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Association Analysis of Fetal Alcohol Syndrome and Hypertension Status in Children,

Adolescents, and Young Adults

By

Jonathan C. Cook

A Thesis Submitted to the Graduate Faculty

of Georgia State University in Partial Fulfillment

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Abstract:

Background:

Fetal Alcohol Syndrome (FAS), located on the severe end of a spectrum of disorders known as Fetal Alcohol Spectrum Disorders (FASDs), is one of the most detrimental, and publicized, teratogenic outcome of alcohol consumption during pregnancy within the United States. During pregnancy, alcohol that is consumed by the mother passes through the placenta and transfers to the baby via the umbilical cord. The same prenatal transference of alcohol that leads to FAS and FASDs might also be contributing to an increased likelihood of hypertension in youth. Additionally, factors such as stress influenced by familial instability, an increased likelihood of developing congenital and conotruncal heart defects, and a reduction in nephron count might be leading to an increased likelihood of hypertension in FAS-affected youth. The purpose of this study is to examine the relationship between prenatal exposure to alcohol, manifested through FAS, and hypertension in children, adolescents, and young adults.

Methods:

A case-control study design was incorporated to analyze the association between FAS status and hypertension status; cases (n=165) were collected from a FAS clinical database in Atlanta, Georgia. Controls (n=177) were taken from the National Health and Nutrition Examination Survey (NHANES).

Chi-square analyses were used to examine the extent to which FAS status, sex, race/ethnicity, medication use, and obesity status each relate to hypertension status. A logistic regression was performed analyzing the relationship between FAS status (y/n: independent) and hypertension status (y/n: dependent) whilst controlling for sex, race/ethnicity, medication use, and obesity status.

Results:

The univariate relationships between FAS status and hypertension status (OR=4.491, $p<.001$) as well as medication use and hypertension status (OR= 2.951, $p=.002$) proved to be statistically significant ($p<.05$). Through the regression, FAS status significantly predicted hypertension status ($\beta = 1.646$, OR = 5.184, $p< .001$) after accounting for sex, race/ethnicity, medication use, and obesity status. Those with a race/ethnicity categorized as either Non-Hispanic African American ($\beta =1.259$, OR = 3.523, $p = .049$) or Hispanic ($\beta = 1.192$, OR = 3.294, $p = .061$) were significantly more likely to have hypertension than those categorized as non-Hispanic Caucasian.

Conclusion:

The major findings of this study suggest a significant relationship between FAS and hypertension in youth. Race/ethnicity also proved important in predicting hypertensive blood pressure readings independent of FAS diagnosis. The most obvious biological mechanism catalyzing the relationship between FAS and hypertension is prenatal alcohol exposure. Because prenatal alcohol exposure is the primary definitional and diagnostic factor of FAS, associative connectivity may exist independently between prenatal alcohol exposure and blood pressure at various levels of severity along an alcohol exposure dose-response spectrum. Further research is

needed to isolate and measure the effect that prenatal alcohol exposure has on blood pressure independently of FAS as well as to assess the extent to which the risk for hypertension in alcohol-affected individuals increases with age and through the life course.

Table of Contents

Acknowledgements.....	2
Abstract.....	3
Table of contents.....	5
Background.....	7
FAS and FASDs.....	7
Hypertension.....	8
Alcohol exposure and hypertension.....	9
Literature review.....	10
Cardiovascular Defects.....	10
Reduction in nephrons.....	11
Purpose of Study.....	11
Methods.....	12
Design.....	12
Participants.....	12
Measures.....	13
Analytic plan.....	15
Results.....	16
Discussion.....	20
FAS and hypertension.....	20
Race/ethnicity.....	20
Limitations and implications.....	21

Conclusion.....	23
References.....	25

List of tables

Table 1.....	15
Table 2.....	16
Table 3.....	18

Background:

