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Recognized Spontaneous Abortion in Mid-Pregnancy and Patterns of Pregnancy Alcohol Use

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Abstract

Alcohol consumption during pregnancy is one potential risk factor for spontaneous abortion (SAb). Prior research suggested that heavy drinking during pregnancy was associated with significantly increased rates of SAb, but results for lower levels of drinking have been inconsistent. We examined the association between different levels and patterns of prenatal alcohol consumption and SAb in a high-risk inner-city sample. We hypothesized that higher levels, binge patterns, and more frequent drinking would be associated with increased rates of SAb. The quantity and frequency of self-reported peri-conceptional and repeated in-pregnancy maternal drinking volumes per beverage type were assessed with semi-structured interviews in a prospective subsample of 302 African-American mothers. Relations between various measures of prenatal alcohol exposure and SAb were assessed using logistic regression. After controlling for various potential confounders, there was a significant positive relation between average absolute alcohol use per day across pregnancy and SAb. Greater frequency of drinking episodes also predicted SAb: an average of even one day of drinking per week across pregnancy was associated with an increase in the incidence of SAb. However, contrary to our hypothesis, neither the amount of alcohol drunk per drinking day nor a measure of binge drinking were significantly related to SAb after controlling for confounders. Differences in when women who drank at risk levels initiated antenatal care may have under-estimated the impact of alcohol on SAb in this low-SES urban African American sample. Some drinking measures averaged across pregnancy may have

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This research was conducted at Wayne State University

underestimated consumption and overestimated risk of SAb, but others risk-drinking measures that avoid this limitation show similar relations to SAb. Identifying fetal risk drinking in pregnant women is critical to increasing the effectiveness of interventions that reduce risk-level alcohol consumption and protect from pregnancy loss.

Keywords

Alcohol; Fetal Alcohol Spectrum Disorder (FASD); Pregnancy; Risk Drinking; Spontaneous Abortion (Miscarriage)

INTRODUCTION

Alcohol consumption during pregnancy is a risk factor for many adverse outcomes (Sokol et al., 2003). Facial dysmorphology, intrauterine growth restriction, and neurodevelopmental problems are the defining features of fetal alcohol syndrome (FAS), and the latter signs are also seen to varying degrees across the gamut of the fetal alcohol spectrum disorders (FASD) (Astley, 2006; Stratton et al., 1996). In addition to these well-documented developmental effects, pregnancy complications including spontaneous abortion, stillbirth, and preterm delivery related to increased consumption of alcohol during pregnancy have been reported although findings are mixed and in some cases conflicting (Abel, 1997; 1998; Allebeck & Olsen, 1998; Bailey & Sokol, 2011). For example, while nearly two dozen published studies examined potential associations between alcohol consumption during pregnancy and preterm birth (i.e., delivery prior to 37 completed weeks of gestation), the assertion that a link exists is controversial (Abel, 1997; Bailey & Sokol, 2008a). Methodological or design limitations or weaknesses, such as small sample size, failure to control adequately for potential confounding factors, or inadequate assessment of alcohol exposure and/or gestational age, may explain why no significant link between exposure and preterm birth was identified in some studies (Bailey & Sokol, 2008a). However, other methodologically sound, well-controlled studies have identified an increased risk of both stillbirth and preterm delivery among women who consume alcohol during pregnancy (Adams et al., 1995; Aliyu et al., 2008b; Bailey & Sokol, 2008a; Kesmodal et al., 2002b; Sokol et al., 2007).

