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Moderate Alcohol Intake during Pregnancy and the Risk of Stillbirth and Death in the First Year of Life

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The authors evaluated the association between alcohol intake during pregnancy and risk of stillbirth and infant death in a cohort of pregnant women receiving routine antenatal care at Aarhus University Hospital (Aarhus, Denmark) between 1989 and 1996. Prospective information on alcohol intake, other lifestyle factors, maternal characteristics, and obstetric risk factors was obtained from self-administered questionnaires and hospital files, and 24,768 singleton pregnancies were included in the analyses (116 stillbirths, 119 infant deaths). The risk ratio for stillbirth among women who consumed ≥5 drinks/week during pregnancy was 2.96 (95% confidence interval: 1.37, 6.41) as compared with women who consumed <1 drink/week. Adjustment for smoking habits, caffeine intake, age, prepregnancy body mass index, marital status, occupational status, education, parity, and sex of the child did not change the conclusions, nor did restriction of the highest intake group to women who consumed 5–14 drinks/week (risk ratio = 3.13, 95% confidence interval: 1.45, 6.77). The rate of stillbirth due to fetoplacental dysfunction increased across alcohol categories, from 1.37 per 1,000 births for women consuming <1 drink/week to 8.83 per 1,000 births for women consuming ≥5 drinks/week. The increased risk could not be attributed to the effect of alcohol on the risk of low birth weight, preterm delivery, or malformations. There was little if any association between alcohol intake and infant death. *Am J Epidemiol* 2002;155:305–12.

alcohol drinking; fetal death; infant mortality; pregnancy

Since the early 1980s, the incidence of stillbirth and infant death has remained relatively constant in Denmark while it has decreased in other countries (1). Attention has been drawn to lifestyle factors as a possible explanation for this stagnation in mortality (2). A larger proportion of women drink alcohol during pregnancy in Denmark than in several other countries (3, 4).

Intake of one or more alcoholic drinks per day during pregnancy has consistently been shown to be associated with reduced birth weight and intrauterine growth restriction (5, 6), and heavy maternal alcohol consumption is consistently found to be associated with malformations (7), mental retardation (8), and behavioral and psychosocial problems in childhood and adolescence (9, 10). Still, the question of whether there is a safe level of drinking during pregnancy remains controversial (8, 11, 12).

Results regarding the relation of alcohol drinking to stillbirth and perinatal, neonatal, and infant mortality have been few and highly inconsistent (13–21). Many studies used retrospective information on alcohol intake (13–18) or did not adequately account for competing risk factors (19–21). Excessive alcohol consumption during pregnancy is potentially preventable; therefore, clarification of the relation between alcohol drinking and infant mortality is important.

We examined the association between maternal alcohol consumption during pregnancy and the risk of stillbirth and death during the first year of life in a Danish cohort of pregnant women. We used information on alcohol intake that had been collected prospectively during pregnancy and took into account a variety of other lifestyle factors, maternal risk factors, and obstetric risk factors.

MATERIALS AND METHODS

Data collection and participants

All Danish-speaking pregnant women receiving routine antenatal care in the Department of Obstetrics and Gynaecology at Aarhus University Hospital, Aarhus, Denmark, between September 1989 and August 1996 were invited to participate in the cohort study. Almost all women in the area (99 percent) participate in the antenatal care program. The women were asked to fill in two self-administered questionnaires prior to their first antenatal care visit: one for the medical record (filled in by 95 percent of the women receiving routine antenatal care) that gathered information on current maternal alcohol intake (drinks/week), smoking habits, age, height, prepregnancy

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Abbreviation: CI, confidence interval.

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weight, and parity, and a research questionnaire that gathered information on caffeine intake, marital status, occupational status, and education. Median gestational age among women filling in the questionnaire for the medical record was 104 days (10th and 90th percentiles: 71 days and 131 days), and for the research questionnaire it was 103 days (10th and 90th percentiles: 72 days and 136 days). Information on birth outcome was obtained from birth registration forms filled in by attending midwives immediately after delivery. To enhance the accuracy of the data, information from the medical-record questionnaire was entered twice into the database, while logical checks were performed for both questionnaires. All birth registration forms were checked manually and compared with the medical records by a research midwife before data entry.

