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Racial and Ethnic Variations in Phthalate Metabolite Concentrations across Pregnancy

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Abstract

Background—Phthalates are associated with adverse reproductive and pregnancy outcomes. In non-pregnant populations, phthalate metabolite levels vary by race/ethnicity. Few studies have evaluated racial/ethnic differences between phthalate metabolite levels at multiple time points across pregnancy.

Objective—To determine whether phthalate metabolite concentrations differ by race/ethnicity across multiple pregnancy time points.

Methods—Women were participants in a prospectively collected pregnancy cohort who delivered at term and had available phthalate metabolite levels for 3 time points across pregnancy (n=350 women). We assessed nine phthalate metabolites that were log-transformed and specific gravity-adjusted. We evaluated the potential racial/ethnic differences in phthalate metabolite levels at baseline (median 10 weeks gestation) using ANOVA and across pregnancy using linear mixed models to calculate percent change and 95% confidence intervals adjusted for sociodemographic and lifestyle factors.

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Results—Almost 30% of the population was non-Hispanic black or Hispanic. With the exception of MCP and DEHP metabolites, baseline levels of phthalate metabolites were significantly higher in non-whites ($p < 0.05$). When evaluating patterns by race/ethnicity, MEP and MCP had significant percent changes across pregnancy. MEP was higher in Hispanics at baseline and decreased in mid pregnancy, but increased in late pregnancy for non-Hispanic blacks. MCP was substantially higher in non-Hispanic blacks at baseline, but decreased between mid- and late pregnancy.

Conclusions—Across pregnancy, non-Hispanic black and Hispanic women had higher concentrations of certain phthalate metabolites. These differences may have implications for racial/ethnic differences in adverse pregnancy outcomes.

Keywords

pregnancy; race; ethnicity; blacks; Hispanics; phthalates

Introduction

A growing body of evidence suggests that exposure to certain environmental chemicals during pregnancy, such as ortho-phthalates, may affect the short- and long-term health of both mothers and their offspring.^{1–6} Phthalates may be a particularly important class of environmental toxicants, given their ability to modulate hormone levels⁷ and bind to nuclear receptors known as peroxisome proliferator-activated receptors (PPAR).^{8–9} These chemicals are used in the production of a variety of consumer products, such as plasticizers, solvents, stabilizers, and lubricants.⁸ They can be ingested, inhaled, and absorbed through the skin.⁸

In non-pregnant populations, having higher phthalate metabolite levels is associated with diabetes,^{10–12} endometriosis,^{13–15} and fibroids¹⁶ in women. Also, data from a non-pregnant population suggest that there are both gender and racial/ethnic differences, with women and non-whites having higher phthalate metabolite levels.^{17–18} Less is known about racial/ethnic differences in pregnancy, with implications on adverse pregnancy outcomes. For example, in pregnant women, higher urinary phthalate metabolite concentrations are associated with preterm birth^{19–20} and intrauterine growth restriction.²¹ In the offspring, in utero exposure to higher levels of phthalates is associated with changes in reproductive organ development,⁵ eczema and allergic conditions,²² as well as adverse neurobehavioral outcomes in children.^{23–25} While previous studies have evaluated the variability of phthalate levels across pregnancy,^{26–27} no study has characterized phthalate metabolite levels by race/ethnicity in a multi-racial population of pregnant women. With changes in sensitive windows across pregnancy that could affect both fetal development and maternal health, evaluating racial/ethnic differences in phthalate metabolite levels across pregnancy may provide important information as to whether differing levels of this class of chemicals across pregnancy could contribute to racial/ethnic disparities in adverse pregnancy outcomes.

