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A brewing concern: A review of the association between caffeine intake during pregnancy and adverse fetal outcomes

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Abstract

Adverse fetal outcomes, such as miscarriage, stillbirth and preterm birth, present serious public health concerns. Maternal caffeine intake during pregnancy may increase these risks; however, research to date has been equivocal. This literature review investigates the association between maternal caffeine intake and miscarriage, stillbirth and preterm birth among women of reproductive age (15–49 years). A search of MEDLINE (Ovid) and PubMed databases identified 8 primary, quantitative studies published in English since 2015. The evidence was inconsistent. Three studies explored miscarriage: one reported a relationship and 2 did not. Two studies explored stillbirth: one identified a relationship and the other reported no relationship. Five studies explored preterm birth: 3 reported a relationship while 2 did not. Variability in study design, exposure assessment and confounder adjustment likely account for these discrepancies. These findings highlight the complexity of evaluating the impact of maternal caffeine intake and the challenge in developing public health recommendations.

Introduction

Adverse fetal outcomes, including miscarriage, stillbirth and preterm birth, pose significant individual and public health challenges (Ohuma et al., 2024; PHAC, 2017). Miscarriage refers to fetal death before 20 gestational weeks (GWs), stillbirth to fetal death at or beyond 20 GWs and preterm birth as delivery before 37 GWs (PHAC, 2017). In Canada, annually approximately 15–25% of clinically recognised pregnancies result in miscarriage, 0.89% in stillbirth and 8.3% in preterm birth (PHAC, 2017; Statistics Canada, 2023; Statistics Canada, 2024). These outcomes have serious physical, psychological and financial impacts on individuals and families, while signalling the likelihood of future pregnancy complications (Quenby et al., 2021).

Maternal nutrition is one of the key determinants of pregnancy outcomes, especially of fetal growth and development (Abu-Saad & Fraser, 2010). Caffeine, a common stimulant in tea, coffee, chocolate, carbonated beverages, energy drinks and certain medications, readily crosses the placenta (Reddy et al., 2024). However, the placenta and fetus cannot efficiently metabolise caffeine, leading to prolonged exposure and potential risks such as impaired growth, disrupted organ development, low birth weight and chromosomal anomalies.

The Public Health Agency of Canada's (PHAC, 2024) recommendation is to limit caffeine intake to under 300 mg/day; however, the evidence linking maternal caffeine intake and adverse fetal outcomes remains inconclusive. This is largely due to conflicting findings and methodological differences across studies. Researchers are limited to observational study designs, as it is unethical to conduct a randomised controlled trial in this area. This review analyses how maternal caffeine intake impacts adverse fetal outcomes, specifically miscarriage, stillbirth and preterm birth, among women of reproductive age (15–49 years), which aims to contribute to the knowledge base for public health recommendations.

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Methods

The studies included in this literature review were selected on a set of predefined inclusion and exclusion criteria. Only primary, quantitative research articles were considered, excluding qualitative articles, systematic reviews and meta-analyses. Eligible studies focused on women aged 15–49 years. The predictor variable examined in the included studies involved the consumption of any caffeine source. The examination focused on adverse fetal outcomes, specifically miscarriage, stillbirth and preterm birth. Animal studies were excluded, as were studies not written in English and those published before 2015. Table 1 summarises the inclusion and exclusion criteria applied in this review.

Eight studies were identified

A search was conducted in MEDLINE (Ovid) and PubMed databases. The author used a combination of terms related to the consumption of caffeine and caffeine-containing sources, including coffee, tea, energy drinks, cacao, chocolate and carbonated beverages. These terms were paired with terms for adverse fetal outcomes encompassed by 3 major categories: miscarriage, stillbirth and preterm birth. Table 2 outlines the databases searched, the predictor and outcome search terms, and the Boolean operators applied in the search strategy.

Results and discussion

Eight studies were identified, including 3 that focused on miscarriage, 2 on stillbirth and 5 on preterm birth. The following sections present key findings, along with an overview of the strengths and limitations of this body of research.

Caffeine intake and miscarriage

Miscarriage is underrepresented in the literature, with only 3 studies including it as an outcome variable (Ding et al., 2023; Hahn et al., 2015; Morales-Suárez-Varela et al., 2017). Two studies found no statistically significant association between caffeine intake and miscarriage (Ding et al., 2023; Morales-Suárez-Varela et al., 2017).

Ding et al. (2023) measured pre-pregnancy caffeine intake, reporting no association with miscarriage after adjusting for multiple confounders, including sociodemographic characteristics, lifestyle behaviours (like smoking status, physical activity and diet quality), marital status, body composition, overall energy intake, use of multivitamin supplements and total years of shift work, with an adjusted odds ratio (aOR) of 0.89 (95% CI: 0.71–1.11). However, alcohol consumption, a potential source of residual confounding, was not considered. The study used a validated food-frequency questionnaire to measure caffeine intake over a one-year period, capturing long-term intake. However, caffeine intake was reported through a frequency-based question: participants were categorised as either consumers or non-consumers. This classification obscures potential dose-dependent effects and does not fully capture variations in levels of intake.

