

Association Between Adverse Childhood Experiences and Adverse Pregnancy Outcomes

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OBJECTIVE: To examine the association between adverse childhood experiences and adverse pregnancy outcomes.

METHODS: This cohort study included individuals who enrolled in a perinatal collaborative mental health care program (COMPASS [the Collaborative Care Model for Perinatal Depression Support Services]) between 2017 and 2021. Participants completed psychosocial self-assessments, including an adverse childhood experiences screen. The primary exposure was adverse childhood experiences measured by the ACE (adverse childhood experience) score, which was evaluated as a dichotomized variable, with a high ACE score defined as greater

than three. Secondary analyses used the ACE score as a continuous variable. Adverse pregnancy outcomes including gestational diabetes, hypertensive disorders of pregnancy, preterm birth, and small-for-gestational-age (SGA) births were abstracted from the electronic health record. Bivariable and multivariable analyses were performed, including mediation analyses.

RESULTS: Of the 1,274 women with a completed adverse childhood experiences screen, 904 (71%) reported one or more adverse childhood experiences, and 290 (23%) reported a high ACE score (more than three adverse childhood experiences). Adverse childhood experience scores were not associated with gestational diabetes or SGA births. After controlling for potential confounders, individuals with high ACE score had 1.55-fold (95% CI 1.06–2.26) increased odds of having hypertensive disorders of pregnancy and 2.03-fold (95% CI 1.38–2.99) increased odds of preterm birth. Each point increase in ACE score was not associated with a statistically increased odds of hypertensive disorders of pregnancy (adjusted odds ratio [aOR] 1.07, 95% CI 0.99–1.15); however, each additional point on the adverse childhood experiences screen was associated with increased odds of preterm birth (aOR 1.13, 95% CI 1.05–1.22). Mediation analyses demonstrated tobacco use, chronic medical problems, and obesity each partially mediated the observed association between high ACE scores and hypertensive disorders of pregnancy. Having chronic medical comorbidities partially mediated the observed association between high ACE scores and preterm birth.

CONCLUSION: One in four individuals referred to a perinatal mental health program who were pregnant or postpartum had a high ACE score. Having a high ACE score was associated with an increased risk of hypertensive disorders of pregnancy and preterm birth. These results underscore how remote events may reverberate through the life course.

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Adverse childhood experiences, traumatic events that occur in childhood including exposures to abuse or neglect, parental separation or divorce, or parental mental health conditions or substance use disorder, are consistently associated with chronic health conditions later in life with a dose–response relationship.^{1,2} Adverse childhood experiences are common, with 62% of Americans reporting at least one adverse childhood experience, 25% reporting at least three, and 16% reporting at least four.^{3,4} Moreover, adverse childhood experiences are disproportionately prevalent among those facing social adversity, including structural racism and poverty.⁵ As adverse childhood experiences may alter life trajectories, including educational attainment and employment status, primary prevention of adverse childhood experiences and mitigation of their effects are essential components of an equity-focused public health strategy.

There is biological plausibility for a relationship between adverse childhood experiences and adverse pregnancy outcomes. Adverse childhood experiences are known to affect the long-term development of the neuroendocrine and immune systems; these alterations, in turn, have been associated with adverse pregnancy outcomes.^{6,7} One mechanism by which adverse childhood experiences affect lifelong health is by altering the internalization of perceived stress through increased cortisol production in the setting of a stress exposure.⁸ High levels of cortisol increase the release of pro-inflammatory cytokines,⁹ which are, in turn, associated with gestational diabetes, hypertensive disorders of pregnancy, preterm birth, and small-for-gestational-age (SGA) births.^{10–15} In addition to these biological pathways, social determinants, including education and income, likely mediate the observed relationship.¹⁵

Prior studies (Appendix 1, available online at <http://links.lww.com/AOG/C460>) that have examined this relationship are limited by small sample sizes,¹³ populations with limited generalizability,^{16,17} or significant concern for confounding bias.^{18–20} To fill this evidence gap, our objective was to examine the association between adverse childhood experiences and adverse perinatal outcomes using a diverse sample of individuals with perinatal mental health conditions. We hypothesized that having a high ACE (adverse childhood experience) score would be associated with an increased prevalence of adverse pregnancy outcomes.

