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Prevalence and predictors of phthalate exposure in pregnant women in Charleston, SC

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Abstract

Phthalates are plasticizers commonly detected in human urine due to widespread exposure from PVC plastics, food packaging, and personal care products. Several phthalates are known antiandrogenic endocrine disruptors, which raises concern for prenatal exposure during critical windows of fetal development. While phthalate exposure is ubiquitous, certain demographics are subject to greater or lesser exposure. We sampled urine from 378 pregnant women during the second trimester of gestation living in Charleston, SC, and measured eight urinary phthalate metabolites as biomarkers of phthalate exposure: monobutyl phthalate (MBP), monobenzyl phthalate (MBzP), mono(2-ethylhexyl) phthalate (MEHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), monoethyl phthalate (MEP), monoisobutyl phthalate (MiBP), and monomethyl phthalate (MMP). Demographic data was collected from questionnaires administered at the time of specimen collection. All phthalate metabolites were detected in over 93% of urine samples. On average, concentrations were highest for MEP (median = 47.0 ng/mL) and lowest for MMP (median = 1.92 ng/mL). Sociodemographic characteristics associated with elevated phthalate concentrations included being unmarried, less educated, having a low income, high body mass index (BMI), and/or being African American.

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Conflicts of interest

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.chemosphere.2017.11.019.

After racial stratification, age, BMI, education, and income were significantly associated with phthalate concentrations in African American women. Marital status was associated with phthalate concentrations in Caucasian women only, with greater concentrations of MBP, MEHHP, MiBP, and MMP in unmarried versus married women. Results of this cross-sectional study provide evidence for significant racial and demographic variations in phthalate exposure.

Keywords

Phthalate; Pregnancy; Biomonitoring; Predictor; Race; Endocrine disruptor

1. Introduction

Phthalates are frequently used in consumer products as plasticizers and solubilizers. Because they are not chemically bound to products they are in, phthalates leach into the environment, resulting in ubiquitous human exposure. Primary routes of phtha-late exposure to humans include dietary consumption of contaminated food and water (Colacino et al., 2010; Serrano et al., 2014), and skin absorption following the use of personal care products (PCPs) (Duty et al., 2005; Guo and Kannan, 2013; Parlett et al., 2013). Two phthalates that are of particular concern due to their antiandrogenic properties are di-2-ethylhexyl phthalate (DEHP) and dibutyl phthalate (DBP). Diethyl phthalate (DEP) is also notable due to its widespread use in PCPs. As a result, the DEP metabolite monoethyl phthalate (MEP) is generally detected in urine at concentrations five to forty times higher than other phthalate metabolites in the U.S. (CDC, 2017; Silva et al., 2004a).

Phthalate exposure is prevalent among pregnant women, raising concern for fetal exposure, especially during critical periods of development (Woodruff et al., 2011). In utero exposure to select phthalates, as approximated by measuring maternal urinary phthalate metabolites, has been positively associated with adverse pregnancy outcomes, including preterm birth and low birth weight (Ferguson et al., 2014; Meeker et al., 2009; Zhang et al., 2009). Additionally, biomarkers of abnormal reproductive development have been noted in males following high-level prenatal phthalate exposure, including reduced anogenital distance, penile size, testosterone concentrations, and incomplete testicular descent (Main et al., 2006; Swan, 2008; Swan et al., 2005; Wagner-Mahler et al., 2011). Recent research suggests that prenatal phthalate exposure may also be associated with more expansive health outcomes later in life, including adverse neurocognitive development (Engel et al., 2009, 2010; Factor-Litvak et al., 2014; Whyatt et al., 2012), asthma (Dodson et al., 2012), diabetes (James-Todd et al., 2012b), and obesity (Desvergne et al., 2009; Trasande et al., 2013).

