

Maternal coffee intake and the risk of bleeding in early pregnancy: a cross-sectional analysis

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Research article

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Abstract

Background: Caffeine can easily cross the placenta, and maternal caffeine intake, thus, has an effect on fetal growth. However, it is still unclear whether coffee consumption is an independent risk factor for bleeding in early pregnancy. The objective of this study was to examine the association between pre-pregnancy coffee consumption patterns and the risk of bleeding in early pregnancy. **Methods:** A cross-sectional analysis was conducted among 3,510 pregnant women from the Korean Pregnancy Outcome Study who underwent baseline examination between 2013 and 2017 and for whom the results of the pregnancy were available. Coffee consumption patterns before pregnancy were examined using a questionnaire. The participants were classified according to the frequency of coffee consumption into seldom (<1 cup/week), light (<1 cup/day), moderate (1 cup/day), and heavy coffee drinker (≥ 2 cups/day) groups. Bleeding in early pregnancy was defined as the occurrence of vaginal bleeding in the first 20 weeks of pregnancy. Multiple logistic regression models were applied to examine the association between pre-pregnancy coffee consumption and the risk of bleeding in early pregnancy, after adjusting for age, body mass index, systolic blood pressure, cigarette smoking and alcohol consumption behavior, previous and current physical activity levels, stress levels, history of depression, presence of antenatal depressive symptoms during the first trimester, type of emesis, parity, and the number of livebirths, stillbirths, miscarriages, and abortions. Odds ratios among light, moderate, and heavy coffee drinkers were determined through comparisons with the seldom coffee drinker group. **Results:** Women who were light, moderate, and heavy coffee drinkers before pregnancy had adjusted odds ratios of 1.086, 1.225, and 1.358, respectively, for bleeding in early pregnancy. However, the association between coffee consumption and the risk of miscarriage or stillbirth was not significant. **Conclusions:** Our results showed that heavy coffee drinking was independently associated with a higher risk of bleeding in early pregnancy among pregnant Korean women, suggesting that caffeine intake before conception and during pregnancy should be reduced. Our study highlights the need for nutritional interventions for healthy coffee drinking among pregnant women in Korea. **Keywords:** caffeine, coffee consumption, fetus, placenta, pregnancy

Background

Coffee is one of the most popular beverages worldwide [1-3]. The Korean National Health and Nutrition Examination Survey reported that the prevalence of daily coffee drinking (1 or more cups/day) greatly increased from 54.6% in 2001 to 65.3% in 2010–2011 among Korean adults [4]. The average coffee consumption among Korean adults is 11.3 times/week – more than five times greater than that in other countries in the Asia-Pacific region [3]. Coffee contains several physiologically active substances; caffeine, in particular, is an important component of coffee [5, 6]. Other caffeinated beverages or foods do not contribute significantly to the daily caffeine intake among Koreans [7]. Therefore, it is important to examine the effect of coffee consumption on health.

Interestingly, among all the dietary ingredients with a potential to adversely affect fetoplacental development, caffeine is the most commonly consumed by pregnant women. Maternal caffeine intake during pregnancy affects fetal growth because caffeine can easily cross the placenta and decrease blood

flow to the placenta [8, 9]. There are ongoing concerns that coffee intake could increase among pregnant women in particular and result in adverse health effects. However, the specific effects of caffeine on the fetus remain unknown. Moreover, it is still unclear whether coffee consumption is an independent risk factor for bleeding in early pregnancy, which is the most common complication of pregnancy (noted in 15–20% of all ongoing pregnancies) [10, 11] and may indicate underlying placental dysfunction that could induce complications in later phases of pregnancy [12, 13].

Therefore, the aim of this study was to examine pre-pregnancy coffee consumption patterns and their association with the risk of bleeding in early pregnancy among pregnant Korean women.

Methods

Study participants

Data for the present study were derived from the Korean Pregnancy Outcome Study (KPOS), a prospective cohort study. Between March 2013 and January 2017, all pregnant women who visited Cheil General Hospital and CHA Hospital for antenatal care during the first trimester were asked to participate in the KPOS. Women were excluded from enrolment if they were not Korean or were pregnant with triplets or higher-order multiple gestations. Gestational age was determined based on the date of the last menstrual period in women who had conceived naturally, and was confirmed by the first trimester ultrasound. After the first antenatal visit, eligible participants were requested to complete several sets of questionnaires or examinations at each of the following visits: visit 1 in the first trimester (around 12 weeks of gestation); visit 2 in the second trimester (around 24 weeks of gestation); visit 3 in the third trimester (around 36 weeks of gestation); visit 4 at birth; and visit 5 at 4–6 weeks after birth.

