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Volume and Type of Alcohol during Early Pregnancy and the Risk of Miscarriage

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Abstract

This study addresses the relationship between alcohol use during pregnancy and miscarriage. A cohort study of pregnant women (n=1061) recruited from 1996 –1998 in the San Francisco area. 3% (n=32) drank 4 or more drinks per week, 38% (n=403) consumed <4 drinks per week and 59% (n= 626) reported no alcohol intake. Women were also categorized by the type of alcohol consumed. An increased risk of miscarriage was found for 1) women who drank four or more drinks a week and 2) women who drank spirits. Future research assessing miscarriage risk should consider the volume and type of alcohol consumed.

Keywords

alcohol volume; miscarriage; spirits; wine; beer

Introduction

Research on the relationship between alcohol consumption during pregnancy and the risk of miscarriage has spanned more than three decades. However, the literature has yielded inconsistent results regarding the existence of an association. Several studies have found an association between alcohol consumption during pregnancy and miscarriage(Andersen, Andersen, Olsen, Gronbaek, & Strandberg-Larsen, 2012; Armstrong, McDonald, & Sloan, 1992; Chiodo et al., 2012; Harlap & Shiono, 1980; Henriksen et al., 2004; Kesmodel, Wisborg, Olsen, Henriksen, & Secher, 2002; Kline, Shrout, Stein, Susser, & Warburton, 1980; Maconochie, Doyle, Prior, & Simmons, 2007; Rasch, 2003; Windham, Von Behren, Fenster, Schaefer, & Swan, 1997). However, others, including two systematic reviews published in 2006 and 2007, have not(Cavallo, Russo, Zotti, Camerlengo, & Ruggenini,

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1995; Henderson, Gray, & Brocklehurst, 2007; Parazzini et al., 1994; Tolstrup et al., 2003; Zhang & Bracken, 1996).

One possible explanation for the inconclusive findings is the variation in the conceptualization of alcohol consumption. Some studies categorize alcohol use as complete abstention vs. any alcohol use; others by pattern, such as binge drinking; others categorize alcohol use by level of use (i.e. volume or frequency); and others by type of alcohol (i.e. beer, wine, or spirits). Of the studies comparing abstention to any use, no study has found a relationship between alcohol and miscarriage(Harlap & Shiono, 1980; Zhang & Bracken, 1996). Regarding pattern of drinking, a recent systematic review found no association between binge drinking and spontaneous abortion(Henderson, Kesmodel, & Gray, 2007). A recent study confirmed this finding for early miscarriage and for infrequent binge drinking(Strandberg-Larsen et al., 2008), although this study did find an association with later miscarriage/stillbirth for higher frequency binge drinking and women reporting both multiple binges and higher volume drinking(Strandberg-Larsen, et al., 2008).

Studies evaluating alcohol consumption in continuous or discrete levels of intake have produced more mixed results(Andersen, et al., 2012; Armstrong, et al., 1992; Cavallo, et al., 1995; Chiodo, et al., 2012; Harlap & Shiono, 1980; Henriksen, et al., 2004; Kesmodel, et al., 2002; Kline, et al., 1980; Maconochie, et al., 2007; Parazzini, et al., 1994; Rasch, 2003; Windham, Fenster, & Swan, 1992; Windham, et al., 1997). Most research examining levels of alcohol use has found evidence of a threshold between two to four drinks per week at which alcohol use during pregnancy is related to miscarriage(Andersen, et al., 2012; Armstrong, et al., 1992; Harlap & Shiono, 1980; Henriksen, et al., 2004; Kesmodel, et al., 2002; Kline, et al., 1980; Maconochie, et al., 2007; Rasch, 2003; Windham, et al., 1992; Windham, et al., 1997). This is especially the case for early miscarriage, see Andersen et al(Andersen, et al., 2012). However, a few studies did not find evidence of a threshold(Cavallo, et al., 1995; Chiodo, et al., 2012; Parazzini, et al., 1994).

Although consumption of one standard drink of wine, beer or spirits results in similar exposure to ethanol(NIAAA, 2005), little is known about the possible differential effects of different types and amounts of other substances (e.g., lead, iron, cobalt, histamines, additives, coloring agents, tannins) and congeners (e.g., acetaldehyde, ethylene) present within various types of alcohol(Greizerstein, 1981). Some research has suggested that these congeners may differ in toxicity, metabolic rates and chronic effects(Auty & Branch, 1977; Greenberg, 1970; Hillbom, Franssila, & Forsander, 1974). Thus, congeners in addition to the other substances could also potentially affect the fetus. While these congeners could plausibly affect the developing fetus differently from exposure to ethanol alone, only limited research—including one study in rats—has examined alcohol type in relation to miscarriage(Abel, Dintcheff, & Bush, 1981; Kline, et al., 1980; Parazzini, et al., 1994). The two epidemiological studies that have assessed associations between specific types of alcohol, i.e. beer, wine, or spirits, and miscarriage have found mixed results(Kline, et al., 1980; Parazzini, et al., 1994). One study focusing on wine only failed to find an association with miscarriage, regardless of the number of drinks consumed per week(Parazzini, et al., 1994). The other study found significant associations between wine, spirits and beer consumed two or more times per week and miscarriage(Kline, et al., 1980). However, the

association between beer and miscarriage was weaker than the associations between wine and miscarriage and spirits and miscarriage.