In this study, we evaluated the association between racial/ethnic differences in phthalate metabolite levels in pregnant women at early, mid, and late pregnancy. We assessed mean phthalate levels across each trimester of pregnancy, as well as overall mean phthalate levels

across pregnancy by race/ethnicity. We also evaluated change in phthalate metabolites from early to late pregnancy stratified by race/ethnicity adjusting for potential confounders. For comparison with previous studies,^{26–27} we provide estimates of reproducibility of phthalate metabolite concentrations across pregnancy. The goal of the study was to characterize the study population's phthalate levels during pregnancy to provide needed information about exposure patterns during pregnancy by race/ethnicity. Given racial/ethnic disparities in certain pregnancy and child health outcomes, such as preterm birth and small-for-gestational age, understanding variations in phthalate metabolite levels across pregnancy in a diverse population may provide needed information as to whether phthalates could explain a portion of racial/ethnic differences in adverse pregnancy outcomes.

Methods

Study population

The Lifecodes pregnancy cohort is an ongoing study of women who delivered at Brigham and Women's Hospital (Boston, MA). Starting in 2006, women were recruited into the cohort during the first trimester of pregnancy (at a median of 10 weeks gestation). Blood and urine samples were collected at 4 different study visits and study participants completed a demographic questionnaire querying sociodemographic and lifestyle factors. Blood plasma and serum were stored at –20C and urine was stored at –80C.

In 2011, a nested case-control study was initiated among women who delivered between 2006 and 2008 to assess the association between phthalate exposure and preterm birth in this study population. Details regarding this nested case-control study are presented elsewhere.⁴ From those women who delivered at term (>37 weeks gestation; n=350 women), we utilized existing data from completed questionnaires and urinary phthalate metabolite levels from the 4 pregnancy time points. We selected term births, as they represent women who were able to complete pregnancy and had the greatest number of urine samples across pregnancy, in order to evaluate changes in urinary phthalate metabolites across the entire pregnancy. All women provided informed consent. This study was approved by the Partners Human Subjects Committee at Brigham and Women's Hospital, as well as the University of Michigan's Health Sciences Institutional Review Board.

Urinary Phthalate Metabolites

Phthalate metabolites were measured in spot urine samples collected at 4 time points across pregnancy. Urine samples were collected at visits occurring at the following median gestation weeks: visit 1: 9.9 weeks gestation; visit 2: 17.9 weeks gestation; visit 3: 26.1 weeks gestation; and visit 4: 35.3 weeks gestation. Of the 350 possible samples at each time point, 99% were available at visit 1; 87% were available at visit 2; 86% were available at visit 3, and 90% were available at visit 4. We measured mono-n-butyl phthalate (MBP), mono-ethyl phthalate (MEP), mono-isobutyl phthalate (MiBP), mono-benzyl phthalate (MBzP), mono-(3-carboxypropyl) phthalate (MCPP), mono-(2-ethyl)-3-hexyl phthalate (MEHP), Mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), and mono-2-ethyl-5-oxohexyl phthalate (MEOHP). Two summary measures were developed for metabolites of DEHP using the sum of the molar

concentrations of its metabolites –one included all four metabolites (MEHHP, MECPP, MEOHP, and MEHP) and the other included the three oxidative metabolites excluding MEHP.

For each sample nine phthalate metabolites were assessed by NSF International, Inc. (Ann Arbor, MI) using the Centers for Disease Control and Prevention protocol described elsewhere.⁴²⁸ In brief, phthalate metabolites were converted from their glucuronidated form by enzymatic deconjugation followed by solid phase extraction and separation using high performance liquid chromatography. Tandem mass spectrometry was used for detection with limits ranging in the low nanogram per milliliter levels. When levels were below the limit of detection, we assigned a value of the limit of detection divided by the square root of 2.²⁹ To account for urine concentration, we adjusted for specific gravity (SG) in this analysis using the following formula: $P_c = P[(1.015 - 1)/SG - 1]$, where P_c represents the SG-adjusted concentration, P represents the measured urinary concentration, SG represents the SG for the individual sample and 1.015 is the median SG over all samples.⁴¹⁹ Urine samples with $SG > 1.04$ were excluded.³⁰

Race/Ethnicity

At study entry (8–10 weeks), women completed a baseline questionnaire, which collected information on a variety of sociodemographic factors. Women responded to a two-part question: First, women were asked: “What race do you consider yourself: Black, White, South Asian, East Asian, Native American/Pacific Islander, More than one race, Other.” Second, women were asked to respond to the question “Do you consider yourself to have a Hispanic or Latino background?: Yes or No.” Women were able to select more than one category for race. Women who selected “Other,” “More than one race,” or who marked more than one racial category were categorized as “Other.” Women who selected “Yes” for the second question regarding Hispanic or Latino ethnicity were categorized as Hispanic, regardless of the race they selected in the first question. Due to small numbers, we collapsed “South Asian” and “East Asian” into a single category of “Asian”. Given few Native American/Pacific Islanders in our study population, women selecting this racial category were categorized as “Other.”