Information on stillbirths, including causes of death, was obtained from one of the birth registration forms and from the Danish Medical Birth Register through record linkage, using the mother's unique personal identification number. Information on deaths occurring during the first year of life was obtained from the Registry of Causes of Death, which is administered by the Danish National Board of Health, and from the Civil Registration System. Four children listed as deceased according to the Civil Registration System were not registered in the Registry of Causes of Death. The medical records were checked, and according to the records all four children were dead.

Stillbirth was defined as delivery of a dead fetus at 28 completed weeks of gestation or later in pregnancy. Infant death was defined as death within the first year of life among liveborn babies. Causes of stillbirth were categorized according to the classification suggested by Andersen et al. (22), based on categorizations suggested by Cole et al. (23) and Hey et al. (24). The classification identifies the factor which probably initiated the chain of events leading to death (22). In Danish data, this categorization was previously shown to yield fewer unexplained deaths than the categorization suggested by Cole et al. (22, 23), as well as a more detailed description of the category labeled "antepartum asphyxia" in the classification by Hey et al. (22, 24). For deaths that could not be unambiguously classified on the basis of the register data, the medical records and autopsy reports were consulted before classification.

Danish women with singleton pregnancies who did not have an induced abortion and who completed the questionnaire for the medical record were eligible for this study (n = 25,788). We excluded the following types of pregnancies from the study: pregnancies that ended with a spontaneous abortion (defined as delivery of a dead fetus before 28 completed weeks of gestation) (n = 346); pregnancies included in the cohort after birth had occurred (n = 7); and pregnancies for which there was no information on alcohol intake (n = 667). This left 24,768 pregnancies for analysis (116 stillbirths, 119 infant deaths). All livebirths, including infant deaths, were included in the analyses irrespective of gestational age at the time of delivery. For analysis of infant deaths, stillbirths were excluded from the denominator. All participants in the study had filled in the questionnaire for the medical record, whereas 18,287 (74 percent) had filled in the research questionnaire.

In the medical-record questionnaire, the following question on alcohol intake was asked: "How many drinks do you approximately drink per week (one drink is the equivalent of one [bottle of] beer, one glass of wine, or one schnapps)?" This question has been shown to yield information comparable to that obtained from a more extensive research questionnaire (25), and it has been validated in a study comparing it with an extensive interview and with diaries (26). Possible responses to the question on alcohol consumption were precoded as <1, 1–2, 3–4, 5–9, 10–14, 15–19, 20–29, 30–39, and ≥40 drinks/week. Because of small numbers in the highest alcohol intake categories (table 1), information on alcohol intake was categorized into four groups for these analyses (<1, 1–2, 3–4, and ≥5 drinks/week). The definition of a drink followed the definition of the Danish National Board of Health: One drink contains 12 g or 15 ml of pure alcohol, the equivalent of one normal beer, one glass of wine, or 4 cl (40 ml) of spirits. Caffeine intake was calculated from average daily consumption of coffee (one cup = 104 mg), tea (one cup = 46 mg), liquid chocolate (one cup = 13 mg), and cola (one bottle or 250 ml = 45 mg) (27). Potentially confounding factors were categorized as shown in table 2.

TABLE 1. Distribution of livebirths, stillbirths, and infant deaths by self-reported alcohol intake within precoded categories, Aarhus, Denmark, 1989–1996

Alcohol intake (drinks/week) during pregnancy	No. of livebirths	Stillbirths		Infant deaths	
		No.	‰*	No.	‰†
<1	16,698	70	4.2	84	5.0
1–2	5,633	29	5.1	23	4.1
3–4	1,762	10	5.6	8	4.5
5–9	467	5	10.6	3	6.4
10–14	62	2	31.3	0	0.0
15–19	16	0	0.0	1	62.5
20–29	6	0	0.0	0	0.0
30–39	5	0	0.0	0	0.0
≥40	3	0	0.0	0	0.0
Missing data‡	667	1	1.5	5	7.5

* Proportion (per thousand) of all births.
† Proportion (per thousand) of all livebirths.
‡ Pregnancies with missing information on alcohol intake.