FAS and FASDs

Fetal Alcohol Syndrome (FAS), located on the severe end of a spectrum of disorders known as Fetal Alcohol Spectrum Disorders (FASDs), was first identified in 1973 and remains one of the most detrimental, publicized, and teratogenic outcomes of alcohol consumption during pregnancy within the United States.^{1,2} FAS has been estimated to impact anywhere between 0.5 to 2 live births per 1000 whilst FASDs are believed to affect 3 times as many people as FAS.³ The diagnostic criteria for FAS include diminished anthropometric growth (typically below the 10th percentile), facial abnormalities (smooth philtrum and reduced palpebral fissures), and impaired cognitive development.^{4,5,6} Those affected by FAS experience an increased risk for a range of health burdens including brain dysfunction, mental impairment, physical dysmorphia/abnormalities, psychological disorders, learning disabilities, spontaneous abortion, and death.⁷ There is no cure for FAS, but the causes are 100% preventable.^{8,66}

Treatment for FAS is often focused on reducing disability through mental health and medical services.⁹ Many of the neurodevelopmental conditions that result from FAS impair academic and adaptive functioning throughout childhood and into adulthood. Research shows that early diagnosis is key in ensuring optimal developmental outcomes for children with FAS.^{10,11} But health burdens relating to FAS reach far beyond impaired physical and cognitive capacity. Some research has shown that having FAS increases the likelihood of incarceration into adulthood; although these findings remain inconsistent within the literature.^{12,75,76} The actual prevalence of FASDs in the correctional system is estimated to be about 9.1 per 1,000 inmates.⁷⁴ Children with FAS, similar to children with other disabilities, have also shown to be much more

likely to face caregiver, familial, and residential instability.^{13,14} Instabilities faced by these children places them at a greater risk for stress; a primary determinant of hypertension.^{15,16}

Hypertension

It is estimated that almost a third of all non-institutionalized adults are classified as hypertensive within the United States.^{17,18,19} For youth in particular, the rates of high blood pressure, or hypertension, have shown to be significantly increasing.^{20,21} This marked increase has been correlated with factors such as an uptick in the overall prevalence of obesity in children and the overconsumption of sodium (Na) in the U.S.²² High blood pressure has a particularly high health burden because its prognosis is multifaceted. Hypertension elevates the risk for serious conditions such as renal failure, heart attack, stroke, and brain damage whilst often producing no obvious signs or symptoms in the patient.^{23,24} National medical costs directly related to hypertension are projected to increase to an annual total of \$200.3 billion dollars by 2030.²⁵ Much of this heightened national cost is attributable to the increased likelihood of progressive morbidity and mortality faced by hypertensive patients.²⁶ Hypertension is also listed as one of the leading risk factors for cardiovascular disease; a disease that accounts for around 25% of all deaths in the U.S.²⁷

Though it can be a devastating burden to an individual's health, hypertension is a condition that is both preventable and reversible.²⁸ One of the most effective methods of preventing hypertension and prehypertension is the continuous monitoring of blood pressure of at-risk individuals.²⁹ Normal blood pressure readings tend to be those that are less than 120/80 mmHg, but this varies by age.³⁰ Another effective method of maintaining healthy blood pressure

levels in youth relates to the reduction of alcohol consumption; the overconsumption of alcohol often leads to the increasingly-prevalent condition of alcohol-induced hypertension.³¹

Alcohol Exposure and Hypertension

Alcohol abuse continues to be one of the most frequent preventable contributors to high blood pressure and prehypertension in the U.S.^{32,33} There is a dose-response relationship between the levels of alcohol consumed and blood pressure; greater consumption of alcohol results in an increased likelihood of high blood pressure.³⁴ Other health effects related to the abuse of alcohol include cardiovascular problems, cancer, liver diseases, gastrointestinal issues, and social dysfunction.³⁵ Alcohol can also directly affect the nervous system causing conditions such as neuropathy, dementia, psychosis, Wernicke's encephalopathy (which presents as paralyzed eye movements, difficulty walking, and confusion), stroke, and death.³⁶ Although the health effects of alcohol and blood pressure have been studied abundantly, most of this research has centered on alcohol as an exposure through consumption by adults. Another exposure pathway in which alcohol may be affecting the prevalence of childhood hypertension is through prenatal exposure.

