Marijuana Use and Maternal Experiences of Severe Nausea During Pregnancy in Hawai‘i

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Abstract
Recreational use of marijuana is relatively common in the United States, and medicinal use is gaining popular and legal support. Marijuana has been proposed as a potential treatment for hyperemesis gravidarum. Research into this topic is complicated by associations between marijuana use and poor birth outcomes. Cannabinoid hyperemesis syndrome, which can cause severe nausea and vomiting in marijuana users, is another complicating factor. Hawai‘i Pregnancy Risk Assessment Monitoring System data from 4,735 respondents were used to estimate prevalence of self-reported marijuana use during and in the month before pregnancy, as well as severe nausea during pregnancy. Data were weighted to be representative of all pregnancies resulting in live births in Hawai‘i between 2009 and 2011. Prevalence ratios (PR) and 95% confidence intervals (CI) were computed to estimate associations. Of recently-pregnant women in Hawai‘i, 6.0% reported using marijuana in the month before pregnancy, and 2.6% reported using marijuana during pregnancy. Approximately 21.2% reported severe nausea during pregnancy. Women who reported severe nausea during pregnancy were significantly more likely to report marijuana use during pregnancy (3.7% vs 2.3%; PR=1.63, 95% CI: 1.08-2.44). More research is needed to investigate the relationship between marijuana use and severe nausea during pregnancy, and to quantify associated risks to mother and fetus.

Keywords
Marijuana, Pregnancy

Introduction
Recreational use of marijuana is relatively common in the United States, and medicinal use is increasingly gaining popular and legal support. In 2012, approximately 38.1% of American women aged 12 and over reported ever using marijuana and 9.2% reported using it in the past year, making it the most common illicit drug used by women in the United States. One of the primary medicinal uses of marijuana is as an anti-emetic, and marijuana has been used in some cultures as treatment for nausea during pregnancy. Research is currently underway examining potential use of the drug as treatment for hyperemesis gravidarum, a severe form of nausea and vomiting during pregnancy that often requires hospitalization. However, there are significant concerns regarding use of marijuana during pregnancy. Results of recent studies examining perinatal marijuana use and birth outcomes have been mixed. Some show an association between marijuana use during pregnancy and poor birth outcomes, while others do not. Potential investigation of marijuana as treatment for severe nausea or hyperemesis gravidarum is complicated not only by associations with poor birth outcomes, but also by the existence of cannabinoid hyperemesis syndrome (CHS), which can cause cyclic nausea and vomiting in some long-term marijuana users. This study sought to (1) determine the prevalence of marijuana use during and immediately before pregnancy in Hawai‘i and (2) describe differences in marijuana use during and immediately before pregnancy in Hawai‘i by maternal report of severe nausea during pregnancy.

Methods
Data Source
A secondary analysis of Hawai‘i Pregnancy Risk Assessment Monitoring System (PRAMS) data from 2009 to 2011 was conducted. PRAMS is a self-reported survey of recent mothers designed to collect information on maternal behaviors, attitudes, and experiences before, during, and immediately following pregnancy. It is a partnership project between the Centers for Disease Control and Prevention (CDC) and selected state and city health departments. PRAMS programs follow a standardized data collection protocol centering on self-administered mailed questionnaires with telephone follow-up for non-responders. Women are selected for participation in the Hawai‘i PRAMS survey as part of a stratified sample drawn from the certificates of live births in Hawai‘i. Participants complete the survey 3-8 months postpartum, with the majority responding 3-4 months postpartum. The Hawai‘i PRAMS analytic dataset includes information collected from survey questions as well as from selected linked birth certificate variables. Data are annually weighted for nonresponse and other demographic factors by the CDC to create an analytic dataset which is representative of all pregnancies resulting in live births in Hawai‘i in a given year. All PRAMS program sites must achieve a minimum weighted response rate of 65% in order for survey results to be considered generalizable to all live births in a given year. Hawai‘i PRAMS annual response rates have not fallen below 65% since data collection began in 2000, and the response rates for the years presented in this analysis ranged from 71-73%. Detailed information on PRAMS methodology can be found at: http://www.cdc.gov/prams/methodology.htm.