TABLE 2. Distribution of and unadjusted risk ratios for stillbirth and infant death within categories of lifestyle factors, maternal characteristics, and obstetric characteristics, Aarhus, Denmark, 1989–1996

	Stillbirth (*n* = 24,768; 116 stillbirths)*				Infant death (*n* = 24,652; 119 infant deaths)*			
	No. of births	No. of stillbirths	Risk ratio	95% confidence interval	No. of livebirths	No. of infant deaths	Risk ratio	95% confidence interval
Alcohol intake (drinks/week)								
<1	16,768	70	1.00 †		16,698	84	1.00 †	
1–2	5,662	29	1.23	0.80, 1.89	5,633	23	0.81	0.51, 1.29
3–4	1,772	10	1.35	0.70, 2.62	1,762	8	0.90	0.44, 1.86
≥5	566	7	2.96	1.37, 6.41	559	4	1.42	0.52, 3.87
Smoking (cigarettes/day)								
0	17,197	65	1.00		17,132	66	1.00	
1–9	3,160	18	1.51	0.90. 2.54	3,142	26	2.15	1.37, 3.38
≥10	3,801	32	2.23	1.46, 3.40	3,769	22	1.52	0.94, 2.45
Caffeine (mg/day)								
<200	7,310	29	1.00		7,281	33	1.00	
200–399	5,326	16	0.76	0.41, 1.39	5,310	26	1.08	0.65, 1.80
≥400	5,514	37	1.69	1.04, 2.75	5,477	23	0.93	0.55, 1.58
Maternal age (years)								
<25	3,701	15	0.87	0.49, 1.56	3,686	23	1.31	0.80, 2.15
25–29	10,129	47	1.00		10,082	48	1.00	
≥30	10,938	54	1.06	0.72, 1.57	10,884	48	0.93	0.62, 1.38
Prepregnancy body mass index‡								
<18.5	1,764	11	1.47	0.78, 2.75	1,753	11	1.35	0.72, 2.52
18.5–24	18,793	80	1.00		18,713	87	1.00	
25–29	2,498	13	1.22	0.68, 2.19	2,485	11	0.95	0.51, 1.78
≥30	917	11	2.82	1.51, 5.27	906	9	2.14	1.08, 4.23
Marital status								
Married/cohabiting	20,026	94	1.00		19,932	92	1.00	
Single	868	3	0.74	0.23, 2.32	865	6	1.50	0.66, 3.42
Occupational status								
Employed	11,906	54	1.00		11,852	53	1.00	
Not employed	3,724	19	1.13	0.67, 1.90	3,705	20	1.21	0.72, 2.02
Student	1,886	7	0.82	0.37, 1.80	1,879	6	0.71	0.31, 1.66
Education (years)								
<10	1,787	8	1.04	0.49, 2.21	1,779	6	0.73	0.32, 1.71
10	5,544	24	1.01	0.62, 1.66	5,520	26	1.03	0.64, 1.65
>10	10,492	45	1.00		10,447	48	1.00	
Parity								
0	12,368	62	1.00		12,306	66	1.00	
≥1	12,364	54	0.87	0.61, 1.25	12,310	52	0.79	0.55, 1.13
Sex of child								
Boy	12,759	68	1.00		12,691	68	1.00	
Girl	12,007	47	0.73	0.51, 1.06	11,960	51	0.80	0.55, 1.14
Preterm delivery								
No	23,777	61	1.00		23,716	82	1.00	
Yes	987	55	21.72	15.17, 31.10	932	37	11.48	7.83, 16.83
Birth weight (g)								
<2,500	816	57	29.29	20.43, 42.00	759	35	13.41	9.09, 19.79
≥2,500	23,902	57	1.00		23,845	82	1.00	

* For some variables, numbers given do not sum to the total because of missing data.
† Referent.
‡ Weight (kg)/height (m)^2.

