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Maternal consumption of coffee during pregnancy and stillbirth and infant death in first year of life: prospective study

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Abstract

Objective To study the association between coffee consumption during pregnancy and the risk of stillbirth and infant death in the first year of life.

Design Prospective follow up study.

Setting Aarhus University Hospital, Denmark, 1989-96.

Participants 18 478 singleton pregnancies in women with valid information about coffee consumption during pregnancy.

Main outcome measures Stillbirth (delivery of a dead fetus at ≥ 28 weeks' gestation) and infant death (death of a liveborn infant during the first year of life).

Results Pregnant women who drank eight or more cups of coffee per day during pregnancy had an increased risk of stillbirth compared with women who did not drink coffee (odds ratio=3.0, 95% confidence interval 1.5 to 5.9). After adjustment for smoking habits and alcohol intake during pregnancy, the relative risk of stillbirth decreased slightly. Adjustment for parity, maternal age, marital status, years of education, occupational status, and body mass index did not substantially change the estimates of association. There was no significant association between coffee consumption and death in the first year of life after adjustment for smoking habits during pregnancy.

Conclusion Drinking coffee during pregnancy is associated with an increased risk of stillbirth but not with infant death.

Introduction

Caffeine, the key component in studies of the potential effects of coffee, is also found in tea, drinking chocolate, and cola. Exposure to caffeine during pregnancy has been associated with an increased risk of spontaneous abortion^{1 2} and low birth weight.^{3 4} High daily doses of caffeine in pregnant monkeys increase the risk of stillbirth.⁵

Caffeine may increase the risk of late fetal death in different ways. It increases the release of catecholamines from the renal medulla, possibly leading to vasoconstriction in the uteroplacental circulation and fetal hypoxia.^{6 7} Caffeine may also have a direct effect on the cardiovascular system of the fetus leading to tachycardia and other arrhythmias.⁸ Other lifestyle factors associated with coffee drinking, however, such as smoking and drinking alcohol, may also explain the apparent association between caffeine and stillbirth and infant death in the first year of life.^{9 10}

Participants and methods

We invited all pregnant women booking for delivery at the Department of Obstetrics and Gynaecology,

Aarhus University Hospital, from September 1989 to August 1996 to participate in the study. Nearly all women in the area comply with the antenatal care programme. The women completed two questionnaires before the first visit for routine antenatal care at about 16 weeks of gestation.

We used information from the first questionnaire to obtain data on medical and obstetric history, maternal age, smoking habits before pregnancy and during the first trimester, and alcohol intake during pregnancy. From the second questionnaire we obtained information on intake of coffee, tea, drinking chocolate, and cola and marital status, education, and employment status. We asked about current intake of coffee, tea, drinking chocolate, and cola, and women could indicate any whole number of daily cups of coffee, tea, and drinking chocolate, or bottles of cola. Information about delivery was obtained from birth registration forms filled in by the attending midwife immediately after delivery. Before data entry, all birth registration forms were manually checked and compared with the medical records by a research midwife.

Information about stillbirths was obtained from the obstetric department and from the Danish medical birth register^{11 12} through record linkage using the mother's personal identification number. Information about deaths during the first year of life was obtained from the registry of causes of death,¹³ administered by the Danish National Board of Health, and from the civil registration system.

The study population was restricted to singleton pregnancies among Danish speaking women who filled in the first questionnaire and who delivered after 28 completed weeks of gestation (n=25 395). The study population was further restricted to those with valid information about coffee intake during pregnancy (n=18 478).

We analysed coffee intake as number of cups and in ordered categories (0, 1-3, 4-7, and ≥ 8 cups/day). One cup of coffee corresponds to about 100 mg of caffeine.¹⁴ The intake of decaffeinated coffee in Denmark was negligible during the study period. We also obtained information on consumption of tea, drinking chocolate, and cola, but only a few women were exposed to high doses of caffeine from tea and hardly any from drinking chocolate or cola. Therefore we could not fully explore the effects of consumption of caffeine from sources other than coffee.

Statistical analyses

We looked at the association between intake of coffee and stillbirth and infant death, and then evaluated effect modification by other variables by stratified analyses. We also tested linear association between different levels of coffee intake by χ^2 test for trend. See bmj.com for details of statistical analysis.

