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RESEARCH ARTICLE

Maternal childhood adversity as an upstream vulnerability for prenatal alcohol use and maternal mental health

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Abstract

Background: Maternal mental health and substance use during pregnancy often co-occur, yet antecedent factors contributing to both remain understudied. This analysis examined associations between maternal adverse childhood experiences (mACEs) and (a) alcohol use and (b) stress, mood, and trauma symptoms during pregnancy.

Methods: The ENRICH-2 cohort recruited pregnant individuals into mild-to-moderate Alcohol and Control groups. Alcohol use was assessed via prospective interviews and ethanol biomarkers. Maternal childhood adversity was measured with a 10-item Adverse Childhood Experiences (ACE) questionnaire, and maternal mental health was evaluated using the Perceived Stress Scale (PSS), Edinburgh Depression Scale (EDS), Generalized Anxiety Disorder-7 (GAD-7), and PTSD Checklist for DSM-5 (PCL-5). Prevalence of High mACEs (≥4) and specific ACE categories were compared using chi-squared tests. Spearman correlation examined the association between absolute alcohol per day (AAD) and mACEs in the Alcohol group. Mean mental health scores across Control, High mACEs, Alcohol, and Alcohol+High mACEs groups were compared by ANOVA and multivariable linear regression.

Results: Among 164 participants (58 Alcohol, 106 Control), the prevalence of High mACEs was almost double in the Alcohol compared to the Control group (37.9% vs. 20.8%, $p = 0.02$). For the Alcohol group, there was a positive correlation between AAD and mACEs ($\rho = 0.18$, $p = 0.02$). The mACEs categories of physical abuse, household exposure to substance use, and incarceration of a family member were significantly higher in the Alcohol group (all $p < 0.05$). Adjusted regression models demonstrated that both High mACEs and Alcohol groups were associated with increases in maternal mental health symptom scores, with the Alcohol+High mACEs group showing the largest model-estimated increases across all outcomes (all p values < 0.01).

Conclusions: Results highlight mACEs as an upstream vulnerability associated with prenatal alcohol use and poorer maternal mental health, suggesting that mACEs—or their sequelae—may function as a contextual risk factor in pregnancy.

KEYWORDS
adverse childhood experience, alcohol, early life adversity, mental health, pregnancy

INTRODUCTION

Alcohol remains one of the most common substances used in pregnancy with prevalence estimates ranging from 8.9% to 11.1% (Popova et al., 2018). Prenatal alcohol exposure (PAE) is associated with a range of physical, cognitive, and behavioral impairments collectively known as Fetal Alcohol Spectrum Disorder (FASD). While early diagnostic efforts focused on the physical features of FASD, research has since emphasized the enduring cognitive and behavioral impacts on the developing brain that follow from an alcohol-exposed pregnancy (Riley et al., 2011). Individuals with FASD can experience a wide range of outcomes, including growth restrictions, neurodevelopmental deficits, and intellectual and behavioral disabilities (Wozniak et al., 2019). These primary disabilities often persist into adulthood, manifesting into lifelong daily challenges, particularly if interlinked to certain environmental and social adversities that lead to further external care (Popova et al., 2017). Active case ascertainment studies in the United States estimated prevalence of FASD to affect as many as 1.1%–5% of school-age children, making it one of the most common neurodevelopmental disorders (May et al., 2018).

Predictors and correlates of alcohol use in pregnancy are heterogeneous and vary by study population. Consumption patterns vary across subpopulations due to—but not limited to—differences across age, race/ethnicity, and education (Perreira & Cortes, 2006). In the United States, alcohol use among women of childbearing age continues to rise despite the strong recommendations against drinking during pregnancy (Conant et al., 2021). Several risk factors have been consistently associated with PAE, including being single (Leonardson & Loudenburg, 2003), tobacco use, having peers who use substances, at-risk alcohol use prior to pregnancy (Chang et al., 2006), and maternal depression or anxiety (Skagerström et al., 2011). Conversely, a strong social and family support network has been shown to improve maternal mental health and reduce the likelihood of alcohol consumption during pregnancy (Ward et al., 2021). Additionally, a history of physical and/or sexual abuse—regardless of timing—has been associated with increased risk of alcohol use during pregnancy (Haynes et al., 2003). Prenatal alcohol use largely reflects continuation of prepregnancy drinking patterns, particularly before pregnancy recognition (McCormack et al., 2017). Nevertheless, alcohol use *during pregnancy* occurs in a distinct clinical and social context due to its teratogenic risk, and factors such as unplanned pregnancy, delayed pregnancy recognition, heavy drinking by a partner, and history of trauma and interpersonal violence have been shown to particularly elevate risk (Pryor et al., 2017; Skagerström et al., 2011). Given the long-term adverse outcomes associated with PAE, identifying modifiable and/or mitigatable risk and resilience factors is critical for both primary and secondary prevention efforts.