Statistical analyses

We used risk ratios and odds ratios to express the unadjusted associations between alcohol intake and mortality, and we used odds ratios to express the adjusted associations. The lowest alcohol intake group (<1 drink/week) was designated the reference category. Multivariate logistic regression analyses were performed in two ways (28), using 1) a change-in-estimate approach, including all the covariates in table 2 that changed the unadjusted point estimates of the alcohol categories by more than 10 percent when included in the model one at a time and 2) a model including all of the covariates in table 2 based on a priori information that they might potentially confound the results (13, 18, 29, 30). The models yielded comparable results; hence, only results from the latter model are presented. Because exclusion of missing values shifted associations between alcohol and outcome measures towards higher risk estimates, we included missing values as a separate category when we adjusted for the covariates in logistic regression analyses. All covariates were entered as dummy variables equal to the number of categories (including a category for missing values) minus 1. Effect modification was evaluated in stratified analyses using the Mantel-Haenszel method (31), as well as in logistic regression models with interaction terms. For the stratified analyses, p values refer to the test of heterogeneity of the odds ratios over the strata ($p > 0.05$ signifying no heterogeneity); for interaction terms, p values refer to the significance of the product terms included in the analyses.

The study was approved by the regional ethics committee, the Danish Data Protection Agency, and the Danish National Board of Health.

RESULTS

Overall rates of stillbirth and infant mortality in the study were 4.7 per 1,000 births and 4.8 per 1,000 livebirths, respectively.

Stillbirth

Bivariate analyses showed that the risk of stillbirth increased with increasing alcohol intake across alcohol categories (Mantel-Haenszel χ^2 test for trend: $p = 0.02$; test for departure from a linear trend: $p > 0.2$). Women who consumed ≥5 drinks/week had a risk of stillbirth nearly three times greater than that of women who consumed <1 drink/week (table 2). Restricting analyses to each woman's first pregnancy registered in the cohort during the study period did not change this conclusion. There was no interaction with smoking ($p > 0.1$) or effect modification by smoking ($p > 0.1$) at any alcohol intake level. Multivariate logistic regression analysis, which included maternal smoking habits, caffeine intake, age, prepregnancy body mass index (weight (kg)/height (m)^2), marital status, occupational status, education, parity, and sex of the child, yielded comparable results (table 3). For comparison, the unadjusted and adjusted odds ratios for the subset of women with no missing information on any of the potential confounders are also shown in table 3. Alcohol may increase the risk of low birth weight and preterm delivery, and these factors may also increase the risk of stillbirth (table 2); yet stratification by birth weight and preterm delivery (dichotomized) did not change the conclusions (all p's > 0.1), nor did inclusion of these variables in the regression model (the odds ratio for women who consumed ≥5 drinks/week was 2.69 (95 percent confidence interval (CI): 1.14, 6.31)).

To eliminate any effects of excessive alcohol use, we reanalyzed the data after truncating the highest alcohol intake group at 14 drinks/week. This categorization resulted

TABLE 3. Unadjusted and adjusted odds ratios for stillbirth within categories of alcohol intake for all pregnancies and for pregnancies with no missing information on potentially confounding factors, Aarhus, Denmark, 1989–1996

