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BPA Levels in Atlanta-Area African American Women: A Tale of Two Communities

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Abstract

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Introduction: Exposure to environmental chemicals is pervasive in the United States. African Americans (AA) are disproportionately exposed to many environmental chemicals such as BPA. Some AA populations see higher rates of food insecurity and have higher exposures to processed foods, which can lead to more exposure to BPA. Disproportionate BPA exposure may translate to an increased likelihood of a pregnant AA woman having a preterm birth. Health disparities begin before the child is born; every aspect of a pregnant woman's environment contributes to the health of her unborn child. The purpose of this project is to determine the relation between BPA exposure and preterm birth among Atlanta AA women delivering at two economically distinct Atlanta hospitals, Emory University Hospital Midtown and Grady Health System. **Methods**: We performed a descriptive analysis to characterize urinary BPA levels, being assessed among the mothers, and summarize gestational age, being assessed among the infants, among AA women and their offspring, respectively. Additionally, we explored the relation between urinary BPA levels and early birth (a summary variable that includes preterm and early term (<37-38 weeks)) using logistic regression analysis. **Results**: The patients attending their prenatal visits at Emory had a mean age of 27 (± 4.73) years of age while those attending Grady were on average 24 (± 3.89) years of age which were significantly different ($p=0.001$). The mean parity, the number of viable pregnancies taken to birth or the number of live births, for both Emory and Grady are approximately 1 birth ($p=0.5524$). Emory had an even split of patients covered by Medicaid and private insurance while only one patient at Grady was covered by private insurance ($p <0.0001$). Accounting for the covariates, hospital sites are significantly associated with odds of delivering preterm or early term. At Grady, there is an increased odd of delivering preterm or early term, whereas delivering at Emory is protective against delivering preterm or early term. **Conclusion**: More research needs to be conducted on the health impacts of BPA, health disparities among races, and long-term morbidity of preterm and early term birth.

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Introduction

Exposure to environmental chemicals is pervasive in the United States. The Centers for Disease Control and Prevention presented data on human exposure to more than 250 environmental chemicals in 2019, with endocrine disrupting chemicals used during the manufacturing of plasticizers and personal care products being among the most highly detected. Among a U.S. nationally representative sample from the National Health and Nutrition Examination Survey (NHANES) in 2013-2014, 93% of the urine samples tested contained detectable levels of bisphenol A (BPA).[1] The wide exposure of BPA can be attributed to food and beverages containing this chemical.[1] Plastic water bottles, food storage containers, even canned products contain BPA and ingestion may be a primary route of exposure.[1] The endocrine disrupting compound, BPA, binds to estrogen membrane receptors, mimicking normal estrogenic actions.[2] This can lead to potentially alarming health consequences. Maternal exposure to bisphenols has been associated with pregnancy outcomes such as preterm (< 37 weeks gestation) delivery.[3] African Americans (AA) are disproportionately exposed to many environmental chemicals such as BPA.[4] Some AA populations see higher rates of food insecurity and have higher exposures to processed foods, which can lead to more exposure to BPA. Disproportionate BPA exposure may translate to an increased likelihood of a pregnant AA woman having a preterm birth.[4] Health

[1] https://www.niehs.nih.gov/health/topics/agents/sya-bpa/index.cfm
[2] Galea, L., & Barha, C. (2011). Maternal bisphenol A (BPA) decreases attractiveness of male offspring. Proceedings of the National Academy of Sciences of the United States of America, 108(28), 11305-11306. Retrieved February 5, 2020, from www.jstor.org/stable/27978792
[3] Derakhshan, A., Shu, H., Peeters, R. P., Kortenkamp, A., Lindh, C. H., Demeneix, B., . . . Korevaar, T. I. M. (2019). Association of urinary bisphenols and triclosan with thyroid function during early pregnancy. Environ Int, 133(Pt A), 105123.doi:10.1016/j.envint.2019.105123
[4] Ranjit, N., Siefert, K., & Padmanabhan, V. (2010). Bisphenol-A and disparities in birth outcomes: a review and directions for future research. Journal of perinatology : official journal of the California Perinatal Association, 30(1), 2–9. doi:10.1038/jp.2009.90

disparities begin before the child is born; every aspect of a pregnant woman's environment contributes to the health of her unborn child.