As shown in Supplementary Figure 1 [see Additional file 1], after excluding 55 individuals with missing dietary data, we performed a cross-sectional analysis of 3,510 women who had positive pregnancy results. Trained research nurses explained the study in detail, obtained written informed consents, and completed questionnaires. All participants provided written informed consent, and the study protocol was approved by the Institutional Review Board (IRB) of Cheil General Hospital (IRB number: CGH-IRB-2013-10) and CHA Hospital (IRB number: 2013-14-KNC13-018), separately. It was clearly explained to all participants that they were free to withdraw from any part of the study at any point in time.

Measurements

A face-to-face interview was conducted to evaluate participants' socio-demographic profiles, medical and family history, reproductive information, health-related behaviors, and psychological health.

Data on socio-demographic status included age, educational level, household income, employment status, marital status, cohabiting family composition, and information on spouses. Family history of

hypertension, diabetes, gestational diabetes mellitus, preeclampsia, depression, and other mental illness was also taken.

Participants underwent clinical and laboratory examinations, including anthropometric measurements, blood pressure measurements, and blood and urine laboratory tests, during pregnancy. Asian classification of obesity used in this study using the body mass index (BMI) [13]. Symptoms of depression were assessed using the Korean version of the Edinburgh Postnatal Depression Scale (K-EPDS), which is a reliable measurement for peripartum depression and validated questionnaire with 10 items; those with K-EPDS scores ≥ 10 were considered to have symptoms of antenatal depression [14, 15]. Those taking anti-depressant drugs and those with a self-reported physician's diagnosis of depression were considered to have a history of depression. Cigarette smoking, alcohol intake, and supplement intake were evaluated during each visit. Physical activity was assessed during each visit with a self-reported questionnaire.

Dietary intake patterns were evaluated using a questionnaire during the first visit. The coffee consumption pattern before conception was determined through the question, "How often did you drink coffee before the pregnancy?" on the questionnaire. Coffee consumption was categorized into five groups (seldom, 2–3 cups/week, 4–6 cups/week, 1 cup/day, and 2 or more cups/day). In the analysis, participants were divided into four groups based on their reported amount of coffee consumption: ≥ 2 cups/day, "heavy coffee drinkers"; 1 cup/day, "moderate coffee drinkers"; < 1 cup/day, "light coffee drinkers"; and < 1 cup/week, "seldom coffee drinkers" (reference group). Preferences for the following types of coffee were noted: black coffee, black coffee with sugar, black coffee with creamer, and instant coffee mix (instant coffee with creamer and sugar).

We obtained information on antenatal pregnancy complications and birth details. First trimester complications, including emesis and bleeding in early pregnancy, were assessed during the first visit. In this study, bleeding in early pregnancy was defined as the occurrence of vaginal bleeding in the first 20 weeks of pregnancy, confirmed using ultrasonographic examinations by a physician [16, 17]. The birth outcomes included gestational age at birth, type of labor (induced or spontaneous), type of birth, indication for Caesarean birth, and birth complications.

Blood pressure was measured during every visit using the automatic oscillometric technique, but a diagnosis of hypertensive disorders of pregnancy was confirmed by manual measurements using blood pressure cuffs and auscultation. Blood samples and placenta were stored in -70 °C freezers at a controlled temperature and humidity. All biological samples were marked with barcodes and stored in the National Biobank of Korea. We uploaded the data from all questionnaires and examinations to a web-based clinical data management system (iCReaT) managed by the Korea National Institute of Health.

Statistical analysis

We summarized the general characteristics of study participants using means and standard deviations for continuous variables and observed numbers and percentages for categorical variables. To statistically analyze differences among groups, a general linear model and the chi-square test were used for continuous and categorical variables, respectively. The Bonferroni post-hoc test was used to identify groups showing significant differences. For some analyses, the lower categories of exposure variables were combined into a single stratum because of the small number of subjects in these categories. Multivariate logistic regression analysis was used to estimate odds ratios (ORs) with 95% confidence intervals (CIs) for the association between coffee consumption and bleeding in early pregnancy. Age, BMI, systolic blood pressure, cigarette smoking and alcohol consumption behavior, previous and current physical activity levels, stress levels, history of depression, presence of antenatal depressive symptom during the first trimester, type of emesis, parity, and the number of livebirths, stillbirths, miscarriages, and abortions were considered as covariates in the adjusted model.

An additional sensitivity analysis was performed with stratification according to age and BMI. We also performed an additional multiple logistic regression analysis to estimate the association between the type of coffee preferred and the risk of bleeding in early pregnancy, as well as the association between coffee consumption and the risk of miscarriage and stillbirth. All statistical analyses were performed using the SAS software (version 9.4, SAS; NC, USA), and two-sided p-values less than 0.05 were considered indicators of statistical significance.