Statistical Analysis

For all analyses, we used log₁₀-transformed SG-adjusted urinary phthalate metabolite concentrations. First, we evaluated characteristics of the study population stratified by race/ethnicity, calculating mean and standard deviations for continuous variables and percentages for categorical variables. Second, we calculated the geometric means of each phthalate metabolite at baseline (median 10 weeks) for the overall population, as well as for each racial/ethnic group. We used ANOVA to determine whether baseline levels significantly differed by race/ethnicity. Third, to capture the overall change in phthalate exposure during pregnancy, we used linear mixed models with a random intercept to estimate the percent change and 95% confidence intervals in phthalate metabolite levels comparing each later pregnancy measure (i.e. 16–18, 22–26, and 33–35 weeks) to the baseline measure at 8–10 weeks gestation. Percent change and 95% confidence intervals were calculated for the overall population, as well as for each racial/ethnic group. We constructed 3 models: model

1) unadjusted; model 2) adjusted for weight at time-specific gestational age; and model 3) adjusted for maternal age, education, weight at time specific gestational age, alcohol use, and smoking status. We also plotted the adjusted phthalate metabolite concentrations stratified by race/ethnicity. Multivariable-adjusted least squares geometric means of each phthalate metabolite were calculated by race/ethnicity at each time point in pregnancy (8–10 weeks, 16–18 weeks, 22–26 weeks, and 33–35 weeks gestation), and plotted. A previous study has evaluated reproducibility of phthalate metabolite levels in this pregnancy cohort, with low to moderate reproducibility.¹⁹

Results

In Table 1, we present baseline (8–10 weeks gestation) study population characteristics stratified by race/ethnicity. Women were of a diverse background with 16% African-American, 14% Hispanic, 5% Asian, and 59% white. The mean age was 31.9 years (SD=5.5) for the overall study population, with the baseline BMI being 25.9 (SD=5.7). A large proportion of the population were college graduates or higher (43.1%). Most women were never smokers (94.6%) and did not currently use alcohol during pregnancy (94.6%).

Table 2 presents SG-adjusted geometric means and 25th and 75th percentiles for baseline urinary phthalate metabolite levels for the overall population and by race/ethnicity. With the exception of the DEHP metabolites (i.e. MEHP, MEHHP, MEOHP, and MECPP), all baseline phthalate metabolites varied significantly by race/ethnicity, with the highest levels being among non-Hispanic blacks, Hispanics, and those who selected “Other” race/ethnicity. In fact, non-Hispanic blacks had a baseline SG-adjusted geometric mean MEP level of 286.0µg/L compared to 98.7µg/L for whites. Also, SG-adjusted geometric means for MBzP were considerably higher for Hispanics and non-Hispanic blacks compared to whites: 11.6 µg/L, 10.2µg/L, and 5.4 µg/L, respectively. Phthalate metabolite levels had low to moderate reproducibility among these pregnant women who made it to term with intra-class correlation coefficients ranging from 0.21 for the DEHP metabolites to 0.58 for MBzP in pregnancy (See Supplemental Tables 1 and 2 for details).