Adverse childhood experiences (ACEs) are defined as potentially traumatic events occurring during childhood, including maltreatment, violence exposure, or family dysfunction (Felitti et al., 1998). A substantial body of literature has linked ACEs to long-term adverse physical and mental health challenges across the lifespan (Racine et al., 2018). In the FASD literature, studies examining *child* ACEs have shown that exposure to adversity following PAE increases risk for neurodevelopmental and behavioral problems, including problems with attention, memory, and language development (Kambeitz et al., 2019; Koponen et al., 2023; Racine et al., 2020; Ward et al., 2021; Wozniak et al., 2019). In addition, a pregnant person's early life adversity during childhood or *maternal* ACEs (*mACEs*) might be a risk factor for substance use, impaired mental health in pregnancy, and adverse perinatal outcomes. Prior research indicated that mACEs were associated with a higher prevalence of substance use, including alcohol use, in pregnancy (Chang et al., 2006; May et al., 2018), including evidence of a dose–response relationship that remained after controlling for prepregnancy alcohol use and other covariates (May et al., 2018). These findings support conceptualizing mACEs as a temporally antecedent factor that may contribute both to PAE and to elevated stress, mood, and trauma symptoms during pregnancy.

Despite emerging evidence, the consistency of these associations across different populations, the specific maternal adversity factors most strongly linked to alcohol use, and the combined effects of mACEs and prenatal alcohol use on maternal mental health remain poorly understood.

This study aimed to address this gap by first examining the association between mACEs and PAE, and then evaluating independent and joint effect of mACEs and PAE on impaired mental health during pregnancy. We hypothesized that higher mACEs exposure would be associated with (a) greater likelihood of alcohol use during pregnancy and (b) worse maternal mental health outcomes.

METHODS

Study data and population

This investigation was conducted using data collected from the ENRICH-2 prospective cohort, a prospective cohort conducted at the University of New Mexico (UNM) between 2018 and 2022 (Maxwell et al., 2024). Briefly, pregnant women were recruited from prenatal care clinics affiliated with the UNM Health Sciences Center. The cohort study incorporated four prospective visits at the following time frames: (V1) second-trimester, (V2) third-trimester, (V3) hospitalization for delivery/birth, (V4) infant neurodevelopmental assessment at approximately 6 months after birth. All participants provided written informed consent for the study, which was approved by the UNM Human Research Protections Office. The following inclusion criteria were applied at enrollment: (1) age ≥18 years; (2) singleton pregnancy; (3) 12–38 weeks gestation; (4) able to give informed consent in English; (5) planning to deliver at UNM Hospital. Individuals with the following characteristics were excluded from analyses: (1) indication of more than occasional (≥1 urine drug test or

more frequent than monthly use per self-report) use of cocaine, methamphetamines, or 3,4-methylenedioxymethamphetamine (MDMA) during the first trimester and any use of these substances in the second or third trimester; (2) gestational age at delivery ≤35 weeks; (3) fetal diagnosis of a major structural anomaly or severe fetal complications requiring prolonged hospital stay; (4) maternal or fetal administration of corticosteroids. Participants who completed V1 and V2 were included in this analysis, and assessment descriptions in this summary pertain to these visits.

Assessment of PAE and other substances

Alcohol use was assessed by a combination of screening questionnaires (AUDIT-C and AUDIT) (Bradley et al., 1998), prospective repeated 4-week Timeline Follow-Back (TLFB) interviews (Sobell et al., 2003; Sobell & Sobell, 1992), targeted questions about binge drinking episodes outside of the TLFB reported windows, and ethanol biomarkers. TLFB interviews captured alcohol use during the periconceptional period ($TLFB_1$), 30 days before V1 ($TLFB_2$), and 30 days before V2 ($TLFB_3$). The following summary measures were estimated: absolute alcohol per day (AAD, ounces) and number of binge episodes (≥4 standard drinks) per each TLFB reported windows and cumulatively during pregnancy $TLFB_{2\text{-}3}$. A panel of ethanol biomarkers (maternal samples collected at V1) consisted of maternal serum gamma-glutamyltransferase (GGT), carbohydrate-deficient transferrin (%dCDT), phosphatidyl ethanol (PEth), urinary ethyl glucuronide (uEtG), and urinary ethyl sulfate (uEtS).

