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MODERATE ALCOHOL INTAKE IN PREGNANCY AND THE RISK OF SPONTANEOUS ABORTION

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Abstract — Women attending routine antenatal care at Aarhus University Hospital, Denmark, from 1989 to 1996 were eligible for this cohort study on the association between alcohol intake in pregnancy and the risk of spontaneous abortion. We included 24 679 singleton pregnancies in the study. We used Cox regression analyses with delayed entry for the analyses. We found an increased risk of spontaneous abortion in the first trimester (7–11 completed weeks of gestation) for women consuming ≥5 drinks/week. We found no association between alcohol intake and spontaneous abortion during the second trimester. Common methodological problems in relation to studies on spontaneous abortions are discussed, as are problems with possible under-reporting of alcohol consumption. We conclude that women consuming ≥5 drinks/week are at increased risk of first trimester spontaneous abortion.

INTRODUCTION

Intake of an average of ~1 drink/day or more has been shown to be associated with reduced birthweight and intrauterine growth restriction (Passaro *et al*., 1996; Lundsberg *et al*., 1997), and heavy maternal alcohol consumption is associated with malformations (Mills and Graubard, 1987; American Academy of Pediatrics Committee on Substance Abuse, 1993), mental retardation, as well as behavioural and psychosocial problems in childhood and adolescence (Spohr *et al*., 1993; Nordberg *et al*., 1994). It remains controversial whether there is a safe level of drinking during pregnancy (American Academy of Pediatrics Committee on Substance Abuse, 1993; Midirs & NHS Centre for Reviews and Dissemination, 1996; Kesmodel, 1999).

Previous studies on alcohol and spontaneous abortions have yielded inconsistent results: increased risk has been reported in alcoholics (Sokol, 1980; Sokol *et al*., 1980) and in women drinking ≥7 drinks/week on average (Harlap and Shiono, 1980; Windham *et al*., 1992), and in one study increased risk has been reported at lower levels (Windham *et al*., 1997). Parazzini *et al*. (1994) reported a decreased risk of spontaneous abortion for women drinking >7 drinks of wine/week on average prior to pregnancy, and several studies have found no association between alcohol and spontaneous abortion (Becker *et al*., 1989; Parazzini *et al*., 1990, 1994; Cavallo *et al*., 1995; Dlugosz *et al*., 1996; Zhang and Bracken, 1996). Excessive alcohol consumption during pregnancy is potentially preventable, and clarification of the relationship between alcohol and spontaneous abortions is therefore important.

In the present study, we examined the association between maternal alcohol consumption during pregnancy and the risk of spontaneous abortion in a Danish cohort of pregnant women, using information on alcohol intake collected during pregnancy, and taking into account a variety of other lifestyle factors, maternal risk factors and obstetric risk factors.

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MATERIALS AND METHODS

All Danish-speaking pregnant women attending routine antenatal care at the Department of Obstetrics and Gynaecology, Aarhus University Hospital, Denmark, from September 1989 till August 1996 were invited to participate in the cohort study. The department serves all pregnant women in the area (high as well as low risk), and nearly all women in the area comply with the antenatal care programme. The women were asked to fill in two self-administered questionnaires: one for the medical record, which provided information on current maternal alcohol intake (drinks/week) and smoking habits, maternal age, height, pre-pregnant weight, parity, and previous spontaneous abortions; and a research questionnaire providing information on caffeine intake, marital status, occupational status, and school education. Both questionnaires were mailed together to each woman's home address. Information on birth outcome was obtained from birth registration forms filled in by the attending midwife immediately after delivery. In order to enhance the accuracy of the data, information from the questionnaire for the medical record was entered twice into the database, while logical checks regarding the reasonableness of the distribution of each variable and impossible and unusual values were performed for both questionnaires. All birth registration forms were manually checked and compared with the medical records by a research midwife before data entry.

Information on spontaneous and induced abortions was obtained from the cohort, as well as from the Danish National Patient Registry through record linkage, using the pregnant woman's unique personal identification number. For pregnancies with ICD-8 and ICD-10 codes for spontaneous abortions (including codes for missed abortions and habitual abortions) and induced abortions, and for women with no information on birth outcome, the information on pregnancy outcome was manually checked in the medical records by the first two authors (U.K., K.W.). For spontaneous abortions, we used the date the fetus was assessed to be non-viable as the date of the abortion.