While phthalate exposure is ubiquitous, larger bioburdens have been associated with people of certain ethnicities, demographics, physical build, and socioeconomic class; however, these trends lack consistency across different studies (Casas et al., 2011). Previous surveys of phthalate concentrations in pregnant women have been conducted along the West Coast and in the Northeastern U.S.; the Southeast is a region with unique culture, climate, diet, lifestyle, and racial makeup that could introduce novel patterns of phthalate exposure. Because of the potential for adverse health outcomes, it is important to further our

understanding of patterns and sources of phthalate exposure across all populations. The aim of this cross-sectional study was to identify potential predictors of phthalate exposure in pregnant women residing in the Charleston, South Carolina metropolitan area.

2. Materials and methods

2.1. Study population

From 2011 to 2014, women from the Charleston area who planned to deliver at the Medical University of South Carolina (MUSC) were recruited to participate in a larger study designed to examine the relationship between maternal phthalate concentration and prenatal and neonatal genital measurements. Eligibility criteria to participate included being at least 18 years of age, carrying a singleton fetus, and having pregnancy dating confirmed by a first trimester ultrasound. Women were excluded if they were carrying a fetus with genetic anomalies or aneuploidy, using progesterone or other steroids, or had pre-gestational diabetes mellitus, hypo- or hyperthyroidism, or any other known endocrine disorders.

Between 18 and 22 (median 20) completed weeks of gestation, participants answered a study questionnaire, provided a urine specimen, and were evaluated for physical condition and relevant pregnancy characteristics. This study and all survey protocols were approved by the institutional review board of MUSC. All participants signed informed consent prior to enrollment.

2.2. Questionnaire

Demographic information was obtained through a questionnaire administered to women upon enrollment into the study. Clinical data was abstracted from medical records. Variables collected and evaluated in this study as potential determinants of phthalate exposure included maternal age, body mass index (BMI), race, parity, tobacco use, medication use, prenatal vitamin use, nutritional supplement use, contraceptive choice, marital status, education level, employment status, smoking status, annual household income, and season and year of sample collection. BMI was calculated from physician-recorded height and weight at time of enrollment. Race was self-categorized as either African American or Caucasian. Maternal education was classified into four ordinal categories: less than high school degree, high school graduate or equivalent, some college or technical school, and college graduate or above. Marital status was classified as two categories: married or living as married, and single (including single, separated, divorced, and widowed). Annual household income was classified into four categories for analysis: less than $25 000, $25 000 to $65 000, greater than $65 000, and do not know. Age, BMI, and education were treated as continuous variables, and race, marital status, and household income were treated as categorical variables.

2.3. Phthalate metabolite analysis

Urine from 378 women was analyzed for eight phthalate metabolites, including monobutyl phthalate (MBP), monobenzyl phthalate (MBzP), mono(2-ethylhexyl) phthalate (MEHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), monoisobutyl phthalate (MiBP), MEP, and monomethyl phthalate (MMP). Spot

urine specimens were collected in sterile glass jars in the obstetrical clinics at MUSC and transferred to the Hollings Marine Laboratory (Charleston, South Carolina) for analysis. After measuring specific gravity (SG) at room temperature using a handheld refractometer (Atago U.S.A., Inc. Bellevue, WA, USA), urine was divided into 1 mL aliquots and stored under appropriate conditions (−20° C) until analysis.

Extraction and analysis methods were based on those previously developed by the U.S. Centers for Disease Control and Prevention, described elsewhere (Silva et al., 2004b). Method details and modifications can be found in the Supplementary Material. Briefly, β-glucuronidase was added to 1 mL urine to enzymatically deconjugate phthalate metabolites from their glucuronidated form. Urine samples were processed on automated solid-phase extraction workstations (RapidTrace, Biotage, Uppsala, Sweden) fitted with polymeric sorbent-filled cartridges (60 mg, 3 mL; Bond Elut NEXUS, Agilent Technologies, Santa Clara, CA, USA) and eluted with acetonitrile and ethyl acetate. Eluates were evaporated to dryness and reconstituted in 200 μL water for analysis.