To be initially classified into the Alcohol group, participants met the following criteria: (1) AUDIT-C score ≥2 and (2) reported ≥2 binge episodes (≥4 drinks per occasion) or >13 standard drinks during the periconceptional period. For continuation within the Alcohol group, participants met at least one of the following: (1) >13 standard drinks in the $TLFB_{2\text{-}4}$, (2) ≥1 binge drinking episode during pregnancy, (3) positive for ≥1 ethanol biomarkers. Participants in the Control group met the following criteria: (1) AUDIT-C score <2, no binge episodes, and ≤13 standard drinks in the periconceptional period; (2) no reported alcohol use in pregnancy ($TLFB_{2\text{-}3}$); and (3) negative on all ethanol biomarkers.

Exposures to other substances were characterized by self-report, biomarkers, and review of medical records. The National Survey on Drug Use and Health questionnaire was used to inquire about use of the following with or without a prescription during pregnancy: cannabis (including smoked, vaped, and edible forms), cocaine, crack cocaine, heroin/opium, methamphetamines, methadone, buprenorphine, ecstasy, inhalants (liquids, sprays, gasses), pain relievers (oxycontin, Vicodin®, Percocet®, hydrocodone, morphine, fentanyl, codeine), benzodiazepines, barbiturates, and nicotine products, including combustible tobacco, e-cigarettes, and nicotine replacement products. Self-reported substance use was supplemented with a 7-panel drug test administered at the first study visit (V1) screening for opioids (codeine, morphine, heroin, oxycodone, hydrocodone), amphetamines, cocaine, phencyclidine, cannabis, and MDMA.

Sociodemographic characteristics, maternal mental health, and prenatal environment

Maternal sociodemographic characteristics (age at enrollment, marital status, race, ethnicity, predominant language spoken at home, education attainment, family annual income, employment, and health insurance status) were collected at V1. At V2 (third trimester), validated questionnaires were administered to assess maternal psychosocial stress and mental health. These measures included the Perceived Stress Scale (PSS; Cohen et al., 1994), the Generalized Anxiety Disorders-7 questionnaire (GAD-7; Simpson et al., 2014), the Edinburgh Depression Scale (EDS; Bergink et al., 2011; Gibson et al., 2009), and the Posttraumatic Stress Disorder Checklist for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (PCL-5; Levey et al., 2018).

The PSS is a 10-item self-report measure of perceived stress over the past 30 days, assessing the extent to which individuals view their lives as unpredictable, uncontrollable, and overloaded. The PSS-10 has demonstrated acceptable psychometric properties, with internal consistency reliability (Cronbach's α) exceeding 0.70 across studies (Lee, 2012). The GAD-7 is a 7-item self-report measure assessing symptoms of worry and generalized anxiety, with excellent internal consistency (Cronbach's $\alpha = 0.92$). Items are rated on a 4-point Likert scale (0–3), yielding total scores ranging from 0 to 21; scores ≥10 indicate clinically significant anxiety (Johnson et al., 2019; Spitzer et al., 2006). The EDS assesses depressive symptoms experienced over the past 7 days and demonstrates good internal consistency (Cronbach's $\alpha = 0.94$; Moyer et al., 2024). Items are scored on a 4-point scale, with a total score ≥10 indicating probable minor depression and a score ≥13 indicating probable major depression (Matthey, 2008). The PCL-5 is a 20-item self-report measure that assesses posttraumatic stress symptoms severity over the past month, with items rated from 0 (not at all) to 4 (extremely), and has excellent internal consistency (Cronbach's $\alpha = 0.94$; Blevins et al., 2015). Additionally, the 10-item ACEs questionnaire that queried participants about childhood abuse, household challenges, and neglect (Felitti et al., 1998) was administered. Participants with ≥4 adverse childhood experiences were categorized as High mACEs, consistent with established literature identifying ACE ≥4 as a high-risk threshold (Campbell et al., 2016).