Spontaneous abortion was defined as spontaneous intrauterine fetal death and termination of pregnancy before 28 completed weeks of gestation. Gestational age for abortions was calculated from the last menstrual date, and if this date was missing or the woman had irregular menstrual cycles, information on gestational age was obtained from ultrasonographic measurements.

Danish women with singleton pregnancies, who had completed the questionnaire for the medical records, were eligible for this study (n = 25 896). We excluded pregnancies with a hydatidiform mole (n = 2), pregnancies with missing information on gestational age (n = 5), pregnancies included in the cohort after 28 completed weeks of gestation (n = 532), pregnancies included in the cohort after abortion or birth had occurred (n = 8), pregnancies for which no valid date of completing the questionnaire was available (n = 4), and pregnancies with no information on alcohol intake (n = 666), thus leaving 24 679 pregnancies for analysis, including 321 spontaneous abortions and 98 induced abortions. All participants had filled in the questionnaire for the medical record, whereas 18 226 (74%) had filled in the research questionnaire.

In the questionnaire the following question on current average, weekly alcohol intake was asked: 'How many drinks do you approximately drink per week (one drink is the equivalent of 1 [bottle of] beer, 1 glass of wine, or 1 schnaps)?'. The question has been shown to yield information comparable with that from a more extensive research questionnaire (Kesmodel *et al*., 2001), and it has been validated in a study comparing it with an extensive interview and information from diaries (Kesmodel and Olsen, 2001). Response to questions on alcohol consumption was precoded into <1, 1–2, 3–4, 5–9, 10–14, 15–19, 20–29, 30–39 and ≥40 drinks/week. Due to small numbers in the highest alcohol intake categories (31 reported intake of ≥15 drinks/week) information on alcohol was categorized into four groups for analysis (<1, 1–2, 3–4, ≥5 drinks/week). The definition of a drink complied with the definition from the Danish National Board of Health, one drink containing 12 g or 15 ml of pure alcohol, the equivalent of one normal beer, one glass of wine, or 4 cl of spirits. Caffeine intake was calculated from average daily consumption of coffee (1 cup = 104 mg), tea (1 cup = 46 mg), drinking chocolate (1 cup = 13 mg) and cola (1 bottle or 250 ml = 45 mg) (Bunker and McWilliams, 1979). Potential confounders were categorized as in Table 1.

Statistical methods

We used Cox regression analyses with delayed entry (left truncation) for analyses (Cox and Oakes, 1984), and hazard ratios (HR) to express the association between alcohol intake and spontaneous abortion. The lowest alcohol intake group (<1 drink/week) was used as the reference category. The risk was calculated for first and second trimester spontaneous abortions, respectively. Each pregnancy contributed time at risk from the date the woman completed the questionnaire for the medical record. For analyses of first trimester abortions, each pregnancy contributed time at risk until the date the fetus was assessed to be non-viable (spontaneous abortions), the date of the induced abortion, or at 12 completed weeks of gestation (84 days). For analyses of second trimester abortions, we excluded first trimester spontaneous and induced abortions. Each pregnancy contributed time at risk until the date the fetus was assessed to be non-viable (spontaneous abortions), the date of the induced abortion, the date of birth if occurring before 28 completed weeks of gestation, or at 28 completed weeks of gestation (pregnancies ending with a livebirth or a stillbirth) as appropriate. Multivariate analyses were performed, using a model including all the covariates in Table 1 (except previous spontaneous abortion and gravidity) based on *a priori* information that they might potentially confound the results (Greenland, 1989). Subsequently, parity was replaced with respectively previous spontaneous abortions and gravidity, which are also risk factors, the inclusion of which, however, may result in serious over-adjustment if previous abortions were also due to high alcohol intake (Weinberg *et al*., 1993; Weinberg and Wilcox, 1998). Missing values were included as a separate category when adjusting for the covariates in multivariate analyses, since exclusion of missing values changed the association between alcohol and outcome measures towards substantially higher hazard ratios.

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

RESULTS

For all births, median gestational age when filling in the questionnaire for the medical record was 103 days (10th/90th percentiles = 71/128 days), and, for the research questionnaire, it was 102 days (10th/90th percentiles = 71/132 days). For spontaneous abortions, median gestational age when filling in the questionnaire for the medical record was 77 days (10th/90th percentiles = 51/113 days), and for the research questionnaire it was 79 days (10th/90th percentiles = 51/113 days). The distribution of characteristics of the study population and their association with alcohol intake are shown in Table 1.