Spontaneous abortion (SAb), defined in North America as fetal demise prior to 20 completed weeks of gestation (Cunningham et al., 2010; Stirrat, 1990), is the most common negative outcome of pregnancy. In their review, Kline et al. (1989) reported that loss estimates prior to the 28th week of pregnancy range from 14% to 22%. The cause(s) of fetal loss are often unknown although certain factors are suspected including family history of miscarriage, or increased stress (e.g., Arck et al., 2008; Baba et al., 2011; Zeng et al., 2007; Zhang et al., 2010) and a wide variety of drugs and medicines. There is evidence that smoking at both advanced maternal age and in young teen mothers increases the risk for SAb (Aliyu et al., 2008a; 2010), and environmental tobacco smoke can also be a factor (Kharrazi et al., 2004). There is evidence for increased risk for SAb with obesity or high body mass index (BMI; ASRM, 2008; Jarvie & Ramsay, 2010). Maternal alcohol consumption during pregnancy has been examined as another potential risk factor for SAb (e.g., Abel, 1997; Aliyu et al., 2008b; Henderson et al., 2007a; 2007b; Kesmodel et al., 2002a; 200b). Early research suggested that heavy drinking during pregnancy was associated with a significantly increased rate of SAb (Sokol, 1980). Women who consumed an average of at least one alcoholic beverage per day during pregnancy had more SAb than women who did not drink or drank lesser amounts. Other studies at that time also showed that women who consumed more than three drinks daily had a more than three-fold increased risk for SAb (Harlap & Shiono, 1980; Kline et al., 1980).

Binge patterns of drinking by women, defined as four or five or more drinks per occasion (ACOG, 2006; Bertrand et al., 2004; 2005; NIAAA, 2004b), may further increase the risk for adverse pregnancy outcomes including SAb. In a systematic review of the literature by Henderson et al. (2007b), no consensus was found for a significant association between maternal binge drinking during pregnancy and pregnancy outcome, however, no published studies were included that specifically examined SAb. Many studies have identified a link between pregnancy binge drinking and poor child outcome (e.g., Nordstrom Bailey et al., 2004; Nulman et al., 2004). A significant association between prenatal binge drinking and infant mortality has also been found (Strandberg-Larsen et al., 2009). Finally, while a prospective epidemiological study of binge drinking in pregnancy from the Danish National Birth Cohort reported that neither drinking frequency nor bingeing (i.e., 5 drinks/occasion) were related to the risk of SAb (defined there as fetal death <22 weeks of completed gestation), the study did find that having 3 episodes of bingeing during pregnancy increased the likelihood of stillbirth (i.e., fetal death at 22 completed weeks of gestation) by 50% compared to women who did not binge this often (Strandberg-Larsen et al., 2008).

Other studies have focused on the potential negative effects of relatively moderate levels of alcohol consumption during pregnancy, that is, levels averaging less than one drink/day. In one large-scale prospective cohort study, consumption of >3 drinks/week during the first trimester was associated with a significantly increased risk of SAb (OR=2.3) (Windham et al., 1997). In another study, women who consumed 5 drinks/week in the first trimester had a five-fold increased risk of first-trimester SAb (Kesmodal et al., 2002a). Rasch (2003) also reported that consumption of 5 drinks/week was associated with a five-fold increased risk for SAb, although no link was found between consumption of one to four drinks/week and SAb. In all three of these studies, effects remained significant after control for potentially confounding maternal factors, including age, parity, socioeconomic status (SES), and use of other substances.

In light of these findings, the present investigation examined the association between prenatal maternal alcohol consumption and SAb in a prospective sample of high-risk inner-city pregnant African American women recruited on the basis of their self-reported periconceptional drinking. Specifically, we assessed the incidence of recognized SAb in mid-pregnancy associated with different levels and patterns of alcohol consumption while controlling for specific potentially confounding factors. It was hypothesized that greater average amounts of alcohol consumption across pregnancy in this sample – drinking more alcohol/drinking day, binge patterns of prenatal drinking, and more frequent drinking – would each be associated with increased rates of SAb compared to the women in this sample who were reporting lower levels of drinking.

MATERIALS AND METHODS

Data collection for this study was reviewed and approved by the Wayne State University Institutional Review Board prior to all phases of the study. All adult participants provided informed consent prior to participation.