Change in phthalate metabolites across pregnancy—overall population

In Table 3, we present the change in pregnancy phthalate metabolite concentrations for the overall study population. While phthalate metabolite levels did not significantly change from 8–10 weeks to 16–18 weeks for any of the measured metabolites, when comparing 8–10 weeks to 22–26 weeks, we saw significant changes in MCPP and the DEHP metabolites. In fact, there was a 16.0% decrease (95% CI: –27.4, –2.8) in MCPP after adjustment for age, race/ethnicity, education, period-specific weight, alcohol use, and smoking status. For the total DEHP metabolites, after full-adjustment, there was a 30.6% decrease (95% CI: –40.9, –18.4), which was similar for the oxidative metabolites for DEHP. When comparing the change from 8–10 weeks to levels at 33–35 weeks gestation, there was no longer a significant change in MCPP, but MEHP, a metabolite of DEHP, continued to show a decrease compared to baseline (fully adjusted: –20.2%; 95% CI: –33.2, –4.6). MiBP at 33–35 weeks had a 18.6% increase (95% CI: 7.8, 30.5) after adjustment for weight. MBzP also

showed a significant increase (crude: 12.1%; 95% CI: 0.7, 24.8), but this did not hold after full adjustment (fully adjusted: 9.0; 95% CI: -4.0, 23.7).

Phthalate metabolites at multiple pregnancy time points by race/ethnicity

In Figure 1 (panels A-J), we present fully-adjusted least squares geometric means of each phthalate metabolite by race/ethnicity. (See Supplemental tables 1–3 for corresponding estimates of percent change). At all time points across pregnancy, non-Hispanic blacks had the highest concentrations of MCPP and the DEHP metabolites across pregnancy compared to any other racial/ethnic groups. Whereas, Hispanics had higher levels of MBP and MBzP compared to other racial/ethnic groups at all time points in pregnancy. Concentrations of MEP and MiBP were higher in non-Hispanic blacks and Hispanics compared to whites across all pregnancy time points.

Patterns across pregnancy differed for each phthalate metabolite, with MEP and MCPP having statistically significant differences by race/ethnicity (p for interaction for MEP=0.04 and p for interaction for MCPP=0.02). Levels of MEP decreased in second and third trimesters for Hispanic women, but remained relatively constant and high for non-Hispanic black women throughout pregnancy. White women had low levels of this phthalate metabolite, which remained fairly constant throughout pregnancy. For MCPP levels in non-Hispanic blacks were higher than in whites and Hispanics for the first two trimesters of pregnancy and decreased substantially at 22–26 weeks and 33–35 weeks gestation. On the other hand, Hispanics had a slight increase across pregnancy, with levels being higher than non-Hispanic blacks by third trimester. Whites maintained relatively constant levels of this phthalate metabolite.

Interestingly, MiBP increased during pregnancy for all racial/ethnic groups. On the other hand, DEHP modestly declined across pregnancy until late second trimester and then slightly increased by 33–35 weeks gestation. However, racial/ethnic differences in the patterns of these phthalates across pregnancy did not reach statistical significance.

Discussion

We found significant racial/ethnic differences for certain phthalate metabolite levels across pregnancy. Phthalate metabolite levels were higher in non-Hispanic black and Hispanic women across all pregnancy time points. In the overall population, levels of MCPP and DEHP metabolites significantly decreased, while levels of MiBP increased across pregnancy. Patterns of MEP and MCPP significantly differed by race/ethnicity across pregnancy, with decreasing levels in mid-pregnancy in non-Hispanic black and Hispanic women for MCPP and MEP, respectively. However, levels of these and all other phthalate metabolites remained higher among non-whites. These racial/ethnic differences for phthalate metabolite concentrations across pregnancy raise implications of different sensitivity windows in fetal development as a function of maternal race, as well as maternal health outcomes associated with elevated phthalate metabolite levels in pregnancy. Additionally, these racial/ethnic differences strongly suggest that exposure is itself a product of unique and specific behaviors or practices related to race/ethnicity. As such, our study provides needed information on racial/ethnic phthalate metabolite concentrations across pregnancy

that can inform future analyses to evaluate racial/ethnic differences in disease patterns associated with higher phthalate metabolite concentrations.