METHODS

This cohort study included all pregnant and postpartum individuals who enrolled in COMPASS (the

Collaborative Care Model for Perinatal Depression Support Services) on or after its inception on January 23, 2017, through March 1, 2021, and individuals who delivered after 20 weeks of gestation. COMPASS is a perinatal mental health system embedded within all five of the Northwestern Medicine obstetrics clinics.²¹ Obstetric patients were eligible for enrollment if they had either a history of a mental health condition or current mental health symptoms. COMPASS provides mental health services, guided by collaborative care model principles,²² during pregnancy and up to one year postpartum.

On enrollment in COMPASS, individuals were asked to complete self-reported psychosocial assessments, which included 10 types of adversity that occurred before the age of 18 that are described in the Centers for Disease Control and Prevention's (CDC) Kaiser ACE Study.¹ These assessments were completed directly in a participant registry, housed in REDCap.²³ Individuals who did not complete the adverse childhood experiences screen were excluded from these analyses. Sociodemographic characteristics, which included maternal age, insurance, self-reported race and ethnicity, marital status, medical history including tobacco use, medical conditions, body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) at delivery, obstetric history including parity, and regnancy outcomes such as gestational diabetes, hypertensive disorders of pregnancy, preterm birth, and SGA births were abstracted from the electronic health record. Gestational diabetes was diagnosed by either a glucose challenge test result higher than 200 mg/dL or results from a glucose tolerance test that met the Carpenter-Coustan diagnostic criteria.²⁴ Hypertensive disorders of pregnancy were diagnosed by the attending obstetric clinician, in accordance with criteria defined by the American College of Obstetricians and Gynecologists.²⁵ Gestational age at delivery was calculated from the estimated due date, derived using American College of Obstetricians and Gynecologists standards,²⁶ and preterm birth was defined as delivery before 37 weeks of gestation. Neonates were classified as SGA if their birth weight was below the 10th percentile of normative birth weights for singletons.²⁷

Adverse childhood experiences were evaluated as a categorical variable with a high ACE score defined as greater than three adverse childhood experiences in accordance with prior work.¹ Secondary analyses evaluated adverse childhood experiences as a continuous variable. Bivariable analyses were conducted using *t* tests or Mann Whitney U tests for continuous variables or χ^2 or Fisher exact tests for categorical



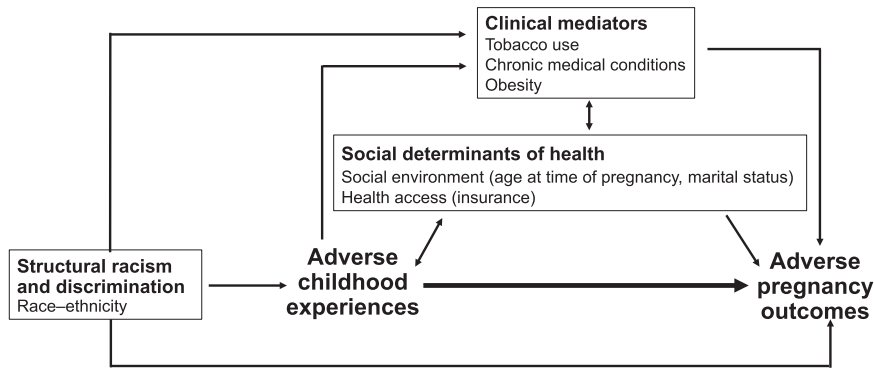


Fig. 1. Directed acyclic graph for the association between adverse childhood experiences and adverse pregnancy outcomes. Miller. *Adverse Childhood Experiences and Adverse Pregnancy Outcomes. Obstet Gynecol* 2021.