The current analysis utilizes a prospective cohort design to extend previous research about the relationship between alcohol and miscarriage. In particular, it seeks to replicate previous research regarding a threshold at which alcohol consumption is associated with miscarriage. More importantly, it seeks to extend previous research by assessing whether associations between alcohol and miscarriage are consistent across beer, wine, and spirits. By assessing the type of alcohol, we hope to shed additional light on some possible mechanisms through which alcohol could affect miscarriage and potentially fetal development. We hypothesize that women who drink four or more drinks a week will have an increased risk for miscarriage compared to abstainers, but that women who consume fewer than four drinks a week will not have an increased risk. Further, we hypothesize the associations between alcohol and miscarriage will not be consistent across type of alcohol.

Materials and Methods

The methods have been described elsewhere (Li et al., 2002). Briefly, the current analysis was conducted utilizing data from a population-based prospective cohort study in Kaiser Permanente Northern California (KPNC). All KPNC women members who had a positive pregnancy test at facilities in the San Francisco area from October 1996 to October 1998 were identified for participation. English-speaking women who intended to carry their pregnancy to term and whose gestational age at the pregnancy test was less than or equal to 10 complete weeks were eligible for the study. To avoid non-independent observations, a woman's second pregnancy, if any, during the study period was not eligible for the study.

A total of 2,729 pregnant women were eligible for the original study (Figure 1). Of these women, 1,380 (50.6%) agreed to participate in the study, of whom 1,061 (39%) completed an in-person interview.

Measures

Miscarriage

Miscarriage was defined as a fetal loss occurring prior to 20 complete weeks of gestation. Miscarriage was ascertained for all participants through one of the following methods: linking electronic KPMCP databases, reviewing medical charts, and telephoning women whose outcomes could not be identified (<7%). Miscarriage outcome was ascertained for all participants.

Alcohol Intake

Women were asked the “total number of beers (one beer is equal to 12 ounces),” “total number of glasses of wine or champagne (one glass is equal to 4 ounces),” and “total number of mixed drinks (one drink is equal to 1 ounce of hard liquor) consumed since becoming pregnant or since your last menstrual period, LMP.” The average number of drinks consumed per week was calculated by adding the total number of drinks consumed, and dividing by the gestational age in weeks at the interview date. Based on the distribution

of the ***average number of drinks per week in our sample***, our sample size, and previous research, alcohol consumption was further categorized into three mutually exclusive categories: 1) no alcohol intake (n=626), 2) less than 4 drinks per week (n=403), and 3) 4 or more drinks per week (n=33).

A five category variable was constructed to assess ***beverage type***. Each category was mutually exclusive; 1) spirits only (n=56), 2) wine only (n=160), 3) beer only (n=47), 4) combination of any two or more types of alcohol (n=173), and 5) no alcohol intake (n=626). Of the combination group, 24% (n=41) reported drinking all three types of alcohol, 44% (n=75) drank beer and wine, 22% (n=37) drank wine and spirits and 11% (n=19) drank a combination of beer and spirits.

Covariates

Participants were asked whether they used any illicit drugs, engaged in regular exercise (physical activity for 30 minutes at least three times a week), smoked cigarettes, or consumed caffeine during pregnancy, and their height and weight. Pre-pregnancy Body Mass Index (BMI) was calculated (kg/m^2) and categorized into underweight/normal ≤ 24.9 and overweight/obese 25+. Other demographic characteristics considered were race (Black, Asian, White, Hispanic, and Other), education (≤ some college/technical training vs. graduated from college or more) and marital status (married, partnered, single). Women were also asked about income and classified into four categories: <$35k, $35k-$59k, $60k+, non-responders (forty-two or 5% of the women). Age was dichotomized as less than or equal to 35 and 36 or older, because pregnancies occurring among women aged 36 or older are considered high risk. Finally, we considered whether this pregnancy was intended and previous miscarriage history.

Data Analysis

Pearson chi-square tests were conducted to test differences between categorical variables. A t-test or ANOVA was used to test any mean differences between groups.

Cox Proportional Hazards Models were conducted to examine the relationship between alcohol exposure and miscarriage while adjusting for possible confounders. These analyses considered all covariates significantly associated with both alcohol consumption and miscarriage. The period for which a woman was considered at risk began at the gestational age when she had a positive pregnancy test (study entry) and continued until she had a miscarriage, ectopic pregnancy or induced abortion (3.6%), or was censored at 20 weeks gestation. Women who remained pregnant beyond 20 weeks of gestation were censored at 20 weeks (80%), because, by definition, miscarriage occurs prior to 20 weeks gestation.