Participants

The sample of 302 pregnant women was a subset of a larger cohort of 443 African-American inner-city mothers who were participants in a study of long-term effects of prenatal alcohol and under-nutrition on perinatal development (cf., Beblo et al., 2005; Stark et al., 2005a; 2005b). The mothers were recruited initially at their first antenatal visit to a large, inner-city maternity clinic serving primarily (~92%) African-American women. Since the vast majority of the women were African American, the sample was restricted to this group (Beblo et al., 2005; Chiodo et al., 2009; Stark et al., 2005a; 2005b). Recruitment in

the parent study oversampled drinking women. All women reporting peri-conceptional alcohol consumption averaging at least 1.0 ounce of absolute alcohol/day (AAD) – the equivalent of about two standard American drinks/day on average – were included. Low-level drinking women and abstainers were chosen randomly from the total available sample. Approximately 8% of all the lower-level drinkers and abstainers screened in the clinic were invited to participate and formed the comparison group. The final sample had close to equal numbers of low-level drinkers/abstainers and moderate/heavy drinking women.

All women in the original recruitment study had initiated prenatal care by the 28th week of pregnancy. A first antenatal visit later than the 28th week of gestation was an exclusion criterion for the parent study. Other maternal exclusion criteria were multiple gestation (i.e., twins & triplets: 9 pregnancies & 20 neonates), metabolic disorders, and known HIV-positive status. For the purposes of the current analyses, we also excluded women who were enrolled after 20 weeks gestation because, by the North American definition of SAb, they could not suffer a SAb, that is, fetal demise occurring prior to 20 completed weeks of gestation. The final sample included 302 women.

Assessing Maternal Alcohol Use

Details for assessment of maternal alcohol use are given in Chiodo et al. (2009). Briefly, antenatal interviews at each prenatal clinic visit examined mothers' day-by-day alcohol and drug use during the previous two weeks. Each mother was asked about her alcohol consumption, both at the time of the first visit and retrospectively about drinking around the time of conception, using a semi-structured interview (Sokol et al., 1985). Drinking volumes were converted to ounces of absolute alcohol/day (AAD) based on beverage type, and averaged across visits to create variables reflecting average drinking across pregnancy from reports at all visits (AADXP). Average ounces of absolute alcohol drunk per day (AAD0) and the proportion of drinking days/week (PROPDD0) around the time the woman become pregnant were also calculated. This AAD0 retrospective report of peri-conceptional drinking was analyzed separately and included in the within-pregnancy estimate of average across-pregnancy drinking for all women (Burden et al., 2005; Jacobson et al., 1993; Jacobson et al., 1994; Nordstrom Bailey et al., 2004). The AADXP variable represented overall amount of alcohol consumed during pregnancy, including the third trimester (Hannigan et al., 2010). Further, average ounces of absolute alcohol drunk per drinking day across pregnancy (AADDXP) and proportion of drinking days/week across pregnancy (PROPDDXP) were also calculated. These variables reflected different aspects of the pattern of drinking, the former (AADDXP) represented the amount of alcohol consumed on those days when the women drank, while the latter (PROPDDXP) represented how frequently – by days per two-week reporting period – alcohol in any amount was consumed during pregnancy. Each of these measures has been used effectively for years to predict prenatal alcohol-related outcomes (Beblo et al., 2005; Burden et al., 2005; Hannigan et al., 2010; Jacobson et al., 1994, 1998, 2002; Nordstrom Bailey et al., 2004). In addition, the continuous AADDXP variable was used to categorize women as “binge drinkers” when AADDXP ≥ 2.0 ounces absolute alcohol per drinking day (i.e., 4 drinks/day), reflecting the NIAAA and ACOG definitions of binge drinking in females (ACOG, 2006; NIAAA, 2004).