The Center for Children's Health, the Environment, the Microbiome, and Metabolomics (CCHEM2) at Emory University is working to improve children's health and reduce health disparities by better understanding how environmental exposures during and after pregnancy affect AA women and their children in Atlanta.[5] Currently, the first of its kind in the Southeast, particularly in African American populations, this program involves transdisciplinary collaboration that spans across four schools at Emory University to contribute to a healthier society for mothers and children.[5]

The purpose of this project is to determine the relation between BPA exposure and preterm birth among Atlanta AA women delivering at two economically distinct Atlanta hospitals, Emory University Hospital Midtown and Grady Health System. This study may inform our understanding of the health effects of maternal exposure leading to adverse birth outcomes, including preterm and early term birth, which may also be on a causal pathway to other health problems for the child. Additionally, understanding the burden of environmental exposures on AA women may lead to targeted interventions for this community.

Emory Midtown, located in the midst of the South of North Avenue community of Atlanta, is a teaching hospital affiliated with Emory Healthcare with 1,200 Emory Clinic and 440 private-

[5] C-CHEM² About Us: Nell Hodgson Woodruff School of Nursing: Emory University: Atlanta GA. (n.d.). Retrieved from http://www.nursing.emory.edu/c-chem2/about.html.

practice in 28 specialties.[6] Many gynecologists and obstetricians at Emory Midtown serve as faculty members at Emory University School of medicine. Well known for women's services including prenatal and postnatal education along with a specialization in high-risk pregnancies, Emory has a level III neonatal intensive care unit.[6]

Grady Hospital is the largest in the state of Georgia and 5th largest public hospital in the United States. As the public hospital for the city of Atlanta, it is one of the busiest level I trauma centers in the country. With 697,000 patient visits each year, Grady also includes pregnancy and obstetrics care, neonatal intensive care unit (NICU) services, and confidential reproductive health education at the Grady Teen Center.[7]

The usual length of pregnancy lasts 39 to 41 weeks of gestation. A child delivered before 37 weeks is considered preterm whereas an early term birth is at 37 to 38 weeks of gestation. Many understand the health consequences of a preterm birth. Evidence shows adverse health outcomes for early term birth including having higher neonatal morbidity, more frequent neonatal intensive care admissions, and respiratory complications at birth, among others.[8] Preterm and early term birth can cause longer-term morbidity in childhood and adulthood.[8]

We propose two specific aims for this project.

[6] Emory University Hospital Midtown. (2019). Retrieved 2020, from https://www.emoryhealthcare.org/locations/hospitals/emory-university-hospital-midtown/index.html
[7] Women's Center. (2019, September 25). Retrieved from https://www.gradyhealth.org/care-treatment/obgyn-center/
[8] Delnord, M., & Zeitlin, J. (2019). Epidemiology of late preterm and early term births – An international perspective. Seminars in Fetal and Neonatal Medicine, 24(1), 3–10. doi: 10.1016/j.siny.2018.09.001

Aim 1: Perform a descriptive analysis to characterize urinary BPA levels, being assessed among the mothers, and summarize gestational age, being assessed among the infants, among AA women and their offspring, respectively.

Hypothesis: We hypothesize the urinary BPA levels among AA women enrolled in CCHEM2 will be higher than those in the general US population (2015-2016 NHANES). We also hypothesize the offspring outcome gestational age at birth will be different among women and offspring at the two hospitals (Emory and Grady)

Aim 2: Explore the relation between urinary BPA levels and early birth (a summary variable that includes preterm and early term (<37-38 weeks)) using logistic regression analysis.

Hypothesis: We hypothesize the association between BPA levels and early birth will vary depending on other determining factors.

Methods

Ethics Statement:

Institutional Review Board (IRB) approval was obtained for human subjects research by Emory University. Informed consent was provided for all participants. The Collaborative IRB Training Initiative Program (CITI) offers curricula in human subjects research as well as the responsible conduct of research. All researchers have received CITI training.