Statistical analyses

Participant demographic and clinical characteristics were summarized with frequencies for categorical variables and mean/standard deviations for numeric variables. Chi-square (or Fisher's exact test as an equivalent) was used for comparisons between Alcohol and Control groups of categorical variables, and Mann–Whitney test was used for comparisons of continuous variables between the groups. Prevalence of High mACEs and specific types of childhood adversity, which are captured by the ACE

questionnaire, were compared between Alcohol and Control groups by chi-square test. Spearman correlation was used to assess the association between mACE score and AAD within the Alcohol group. To further examine the independent effects of Alcohol and mACEs and their combination, mean scores derived from mental health questionnaires (PSS, GAD-7, EDS, and PCL-5) were compared among the 4 groups: Control ($n=84$), High mACEs ($n=22$), Alcohol ($n=36$), and Alcohol + High mACEs ($n=22$) by analysis of variance (ANOVA). Subsequently, these associations were further examined in a multivariable linear regression that included adjustment for marijuana and nicotine use in pregnancy—two variables that differed significantly among the study groups and were included to reduce confounding, particularly given their known associations with maternal mental health in prior studies. Since participants did not vary on sociodemographic characteristics (either in 2- or 4-group analyses), these variables were not included in the multivariable models. Household income was additionally evaluated in sensitivity analyses. Percent of variability explained by the predictors (R^2) in regressions was estimated for each mental health outcome. Statistical analyses were conducted using the SAS software (version 9.4; SAS institute, Cary, NC, USA). An alpha level of 0.05 was considered statistically significant.

RESULTS

The sample represented diverse sociodemographic backgrounds, with 66.5% self-identifying as Hispanic/Latine, 3.0% as American Indian, and 16.5% as multiracial or other. Participants represented the full spectrum of educational attainment, with 36.0% having a high school education or less and 40.2% holding a college degree or higher; 37.2% having income below $30,000 and 26.8% with income at or over $70,000. There were no differences in sociodemographic characteristics or gestational age at enrollment into the study among Alcohol and Control groups (all p values >0.05; Table 1). However, participants classified into the Alcohol group had a significantly higher prevalence of cannabis (39.7% vs. 9.4%) and nicotine (19.0% vs. 1.9%) exposure compared to the Control group (both p values <0.001). Among participants categorized into the Alcohol group, the average alcohol consumption across the periconceptional period and during pregnancy was approximately 2.9 drinks per week (AAD: 0.204 ± 0.343); 87.9% reported ≥1 binge episode since the last menstrual period (mostly before pregnancy recognition), and 25.9% tested positive for ≥1 ethanol biomarker at V1.

As shown in Table 2, mean mACEs score was higher in the Alcohol group (3.03 ± 2.93 vs. 2.04 ± 2.20; $p=0.02$), and the proportion of participants with mACEs≥4 was almost twice as high (37.9% vs. 20.8%; $p=0.02$) compared to the Control group. Within the Alcohol group, there was a significant positive association between mACEs score and AAD across the periconceptual period and pregnancy ($\rho=0.18$, $p=0.02$). With respect to specific types of mACEs,

TABLE 1 Demographic and medical characteristics of study participants ($n=164$).

Characteristics	Alcohol ($n=58$) N (%)	Control ($n=106$) N (%)	p
Ethnicity (Hispanic/Latine)	40 (69.0%)	69 (65.1%)	0.62[a]
Race			
White	44 (75.9%)	67 (63.2%)	0.54[b]
Black or African American	2 (3.4%)	3 (2.8%)	
American Indian or Alaskan Native	3 (5.2%)	8 (7.5%)	
Multi-racial/other	7 (12.0%)	20 (18.9%)	
Prefer not to report	2 (3.4%)	8 (7.6%)	
Education			
High school or less	21 (36.2%)	38 (35.8%)	0.39[b]
Some college or vocational school	17 (29.3%)	22 (20.8%)	
College degree or higher	20 (34.5%)	46 (43.4%)	
Family income			
Not reported	1 (1.7%)	1 (0.9%)	0.22[b]
Under $30,000	22 (37.9%)	39 (36.8%)	
$30,000–49,000	17 (29.3%)	18 (17.0%)	
$50,000–69,000	6 (10.3%)	16 (15.1%)	
$70,000 or over	12 (20.7%)	32 (30.2%)	
Cannabis use	23 (39.7%)	10 (9.4%)	<0.001[b]
Tobacco use	11 (19.0%)	2 (1.9%)	<0.001[b]
	Mean ± SD	Mean ± SD	
Maternal age at enrollment	29.26 ± 5.92	29.31 ± 6.10	0.96[c]
Gestational age at enrollment	25.25 ± 6.39	24.41 ± 6.24	0.42[c]
Gestational age at V2	32.23 ± 2.86	31.55 ± 2.97	0.17[c]
Alcohol use			
AAD averaged across periconceptional period and during pregnancy	0.204 ± 0.343	0.002 ± 0.006	<0.001[d]
≥1 binge episode during pregnancy	51 (87.9%)	0 (0.0%)	<0.001[b]
Positive for ≥1 ethanol biomarker	15 (25.9%)	0 (0.0%)	<0.001[b]

Abbreviations: AAD, absolute alcohol per day (oz).