Spontaneous Abortion

Information about pregnancy outcome was obtained from medical chart records. Spontaneous abortion (SAb) was defined as fetal demise prior to 20 completed weeks of gestation (Cunningham et al., 2010; Stirrat, 1990). Within this sample, 23 pregnancies aborted spontaneously prior to the end of the 20th week of pregnancy based on last menstrual period. Over half of the recognized SAb (58%) occurred during the first trimester (i.e., before week 14); 42% occurred within the second trimester and before the end of the

20th week. One fetal stillbirth (< 500 g) occurred during the 22nd week of gestation. This fetus could have been classified a SAb according to the European criterion of 22 weeks (e.g., as in Strandberg-Larsen et al., 2008), or according to other guidelines that classify a later aborted fetuses weighing <500g as a SAb (Cunningham et al., 2010; Stirrat, 1990). However, the case was dropped from analyses since fetal death occurred after the 20th week of pregnancy to be consistent with the North American definition of SAb.

Covariates

In addition to alcohol consumption and pregnancy outcome, other data were collected for purposes of sample description and statistical control. Variables included other prenatal substance use (cocaine and smoking), maternal age at the time of conception (years), maternal pre-pregnancy BMI (PPBMI), maternal education (years), socio-economic status (SES), maternal marital status (married/not married), and gestational age at birth. SES was estimated with the widely used Hollingshead four-factor index (Hollingshead, 1975).

Data Analyses

Prior to analyses, checks were performed for missing and out-of-range data and for deviations from normality. Univariate outliers were 'winsorized' to reduce their potential inordinate influence in the analyses. Using this standard procedure, all values three standard deviations above the mean were re-coded to that cut-point value. Logistic regression was used to assess relations between alcohol variables and pregnancy outcome (SAb vs no SAb), controlling for maternal age, maternal education, SES classification, marital status, and prenatal exposure to cigarettes (number smoked/day). For the analysis of binge drinking, the amount of alcohol consumed per drinking day was dichotomized at either 4 or 5 drinks/day to create two binge drinking variables. Women who drank at or above these levels were given a binge score of '1', while women below these levels were given a score of '0' on each of the respective binge measures. Each alcohol consumption measure was analyzed separately. All variables were entered simultaneously into the regression equations. In addition, a visual examination of the distribution of SAb across AADDXP was performed to see if an obvious threshold was present.

RESULTS

Pre-pregnancy BMI data were missing for 22 of the 302 mothers. The bivariate relationship between BMI and SAb was not significant ($\beta=0.01$, $p=0.63$). Maternal BMI was also unrelated to any of the alcohol measures (p values ranged from 0.25 to 0.58). Due to the lack of significant association of BMI with both the outcome (SAb) and the predictor (prenatal alcohol exposure) in this sample, BMI was excluded as a factor from further analyses and the 22 women missing data for this variable were retained in the sample for analysis. The proportion of drinking days variable (PROPDDXP) had two univariate outliers that were 'winsorized.' Absolute alcohol per day, both the perinatal (AAD0) and across pregnancy (AADXP) measures, and absolute alcohol per drinking day, both the perinatal (AADD0) and across pregnancy (AADDXP) measures, each had one univariate outlier that was also 'winsorized.' The relationship between prenatal cocaine exposure ('yes/no') and SAb contained an empty cell, with none of the mothers admitting to cocaine use having had a SAb. Since an exact test showed no relationship between prenatal cocaine exposure and SAb ($p=0.62$), pregnancy cocaine use was excluded from further analyses.

Sample Characteristics

The mean gestational age at the initial antenatal clinic visit for the 302 mothers was 12.3 weeks ($SD = \pm 4.3$; range = 4 to 20 weeks; median=12.0). Mothers were poorly educated: >35% had not graduated from high school, only 12% attended some college, and fewer than

4.5% had a college degree (Table 1). Mothers were predominantly lower SES and unmarried, average maternal age at the first prenatal visit was 25.0 years, and only 4% were <18 years of age at the time of delivery.

Analyses were performed comparing excluded women (i.e., those enrolled after the 20th week) to those retained on several demographic characteristics such as marital status, maternal education, maternal age, socio-economic status, alcohol use at conception, and alcohol use across pregnancy. There were no significant differences between these two groups.