Urinary phthalate metabolites were separated with an Agilent 1100 Series liquid chromatography system using a 3 mm, 150 mm × 2.1 mm Betasil phenyl column (Table S1; Thermo Fisher Scientific, Waltham, MA, USA), and detected by tandem mass spectrometry on an API 4000 triple quadrupole mass spectrometer (Table S2; Applied Biosystems MDS/Sciex, Foster City, CA, USA). Pooled urine control material, a standard reference material (SRM 3673, Organic Contaminants in Non-Smokers' Urine, National Institute of Standards and Technology, Gaithersburg, MD, USA), and reagent blank samples were included in each analytical batch along with unknown samples. In addition to analyzing eight individual phthalate metabolites, molar sums of the three measured DEHP metabolites were also calculated: ΣDEHP = (MEHP/278) + (MEOHP/292) + (MEHHP/294), in nmol/L.

2.4. Statistical analyses

The limit of detection (LOD) for each metabolite was estimated as the mean of the control blanks plus three times the standard deviation of the mean, or the concentration of the lowest detectable calibrant successfully measured using a signal to noise ratio of three. The higher LOD was applied, providing conservative and analyte-specific LODs linked to the recovery of mass-labeled internal standards (Ragland et al., 2014). Urinary concentrations of phthalate metabolites below the LOD were assigned a value equal to half the LOD for statistical analysis. Specific gravity was used to correct for urine dilution according to the following formula: $P_c = P((1.016-1)/(SG - 1))$, where P_c is the SG-corrected phthalate concentration (ng/mL), 1.016 is the mean SG for all study participant urine samples, and SG is the individual specific gravity of urine (Boeniger et al., 1993). The concentrations of all phthalate metabolites were natural log-transformed in order to meet the assumptions for statistical analysis.

Associations between race and nominal variables were evaluated using chi-square tests. Associations between race and ordinal variables were evaluated using the Cochran-Armitage trend test, and associations with continuous variables were evaluated using the Mann-Whitney *U* test. We assessed univariate associations between individual covariates and phthalate concentrations by Pearson correlations, Student's t-test, or one-way analysis of

variance (ANOVA), as appropriate. To evaluate the impact of clinical and sociocultural factors on phthalate concentrations, we employed multiple linear regression models that included a priori-selected predictors consistently reported in the literature as associated with phthalate exposure (Casas et al., 2011; Kobrosly et al., 2012; Koo et al., 2002; Valvi et al., 2015). These variables include maternal age, race, education, and household income as a proxy for socioeconomic status (SES), as well as BMI during the current pregnancy. Other variables evaluated included parity, smoking status, medication use, prenatal vitamin use, nutritional supplement use, contraceptive choice, and season and year of enrollment, but these variables were not incorporated into the final model due to lack of significance in univariate analyses. Race was strongly associated with other independent variables in the analysis and modified their relationships with phthalate concentrations; therefore, we also conducted the analysis stratified by race. Statistical analyses were performed using IBM SPSS Statistics, version 22 (IBM Corp. Armonk, NY, USA) and R, version 3.2.5 (R Core Team, 2016) with the significance level set at $\alpha = 0.05$.

3. Results

3.1. Study population

Descriptive statistics of the clinical and sociocultural characteristics are presented in Table 1 for the population overall and by race. Of the women enrolled in the study, 49.2% were African American and 50.8% were Caucasian. The median (interquartile range) age of all participants was 27 (8) years and the second trimester BMI was 27.2 (8.5) kg/m^2. Over 67% of the enrolled women had at least some college education, and 88.3% were non-smokers. Racial differences emerged for several variables; most notably, Caucasian women were significantly older, had lower BMIs, and were more likely to be nulliparous, compared to African American women ($p < 0.001$). A greater percentage of Caucasian women were more likely to be married (83.2 vs. 25.1%), have a college education (63.6 vs. 21.8%), and earn over $65 000 per year(46.4 vs. 2.9%), compared to African American women (all $p < 0.05$).