	All pregnancies (n = 24,768; 116 stillbirths)						Pregnancies with no missing information (n = 16,010; 74 stillbirths)					
Alcohol intake (drinks/week)	No. of pregnancies	No. of stillbirths	Unadjusted odds ratio	95% confidence interval	Adjusted odds ratio*	95% confidence interval	No. of pregnancies	No. of stillbirths	Unadjusted odds ratio	95% confidence interval	Adjusted odds ratio*	95% confidence interval
<1	16,768	70	1.00†		1.00†		10,725	43	1.00†		1.00†	
1–2	5,662	29	1.23	0.80, 1.90	1.27	0.81, 1.98	3,757	16	1.06	0.60, 1.89	1.12	0.62, 2.02
3–4	1,772	10	1.35	0.70, 2.63	1.25	0.63, 2.47	1,161	9	1.94	0.94, 4.00	1.83	0.86, 3.86
≥5	566	7	2.99	1.37, 6.53	2.65	1.18, 5.97	367	6	4.13	1.75, 9.76	3.65	1.47, 9.07

* Adjusted for maternal smoking habits, caffeine intake, age, prepregnancy body mass index, marital status, occupational status, education, parity, and sex of the child.
† Referent.

in a risk ratio for stillbirth of 3.13 (95 percent CI: 1.45, 6.77) among women consuming 5–14 drinks/week. This estimate was little changed in multivariate analyses (odds ratio = 2.80, 95 percent CI: 1.24, 6.30)).

The risk of stillbirth due to fetoplacental dysfunction increased across alcohol categories, from 1.37 per 1,000 for women consuming <1 drink/week to 8.83 per 1,000 for women consuming ≥5 drinks/week (table 4). When we included only stillbirths due to fetoplacental dysfunction in the analyses, the adjusted odds ratios for women consuming 1–2, 3–4, and ≥5 drinks/week were 1.45 (95 percent CI: 0.67, 3.11), 1.79 (95 percent CI: 0.60, 5.37), and 7.92 (95 percent CI: 2.80, 22.40), respectively. The increased risk of stillbirth did not seem to be mediated through an increased risk of malformations (table 4).

Infant death

Bivariate analyses showed a slight but insignificant increase in risk of infant death for women consuming ≥5 drinks/week (table 2). Restricting analyses to each woman's first pregnancy registered in the cohort did not change this conclusion. There was no interaction (all *p*'s > 0.1) or effect modification (all *p*'s > 0.1) with smoking, birth weight, or preterm delivery at any alcohol intake level.

Multivariate logistic regression analyses with adjustment for potential confounding by maternal smoking, caffeine intake, age, prepregnancy body mass index, marital status, occupational status, education, parity, and sex of the child yielded comparable results (table 5), as did inclusion of birth weight and preterm delivery in the regression model (the odds ratio for women consuming ≥5 drinks/week was 1.39 (95 percent CI: 0.49, 3.95)).

DISCUSSION

In this study, we found an increasing risk of stillbirth with increasing moderate alcohol intake. Women who consumed ≥5 drinks/week had a 2–3 times increased risk of experiencing a stillbirth, mainly because of fetoplacental dysfunction. Little if any association was seen between moderate alcohol intake and infant mortality.

Previous studies of mortality have yielded highly inconsistent results (13–21, 32). One study which used prospective information on alcohol intake showed a 2.5 times increased risk of stillbirth for women consuming >3 drinks/day (32); another study showed a linear relation for stillbirth and infant mortality, each drink increasing the risk of stillbirth by 1 percent (16). However, the unadjusted data from the latter study suggest a threshold effect for both outcomes at a level of approximately 6 drinks/week rather than a linear relation. Yet another study showed an increased risk of intrapartum stillbirth (13) and perinatal mortality (13, 20) for abstainers. Other studies have found no association between alcohol and stillbirth (14, 15, 17, 19, 21), perinatal mortality (21), early neonatal (17) or neonatal (19, 21) mortality, or sudden infant death syndrome (18). However, in most of these studies, investigators used retrospective information on alcohol intake (collected after death had

TABLE 4. Distribution of stillbirths and rates of stillbirth per 1,000 births, by cause, Aarhus, Denmark, 1989–1996*