Alcohol Consumption

Just under one quarter of the sample of 302 women (22%) reported abstaining from drinking during pregnancy (Table 1). 16% of the women reported drinking at levels consistent with prior reported alcohol-related effects on the across-pregnancy measure (average ounces of absolute alcohol/day during pregnancy - AADXP), 36.8% reported similarly defined risk drinking on the peri-conceptional measure (AAD0), whereas 38% were identified as consuming risk levels of alcohol per drinking day (AADDXP 2.5) (ACOG, 2006; Jacobson & Jacobson, 1994; Russell et al., 1994). Also, based upon the two definitions of binge drinking (4 and 5 drinks/drinking day, respectively), 47.7% and 40.4% of the women in the sample were classified as binge drinkers. Regarding drinking frequency across pregnancy (PROPDDXP), 82.5% drank one day or less per week, 9.2% drank 2 days per week, and the remaining 8.3% drank 3 days per week during pregnancy, in contrast to peri-conceptional reports of drinking frequency (PROPXX0) when a 36.1% drank one day or less per week, 31.5% drank 2 days per week, and the remaining 32.4% drank 3 days per week during pregnancy.

Prenatal Alcohol Exposure and Spontaneous Abortion

Average amount of alcohol – in estimated ounces (oz.) of absolute alcohol – per day across pregnancy (AADXP), peri-conceptionally (AAD0), and per drinking day across pregnancy (AADDXP), as well as the proportion of days drinking/week peri-conceptionally (PROPDD0) and across pregnancy (PROPDDXP), were each examined in relation to SAb in separate logistic regression analyses (Table 2). After controlling for multiple demographic characteristics and other prenatal exposures, including smoking, the frequency of alcohol consumption during pregnancy (PROPDDXP) or periconceptionally (PROPDD0) ($\beta=10.12$, $p<0.001$, & $\beta=2.78$, $p=0.001$, respectively) and the amount of absolute alcohol per day periconceptionally (AAD0) and across pregnancy (AADXP) were each related positively to the incidence of SAb ($\beta=0.33$, $p=0.012$, & $\beta=0.86$, $p=0.008$, respectively). Based on the logistic regression models, the odds of having an SAb increased by 2.59 times for each additional drinking day per week (e.g., 1 day [$\text{PROPDDXP} = 1/7 * 100 = 14.3$] compared to 0 days). In this sample, none of the women who abstained from alcohol had a SAb, while 7.4% of the pregnancies of women who drank up to 1 day per week ended in a SAb. In addition, those who drank two, three and >3 days per week had SAb rates of 10.7%, 15.0%, and 40.0% respectively (Table 3), indicating an average drinking frequency-dependent association between level of drinking and SAb. However, contrary to our hypothesis, after control for confounding factors, SAb was not related significantly to pattern of average heavy daily alcohol drinking (AADDXP and AADD0); $\beta=0.13$, $p=0.07$; $\beta=0.14$, $p=0.109$, or to bingeing defined as either 4 or 5 drinks/drinking day ($\beta=0.16$, $p=0.727$ & $\beta=0.09$, $p=0.849$ respectively).

DISCUSSION

Consistent with our hypotheses, a significant relation between alcohol use/day across pregnancy (i.e., AADXP) and spontaneous abortion (SAb) was identified in this selected sample of high-risk, urban African American women. Similarly, the average amount of drinking reported per day around the time the woman become pregnant (i.e., AAD0), which is a reliable predictor of the growth and neurobehavioral effects of prenatal alcohol exposure (e.g., Jacobson et al., 1994; 2002), was related significantly to SAb. Drinking frequency (i.e., proportion of drinking days during pregnancy – PROPDDXP) also predicted SAb, with an average of even one day of drinking per week across pregnancy associated with a significantly increased incidence of SAb: women who drank at least one day/week were 2.59 times more likely to have a SAb compared to women who abstained from alcohol use during pregnancy. Additionally, the risk of a SAb increased as the daily frequency of drinking increased within this sample. These current results are consistent with a recent study that also reported significant increases in SAb related to frequency of drinking using a categorical variable reflecting frequency of in-pregnancy drinking (i.e., none *vs* <4 drinks/week *vs* 4 drinks/week), rather than “days drinking /week,” as in the current study (Ammon Avalos et al., 2009).