Study Design:

CCHEM2 includes pregnant Atlanta-area AA women of various socioeconomic status (SES) at least 18 years of age. Participants were recruited at Emory University Hospital Midtown and Grady Health System to ensure SES diversity. Enrollment of pregnant AA women for this study

began in January 2016 and continues. The study occurred in three key parts: initial hospital visit, home visit, and a second hospital visit. The first hospital visit occurs when the woman is 8-14 weeks pregnant. Women are asked to join the study and blood and urine are collected. The home visit occurs at 20-24 weeks gestation. Urine samples are again taken, and dust samples are collected via vacuum. A questionnaire is administered to gather insight into the cleaning and personal care products used by the mother. The final hospital visit occurs between 28- and 30-weeks gestation when blood and urine samples are taken once again. For this analysis, we have urinary BPA data on 284 unique participants.

Data Sources & Sample Size:

Three sets of data were used in this analysis: BPA levels of patients at Emory and Grady, demographic data obtained by the questionnaires, and national BPA levels of AA and White women from the 2015-2016 NHANES survey. Because BPA levels were assessed on three occasions for the Emory/Grady CCHEM2 cohort, all three BPA measurements were first matched with the appropriate subject IDs. Then, they were matched with their responses to the demographic data, including age, parity, etc. If demographic data were not available for a subject, they were removed from the analysis. This exclusion left 100 subjects (40 from Emory and 60 from Grady). However, many subjects (n=81) had multiple BPA measurements from the three visits. This allowed for 226 total BPA measurements (87 from Emory and 139 from Grady). From the NHANES data, we reduced our scope to urinary BPA data for AA women and White women (n=761 women). There were not enough pregnant women (< 1%) in the 2015-2016 survey sample to include this population in the scope of the present analysis.

Variables & Statistical Methods:

Each specific aim called for an analysis of a set of different variables.

The first aim of this project was to perform descriptive analysis of urinary BPA levels (the exposure) and gestational age (the outcome). The variables included were urinary BPA levels of patients attending Emory and Grady, as well as African American and White women's BPA levels from the National Health and Nutrition Examination Survey (NHANES). BPA is not a measurement that is normally distributed, so the data were log transformed and geometric means were calculated. Without this crucial step, an outlier in the BPA levels can greatly skew the distribution and a clear comparison may not be possible. The arithmetic means of the gestational ages for Emory and Grady were also calculated; prevalence of preterm and early term infants were estimated. The variables preterm and early term were combined as one variable because the relatively small sample size (n=100) would not support statistical power to analyze the two variables individually. A t-test of significance was undertaken to detect if there was a significant difference between the geometric means of urinary BPA concentrations and mean gestational age at birth of Emory and Grady patients.

Our hypothesis of exposure and outcome differences between patients at the two hospitals are contingent on a difference in demographics. The demographic variables used to assess this difference included age, parity, and insurance type. Mean age and parity were calculated, and the distribution of insurance type was assessed. An assessment of whether the differences in demographic data of participants between the two hospital sites were significant was conducted. A chi-square test of significance was performed to test the significance of the difference in

insurance type while a t-test of significance was performed for age and parity. Insurance type was categorized as either covered by Medicaid or private insurance. Those covered by private insurance included if they received their insurance through their employer or the marketplace healthcare exchange.

The next aim was to explore the relation between BPA levels and early birth. The first step of this analysis was to identify a list of potential covariates that could be effect modifiers or confounders on BPA exposure and the odds of delivering preterm or early term. We identified age, parity, site, and insurance type as potential effect modifiers. Among these possible modifiers, we performed a test of collinearity to determine if these variables should be included in the logistic regression analysis. If there is an issue of collinearity, there is potential for bias. Variance Inflation (VIF) allows for the determination of the presence of collinearity. For the purposes of this project, collinearity problems are indicated when VIF > 10. To assist in model specification and identify which variables would be necessary in the final logistic model, we conducted a backward regression analysis. Because of the small sample size, we need to identify the variables that truly explain the variance in the model. Backward elimination removed the covariates at an alpha level of 0.1 due to the low statistical power. Backward logistic regression eliminated all variables except the interaction between BPA and site, and BPA and parity. Still, we decided to also include the main effects (site and parity) in regression models. Furthermore, because these were non-time varying variables, we assumed these interaction terms would remain significant throughout the study and included these interaction terms for each model of maternal urinary BPA at three time points across pregnancy.

