/mg Cr THC-COOH increment).

Precis:

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Cannabis use as ascertained by urine assay for marijuana metabolite was associated with a higher likelihood of moderate-to-severe nausea and vomiting in early pregnancy.

Introduction:

Cannabis use is increasing among pregnant individuals[1], with many perceiving that it relieves nausea and vomiting. Our objective was to evaluate whether cannabis use was associated with nausea and vomiting in early pregnancy.

Methods:

This was an ancillary study of a prospective cohort of nulliparous individuals recruited from October 2010-September 2013 at eight academic U.S. centers as part of the Nulliparous Pregnancy Outcomes Study: Monitoring Nulliparous Mothers-to-be (nuMoM2b) study.[2] Participants who completed a Pregnancy-Unique Quantification of Emesis (PUQE) questionnaire [3] and provided a urine sample at the first study visit were included. The nuMoM2b study was approved by institutional review boards at participating centers. This ancillary analysis was considered non-human subjects research as all data and specimens were deidentified.

Stored urine specimens were thawed and cannabis exposure ascertained based on detection of 11-nor-9-carboxy-delta-9-tetrahydrocannabinol (THC-COOH) by immunoassay (limit of detection 20 ng/mL); positive results were confirmed with liquid chromatography tandem mass spectrometry (limit of detection 15 ng/mL) and quantitative values were normalized with urine creatinine (Cr).[4]

The primary outcome was selected a priori as moderate-to-severe nausea on the PUQE score (i.e., total PUQE score ≥ 7). Secondary outcomes were components of the PUQE score.

For baseline characteristics, primary and secondary outcomes, comparisons between those with and without detectable THC-COOH were made using chi square and t tests. In multivariable logistic regression, THC-COOH exposure was modeled as a continuous measure, with an odds ratio reported for a 500ng/mg Cr incremental difference, and the primary and secondary outcomes were dichotomized as present or absent. Covariates were selected based on clinical importance including maternal age, body mass index, prescription antiemetics, and gestational age. P value <0.05 was considered statistically significant. Analyses were performed in SAS 9.4.

Results:

Overall, 9250 of 10,038 nuMoM2b participants were included (Table 1) of whom 5.8% (95% CI 5.4-6.3%) had detectable urine THC-COOH. In total, 1159 (13%) reported antiemetic use; those with detectable urine THC-COOH were more likely to use antiemetics (Table 1).

In the cohort, 4257 (46.0%) reported no nausea, 3531 (38.2%) mild nausea, and 1462 (15.8%) were categorized as having moderate-to-severe nausea. Descriptive PUQE score

data are provided in Figure 1A–1D. In adjusted analyses, higher THC-COOH levels were associated with greater odds of moderate-to-severe nausea (20.7% vs 15.5%, aOR 1.6, 95% CI 1.1-2.2 for a 500ng/mg Cr THC-COOH increment), and with the secondary outcomes of vomiting and dry heaves (Figure 1E).

Discussion:

In a large, multicenter cohort, cannabis use was associated with a higher likelihood of moderate-to-severe nausea and vomiting in early pregnancy. This result is consistent with existing literature demonstrating a link between nausea in pregnancy and cannabis use.[5–6]

Prescription antiemetic use was more frequent in those with detectable THC-COOH. It is unknown whether individuals in this study were using cannabis to treat nausea, for other perceived benefit, or dependence.

The study has limitations. THC-COOH can be detected in urine for days to weeks after exposure whereas the PUQE score focuses on nausea symptoms over the prior 12 hours. Further, the cohort was created prior to widespread legal availability of cannabidiol products and may not reflect contemporary reasons for and rates of use.

Strengths include the use of biologic sampling to more accurately ascertain cannabis use in pregnancy.[4] Universal assessment for THC-COOH avoids bias observed in other studies that rely on testing at clinical discretion. In addition, we used a standardized, validated[3, 7–9] and widely used questionnaire to evaluate nausea rather than subjective recall or diagnostic codes. The cohort is multicenter with geographic and racial diversity representative of the U.S. population.