Two sets of three Cox Proportional Hazard models were conducted. The first model assessed miscarriage occurring at any time up through 20 weeks gestation and is shown in the tables. Two additional models were conducted to evaluate early and late gestation miscarriages separately. Of these, the first evaluated the association between alcohol consumption and early miscarriage (prior to 10 weeks gestation). The other model evaluated the relationship between alcohol consumption and miscarriage which occurred between

weeks 10 and 20 of gestation. Each of the three models was conducted to evaluate the relationship between 1) the average frequency of alcohol consumption and miscarriage and 2) alcohol type and miscarriage.

Post-hoc analyses—We conducted post-hoc analyses to assess the robustness of our findings. First we conducted additional analyses adjusting for two covariates which were not significantly associated with our exposure and outcome, but may theoretically be considered confounders. Education and income were both included in a post-hoc analyses of the relationship between both alcohol intake and beverage type and miscarriage. We also conducted an analysis in which we excluded women with a previous miscarriage.

A final post-hoc sensitivity analysis was conducted in an attempt to compare our findings with findings by Kline(Kline, et al., 1980) which reported a minimum threshold of two drinks a week.

Results

Sixteen percent (n=172) of the women had a miscarriage. Forty-one percent of the women reported drinking any alcohol with 3% drinking at a high frequency, 5% drinking only spirits, 15% drinking only wine, 4% drinking only beer and 16% drinking a combination of any of the three types of alcohol (Table 1).

Few potential confounders were significantly associated with miscarriage and alcohol intake (Table 1). While not statistically significant at $p<0.05$, a trend emerged and the data suggest women who drank any caffeinated drinks (17%) were more likely to have a miscarriage compared to women who did not (13%, $p=0.059$). Maternal caffeine intake along with the four other variables significantly associated with both miscarriage and alcohol consumption (marital status, vitamin supplementation, pregnancy intention, and maternal age) were included in all multivariable analyses.

Women who drank four or more drinks a week were 2.65 times more likely to have a miscarriage compared to women who abstained, after adjusting for potential confounders (95% CI: 1.38, 5.10) (Table 2). The risk of early fetal loss was also elevated for women who drank four or more drinks a week (adjusted Hazards Ratio (aHR): 2.79, (95% CI: 1.29, 6.07)). While a similar pattern emerged for late fetal loss the magnitude of effect was not as strong and the results were not significant (aHR: 2.16, (95% CI: 0.64, 7.29)). However, women who drank fewer than four drinks a week did not have a statistically significant increased risk of miscarriage compared to women who abstained. Drinking fewer than 4 drinks a week did not have an effect on early or late miscarriage.

No statistically significant differences in the risk of miscarriage were found for women who drank beer only, wine only, or a combination of beer, wine or spirits compared to women who abstained (Table 3). However, women who drank spirits only were at a significantly increased risk of miscarriage compared to abstainers (aHR: 2.24, (95% CI: 1.32, 3.80)). An increased risk of early fetal loss was also found for spirits only drinkers (aHR: 2.50, (95% CI: 1.28, 4.86)). While not significant, a similar trend was found for late fetal loss (aHR: 1.88, (95% CI: 0.78, 4.51)). No increased risk was found for women who drank beer only,

wine only or a combination of beer, wine or spirits regardless of whether fetal loss occurred early or late in gestation.

Women who drank a combination of spirits, beer and wine drank significantly more drinks per week than women who drank spirits only, beer only and wine only (Mean: 1.97 vs. 0.66 vs. 0.53 vs. 0.88, $p<0.001$, respectively) (Table 4). Calculation of the geometric mean produced similar results (results not shown).

Post-hoc Analyses

In our post-hoc analyses also adjusting for education and income in the relationship between both alcohol intake and beverage type and miscarriage, similar results emerged. In addition, after excluding women with a previous miscarriage (n=219), a slightly higher hazard ratio was found for women who drank four or more drinks a week (aHR: 3.33, (95% CI: 1.59, 6.94)) while similar results were found for women who drank only spirits (aHR: 2.42, (95% CI: 1.33, 4.42)).

Additional post-hoc analyses were conducted in an attempt to further understand the findings by Kline (Kline, et al., 1980) which reported a minimum threshold of two drinks a week. Similar to their study, we combined all women who drank two or more drinks a week into one category, women who drank fewer than two drinks a week into a second category, and compared them to abstainers. An increased risk of miscarriage for women who drank two or more drinks a week was found (aHR: 1.95, (95% CI: 1.14, 3.32)). Second, we created four categories of the average number of drinks a week: four or more drinks per week, two to less than four drinks per week, fewer than 2 drinks a week, and abstainers. A significant increase in the risk of miscarriage did not emerge for women who drank two to less than four drinks a week (aHR: 1.17, (95% CI: 0.47, 2.92)). To further assess the threshold of four drinks a week we separated women who consumed four drinks a week from women who drank five or more drinks a week. Only nine women reported drinking four drinks a week and while not significant, a nearly twofold increase in risk of miscarriage was found (aHR: 1.69, (95% CI: 0.52, 5.51)).