Cause of stillbirth	Alcohol intake (drinks/week) during pregnancy: <1			1–2			3–4			≥5			Total		
	No. of stillbirths	Rate per 1,000 births	95% CI†	No. of stillbirths	Rate per 1,000 births	95% CI	No. of stillbirths	Rate per 1,000 births	95% CI	No. of stillbirths	Rate per 1,000 births	95% CI	No. of stillbirths	Rate per 1,000 births	95% CI
Congenital malformations	7	0.42	0.17, 0.86	1	0.18	0.00, 0.98	0			0			8	0.32	0.14, 0.64
Unexplained intrauterine death	11	0.66	0.33, 1.17	8	1.41	0.61, 2.78	1	0.56	0.01, 3.14	1	1.77	0.04, 9.80	21	0.85	0.52, 1.30
Fetoplacental dysfunction	23	1.37	0.87, 2.06	10	1.77	0.85, 3.25	4	2.26	0.62, 5.77	5	8.83	2.87, 20.49	42	1.70	1.22, 2.29
Antepartum hemorrhage	13	0.78	0.41, 1.33	2	0.35	0.04, 1.28	1	0.56	0.01, 3.14	1	1.77	0.04, 9.80	17	0.69	0.40, 1.10
Maternal disease	4	0.24	0.07, 0.61	4	0.71	0.19, 1.81	1	0.56	0.01, 3.14	0			9	0.36	0.17, 0.69
Intrapartum event	6	0.36	0.13, 0.78	2	0.35	0.04, 1.28	2	1.13	0.14, 4.07	0			10	0.40	0.19, 0.74
Conditions due to preterm delivery	0			0			0			0			0		
Infections	3	0.18	0.04, 0.52	2	0.35	0.04, 1.28	1	0.56	0.01, 3.14	0			6	0.24	0.09, 0.53
Other specific conditions	3	0.18	0.04, 0.52	0			0			0			3	0.12	0.03, 0.35
Unclassifiable	0			0			0			0			0		
Total	70	4.17	3.26, 5.27	29	5.12	3.43, 7.35	10	5.64	2.71, 10.35	7	12.37	4.99, 25.31	116	4.68	3.87, 5.61

* Classification was based on that of Andersen et al. (22).
† CI, confidence interval.

TABLE 5. Unadjusted and adjusted odds ratios for infant death within categories of alcohol intake (*n* = 24,652 livebirths; 119 infant deaths), Aarhus, Denmark, 1989–1996

	No. of livebirths	No. of infant deaths	Unadjusted odds ratio	95% confidence interval	Adjusted odds ratio*	95% confidence interval
Alcohol intake (drinks/week)						
<1	16,698	84	1.00†		1.00†	
1–2	5,633	23	0.81	0.51, 1.29	0.85	0.53, 1.36
3–4	1,762	8	0.90	0.44, 1.87	0.90	0.43, 1.89
≥5	559	4	1.43	0.52, 3.90	1.38	0.50, 3.86

* Adjusted for maternal smoking habits, caffeine intake, age, prepregnancy body mass index, marital status, occupational status, education, parity, and sex of the child.
† Referent.

occurred) (13–18), and in some of the studies they did not adequately control for potentially confounding factors (19–21).

Preterm delivery and low birth weight are important contributors to neonatal mortality (33, 34). We previously found that alcohol was associated with increased risk of preterm delivery (35), and it has consistently been found that alcohol is associated with increased risk of low birth weight (5, 6). However, our analyses suggested that the association of stillbirth with alcohol consumption was not mediated by an effect of alcohol on preterm delivery and birth weight, nor did it seem to be mediated by an effect of alcohol on malformations.