variables, as appropriate. Given the complex interrelatedness of social determinants of health, a directed acyclic graph (Fig. 1) was generated to represent potential causal networks and inform covariate adjustment. Variables with plausible roles as confounders in the directed acyclic graph that were significantly different in bivariable analyses were considered as potential confounders. Although race and ethnicity have been associated with both adverse childhood experiences and adverse pregnancy outcomes,^{8,28} their roles as a surrogate for structural racism and discrimination were felt to be potentially antecedent to the adverse childhood experiences exposure; without metrics to ascribe temporality to these lived experiences, race and ethnicity were not included as confounders. Bivariable analyses were performed to evaluate associations between participant characteristics and missing data for the adverse childhood experiences screen. These associations were used to perform a sensitivity analysis using multiple imputation. Given the specific pregnancy risks faced by people in their first pregnancies, additional sensitivity analyses were performed including just those who were nulliparous.

For adverse pregnancy outcomes with significant associations with ACE score in bivariable analyses, mediation analyses were performed to inform the underlying pathways of the association.^{29,30} Variables considered as potential mediators were identified using the directed acyclic graph (Fig. 1). The percentage of the total effect that was mediated by a given factor was calculated by dividing the beta coefficient of the indirect pathway by the summation of the beta coefficients of the indirect and direct pathways. As indirect effects are often nonparametric, standard errors and CIs for each mediator were estimated using bootstrapping with 5,000 replications and bias correction. STATA 15.0 was used for analyses. This study was approved by Northwestern University's Institutional Review Board before its initiation.

RESULTS

During the study period, 2,016 individuals were referred to COMPASS for mental health care and met eligibility criteria; 742 (37%) were excluded because they did not complete the adverse childhood experiences screen. ACE scores for the remaining 1,274 participants are shown in Figure 2. Of the individuals included, 904 (71%) reported one or more adverse childhood experiences, and 290 (23%) reported a high ACE score (ie, a score greater than three).

Sociodemographic and clinical characteristics of the sample, stratified by high ACE score, are shown in Table 1. Patients with high ACE scores (higher than 3) were more likely to be younger at time of delivery, have government-supported insurance (eg, Medicaid), use tobacco, have a chronic medical condition, and have a higher BMI at delivery. Patients with high ACE scores were less likely to be married. Self-identified race and ethnicity also differed by adverse

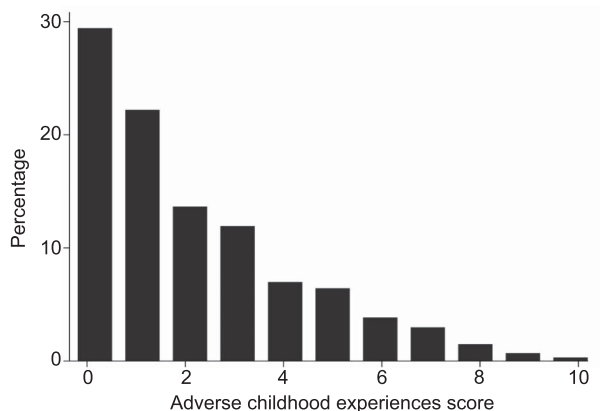


Fig. 2. Distribution of adverse childhood experiences scores.

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Table 1. Sociodemographic and Clinical Characteristics, Stratified by High Adverse Childhood Experiences Score