Among women drinking <1 drink/week, 1.4% experienced a spontaneous abortion in the first trimester, whereas this was the case for 8.9% among women drinking ≥5 drinks/week (Table 2), the excess risk of first trimester spontaneous abortion being 75/1000 pregnancies (95% CI: 32–119/1000). Thus, women drinking ≥5 drinks/week had a 5-fold increased risk of first trimester spontaneous abortion (7–11 completed weeks of gestation), compared with women drinking <1 drink/week (Table 2). In multivariate analyses allowing for potential confounding by maternal smoking habits, caffeine intake, age, pre-pregnant body mass index (BMI), marital status, occupational status, education, and parity, the HR was reduced, but the conclusions remained the same (Table 2). Including gestational age at the time of study entry into the multivariate models did not change the results, and for each of the weeks 7, 8, 9, 10 and 11 (completed weeks of gestation), the adjusted HRs for women drinking ≥5 drinks/week were 5.6 (0.4–81.4), 2.5 (0.5–13.8), 4.9 (1.6–15.0), 3.4 (1.0–11.0) and 3.3 (0.6–16.9), respectively. Including previous spontaneous abortions in the multivariate analyses, instead of parity, changed the results very little [HR = 3.8 (2.1–7.0) for women drinking ≥5 drinks/week]

Table 1. Distribution of alcohol intake within categories of lifestyle factors, maternal characteristics and obstetric risk factors which served as potential confounders (n = 24679) Aarhus, Denmark, 1989–1996