Results

Table 1 presents the baseline characteristics of all study participants according to the frequency of coffee consumption before pregnancy. Of the 3,510 participants, 1,077 were seldom coffee drinkers (30.7%), 595 were light coffee drinkers (17.0%), 1,202 were moderate coffee drinkers (34.2%), and 636 were heavy coffee drinkers (18.1%). The mean age of all pregnant women was 33.3 years. Heavy coffee drinkers were more likely to be significantly older; have a higher economic status, BMI, and frequency of history of depression; and be former smokers and drinkers. The overall prevalence of bleeding in early pregnancy among these pregnant women was 18.1%. In Supplementary Table 1, a total of 46 miscarriage or abortion occurred, however, it was not significantly different according to coffee consumption. As shown in Figure 1, heavy coffee drinkers showed the highest prevalence of bleeding in early pregnancy; this group, in particular, tended to require drug therapy or inpatient treatment for bleeding in early pregnancy.

Age- and BMI-dependent adjusted ORs for bleeding in early pregnancy in the different coffee consumption groups are presented in Tables 2 and 3, respectively. The group with the highest coffee consumption showed a high risk of bleeding in early pregnancy, and this association was significant both before and after additional adjustment for covariates. As shown in Figure 2, heavy coffee drinkers showed a significantly higher prevalence of bleeding in early pregnancy than did seldom coffee drinkers. Light, moderate, and heavy coffee drinkers showed adjusted ORs of 1.086, 1.225, and 1.358, respectively, for bleeding in early pregnancy. This association was significant in all age groups, except for in women

older than 35-40 years, who are already at risk for pregnancy complications (Table 2 and Supplementary Table 2) [see Additional file 1].

Regarding BMI, a higher consumption of coffee was significantly associated with the risk of bleeding in early pregnancy in women with normal BMI (Table 3). However, this association was not statistically significant in overweight or obese pregnant women

As shown in Supplementary Table 3 [see Additional file 1], no significant associations were observed between the type of coffee and additives and the risk of bleeding in early pregnancy. An additional sensitivity analysis, summarized in Supplementary Table 4 [see Additional file 1], revealed that the frequency of coffee consumption was not significantly associated with the risk of miscarriage or stillbirth.

Discussion

As younger women continue to partake in the western coffee culture and demand high-quality coffee beans, the current trends of coffee consumption are expected to continue. The properties of coffee make it a double-edged sword, and the balance between its beneficial and harmful health impacts should be considered. In this study, we examined coffee consumption patterns before pregnancy and their association with the risk of bleeding in early pregnancy among pregnant Korean women. Our study showed that women who were habitual coffee drinkers before pregnancy constituted a larger fraction of those experiencing bleeding in early pregnancy than women who were seldom coffee drinkers. We found that habitual coffee consumption of one or more cup/day before pregnancy was significantly associated with an increased risk of bleeding in early pregnancy, even after adjustment for cigarette smoking and alcohol consumption. However, the type of coffee consumed did not significantly affect the risk of bleeding in early pregnancy.

In the present study, among 3,510 pregnant women, the overall prevalence of bleeding in early pregnancy was 18.1%, even though the average maternal age of participants was relatively high, which is consistent with previous results. Bleeding in early pregnancy is associated with an increased risk of poor pregnancy outcomes, and approximately 50% of pregnant women who experience bleeding in early pregnancy eventually have miscarriages. Therefore, thorough prevention and management in early pregnancy are required to prevent fetal mortalities and morbidities. However, information on risk factors for bleeding in early pregnancy in the first trimester is insufficient and methods of prevention are still lacking [12, 18-21].

Coffee consumption is one possible risk factor for bleeding in early pregnancy in the first trimester. Even though the market for caffeinated beverages has increased in the past decades, coffee remains the most frequently consumed caffeinated beverage [1, 7]. A standard cup of coffee is generally expected to provide 100 mg of caffeine; however, this varies according to portion size, brewing method, and brand [1-3, 6, 7, 22]. Although other beverages have some caffeine content (one cup of tea, 64.0 mg of caffeine; 12 oz of coke, 46.0 mg of caffeine; one cup of hot chocolate, 16.0 mg of caffeine; and caffeinated soda, 46.0 mg of caffeine), these caffeinated beverages do not significantly affect daily caffeine consumption

among Koreans [7, 23]. Nisenblat et al. reported that caffeine intake is not associated with an increased risk of bleeding in early pregnancy, with the possible exception of very high levels of caffeine intake [22]. However, caffeine and its metabolites easily cross the placenta and may be present in considerable quantities in the amniotic fluid and fetal blood [8, 24]. Moreover, the fetus metabolizes caffeine very slowly, and even extremely small amounts of maternal caffeine intake could lead to long-term fetal caffeine exposure [22, 24]. Experimental and human studies have shown that caffeine exposure induces angiotensin II by stimulating the generation of reactive oxygen species, which ultimately inhibits angiogenesis and negatively affects the developing embryo [25]. In addition, caffeine consumption could increase the generation of circulating catecholamines, which could cause uteroplacental vasoconstriction, leading to fetal hypoxia [22, 26, 27]. Moreover, although a threshold for the adverse effects of caffeine on pregnant women was not well established, a few studies showed that high levels of caffeine intake could have adverse effects, such as miscarriage, fetal growth restriction, and long-term behavioral effects in offspring [9, 11, 16, 22, 23, 28, 29].