During pregnancy, alcohol that is consumed by the mother passes through the placenta and transfers to the baby via the umbilical cord.³⁷ Within the U.S., it is estimated that approximately 12% of pregnant mothers drink alcohol; despite the recommendations of experts, including the Surgeon General, who report that there is no level of alcohol consumed during pregnancy that is considered safe for the mother and the developing fetus.³⁸ The same prenatal transference of alcohol that leads to FAS and FASDs might also be contributing to an increased likelihood of hypertension in youth. The purpose of this study is to examine the relationship

between prenatal exposure to alcohol, manifested through FAS, and hypertension in children, adolescents, and young adults.

Literature Review:

Although there has been much study on FASDs, FASD research is still lacking compared with the abundance of research on other developmental disorders, such as autism and ADHD, which have consistently been improving in overall awareness.^{40,41} In particular, there is virtually no research that has been conducted which specifically connects Fetal Alcohol Syndrome (FAS) with blood pressure outcomes.

Cardiovascular Defects

One of the most damaging outcomes of FASD is the impact that maternal alcohol use has on the developing fetal cardiovascular system. Research has shown that prenatal alcohol exposure, manifested through FASDs, significantly increases the likelihood of congenital and conotruncal heart defects.^{42,43} Congenital heart defects frequently lead to cardiovascular abnormalities such as holes in the heart and narrowed vessels; conditions which often present clinically as hypertension.^{44, 69} Conotruncal heart defects, which often result in right ventricular hypertrophy and pulmonary hypertension, also have been shown to be more likely to present in offspring whose mothers consumed alcohol during the periconceptional phase of pregnancy.⁶⁸ Additionally, FAS has been identified in individuals with mid-aortic syndrome; a rare condition that narrows the abdominal aorta and presents as untreatable hypertension.⁶⁷

Recently it has been found that reversed blood flow within the developing heart, influenced by prenatal alcohol exposure, may be the primary catalyst for defective heart formation during the critical stages of embryonic development.⁴⁵ Specifically, alcohol-exposed

fetuses have an increased risk of developing defects such as ventricular septal defects (VSDs), Patent Ductus Arteriosus (PDA), and narrowed valves.^{72,73} Heart defects such as these often symptomatically present as high blood pressure in the affected individual.^{46,47,48}

Reduction in Nephrons

Research has also shown that prenatal alcohol exposure results in an overall reduction of nephrons in the developing fetus.⁴⁹ Nephrons are the primary functional unit of the kidneys and are critical in the regulation of water and sodium through blood filtration.⁵⁰ A reduction in nephrons results in a weakening of the cardiovascular system and impaired renal function.⁷⁷ Specifically, reduced nephrons have been shown to correlate with an overall increase in mean arterial pressure (MAP).⁵¹ Impaired cardiovascular and renal function have also been proven, independently, to correlate with non-normative blood pressure readings and an increased likelihood of hypertension.^{52,53} There are no studies, however, examining the relationship between FAS and hypertension status within this context.

Purpose of Study

This study is aimed at bringing to light the potentiality of prenatal alcohol exposure as a determinant of high blood pressure in youth. The study samples contain data from participants ages 3 to 17 (n=342) and includes 165 cases diagnosed with either fetal alcohol syndrome (FAS) or partial fetal alcohol syndrome (pFAS) compared to 177 controls without a diagnosis of FAS or pFAS. The findings will shed light on the potential outcomes of drinking alcohol while pregnant and provide the basis for a more comprehensive health screening process when evaluating FAS-affected patients.⁵⁴

Methods:

Design

A case-control design was used for the purposes of this research study. Data comes two distinct sources. Cases (n=165) were taken from a clinical database abstracted from the Fetal Alcohol Syndrome and Drug Exposure Center at the Marcus Autism Center in Atlanta, Georgia. Information on cases was collected through patient medical records, cognitive and intellectual-assessment evaluations, and demographic/family-history surveys. The database houses patient data during initial and follow-up FAS clinic sessions and includes records spanning from 2000 through 2006. Controls (n=177) were taken from the National Health and Nutrition Examination Survey (NHANES) from the 2005-2006 dataset. NHANES is a nationally-representative survey administered by the Centers for Disease Control and Prevention (CDC) designed to assess the health and nutrition of the U.S. population. NHANES houses both interviews and physical examinations and contains dietary information, demographics, medical conditions, and laboratory tests.