While cause and effect cannot be determined, the association between cannabis use and nausea is clinically important. Patients may be insufficiently treated for nausea and may seek other options including cannabis. Alternatively, cannabis may result in nausea of pregnancy, especially with heavy use. Obstetricians should continue to educate patients about concerns for adverse effects of cannabis use[10] and offer prescription antiemetics as appropriate to control symptoms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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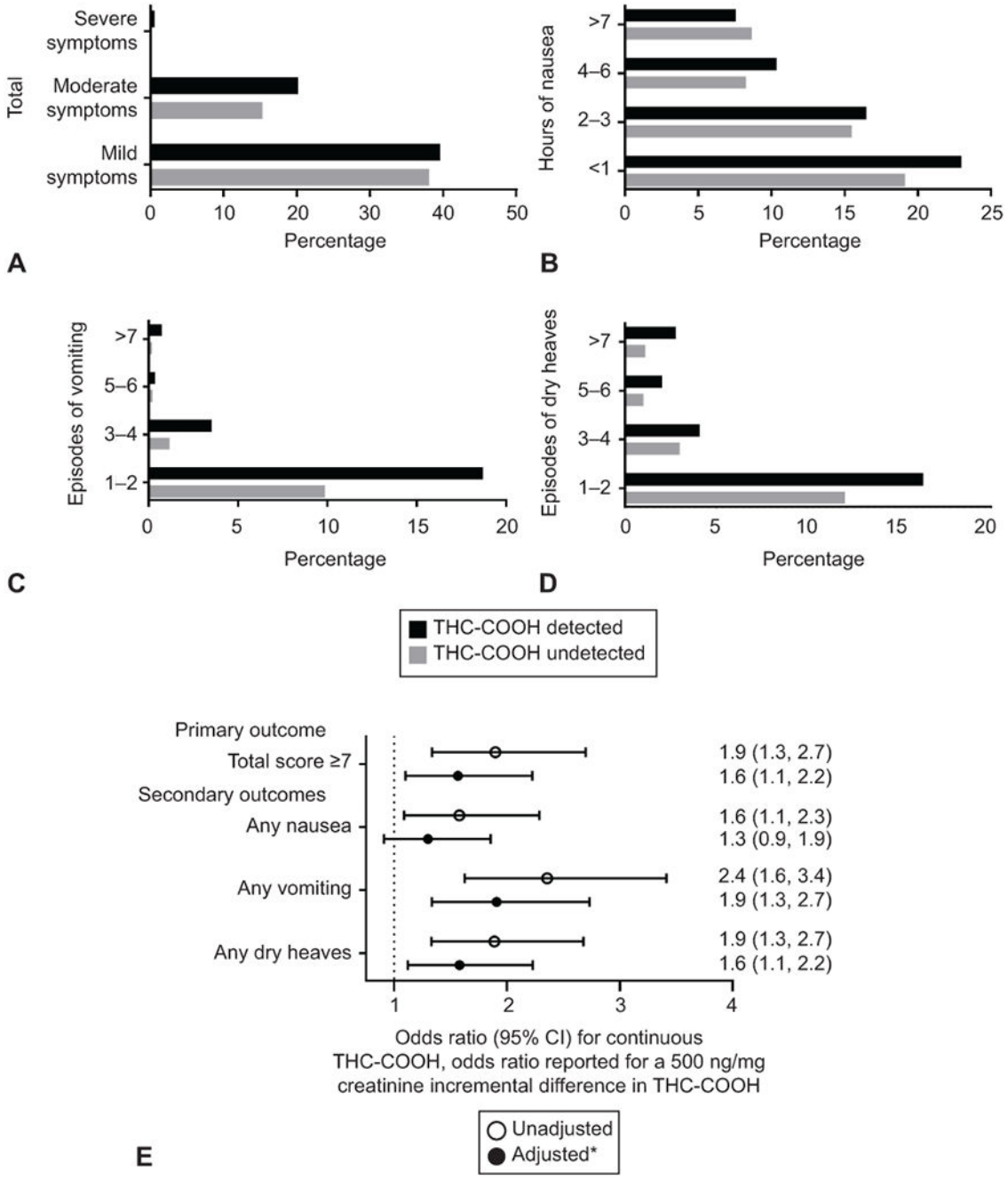

Figure 1.