Recently, some epidemiologic studies have found a significant association between a caffeine intake of 300 mg or more/day and the risk of spontaneous abortion [23, 30, 31]. Consistent with previous reports, in the present study, we found that pregnant women who were heavy coffee drinkers had a significantly higher risk of bleeding in early pregnancy. In a Chinese prospective study, caffeine intake before pregnancy was not found to increase the risk of spontaneous abortion, but caffeine intake of more than 300 mg/day during the first trimester appeared to significantly increase this risk [23]. A UK case-control study showed that caffeine consumption of more than 300 mg/day during pregnancy approximately doubles the risk of miscarriage, and this effect is driven by coffee consumption [30]. Similarly, a study found that the adjusted risk of spontaneous abortion among Danish women who consumed more than 375 mg of caffeine/day was 2.21 [31].

A meta-analysis found that the risk of pregnancy loss increased by 3% for every increase in coffee consumption of two cups/day [28]. Hence, most women try to reduce their caffeine intake considerably during pregnancy, especially from the time they start preparing for pregnancy to the first trimester [9, 29]. The current guidelines of the World Health Organization recommend a caffeine intake below 300 mg/day, whereas the American College of Obstetricians and Gynecologists recommend a maximum caffeine intake of 200 mg/day [32, 33]. Different recommendations in guidelines can lead to confusion in preparing for pregnancy or during pregnancy. Moreover, knowing the exact caffeine content is difficult, because the amount varies depending on the serving size of the coffee.

The present study has some limitations that should be noted. The main limitation of the present study relates to the inaccurate assessment of the coffee consumption pattern, because the caffeine consumed in a “cup” of coffee varies according to portion size, brewing method, and brand type. Despite the huge popularity of decaffeinated coffee, we could not examine the consumption of decaffeinated coffee, especially in pregnant women. In future studies, objective measurements, combining caffeine exposure biomarkers from blood, urine, and saliva with 24-hour dietary recall measurements, should be used to assess precise coffee consumption. Second, recall bias due to the retrospective assessment of caffeine

consumption should be considered. However, since we examined coffee consumption before the onset of bleeding in early pregnancy, the impact of recall bias may have reduced. Third, coffee consumption patterns before pregnancy at a single time point may not reflect chronic exposure over the years, because women who prepare to conceive tend to maintain healthy eating habits. To address this concern in future studies, we should measure coffee consumption before pregnancy and evaluate the reliability of the FFQ. Finally, although we controlled for several potential confounders in our analysis, residual confounding by diet or other lifestyle factor effects may have been present. In addition, a causal relationship between coffee consumption and bleeding in early pregnancy could not be assessed due to the observational design of the study.

Conclusions

Our results revealed a higher risk of bleeding in early pregnancy among those with heavy coffee consumption before pregnancy. Considering that coffee consumption is a potentially modifiable risk factor, our results indicate that caffeine intake before conception and during pregnancy should be reduced. Moreover, our study provides potentially useful information that can be used to address the need for nutritional interventions for healthy coffee drinking among pregnant women in Korea. However, further prospective studies are needed to confirm our findings and establish the causal associations between the potential negative effects of coffee consumption and the risk of bleeding in early pregnancy.

Abbreviations

Korean Pregnancy Outcome Study (KPOS)

Institutional Review Board (IRB)

International Physical Activity Questionnaire (IPAQ)

Odds ratios (OR)

Confidence intervals (CI)

Declarations

Ethics approval and consent to participate

All procedures were approved by the Institutional Review Boards (IRB) of Cheil General Hospital (IRB number: CGH-IRB-2013-10) and CHA Hospital (IRB number: 2013-14-KNC13-018), separately. All participants provided written informed consent prior to participation, and it was clearly explained to all participants that they were free to withdraw from any part of the study at any point in time.

Consent for publication

Not applicable

Availability of data and material

The KPOS is being conducted mainly at the Cheil General Hospital & Women's Healthcare Center and CHA Gangnam Medical Center, where the staff are responsible for the collection, management, and distribution of data. All data are stored electronically in an anonymous format and are currently only available to KPOS researchers; however, data analysis collaborations may be possible through specific research proposals. Further information can be requested by e-mailing the principal investigator (hmryu2012@naver.com).

Competing interests

The authors declare that they have no conflict of interest.

