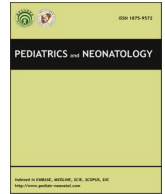




Contents lists available at ScienceDirect

Pediatrics & Neonatology

journal homepage: www.pediatr-neonol.com

Prenatal cannabis use and adverse health outcomes in neonates and early childhood

Panagiota Kitsantas^{a,*}, Katerina Benson^b, Alexandra Rubenstein^c, Maria Carmenza Mejia^{a,d}, Robert S. Levine^{a,d}, Charles H. Hennekens^a, Sarah K. Wood^d

^a Department of Population Health and Social Medicine, Charles E. Schmidt College of Medicine, Florida Atlantic University, USA

^b Florida Atlantic University, USA

^c Tufts University School of Medicine, Tufts University, USA

^d Harvard Macy Institute, Harvard Medical School, USA

In the United States (US), the use of cannabis sativa, the medical term for marijuana, has been influenced by federal and state legalization. This trend began with medicinal use which refers to a health provider prescribing this drug to treat symptoms of their sick patients, which were initially those with metastatic cancer. Medicinal use of cannabis today is legal in 38 US states. In addition, recreational use of cannabis is currently legal in 24 US states.

Due at least in part to these circumstances, cannabis is the drug most frequently used during pregnancy in the US. In pregnant US women, the estimated use of cannabis ranges from 4.6% to 10.7% [1]. From 2002 to 2017 prenatal cannabis use increased about 2.1-fold from 3.4% to 7.0% [2]. In addition, among women who use cannabis during pregnancy, an estimated 19% have cannabis dependence [1]. The self-reported reasons for cannabis use during pregnancy include the alleviation of nausea, stress, anxiety, and depression. Many women perceive cannabis as a natural, safer alternative to prescription medications or other substances such as alcohol and tobacco. Cannabis use during pregnancy, however, can adversely impact the health of mothers and their neonates as well as growing children. From this perspective, we briefly review the available evidence concerning prenatal cannabis exposure and adverse health outcomes in neonates and early childhood. Our conclusions are consistent with those of other committees that recommend against the use of prenatal cannabis.

Exposure to cannabis during pregnancy has been linked to low birth weight, preterm delivery, perinatal mortality, lower Apgar scores, and neonatal intensive care unit admissions [3–5]. Moreover, studies indicate potential links to gastrointestinal malformations [6]. It is important to note that the available data concerning cannabis use during pregnancy and birth defects are largely based on descriptive studies or analytic studies with inherent biases as well as failure to control

confounding. At present the totality of evidence is incomplete and so analytic studies designed a priori to test the hypothesis and adequately address bias and confounding as well as chance are necessary [7]. Thus, studies of prenatal cannabis exposure and structural birth defects show inconsistent results, with many failing to consider the biases inherent in their study designs and uncontrolled confounding [6]. Overall, studies on adverse health effects (e.g., low birth weight, etc.) associated with prenatal cannabis exposure are characterized by methodological issues, including small sample sizes, varied cannabis potency, measurement of cannabis use and health outcomes as well as confounding factors such as co-use of tobacco or alcohol [5].

In addition, prenatal exposure to cannabis beyond the first trimester suggests an increased likelihood of high levels of seeking out and over-attention to visual stimulation in 15-month-old children [8]. Prospective studies among offspring exposed to prenatal cannabis also show increased deficits in cognitive domains which include language comprehension and memory [9]. Recent findings suggest that continued use of cannabis after pregnancy recognition may increase the likelihood of psychopathology in middle childhood [10]. Although prenatal cannabis exposure may result in poorer attention and externalizing behaviors in infancy and early childhood, data to support cognitive impairments or internalizing behaviors are sparse [5]. Cannabis exposure during fetal development may disturb the normal functioning of several systems, including the endogenous opioid system which may affect mood and pain perception as well as altering dopaminergic receptor densities that are implicated in psychiatric and substance use disorders [5]. These findings suggest that children exposed to parental cannabis may have long-term adverse outcomes.

From our perspective, further research should include descriptive studies that are useful to formulate hypotheses and analytic studies (e.g.,

* Corresponding author.

E-mail address: pkitsanta@health.fau.edu (P. Kitsantas).

<https://doi.org/10.1016/j.pedneo.2024.11.004>

Received 8 May 2024; Received in revised form 17 October 2024; Accepted 12 November 2024

Available online 9 January 2025

1875-9572/© 2024 Taiwan Pediatric Association.