Descriptive survey data from the Pregnancy-Unique Quantification of Emesis (PUQE) tool for the total PUQE score (**A**) and components of PUQE score (hours of nausea [**B**], episodes of vomiting [**C**], and episodes of dry heaves [**D**]) among those with and without detectable urine 11-nor-9-carboxy-delta-9-tetrahydrocannabinol (THC-COOH). PUQE score evaluates symptoms over the last 12 hours. **E.** Logistic regression model results for the association between THC-COOH and the primary outcome (total score ≥7 which is consistent with moderate-to-severe nausea), and the secondary outcomes which were components of the

PUQE score including any nausea, vomiting or dry heaves. *Adjusted for maternal age (<18, 18 to <30, or ≥30 years), body mass index (≥30 or <30), prescription antiemetic use (yes or no), and gestational age at visit (<10 or ≥10 weeks).

Table 1.

Baseline Characteristics of Study Population and Study Outcomes

	THC-COOH detected	THC-COOH undetected	P value[a]
Baseline Characteristics	**n=540**	**n=8710**	
Gestational age at study visit[b]	12 (10, 13)	12 (11, 13)	<0.001
Age (years)			<0.001
13-17	27 (5.0)	192 (2.2)	
18-34	504 (93.3)	7667 (88.0)	
35 and older	9 (1.7)	851 (9.8)	
Race and ethnicity[c]			<0.001
Asian	3 (0.6)	372 (4.3)	
Hispanic	77 (14.3)	1458 (16.7)	
Non-Hispanic Black	215 (39.8)	1038 (11.9)	
Non-Hispanic White	192 (35.6)	5439 (62.4)	
Body mass index (kg/m^2)[d]	26.8 (26.2, 27.4)	25.6 (25.5, 25.7)	<0.001
Body mass index category (kg/m^2)			<0.001
< 18.5 (underweight)	27 (5.1)	181 (2.1)	
18.5-24.9 (normal weight)	214 (40.5)	4430 (51.7)	
25-29.9 (overweight)	112 (21.2)	2132 (24.9)	
30-34.9 (obese)	83 (15.7)	1008 (11.8)	
≥ 35 (morbidly obese)	92 (17.4)	815 (9.5)	
Insurance			
Public insurance	377 (71.3)	2179 (25.2)	<0.001
Military insurance	1 (0.2)	58 (0.7)	0.179
Commercial insurance	138 (26.1)	6195 (71.5)	<.001
Personal income	22 (4.2)	1603 (18.5)	<0.001
Other	15 (2.8)	111 (1.3)	0.003
Federal poverty level category			<.001
> 200%	69 (21.7)	5242 (72.4)	
100-200%	71 (22.3)	1002 (13.8)	
< 100%	178 (56.0)	997 (13.8)	
Any prescription antiemetic use[e]	96 (17.8)	1063 (12.2)	<0.001
Number prescription antiemetics			<0.001
One	78 (14.4)	807 (9.3)	
Two	11 (2.0)	118 (1.4)	
Three	3 (0.6)	11 (0.1)	

	THC-COOH detected	THC-COOH undetected	P value[a]
Baseline Characteristics	**n=540**	**n=8710**	
Four	1 (0.2)	0 (0.0)	
Primary and Secondary Outcomes	**n=540**	**n=8710**	
Total PUQE score ≥ 7 (moderate-to-severe symptoms)	112 (20.7)	1350 (15.5)	0.001
Any nausea	310 (57.4)	4489 (51.5)	0.008
Any vomiting	126 (23.3)	997 (11.4)	<0.001
Any dry heaves	136 (25.2)	1496 (17.2)	<0.001

Data are n (%) unless otherwise specified.

[a] P value from Wilcoxon rank sum test for gestational age, t test for body mass index, and chi-square otherwise.

[b] Median (interquartile range).

[c] Race and ethnicity were included to describe the racial demographics of the included population for assessment of generalizability. Of note, n=53 in the THC-COOH detectable group and n=403 in the THC-COOH undetectable group self-reported a race or ethnicity that was not included on the study data collection forms.

[d] Geometric mean (95% confidence interval).

[e] Antiemetics includes promethazine, ondansetron, emetrol, droperidol, doxylamine or doxylamine and vitamin B6, metoclopramide, and prochlorperazine.