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Authors' contributions

H-YP designed the study and reviewed the manuscript critically. HC analyzed and interpreted the data and contributed to the drafting of the manuscript. SK managed the data and provided clinical outputs. All authors read and approved the final version of the manuscript for submission.

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Tables

Table 1. Baseline characteristics of study participants (n=3510)

Variables	Frequency of coffee consumption				p-value
	Seldom coffee drinkers (n=1077)	Light coffee drinkers (<1 cup/day) (n=595)	Moderate coffee drinkers (1 cup/day) (n=1202)	Heavy coffee drinkers (≥ 2 cups/day) (n=636)	
Maternal age, years	32.8 ± 3.8	33.1 ± 3.8	33.4 ± 3.6	34.1 ± 3.8	<0.001
20-24	11 (1.0)	7 (1.2)	5 (0.4)	1 (0.2)	<0.001
25-29	203 (18.8)	99 (16.6)	184 (15.3)	62 (9.7)	
30-34	515 (47.8)	277 (46.6)	558 (46.4)	292 (45.9)	
35-39	303 (28.1)	185 (31.1)	392 (32.6)	220 (34.6)	
≥40	45 (4.2)	27 (4.5)	63 (5.2)	61 (9.6)	
Marital status					
Married	1055 (98.0)	581 (97.6)	1184 (98.5)	620 (97.5)	0.446
Unmarried	22 (2.0)	13 (2.2)	18 (1.5)	15 (2.4)	
Divorced/ Widowed/ Separated	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)	
Educational status					
≤High school	92 (8.5)	54 (9.1)	83 (6.9)	64 (10.1)	0.075
College or university	810 (75.2)	442 (74.3)	923 (76.8)	447 (70.3)	
≥Graduate school	175 (16.2)	99 (16.6)	196 (16.3)	125 (19.7)	
Systolic blood pressure, mmHg	113.1 ± 13.1	114.6 ± 14.1	114.1 ± 13.3	114.6 ± 13.0	0.068
BMI, kg/m ² *	21.3 ± 3.1	21.8 ± 3.2	21.7 ± 3.0	22.2 ± 3.1	<0.001
<18.5	155 (14.4)	52 (8.7)	116 (9.7)	50 (7.9)	<0.001
18.5-22.9	677 (62.9)	379 (63.7)	772 (64.2)	379 (59.6)	
23.0-24.9	134 (12.4)	81 (13.6)	157 (13.1)	104 (16.4)	
25.0-29.9	91 (8.4)	67 (11.3)	137 (11.4)	86 (13.5)	
≥30.0	20 (1.9)	16 (2.7)	20 (1.7)	17 (2.7)	
Emesis	801 (74.4)	447 (75.1)	942 (78.4)	497 (78.1)	0.085
Bleeding in early pregnancy	173 (16.1)	103 (17.3)	226 (18.8)	134 (21.1)	0.059
Stabilization	130 (75.1)	80 (77.7)	172 (76.1)	98 (73.1)	0.987
Drug treatment	34 (19.7)	19 (18.4)	42 (18.6)	29 (21.6)	

Inpatient treatment	9 (5.2)	4 (3.9)	12 (5.3)	7 (5.2)	
Number of fetus					
Singleton	1061 (98.5)	584 (98.2)	1188 (98.8)	623 (98.0)	0.461
Twin	16 (1.5)	11 (1.8)	14 (1.2)	13 (2.0)	
Parity	0.4 ± 0.6	0.5 ± 0.6	0.5 ± 0.6	0.4 ± 0.6	0.005
0	677 (62.9)	341 (57.3)	681 (56.7)	399 (62.7)	0.001
1	362 (33.6)	223 (37.5)	454 (37.8)	192 (30.2)	
≥2	38 (3.5)	31 (5.2)	67 (5.6)	45 (7.1)	
History of depression	5 (0.5)	3 (0.5)	8 (0.7)	5 (0.8)	0.037
Antenatal depressive symptoms	194 (18.0)	113 (19.0)	217 (18.1)	141 (22.2)	0.136
Type of Coffee (n=2394)					
Black coffee		355 (60.4)	781 (65.9)	402 (64.7)	<0.001
Black coffee with sugar		50 (8.5)	96 (8.1)	23 (3.7)	
Black coffee with non-dairy creamer		28 (4.8)	47 (4.0)	15 (2.4)	
Instant coffee with sugar and non-dairy creamer		155 (26.4)	261 (22.0)	181 (29.1)	
Cigarette smoking					
Never smoked	970 (90.1)	546 (91.8)	1081 (89.9)	538 (84.6)	<0.001
Former smoker	107 (9.9)	47 (7.9)	121 (10.1)	96 (15.1)	
Current smoker	0 (0.0)	2 (0.3)	0 (0.0)	2 (0.3)	
Alcohol consumption					
Never drank	245 (22.7)	129 (21.7)	193 (16.1)	98 (15.4)	<0.001
Former drinker	830 (77.1)	465 (78.2)	1009 (83.9)	537 (84.4)	
Current drinker	2 (0.2)	1 (0.2)	0 (0.0)	1 (0.2)	
Physical activity (n=3459)					
Static activity	265 (24.9)	132 (22.5)	259 (21.9)	136 (21.8)	<0.001
Light activity	551 (51.8)	352 (60.0)	693 (58.5)	387 (61.9)	
Moderate activity	246 (23.1)	103 (17.5)	232 (19.6)	100 (16.0)	
≤Vigorous activity	1 (0.1)	0 (0.0)	0 (0.0)	2 (0.3)	