Racial/ethnic differences in urinary phthalate metabolite concentrations have been evaluated in a non-pregnant population comprised of a representative sample of the U.S. population participating in the National Health and Nutrition Examination Survey (NHANES 2001–2008). When comparing our study of pregnant women to this non-pregnant population, levels of MnBP were higher in pregnant non-Hispanic blacks and Hispanics participating in the present cohort.¹⁸ Urinary concentrations of MiBP and MBzP were also higher in our population of pregnant women, regardless of race/ethnicity relative to the non-pregnant NHANES population.¹⁸ MEP was lower in pregnant white women participating in our pregnancy cohort, but higher in pregnant non-Hispanic black and Hispanic women participating in our pregnancy cohort.¹⁸

Another study evaluated overall phthalate metabolite concentrations in pregnant women. Specifically, Zota et al compared pregnant versus non-pregnant women who participated in NHANES 2003–2004, which showed lower levels among pregnant women for MBP, MEP, and MiBP, but slightly higher levels of MBzP compared to non-pregnant women participating in NHANES. Urinary phthalate metabolite concentrations differed between our population and NHANES pregnant women from this earlier time period. Our overall population of pregnant women had lower levels of MBzP and MEP and higher levels of MiBP compared to pregnant women in NHANES 2003–2004.³¹ However, NHANES 2003–2004 levels of MEP were similar to that of our non-Hispanic black and Hispanic pregnant population.³¹ When evaluating other studies that examined phthalate levels in pregnant populations, we found levels of MEP and MnBP to be lower in our overall pregnant population compared to a study of black and Dominican women.²⁷ Levels were similar for MiBP in blacks and Hispanics and substantially lower for MBzP.²⁷ Differences in phthalate metabolite levels across these populations could be attributed to differences in laboratories across the various studies of pregnant women or changes in the use of certain phthalates over time. In fact a recent study found decreasing levels of many phthalate metabolites, with an increase in the use of di-isobutyl phthalate when evaluating a subset of NHANES participants between 2001 and 2010.³²

Reasons for racial/ethnic variations in urinary phthalate metabolite concentrations could be due to differences in exposure to phthalate containing consumer products. A recently published study found associations between self-reported personal care product use during pregnancy from a short questionnaire and phthalate metabolite concentrations in pregnant women.³³ Another study of pregnant women, suggested that differences in the use of perfumes could contribute to racial/ethnic variations in levels of MEP, as 45% of blacks and 41% of Dominicans used perfumes, with many using perfumes daily.²⁷ A different study of predominantly pregnant white women found a prevalence of perfume use of 31%.³³ Another alternative is that certain personal care products are predominantly used by one specific racial/ethnic group. In 2004, Silva et al posited that higher levels in non-pregnant, non-Hispanic blacks could be attributed to the use of certain types of hair products.¹⁷ Interestingly, a previous study found that non-pregnant black women were more likely to use hair products containing endocrine disrupting chemicals based on hair product labels

compared to white women (~50% of non-Hispanic black women compared to ~8% of white women).³⁴ However, phthalates are not required to be listed on the labels of personal care products. Furthermore, little is known about racial/ethnic differences in patterns of personal care product use related to phthalate exposure. Future studies will need to evaluate sources of exposure in a racially/ethnically diverse population accounting for product types that may differ across racial/ethnic groups to determine whether patterns of personal care product use could partially explain the significant differences for certain phthalate metabolite levels in pregnant women.

Higher phthalate metabolite levels in utero could explain some racial/ethnic differences in pregnancy outcomes. For example, a recent study found associations between higher in utero exposure to certain phthalate metabolites and intrauterine growth restriction.²¹ Interestingly, a greater proportion of Non-Hispanic black women have infants born small-for-gestational age compared to other racial/ethnic groups,³⁵ which is likely related to a host of factors, but could also be partly due to higher phthalate exposure in utero. Higher phthalate levels could explain some portion of racial/ethnic differences in maternal health outcomes. A recent study, using the same population as the present study, found an association between higher phthalate metabolites and an increased risk of preterm birth.⁴ Non-Hispanic black women have a significantly higher preterm birth rate than white women.³⁶ Future studies will need to confirm racial/ethnic differences in phthalate metabolite concentrations, as well as determine whether these differences could contribute to racial/ethnic disparities in poor infant or maternal health outcomes. If associations are found, interventions focusing on changing the use of certain products known to be associated with increased levels of these chemicals could reduce phthalate levels in pregnancy,²²³³ with implications on maternal and child health.