Participants

The sample includes participants' ages 3 to 17 (mean age = 10.48, SD = 4.21) who provided consent for their information to be used in further research. Participants under the age of 3 were eliminated from the sample in order to remain consistent with the National Heart, Lung, and Blood Institute's blood pressure measurement conventions for children and young adults; which does not indicate standard blood pressure thresholds for those under 3 years of age.⁵⁸ The sex of the sample participants was relatively evenly distributed with 53.5% of the sample being male (n=183) and 46.5% female (n=159). There were greater number of non-

Hispanic Blacks (NHBs) in the sample (n=143; 41.8%) than other race/ethnicities; this was in congruence with the race/ethnicity distribution of patients regularly seen at the FAS clinic. Non-Hispanic Whites within the sample totaled to 124 (36.3%), Hispanics totaled to 53 (15.5%), and all others totaled to 22 (6.4%). FAS-status was the primary independent variable of interest and was treated as an indicative determinant of hypertension status.

Measures

FAS-status is assessed by diagnoses taken from the FAS Team Interdisciplinary Evaluation Form; a form summarizing the diagnoses and recommendations for the patient from a multidisciplinary panel of experts. The presence or absence of FAS in each patient within the sample is categorized based upon confirmed vs. non-confirmed diagnoses. Diagnosis of fully-developed FAS includes 4 diagnostic criteria: facial dysmorphism, growth problems, central nervous system abnormalities, and confirmed maternal alcohol exposure.⁵⁶ Partial fetal alcohol syndrome, or pFAS, is diagnosed when there is confirmation of both maternal alcohol exposure and facial abnormalities in addition to either growth retardation, central nervous system abnormalities, or delayed cognitive and behavioral development without an otherwise specified cause.⁵⁷ Because of the similarities of the alcohol exposure mechanisms and diagnostic criteria of FAS and pFAS, both were categorized with a positive FAS-status.

The blood pressure of the cases was measured through systolic and diastolic readings taken from the arm by a licensed nurse practitioner during FAS evaluation visits to the Marcus Autism Center. Hypertension status was assessed by categorizing blood pressure readings into a variable that labels participants as having either a non-risk or at-risk blood pressure level. At-risk levels include those whose blood pressure reading is in the range of hypertension; a condition

which is considered to be “at-risk” for atherosclerosis, heart disease, stroke, congestive heart failure, blindness, and kidney disease.⁵⁹ Non-risk levels are coded as blood pressure readings below the systolic/diastolic threshold for hypertension; non-risk levels also include blood pressure levels in the range of prehypertension. In patients between the ages of 3 and 17, at-risk blood pressure thresholds are assessed by conventions set within the National High Blood Pressure Committee's Fourth Report; which sets hypertension thresholds based upon sex, height, and age (in years) categorical.⁵⁵

To address potential confounding, race and ethnicity are factored into the analysis and aggregated into one variable which is categorized as either Hispanic, non-Hispanic White, non-Hispanic Black, or other; sex is categorized into either male or female. Case data relating to race, ethnicity, and sex are abstracted from the FAS Team Interdisciplinary Report, which includes data on demographic factors ascertained through guardian/caregiver self-report from Marcus Autism Center and the Fetal Alcohol Syndrome and Drug Exposure Center medical records. Control demographic data was taken directly from the 2005-2006 NHANES. Age is measured in whole and half-years and calculated by subtracting the birthdate from the exam date and truncating the resulting value. Medications in use by the patient, obtained through patient medical records, guardian/caregiver report, and NHANES, are aggregated into the analysis in order to avoid potential confounding that may result from medicinally-elevated blood pressure readings. A bivariate variable was created that categorized each participant as either on medication or off medication at the time of examination. Obesity has been shown to be directly correlated with hypertension and, thus, was also factored into the analysis as a potential confounder.⁶⁰ Obesity was measured as having a body mass index (BMI) of 30 or greater; calculated as weight (in kg) divided by height² (in cm).⁶¹

Analytic Plan

Chi-square analyses were used to examine the extent to which FAS status, sex, race/ethnicity, medication use, and obesity status each relate to hypertension status. A logistic regression was performed to analyze the association between the diagnosis of FAS and hypertension status. Categorical variables relating to FAS-status, race/ethnicity, sex, obesity, and medication use were included into the regression as possible predictors of hypertension status; hypertension status was the primary outcome measure and was coded as 0 = hypertensive, 1 = not hypertensive.