Table 1: Eligibility criteria

Category	Description
Study design	Primary, quantitative research articles only
Population	Women aged 15–49 years
Predictor variable	Consumption of any caffeine source
Outcome variables	Adverse fetal outcomes: miscarriage, stillbirth and preterm birth
Exclusions	Animal studies, non-English publications, studies published before 2015

Table 2: Database search strategy

Component	Description
Databases	MEDLINE (Ovid), PubMed
Search terms for predictor variable	caffeine; coffee; energy drinks; chocolate; cacao; carbonated beverages; tea (combined using the OR Boolean operator)
Search terms for outcome variable	miscarriage; spontaneous abortion; stillbirth; preterm birth; premature birth (combined using the OR Boolean operator)
Search structure	All the search terms for the predictor variable were paired with all the search terms for outcome variable using the AND Boolean operator.

Morales-Suárez-Varela et al. (2017) reported comparable findings, with a slightly elevated but not statistically significant risk of miscarriage among women consuming ≤3 cups/day (adjusted Hazard Ratio [aHR]: 1.05, 95% CI: 0.87–1.27) and >3 cups/day (aHR: 1.22, 95% CI: 0.91–1.63), after adjusting for maternal age, parity, socioeconomic status, physical activity, alcohol intake and pre-pregnancy body mass index (BMI). However, the authors did not adjust for dietary factors, a potential limitation given that overall diet quality may influence miscarriage risks. This was the only study that explored the combined effect of caffeine intake and smoking on miscarriage and preterm birth. Individuals who smoked >10 cigarettes and drank >3 cups of coffee had an elevated risk (aHR: 1.82, 95% CI: 1.25–2.64). However, it is not possible to conclude that smoking and high caffeine intake amplify the risk beyond their separate contributions (interaction contrast ratio [ICR]: 0.55, 95% CI: -0.38, 1.45). Participants were stratified into 3 tiers of caffeine intake, allowing for an assessment of dose–response relationships. However, potential coding inconsistencies were noted, as participants consuming >1 cup/day were recoded as consuming only 0.5 cup/day, which might have resulted in an underestimation of true intake.

A key limitation of both studies is their narrow focus on a single caffeine source: Ding et al. (2023) assessed energy drinks, while Morales-Suárez-Varela et al. (2017) assessed coffee. This limited exposure assessment likely led to an underestimation of overall caffeine intake and its possible impact on miscarriage.

Hahn et al. (2015) accounted for multiple caffeine sources and identified a modest association that was contingent on dose and timing of consumption. A slightly elevated likelihood of late miscarriage (≥8 GWs) was associated with pre-pregnancy intake of ≥300 mg/day of caffeine (aHR: 1.40; 95% CI: 1.00–1.96). Early pregnancy intake was linked to an increased miscarriage risk at 100–199 mg/day (aHR: 1.62, 95% CI: 1.19–2.22) and 200–299 mg/day (HR: 1.48; 95% CI: 1.03–2.13). These associations were adjusted for maternal age, physical activity, number of previous births, BMI, educational background, smoking status, alcohol consumption and prior miscarriages.

Unlike the first 2 studies, Hahn et al. (2015) distinguished between caffeine intake before and during early pregnancy, acknowledging potential behavioural changes following conception. While this approach improved exposure assessment by incorporating multiple caffeine sources, it still excluded relevant sources, including chocolate, energy drinks, certain teas and medication. All studies relied on hospital registry and/or self-reporting to assess miscarriage, potentially leading to underreporting, particularly of early pregnancy losses that did not require medical intervention or were unrecognised by individuals. The omission of early miscarriage may have introduced misclassification bias and underestimation of caffeine's true effect on pregnancy loss. Consequently, studies may have underestimated the strength of the association, as early losses linked to caffeine intake may have gone undetected.

Adjustment for confounding variables varied across the 3 studies. Only Ding et al. (2023) accounted for dietary factors that could influence miscarriage risk in conjunction with caffeine intake. Furthermore, definitions of miscarriage varied: <20 GWs (Ding et al., 2023), <22 GWs (Hahn et al., 2015) and <28 GWs (Morales-Suárez-Varela et al., 2017). The varying definitions of miscarriage impact comparability, potentially weakening or amplifying the observed link between caffeine intake and miscarriage.

Given the limited and heterogeneous evidence from 3 studies on caffeine intake and miscarriage risk, variations in study methodologies, exposure assessment and miscarriage definitions, coupled with potential biases such as underreporting of early losses, the true relationship between caffeine intake and miscarriage may not be fully captured by current findings.