Data expressed as mean \pm standard deviation or number (percentage)

* Asian classification of obesity used in this study [13].

Table 2. Association between coffee consumption frequency and the risk of bleeding in early pregnancy according to age (n=3510)

	Total No.	No. (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^a
Overall	3510	636(18.1)		
Seldom coffee drinkers	1077	173(16.1)	1.000	1.000
Light coffee drinkers (<1 cup/day)	595	103(17.3)	1.094(0.837-1.429)	1.086(0.827-1.425)
Moderate coffee drinkers (1 cup/day)	1202	226(18.8)	1.210(0.973-1.504)	1.225(0.981-1.530)
Heavy coffee drinkers (≥2 cups/day)	636	134(21.1)	1.395(1.086-1.792)	1.358(1.050-1.757)
aged <35 years	2214	372(16.8)		
Seldom coffee drinkers	729	111(15.2)	1.000	1.000
Light coffee drinkers (<1 cup/day)	383	57(14.9)	0.973(0.688-1.376)	0.993(0.699-1.411)
Moderate coffee drinkers (1 cup/day)	747	125(16.7)	1.119(0.847-1.479)	1.163(0.875-1.547)
Heavy coffee drinkers (≥2 cups/day)	355	79(22.3)	1.594(1.155-2.198)	1.680(1.207-2.338)
aged ≥35 years	1296	264(20.4)		
Seldom coffee drinkers	348	62(17.8)	1.000	1.000
Light coffee drinkers (<1 cup/day)	212	46(21.7)	0.973(0.688-1.376)	1.278(0.834-1.958)
Moderate coffee drinkers (1 cup/day)	455	101(22.2)	1.119(0.847-1.479)	1.316(0.925-1.872)
Heavy coffee drinkers (≥2 cups/day)	281	55(19.6)	1.594(1.155-2.198)	1.123(0.750-1.679)

^aadjusted for age, body mass index, systolic blood pressure, cigarette smoking and alcohol

consumption behavior, previous and current physical activity levels, stress levels, history of depression, presence of antenatal depressive symptoms during the first trimester, type of delivery, parity, and the number of livebirths, stillbirths, miscarriages, and abortions

Table 3. Association between coffee consumption frequency and the risk of bleeding in early pregnancy according to BMI (n=3510)

BMI	Total No.	No. (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^a
Underweight, <18.5 kg/m ²	373	80 (21.4)		
Seldom coffee drinkers	155	33 (21.3)	1.000	1.000
Light coffee drinkers (<1 cup/day)	52	11 (21.2)	0.992 (0.460-2.139)	0.780 (0.331-1.837)
Moderate coffee drinkers (1 cup/day)	116	26 (22.4)	1.068 (0.597-1.911)	1.213 (0.650-2.265)
Heavy coffee drinkers (≥2 cups/day)	50	10 (20.0)	0.924 (0.418-2.042)	0.990 (0.414-2.367)
Normal, 18.5-24.9 kg/m ²	2683	463 (17.3)		
Seldom coffee drinkers	811	119 (14.7)	1.000	1.000
Light coffee drinkers (<1 cup/day)	460	80 (17.4)	1.224 (0.898-1.669)	1.249 (0.912-1.712)
Moderate coffee drinkers (1 cup/day)	929	168 (18.1)	1.284 (0.993-1.659)	1.314 (1.012-1.706)
Heavy coffee drinkers (≥2 cups/day)	483	96 (19.9)	1.442 (1.073-1.940)	1.389 (1.025-1.884)
Overweight + Obese, ≥25.0 kg/m ²	454	93 (20.5)		
Seldom coffee drinkers	111	21 (18.9)	1.000	1.000
Light coffee drinkers (<1 cup/day)	83	12 (14.5)	0.724 (0.334-1.571)	0.699 (0.315-1.551)
Moderate coffee drinkers (1 cup/day)	157	32 (20.4)	1.097 (0.594-2.026)	1.059 (0.554-2.025)
Heavy coffee drinkers (≥2 cups/day)	103	28 (27.2)	1.600 (0.841-3.045)	1.574 (0.801-3.093)

cups/day)