Discussion

We found that women who consumed four or more drinks per week had a twofold increase in the risk of miscarriage compared to women who abstained. Women who drank fewer than four drinks a week did not have a significantly increased risk. The risk of miscarriage was primarily seen for early (<10 weeks gestation) miscarriage. These findings replicate previous results which have found an association between alcohol consumption during pregnancy and miscarriage and suggest a higher threshold than reported in some other studies(Andersen, et al., 2012; Cavallo, et al., 1995; Chiodo, et al., 2012; Harlap & Shiono, 1980; Henriksen, et al., 2004; Kesmodel, et al., 2002; Maconochie, et al., 2007; Rasch, 2003; Windham, et al., 1992; Windham, et al., 1997). Importantly, we confirm previous research that found no association between wine consumption and miscarriage(Parazzini, et al., 1994) and extend previous research by finding that the risk of miscarriage is increased for women consuming spirits.

Our finding suggesting a threshold of four drinks per week for miscarriage risk was further supported by our posthoc analyses. However, the threshold may depend on the type of alcohol consumed. Spirits was the only type of alcohol specifically significantly associated with an increased risk of miscarriage. We acknowledge that trend emerged for women consuming only beer, but these results were based on a small number of women. Thus, we are cautious in our interpretation of the beer-only results. This significant increased risk was not due to a reported higher consumption of alcohol by spirits drinkers.

Of the spirits drinkers, only 4% of them drank four or more drinks a week. Further, there was no difference in the mean number of drinks consumed between women who drank spirits only, wine only and beer only. We conducted additional analyses to assess the threshold for spirits only drinkers and nearly a two-fold, though non-significant, increase in risk remained at equal to or less than half a drink of spirits a week.

There are several possibilities as to why spirits may be more harmful than other types of alcohol. First, spirits may contain different types and amounts of congeners found in beer or wine thus leading to a differential effect of spirits on miscarriage(Greizerstein, 1981). Another possibility is that the behaviors women engage in as they drink spirits may contribute to the increased toxicity of spirits. For example, eating food may impact the accumulation of alcohol in the body and alcohol's toxicity. If sprits drinkers are less likely than wine drinkers to eat while drinking alcohol(Klein & Pittman, 1990), the spirits may have a larger effect on the fetus.

Third, women who drink spirits may unintentionally underreport the amount of spirits they consume, as they may not be aware of the actual amount of alcohol in their mixed drinks. Previous research suggests pregnant respondents, like the general population, do not know the amount of wine, beer or spirits in a given glass(Kaskutas & Graves, 2000); (Kerr, Greenfield, Tujague, & Brown, 2005). In the United States, a standard drink is equivalent to 0.6 ounces of pure alcohol and the liquid volume equaling a standard drink varies by the type of beverage. In general the standard sizes are 12 ounces of beer, 5 ounces of wine, and 1.5 ounces of spirits. Research in the US attempting to elucidate the actual alcohol content in a person's glass found that the mean drink content for women in the general population who drank spirits was 43% larger (0.85 ounces) than the standard drink of 0.6 ounces of pure alcohol(Kerr, et al., 2005). In addition, women were asked to report the number of drinks of spirits consumed per month which was then compared to the actual measured ethanol content. For women, the actual average alcohol intake from spirits was 61% more than what was self-reported. The mean drink alcohol content for women beer drinkers was 0.6, exactly a standard drink, while the standard drink content for wine was 15% larger (0.66 ounces) compared to the standard drink of 0.6 ounces. Thus, the apparent low frequency of alcohol consumption reported by spirits only drinkers may be an artifact due to a lack of knowledge about drink size among these women. Future research should assess the relationship between the type of alcohol consumed and miscarriage taking into account the ascertainment of alcohol intake and the behaviors women engage in while drinking.

We also examined the effect of alcohol consumption during pregnancy on early and late miscarriage (<10 weeks versus ≥10 weeks), as these periods may differ in their sensitivity to

alcohol exposure. The literature to date assessing this relationship is inconsistent with three studies finding a differential effect(Andersen, et al., 2012; Kesmodel, et al., 2002; Windham, et al., 1997) and two studies failing to demonstrate a differential effect(Harlap & Shiono, 1980; Henriksen, et al., 2004). Our results revealed elevated rates of miscarriage attributed to drinking four or more drinks a week for both early and late miscarriages, yet the relationship was stronger for early miscarriage. These patterns did not persist for alcohol consumption during pregnancy at less than four drinks a week. However, patterns similar to those found for prenatal alcohol exposure to four or more drinks a week emerged for spirits only intake. Our results suggest alcohol intake during pregnancy may have the largest effect on the embryo or fetus at the period in which they are much more sensitive to environmental insults. Yet, there appears to be a threshold with regards to the amount of alcohol consumed.

Limitations

These findings should be interpreted in light of certain limitations. First, it is important to note that miscarriage was based on a clinical diagnosis. In addition, 61% of the women who had a miscarriage were interviewed after the miscarriage. However, the proportion of women who reported alcohol use during pregnancy was the same for women interviewed either pre- or post- miscarriage (44% for both), with no indication of differential reporting due to the timing of interview in relation to miscarriage.