3.2. Phthalate prevalence

Every phthalate metabolite measured in this study was detected at levels above the LOD in at least 93% of urine samples (Table 2). MEHHP and MiBP were present in 100% and MEHP, MEOHP, MBP, MBzP, and MEP were present in over 95% of samples. The least prevalent metabolite was MMP, which was detected in 93.7% of samples. Both SG-adjusted and unadjusted geometric means and 95% confidence intervals (CIs) of the eight phthalate metabolites are presented in Table 2. Consistent with previous studies and the National Health and Nutrition Examination Survey (NHANES) concentrations from 2011 to 2012 (CDC, 2017), concentrations of MEP were noticeably higher than any other metabolite. The metabolite with the lowest concentration in both this study and in NHANES was MMP (CDC, 2017). Urinary phthalate metabolites displayed significant positive correlations with each other ($p < 0.05$), ranging from $r = 0.11$ for MEP with MEHP, to $r = 0.97$ for MEHHP with MEOHP and ΣDEHP (Table S3).

3.3. Univariate analysis

Other studies have shown phthalate concentrations to be associated with certain demographics. Initially, univariate analyses were conducted to determine if phthalate concentrations were associated with age, BMI, race, education, marital status, or household income in our study population (Table S4).

We found a significant inverse correlation between age and phthalate concentrations for four metabolites (MBzP, MEHP, MiBP, and MEP), and a significant positive correlation between BMI and phthalate concentration for all except two metabolites (MEHP and ΣDEHP; $p < 0.05$). Significantly elevated concentrations of six phthalate metabolites were observed in African American women compared to Caucasian women ($p < 0.005$). In addition, concentrations of MEOHP, MEHHP, and ΣDEHP were higher in African Americans than in Caucasians, though the differences were not statistically significant. College-educated women had the lowest phthalate concentrations, and this difference was significant for MBP, MBzP, MiBP, MEP, and MMP ($p < 0.005$). Women who were married or living as married had significantly lower phthalate levels than unmarried women ($p < 0.05$), with the exception of MEHP. Lastly, women whose annual household income was less than $25 000 or who did not know their household income exhibited significantly higher phthalate concentrations than women earning $65 000 or more per year ($p < 0.05$ for MBP, MBzP, MiBP, MEP, and MMP).

3.4. Multivariate analysis

Urinary phthalate metabolite concentrations in the overall population of pregnant women showed significant differences after controlling for age, BMI, race, education, marital status, and household income (Table 3). After adjusting for age, BMI, education, marital status, and household income, race remained significantly associated with concentrations of MBzP, MiBP, MEP, and MMP ($p < 0.05$), with African Americans displaying higher phthalate levels than Caucasians. The greatest difference was seen with MEP, which was 62% higher in African Americans than in Caucasians (Fig. S1).

After adjusting for age, race, education, marital status, and household income, BMI remained positively associated with concentrations of MBP, MBzP, and MiBP ($p < 0.05$). Maternal education level was inversely correlated with MBP, MiBP, and MEP concentrations ($p < 0.05$). Concentrations of MEP decreased by 21% for every one-level increase in educational attainment (from less than high school, to high school, to some college, to a college education or greater). Age and marital status were significantly associated with concentrations of MBP ($p < 0.05$), with a one-year increase in age resulting in a 3% increase, and being single versus married resulting in a 27% increase in MBP, controlling for other factors. Household income was significantly associated with MBP and MBzP ($p < 0.05$), with women making over $65 000 per year having lower concentrations than women making less than $25 000 per year.

When stratified by race, significant predictors of phthalate exposure varied from those for the overall population (Tables 4 and 5). The multivariate analysis of African American women only is presented in Table 4. Maternal education was a stronger predictor of

phthalate exposure for African American women than it was for the overall population, with increasing educational attainment resulting in significantly reduced concentrations of four phthalate metabolites (MBP, MBzP, MiBP, and MEP; $p < 0.05$; Fig. S2). Marital status was no longer significantly associated with MBP concentrations, and the significant association between household income and MBzP disappeared when considering only African American women (Figs S3 and S4). There were no associations between marital status and phthalates for African American women; conversely, marital status was the only significant predictor of phthalate concentration for Caucasian women, with married women having lower concentrations of MBP, MEOHP, MiBP, and MMP than single women ($p < 0.05$; Table 5 & Fig. S3).