Data were available for 4,735 respondents, weighted to be representative of all pregnancies resulting in live births in Hawai‘i between 2009 and 2011 (approximately 55,690 live births). Survey responses related to the three main outcomes of interest were missing in less than 3% of weighted cases. Secondary analysis of Hawai‘i PRAMS data is covered under pre-existing approvals granted by the Institutional Review Board of the Human Research Protection Office of the CDC, as well as by the Hawai‘i State Department of Health Institutional Review Board.

Measures
The following questions pertaining to severe nausea during
pregnancy and marijuana use in the month before and during pregnancy were used for this analysis:

Did you have any of the following problems during your most recent pregnancy? For each item, circle Y (Yes) if you had the problem or circle N (No) if you did not.

- c. Severe nausea, vomiting, or dehydration  N Y

Did you use any of these drugs in the month before you got pregnant? For each item, circle Y (Yes) if you used it or circle N (No) if you did not.

- b. Marijuana (pot, bud) or hashish (hash)  N Y

Prevalence estimates, confidence intervals, and P-values were generated using SAS 9.2 (SAS Institute Inc., Cary, NC) and SAS-callable SUDAAN 10.0 (RTI International, Research Triangle Park, NC) to account for complex sampling. Chi-square tests were calculated to determine statistical significance.

Maternal age, race/ethnicity, nativity, education, and parity were determined based on linked birth certificate variables included in the Hawai‘i PRAMS dataset. Although approximately 23% of the population of Hawai‘i identifies as mixed race, maternal race/ethnicity variables included in the Hawai‘i PRAMS dataset have been sorted into single race groups based on a standard algorithm used by the Hawai‘i State Department of Health Office of Health Status and Monitoring. Federal Poverty Level (FPL) was based on maternal report of household annual income and number of dependents in the year before delivery and was calculated according to Hawai‘i-specific threshold guidelines.

Results

Of women with recent live births in Hawai‘i, 6.0% (95% CI: 5.2-6.8) reported using marijuana in the month before their most recent pregnancy, and 2.6% (95% CI: 2.2-3.2) reported using marijuana during their most recent pregnancy. The demographic groups reporting the highest estimates of pre-pregnancy marijuana use were women of other or unknown race/ethnicity (12.1%; 95% CI: 7.8-18.1), women below age 20 (10.3%; 95% CI: 7.2-14.5), primiparous women (9.1%; 95% CI: 7.6-10.8), and women with less than a high school education (8.9%; 95% CI: 5.8-13.2). The demographic groups reporting the highest estimates of marijuana use during pregnancy were women of other or unknown race/ethnicity (4.6%; 95% CI: 2.7-7.7), women at or below 100% of the Federal Poverty Level (4.1%; 95% CI: 3.1-5.5), white women (3.8%; 95% CI: 2.8-5.3), and women with 1-3 years of college education (3.8%; 95% CI: 2.6-5.5). A complete breakdown of these prevalence estimates by maternal characteristics can be seen in Table 1.

Approximately 21.2% (95% CI: 19.8-22.8) of women with live births in Hawai‘i reported severe nausea during their most recent pregnancy. Compared to those who did not report severe nausea during pregnancy, women who reported severe nausea during pregnancy were more likely to report marijuana use during pregnancy (3.7% vs 2.3%; PR = 1.63, 95% CI: 1.08-2.44) (Table 1). This association was statistically significant (P = .034). Women who reported severe nausea during pregnancy also had a higher prevalence of marijuana use before pregnancy compared to women who did not report severe nausea during pregnancy (7.0% vs 5.5%; PR = 1.27, 95% CI: 0.94-1.72), however the association between marijuana use before pregnancy and severe nausea during pregnancy was not statistically significant (P = .134).