					Alcohol intake (drinks/week)							
					<1		1–2		3–4		≥5	
Parameter	*N*	(%)	SAB	(%)	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Maternal age (years)												
<25	3649	(14.8)	31	(0.8)	3023	(82.8)	487	(13.3)	112	(3.1)	27	(0.7)
25–29	10 015	(40.6)	85	(0.8)	7235	(72.2)	2125	(21.2)	525	(5.2)	130	(1.3)
≥30	11 015	(44.6)	205	(1.9)	6432	(58.4)	3032	(27.5)	1130	(10.3)	421	(3.8)
Missing	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Smoking (cigarettes/day)												
0	17 157	(69.5)	226	(1.3)	11 747	(68.5)	4051	(23.6)	1084	(6.3)	275	(1.6)
1–9	3144	(12.7)	42	(1.3)	2031	(64.6)	718	(22.8)	296	(9.4)	99	(3.1)
≥10	3771	(15.3)	43	(1.1)	2510	(66.6)	735	(19.5)	341	(9.0)	185	(4.9)
Missing	607	(2.5)	10	(1.6)	402	(66.2)	140	(23.1)	46	(7.6)	19	(3.1)
Caffeine (mg/day)												
<200	7278	(29.5)	77	(1.1)	5750	(79.0)	1239	(17.0)	248	(3.4)	41	(0.6)
200–399	5289	(21.4)	55	(1.0)	3312	(62.6)	1457	(27.5)	396	(7.5)	124	(2.3)
≥400	5524	(22.4)	87	(1.6)	3109	(56.3)	1500	(27.2)	659	(11.9)	256	(4.6)
Missing	6588	(26.7)	102	(1.5)	4519	(68.6)	1448	(22.0)	464	(7.0)	157	(2.4)
Pre-pregnant BMI												
<18.5	1758	(7.1)	17	(1.0)	1243	(70.7)	367	(20.9)	115	(6.5)	33	(1.9)
18.5–24	18 711	(75.8)	221	(1.2)	12 320	(65.8)	4488	(24.0)	1430	(7.6)	473	(2.5)
25–29	2497	(10.1)	46	(1.8)	1814	(72.6)	497	(19.9)	138	(5.5)	48	(1.9)
≥30	926	(3.8)	24	(2.6)	750	(81.0)	136	(14.7)	36	(3.9)	4	(0.4)
Missing	787	(3.2)	13	(1.7)	563	(71.5)	156	(19.8)	48	(6.1)	20	(2.5)
Marital status												
Married/co-habiting	19 909	(80.7)	202	(1.0)	13 419	(67.4)	4627	(23.2)	1415	(7.1)	448	(2.3)
Single	853	(3.5)	15	(1.8)	582	(68.2)	177	(20.8)	64	(7.5)	30	(3.5)
Missing	3917	(15.9)	104	(2.7)	2689	(68.6)	840	(21.4)	288	(7.4)	100	(2.6)
Occupation												
Employed	11 938	(48.4)	156	(1.3)	7744	(64.9)	2991	(25.1)	917	(7.7)	286	(2.4)
Not employed	3656	(14.8)	37	(1.0)	2652	(72.5)	668	(18.3)	238	(6.5)	98	(2.7)
Student	1869	(7.6)	17	(0.9)	1332	(71.3)	416	(22.3)	101	(5.4)	20	(1.1)
Missing	7216	(29.2)	111	(1.5)	4962	(68.8)	1569	(21.7)	511	(7.1)	174	(2.4)
Education (years)												
<10	1787	(7.2)	22	(1.2)	1367	(76.5)	299	(16.7)	85	(4.8)	36	(2.0)
10	5526	(22.4)	62	(1.1)	3977	(72.0)	1085	(19.6)	352	(6.4)	112	(2.0)
>10	10 453	(42.4)	133	(1.3)	6594	(63.1)	2743	(26.2)	845	(8.1)	271	(2.6)
Missing	6913	(28.0)	104	(1.5)	4752	(68.7)	1517	(21.9)	485	(7.0)	159	(2.3)
Parity												
0	12 247	(49.6)	120	(1.0)	8539	(69.7)	2674	(21.8)	795	(6.5)	239	(2.0)
1	8802	(35.7)	105	(1.2)	5811	(66.0)	2149	(24.4)	641	(7.3)	201	(2.3)
≥2	3592	(14.6)	92	(2.6)	2315	(64.4)	812	(22.6)	329	(9.2)	136	(3.8)
Missing	38	(0.2)	4	(10.5)	25	(65.8)	9	(23.7)	2	(5.3)	2	(5.3)
Previous spontaneous abortions												
0	19 934	(80.8)	210	(1.1)	13 533	(67.9)	4551	(22.8)	1392	(7.0)	458	(2.3)
1	3537	(14.3)	68	(1.9)	2362	(66.8)	811	(22.9)	273	(7.7)	91	(2.6)
≥2	905	(3.7)	39	(4.3)	568	(62.8)	224	(24.8)	90	(9.9)	23	(2.5)
Missing	303	(1.2)	4	(1.3)	227	(74.9)	58	(19.1)	12	(4.0)	6	(2.0)
Gravidity												
0	8429	(34.2)	64	(0.8)	5978	(70.9)	1810	(21.5)	499	(5.9)	142	(1.7)
1	7815	(31.7)	77	(1.0)	5296	(67.8)	1851	(23.7)	511	(6.5)	157	(2.0)
≥2	8132	(33.0)	176	(2.2)	5189	(63.8)	1925	(23.7)	745	(9.2)	273	(3.4)
Missing	303	(1.2)	4	(1.3)	227	(74.9)	58	(19.1)	12	(4.0)	6	(2.0)

N, total number of pregnancies (column percentage); SAB, number of spontaneous abortions (percentage of total number of pregnancies); *n*, number of pregnancies at each drinking level (row percentage); BMI, body mass index.

as did inclusion of gravidity [HR = 3.7 (2.0–6.8) for women drinking ≥5 drinks/week]. We found no interaction between alcohol and smoking. No increased risk could be detected in the second trimester; indeed, if anything the risk tended to be reduced (Table 2). To eliminate any effects of excessive use of alcohol, we re-analysed data truncating the highest alcohol intake group at 14 drinks/week. This categorization resulted in an adjusted hazard ratio for the group of women drinking 5–14 drinks/week (n = 547, 18 spontaneous abortions) of 3.8 (2.1–7.0) for first trimester spontaneous abortions, and 0.6 (0.2–2.0) for second trimester spontaneous abortions. Restricting analyses to the women's first pregnancy in the

Table 2. Unadjusted (HR_u) and adjusted[a] (HR_a) hazard ratios of first and second trimester spontaneous abortions, Aarhus, Denmark, 1989–1996