4. Discussion

In this cross-sectional study of 378 pregnant women, we detected two phthalate metabolites in all participants and all other metabolites in at least 93% of subjects. We identified several sociocultural characteristics that were associated with above average phthalate concentrations, with race being the most influential. After stratifying by race, age, BMI, education, and income were significantly associated with phthalate concentrations in African American women, while only marital status was significantly associated with phthalate concentrations in Caucasian women.

Participants in this study were generally younger and more racially diverse than pregnant women in similar studies (Bustamante-Montes et al., 2013; Suzuki et al., 2012; Swan et al., 2015). Phthalate exposure in our study population was ubiquitous, supporting findings from similar exposure assessments that have detected phthalates in 98–100% of pregnant women both nationally (Cantonwine et al., 2016; Just et al., 2010; Woodruff et al., 2011) and internationally (Casas et al., 2011; Enke et al., 2013; Frederiksen et al., 2014; Lin et al., 2011). Similar to NHANES, the high concentrations of MEP found in our study likely reflect the frequent use of DEP-containing PCPs (Parlett et al., 2013).

Relative to similar studies conducted in the U.S. phthalate concentrations observed in our study population were slightly higher than those reported for The Infant Development and the Environment Study (Swan et al., 2015), and were also higher than reported values for all U.S. females from 2011 to 2012 (CDC, 2017). Concentrations of phthalates reported here were generally lower than those in pregnant women from Spain and Taiwan (Lin et al., 2011; Valvi et al., 2015), but were similar to concentrations reported in pregnant women in Germany (Enke et al., 2013) and Denmark (Jensen et al., 2016). When considering these trends, it is important to remember that phthalate concentrations can be difficult to compare among different studies due to variations in extraction, analytical, and urine dilution adjustment methods.

Several studies suggest that exposure to certain phthalates (benzyl butyl phthalate [BBzP], DBP, and DEHP) has decreased over the past decade following implementation of government regulation and voluntary removal, while exposure to other phthalates (diisononyl phthalate, diisobutyl phthalate) and phthalate substitutes (diisononyl cyclohexane-1,2-dicarboxylate [DINCH], di-2-ethylhexyl terephthalate [DEHTP]) is

increasing (Calafat et al., 2015; Silva et al., 2013; Zota et al., 2014). In this study, concentrations of all phthalate metabolites except MEHP were higher in 2011 and 2013 than in 2012 and 2014, although the differences were not statistically significant. MEHP concentrations were significantly higher in 2011 than in any subsequent year ($p < 0.001$, data not shown), indicating a potential decrease in exposure to its parent compound DEHP; however, the other DEHP metabolites measured here did not corroborate this trend. Additionally, we did not identify any seasonal patterns of phthalate exposure.

In the overall adjusted model and in the stratified model for African Americans, MBP concentrations were positively associated with age (Fig. S5). Previous studies have not found associations between age and phthalate concentration in men (Duty et al., 2005), or in pregnant Spanish women (Valvi et al., 2015). After adjusting for other variables, there were also significant positive associations between BMI and MBP, MBzP, and MiBP. These associations also remained significant for African Americans in the race-stratified model (Fig. S6). Several previous studies corroborate this relationship between BMI and phthalate concentrations (Buser et al., 2014; Peck et al., 2010; Stahlhut et al., 2007; Valvi et al., 2015; Yaghjyan et al., 2015), including a study of pregnant women in which nine phthalate metabolites exhibited a positive correlation with BMI (Wolff et al., 2008). Obesity disproportionately affects minorities and those of lower income (Mitchell et al., 2011), which could explain why BMI is significantly associated with phthalate concentrations in African Americans but not in Caucasians.