^aadjusted for age, body mass index, systolic blood pressure, cigarette smoking and alcohol consumption behavior, previous and current physical activity levels, stress levels, history of depression, presence of antenatal depressive symptoms during the first trimester, type of emesis, parity, and the number of livebirths, stillbirths, miscarriages, and abortions

Figures

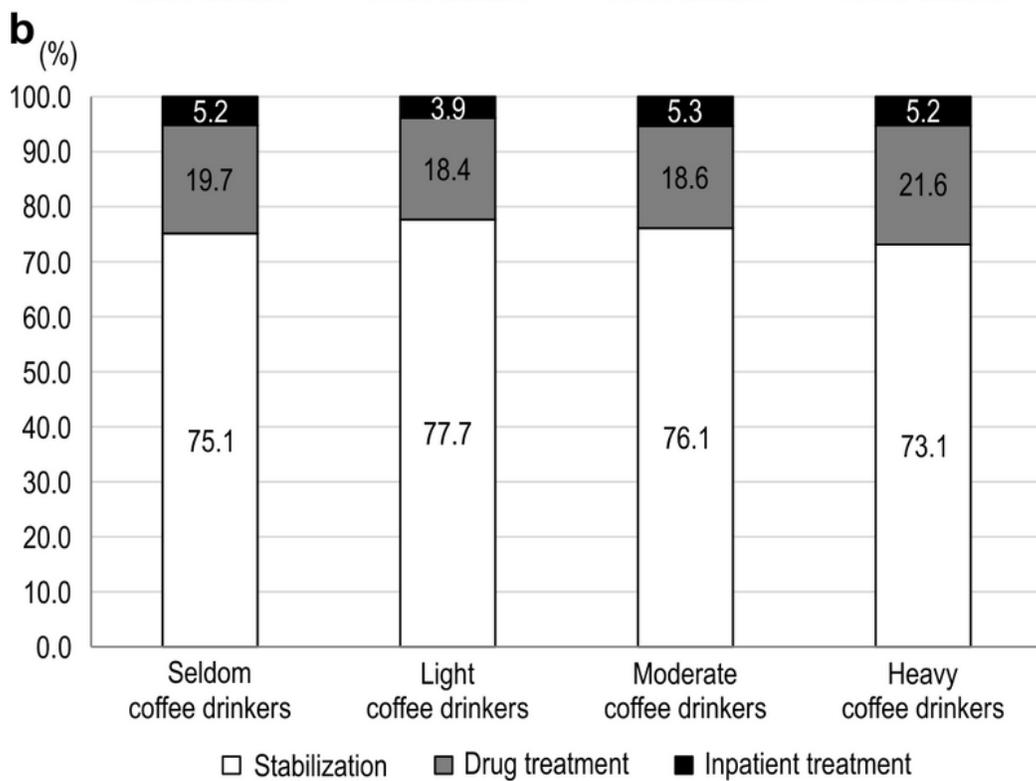
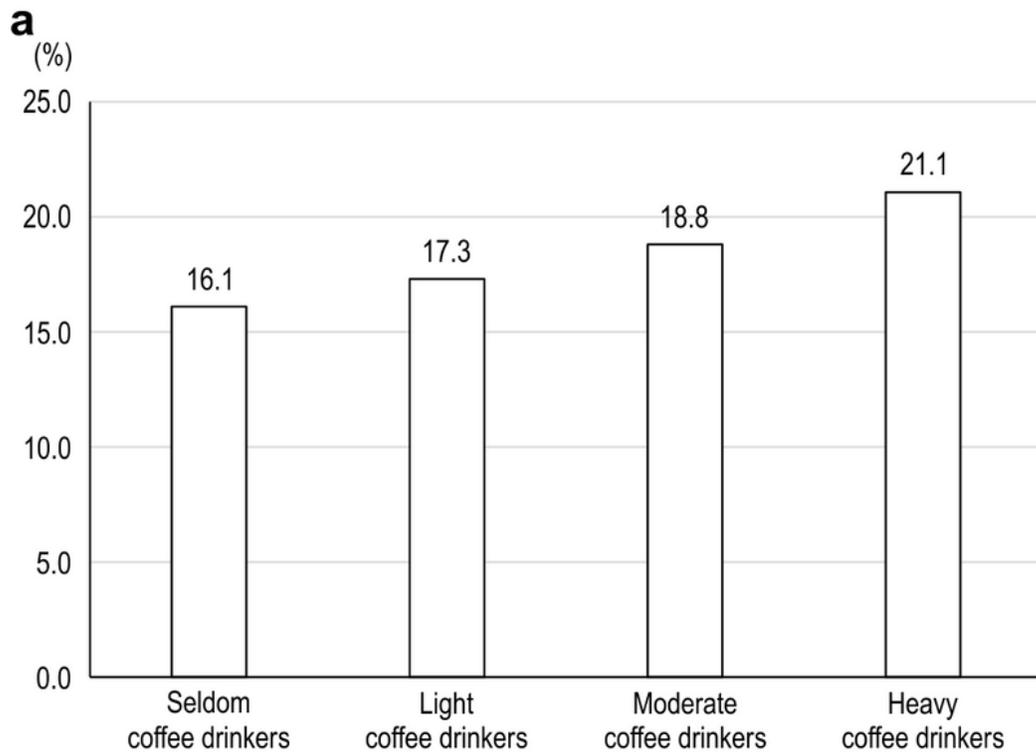


