



Brief communication

Prenatal alcohol exposure and offspring alcohol use and misuse at 22 years of age: A prospective longitudinal study

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ABSTRACT

Studies have shown that prenatal alcohol exposure (PAE) is related to drinking problems during adulthood, but the level of prenatal exposure associated with young adults' quantity and frequency of alcohol use and drinking problems has not yet been established. The relation between PAE and offspring levels of alcohol use and alcohol abuse/dependency was examined in 608 22-year-olds. Mothers were recruited in early pregnancy and maternal alcohol use data were collected for each trimester of pregnancy. The offspring were assessed at multiple phases from birth to young adulthood. The average daily volume of drinking was calculated based on a self-report questionnaire developed by the Maternal Health Practices and Child Development Project and alcohol abuse/dependence was assessed using the Diagnostic Interview Schedule-IV. Exposure to one or more drinks/day during the first trimester of pregnancy was significantly related to increased levels of drinking at 22 years of age, controlling for other predictors of alcohol use. PAE was also related to two or more symptoms of Alcohol Use Disorder, but not to a full diagnosis of young adult alcohol abuse/dependence. These results indicate that individuals exposed to as little as one drink per day during gestation are at risk of higher levels of drinking and more problems with alcohol by age 22.

1. Introduction

Despite the potential negative consequences of alcohol use, such as injury, death, and assault, drinking and excessive alcohol use are common among young adults. In the National Survey on Drug Use and Health, 57% of 18- to 25-year-olds had used alcohol in the past month (Substance Abuse and Mental Health Services Administration, 2017). In the National Epidemiologic Survey on Alcohol and Related Conditions, 50% of young adult drinkers exceeded the recommended daily drinking limit, defined as four drinks in a single day for men and three drinks for women (Chen et al., 2004). In addition to characteristics such as gender, ethnicity, and family history of alcohol problems that are related to alcohol use (Courtney and Polich, 2009; Cranford et al., 2006; Hill et al., 2000; Jackson et al., 2001; NIAAA Alcohol Alert, 2006), it is important to identify other potentially modifiable factors that may be related to higher levels of drinking.

Longitudinal studies examining the relation between prenatal alcohol exposure (PAE) and offspring alcohol use during young adulthood are scarce. Baer et al. (2003) reported a significant association between PAE and higher number of negative consequences and symptoms of

alcohol dependence at 21 years in the Seattle Prospective Longitudinal Study. This study controlled for family environment, including history of alcohol problems. No statistically significant relation was found between PAE and quantity and frequency of alcohol use by the offspring. However, several measures of prenatal alcohol use, including heavy episodes of drinking, were combined to represent PAE, so the level of PAE associated with offspring alcohol use is unknown. Results from the Mater-University of Queensland Study of Pregnancy showed that exposure to 3 or more drinks per occasion in early pregnancy increased the risk of Alcohol Use Disorders (AUD) at age 21 by 2.95 times compared to those who were exposed to lesser amounts or none (Alati et al., 2006). The results remained stable when subjects with fathers or siblings with alcohol problems were excluded. Although this was a large study and environmental effects were considered, an integrated measure of quantity by frequency of PAE was not available.

In an earlier report from our research group, a significant direct relation was found between heavy (≥ 1 drink/day) first trimester PAE and alcohol drinking among the 16-year-old offspring (Cornelius et al., 2016a). This relation was not mediated by childhood externalizing behavior problems. The frequency and quantity of alcohol use changes

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from adolescence into young adulthood, and different patterns of use have been reported in the literature. Colder et al. (2002) identified not only stable users and those who escalate their use, but also a distinguishable class of individuals who started at a high level and reduced their use over time. Therefore, it is important to examine the relation between PAE and alcohol use at young adulthood to determine if PAE continues to predict levels of drinking among adult offspring.