Contrary to our hypothesis, measures of a pattern of heavy drinking or number of drinks per drinking day were not associated with SAb after control for potentially confounding factors, although some analyses were marginal (i.e., at $p < 0.07$ to 0.09). This was not due to our use of a continuous variable for number of drinks/drinking day because dichotomous variables representing binge drinking based on 4 or 5 drinks/drinking day were also unrelated to the incidence of SAb. Also, our AADXP measure of average amount drunk on drinking days across pregnancy may have been a more stringent definition of “binge” drinking than other studies that categorized women as binge drinkers based on a single episode drinking 4 drinks/day anytime during pregnancy (Kesmodal et al., 2002a; Rasch, 2003; Strandberg-Larsen et al., 2008; Windham et al., 1997), or in current clinical screens with similar criteria of binge drinking (e.g., ACOG, 2006). The lack of a significant relation between SAb and binge drinking in our current data is partially consistent with recent reviews that examined the impact of prenatal bingeing (Henderson et al., 2007b) or light to moderate prenatal alcohol exposure (Henderson et al., 2007a) and SAb. Both reviews concluded that there is no consistent evidence for an increased risk of SAb after either bingeing or lower levels of exposure (Henderson et al., 2007a; 2007b). In contrast, our data are consistent with earlier assessments of pregnancy risk associated with the frequency of alcohol consumption. Harlap and Shiono (1980) reported that while women who drank less than 1 drink per day had no increased risk of SAb, when alcohol intake increased to 1–2 drinks daily there was a 1.98-fold increase in the rate of SAb. In Kline et al. (1980), pregnancy alcohol consumption by women who spontaneously aborted (cases) was compared to women who remained pregnant at least beyond the 28th week of gestation (non-cases). Among the cases, 17% of women drank at least two times per week compared to only 8.1% of non-cases. Kline et al. (1980) concluded that drinking 2 or more days per week significantly increased the frequency of SAb.

How prenatal alcohol exposure is assessed may explain apparent discrepancies among studies that have examined associations between pregnancy alcohol consumption and SAb. Alcohol consumption data are typically collected via maternal self-report. Given the increasing awareness of the dangers of pregnancy drinking and the consequent social stigma, women who consume alcohol are more likely to either deny use or significantly under-report the amount that they drink (ACOG, 2006; Ernhart et al., 1988). Thus, the entire distribution of reported amounts of alcohol consumed may be shifted significantly lower than the actual values (Sokol et al., 1980) which could bias assessment of the overall impact of alcohol on

the frequency of alcohol use simply by associating the lower reported drinking levels with effects of what are actually higher levels of exposure. Also, the present analysis does not address how some women and/or their fetuses are likely to have a greater susceptibility to deleterious effects of alcohol consumption during pregnancy than others. In some studies, for example, maternal age appears to be one critical risk factor: women over 30 years old, compared to younger women, have an increased risk for other poor pregnancy outcomes related to in-pregnancy drinking (Chiodo et al., 2010; Sokol et al., 2007). In the present study, maternal age marginally predicted increased SAb in the regression model assessing AADDXP ($\beta=0.13$, $p=0.07$). Other susceptibility factors that may also increase the risk of adverse effects due to prenatal alcohol exposure include cultural, racial and ethnic backgrounds (Abel, 1998; Abel & Hannigan, 1995). Since the data reported here are from an African American, high-risk, low-SES sample, the role these factors may play in the reported associations cannot be determined for our data. Finally, differences in the temporal patterns of alcohol consumption during pregnancy – especially greater risk drinking earlier in the first trimester – may also influence the likelihood of SAb. In particular, since women drinking alcohol at risk levels tend to have their first antenatal clinic visit later in pregnancy than non-drinking women, it is likely that risk-drinking women were more likely to have had a SAb prior to possible recruitment than non-drinking women. This potential sampling bias, however, would under-estimate the relationship between drinking and SAb, leading to a Type II error and not a Type I error.