Characteristic	ACE Score		P
	3 or Lower (n=984 [77])	Higher Than 3 (n=290 [23])	
Maternal age (y)	33±5	32±6	<.001
Public insurance (n=1,225)	138 (14.6)	106 (37.7)	<.001
Race (n=1,225)			<.001
White	555 (58.8)	112 (39.9)	
African American or Black	146 (15.5)	104 (37.0)	
Asian	58 (6.1)	10 (3.6)	
Other*	84 (8.9)	30 (10.7)	
Unknown	101 (10.7)	25 (8.9)	
Latinx ethnicity (n=1,146)	131 (14.8)	56 (21.3)	.013
Married (n=1,224)	692 (73.4)	131 (46.6)	<.001
Ever used tobacco (n=1,216)	144 (15.4)	84 (30.2)	<.001
Any chronic medical condition (n=1,215)	425 (45.4)	154 (55.4)	.003
Preexisting diabetes	36 (3.7)	14 (4.8)	.37
Chronic hypertension	58 (5.9)	21 (7.2)	.40
BMI at delivery (kg/m ²) (n=1,157)	32±7	33±7	.002
Higher than 30	458 (51.4)	164 (61.9)	.003
Nulliparous	538 (54.7)	140 (48.3)	.055
Prior history of preterm birth (n=1,219)	54 (5.7)	31 (11.1)	.002

ACE, adverse childhood experiences; BMI, body mass index.

Data are mean±SD or n (%) unless otherwise specified.

* Includes individuals who self-identified as American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, or other.

childhood experiences exposure, with people identifying as White or Asian less likely to have a high ACE score than those who identified as Black.

Associations between high ACE score and adverse pregnancy outcomes are described in Table 2. After controlling for potential confounders (including maternal age, insurance, marital status, tobacco use, chronic medical conditions, and obesity), individuals with high ACE score had 1.6-fold increased odds of having a hypertensive disorder of pregnancy and 2.0-fold increased odds of preterm birth. No differences were observed in gestational diabetes or SGA births, though it should be noted that the point estimates for

each of these outcomes were higher in those with high ACE scores compared with those without a high ACE score.

As a secondary analysis, ACE score was analyzed as a continuous variable. Each additional point on the adverse childhood experiences screen was associated with 10% increased odds of hypertensive disorders of pregnancy (odds ratio 1.10, 95% CI 1.03–1.18); however, this finding did not remain significant in multivariable analyses (adjusted odds ratio 1.07, 95% CI 0.99–1.15). Each additional point on the adverse childhood experiences screen also was associated with 15% increased odds of preterm birth (odds ratio 1.15,

Table 2. Bivariable and Multivariable Analyses of the Associations Between Adverse Childhood Experiences and Adverse Pregnancy Outcomes

Outcome	ACE Score		OR (95% CI)	aOR (95% CI)*
	3 or Lower	Higher Than 3		
Gestational diabetes (n=1,170)	60 (6.7)	20 (7.4)	1.11 (0.66–1.88)	1.21 (0.70–2.11)
HDP	126 (12.8)	58 (20.0)	1.58 (1.08–2.32)	1.55 (1.06–2.26)
Preterm birth (n=1,271)	120 (12.2)	67 (23.1)	2.16 (1.54–3.01)	2.03 (1.38–2.99)
SGA (n=1,149)	39 (4.4)	14 (5.3)	1.20 (0.64–2.25)	— [†]

ACE, adverse childhood experiences; OR, odds ratio; aOR, adjusted odds ratio; HDP, hypertensive disorder of pregnancy; SGA, small for gestation age.

Data are n (%) unless otherwise specified.

* Multivariable analyses adjusted for maternal age, insurance, marital status, tobacco use, chronic medical conditions, and obesity.

[†] Cell count too small for multivariable analysis.



Table 3. Mediation Analyses

	Proportion of Total Effect Mediated (%)	95% CI (%)
HDP		
Tobacco use	5.3	4.2–6.7
Any chronic medical comorbidity	11.5	9.8–13.4
Obesity	17.4	15.4–19.6
Preterm birth		
Tobacco use	0.4	0.2–1.0
Any chronic medical comorbidity	6.7	5.3–8.2
Obesity	0.1	0.0–0.4

HDP, hypertensive disorder of pregnancy.

Obesity was defined as body mass index higher than 30 at delivery.

95% CI 1.08–1.23); this association remained significant in multivariable analyses (adjusted odds ratio 1.13, 95% CI 1.05–1.22).