The data for the current study are from the Maternal Health Practices and Child Development (MHPCD) Project, a longitudinal study designed to examine the long-term effects of PAE. Pregnant women were selected from a low-income prenatal clinic (half were African-American and half were Caucasian, reflecting the distribution in the clinic). Detailed measures of PAE during each trimester of pregnancy allow us to define the level of exposure more accurately than in previous studies. The main aims of the present study are to test whether the offspring exposed to alcohol during gestation exhibit higher rates of alcohol use and abuse at age 22 and to determine what level of PAE is associated with alcohol problems in adult offspring. The outcome variables included both frequency and quantity of alcohol use, and alcohol abuse/dependence. Other variables that may influence young adult alcohol use such as family history of alcohol and drug problems, parenthood, employment, and life events (Lynch et al., 2003; NIAAA Alcohol Alert, 2006) were included in the analyses.

2. Method

2.1. Study design

Recruitment for the MHPCD Project occurred during the fourth or fifth month of pregnancy from 1982 to 1985. The women were recruited from the Magee-Womens Hospital prenatal clinic to study the effects of prenatal alcohol and marijuana exposure. Women were selected for the study of PAE if they drank ≥ 3 drinks/week, along with the next woman who drank less than that amount. Women were selected for the study of prenatal marijuana exposure (PME) if they used at least two times per month, along with the next woman who used less. Women selected for the study were interviewed again at the seventh month of pregnancy and after delivery. There were 763 live singleton infants at birth. Women and their children were assessed at 8 and 18 months and at 3, 6, 10, 14, 16, and 22 years. At the 22-year phase, the cohort consisted of 608 subjects, of whom 64.5% were exposed to alcohol during first trimester. Missing were 11 offspring who died, 3 were adopted, 18 were institutionalized (military, jail), 8 with low cognitive functioning, 29 moved out of the area, 56 could not be located, and 30 refused to participate. The attrition was unrelated to PAE, prenatal exposure to other substances, income, or race. The 22-year assessment was completed between 2006 and 2009.

2.2. Sample characteristics

The pregnant women recruited for this study were ≥ 18 years (mean age = 23, SD = 4). They were of lower socioeconomic status with a mean family income of \$343/month (SD = 300) at recruitment. At delivery, 49% lived with a husband/boyfriend, 24% lived with parents/other adults, 18% lived alone with children (< 18 years), and 9% lived alone.

The mean age of the young adult offspring participants was 22.8 years (range 21–26). The sample consisted of 264 Caucasian (43%) and 344 African-American (57%) participants and 289 (48%) men and 319 (52%) women. Forty-eight percent reported post-high school education, 27% were still attending school, 4% were in the military, and 60% worked. The mean personal income/month among those who worked was \$1372 (range: 100–5000). Twenty-eight percent lived with their partners and 35% lived with their parents.

2.3. Measures

2.3.1. Independent variable

PAE was calculated separately for each trimester of pregnancy. First trimester exposure was an average of daily alcohol use by the mothers weighted based on the number of days in each of these three time periods: between 1) conception to recognition of pregnancy, 2) recognition to confirmation of pregnancy, and 3) diagnosis confirmation to the end of the first trimester (see Day and Robles, 1989 for further details). Women were also interviewed at the 7th prenatal month and at birth, when they were asked about their second and third trimester alcohol use, respectively.

2.3.2. Dependent variables

At 22 years, the offspring reported their past year frequency and quantity of alcohol use, including wine, beer, wine and beer coolers, liquor, and malt liquor (Day and Robles, 1989). The frequency of use was measured using a Likert scale ranging from every day to 1–5 times/year. The offspring were asked how much they usually drank, how often they drank more than usual, and how often they drank a smaller amount. The responses were combined and transformed to average daily volume of use (ADV). Since ADV was highly skewed (skewness = 7.4, range: 0–38 drinks/day), subjects were categorized into three groups for the analyses based on ADV lower and upper quartiles: none to 5 drinks/month, > 5 drinks/month to 2 drinks/day, and > 2 drinks/day.

Diagnoses for lifetime alcohol abuse and dependence were assessed using the Diagnostic Interview Schedule-IV (Robins et al., 2000). Abuse criteria consist of four symptoms and dependence criteria include seven different symptoms. An individual is diagnosed with abuse if he/she meets one or more symptoms of alcohol abuse. Dependence diagnosis is based on endorsing three or more criteria related to excessive drinking within a 12-month period (American Psychiatric Association, 1994). The symptoms listed under DSM-5 differ from those of the DSM-IV by one question: *legal problems because of drinking* has been replaced by a *craving symptom*. However, in the DSM-5, symptoms of abuse and dependence are combined, and a diagnosis of Alcohol Use Disorder (AUD) is assigned to individuals with 2 or more symptoms.