[a]Based on chi-square test.

[b]Based on Fisher's exact test.

[c]Based on t-test.

[d]Based on Mann–Whitney test.

the Alcohol group had a significantly higher prevalence of physical abuse (31.0% vs. 16.0%), exposure to substance abuse in the household (46.6% vs. 24.5%), and incarceration of a family member (25.9% vs. 11.3%; all p values <0.05).

To examine independent and cumulative effects of PAE and mACEs, subsequent analyses were conducted based on four groups: Control, High mACEs (mACEs≥4), Alcohol, and Alcohol + High mACEs. Figure 1 shows mean scores for each mental health instrument by four groups. One-way ANOVAs conducted for each outcome (stress, depression, anxiety, PTSD) revealed significant omnibus group differences (all p values <0.001); detailed F statistics and degrees of freedom are provided in Figure 1. Significant differences among the 4 groups were observed for all mental health outcomes ($p<0.001$). Across all outcomes, the group means followed the same ordering: lowest in the Control group and highest in the Alcohol + High mACEs group, with Alcohol and High ACE falling in between. Formal pairwise comparisons were not performed due to concerns about multiple testing.

TABLE 2 Distribution of mACEs among Alcohol and Control groups ($n=164$).

mACEs	Alcohol ($N=58$)	Control ($N=106$)	p
Overall mACEs ≥ 4	22 (37.9%)	22 (20.8%)	0.02
Mean mACEs score	3.03 ± 2.93	2.04 ± 2.20	0.02
Specific types of mACEs			
Abuse			
Psychological abuse	17 (29.3%)	31 (29.2%)	0.94
Physical abuse	18 (31.0%)	17 (16.0%)	0.02
Sexual abuse	15 (25.9%)	17 (16.0%)	0.14
Neglect			
Lack of support	18 (31.0%)	21 (19.8%)	0.11
Basic needs unmet	6 (10.3%)	5 (4.7%)	0.20
Household dysfunction			
Violent treatment of mother/stepmother	12 (20.7%)	13 (12.3%)	0.15
Exposure to substance abuse	27 (46.6%)	26 (24.5%)	<0.01
Mental illness/suicide in the household	22 (37.9%)	27 (25.5%)	0.10
Parental separation	26 (44.8%)	47 (44.3%)	0.95
Incarceration of a family member	15 (25.9%)	12 (11.3%)	0.02

Note: p-values calculated using chi-square test (or Fisher's exact) for frequencies and t-test for the mean ACE score.

In multivariable analysis (Table 3), after adjusting for marijuana and tobacco use, the High mACEs and Alcohol + High mACEs groups had significantly higher regression-estimated symptom scores across all mental health outcomes compared with the Control group (all $ps<0.01$). Alcohol group was associated with an increase in PSS and EDS scores (p values <0.01) compared to Controls. After adjusting for study-group status, neither cannabis nor nicotine use demonstrated an independent association with any of the mental health outcomes (all p values >0.05). In sensitivity analyses, household income was not significantly associated with any of the four mental health outcomes and did not alter the effect estimates for mACEs, alcohol use, or their combination (data not shown). Proportion of variance in the outcome explained by the model predictors varied from 0.12 to 0.19 with the highest R^2 observed for the PCL-5 scores.

DISCUSSION

Results of this study demonstrate a strong association between maternal ACEs and alcohol use in pregnancy. In our study population, the prevalence of 4 or more ACEs in the Alcohol group was almost twice as high as in the Control group (38% vs. 21%). Participants with a history of physical abuse, substance use in the household, and incarceration of family members were particularly overrepresented among those who used alcohol in pregnancy. Our study not only demonstrated an association between High mACEs and alcohol use but also found a significant dose–response relationship between the number of mACEs (severity) and intensity of alcohol use. By design, the ENRICH-2 study focused on mild-to-moderate alcohol use in pregnancy, a far more prevalent exposure than heavy use or Alcohol Use Disorder (AUD). It is possible that the prevalence and impact of mACEs could be even greater among pregnant individuals with heavier alcohol use or AUD, underscoring the public health relevance of these findings.

