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Heavy prenatal alcohol exposure and risk of stillbirth and preterm delivery

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Abstract

We prospectively identified 96 women consuming at least 4 drinks/day during pregnancy by screening 9628 pregnant women. In these women with heavy prenatal alcohol use, there were three stillbirths and one preterm delivery; 98 matched nondrinking women had no stillbirths and two preterm births. Preterm rates did not differ significantly. The stillbirth rate was higher in the exposed group ($p = 0.06$). Additional investigation showed the stillbirth rate in the exposed population (3.1%) was significantly higher ($p = 0.019$) than the reported Chilean population rate (0.45%). Our data suggest that heavy alcohol consumption may increase the risk for stillbirth but not preterm delivery.

Keywords

alcohol; pregnancy; stillbirth; preterm delivery; binge drinking

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Introduction

Heavy alcohol intake during pregnancy is known to cause functional deficits and anatomical abnormalities in offspring, but it is unclear whether it affects stillbirth and preterm delivery rates. Previous studies have reported increased, decreased, and unchanged risks [1-5]. Due to the known fetal risks of prenatal alcohol exposure, studies are often limited by the stigma associated with drinking during pregnancy. This may make the collection of accurate and detailed alcohol consumption data difficult.

We prospectively screened a large unselected population of women at their first prenatal visit to a clinic in Chile to identify heavy drinkers. We enrolled and monitored the women throughout their pregnancy. We collected detailed data on alcohol consumption during their pregnancies enabling us to examine the effects of quantity and patterns of maternal alcohol intake on stillbirth and preterm birth.

Methods

The study design of the National Institute of Child Health and Human Development (NICHD)–University of Chile Alcohol in Pregnancy Study has been reported in detail previously [6]. Briefly, 9628 (of 10,917) women registering for prenatal care at a health clinic in Santiago, Chile between August 1995 and July 2000 were screened for prenatal alcohol use. Through a screening questionnaire and confirmatory home visit, a group of 101 women with reported alcohol consumption of at least four drinks (48 g) daily and 101 women who reported no alcohol consumption during pregnancy, frequency matched for maternal age (± 2 years) and parity (0 or ≥1), were recruited. Detailed alcohol consumption data were collected during the pregnancy for two representative weeks, one from conception until the woman realized she was pregnant and one after the woman realized she was pregnant. The mother was asked to describe the number, amount and type of alcohol drinks consumed each day of the week. Data were recorded in grams and standardized with one drink equaling 12 g. Home visits were conducted for all exposed and unexposed women to validate the self reported alcohol data and assess the reliability of the women. Alcohol consumption was then classified by total amount (in grams) consumed during the week, average amount (in grams) consumed on days when alcohol was consumed, the peak alcohol intake (in grams) on the day in which the most alcohol was consumed, and the number of days in which >60 grams of alcohol was consumed (bingeing). The weeks from conception to recognition of pregnancy and after recognition of pregnancy were analyzed separately and examined for any change in consumption. Participants were followed to assess pregnancy and child outcomes. Institutional review boards at the University of Chile and NICHD approved the study. All women provided written informed consent.

The characteristics of the exposed and unexposed groups were compared using the Wilcoxon rank sum test and the Fisher’s exact test. Stillbirth and preterm birth were compared between exposed and unexposed groups with proportional hazards models and the log rank test using the fetuses-at-risk approach [7]. Unconditional logistic regression was used to compute odds ratios and 95% confidence intervals for associations between classifications of alcohol use and pregnancy outcomes. Covariates associated with still- and

preterm births that changed the exposure effect estimate by >10% were included. Any classifications of alcohol intake that were associated with the outcomes in unadjusted analyses ($p < 0.05$) were used as main exposure variables in separate logistic regression models. We compared stillbirth (fetal death ≥20 weeks) and preterm delivery (<37 weeks) rates with Chilean population rates by the exact binomial test [8]. Analyses were conducted using SAS 9.1 and 9.2 (SAS Institute, Cary, NC).

Results

Ninety-six exposed (95.0%) and 98 (97.0%) unexposed mothers were followed to parturition; 5 (5.0%) exposed and 3 (3.0%) unexposed were lost to follow-up. Exposed mothers were more likely to be less educated, single, and to have enrolled in the study later in pregnancy (Table I).

From conception to the time the exposed women learned they were pregnant, they consumed on average 20 ± 15 (mean ± SD) drinks per drinking day. After they knew they were pregnant, women reduced intake by approximately half; however, on average the women still consumed almost 11 ± 14 (mean ± SD) drinks per drinking day. Fourteen of the 96 exposed women (14.6%) abstained completely once they became aware of the pregnancy.