Other factors that may affect fetal viability include smoking and other drug use, which frequently co-occur with risk drinking (Flynn & Chermack, 2008; Leonardson et al., 2007; Odendaal et al., 2009) and exposure to environmental contaminants such as lead (Bellinger, 2005). These factors are also likely to interact with maternal alcohol consumption in pregnancy to produce increased risk for SAb and FASD (Abel & Hannigan, 1995). Although animal studies and well-controlled human studies have indicated that alcohol itself appears to have direct influences on pregnancy outcome (e.g., Burd et al., 2007), this does not exclude the potential impact of other known, interacting risk factors on pregnancy outcomes.

We emphasize that limiting the current analyses to women who were enrolled prior to the 20th week of gestation could bias the estimated magnitude of the overall impact of alcohol on the frequency of SAb in this cohort, especially since the reported levels of alcohol consumption were the same among the excluded mothers. However, follow-up analyses (not presented) that included those enrolled after the 20th week of gestation revealed the same pattern of significant effects. Another potentially biasing factor is how late on average the drinking women in this population first seek prenatal care. With a later first prenatal care visit, it is possible that a higher proportion of drinking women may not have had a chance to enroll in this study since many pregnancies and/or early pregnancy losses due to alcohol were never recognized and SAb would never be reported. This possible enrollment bias (“left truncation”) would under-estimate the total number of SAb in the population and could potentially also under-estimate the impact of alcohol on SAb.

The current study has other limitations. The results may have poor generalizability since the cohort was restricted to low-SES urban African-American women, and oversampled drinkers, and the reliability of assessments of maternal alcohol use or abuse can differ across populations (Bradley et al., 1998; Chan et al., 1993; Ewing, 1984; Nardini et al., 2005; Sokol et al., 1989). In addition, some data were limited to trimester-specific information about when a SAb occurred. This lack of detail in some cases regarding SAb timing meant further, more detailed exploration was not feasible. For all these reasons, the results cannot be extrapolated to make population-wide estimates of the risk of an SAb after alcohol consumption.

A final limitation may reside in the AADDXP measure of prenatal alcohol exposure which is an across-pregnancy average that includes maternal reports made after the 20th week of pregnancy, after a SAb is no longer possible by definition. This means that AADDXP could underestimate drinking levels prior to 20 weeks gestation, if drinking were lower in the third trimester, and may thereby overestimate the risk of alcohol for SAb. However, third-trimester drinking may actually increase relative to the second trimester (Chiodo, 2002), and relations between peri-conceptional drinking (AAD0) and SAb were similar to those for AADDXP, and the proportion drinking days (PROPDDXP) also significantly predicted SAb.

Pregnancy alcohol consumption has wide-reaching effects. In addition to the FASD-related outcomes, other adverse pregnancy and birth outcomes have been linked to prenatal alcohol exposure, including prematurity and SAb. The current study identified increased risk of SAb at relatively low levels of alcohol use, and with a relatively small frequency of alcohol drinking across pregnancy. It is incumbent upon prenatal care providers to identify, address, and seek to reduce pregnancy alcohol use in their patients. Brief, reliable screening tools are available, and interventions with pregnant women to reduce or eliminate their alcohol consumption are easy to implement and known to be effective (ACOG, 2006; Bailey & Sokol, 2008b). Currently, there are no clearly defined thresholds for the effects of alcohol on embryos or fetuses (Abel, 2006; Henderson et al., 2007a; Jacobson & Jacobson, 1994; Martinez-Frías et al., 2004; Sampson et al., 2000). As a result, current standards of care and public health mandates advise health care providers to carefully monitor their pregnant patients' drinking and counsel that "no amount of alcohol consumption can be considered safe during pregnancy" (ACOG, 2006; Bertrand et al., 2005b; Chang, 2005; NIAAA, 2000; 2004, 2005a; USDHHS, 2005). Identification and treatment of alcohol use during pregnancy is critical for prevention of FASD and spontaneous abortions related to prenatal alcohol exposure.