Our study also demonstrated that both maternal alcohol use and mACEs were independently associated with worse maternal mental health scores. Consistent with our hypothesis, visual inspection

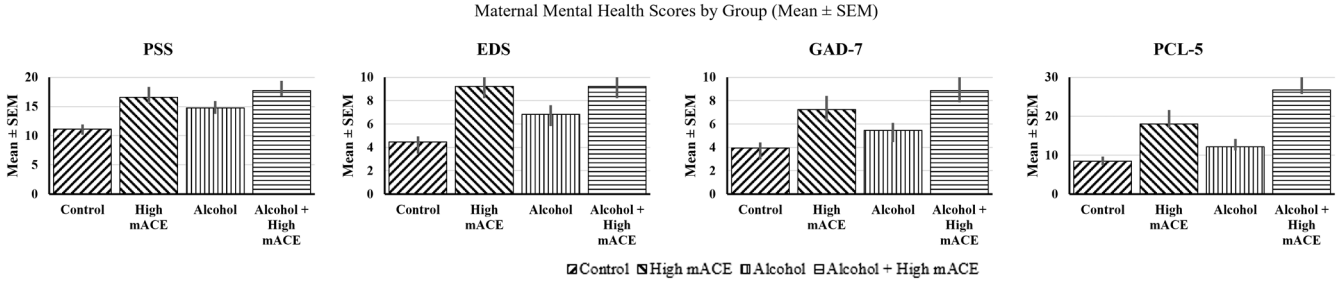

FIGURE 1 Mean differences in maternal mental health scores by PAE and mACEs. PSS: $F=6.81$, df = 3, $p<0.001$; EDS: $F=7.46$, df = 3, $p<0.001$; GAD-7: $F=8.05$, df = 3, $p<0.001$; PCL-5: $F=11.49$, df = 3, $p<0.001$.

TABLE 3 Associations between study groups and maternal mental health outcomes: Results of multivariable linear regression.

	Maternal mental health outcomes							
	PSS		GAD-7		EDS		PCL-5	
Predictors	Estimate (SE)	*p*	Estimate (SE)	*p*	Estimate (SE)	*p*	Estimate (SE)	*p*
Intercept	11.19 (0.82)	<0.001	4.04 (0.53)	<0.001	4.46 (0.58)	<0.001	8.29 (1.51)	<0.001
Study group								
Control (Ref.)	—		—		—		—	
High mACEs	5.27 (1.80)	<0.01	3.32 (1.16)	<0.01	4.66 (1.29)	<0.001	8.82 (3.33)	<0.01
Alcohol	3.70 (1.50)	0.01	1.71 (0.97)	0.08	2.40 (1.07)	0.03	3.53 (2.77)	0.21
Alcohol + High mACEs	7.21 (2.25)	<0.01	6.09 (1.45)	<0.001	4.96 (1.61)	<0.01	17.38 (4.16)	<0.001
Cannabis	0.37 (1.72)	0.83	−0.58 (1.11)	0.60	0.48 (1.23)	0.70	3.91 (3.18)	0.22
Nicotine	−2.61 (2.37)	0.27	−2.34 (1.53)	0.13	−1.48 (1.70)	0.39	−4.90 (4.38)	0.26
% Variance explained	$R^2 = 0.12$		$R^2 = 0.14$		$R^2 = 0.14$		$R^2 = 0.19$	

Note: Each mental health outcome was modeled using a multivariable linear regression including all predictors listed in the table.

of group means showed a graded distribution across the four study groups, with the Alcohol + High mACEs group displaying the highest average levels of prenatal stress, depressive symptoms, anxiety, and PTSD-related symptoms. These observations are descriptive only, as no pairwise comparisons were conducted. In multivariable regression models adjusting for other substances, high maternal ACEs exposure was associated with larger increases in mental health symptomatology than the effect of mild-to-moderate alcohol use alone, and the combined Alcohol + High mACEs group showed the greatest elevations across all outcomes. This observed pattern aligns with evidence that cumulative childhood adversity can have enduring effects on stress regulation and emotional functioning later in life (Kalia & Knauft, 2020; Miu et al., 2022), while the effects of mild-to-moderate alcohol use on mental health are more variable (Boden et al., 2016). It is also important to emphasize that the associations between PAE and mental health are likely bidirectional. Moreover, given that the ENRICH-2 cohort was designed to focus on mild-to-moderate PAE and none of the individuals were diagnosed with AUD, the observed associations in the Alcohol group may be attenuated relative to those expected with heavier exposure or AUD. Overall, these results suggest that both maternal ACE exposure and PAE are associated with poorer maternal mental health during pregnancy, with the greatest symptom burden observed among women experiencing both exposures. These findings underscore the value of incorporating ACE-informed assessment into prenatal care to better identify women who may need additional support.