The low response rate may limit the generalizability of the findings. We cannot rule out with certainty that participation was not associated with factors related to alcohol consumption; but the requirements of participation in the original study, which had nothing to do with alcohol, resulted in many refusals. Using KPMCP electronic databases we were able to obtain the percent of miscarriages among non-participants. This percent was similar to that of participants (17.2% versus 16.4%, respectively), somewhat reducing this concern. In addition, other papers published from these data have reported findings consistent with previous research(Li, Janevic, Odouli, & Liu, 2003; Li, et al., 2002; Weng, Odouli, & Li, 2008). Nevertheless, we acknowledge that low participation could potentially impact the interpretation of the findings.

Interpretations of our findings should consider limitations with the measurement of alcohol exposure. Misclassification of 4 or more drinks a week and 4 or fewer drinks a week is a possibility. However, misclassification of the average weekly number of drinks is unlikely. While women in the less than four drinks a week category were interviewed at a later gestational age (70 days compared to 61 days), there was a large difference in the mean number of total drinks consumed during pregnancy between these two categories. The mean number of total drinks prior to interview in the four or more drinks a week category was 65 compared to 7 drinks in the less than four drinks a week group.

It was not possible to assess the impact of binge-drinking due to the manner in which alcohol intake was ascertained. However, as seen in our post-hoc analyses, similar patterns emerged when additional analyses were conducted modifying the cut-points for alcohol consumption. We also acknowledge that the sample size of women drinking four or more drinks a week likely contributed to the lack of a statistically significant result for the relationship with late miscarriage.

Nutritional intake may impact the relationships addressed in this study. Our analyses were all adjusted for multivitamin use, but we were not able to take into account any other nutritional factors.

Finally, we recognize this study recruited women from 1996-1998. However, the relationships of interest in this study are not impacted by time period. The implications from this study transcend time and are important for pregnant women consuming alcohol regardless of the time period.

Conclusions

In conclusion, our findings support previous research that has found a relationship between four or more drinks a week and miscarriage. We also found the relationship between alcohol intake during pregnancy and miscarriage was strongest for early miscarriage. In addition, we contribute new results which suggest an increased risk of miscarriage for women who drink only spirits as compared to other types of alcohol during pregnancy. Future research on alcohol and miscarriage should consider type of alcohol in their analyses.

References

Abel EL, Dintcheff BA, Bush R. Effects of beer, wine, whiskey, and ethanol on pregnant rats and their offspring. Teratology. 1981; 23(2):217–222. [PubMed: 7268638]

Andersen AM, Andersen PK, Olsen J, Gronbaek M, Strandberg-Larsen K. Moderate alcohol intake during pregnancy and risk of fetal death. [Research Support, Non-U.S. Gov't]. International journal of epidemiology. 2012; 41(2):405–413. [PubMed: 22253313]

Armstrong BG, McDonald AD, Sloan M. Cigarette, alcohol, and coffee consumption and spontaneous abortion. Am J Public Health. 1992; 82(1):85–87. [PubMed: 1536340]

Auty RM, Branch RA. Pharmacokinetics and pharmacodynamics of ethanol, whiskey, and ethanol with n-propyl, n-butyl, and iso-amyl alcohols. Clinical pharmacology and therapeutics. 1977; 22(2): 242–249. [PubMed: 884925]

Cavallo F, Russo R, Zotti C, Camerlengo A, Ruggenini AM. Moderate alcohol consumption and spontaneous abortion. Alcohol Alcohol. 1995; 30(2):195–201. [PubMed: 7662038]

Chiodo LM, Bailey BA, Sokol RJ, Janisse J, Delaney-Black V, Hannigan JH. Recognized spontaneous abortion in mid-pregnancy and patterns of pregnancy alcohol use. [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. Alcohol. 2012; 46(3):261–267. [PubMed: 22440690]

Greenberg LA. The appearance of some congeners of alcoholic beverages and their metabolites in blood. Quarterly journal of studies on alcohol. 1970; 5(Suppl 5):20–25. [PubMed: 5450661]

Greizerstein HB. Congener contents of alcoholic beverages. Journal of studies on alcohol. 1981; 42(11):1030–1037. [PubMed: 7334803]

Harlap S, Shiono PH. Alcohol, smoking, and incidence of spontaneous abortions in the first and second trimester. Lancet. 1980; 2(8187):173–176. [PubMed: 6105340]

Henderson J, Gray R, Brocklehurst P. Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. [Research Support, Non-U.S. Gov't Review]. BJOG : an international journal of obstetrics and gynaecology. 2007; 114(3):243–252. [PubMed: 17233797]

Henderson J, Kesmodel U, Gray R. Systematic review of the fetal effects of prenatal binge-drinking. [Research Support, Non-U.S. Gov't Review]. Journal of epidemiology and community health. 2007; 61(12):1069–1073. [PubMed: 18000129]