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Caffeine intake and stillbirth

Stillbirth is even more poorly represented in the literature than miscarriage, with only 2 studies examining miscarriage as the outcome variable (Heazell et al., 2021; Morales-Suárez-Varela et al., 2017). Both studies employed the same definition for stillbirth as pregnancy loss after 28 GWs. The findings from these studies conflict, with Heazell et al. (2021) identifying an association, while Morales-Suárez-Varela et al. (2017) reporting no association.

Heazell et al. (2021) conducted a case-control study, which is well suited as it adjusted for key confounders and efficiently examined this rare outcome. The authors discovered that for every additional 100 mg of daily caffeine intake, the risks for stillbirth increased by 27% (aOR: 1.27, 95% CI 1.14–1.43), indicating a linear relationship rather than a threshold effect.

The existing studies on caffeine intake and stillbirth are limited

Furthermore, daily caffeine intake of over 300 mg doubled the risk of stillbirth (aOR: 2.30; 95% CI: 1.40–4.24). The analysis accounted for demographic factors, physical health indicators, lifestyle behaviours (including smoking and supplement use), educational background, parity and key fetal growth and development measures. However, the possibility of residual confounding from unmeasured factors, such as physical activity and alcohol consumption, cannot be entirely ruled out. The study applied the Bradford-Hill criteria, supporting a moderate association of caffeine intake >300 mg/day and stillbirth. A key strength of this study is the inclusion of nearly all dietary sources of caffeine, except for medications, improving exposure assessment and minimising misclassification bias.

In contrast, Morales-Suárez-Varela et al. (2017) assessed caffeine intake solely from coffee, likely underestimating the total intake and potentially leading to a misrepresentation of caffeine's true effect on stillbirth risk. Conversely, the authors employed a population-based cohort study design, which may have provided a more representative sample of at-risk individuals, in this case, women of reproductive age. This approach also reduced recall bias, a common limitation in retrospective studies. However, the study's lack of association between caffeine intake and stillbirth aligns with its findings for miscarriage, potentially reflecting limitations in caffeine exposure assessment rather than a true absence of effect. When examining the combined effect of smoking and caffeine intake, elevated risks were observed among individuals who smoked ≤10 cigarettes/day (aHR: 1.77, 95% CI: 1.08–2.90) and >10 cigarettes/day (aHR: 1.92, 95% CI: 0.99–3.70) at >3 cups/day. Like the results on miscarriage, there is no strong evidence that smoking and high caffeine intake interact synergistically.

The existing studies on caffeine intake and stillbirth are limited and present conflicting findings with methodological differences, including variations in caffeine exposure assessment and the adjustment for confounding factors.

Caffeine intake and preterm birth

Preterm birth was well depicted, with 5 studies including it as the outcome variable (Chen et al., 2018; Ding et al., 2023; Huang et al., 2016; Okubo et al., 2015; Vitti et al., 2018). Preterm birth was consistently defined across the literature as delivery before 37 GWs, allowing for ease of comparison.

While Ding et al. (2023) and Vitti et al. (2018) reported no significant associations, their findings may have been influenced by methodological limitations. Specifically, Ding et al. (2023) reported no significant association for caffeine intake between 20 and 25 GWs (aOR: 1.13; 95% CI: 0.35–3.60), while Vitti et al. (2018) further recorded caffeine intake for each trimester, reported no differences in intake across all three trimesters and no association with greater risk of preterm birth (adjusted relative risks [aRR]:1.10, 95% CI: 0.96–1.26 for <300 mg/day; aRR: 1.03, 95% CI: 0.65–1.63 for ≥300 mg/day). Vitti et al. (2018) adjusted for key sociodemographic, obstetric and health-related factors, including maternal age, education, ethnicity, marital and employment status, obstetric history, pregnancy complications, substance use, infections and dental treatments during pregnancy.

Both studies assessed caffeine intake from a single source: energy drinks in Ding et al. (2023) and coffee in Vitti et al. (2018), which likely led to an underestimation of true intake, thus weakening the observed associations. Additionally, Ding et al. (2023) included a cohort of nurses, a population with higher perinatal and overall health awareness, and distinct health behaviours, potentially underestimating risk and further limiting the generalisability of findings.

In contrast, Huang et al. (2016), despite also analysing a single caffeine source (tea), found a significant association (aOR: 1.36, 95% CI: 1.09–1.69), with variations depending on preterm birth subtype (moderate, very, medically indicated and spontaneous) and timing of consumption (before, during, before and during). This estimate was adjusted for maternal age, education, employment status, income, parity, hypertensive disorders, pre-pregnancy BMI, alcohol use, active and passive smoking, and prior preterm birth.

