

## The Effect of Caffeine on Pregnancy-Fact or Myth?

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### Abstract

Caffeine crosses the placenta and causes a number of complications. This study aims to review the effect of caffeine during pregnancy. Because of ion trapping weak bases that are non-ionized and lipophilic like caffeine diffuse across the placental barrier and become ionized in the more acidic fetal blood. A number of studies have reported the effect of caffeine on pregnancy. Some of the effects are diminishing fetal skeleton growth; risk of low birth weight (LBW); retardation of fetal development and/or intrauterine growth retardation (IUGR); adverse offspring childhood body fat distribution; increased risk of obesity; risk of type two diabetes mellitus; and Increased risk abortion. Even though a number of effects of caffeine are reported to be associated with pregnancy there are only a limited data showing causal association. Hence, avoiding the consumption of coffee, chocolate and tea during pregnancy appears prudent until more reliable evidences are emerging.

**Keywords:** Caffeine; Pregnancy; Fetal skeleton growth

### Introduction

Caffeine is the most widely consumed psychoactive substance in the world [1]. An easy access to products containing caffeine due to its presence in drugs, coffee, tea and chocolate makes it widely consumed by the general population, including pregnant women [2,3].

Caffeine is an alkaloid [3] that can block adenosine receptors [4]. The adenosine is one of the major endogenous neuromodulator that can inhibit the overactive excitatory neurotransmission [5] and therefore, the stimulatory effect of caffeine is mainly due to antagonism of adenosine actions [1].

Caffeine crosses the placenta and has a prolonged metabolism in pregnant women (15.08 h half-life) compared with non-pregnant women (4.71 h half-life). The objective of this review is to overview the effect of caffeine during pregnancy; and thereby to forward the current information to the scientific community.

### Mechanism of Fetal Toxicity

One of the mechanisms that can lead to prolonged effects of drugs in the fetal compartment is via ion trapping. Ion trapping occurs because the fetal plasma pH is more acidic than the maternal plasma, causing weak bases (e.g. usually nonionized and lipophilic substances such as caffeine) to diffuse across the placental barrier and become ionized in the more acidic fetal blood [6], resulting the compound to pass to offspring through the placental barrier and to cause a number of complications [1]. Some of the complications of prenatal caffeine exposure (PCE) are reduction in the formation, growth, and mass of bone by targeting mesenchymal stem cells that are responsible for generating the entire fetal skeleton [3]; risk of low birth weight (LBW) [7]; retardation of fetal development [8] or intrauterine growth

retardation (IUGR) [9]; adverse offspring childhood body fat distribution [10]; increased risk of obesity [11,12]; potentially abnormal glucose homeostasis to result in increased risk of type to diabetes mellitus (T2DM) in the offspring adulthood [13] and Increase the risk of pregnancy loss or abortion [14].

### Threshold of Toxicity

Reducing the consumption of caffeinated coffee to 180 mg of caffeine, which is approximately equivalent to 2 cups per day after 16 weeks' of gestation, has been reported to cause no effect on birth weight [15]. Some even reported that it is safer for the pregnancy at lower than this dose [16]. However, the metabolism of caffeine is greatly influenced by the stage of pregnancy and at third trimester, its metabolism reduced and cause increased serum level of the active metabolites including theophylline [17].

Consuming more than 300 mg of caffeine per day has been associated with a clinically trivial, and statistically insignificant (less than 1 ounce), reduction in birth weight, compared to women consumed no caffeine during pregnancy [15]. Higher maternal caffeine intake (>300 mg) has also associated with a higher risk of pregnancy loss [18]. Nursing mothers should also drink coffee sparingly and immediately and avoid coffee or caffeinated beverages for at least 4 h prior to breastfeeding to minimize the infant's exposure to caffeine.

### Benefits from PCE

PCE and early commencement of caffeine in preterm infant with bronchopulmonary dysplasia (BPD) has been associated with improved health circumstances and survival [19]. The frequency of severe intra ventricular hemorrhage and patent ductus arteriosus (PDA) was also lower and the length of hospitalization was shorter in infants receiving early caffeine therapy [20] (Table 1).

Estimate your daily caffeine intake			
Sr. No.	Coffee source	Volume in OZ	Strength in mg
1	Starbucks Grande Coffee	16	400
2	Starbucks House Blend Coffee	16	259
3	Dr. Pepper	12	37
4	7 Eleven Big Gulp Diet Coke	32	124
5	7 Eleven Big Gulp Coca-Cola	32	92
6	Ben and Jerry's Coffee Buzz Ice Cream	8	72
7	Baker's chocolate	1	26
8	Green tea	6	40
9	Black tea	6	45
10	Excedrin	capsule	65
1 OZ=28.349 g=29.574 mL			

**Table 1:** Showing description of coffee source type with its approximate caffeine strength.

### Conclusion

A number of studies showed the effect of caffeine on pregnancy but with only a limited data of causal association. Hence, avoiding the consumption of coffee, chocolate and tea during pregnancy appears prudent until more reliable evidences are emerging.

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MAW has conceptualized the paper, wrote the first draft, reviewed and added substantive edits to the paper.

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