Henriksen TB, Hjollund NH, Jensen TK, Bonde JP, Andersson AM, Kolstad H, et al. Alcohol consumption at the time of conception and spontaneous abortion. Am J Epidemiol. 2004; 160(7): 661–667. [PubMed: 15383410]

Hillbom ME, Franssila K, Forsander OA. Effects of chronic ingestion of some lower aliphatic alcohols in rats. Research communications in chemical pathology and pharmacology. 1974; 9(1):177–180. [PubMed: 4140561]

Kaskutas LA, Graves K. An alternative to standard drinks as a measure of alcohol consumption. Journal of Substance Abuse. 2000; 12(1-2):67–78. [PubMed: 11288475]

Kerr WC, Greenfield TK, Tujague J, Brown S. A drink is a drink? Variation in the alcohol content of beer, wine, and spirits drinks in a U.S. methodological sample. Alcoholism: Clinical and Experimental Research. 2005; 29(11):2015–2021.

Kesmodel U, Wisborg K, Olsen SF, Henriksen TB, Secher NJ. Moderate alcohol intake in pregnancy and the risk of spontaneous abortion. Alcohol Alcohol. 2002; 37(1):87–92. [PubMed: 11825863]

Klein H, Pittman DJ. Drinker prototypes in American society. Journal of substance abuse. 1990; 2(3): 299–316. [PubMed: 2136117]

Kline J, Shrout P, Stein Z, Susser M, Warburton D. Drinking during pregnancy and spontaneous abortion. Lancet. 1980; 2(8187):176–180. [PubMed: 6105341]

Li DK, Janevic T, Odouli R, Liu L. Hot tub use during pregnancy and the risk of miscarriage. Am J Epidemiol. 2003; 158(10):931–937. [PubMed: 14607798]

Li DK, Odouli R, Wi S, Janevic T, Golditch I, Bracken TD, et al. A population-based prospective cohort study of personal exposure to magnetic fields during pregnancy and the risk of miscarriage. Epidemiology. 2002; 13(1):9–20. [PubMed: 11805581]

Maconochie N, Doyle P, Prior S, Simmons R. Risk factors for first trimester miscarriage--results from a UK-population-based case-control study. [Research Support, Non-U.S. Gov't]. BJOG : an international journal of obstetrics and gynaecology. 2007; 114(2):170–186. [PubMed: 17305901]

NIAAA. What is a Standard Drink? A Pocket Guide for Alcohol Screening and Brief Intervention. 2005. Retrieved from http://pubs.niaaa.nih.gov/publications/Practitioner/pocketguide/pocket_guide2.htm

Parazzini F, Tozzi L, Chatenoud L, Restelli S, Luchini L, La Vecchia C. Alcohol and risk of spontaneous abortion. Hum Reprod. 1994; 9(10):1950–1953. [PubMed: 7844232]

Rasch V. Cigarette, alcohol, and caffeine consumption: risk factors for spontaneous abortion. Acta Obstet Gynecol Scand. 2003; 82(2):182–188. [PubMed: 12648183]

Strandberg-Larsen K, Nielsen NR, Gronbaek M, Andersen PK, Olsen J, Andersen AM. Binge drinking in pregnancy and risk of fetal death. [Research Support, Non-U.S. Gov't]. Obstetrics and gynecology. 2008; 111(3):602–609. [PubMed: 18310362]

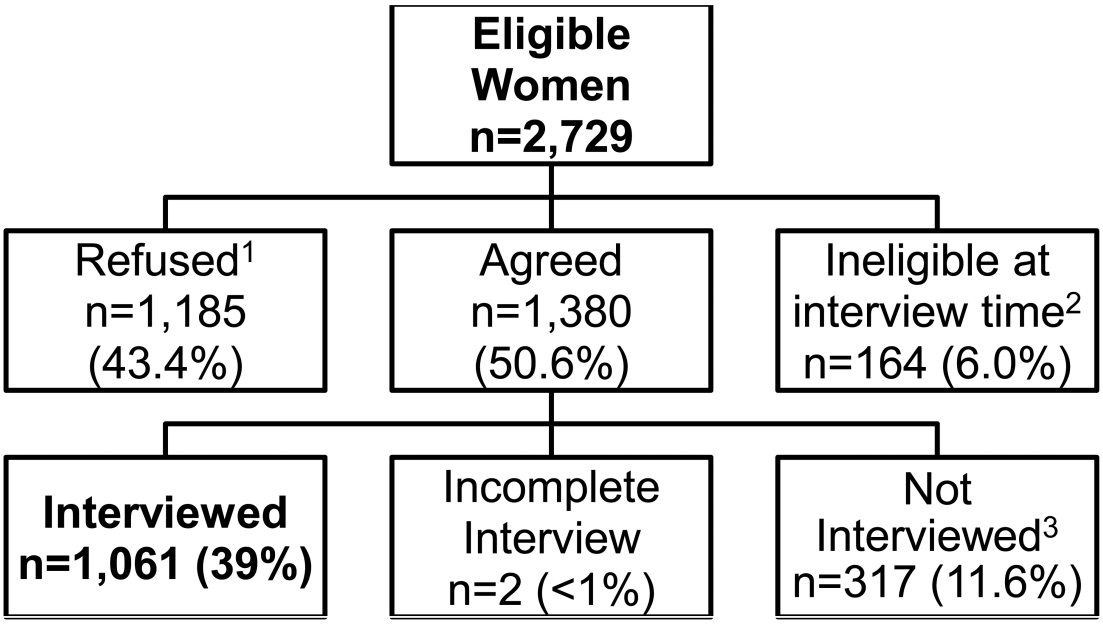
Tolstrup JS, Kjaer SK, Munk C, Madsen LB, Ottesen B, Bergholt T, et al. Does caffeine and alcohol intake before pregnancy predict the occurrence of spontaneous abortion? Human reproduction. 2003; 18(12):2704–2710. [PubMed: 14645195]