Alcohol (drinks/week)	Weeks 7–11 (1st trimester)[b]							Weeks 12–27 (2nd trimester)[b]						
	N	Risk weeks	*n*	HR_u	95% CI	HR_a	95% CI	*N*	Risk weeks	*n*	HR_u	95% CI	HR_a	95% CI
<1	3813	7378	53	1.0	—	1.0	—	16 628	214 592	136	1.0	—	1.0	—
1–2	1229	2472	28	1.5	1.0–2.4	1.3	0.8–2.0	5613	71 840	57	1.3	0.9–1.7	1.2	0.9–1.7
3–4	403	895	8	1.2	0.6–2.5	0.8	0.4–1.7	1759	22 605	21	1.3	0.8–2.1	1.1	0.7–1.9
≥5	168	377	15	5.2	2.9–9.2	3.7	2.0–6.8	559	7214	3	0.7	0.2–2.0	0.6	0.2–1.9

[a]Adjusted to maternal smoking habits, caffeine intake, age, pre-pregnant body mass index, marital status, occupational status, education, and parity.
N, total number of pregnancies; *n*, number of spontaneous abortions.
[b]Completed weeks of gestation.

cohort yielded adjusted hazard ratios of a similar magnitude: 4.0 (2.0–8.0) for first trimester spontaneous abortions, and 0.8 (0.2–2.4) for second trimester spontaneous abortions for women drinking ≥5 drinks/week.

Given the low proportion of spontaneous abortions, particularly in the first trimester, one might suspect that the women who entered the study early were women with planned pregnancies, and also that such women with planned pregnancies would be more likely to have a drinking pattern different from that of women who entered the study later in pregnancy. However, when we stratified the distribution of alcohol intake by week of study entry, the distribution of intake was almost the same for each week. With regard to pregnancy planning, restricting analyses to unplanned pregnancies yielded adjusted estimates of a magnitude very similar to that for the entire group, in spite of the low numbers: for women drinking ≥5 drinks/week, the HR was 3.1 (0.9–10.5) for first trimester spontaneous abortions.

DISCUSSION

We found a more than 3-fold increased risk of first trimester spontaneous abortion for women drinking on average ≥5 drinks/week. There was, however, no association between alcohol intake and second trimester spontaneous abortion.

A recent study found results very similar to ours, namely a 3.8-fold increased risk of first trimester spontaneous abortion for women reporting an average intake of >3 drinks/week, but only a small and insignificantly increased risk of second trimester spontaneous abortion (Windham *et al*., 1997). The risk increased during the first trimester, peaking at 9 weeks of gestation (Windham *et al*., 1997). Two studies have found a 2-fold increased risk of spontaneous abortion in the first trimester (Windham *et al*., 1992) or in the second trimester (Harlap and Shiono, 1980; Windham *et al*., 1992) for women drinking ≥7 drinks/week on average, and increased risk has also been reported in alcoholics (Sokol, 1980; Sokol *et al*., 1980). Three of the above studies were large prospective follow-up studies including >5000 pregnancies each (Harlap and Shiono, 1980; Sokol, 1980; Sokol *et al*., 1980; Windham *et al*., 1997). Several case-referent and follow-up studies have found increasing risk with increasing alcohol intake (Harlap and Shiono, 1980; Kline *et al*., 1980, 1981; Russell and Skinner, 1988; Armstrong *et al*., 1992). However, a number of studies have found no association between alcohol intake in pregnancy and spontaneous abortion (Becker *et al*., 1989; Parazzini *et al*., 1990, 1994; Cavallo *et al*., 1995; Dlugosz *et al*., 1996; Zhang and Bracken, 1996). These latter studies were a mixture of case-referent and follow-up studies including <3000 pregnancies each. This suggests that study size may account for at least some of the variation seen in previous studies, and our results as presented here fit well into this pattern.

Also the analytical methods applied are likely to account for some of the variability between results of different studies. A common methodological problem in relation to studies on spontaneous abortions is variation in self-testing behaviour, since women testing themselves very early in pregnancy will appear to have higher abortion rates than women who do not (Weinberg and Wilcox, 1998). By applying conventional logistic regression analysis, as most studies do, one will tend to over-estimate the risk for early spontaneous abortions. This problem may be dealt with by applying survival analysis, so that women are not included in the analyses until recognition of pregnancy. In this way, women do not inappropriately contribute time at risk before recognition of pregnancy (Weinberg and Wilcox, 1998). Survival analysis also allows pregnancies that end in induced abortion to contribute time at risk to the analyses, since such pregnancies are also at risk of spontaneous abortion until the day of the induced abortion (Weinberg and Wilcox, 1998). In our cohort, women with very early spontaneous abortions have not completed the questionnaire, either because they did not know they were pregnant at the time of abortion, because they had not contacted our Department for antenatal care before the abortion, or because the abortion happened before the questionnaire was filled in. We have no information on spontaneous abortions before 7 completed weeks of gestation, and, for spontaneous abortions in the following weeks, our study included fewer than the total number of spontaneous abortions, since women who miscarried often did not enter the cohort before the miscarriage. This may explain partly the low rate of spontaneous abortions (1.3%) compared with that expected (~8.4%) (Nybo Andersen *et al*., 2000), particularly in the first trimester. In any case, our results on early spontaneous abortions do not apply to very early spontaneous abortions during weeks 0–6. As for the earliest abortions in our study, we dealt with the potential bias problem by applying survival analysis techniques with delayed entry or left truncation (Weinberg and Wilcox, 1998). Only one study has previously addressed these problems by using Cox proportional hazard models with delayed entry