Discussion

Hawai‘i women who reported severe nausea during pregnancy were significantly more likely to report use of marijuana during pregnancy than those who did not report severe nausea during pregnancy. As medical marijuana use has been legal in the state of Hawai‘i since the year 2000, this finding could indicate use of marijuana as an anti-emetic (either with or without a prescription from a licensed health care provider) among those experiencing severe morning sickness. However, marijuana use before pregnancy was also associated with an increased likelihood of severe nausea during pregnancy, although the difference was not statistically significant. These preliminary findings warrant further research into the subject, with special attention paid to the relatively rare, but increasingly documented cannabinoid hyperemesis syndrome (CHS). While CHS is still being fully described as a medical condition, current reports describe it as being characterized by cyclic nausea and vomiting in long-term marijuana users. In light of this, the relationship between marijuana use, CHS, and severe nausea during pregnancy is a bit more complicated. Are regular marijuana users who become pregnant more likely to report severe nausea during pregnancy due to undiagnosed CHS? Are women with severe nausea during pregnancy opting to use marijuana (legally or illegally) in order to relieve their symptoms, with CHS playing a role only as a minor complicating factor? The body of literature available does not appear sufficient to make a clear determination at this time.

As current information on CHS relies mainly on case reports from the past decade, population prevalence estimates are not yet available. However, CHS has been observed and described in Hawai‘i. There has also been at least one published case report of CHS during pregnancy to date, and the first documented report of CHS in the literature (in 2004) stated that two female CHS patients reported a history of severe hyperemesis gravidarum which had required hospital admission and administration of intravenous fluids. An important point from the 2011 case report of CHS during pregnancy regarded misdiagnosis of CHS as hyperemesis gravidarum. The researchers in that study suggested that pregnant patients with tentative diagnoses of hyperemesis gravidarum who do not respond to treatment might benefit from investigation of CHS as a possible cause, along with potentially adjusting treatment accordingly. Currently, the principle treatments for CHS include utilizing hot...
Table 1. Marijuana Use By Maternal Characteristics, Hawai‘i PRAMS, 2009-2011