A review of missing data demonstrated that those with missing adverse childhood experiences data were younger (33 [interquartile range 30–36] vs 33 [interquartile range 29–36], $P < .001$); were more likely to have public insurance (25% vs 20%, $P = .012$), identify as Black (27% vs 20%, $P = .002$), be married (60% vs 67%, $P = .002$); and were less likely to be nulliparous (48% vs 53%, $P = .018$). These identified associations were used to perform multiple imputation. Bivariable and multivariable analyses were conducted with these imputed data with results depicted in Appendix 2, available online at <http://links.lww.com/AOG/C460>. After multiple imputation, the associations between a high ACE score and preterm birth, and between a high ACE score and hypertensive disorders of pregnancy were not changed. Analyses including only those who were nulliparous similarly did not change the results.

Mediation analyses were conducted for the outcomes of hypertensive disorders of pregnancy and preterm birth. Tobacco use, chronic medical problems, and obesity each partially mediated the observed association between high ACE scores and hypertensive disorders of pregnancy (Table 3). Having chronic medical comorbidities partially mediated the observed association between high ACE scores and preterm birth (Table 3). There was no other statistically significant mediation present.

DISCUSSION

In this study, one in four pregnant or postpartum individuals referred for perinatal mental health care had a high ACE score, consistent with national CDC and Behavioral Risk Factor Surveillance System estimates.^{4,5} We found that a high ACE score was associated with hypertensive disorders of pregnancy and preterm birth. These data amplify the importance of

the CDC's campaign to prevent adverse childhood experiences to improve U.S. health³¹ and emphasize the potential of prevention to mitigate the intergenerational transmission of trauma. The association of adverse childhood experiences with hypertensive disorders of pregnancy was mediated by tobacco use, chronic medical comorbidities, and obesity, whereas the association with preterm birth was partially associated with chronic medical comorbidities. These mediation analyses suggest avenues for secondary prevention when adverse childhood experiences are identified.

In Felitti's study on adverse childhood experiences, seven categories of negative experiences occurring in childhood were associated with negative health outcomes later in life.¹ Subsequently, many investigators expanded the understanding of health outcomes related to adverse childhood experiences, finding a dose–response relationship as well.^{1,32} Recently, maternal adverse childhood experiences were associated with abnormal development of their children through at least 4 years of age.^{33–36} Our findings underscore the potential intergenerational reverberation of adverse childhood experiences, because children born to individuals exposed to trauma were more likely to be born preterm.

Our study narrows the focus from childhood outcomes to birth outcomes, linking adverse childhood experiences to adverse pregnancy outcomes including preterm birth. Results from our study are consistent with prior results linking adverse childhood experiences to preterm birth.^{13,37} Less research has been conducted to evaluate the association between adverse childhood experiences and other adverse pregnancy outcomes (Table 1). Our study builds on the existing literature through its larger sample size, lessening the potential for type II error. In addition, the breadth of sociodemographic diversity of our study population improves external generalizability. Finally, the development of a directed acyclic graph



and the use of mediation analysis provide insights into the pathways that contribute to observed associations.

The study is limited by recall bias inherent in detailing adverse childhood experiences. Underreporting of negative childhood experiences is common due to incomplete memories or stigma.³⁸ This dynamic, however, would bias our results toward the null and may have masked relationships between adverse childhood experiences and other adverse pregnancy outcomes. In addition, this study included individuals with an identified history or current symptoms of a mental health condition. Whether the association between adverse childhood experiences and adverse perinatal outcomes is different in this population compared with a more general population remains unknown. Finally, although the directed acyclic graph informed development of our model, we recognize that complex interactions across social and structural determinants of health exist and cannot be represented in any one model.

These data are particularly salient in the context of the coronavirus disease 2019 (COVID-19) pandemic, as rates of intimate partner violence and child neglect are rising.³⁹ Health care professionals play an important role in identifying and intervening when abuse or neglect is suspected. In addition, the observed racial disparity in the prevalence of adverse childhood experiences emphasizes the importance of equity-focused research and programs designed to mitigate these risks.

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