Logistic regression analysis was performed to assess a significant association between maternal BPA levels and odds of having either a preterm or early term delivery at the three different time points (first and second hospital visits and the home visit). From this regression analysis, odds ratios and 95% Wald Confidence Intervals were adjusted for each covariate (parity, age, insurance, site) along with BPA concentration from each visit (first, home, and second) , separately. Logistic regression models also included interaction terms deemed significant from the backward elimination step. Significance was defined at an alpha level of 0.05.

Results

The patients attending their prenatal visits at Emory had a mean age of 27 (± 4.73) years of age while those attending Grady were on average 24 (± 3.89) years of age which were significantly different (p=0.001). The mean parity, the number of viable pregnancies taken to birth or the number of live births, for both Emory and Grady are approximately 1 birth (p=0.5524). Emory had an even split of patients covered by Medicaid and private insurance while only one patient at Grady was covered by private insurance (p <0.0001). Age and parity data may be found in Table 1. Insurance type distribution can be found in Table 2.

The geometric means were compiled into Table 3. The mean BPA for Emory and Grady participants was 0.90 ng/mL and 1.43 ng/mL (p=0.02). Emory's geometric mean BPA was lower than the national average even when stratified by race. Grady's mean BPA level was similar to the national AA mean BPA level but higher than the mean for White women (Table 4). There was not a significant difference in mean gestational age at birth of infants between Emory and Grady (p=0.13) participants. However, the mean gestational age for Emory's population was

lower, at 39.47% preterm or early term, as compared to Grady, at 50.94%. There was no national data on gestational age.

Including the mean BPA concentrations at each visit, age, parity, insurance, and site to the logistic model, the collinearity assessment produced no variance inflation (VIF) higher than 10, as presented in Table 5. This means there was no collinearity problem.

The odds ratios of each visit after running cross-sectional analysis with each covariate produced a non-significant result. Accounting for parity, age, insurance, and hospital site, we found that across the three time points, there were no significant associations between maternal BPA concentrations and the odds of delivering preterm or early term. The odd ratios and confidence intervals for each visit, accounting for the covariates, may be found in Table 6.

Logistic regression analysis assessed the interaction between maternal BPA concentration and parity as well as BPA and hospital site. There was nominally significant interaction ($p<0.1$) for both (Table 7). Maternal BPA levels at visit one and parity were not significant. To be conservative, odds ratios for the interaction term of maternal BPA concentration and site, were assessed. Accounting for the covariates, hospital sites are significantly associated with odds of delivering preterm or early term. At Grady, there is an increased odd of delivering preterm or early term, whereas delivering at Emory is protective against delivering preterm or early term (Table 8).

Discussion

Key Findings:

We hypothesized there would be a difference in BPA levels across the two hospitals because the patients attending them are socioeconomically different. The women attending prenatal visits at both Emory and Grady are about the same age and parity. The disparities were depicted in insurance type. Using health insurance as a proxy for SES status, it is clear there is a difference in the pregnant patients attending these two hospitals. Those with a higher SES status may have more buying power to opt out of purchasing products containing BPA. Canned shelf-stable foods, soda cans, among other products high in BPA, are often cheaper and more accessible to lower-income individuals. This may make them at greater risk of exposure and have higher urinary BPA levels, as shown in the Grady population. There is a significant difference between the geometric mean BPA levels of the women visiting Emory and Grady hospitals. At Grady, there is an increased odd of delivering preterm or early term, whereas delivering at Emory is protective against delivering preterm or early term. Additionally, differences in insurance type may explain differences in access to, and type of healthcare received by the women attending the various hospitals.

Evidence shows BPA and its derivatives may cause preterm and early term birth. From this project, the mean gestational ages for both hospitals were between 37 and 38 weeks, these are considered early term births. This is consistent with previous research of AA women being more at risk for preterm and early term birth. Although Emory had a higher proportion of patients privately insured, these AA women still had a good proportion of preterm or early term births. There was not a significant difference in gestational ages between the two populations. However,

by increasing the number of subjects in the study, the difference could become significant. Additionally, early term infants are generally healthier and at less risk of morbidities or mortality than those delivered preterm. So, this grouping of the two as one variable may be resulting in misclassification. This misclassification is probably non-differential with regards to maternal BPA levels and as such, biases the ORs toward the null.

Neither age, parity, insurance, or hospital site (predictors in model) are highly correlated with other variables in model. This is a strength of the analysis. The association between BPA and gestational age is not statistically significant, however the small sample size is a limitation. Although, there was a hospital site specific difference in women delivering at the Emory and Grady.