<table>
<thead>
<tr>
<th></th>
<th>Percent of total birth population* (95% CI)</th>
<th>Percent reporting marijuana use before pregnancy* (95% CI)</th>
<th>P–Value</th>
<th>Percent reporting marijuana use during pregnancy* (95% CI)</th>
<th>P–Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>100</td>
<td>6.0 (5.2 – 6.8)</td>
<td></td>
<td>2.6 (2.2 – 3.2)</td>
<td></td>
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<tr>
<td>Age (years)</td>
<td></td>
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<tr>
<td>&lt; 20</td>
<td>7.3 (6.4 – 8.3)</td>
<td>10.3 (7.2 – 14.5)</td>
<td>P &lt; .001</td>
<td>3.2 (1.7 – 5.7)</td>
<td>P = .196</td>
</tr>
<tr>
<td>20-24</td>
<td>23.6 (22.1 – 25.3)</td>
<td>8.6 (6.8 – 10.9)</td>
<td></td>
<td>3.6 (2.6 – 5.2)</td>
<td></td>
</tr>
<tr>
<td>25-29</td>
<td>27.3 (25.7 – 29.0)</td>
<td>5.3 (4.0 – 6.9)</td>
<td></td>
<td>1.9 (1.3 – 2.8)</td>
<td></td>
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<tr>
<td>30-34</td>
<td>24.4 (22.9 – 26.0)</td>
<td>4.5 (3.3 – 6.2)</td>
<td></td>
<td>2.6 (1.7 – 3.9)</td>
<td></td>
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<tr>
<td>35+</td>
<td>17.4 (16.1 – 18.8)</td>
<td>3.6 (2.3 – 5.5)</td>
<td></td>
<td>2.1 (1.2 – 3.8)</td>
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<tr>
<td>Race</td>
<td></td>
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<tr>
<td>Hawaiian or other Pacific Islander*</td>
<td>37.4 (35.7 – 39.2)</td>
<td>6.2 (5.0 – 7.6)</td>
<td>P &lt; .001</td>
<td>2.8 (2.1 – 3.8)</td>
<td>P = .001</td>
</tr>
<tr>
<td>Asianb</td>
<td>34.4 (32.7 – 36.2)</td>
<td>2.9 (2.0 – 4.2)</td>
<td></td>
<td>1.4 (0.8 – 2.4)</td>
<td></td>
</tr>
<tr>
<td>Whiteb</td>
<td>23.0 (21.5 – 24.6)</td>
<td>8.8 (7.1 – 11.0)</td>
<td></td>
<td>3.8 (2.8 – 5.3)</td>
<td></td>
</tr>
<tr>
<td>Other or unknownc</td>
<td>5.2 (4.4 – 6.1)</td>
<td>12.1 (7.8 – 18.1)</td>
<td></td>
<td>4.6 (2.7 – 7.7)</td>
<td></td>
</tr>
<tr>
<td>Nativity</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Born in US</td>
<td>74.8 (73.1 – 76.4)</td>
<td>7.3 (6.4 – 8.4)</td>
<td>P &lt; .001</td>
<td>3.3 (2.7 – 4.0)</td>
<td>P &lt; .001</td>
</tr>
<tr>
<td>Born outside US</td>
<td>25.2 (23.7 – 26.9)</td>
<td>1.8 (1.1 – 3.1)</td>
<td></td>
<td>0.7 (0.4 – 1.3)</td>
<td></td>
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<tr>
<td>Education Level</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Less than high school</td>
<td>7.5 (6.6 – 8.5)</td>
<td>8.9 (5.8 – 13.2)</td>
<td>P &lt; .001</td>
<td>3.0 (1.6 – 5.5)</td>
<td>P = .045</td>
</tr>
<tr>
<td>High school graduate</td>
<td>39.7 (37.9 – 41.5)</td>
<td>6.5 (5.3 – 8.0)</td>
<td></td>
<td>2.4 (1.8 – 3.3)</td>
<td></td>
</tr>
<tr>
<td>1-3 years of college</td>
<td>23.5 (22.0 – 25.1)</td>
<td>6.0 (4.5 – 7.9)</td>
<td></td>
<td>3.8 (2.6 – 5.5)</td>
<td></td>
</tr>
<tr>
<td>4 or more years of college</td>
<td>29.3 (27.3 – 31.0)</td>
<td>4.1 (3.0 – 5.5)</td>
<td></td>
<td>1.7 (1.1 – 2.5)</td>
<td></td>
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<tr>
<td>Federal Poverty Level (%)</td>
<td></td>
<td></td>
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<tr>
<td>≤ 100%</td>
<td>29.3 (27.6 – 31.0)</td>
<td>8.7 (7.1 – 10.7)</td>
<td>P &lt; .001</td>
<td>4.1 (3.1 – 5.5)</td>
<td>P = .007</td>
</tr>
<tr>
<td>101-200%</td>
<td>26.0 (24.4 – 27.7)</td>
<td>6.2 (4.6 – 8.2)</td>
<td></td>
<td>2.2 (1.5 – 3.3)</td>
<td></td>
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<tr>
<td>201% +</td>
<td>44.7 (42.8 – 46.6)</td>
<td>4.1 (3.2 – 5.3)</td>
<td></td>
<td>2.0 (1.4 – 2.9)</td>
<td></td>
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<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>First live birth</td>
<td>40.6 (38.8 – 42.4)</td>
<td>9.1 (7.6 – 10.8)</td>
<td>P &lt; .001</td>
<td>3.7 (2.9 – 4.8)</td>
<td>P = .001</td>
</tr>
<tr>
<td>Not first live birth</td>
<td>59.4 (57.6 – 61.2)</td>
<td>3.8 (3.1 – 4.7)</td>
<td></td>
<td>1.9 (1.4 – 2.5)</td>
<td></td>
</tr>
<tr>
<td>Severe Nausea During Pregnancy</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>78.8 (77.2 – 80.2)</td>
<td>5.5 (4.7 – 6.5)</td>
<td>P = .134</td>
<td>2.3 (1.8 – 2.9)</td>
<td>P = .034</td>
</tr>
<tr>
<td>Yes</td>
<td>21.2 (19.8 – 22.8)</td>
<td>7.0 (5.4 – 9.0)</td>
<td></td>
<td>3.7 (2.7 – 5.1)</td>
<td></td>
</tr>
</tbody>
</table>