Published by Elsevier Taiwan LLC. This is an open access article under the CC BY license

(<http://creativecommons.org/licenses/by/4.0/>).

matched-case control studies, etc.) designed to test the hypotheses. Hypothesis testing of moderate to large effects can rely on observational analytic studies of cohort and case-control. For smaller effects, however, the amount of uncontrolled and uncontrollable confounding inherent in these designs may be as large as the postulated effect sizes. Although large-scale randomized trials are a particularly crucial component of the future totality of the evidence, in these circumstances involving prenatal cannabis exposure, randomized trials have major limitations including ethics, costs, and feasibility [7].

Large-scale prospective studies will be important potential contributors if they adequately address confounding, and the need for standardized measures to assess cannabis use including routes of administration, products, cannabis potency, and dose. The availability of such evidence should produce a clearer understanding of the relationship between prenatal cannabis use and health outcomes in neonates and early childhood. Prospective data would also allow assessments of the effects of prenatal cannabis exposure across developmental stages and lifespan transitions. Enhancing data collection and metrics associated with cannabis, along with developing community-based databanks, can lead to greater accuracy in the results. Furthermore, the recreational use of cannabis and its medical analog for certain diseases may have different effects on the fetus, warranting separate investigations for these two populations. It is also necessary to explore the potential impact of cannabis exposure through breastmilk and second-hand cannabis smoke and the potential for bidirectional and generational epigenetic effects. If there is a conclusion of a valid statistical association, then belief in causality would be enhanced by the consistency of findings from different investigators using different methodologies [7]. The integration of qualitative research and triangulation methods can also offer a more comprehensive understanding of the context and consequences of prenatal cannabis exposure.

When the evidence becomes complete, it will be possible to make the most rational individual decisions for patients as well as policy decisions for the health of the general public [7].

For now, we should not let the perfect be the enemy of the good. In regards to the use of cannabis during pregnancy and breastfeeding, we concur with the Surgeon General of the US as well as the American College of Obstetrics and Gynecology, and the American Academy of Pediatrics, all of whom advocate against prenatal cannabis use.

Healthcare providers should incorporate routine screening for cannabis use during prenatal visits and offer evidence-based counseling on potential risks, emphasizing harm reduction when abstinence is not feasible.

In conclusion, while evidence on prenatal cannabis exposure is still developing, the current research suggests significant risks to infants and children. Until more conclusive data are available, healthcare providers and public health authorities should follow established guidelines and advise against cannabis use during pregnancy and breastfeeding, prioritizing the health and safety of both mothers and children.

Declarations of interest

None.

References

- [1] Alshaarawy O, Anthony JC. Cannabis use among women of reproductive age in the United States: 2002–2017. *Addict Behav* 2019;99:106082.
- [2] Volkow ND, Han B, Compton WM, McCance-Katz EF. Self-reported medical and nonmedical cannabis use among pregnant women in the United States. *JAMA* 2019;322:167–9.
- [3] Bailey BA, Wood DL, Shah D. Impact of pregnancy marijuana use on birth outcomes: results from two matched population-based cohorts. *J Perinatol* 2020;40:1477–82.
- [4] Lo JO, Shaw B, Robalino S, Ayers CK, Durbin S, Rushkin MC, et al. Cannabis use in pregnancy and neonatal outcomes: a systematic review and meta-analysis. *Cannabis Cannabinoid Res* 2024;9:470–85.
- [5] Sorkhou M, Singla DR, Castle DJ, George TP. Birth, cognitive and behavioral effects of intrauterine cannabis exposure in infants and children: a systematic review and meta-analysis. *Addiction* 2024;119:411–37.
- [6] Delker E, Hayes S, Kelly AE, Jones KL, Chambers C, Bandoli G. Prenatal exposure to cannabis and risk of major structural birth defects: a systematic review and meta-analysis. *Obstet Gynecol* 2023;142:269–83.
- [7] Hennekens CH, DeMets D. Statistical association and causation: contributions of different types of evidence. *JAMA* 2011;305:1134–5.
- [8] Bailey BA, Osborne JB. Prenatal marijuana exposure and visual perception in toddlers: evidence of a sensory processing deficit. *Front Pediatr* 2023;11:1113047.
- [9] Day NL, Richardson GA, Goldschmidt L, Robles N, Taylor PM, Stoffer DS, et al. Effect of prenatal marijuana exposure on the cognitive development of offspring at age three. *Neurotoxicol Teratol* 1994;16:169–75.
- [10] Paul SE, Hatoum AS, Fine JD, Johnson EC, Hansen I, Karcher NR, et al. Associations between prenatal cannabis exposure and childhood outcomes: results from the ABCD study. *JAMA Psychiatry* 2021;78:64–76.