This study has several limitations. First, we only evaluated women who had term births. A previous study showed an association between higher phthalate metabolite levels and preterm birth in this population.⁴ As such, we possibly have a restricted subset of the population that is generally healthier and has somewhat lower phthalate metabolite concentrations than all pregnant women. As such, patterns could differ by race/ethnicity for women with preterm births or those with more co-morbid conditions that could result in preterm birth. Second, we did not have data on diet or lifestyle factors, including personal care product use for the study population. As major sources of phthalate exposure,⁸³³³⁷ data on these factors could provide insight into reasons for differences across racial/ethnic groups based on behavior patterns. Future studies will need to evaluate whether diet or lifestyle factors explains some of the racial/ethnic differences found in the present study. Third, our stratified analyses are based on a somewhat small subset of non-Hispanic black and Hispanic women. We could not evaluate Asian women in the longitudinal analysis across pregnancy due to small numbers. However, we did find statistically significant associations between racial/ethnic groups that are not likely due to chance alone. We also cannot rule out the possibility of differences in phthalate metabolism that could impact urinary concentrations based on geographic heritage, as well as a variety of other social and environmental factors.

Despite these limitations, this study has several strengths. First, we measured phthalate metabolite concentrations across 4 time points in pregnancy, with the majority of women in

the population having data on all 4 time points. Second, we were able to assess patterns of several different phthalate metabolite concentrations, as well as the DEHP metabolites in 3 different racial/ethnic groups. Third, we evaluated percent change in phthalate metabolites for the overall population and stratified by race/ethnicity controlling for potential confounders. As such we were able to evaluate patterns and changes in phthalate metabolites during early, mid, and late pregnancy to determine whether racial/ethnic differences in this environmental toxicant existed.

In conclusion, we found certain phthalate metabolite concentrations to vary by race/ethnicity across pregnancy. Concentrations of MBP, MEP, MiBP, and MBzP were significantly higher among non-Hispanic blacks and Hispanics during early first trimester, with significant changes in MiBP, MCPP and the DEHP metabolites across pregnancy for the overall population. Across pregnancy, MEP and MCPP varied significantly by race/ethnicity, with non-Hispanic black and Hispanic women having different patterns than white women. These data suggest that phthalate metabolite levels vary over pregnancy, but certain racial/ethnic groups may be more likely to have higher levels of these chemicals, with implications for poor health effects related to higher phthalate exposure in both mothers and their developing fetuses. Therefore, non-Hispanic black and Hispanic pregnant women may benefit from interventions to decrease phthalate metabolite exposure during pregnancy to improve their health and the health of their offspring.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Panel A: Mono-butyl phthalate

Panel D: Mono-benzyl phthalate

Panel B: Mono-ethyl phthalate

Panel E: Mono-(3-carboxypropyl) phthalate

Panel C: Mono-isobutyl phthalate

Panel F: Mono-(2-ethyl)-3-hexyl phthalate

Panel G: Σ DEHP metabolites Panel H: Oxidative Σ DEHP metabolites

Figure 1.
Adjusted phthalate metabolite concentrations across pregnancy by race/ethnicity

^a Adjusted for age (<25, 25–<30, 30–<35, 35–<40, >40), education (high school or less, technical school, some college, college graduate or higher), period-specific weight (continuous), alcohol drinking (yes, no) and smoking (current, past, never)