2.3.3. Covariates

PME was measured in a similar way to alcohol use: Average daily joints (ADJ) was used in the analyses. Cigarette smoking during pregnancy was measured as number of packs smoked per day and was translated to the number of cigarettes per day (1 pack = 20 cigarettes).

At 22 years, the young adult offspring were asked whether anyone in their immediate family ever had a serious drinking problem, defined as the attempt to stop drinking but unable to do so, having marital or job problems due to drinking, or seeking treatment. Two variables were created indicating whether the biological mother or the biological father had serious drinking problems (yes = 1/no = 0).

Stressful life events in the young adults over the past year were measured using questions adapted from the Recent Life Changes Questionnaire (RLCQ; Miller and Rahe, 1997), which covers events related to health, work, home and family, personal and social, and finance. Both positive and negative life changes, such as marriage and divorce, were included in the checklist. Other covariates included in the analyses, based on the literature, were parenthood (having any children versus none), employment (yes/no), and military service (yes/no).

2.4. Statistical analysis

Prior to regression analyses, the frequency distributions of the outcome variables at different levels of PAE (non-exposed, exposed to $ADV < 1$, exposed to $ADV \geq 1$) were explored to determine whether there was a negative relation at any level of exposure or only at higher levels of exposure. Regression analyses were applied to estimate PAE

effects on offspring alcohol consumption at 22 years, adjusting for possible covariates. Regular logistic regression was applied for the dichotomous outcome variable abuse/dependence, and ordinal logistic regression was applied to estimate the relation between PAE and the offspring levels of drinking. The covariates included in the models were offspring age at the time of assessment, gender, ethnicity, parents' history of serious drinking problems, life events, parenthood, employment, military service, and prenatal exposure to marijuana and tobacco. The analyses proceeded in a stepwise manner with forward entry and variables significant at an alpha level of 0.05 were included in the model. The odds ratios (OR) for the logistic regression and cumulative odds ratios (COR) for the ordinal regression are presented.

3. Results

During the first trimester of pregnancy, 64.5% of the mothers reported drinking and 18.3% drank one or more drinks/day. In general, most women decreased their use across pregnancy. By the third trimester, 31% of the women reported drinking, and 4% drank heavily (ADV ≥ 1). At 22 years, 76% of the mothers reported any alcohol use. Among the covariates, first trimester PAE was significantly related to prenatal tobacco exposure (mean 6.6 cigarettes/day among non-exposed versus 11.2 among heavily exposed, $p < 0.001$), PME (ADJ of 0.29 in non-exposed versus 0.59 in heavily exposed, $p < 0.01$), and maternal history of alcohol problems (6.6% among non-exposed compared to 23.6% among heavily exposed, $p < 0.001$).

Levels of drinking: Table 1 depicts the bivariate relations between offspring alcohol use and PAE and the covariates. As explained above, offspring drinking was categorized into three groups for the analyses. Heavier offspring drinking was associated with being male, having more life events, and being less likely to have children. Bivariately, offspring drinking was significantly associated with first trimester heavy exposure (≥ 1 drink/day). Although third trimester exposure was positively related to offspring alcohol use, it did not reach statistical significance (Table 1).

The results of the ordinal logistic regression are presented in Table 2. Exposure to one or more drinks/day during the first trimester of pregnancy was significantly related to levels of offspring drinking with a COR of 1.6 from one level of drinking to the next (95% CI = 1.1–2.4, $p < 0.05$). Other significant predictors were male gender and offspring life events.

Alcohol abuse/dependence: There was no significant relation between PAE and this outcome variable. The frequencies of abuse/dependence among first trimester non-exposed, non-heavily exposed, and

heavily exposed (ADV ≥ 1) were 18%, 16%, and 16%, respectively. Using logistic regression, significant predictors of abuse/dependence were life events (OR = 1.09, 95% CI = 1.05–1.14, $p < 0.001$), biological father's alcohol problems (OR = 2.12, CI = 1.3–3.46, $p < 0.005$), male gender (OR = 2.0, CI = 1.24–3.11, $p < 0.005$), Caucasian race (OR = 1.85, CI = 1.17–2.92, $p < 0.01$), and lack of employment (OR = 0.59, CI = 0.37–0.93, $p < 0.05$).