Weng X, Odouli R, Li D-K. Maternal caffeine consumption during pregnancy and the risk of miscarriage: a prospective cohort study. American Journal of Obstetrics and Gynecology. 2008; 198(3):279.e271–279.e278. [PubMed: 18221932]

Windham GC, Fenster L, Swan SH. Moderate maternal and paternal alcohol consumption and the risk of spontaneous abortion. Epidemiology. 1992; 3(4):364–370. [PubMed: 1637900]

Windham GC, Von Behren J, Fenster L, Schaefer C, Swan SH. Moderate maternal alcohol consumption and risk of spontaneous abortion. Epidemiology. 1997; 8(5):509–514. [PubMed: 9270952]

Zhang H, Bracken MB. Tree-based, two-stage risk factor analysis for spontaneous abortion. Am J Epidemiol. 1996; 144(10):989–996. [PubMed: 8916510]



[1]Main reasons for refusing participation were 1) too busy/not interested/too stressful to participate (47.9%), 2) husband's objection (11.1%), 3) had miscarried already and would rather not talk about it (7.3%), 4) unwilling to wear the meter (required for the original study) (6.2%), 5) other miscellaneous reasons (8.3%), and 6) no specific reasons given (19%).

[2]Participants were not interviewed because they were too far along in their pregnancy (>15 weeks gestation) when they were reached by the interviewers

[3]Participants were never able to schedule an interview.

Figure 1.
Recruitment Process and Study Sample

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Table 1

Demographic Characteristics, Pregnancy Behaviors and Previous Miscarriage History by Miscarriage and Alcohol Intake

	Total Sample n=1061 n (%)	Miscarriage n=172 n (%)	p-value[a]	4+ Drinks per Week n=32 n(%)	<4 Drinks per Week n=403 n(%)	No Alcohol Intake n=626 n(%)	p-value[b]
Demographic Characteristics							
Race							
White	449 (43)	74 (16)	0.76	26 (6)	241 (54)	182 (41)	<0.001
Black	82 (8)	15 (18)		1 (1)	28 (34)	53 (65)	
Hispanic	219 (21)	38 (17)		2 (4)	78 (36)	139 (63)	
Native American	13 (1)	1 (8)		0 (0)	4 (31)	9 (69)	
Asian	291 (28)	42 (14)		3 (1)	50 (17)	238 (82)	
Marital Status							
Single	97 (9)	24 (25)	0.026	8 (8)	43 (44)	46 (47)	<0.001
Married	850 (80)	134 (16)		15 (7)	314 (37)	520 (61)	
Partner	114 (11)	13 (11)		9 (8)	45 (40)	59 (52)	
Age							
Maternal age 36 +	208 (20)	52 (25)	<0.001	14 (7)	92 (44)	101 (49)	<0.001
Maternal age < 36	855 (80)	120 (14)		18 (2)	311 (36)	525 (61)	
Income							
<$35k	289 (27)	52 (18)	0.56	8 (3)	86 (30)	195 (67)	<0.001
$35K-$59K	326 (31)	46 (14)		8 (2)	110 (33)	208 (64)	
$60k+	388 (37	63 (16)		13 (3)	110 (48)	188 (48)	
non-responders	58 (5)	11 (19)		3 (5)	20 (34)	35 (60)	
Education							
<=HS	250 (24)	43 (17)	0.756	8 (3)	87 (34)	155 (62)	<0.001
some college/tech	339 (32)	51 (15)		5 (1)	107 (32)	22 (67)	
graduated college	307 (29)	47 (15)		11 (4)	124 (41)	170 (56)	
grad school	164 (15)	30 (18)		8 (5)	83 (51)	73 (45)	
Pregnancy Behaviors							
Illicit Drug Use							
Drug User	60 (6)	10 (17)	0.921	7 (12)	38 (63)	15 (25)	<0.001
Drug non-user	1001 (94)	162 (16)		25 (3)	365 (36)	611 (61)	