Table 1

Study population characteristics stratified by race/ethnicity

	Overall (n=350)	Non-Hispanic whites (n=206)	Non-Hispanic blacks (n=55)	Asians (n=19)	Hispanics (n=50)	Other (n=20)	p-value
Maternal age (mean, (SD))	31.9 (5.5)	33.6 (4.2)	29.3 (5.9)	33.2 (3.3)	27.3 (6.3)	32.0 (6.1)	<0.001
Maternal BMI (mean, (SD))	25.9 (5.7)	24.8 (5.0)	28.6 (6.6)	24.3 (3.7)	27.7 (6.7)	26.4 (5.0)	<0.001
Baseline weight in kg (mean, (SD))	70.4 (15.7)	68.7 (14.7)	78.3 (18.2)	65.2 (9.9)	70.9 (16.5)	70.1 (14.4)	<0.001
Education (%)							<0.001
HS	13.4	3.4	25.5	5.3	42.0	20.0	
Technical School/ Some college	43.5	41.8	60.0	26.4	38.0		
College	43.1	54.9	14.6	68.4	20.0	35.0	
Smoking (%)							0.20
Current	3.1	1.9	3.6	10.5	6.0	0.0	
Past	2.3	1.9	1.8	0.0	6.0	0.0	
Never	94.6	96.1	94.6	89.5	88.0	100.0	
Alcohol use during pregnancy (%)							
Yes	5.4	6.3	1.8	5.3	6.0	5.0	0.76
No	94.6	93.7	98.2	94.7	94.0	95.0	

Baseline (8–10 weeks gestation) urinary phthalate metabolite concentrations by race/ethnicity

Table 2

Baseline phthalate metabolites	SG-adjusted geometric means (25 th , 75 th percentiles)					p-value
	Overall (n=350)	Non-Hispanic whites (n=206)	Non-Hispanic blacks (n=55)	Asians (n=19)	Hispanics (n=50)	Other (n=20)
Mono-butyl phthalate (MBP)	17.1 (10.8, 25.9)	15.5 (10.5, 21.2)	22.1 (11.8, 39.1)	10.3 (8.7, 15.6)	21.7 (14.1, 33.9)	21.1 (15.9, 33.5)
Mono-ethyl phthalate (MEP)	135.0 (47.4, 342.0)	98.7 (41.0, 240.0)	286.0 (136.6, 468.3)	71.9 (27.5, 229.8)	247.4 (72.5, 630.0)	183.3 (101.3, 347.0)
Mono-isobutyl phthalate (MiBP)	7.2 (4.4, 11.1)	6.0 (4.2, 9.6)	10.2 (6.0, 17.3)	8.3 (4.4, 14.4)	8.6 (4.5, 14.2)	10.2 (7.0, 17.2)
Mono-benzyl phthalate (MBzP)	6.9 (3.4, 13.4)	5.4 (3.1, 9.1)	10.2 (4.2, 24.5)	4.9 (2.4, 9.3)	11.6 (4.9, 23.9)	11. (6.4, 22.3)
Mono-(2-ethyl-3-hexyl) phthalate (MEHP)	12.0 (5.0, 23.8)	12.3 (5.1, 25.7)	14.3 (5.8, 25.1)	13.7 (5.6, 26.8)	10.4 (4.4, 16.4)	7.7 (4.0, 16.9)
Mono-(3-carboxypropyl) phthalate (MCPP)	2.1 (1.0, 3.1)	2.0 (1.0, 3.1)	3.2 (1.3, 5.6)	1.6 (1.0, 2.6)	2.0 (0.9, 2.9)	1.8 (1.2, 2.3)
ΣDEHP metabolites	0.4 (0.2, 0.8)	0.4 (0.2, 0.8)	0.4 (0.2, 0.8)	0.5 (0.2, 1.7)	0.4 (0.2, 0.7)	0.3 (0.1, 0.5)
Oxidative ΣDEHP metabolites	0.4 (0.2, 0.7)	0.4 (0.2, 0.8)	0.4 (0.2, 0.6)	0.4 (0.1, 1.6)	0.4 (0.1, 0.6)	0.2 (0.1, 0.4)

Table 3

Percent change of SG-adjusted urinary phthalate metabolites and concentrations during pregnancy (n=350)