Figure 1

Prevalence and severity of bleeding in early pregnancy according to coffee consumption

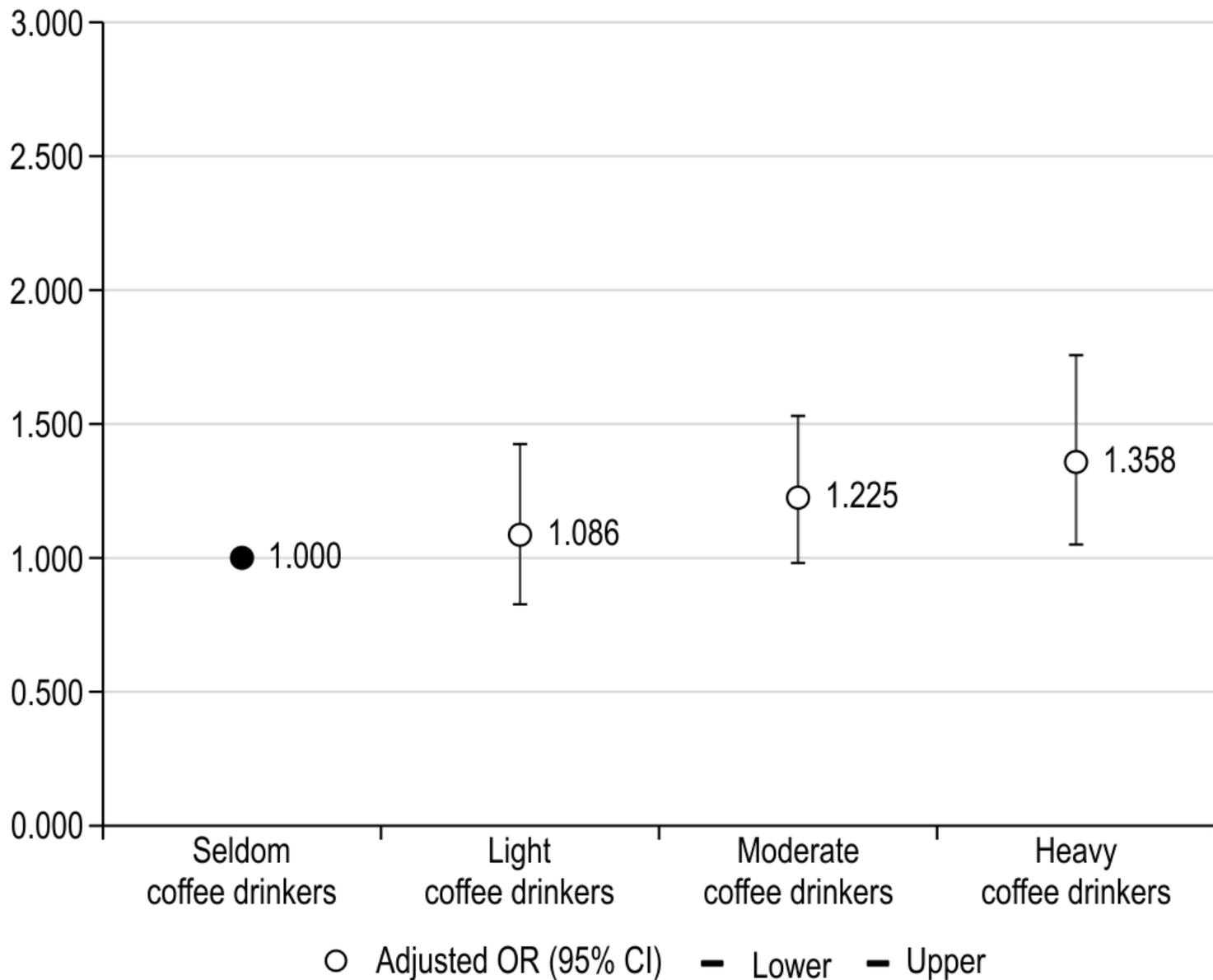


Figure 2

Adjusted odds ratios for the risk of bleeding in early pregnancy according to coffee consumption

Supplementary Files

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