For stillbirth, the test for departure from a linear trend (based on unadjusted data) did not yield a significant result, which suggests a linear effect rather than a threshold effect. On the other hand, considering that the risk for women consuming 1–2 and 3–4 drinks/week was only insignificantly increased in comparison with women drinking less, and considering that the linear trend seemed less evident when the adjusted estimates were examined (table 3), one should be cautious when interpreting the apparent linear dose-response relation. Moreover, although underreporting *usually* has little effect on the association between exposure and outcome (if the reference group is large) (36), underreporting of alcohol intake may mask a true threshold effect as a dose-response relation (36). Indeed, it is well-known that alcohol intake is usually underreported in questionnaires and interviews as compared with diaries (37). When we compared our questionnaire data with information on alcohol intake obtained from a more elaborate questionnaire specifying subtypes of alcohol (25) and with information from an elaborate personal interview and from diaries specifying alcohol subtypes and different time periods during pregnancy, we found a slight tendency towards underreporting in the questionnaire data (26). Therefore, considering that slight underreporting is likely to have occurred (26), a threshold for the effect of alcohol on stillbirth also seems to be a plausible interpretation of our data. In any case, both interpretations are possible because of the small numbers in the highest alcohol intake group.

We had information on alcohol intake at only one point in time during pregnancy, and therefore we were not able to account for different patterns of drinking. Our data did not allow us to distinguish between total abstainers and women reporting an intake of >0 but <1 drink/week. However, a distinction between these two groups of women would be inappropriate in our data in any case. In a recent study, when we focused on low-to-moderate intake, we found that a very large group of women (5–44 percent) who reported being total abstainers on the questionnaire actually reported consuming small amounts of alcohol (>0 but <1 drink/week) in interviews or diaries, and vice versa (26).

Although this was one of the largest studies of this topic to date, the number and distribution of drinkers limited the analytical possibilities. Very few women reported consuming more than 14 drinks/week, which made it impossible to independently assess effects above this level, and the findings for women who consumed ≥5 drinks/week were all based on low numbers.

Women consuming ≥5 drinks/week were older, were more often smokers, had a higher caffeine intake, were more educated, and were more often multiparous than women with a lower alcohol intake. Women with a high alcohol intake may also differ with regard to other sociodemographic factors not included in these analyses, and thus bias from unadjusted confounding may be present. Furthermore, information was missing for some women, particularly with respect to caffeine intake, occupation, and education. However, in order for these variables to act as confounders they must be associated with both alcohol intake and death. Although caffeine intake and education were associated with alcohol intake (based on information obtained from the participants), none of the variables were significantly associated with death (table 2). In any case, causal inferences should be made with caution.

We used the definition of stillbirth that was used officially during the study period—the definition of the Danish Medical Birth Register. We obtained supplementary data on spontaneous abortions occurring in the 27th and 28th weeks of gestation from the Danish National Patient Registry. Including these fetal deaths in the analyses did not change the conclusions: Adjusted odds ratios for women consuming 1–2, 3–4, and ≥5 drinks/week were 1.28 (95 percent CI: 0.82, 1.99), 1.26 (95 percent CI: 0.64, 2.49), and 2.69 (95 percent CI: 1.20, 6.05), respectively, in comparison with women consuming <1 drink/week.

We found an increased risk of stillbirth that was mainly due to fetoplacental dysfunction, including placental infarction, complications related to the umbilical cord, intrauterine growth retardation, and antepartum asphyxia (22). Animal models have shown that increasing alcohol intake may increase the risk of severe intravascular coagulation (38) and decrease blood flow in the placenta (39). A recent study in humans suggested that alcohol abuse among nonpregnant surgical patients may change hemostatic function (40). Other possible pathophysiologic mechanisms may include increased production of prostaglandins, including prostaglandins of the E series (41, 42). Prostaglandins increase cyclic 3′,5′–adenosine monophosphate activity, thereby decreasing cell division (42), and it is possible that increased levels of prostaglandin E_2 and prostaglandin $F_{2\alpha}$ cause fetal death (43). Finally, alcohol drinking may cause hypoglycemia (44), and an association has been found between hypoglycemia and perinatal mortality (45).

Our data suggest that there is an increasing risk of stillbirth with increasing moderate alcohol intake. The data show that women consuming ≥5 drinks/week have a 2–3 times increased risk of stillbirth that is attributable mainly to fetoplacental dysfunction.

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