		Gestational Age			
		8–10 weeks	16–18 weeks	22–26 weeks	33–35 weeks
		Percent change (95% CI)			
MBP					
Unadjusted	Reference	1.2 (−7.7, 11.0)	−4.4 (−12.9, 4.8)	11.9 (2.2, 22.6)	
Weight-adjusted	Reference	−0.3 (−9.2, 9.4)	−9.1 (−17.5, 0.2)	3.2 (−6.9, 14.4)	
Multivariate-adjusted ^a	Reference	0.3 (−8.6, 10.0)	−7.5 (−16.0, 2.0)	5.9 (−4.5, 17.3)	
MEP					
Unadjusted	Reference	2.1 (−14.2, 21.5)	−2.3 (−18.0, 16.3)	10.3 (−7.1, 31.0)	
Weight-adjusted	Reference	−0.9 (−16.8, 18.0)	−10.4 (−25.5, 7.6)	−5.1 (−21.9, 15.3)	
Multivariate-adjusted ^a	Reference	0.7 (−15.5, 20.0)	−6.7 (−22.3, 12.1)	0.7 (−17.1, 22.4)	
MiBP					
Unadjusted	Reference	−4.1 (−11.6, 4.1)	2.0 (−6.0, 10.8)	22.1 (12.6, 32.4)	
Weight-adjusted	Reference	−5.2 (−12.7, 3.0)	−0.9 (−9.3, 8.2)	16.3 (5.6, 28.0)	
Multivariate-adjusted ^a	Reference	−4.7 (−12.3, 3.5)	0.5 (−8.0, 9.7)	18.6 (7.8, 30.5)	
MBzP					
Unadjusted	Reference	−2.2 (−12.2, 9.1)	−2.6 (−12.7, 8.6)	12.1 (0.7, 24.8)	
Weight-adjusted	Reference	−3.8 (−13.8, 7.4)	−7.1 (−17.5, 4.5)	4.6 (−8.1, 18.9)	
Multivariate-adjusted ^a	Reference	−3.0 (−13.1, 8.2)	−4.8 (−15.3, 7.1)	9.0 (−4.0, 23.7)	
MCPP					
Unadjusted	Reference	5.3 (−8.5, 21.1)	−13.8 (−25.1, −0.8)	−3.5 (−16.0, 10.8)	
Weight-adjusted	Reference	3.3 (−10.1, 18.8)	−16.6 (−27.9, −3.6)	−9.1 (−21.9, 5.8)	
Multivariate-adjusted ^a	Reference	3.5 (−10.0, 19.0)	−16.0 (−27.4, −2.8)	−8.1 (−21.1, 7.0)	
MEHP					
Unadjusted	Reference	−12.5 (−25.8, 3.1)	−23.2 (−34.9, −9.4)	−20.6 (−32.5, −6.5)	
Weight-adjusted	Reference	−12.7 (−26.0, 3.0)	−22.6 (−34.7, −8.1)	−19.3 (−32.4, −3.7)	
Multivariate-adjusted ^a	Reference	−12.6 (−26.0, 3.1)	−22.9 (−35.1, −8.5)	−20.2 (−33.2, −4.6)	
ΣDEHP metabolites					
Unadjusted	Reference	−12.5 (−25.3, 2.4)	−28.3 (−38.9, −15.9)	−5.8 (−20.1, 11.0)	
Weight-adjusted	Reference	−13.6 (−26.2, 1.1)	−29.8 (−40.2, −17.4)	−8.2 (−22.3, 8.4)	
Multivariate-adjusted ^a	Reference	−14.0 (−26.5, 0.7)	−30.6 (−40.9, −18.4)	−9.9 (−23.8, 6.4)	
ΣDEHP oxidative metabolites					

Gestational Age				
Unadjusted	Reference	−12.5 (−25.3, 2.5)	−28.8 (−39.3, −16.6)	−4.0 (−17.9, 12.2)
Weight-adjusted	Reference	−13.9 (−26.6, 1.0)	−30.4 (−40.9, −18.1)	−7.1 (−21.5, 10.0)
Multivariate-adjusted ^a	Reference	−14.3 (−26.9, 0.5)	−31.3 (−41.7, −19.0)	−8.8 (−23.0, 7.9)

^a Adjusted for age (<25, 25–<30, 30–<35, 35–<40, >=40), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian, unknown/other), education (high school or less, technical school, some college, college graduate or higher), period-specific weight (continuous), alcohol drinking (yes, no) and smoking (current, past, never)