Most prior studies assessed associations between mACEs and tobacco (Pear et al., 2017), cannabis (Thomas et al., 2023), and illicit drug use or the role of maternal mental health as a mediator between mACEs and adverse perinatal outcomes (Duka et al., 2023; Osofsky et al., 2021). For example, the All Our Families Cohort conducted in Canada reported that women with ≥4 ACEs had almost a fourfold increase in illicit drug use in pregnancy, relative to women with 0–1 ACEs after adjustment for confounders (Currie & Tough, 2021). A pilot study among prenatal care patients at the Kaiser Permanente Northern California demonstrated that patients with ≥1 ACEs had higher odds of anxiety and depressive disorders, depressive symptoms, inter-partner violence, and any prenatal substance use (Foti et al., 2023). Although cannabis and tobacco use have been linked to maternal mental health in prior studies (Brannigan et al., 2022; Brown et al., 2023), neither emerged as an independent predictor of stress, mood, or trauma symptoms in our adjusted models. This likely reflects the stronger influence of mACEs and PAE in this cohort, as well as differences in analytic approaches across studies. Importantly, cannabis and tobacco were included as covariates to reduce confounding rather than as primary exposures of interest. To our knowledge, no prior studies have prospectively examined alcohol use during pregnancy in relation to mACEs using a comprehensive, multimethod assessment approach, highlighting the novel and rigorous contribution of our study to the field.

Our findings also suggest that physical abuse, exposure to substance abuse in the household, and incarceration of a family member may pose a particular risk for alcohol use in pregnancy. Prior studies also suggest that the type of adversity may differentially influence prenatal substance use, although findings regarding which types pose the highest risk are heterogeneous. For example, the Evidence for Better Lives Study, which recruited participants from 8 low- and middle-income countries, reported that pregnant women with emotional abuse and those "highly maltreated" during childhood were more likely to report substance use in pregnancy (Hemady et al., 2022). A cross-sectional study conducted at obstetrics clinics affiliated with a large urban academic hospital in Southern United States, where substance use was assessed by the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) screener (Humeniuk et al., 2008), found that overall mACEs score was associated with tobacco but not alcohol use, whereas household dysfunction was linked to both tobacco and alcohol use during pregnancy (Osofsky et al., 2021). These results, together with our data, underscore the importance of considering specific domains of childhood adversity when examining maternal substance use.

There is an extensive body of literature linking ACEs to adverse mental health outcomes in adulthood. For example, a systematic review and a meta-analyses of 37 studies estimated that having four or more ACEs is strongly (odds ratio [OR] >3 to 6) associated with sexual risk taking, mental ill health, and problematic alcohol use and very strongly associated (OR > 7) with the problematic drug use and interpersonal and self-directed violence later in life (Hughes et al., 2017). Similarly, another meta-analyses of 23 large studies estimated that as many as 30% of cases of anxiety and 40% of cases of depression in North America might be attributable to ACEs (Bellis et al., 2019). While these findings underscore the profound and long-lasting impact of ACEs on adult mental health, far less is known about how maternal childhood adversity affects mental health during the pregnancy and postpartum period. A recent systematic review concluded that mACEs, especially those involving maltreatment during childhood, were predictive of adverse perinatal mental health outcomes, including anxiety, posttraumatic stress disorder, and substance use (Hipke, 2024).

There is also growing interest in how early life adversity can become neurobiologically embedded, exerting lasting effects on neurodevelopment, as well as in recent studies exploring the "transgenerational transmission" of ACEs. Epigenetic changes, fetal programming of serotonin, the hypothalamic–pituitary–adrenal axis, and immune regulatory systems were implicated as possible mechanisms (Bouvette-Turcot et al., 2015; Stenz et al., 2018; Zhou & Ryan, 2023). Recently, the role of the placenta in fetal programming of neurodevelopmental and adult-onset mental health disorders began being recognized, leading to the coinage of the term "placenta-brain-axis" (Rosenfeld, 2021). Several ongoing investigations, including work from our research group, are examining putative placenta-mediated mechanisms involved in transgenerational transmission of ACEs.