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Smoking Status							
Smoker	129 (12)	23 (18)	0.595	15 (12)	57 (44)	57 (44)	<0.001
Non-smoker	932 (88)	149 (16)		17 (2)	46 (3)	569 (61)	
Exercise Status							
Exercised regularly	319 (30)	56 (18)	0.424	14 (4)	145 (45)	160 (50)	<0.001
Did not exercise regularly	738 (70)	115 (16)		18 (2)	256 (35)	464 (63)	
Caffeine Consumption							
Drank any caffeinated beverages	797 (75)	139 (17)	0.059	29 (4)	330 (41)	438 (55)	<0.001
Did not drink caffeinated beverages	264 (25)	33 (13)		3 (1)	73 (28)	188 (71)	
Pregnancy Intention							
Unplanned pregnancy	376 (35)	72 (19)	0.048	13 (3)	160 (43)	203 (54)	0.051
Planned pregnancy	684 (65)	99 (14)		19 (3)	243 (36)	422 (62)	
Multinutrient Supplements							
Multinutrient non-user	291 (28)	68 (23)	<0.001	8 (3)	87 (30)	196 (67)	0.003
Multinutrient user	772 (73)	104 (13)		24 (3)	316 (41)	430 (56)	
Body Mass Index							
Underweight/normal	709 (69)	112 (16)	0.822	24 (3)	271 (38)	414 (58)	0.687
Overweight/obese	318 (31)	52 (16)		8 (3)	118 (37)	192 (60)	
Previous Miscarriage History							
No miscarriage	843 (79)	134 (16)	0.583	9 (4)	74 (34)	135 (62)	0.259
1 + miscarriage	218 (21)	38 (17)		23 (3)	329 (39)	491 (58)	
Timing of Current Miscarriage (n= 172)							
Early (< 10 weeks gestation)		102 (59)	NA	3 (4)	27 (39)	40 (57)	0.637
Late (10-20 weeks gestation)		70 (41)		8 (8)	39 (38)	55 (54)	
Alcohol Consumption							
Any alcohol intake	435 (41)	77 (18)	0.272	32 (7)	403 (93)		na
No alcohol intake	626 (59)	95 (15)					
Average Number of Alcoholic Drinks per Week							
4+ drinks/week	32 (3)	11 (34)	0.016	32 (100)			na
<4 drinks/week	403 (38)	66 (16)			403 (100)		
No alcohol intake	626 (59)	95 (15)				626 (100)	

	Total Sample n=1061 n (%)	Miscarriage n=172 n (%)	p-value[a]	4+ Drinks per Week n=32 n(%)	<4 Drinks per Week n=403 n(%)	No Alcohol Intake n=626 n(%)	p-value[b]
Type of Alcohol							
Spirits	56 (5)	18 (32)	0.013	3 (4)	54 (96)		na
Wine	160 (15)	22 (14)		9 (6)	151 (94)		
Beer	47 (4)	10 (21)		0 (0)	47 (100)		
Combination	172 (16)	27 (16)		21 (12)	151 (88)		
Abstainer	626 (59)	95 (15)		0	0	626(100)	
Distribution of Drinks per Week by Category				**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
	NA	NA		7.7 (5.6)	0.72 (0.8)	0 (0)	-

[a] p-value compares miscarriage to no miscarriage

[b] p-value compares 4+ drinks/week, <4 drinks/week and no alcohol intake

Table 2

Average Drinks of Alcohol per Week during Pregnancy and the Hazard Ratio (HR) and adjusted Hazard Ratio (aHR) for Miscarriage

	Miscarriage (n)	HR_{crude}	95% CI	aHR[a]	95% CI
< 4 drinks/ week	66	1.13	0.82, 1.54	1.12	0.81, 1.55
4+ drinks/week	11	2.79	1.50, 5.22	2.65	1.38, 5.10
No alcohol intake	95	1		1	

[a] adjusted for maternal age, caffeine, vitamins, marital status, unintended pregnancy

Table 3

Type of Alcohol Consumed During Pregnancy and the Hazard Ratio (HR) and adjusted Hazard Ratio (aHR) for Miscarriage

	Miscarriage (n)	HR_{crude}	95% CI	aHR^a	95% CI
Combination	27	1.08	0.70, 1.65	1.11	0.72, 1.73
Beer Only	10	1.51	0.79, 2.90	1.28	0.66, 2.48
Wine Only	22	0.92	0.58, 1.47	0.93	0.58, 1.49
Spirits Only	18	2.58	1.56, 4.27	2.24	1.32, 3.81
No alcohol intake	95	1		1	

[a] adjusted for maternal age, caffeine, vitamins, marital status, unintended pregnancy

Table 4

Mean Number of Drinks per Week by Alcohol Type

	Spirits (n=56) n (%)	Wine (n=160) n (%)	Beer (n=47) n (%)	Combination (n=173) n (%)	p-value
<4 drinks a week	54 (13)	151 (37)	47 (12)	151 (37)	0.009[a]
4+ drinks a week	2 (6)	9 (28)	0 (0)	21 (66)	
Average # of Drinks/Week					
Mean (SD)	0.66 (1.25)	0.88 (1.73)	0.52 (0.74)	1.97 (3.38)	<0.001

[a] p-value is not stable with 2 cells containing less than the expected 5 responses