Similarly, Chen et al. (2018) and Okubo et al. (2015) observed an increased likelihood of preterm birth with every 100 mg/day increase in overall caffeine intake (aOR: 1.28, 95% CI: 1.03–1.58; aOR: 1.36, 95% CI: 1.07–1.74). While both studies adjusted for key maternal lifestyle and pregnancy-related factors, Chen et al. (2018) may have lacked dietary and medical variables, whereas Okubo et al. (2015) did not account for contextual or behavioural factors such as stress and physical activity, leaving room for residual confounding. These results were strengthened by the inclusion of multiple caffeine sources.

None of the studies, regardless of miscarriage, stillbirth, or preterm birth as the outcome variable, accounted for caffeine-containing medications. Chen et al. (2018) also excluded energy drinks. Notably, when the analysis focused on only spontaneous preterm birth, the observed association was slightly weakened (OR: 1.30, 95% CI: 0.98–1.71) in Chen et al. (2018). However, this study only excluded 2 pregnancy complications (gestational diabetes and pre-eclampsia), while other maternal or fetal disorders that may have influenced the onset of preterm labour were not considered (Vogel et al., 2018). This limited exclusion may have resulted in residual confounding, potentially inflating or obscuring the true association between caffeine intake and spontaneous preterm birth.

Four studies used validated dietary assessment tools, such as diet history and food frequency questionnaires, to estimate intake (Chen et al., 2018; Ding et al., 2023; Okubo et al., 2015; Vitti et al., 2018). However, these methods assumed a fixed caffeine content per milligram or per serving, disregarding variations in preparation methods and potentially leading to misclassification of intake. Other studies relied on a simplified, binary classification of intake, limiting the ability to detect dose-response relationships (Ding et al., 2023; Huang et al., 2016). Regardless of the assessment method for caffeine intake, they all relied on self-reported data, which are prone to recall bias and misclassification of intake. Furthermore, a significant imbalance in participant distribution between exposure groups was observed in 3 studies, reducing the ability to recognise statistical associations (Ding et al., 2023; Okubo et al., 2015; Vitti et al., 2018).

Compared with studies on miscarriage and stillbirth, preterm birth studies accounted for maternal medical and birth history, as well as pregnancy complications, to minimise the inclusion of medically indicated preterm birth cases and to isolate the effect of caffeine intake (Chen et al., 2018; Ding et al., 2023; Huang et al., 2016; Okubo et al., 2015; Vitti et al., 2018). However, residual confounders remain potential limitations across studies, most notably dietary quality, multivitamin supplement use, physical activity and medical conditions. Additionally, all studies accounted for smoking status and education level, but only Chen et al. (2018) and Huang et al. (2016) accounted for household income or socioeconomic status. These factors are known to be associated with preterm birth and high caffeine intake (Blumenshine et al., 2010; Heaman et al., 2012). While studies on caffeine intake and preterm birth generally support an association, limitations in exposure assessment, including reliance on single caffeine sources and self-reported data, as well as methodological inconsistencies, may have impacted the strength and consistency of the observed relationships.

Conclusion

This literature review investigated the impact of maternal caffeine intake on adverse fetal outcomes, including miscarriage, stillbirth and preterm birth. Findings were inconclusive, with variability in study designs, exposure assessments and confounding adjustments contributing to discrepancies in results. While some studies report no significant impact of caffeine intake on miscarriage or preterm birth, others indicate an increased risk, particularly at higher intake levels or when intake occurs during early pregnancy. In contrast, stillbirth appears more consistently linked to caffeine intake, with a dose-dependent relationship observed in one study. However, this body of literature includes an underestimation of total caffeine intake and various time points of intake, misclassification and inconsistent definitions of pregnancy outcomes, challenging the strength of these associations.

Only 8 studies were examined in this literature review. A more comprehensive search of the literature may help to better understand the association between maternal caffeine intake during pregnancy and adverse fetal outcomes. However, based on the current review, future research should address methodological inconsistencies to improve clarity on caffeine's role in pregnancy outcomes. Standardising definitions of miscarriage, incorporating more accurate and comprehensive caffeine intake assessments, and considering broader dietary and lifestyle factors in statistical models would enhance study comparability. Moreover, prospective cohort studies with real-time dietary tracking and biomarker validation of caffeine exposure could mitigate recall bias and misclassification. Further investigation into the dose-response relationship and potential critical exposure windows will help refine public health recommendations and provide clearer guidance for pregnant individuals.

This review contributes to the evidence around caffeine intake during pregnancy

This review contributes to the evidence around caffeine intake during pregnancy but does not override any existing government recommendations. From a clinical perspective, healthcare providers should continue to emphasise adherence to existing guidelines, such as PHAC's recommendation to limit caffeine

intake to <300 mg/day. Additionally, to ensure comprehensive risk awareness, patients should be counselled on the diverse sources of caffeine beyond coffee, including energy drinks, certain teas and some medications.

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