Results:

The total proportion of youth classified as hypertensive (12%) was over three times greater than the national average of hypertension in youth (3.6%).⁶² Hypertension prevalence within the FAS-positive cases sampled from the FAS clinic was much higher (19.4%) than the prevalence of hypertension seen in controls sampled from the NHANES (5.1%). Other demographic characteristics are shown in *Table 1*.

Table 1.

Demographic Characteristics of Sample Populations.

Variable	FAS Clinic Sample (cases)	NHANES Sample (controls)	Total
Sample size	165	177	342
Mean age (std dev.)	7.15 (3.58)	13.13 (2.70)	10.25 (4.34)
Sex			
Male (%)	57.6	49.7	53.5

Female (%)	42.4	50.3	46.5
Race/Ethnicity ¹			
NHC (%)	44.8	28.2	36.3
NHAA (%)	49.7	34.5	41.8
Hispanic (%)	.6	29.4	15.5
Other (%)	4.8	7.9	6.4
Medication Use			
Yes (%)	66.1	26.0	45.3
No (%)	33.9	74.0	54.7
Obesity			
Yes (%)	2.4	7.9	5.3
No (%)	97.6	92.1	94.7

1. NHAA is non-Hispanic African American, NHC is non-Hispanic Caucasian.

A chi-square test of independence was performed to examine the relationship between each demographic variable of interest and hypertension status. Results indicated in **Table 2**.

Table 2

Chi-square test of independence and odds ratio for each variable of interest predicting hypertension status.

Variable	%(n) ¹	x ²	df	OR	p
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FAS Status		16.57	1	4.49	>.001
Yes	19.4(165)				
No	5.1(177)				
Sex		.13	1	1.13	.723
Male	12.6(183)				
Female	11.3(159)				
Race/Ethnicity ²					
Non-Hispanic Caucasian	12.1(124)	.00	1	1.02	.963
Non-Hispanic African American	11.9(143)	.00	1	.98	.961
Hispanic	7.5(53)	1.17	1	.56	.279
Other	22.7(22)	2.57	1	2.32	.109
Medication Use		9.92	1	2.95	.002
Yes	18.1(155)				
No	7.0(187)				
Obesity Status		.39	1	1.50	.534
Yes	16.7(18)				
No	11.8(323)				

¹Percentage represents the proportion of participants within each categorical that presented with hypertensive blood pressure readings; n represents the total number of participants in each sub-categorical.

²Difference between groups was tested by Pearson chi-square statistic. Each Race/ethnicity categorical (non-Hispanic Caucasian, non-Hispanic African American, Hispanic, and other) was compared separately against all other races/ethnicities.

The relationships between FAS status and hypertension status (OR=4.49, p<.001) as well as medication use and hypertension status (OR= 2.95, p=.002) proved to be statistically

significant. Those diagnosed with FAS had a larger proportion of respondents who were using medication (66.06%, n=109) than those without a diagnosis of FAS (25.99%, n=46). Additional chi-square analyses found that participants with FAS were also far more likely (OR=5.54, $p<.001$) to be on medication than those without a diagnosis of FAS. The most common types of medications that the FAS-diagnosed youth were using were either stimulants and/or selective serotonin reuptake inhibitors (SSRIs). Expectedly, most of participants with a positive FAS status were also underweight (79.39%); a function of the diagnostic criteria for FAS which includes reduced anthropometric growth. Initial demographic analyses also showed that 23% of the FAS clinic sample were reported as having asthma; a proportion much higher than the national average of asthma which is estimated to be between 7 to 10 percent.⁸⁰ In fact, 25.7% of the FAS clinic sample was on some type of allergy or asthma medication at the time of examination.

In order to assess the potential for an unmediated relationship between FAS and hypertension, a logistic regression was performed that controlled for sex, race/ethnicity, medication use, and obesity status. Results indicated in *Table 2*.