To investigate the possibility that the young adults were too young to be diagnosed with lifetime abuse/dependence at 22 years, we tested whether PAE was significantly related to two or more abuse/dependence symptoms, which is closely related to the definition of AUD in the DSM-5 (Grant et al., 2015). PAE as a continuous variable, as well as heavy exposure (ADV ≥ 1), were both significantly related to increased odd of reporting 2 or more symptoms of AUD, although the goodness of fit was slightly higher with heavy exposure (Table 3). For first trimester exposure, 39%, 42%, and 54% of the non-exposed, non-heavily exposed, and heavily exposed met 2 or more criteria, respectively ($p < 0.05$). A similar pattern was found with third trimester PAE (39%, 50%, and 59%, respectively, $p < 0.05$). After controlling for other significant covariates, heavy PAE during the first trimester of pregnancy was associated with an increase of 84% in ≥ 2 symptoms (Table 3). Other significant correlates were life events, Caucasian race, male gender, and unemployment. Although in bivariate analyses parents' history of alcohol problems was related to 2 or more symptoms, these variables were not significant after controlling for offspring life events.

4. Discussion

This manuscript presented data from the MHPCD Project on the association between trimester-specific levels of PAE and young adult alcohol use and abuse. This was the first study to demonstrate a significant relation between exposure to one or more drinks/day during the first trimester of gestation and quantity and frequency of drinking at 22 years of age. The association between PAE and a DSM-IV diagnosis of alcohol abuse/dependence was not significant. However, PAE was significantly related to reporting two or more symptoms of AUD. This association remained significant after controlling for covariates such as family history of alcohol problems and stressful life events.

In a previous MHPCD report, PAE predicted behavior problems at 22 years of age (Day et al., 2013). The current finding is congruent with those results since young adults' higher level of drinking is significantly related to their externalizing and internalizing behavior problems (Fergusson et al., 2007). The results of this study are also consistent with an earlier report of PAE and levels of drinking during adolescence

Table 1
Offspring levels of alcohol use at 22 years by covariates and PAE.

	0–5 drinks/month N = 157	≤ 2 drinks/day N = 299	> 2 drinks/day N = 152	Overall significance ^a
Mean age at the assessment (years)	22.9	22.8	22.8	N.S.
Gender (% male)	36.9	43.5	66.4	< 0.001
Race (% Caucasian)	37.6	44.8	46.7	N.S.
Father's alcohol problem (% yes)	26.5	19.6	21.7	N.S.
Mother's alcohol problem (% yes)	11.0	10.5	13.2	N.S.
Life events (#)	7.3	9.0	9.6	< 0.001
Parenthood (% yes)	47.1	33.1	34.9	< 0.05
Employment (% yes)	59.2	62.2	57.2	N.S.
Military (% serve)	3.8	4.3	4.6	N.S.
1st trimester marijuana exposure (ADJ) ^b	0.40	0.38	0.34	N.S.
1st trimester tobacco exposure (mean cigarettes/day)	7.7	8.2	8.8	N.S.
1st trimester alcohol exposure (ADV) ^c	0.48	0.59	0.60	N.S.
% 1st trimester ADV ≥ 1	12.7	19.1	22.4	< 0.05
3rd trimester alcohol exposure (ADV) ^c	0.08	0.13	0.17	N.S.
% 3rd trimester ADV ≥ 1	1.3	4.3	4.6	N.S.

^a Based on Ordinary Logistic Regression.

^b ADJ = average daily joints.

^c ADV = average daily volume of alcohol.

Table 2
Results of ordinal logistic regression on offspring levels of drinking at 22 years.

Variable	Coefficient	Cumulative OR [95% CI]	Significance level
Gender (0 = female, 1 = male)	0.80	2.2 [1.6–3.0]	< 0.001
Offspring life events	0.05	1.05 [1.03–1.1]	< 0.001
1st trimester PAE (ADV ≥ 1) ^a	0.47	1.6 [1.1–2.4]	< 0.05

^a ADV = average daily volume of alcohol.