Table 1 Maternal consumption of coffee during pregnancy and unadjusted and adjusted odds ratios for stillbirth, Aarhus, Denmark, 1989-96

Coffee (cups/day)	No of women	No of stillbirths/1000	Odds ratio (95% CI)			
			Unadjusted	Adjusted*	Adjusted†	Adjusted‡
0	7878	31 (3.9)	1	1	1	1
1-3	6362	17 (2.7)	0.7 (0.4 to 1.2)	0.7 (0.4 to 1.2)	0.6 (0.3 to 1.1)	0.6 (0.3 to 1.1)
4-7	3288	23 (7.0)	1.8 (1.0 to 3.1)	1.5 (0.8 to 2.6)	1.6 (0.9 to 2.7)	1.4 (0.8 to 2.5)
≥8	950	11 (11.6)	3.0 (1.5 to 5.9)	2.2 (1.0 to 4.6)	2.6 (1.3 to 5.3)	2.2 (1.0 to 4.7)

*Adjusted for smoking during pregnancy. †Adjusted for alcohol intake during pregnancy.

‡Adjusted for smoking and alcohol intake during pregnancy, parity, maternal age, marital status, years of education, employment status during pregnancy, and maternal body mass index.

Table 2 Maternal consumption of coffee during pregnancy and unadjusted and adjusted odds ratios for infant death, Aarhus, Denmark, 1989-96

Coffee (cups/day)	No of women	No of infant deaths/1000 live births	Odds ratio (95% CI)			
			Unadjusted	Adjusted*	Adjusted†	Adjusted‡
0	7847	34 (4.3)	1	1	1	1
1-3	6345	27 (4.3)	1.0 (0.6 to 1.6)	0.9 (0.6 to 1.5)	1.0 (0.6 to 1.6)	0.9 (0.6 to 1.6)
4-7	3265	4 (1.2)	0.3 (0.1 to 0.8)	0.2 (0.1 to 0.7)	0.3 (0.1 to 0.7)	0.2 (0.1 to 0.7)
≥8	939	9 (9.6)	2.2 (1.1 to 4.7)	1.6 (0.7 to 3.5)	2.1 (1.0 to 4.6)	1.6 (0.7 to 3.6)

*Adjusted for smoking during pregnancy. †Adjusted for alcohol intake during pregnancy.

‡Adjusted for smoking and alcohol intake during pregnancy, parity, maternal age, marital status, years of education, employment status during pregnancy, and maternal body mass index.

Results

The overall risk of stillbirth was 4.4/1000 (n=82) and of infant death was 4.0/1000 (n=74). The risk of stillbirth increased with the number of cups of coffee a day during pregnancy ($P < 0.01$ for trend). Compared with women who did not drink any coffee, women who drank four to seven cups a day had an 80% increased risk of stillbirth, and women who drank eight or more cups a day a 300% increased risk (table 1). When we restricted analyses to non-smokers and to women with an alcohol intake of less than three drinks a week the unadjusted odds ratios were of a similar magnitude as those in table 1. The same was found when we included only primiparous women in the analyses and when we excluded women with chronic diseases from the analyses.

Women with a high intake of coffee were also more likely to smoke and had a higher intake of alcohol. They were older, more often multiparous, more likely to be single, less likely to be students and had fewer years of education. The risk of stillbirth decreased slightly when we controlled for smoking habits and alcohol intake during pregnancy in a logistic regression model (table 1). Further adjustment for parity, maternal age, marital status, years of education, employment status, and body mass index did not substantially change the estimates of association (table 1).

In the crude analyses maternal consumption of eight or more cups of coffee a day during pregnancy was associated with a more than twofold increased risk of infant death (table 2). However, after adjustment for maternal smoking habits the association became insignificant.

Compared with women with valid information about coffee intake during pregnancy, women with missing information were more likely to be smokers, over 30 years of age, multiparous, and unemployed and to have a shorter education. However, we found no difference in the risk of stillbirth in women with missing information about coffee intake compared with women with valid information (odds ratio 1.1, 95% confidence interval 0.8 to 1.7); and the associations between

smoking and stillbirth and between alcohol and stillbirth were similar in the two groups.