In 96 exposed pregnancies, there were three stillbirths (a fetus born dead at ≥20 weeks gestation) and one preterm delivery (birth at <37 weeks gestation). In 98 unexposed pregnancies, there were no stillbirths and two preterm births. The analysis of preterm birth by proportional hazards models showed no significant difference between the exposed and unexposed groups. The model for stillbirth could not be fit because there were no events in the unexposed group; therefore a log rank test was used. This test showed that the stillbirth rate in the exposed group was higher and the difference was of borderline significance ($p = 0.06$). One stillbirth was due to placental abruption, one to multiple malformations, and one cause was undetermined.

To help interpret this borderline result, we compared the stillbirth rate in the exposed group to Chilean national data. The stillbirth rate in the exposed population (3/96, 3.1%) was significantly higher ($p = 0.019$) than reported in the Chilean population from 1995 to 2000 (7087/1,567,315, 0.45%).

Comparison of those women who had stillbirths versus those who had live births regarding amount and pattern of alcohol consumption revealed an association only with binge drinking later in pregnancy in the crude analysis (OR: 1.62, 95% CI: 1.09, 2.41; Table II). Following adjustment for maternal age, maternal education level, and years of any alcohol consumption prior to the pregnancy, no classifications of maternal alcohol exposure remained significant. In order to ensure that years of any alcohol consumption was an independent risk factor, we performed Spearman rank correlation tests that showed no correlation between years of any alcohol consumption and each classification of maternal alcohol exposure ($p > 0.10$). This would imply that that chronic drinking does not predict very well drinking during pregnancy, but since chronic drinking changed the exposure effect estimate by >10% we included years of any alcohol consumption in our model.

Repeating the logistic regression using only the exposed population also showed no significant associations (Table III). Preterm births were not associated with the pattern or amount of alcohol consumption in any analysis.

Discussion

Comparing our exposed and unexposed populations, we found a borderline-significant increase in stillbirths and no increase in preterm deliveries in women consuming ≥48 g alcohol per day. Comparing our exposed population to the Chilean population, we found an impressive increase in stillbirth rate. To our knowledge, this is the first study examining stillbirth and preterm delivery rates in a population with such high alcohol consumption during pregnancy. Additionally, our population is unique due to the detailed alcohol data collected during pregnancy with verification of intake with home visits.

In our population, heavy alcohol consumption did not result in increased rates of preterm delivery. Of note, the rates in both our exposed and unexposed populations were lower than the population rate of 60 per 1000 live births in Chile, suggesting that our population was at low overall risk [9].

We found no significant associations between the amount or pattern of alcohol consumption and stillbirth or preterm delivery, possibly due to our small number of events. We note that our crude, but not our adjusted, analysis detected an association between stillbirth and binge drinking later in pregnancy. Interestingly, previous reports have found an association between binge drinking and stillbirths, warranting investigation in larger trials [5].

In addition to the small number of adverse outcomes, another limitation of our study was the lack of information on some risk factors for stillbirth and preterm delivery. We had one stillbirth of unknown cause; however, one third of stillbirths being of unknown cause is consistent with the literature [10]. Moreover, prenatal alcohol exposure has previously been associated with stillbirth caused by placental abruption, one of the two causes identified here [3]. No causes for the preterm births were identified. Our population may not have been representative of the Chilean national population with regard to risk factors; so this comparison should be interpreted cautiously.

Very few women consume four or more drinks per day during pregnancy. Therefore, a major strength of our study was identifying 96 such women during pregnancy from an unselected population. Furthermore, we limited the problems of recall bias and underreporting by determining alcohol intake before delivery and validating questionnaire responses by home visit.

Our results suggest that pregnancies complicated by exposure to high levels of alcohol may be at increased risk for ending in stillbirth but not preterm delivery and emphasize the need for other large-scale, prospective studies to resolve these issues.

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Table I

Characteristics of study subjects.

	Exposed (*n* = 96)	Unexposed (*n* = 98)	*p*-value[a]
Mothers[b]			
Age (years)	24.5 ± 7.0	24.7 ± 6.9	0.86
Parity			0.89
0	51 (53.1)	54 (55.1)	
≥1	45 (46.9)	44 (44.9)	
Education (years)			0.012
<12	60 (62.5)	43 (43.9)	
12	22 (22.9)	33 (33.7)	
>12	14 (14.6)	22 (22.5)	
Marital status			0.047
Single	72 (75.0)	59 (60.2)	
Married	21 (21.9)	37 (37.8)	
Divorced	3 (3.1)	2 (2.0)	
GA enrollment (weeks)	18.8 ± 7.9	12.4 ± 4.8	<0.0001
Offspring[b]			
GA at birth (weeks)	39.3 ± 1.2	39.1 ± 1.1	0.27
Male	47 (49.0)	46 (46.9)	0.89

Note: GA = gestational age.