Table 3

Logistic regression model of predictors of hypertension status in children, adolescents, and young adults ages 3-17.

Predictor	β	$SE \beta$	Wald's χ^2	df	p	OR	$C.I.(p<.05)$		
Constant	-.86	.97	.78	1	.378	N/A	N/A	N/A	N/A
FAS Status	1.65	.52	10.21	1	.001	5.18	1.89	14.23	
Sex (male is reference)	.02	.35	.00	1	.967	1.02	.51	2.03	

Race/Ethnicity								
White (reference)								
Non-Hispanic African American	1.26	.64	3.86	1	.049	3.52	1.00	12.37
Hispanic	1.19	.64	3.52	1	.061	3.29	.95	11.44
Other	.49	.84	.34	1	.562	1.63	.31	8.46
Medication Use	.64	.39	2.66	1	.103	1.90	.88	4.11
Obesity Status	.98	.73	1.82	1	.177	2.66	.64	11.00

N: The dependent variable used in the regression was hypertension status (yes=0, no=1). Predictors include: FAS status: measured as confirmed diagnosis of FAS or pFAS (yes=0, no=1), sex, medication use (yes=0, no=1), obesity status (yes=0, no=1), and race/ethnicity. The sex categorical compared females to males through the regression (female=0, male=1). The non-Hispanic Caucasian race/ethnicity categorical was used as the reference value during the regression in order to compare outcomes for participants with the races/ethnicities listed (Non-Hispanic African American, Hispanic, Other) against participants classified as non-Hispanic Caucasian.

The results from **Table 3** indicated a significant association between FAS status and hypertension status after controlling for potential confounders. FAS status significantly predicted hypertension status ($\beta = 1.646$, $OR = 5.184$, $p < .001$) after accounting for sex, race/ethnicity, medication use, and obesity status. Similar to findings presented in previous studies, race/ethnicity showed a direct relationship with hypertension status.⁶³ Compared to those having a race/ethnicity classified as non-Hispanic Caucasian, having a minority race/ethnicity classification, which included non-Hispanic African American ($\beta = 1.259$, $OR = 3.523$, $p = .049$) and Hispanic ($\beta = 1.192$, $OR = 3.294$, $p = .061$), seemed to increase the likelihood of having hypertensive blood pressure readings. Though significant in its bivariate relationship with hypertension status, medication use was not significant in the multivariate regression.

Discussion:

FAS and hypertension are conditions that greatly burden healthy functioning, development, and life outcomes in children and adults. FAS and pFAS-affected youth face an increased risk for cardiovascular defects, reduced nephron profusion, and high stress levels; all potential determinants of high blood pressure. Combined, one might expect that these factors elevate the likelihood of developing high blood pressure in individuals with FAS or pFAS and potentially those on the less severe end of the FASD spectrum.

FAS and Hypertension

Results from this study indicated an unmediated relationship between FAS status and hypertension status in children, adolescents, and young adults. The biological mechanism catalyzing this relationship most likely corresponds with the placental transference of alcohol during gestation. Generally, hypertension occurrence in children and adolescents is relatively rare compared with rates seen in older age groups.⁷⁸ In the FAS-affected participants of the study sample, the prevalence of high blood pressure greatly exceeds the national average in youth.⁶² The evidence presented in this report, in addition to previous studies examining the impact age has on the risk of hypertension, suggests that rates of hypertension in FAS-affected individuals may be exponentially higher in adulthood.

Race/Ethnicity

As supported by previous literature, the regression performed showed that race/ethnicity proved important in predicting hypertension status. Ethnic minorities within the sample yielded a much higher likelihood of having hypertension than those classified as non-Hispanic Caucasian. Non-Hispanic African Americans in particular seemed disproportionately burdened with

hypertensive blood pressure readings. Previous research has shown that non-Hispanic African Americans not only face greater severity and mortality in regards to high blood pressure, but are also more likely than others to develop hypertension in childhood.^{63,70} Because the age range of the sample is limited to children and young adults, the prevalence of hypertension might be relatively elevated in non-Hispanic African Americans due to an increased tendency to develop high blood pressure earlier in life. To better examine the extent to which race/ethnicity impacts hypertension status in FAS and alcohol-affected individuals, a longitudinal study following a more ethnically-diverse sample into adulthood is needed.

