# Maternal total caffeine intake, mainly from Japanese and Chinese tea, during pregnancy was associated with risk of preterm birth: the Osaka Maternal and Child Health Study ${ }^{\text {th }}$ 

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#### Abstract

The relation of maternal caffeine intake with birth outcomes is still inconclusive and has not been examined in Japan, where the sources of caffeine intake are different from those in Western countries. We hypothesized that maternal consumption of total caffeine and culture-specific major sources of caffeine would be associated with birth outcomes among Japanese pregnant. The study subjects were 858 Japanese women who delivered singleton infants. Maternal diet during pregnancy was assessed using a validated, self-administered diet history questionnaire. Birth outcomes considered were low birth weight (LBW; <2500 g), preterm birth (PTB; <37 weeks of gestation), and small for gestational age (SGA; <10th percentile). The main caffeine sources were Japanese and Chinese tea (73.5\%), coffee ( $14.3 \%$ ), black tea ( $6.6 \%$ ), and soft drinks ( $3.5 \%$ ). After controlling for confounders, maternal total caffeine intake during pregnancy was significantly associated with an increased risk of PTB (odds ratio per $100 \mathrm{mg} / \mathrm{d}$ caffeine increase, 1.28; 95\% confidence interval, 1.03-1.58; P for trend $=.03$ ). However, no evident relationships were observed between total caffeine intake and risk of LBW or SGA. As for caffeine sources, higher Japanese and Chinese tea consumption was associated with an increased risk of PTB (odds ratio per 1 cup/d increase, 1.14; 95\% confidence interval, 1.00-1.30; P for trend =.04), but not LBW or SGA. There were no associations between consumption of the other beverages examined and birth outcomes. In conclusion, this prospective birth cohort in Japan suggests that higher maternal total caffeine intake, mainly in the form of Japanese and Chinese tea, during pregnancy is associated with a greater risk of PTB.


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## 1. Introduction

Caffeine (1,3,7-trimethylxanthine) is a natural alkaloid found primarily in coffee, tea, colas and some soft drinks, and chocolate and is thus consumed on a daily basis all over the world [1]. During pregnancy, maternal caffeine clearance decreases progressively from the first to the third trimester [2], and caffeine ingested by the mother is known to readily cross the placental barrier and reach the fetus [3,4]. A lack of the principal caffeine metabolism enzyme, cytochrome 1A2 (CYP1A2), in both placenta and fetus leads to increased neonatal exposure to caffeine [5]. Excessive exposure of the fetus to caffeine increases catecholamine levels in the fetus, which may lead to fetal-placental vasoconstriction and hypoxia, and eventually affect fetal growth and development [6]. Thus, maternal caffeine intake during pregnancy has attracted significant attention with regard to its possible effects on birth outcomes.

The relations of maternal caffeine intake with birth outcomes have been examined over the past 30 years with inconsistent results [1,7]. Several comprehensive meta-analyses that examined the association of maternal caffeine intake during pregnancy with the risks of intrauterine growth retardation, stillbirth, preterm birth (PTB), low birth weight (LBW), and small for gestational age (SGA) have been published, but their results are inconclusive [8-10]. It should be noted that all of these studies were from countries with predominantly Western cultures [8-10], and that no epidemiologic studies on this topic have been conducted in Japan to date. In Japan, LBW is an important public health issue; the proportion of LBW has consistently increased from $5.1 \%$ in 1975 to $9.6 \%$ in 2012 [11]. Low birth weight is mostly found in cases of PTB, which has also gradually increased from $4.1 \%$ in 1980 to $5.7 \%$ in 2012 [11]. In addition, the sources of caffeine in the diet are likely to vary among cultures and countries. The major contributors to total caffeine in the diet of Japanese women were Japanese and Chinese tea ( $47.1 \%$ ), coffee ( $46.7 \%$ ), and black tea (4.3\%) [12], whereas coffee $(56 \%-75 \%)$ and black tea ( $15 \%-30 \%$ ) were the major sources of caffeine in the adult diet in North America and some European countries [1,13,14]. Thus, additional studies in regions with different food-cultural backgrounds might provide new insights into matemal total caffeine intake in relation to birth outcomes.