Limitations:

There are several limitations of this project. The small sample size of 100 women is not a representative sample of the pregnant patients attending both hospitals. It does, however, provide a snapshot. This sample size was also too low to adequately evaluate preterm and early term birth separately. Additional statistical analysis needs to be conducted to understand the relation between BPA levels and gestational age.

We compared all Black and White women from the 2015-2016 national survey sample to a cohort of pregnant women from the CCHEM2 cohort. There may be differences in behaviors and bodily functions between non-pregnant and pregnant women that could contribute to differences in urinary BPA levels. This is another potential limitation.

Finally, due to the transient nature of BPA exposure, 1-3 urinary collection samples from the visits may not adequately capture exposure.

Conclusion & Recommendations:

This study is consistent with preliminary results from the larger CCHEM2 study as well as with previous research. More research needs to be conducted on the health impacts of BPA, health disparities among races, and long-term morbidity of preterm and early term birth.

Tables

Table 1: Demographic Data (Age & Parity)

	Mean Age ± Standard Deviation	p-value	Mean Parity	p-value
Emory (n=40)	27.85 ± 4.73	0.001	0.88 ± 0.91	0.5524
Grady (n=60)	24.33 ± 3.89		1.00 ± 1.08	
Total (n=100)	25.74 ± 4.56		0.95 ± 1.01	

Table 2: Demographic Data (Insurance Type)

Insurance Type	Medicaid	Private	Total	p-value <.0001
Emory	20	20	40	Freq.
	50%	50%	100%	Percent
Grady	59	1	60	Freq.
	98.33%	1.67%	100%	Percent
Total	79	21	100	Freq.
	79%	21%	100%	Percent

Table 3: Maternal BPA Concentrations in ng/mL

	1st Visit	Home Visit	2nd Visit	Total
Emory (n=87)	1.15 ± 1.10	0.89 ± 1.25	0.66 ± 1.29	0.90 ± 1.21
Grady (n=139)	1.45 ± 0.90	1.61 ± 1.28	1.24 ± 1.03	1.43 ± 1.07
Total (n=226)	1.32 ± 0.98	1.32 ± 1.29	0.95 ± 1.18	1.20 ± 1.15

*geometric means ± standard deviation

Table 4: CCHEM2 Population BPA Concentrations vs. NHANES National Women BPA Concentrations in ng/mL

		CCHEM Population				National; Women		
		Emory (n=87)	Grady (n=139)	Total (n=226)	p-value	Black (n=346)	White (n=415)	Total (n=761)
Exposure	Mean BPA Level*	0.90 ± 1.21	1.43 ± 1.07	1.20 ± 1.15	0.02	1.31 ± 1.04	1.01 ± 1.02	1.14 ± 1.04
Outcome	Mean Ges. Age	38.87 ± 1.20	37.87 ± 3.52	38.37 ± 0.71	0.13			
	Percent Preterm/ Early term	39.47%	50.94%	46.15%				

*geometric means ± standard deviation

Table 5: Collinearity Assessment

Variable	Variance Inflation
BPA Concentration at Hospital Visit 1	1.11
BPA Concentration at Home Visit	1.69
BPA Concentration at Hospital Visit 2	1.65
Age	1.38
Parity	1.09
Insurance	1.92
Hospital Site	2.00

Table 6: Adjusted* Cross-Sectional Odds Ratios

	Odds Ratio	95% Confidence Interval
BPA Concentration at Hospital Visit 1	0.999	0.829, 1.204
BPA Concentration at Home Visit	1.068	0.923, 1.236
BPA Concentration at Hospital Visit 2	1.038	0.827, 1.302

*Accounting for parity, age, insurance, and hospital site

Table 7: Significant Effect Modifiers

Effects Remaining	p-value
BPA Concentration at Hospital Visit 1*Hospital Site	0.0020
BPA Concentration at Hospital Visit 1*Parity	0.0695

Table 8: Adjusted* Odds Ratios per Hospital Site

	Odds Ratio	Confidence Interval
BPA Concentration at Hospital Visit 1 at Emory	0.862	0.691, 1.075
BPA Concentration at Hospital Visit 1 at Grady	1.612	1.090, 2.386

*Accounting for the interaction between maternal BPA concentration and parity