Limitations and Implications

There are several limitations that arose during the course of this study. As a product of the structural design of the FAS clinic survey and database, income and socioeconomic status (SES) were not available or factored into the analysis. The inclusion of SES into the study would have been beneficial in assessing the extent to which environmental factors play a role in the relationship between FAS and hypertension. FAS-affected youth are often part of households with low socioeconomic status and poor social support.⁶⁴ Research also shows that low SES and being below the poverty line are significantly associated with an increased risk for high blood pressure.⁷¹ This phenomenon could be partly due to the challenges individuals with low SES face in regards to access to healthcare, knowledge about the prevention and control of hypertension, and nutrition.⁷⁹ Through this context, SES could potentially have a mediating affect in the relationship between FAS and hypertension status.

The second major limitation of this study relates to the controls sampled from NHANES. Because NHANES does not contain a variable that specifically contains information on FAS

diagnosis, a lack of diagnosis was assumed due to the relative rarity of confirmed cases of FAS and pFAS present in the general population. Although unlikely, the differential misclassification of exposure of FAS-affected individuals as controls could potentially diminish the statistical power of the relationship between FAS and hypertension and underestimate an otherwise larger predictive value. Establishing an alternative source for controls that incorporates comprehensive diagnostic information, possibly from other clinics or hospitals, would help eliminate this limitation and improve predictive accuracy in future studies relating to FAS and hypertension.

This study was also limited in that, within the FAS clinic sample of cases, blood pressure was only measured at one point in time. To make the hypertension categorization of the controls equivalent to the cases, blood pressure readings from the NHANES were also limited to the first measurement. The most precise diagnoses of hypertension involve approximately three blood pressure readings that are taken on distinctly different days. This is done to reduce the likelihood of white-coat hypertension, and other environmental factors, that may contribute to spiked blood pressure readings during one or more of the measurements.⁶⁵ Although single measurements are not ideal for assessment, initial measurements should not vastly differ statistically from results indicated from multiple readings. In addition, the sample size is large enough to significantly decrease the potential impact of anomalous blood pressure measurements during hypertension categorization and analysis. As such, blood pressure evaluation and hypertension categorization would be more precise if multiple readings were included, but, for the purposes of this study, initial readings prove sufficient.

One major implication of this study is that the findings could be used to develop a more comprehensive health screening process during clinical FAS evaluation. Implementing interval-based sphygmomanometer readings and, where necessary, non-invasive echocardiography into

FAS clinic evaluations could better identify hypertensive patients. This could potentially lead to earlier identification of at-risk blood pressure levels and reduce the overall impact of hypertension in many FAS-affected individuals.

Another implication of this report is that the results shed more light on the diversity and complexity of health burdens faced by individuals diagnosed with FASDs. Identifying hypertension as an additional source of morbidity for youth with FAS could elevate the research interest and overall awareness surrounding the devastating effects of prenatal alcohol exposure. This could potentially lead to more comprehensive and effective maternal alcohol use prevention efforts that incorporate the interaction between prenatal alcohol exposure and hypertension.

Conclusion

The major findings of this study suggest a significant relationship between FAS and hypertension in youth. Race/ethnicity also proved important in predicting hypertensive blood pressure readings independent of FAS diagnosis. The most obvious biological mechanism catalyzing the relationship between FAS and hypertension is prenatal alcohol exposure. Because prenatal alcohol exposure is the primary definitional and diagnostic factor of FAS, associative connectivity may exist independently between prenatal alcohol exposure and blood pressure at various levels of severity along an alcohol-exposure, dose-response spectrum. Further research is needed to isolate and measure the effect that prenatal alcohol exposure has on blood pressure independently of FAS diagnosis whilst assessing the extent to which the risk for hypertension in alcohol-affected individuals increases with age and through the life course. Factoring in SES and a more diverse race/ethnicity categorical would also be beneficial in future studies to further

reduce mediation and improve the statistical power of the relationship between prenatal alcohol exposure, presenting as FAS, and hypertension.

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