(Windham *et al*., 1997). For each of weeks 7–11, women drinking ≥5 drinks/week were at increased risk of experiencing a spontaneous abortion. Also, women who entered the study at different gestational ages had the same distribution of alcohol intake, and restricting analyses to unplanned pregnancies yielded adjusted estimates of a magnitude very similar to that for the entire group. It therefore seems less likely that the low proportion of early spontaneous abortions should invalidate our conclusions.

Animal models have shown that alcohol may increase the risk of resorptions and fetal death (Rasmussen and Christensen, 1980; Henderson, 1982; Webster *et al*., 1983; Stuckey and Berry, 1984; Padmanabhan and Hameed, 1988; Padmanabhan and Pallot, 1995). Possible pathophysiological mechanisms may include alcohol-induced chromosomal defects (McMorrow, 1991; Kaufman, 1983), and since at least 55–60% of clinically recognized spontaneous abortions have chromosome abnormalities (Stein *et al*., 1975; Apgar and Churgay, 1993), this may at least partly explain the association between alcohol and early spontaneous abortion. Also, alcohol may increase the production of prostaglandins, including prostaglandins of the E series (Pennington *et al*., 1983; Pennington, 1988; Anton *et al*., 1990), and alcohol consumption at high levels seems to increase the excretion of prostaglandins and thromboxanes in humans (Ylikorkala *et al*., 1988). Prostaglandins increase the activity of cAMP and suppress the rate of cell division (Pennington *et al*., 1983; Pennington, 1988), the suppression of cell division is proportional to the amount of alcohol ingested (Pennington *et al*., 1983), and an increased level of PGE_2 and $PGF_{2\alpha}$ may possibly increase the risk of spontaneous abortions (Randall *et al*., 1987).

It is well known that alcohol intake is usually under-reported in questionnaires and interviews, compared with diaries (Uchalik, 1979; Poikolainen and Karkkainen, 1983). When we compared our questionnaire data with information on alcohol intake obtained from a more elaborate questionnaire specifying subtypes of alcohol (Kesmodel *et al*., 2001), and with an elaborate personal interview and diaries specifying subtypes of alcohol and different time periods during pregnancy, we found a slight tendency towards under-reporting in the questionnaire (Kesmodel and Olsen, 2001). However, if the reference group is large, under-reporting usually has little effect on the association between exposure and outcome (Verkerk, 1992). Under-reporting of alcohol intake may mask a true threshold effect as a dose–response relation (Verkerk, 1992); however, our finding of a possible threshold effect cannot be attributed to under-reporting.

Even though this is one of the largest studies in this area, very few women reported an intake of >14 drinks/week, which made it impossible to assess separately effects above this level. The fairly low alcohol intake level in the study population is comparable with the average intake level among pregnant Danish women reported elsewhere (Olsen *et al*., 1987; Kesmodel *et al*., 2001; Kesmodel and Olsen, 2001), and the low intake level is due to a pronounced reduction in alcohol consumption, including binge drinking, during the early weeks of pregnancy (Kesmodel, 2001).

Women drinking ≥5 drinks/week were older, were more often smokers, had a higher intake of caffeine, were more educated, and were more often multiparous, than women with a lower alcohol intake (Table 1). Women with a high alcohol intake may also differ with regard to other socio-demographic factors not included in the analyses. Bias due to unadjusted confounding may therefore be present, and causal inferences should be made with caution.

We conclude from our data that women consuming on average ≥5 drinks/week appeared to have a >3-fold increased risk of experiencing a first trimester spontaneous abortion, and that alcohol appeared to have no effect on second trimester spontaneous abortion.

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