Discussion

In this prospective study of 18 478 deliveries the risk of stillbirth increased with the amount of coffee consumed by the mothers during pregnancy. Due to the prospective nature of this study the number of deaths was small, and the risk estimate in women with the highest intake of coffee was based on only 11 stillbirths. However, after adjustment for potential confounding factors the association remained significant.

Compared with women who did not drink any coffee during pregnancy the adjusted risk of stillbirth was lower among women who drank one to three cups per day, slightly increased among women who drank four to seven cups per day, and more than doubled among women who drank eight or more cups of coffee per day. These results seem to indicate a threshold effect around four to seven cups per day.

Women with a high intake of coffee are more likely to be smokers and to have a high intake of alcohol.⁹ Adjustment for several potential confounders changed the association between coffee and stillbirth only slightly. However, adjustment for other factors such as nutritional status and eating habits might further influence the estimated risk. Furthermore, our study was conducted in a homogeneous population with a low overall late fetal mortality, reflecting lower prevalence of competing risks. The association between coffee drinking and stillbirth may be different in populations with higher overall risks of stillbirth.

The association between increased risk of death in the first year of life and intrauterine exposure to coffee became insignificant when we adjusted for smoking during pregnancy. Thus, coffee may not be causally related to infant death.

We measured coffee consumption at 16 weeks of gestation. Estimates of exposure based on questionnaires may be imprecise,¹⁵ and we had no information about size of cups or the type of coffee. However, due to

What is already known on this topic

Results from studies in monkeys suggest that high daily doses of caffeine in pregnancy increase the risk of stillbirth, but evidence from studies in humans has been lacking

What this study adds

Pregnant women who drank eight or more cups of coffee a day had more than twice the risk of stillbirth compared with women who did not drink coffee during pregnancy

the timing of the data collection, our information could not be biased by the women's knowledge about the outcome of pregnancy. Potential misclassification is likely to be non-differential, and our results may thus underestimate the true association between coffee drinking and stillbirth. Due to a higher intake of coffee and a faster metabolism among smokers^{15 16} we hypothesised that the fetotoxic effect of caffeine could depend on smoking habits during pregnancy. However, the risk of stillbirth associated with coffee was similar in smokers and non-smokers.

There did not seem to be one single cause that could explain the increased risk of stillbirth among women with a high intake of coffee (see bmj.com).

Information on coffee intake during pregnancy was missing in a quarter of the population. Women with missing information had a different risk profile than women with valid information. However, we have no reason to believe that the association between coffee and stillbirth among women with non-valid information would be different from the one we found.

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Longitudinal study of childhood wheezy bronchitis and asthma: outcome at age 42

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Longitudinal studies have reported that asthma in childhood has a good prognosis. However, most of these studies have not taken into account the severity of childhood symptoms.¹ The Melbourne Epidemiological Study of Childhood Asthma recruited children at age 7 years and followed them up through adolescence to adulthood.²⁻⁵ This report describes outcome at age 42 years in relation to symptoms in childhood.

Participants, methods, and results

In 1964, 401 children (295 with asthma and 106 controls) were randomly selected from a total of 30 000 7 year olds living in metropolitan Melbourne. A further 83 children with severe asthma were included from the same cohort in 1967, at age 10.^{2 3} Original data were available for 479 participants.

At recruitment, 105 children were classified as controls (children who had never wheezed); 74 had mild wheezy bronchitis (<5 episodes of wheezing associated with respiratory tract infection); 104 had wheezy bronchitis (≥5 episodes of wheezing associated with respiratory tract infection); 113 had asthma (wheezing unassociated with respiratory tract infection); and 83 had severe asthma (onset of asthma symptoms before 3 years of age, persistent symptoms at age of 10, and barrel chest deformity or ratio of forced expiratory volume in one second to forced vital capacity ≤50%).

At each review from the age of 21, participants were classified as follows: no recent asthma (no wheeze in past three years); infrequent asthma (wheezing in past three years but none in past three months); frequent asthma (wheezing in past three months, but less than once a week); or persistent asthma (wheezing in past three months, more than once a week).