We would like to acknowledge several limitations of the study. First, while the study assessed different types of mACEs and their severity, we did not query information about specific timing of early life adversity or duration. Prior research indicates that adversity during particularly sensitive developmental windows, which vary for specific neurobehavioral domains, can have lasting effects on brain development and function (Nelson & Gabard-Durnam, 2020). Additionally, while a well-established ACE questionnaire was used, pregnant women retrospectively recalled their adverse childhood experiences. Second, the generalizability of these findings to other populations may be limited, as participants were recruited from a single geographic region; though the sample included individuals across diverse socio-economic and racial/ethnic backgrounds, enhancing the relevance of the results. Third, a relatively small sample size, especially for subgroup analyses, may have resulted in limited statistical power for detecting smaller effects. Fourth, although we examined four related mental health outcomes in separate multivariable models, which reflects our prespecified analytic plan, testing multiple correlated outcomes may still increase the risk of Type I error. Findings should therefore be interpreted with appropriate caution. Fifth, although still an emerging area of research, there is increasing recognition that positive childhood experiences (PCEs) (Elmore et al., 2020) or protective and compensatory experiences (PACEs) (Morris & Hays-Grudo, 2023) can buffer the effects of childhood adversity. Our study did not assess PACEs, which may moderate the relationships observed between maternal ACEs, mental health, and prenatal alcohol use. Finally, we want to acknowledge that this study does not establish causality between mACEs, maternal mental health, and alcohol use.

The study also had some unique strengths. First, we examined specific ACE categories of maternal early childhood adversity, providing a more granular understanding of the primary risk factors. Second, assessment of alcohol use in pregnancy was done in a prospective manner with repeated biomarkers and a state-of-the-art panel of biomarkers, providing accurate, quantitative exposure data. Additionally, as mentioned earlier, our study focused on the mild-to-moderate level of alcohol exposure, which is particularly important given that the pattern of use is much more prevalent in the general obstetrics population than heavy drinking or AUD. This strengthens the generalizability of the results and further highlights this highly prevalent, often unrecognized, public health concern. Finally, to our knowledge, this is the first study to demonstrate that maternal ACEs and alcohol use during pregnancy independently contribute to worse maternal mental health, and that their co-occurrence identifies women at greatest risk.

In conclusion, this study underscores the lasting influence of early life adversity as a risk factor for both alcohol use during pregnancy and impaired maternal mental health. Given that both maternal childhood adversity (Ciciolla et al., 2021; Hardcastle et al., 2022) and PAE (Garrison et al., 2019) are associated with adverse perinatal and pediatric outcomes, understanding their independent and combined effects is critical for identifying high-risk pregnancies and informing targeted prevention and intervention strategies. Assessing mACEs in prenatal or preconception care may help risk-stratify individuals who could benefit from additional support around trauma-informed care and health behaviors (Seng, 1995), but mACEs should be considered within a broader risk profile rather than as a stand-alone tool for detecting alcohol use during pregnancy. There is emerging evidence that resilience-building interventions among adults might improve coping skills and health behaviors (Chandler et al., 2015). Prior work has demonstrated the effectiveness of multicomponent, harm reduction, home-visitation-based interventions for pregnant and postpartum women with histories of alcohol or substance use histories, such as Parent–Child Assistance and First Steps Programs in Washington State (Grant, 1996; Grant et al., 2005; Rasmussen et al., 2012; Stoner et al., 2023). These programs relied on advocacy-based case management that acknowledges trauma, adversity, mental health challenges, and social instability as contextual contributors to substance use. However, trauma has generally been addressed implicitly rather than through explicit assessment of maternal childhood adversity and active integration of maternal mental health into intervention approaches. Future studies should build on this foundational work by evaluating the effectiveness of multi-factorial interventions, which explicitly address both alcohol

or substance use and maternal trauma, especially given that pregnancy represents not only a unique window of vulnerability but also an opportunity to interrupt transgenerational "transmission" of adversity and psychiatric vulnerability. Future studies should also examine the mechanisms linking maternal ACEs to perinatal alcohol use and mental health, including potential neurobiological and psychosocial pathways. Longitudinal research following mothers and children could clarify the intergenerational impact of ACEs and inform targeted interventions to reduce risk and improve outcomes.

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CONFLICT OF INTEREST STATEMENT

None of the authors have a conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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