*Weighted estimates; *Hawaiian or other Pacific Islander includes Hawaiian, Part Hawaiian, Samoan, Guamanian, and other Pacific Islander; *Asian includes: Chinese, Japanese, Korean, Filipino, Vietnamese, Asian Indian, and other Asian; *Other or unknown includes: African American, American Indian, Puerto Rican, Cuban, Mexican, and all others.

baths or showers for immediate symptom relief, with abstinence from marijuana typically providing long-term resolution of symptoms.5,25 Supportive treatment for dehydration may also be needed.5,25

This study is the first examining the relationship between marijuana use and severe nausea during pregnancy using maternally reported data from the Hawai‘i PRAMS survey. This data source has advantages over smaller studies in that it provides population-based estimates representing all pregnancies resulting in live births in Hawai‘i in a given time period. Another advantage of using Hawai‘i PRAMS as a data source for this study relates to the uniqueness of the state itself. The multiethnic nature of the population of Hawai‘i means that generalizability of research findings from studies conducted outside the state is unclear with regards to many different topics, marijuana use included. The research presented here includes racial and ethnic groups less frequently reported in the scientific literature.

This study does have limitations. Limitations related to the Hawai‘i PRAMS survey itself include that the data are self-reported, and consequently subject to bias due to recall or reporting factors. Due to the sensitive nature of the subject, some bias in reporting due to perceived social desirability of behaviors would be expected.20 However, past research has shown that population prevalence estimates calculated based on maternal self-report of marijuana use during pregnancy tend to be higher than those calculated based on positive urine
tests, suggesting that self-reported survey data is a good starting point for research into this topic. The Hawai‘i PRAMS survey questions related to marijuana use did not have information on amount or frequency of use, pregnancy trimester of usage, or if the marijuana was recreational or prescribed by a physician. The survey question related to severe morning sickness during pregnancy was self-reported and non-validated, so variation may have existed with respect to maternal interpretation of nausea severity.

There may also be some effects due to mode bias (mail versus telephone), as mail respondents were more likely to report all three outcomes of interest than were phone respondents (data not shown). However, phone respondents tend to differ from mail respondents in multiple ways, some of which are thought to be at least partially addressed by PRAMS weighting for demographic characteristics. Previous investigation into mode bias effects on PRAMS survey responses found that most differences by mode were minimal or nonexistent, and attempts to control for mode bias resulted in very small absolute differences in estimates.

In the years examined for this study, 81.0% of survey respondents completed the Hawai‘i PRAMS questionnaire by mail.

Although medical use of marijuana has been legal in Hawai‘i for some time, the issue is still accompanied by significant controversy within the state, as it is in the rest of the country. More research is needed to investigate the exact nature of the relationship between marijuana use and severe nausea during pregnancy, as well as to quantify other risks to mother and fetus associated with marijuana use during pregnancy.

Disclaimer
The findings and conclusions described in this article are those of the authors and do not necessarily represent the official position of the Hawai‘i State Department of Health, the Centers for Disease Control and Prevention, or any other organization.

Conflict of Interest
None of the authors identify a conflict of interest.

Acknowledgements
The researchers would like to thank all of the women who have responded to the Hawai‘i PRAMS survey since the program began as a pilot project in 1999. Without their willingness to share information about their experiences before, during, and after pregnancy, this research would not be possible. Additionally, Brian Morrow, Mathematical Statistician for the CDC PRAMS program, provided valuable guidance with respect to statistical analysis for this project, CDC Statistician Holly B. Shulman provided additional information related to mode bias effects on PRAMS survey responses, and CDC Health Scientist Denise D’Angelo provided feedback on an early draft of this manuscript. The researchers would also like to acknowledge the Hawai‘i State Department of Health, and specifically the Family Health Services Division and Maternal and Child Health Branch, for supporting the Hawai‘i PRAMS program. This study was made possible in part by CDC grant #U01DP003145.

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