[a]Comparisons between exposed and unexposed groups using Wilcoxon rank sum test for maternal age, education, gestational age at enrollment, and gestational age at birth; and using Fisher's exact test for parity, marital status, and proportion of male offspring.

[b]Values are expressed as mean ± standard deviation or number (percent).

Table II

Association between alcohol consumption during pregnancy and stillbirth all women (*n* = 194).

Alcohol exposure classification	Unadjusted OR[a] (95% CI)	*p*-value	Adjusted OR[b] (95% CI)	*p*-value
Conception to pregnancy awareness				
Total consumed during the week (g; effect per gram of alcohol)	1.00 (0.99, 1.00)	0.41	1.00 (1.00, 1.00)	0.44
Average consumed per drinking day (g; effect per gram of alcohol)	1.00 (0.99, 1.01)	0.10	1.00 (1.00, 1.01)	0.48
Maximum alcohol intake on any one drinking day (g; effect per gram of alcohol)	1.00 (0.99, 1.01)	0.28	1.00 (1.00, 1.01)	0.57
Number of drinking days in a week that mother drank >60 g/ day (indicator of binge drinking; effect per each additional day)	1.43 (0.94, 1.01)	0.10	2.08 (0.66, 6.50)	0.21
After pregnancy awareness				
Total consumed during the week (g; effect per gram of alcohol)	1.00 (0.99, 1.00)	0.53	1.00 (1.00, 1.01)	0.60
Average consumed per drinking day (g; effect per gram of alcohol)	1.00 (1.00, 1.01)	0.59	1.01(0.99,1.02)	0.38
Maximum alcohol intake on any one drinking day (g; effect per gram of alcohol)	1.00 (1.00, 1.01)	0.60	1.00 (1.00,1.01)	0.40
Number of drinking days in a week that mother drank >60 g/ day (indicator of binge drinking; effect per each additional day)	1.62 (1.09, 2.41)	0.02	2.23 (0.75, 6.61)	0.15

[a] Logistic regression for the association between alcohol intake and stillbirth.

[b] Adjusted for maternal age, maternal education, and years of alcohol consumption prior to pregnancy. OR = odds ratio, CI = confidence interval.

Table III

Alcohol consumption during pregnancy after the mother was aware that she was pregnant-exposed group mothers (n = 96).

	Alcohol consumption			
	Stillbirths (n = 3)	**Live births[a] (n = 93)**	***p*-value[b]**	**OR[c] (95% CI) effect per gram of alcohol**
Total amount of alcohol consumed in a representative week (g)				
Range	140–691	0–1,941	0.59	1.001
Mean ± SD	379 ± 276	448 ± 533		(0.997, 1.005)
Median (IQ range)	317 (140-681)	213 (53-615)		
Average amount of alcohol consumed / drinking day in a representative week (g)				
Range	70–159	0–773	0.64	1.006
Mean ± SD	109 ± 45	135 ± 164		(0.989, 1.023)
Median (IQ range)	97 (70–159)	80 (21–209)		
Maximum alcohol intake on any one day in a representative week (g)				
Range	70–216	0–1,250	0.73	1.112
Mean ± SD	156 ± 77	197 ± 243		(0.908, 1.362)
Median (IQ range)	183 (70–216)	118 (23–277)		
Number of drinking days in a representative week that mother drank >60 g/day (indicator of binge drinking)				
0	0 (0.0)	37 (39.8)	0.13	
1	0 (0.0)	10 (10.8)		
2	2 (66.7)	26 (28.0)		
3	0 (0.0)	9 (9.7)		
4	0 (0.0)	3 (3.2)		
5	0 (0.0)	1 (1.1)		
6	0 (0.0)	0 (0.0)		
7	1 (33.3)	7 (7.5)		

Note: OR= odds ratio, CI = confidence interval, SD = standard deviation, IQ = Inter-quartile range.

[a] 14 of 93 mothers (15.1%) reported no further alcohol use after becoming aware of the pregnancy.

[b] Wilcoxon rank sum test used to compare alcohol intake (g) between mothers who delivered live births and those who delivered stillbirths.

[c] Logistic regression for the association between alcohol intake and stillbirth; adjusted for maternal age, maternal education, years of any alcohol consumption prior to the pregnancy, duration of maternal alcohol consumption (yrs), number of cigarettes smoked per day.