The objective of this prospective birth cohort was to examine the associations of maternal total caffeine intake and caffeinerich beverage consumption during pregnancy with the risk of LBW, PTB, and SGA among 858 Japanese mothers who participated in the Osaka Maternal and Child Health Study (OMCHS). We hypothesized that higher maternal consumption of total caffeine and caffeine-rich beverages during pregnancy would be associated with increased risk of negative birth outcomes.

## 2. Methods and materials

### 2.1. Study population and procedure

The OMCHS is a prospective cohort study that investigates preventive and risk factors for maternal and child health problems. A detailed description of the rationale, study design,
and protocol has been published elsewhere [15,16]. Briefly, a total of 1002 pregnant women at 5 to 39 weeks of gestation living in Neyagawa City and other municipalities in Osaka Prefecture took part in a baseline survey conducted between November 2001 and March 2003, of whom 867 participated in the follow-up survey at 2 to 9 months postpartum. After exclusion of women with multiple births ( $n=7$ ) or missing information on infant birth weight ( $n=2$ ), the final analyses of the present study comprised 858 women. Written informed consent was obtained from all participating women. The OMCHS was conducted according to the guidelines of the Declaration of Helsinki and approved by the ethics committee of the Osaka City University School of Medicine.

At baseline, each participant filled out a set of 2 selfadministered questionnaires on dietary habits and a wide range of lifestyle behaviors. A third self-administered questionnaire was additionally answered at the follow-up survey (2-9 months postpartum). Participants mailed these completed questionnaires to the data management center at the time of each survey. Research technicians completed missing or illogical data by telephone interview.

### 2.2. Maternal dietary data during pregnancy

At the baseline survey, we collected information on dietary habits using a validated, self-administered dietary history questionnaire (DHQ) [17-23]. The subjects were asked to report their average consumption frequency of 8 categories of foods and beverages over the preceding month, ranging from "never" to " $\geq 2$ times/d" for foods and from " $<1$ time/wk" to " $\geq 6$ times/d" for beverages, and their relative portion size consumed in comparison with a standard portion size given according to 5 categories: " $50 \%$ smaller or less," " $20 \%-30 \%$ smaller," "same," " $20 \%-30 \%$ larger," and " $50 \%$ larger or more" [17]. Estimates of daily intake for 150 food and beverage items, as well as for energy, nutrients, and alcohol, were calculated using an ad hoc computer algorithm for the DHQ which was based on the Standard Tables of Food Composition in Japan [24].

Maternal total caffeine intake during pregnancy was estimated in accordance with a published report [12]. The main food sources of caffeine in this study included Japanese and Chinese tea (eg, green tea and oolong tea), coffee, black tea, cola and sports drinks, hot chocolate, diet cola and non-energycontaining soft drinks, and confectionaries (mainly chocolate). We calculated each participant's total caffeine intake by multiplying the caffeine content of each beverage/food by the participant's reported consumption frequency and portion size and then summing these values. Information on medicines was not used in the calculation of caffeine because of the lack of a reliable composition table for such items in Japan.

Validity of the DHQ with respect to commonly studied nutritional factors has been investigated in several previous studies, using dietary record (DR) [17,20,21], 24-hour urine excretion [18], and serum biomarkers [19,22,23]. In a previous study of 92 Japanese women aged 31 to 69 years, the Pearson correlation coefficients between the DHQ and 16 -day semiweighed DRs were 0.27 to 0.87 for energyproviding nutrients, 0.39 to 0.71 for other nutrients [20], 0.59 for Japanese and Chinese tea, 0.75 for coffee, 0.52 for black tea, 0.28 for soft drinks, and 0.28 for confectionaries

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[^0]:    Abbreviations: DHQ dietary history questionnaire; LBW, low birth weight; OMCHS, Osaka Maternal and Child Health Study; PTB, preterm birth; SGA, small for gestational age.
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