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TABLE 1

Sample Characteristics (N=302^a)

	Mean or %	SD	Min	Max
Demographics				
Marital Status (% married)	7.90	—	—	—
Age at delivery (years)	24.93	5.44	15	41.0
SES classification ^b	3.79	1.09	1	5.0
Education	11.74	1.37	8	16.0
Maternal Weight (pre-pregnancy; lbs)	168.76	48.6	85	490.0
Maternal Height (inches)	64.93	2.93	52	75.0
BMI	30.12	7.88	16.46	70.5
Alcohol Variables				
<u>Periconception</u>				
Average AA ^c per Day (AAD0)	1.20	2.09	0	24.0
AA ^b per Drinking Day (AADD0)	2.73	2.83	0	24.0
Proportion Drinking days per week (PROPDD0)	0.33	0.30	0	1.0
<u>Across Pregnancy</u>				
AA per Day around conception (AADXP)	0.34	0.68	0	8.0
AA ^b per Drinking Day (AADDXP)	2.64	2.78	0	24.0
Proportion Drinking days per week (PROPDDXP)	0.10	0.12	0	0.9
Percent Abstainers	19.80	—	—	—
Percent Drinking 1 day/week	62.71	—	—	—
Percent Drinking 2 days/week	9.24	—	—	—
Percent Drinking 3 days/week	6.60	—	—	—
Percent Drinking >3 days/week	1.65	—	—	—
Binge Drinkers ^d (% 4 drinks per day)	47.70	—	—	—
Binge Drinkers ^d (% 5 drinks per day)	40.40	—	—	—
Other Prenatal Exposures				
Cocaine (% users)	5.70	—	—	—
Cigarettes (# smoked/day)	5.59	8.58	0	40.00

^aWomen enrolled prior to the 20th week of gestation^bSocioeconomic status (Hollingshead, 1975). A score of 3 represents skilled craftsmen as well as clerical & sales workers.^cOunces of absolute alcohol; AA=0.5 is roughly equivalent to one standard U.S. drink.^dBased on an AADDXP 2.0 or 2.5 for 4 or 5 drinks, respectively

Table 2
Regression results for Alcohol Measures and Incidence of Spontaneous Abortion (N=302).

Alcohol Measure	β	Odds Ratio	<i>p</i>	95% Confidence Interval for Odds Ratio	
				Lower	Upper
Average AA ^a per Day around conception (AAD0)	0.33	1.39	0.012	1.08	1.79
Average AA ^a per Day across pregnancy (AADXP)	0.86	2.37	0.008	1.25	4.48
AAa per Drinking Day across pregnancy (AADDXP)	0.13	1.08	0.07	0.92	1.27
Proportion Drinking days per week (PROPDXP) ^b	0.07	1.07	0.001	1.03	1.11
Binge Drinkers (Yes/No; 4 drinks per day)	0.16	1.18	0.727	0.47	2.93
Binge Drinkers (Yes/No; 5 drinks per day)	0.09	1.09	0.849	0.43	2.78

^aOunces of Absolute Alcohol; AA=0.5 is roughly equivalent to one standard U.S. drink.

^bProportion of Drinking Days per week across pregnancy is scaled from 0 to 100.

Table 3

Rates of Spontaneous Abortion (SAb) by Proportion of Days Drinking (N=302)

	Abstainers	1 day/week	2 days/week	3 days/week	> 3 days/week
SAb rate	0/59	14/190	3/28	3/20	2/5
SAb %	0%	7.4%	10.7%	15.0%	40.0%