Table 3
Results of logistic regression on two or more symptoms of DSM-IV alcohol abuse and dependence.^a

Variable	Coefficient	Odds ratio [95% CI]	Significance level
Offspring life events	0.07	1.08 [1.04–1.11]	< 0.001
Race (0 = Black, 1 = White)	0.76	2.14 [1.5–3.03]	< 0.001
Gender (0 = female, 1 = male)	0.71	2.03 [1.44–2.87]	< 0.001
Employment (0 = no, 1 = yes)	–0.38	0.68 [0.48–0.97]	< 0.05
1st trimester PAE (ADV ≥ 1) ^b	0.61	1.84 [1.17–2.88]	< 0.01
3rd trimester PAE (ADV ≥ 1) ^b	1.14	3.14 [1.23–8.0]	< 0.05

^a Closely related to DSM-5 definition of AUD (Grant et al., 2015).

^b Each trimester was analyzed separately but shown in the same table to conserve space. ADV = average daily volume of alcohol.

(Cornelius et al., 2016a), demonstrating continuity of risk from PAE from adolescence to adulthood. Although the measures of PAE, offspring alcohol problems, and covariates in the MHPCD differ from those in the Queensland and Seattle studies, all three studies identified a significant relation between PAE and young adult alcohol problems. However, our study also showed a significant relation between PAE and higher levels of drinking during young adulthood.

There are several theories about how prenatal exposure may increase alcohol consumption among offspring. The theory that PAE enhances the association between alcohol's odor/taste and pleasant consequences in offspring has been supported by several animal studies (Spear and Molina, 2005). Hannigan et al. (2015) tested this theory in young adult humans and found that offspring exposed to higher levels of PAE were significantly more likely to rate alcohol as having a pleasant odor than their peers. Genetic associations between maternal and child drinking are another possibility. Although our study did not have a genetic design, the variance due to parental history of alcohol problems was parceled out using multivariate analysis.

Although this prospective study featured 22 years of longitudinal data, excellent retention rates, and consideration of many possible covariates of young adult alcohol use and abuse, there were some limitations. One, the study was designed to examine the effects of PAE on offspring, so pregnant drinkers were oversampled, with 64.5% of the women reporting alcohol use in the first trimester. However, the full spectrum of prenatal use was represented in this study, from abstainers to women who drank every day during the first trimester, providing adequate variance to test for the effects of levels of PAE on adult offspring alcohol use. Two, the sample was drawn from an urban prenatal clinic associated with a teaching hospital that serves both Caucasian and African-American women. Thus, results may not generalize to offspring with mothers from rural areas or of other race/ethnicities. Three, at the time data were collected on the young adult offspring, the DSM-IV was in use, so our AUD diagnoses were based on the DSM-IV rather than the DSM-5. However, we matched the number of symptoms from the DSM-IV instrument to those used in the DSM-5 to examine the effects of PAE on symptoms of AUD that are comparable to studies using the DSM-5 and found a significant relation with PAE. Four, we have previously shown that persistent alcohol use from ages 14 to 16 was significantly related to PAE (Cornelius et al., 2016b). Further research is needed to examine the effects of PAE on patterns of change in drinking from adolescence to adulthood and to full AUD diagnosis, when parental supervision has less impact and individuals face new adult responsibilities.

Only a small proportion (8%) of participants in the study with

alcohol abuse/dependence had sought treatment for alcohol-related problems. This is even lower than the treatment rates reported in the US general population (Grant et al., 2015; Hasin et al., 2007). According to Hasin et al. (2007), the reason a small proportion seek treatment is not due to lack of health insurance, but because of stigmatization of people with AUD, lack of confidence in the efficacy of treatments, and a general lack of knowledge about new medications and behavioral therapies. Pregnant women are particularly prone to being stigmatized for their drinking. Since PAE has been identified as a risk factor for alcohol problems and higher levels of drinking in the offspring, prevention and information campaigns emphasizing effective treatment options and destigmatization should be targeted to young adults and pregnant women.

Transparency document

The [Transparency document](#) associated this article can be found, in online version.

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