The potential for phthalates to act as obesogens is a research area of growing interest that could potentially explain our findings of a positive association between BMI and phthalate concentrations. Several *in vitro* (Feige et al., 2007; Sargis et al., 2010) and *in vivo* studies (Hao et al., 2012) attribute obesogen activity to the interaction of phthalates with hormone receptors, leading to disrupted metabolism and increased adipogenesis. Specifically, phthalates can bind to peroxisome proliferator-activated receptors alpha and gamma, which regulate glucose metabolism and adipocyte activity (Casals-Casas et al., 2008; Desvergne et al., 2009; Grun and Blumberg, 2007). Epidemiological studies have found that urinary levels of some phthalates were associated with the incidence of diabetes among women (James-Todd et al., 2012b) and faster weight gain over a period of ten years (Song et al., 2014). Additionally, heavier individuals or pregnant women may have greater phthalate concentrations due to increased dietary consumption, indoor exposures, medication, and personal care product use.

Several previous studies have also detected elevated phthalate concentrations in racial minority groups. From 1999 to 2000, non-Hispanic black men and women in the U.S. had significantly higher MEP concentrations than did Mexican Americans or non-Hispanic whites (Silva et al., 2004a). Non-white women of reproductive age in the U.S. from 2001 to 2008 had higher concentrations of MBP, MiBP, MBzP, and MEP, but not DEHP metabolites (Kobrosly et al., 2012). A third study conducted from 2001 to 2008 found that African American men and women aged 12 and up had higher levels of MEP, MBP, MiBP, MBzP, and ΣDEHP than whites or Mexican-Americans (Huang et al., 2014). Our results support findings of higher phthalate concentrations in African Americans compared to Caucasians,

and provide evidence for a significant racial disparity in phthalate exposure in the Southeast U.S.

Genetic polymorphisms can contribute to ethnic variations in phase I metabolism enzymes (Guillemette, 2003; McGraw and Waller, 2012), providing one potential explanation for racial disparities of phthalate concentrations. African Americans may also be subject to higher personal care product or dietary phthalate exposures. Several studies have shown that African American women use more hair products than Caucasians, and that many of these hair products contain hormonally active chemicals (James-Todd et al., 2012a; Li et al., 2002; Tiwary, 1997; Wise et al., 2012). Additionally, a greater proportion of African American women compared to white and Mexican American women report use of vaginal douches, resulting in significantly higher MEP exposure (Branch et al., 2015). African Americans also generally consume more highly processed foods and fast food than Caucasians, which are substantial sources of phthalate exposure (Neff et al., 2009; Zota et al., 2016).

Our results suggest that concentrations of phthalates are likely to increase in single Caucasian women by 79% for MBP, 64% for MMP, 46% for MiBP, and 39% for MEOHP, relative to married Caucasian women (Fig. S3). Low and high molecular weight phthalates were significantly associated with marital status, suggesting that single Caucasian women are exposed to higher levels of phthalates through the use of more PCPs and the consumption of processed foods; both are practices associated with a more social lifestyle. However, marital status was not significantly associated with concentrations of MEP, a metabolite most commonly associated with PCP use. Ultimately, the explanation for this association remains unclear and merits further investigation. To our knowledge, this is the first description of an association between marital status and phthalate concentration.

In the race-stratified analysis, income remained a significant predictor of phthalate exposure in African Americans only. African American women who were unaware of their household income had 87% higher MBP concentrations and 80% higher MEOHP concentrations than African American women making over $65 000 per year. Additionally, African American women with household incomes of less than $25 000 had 80% higher MBP concentrations than African American women with household incomes of greater than $65 000. These results could be influenced by the fact that only 2.9% of African American women in our study population reported an income of over $65 000 per year. Income was not associated with phthalate exposure in Caucasian women.

Results from studies examining associations between SES and phthalate concentrations have varied, with some agreeing with our findings of an inverse association, and others showing a positive association (Adibi et al., 2009; Kobrosly et al., 2012; Koo et al., 2002; Tyrrell et al., 2013; Valvi et al., 2015; Ye et al., 2008). In four epidemiological studies, positive associations were found between social class, education, income, and SES and phthalate exposure (Casas et al., 2011; Kobrosly et al., 2012; Tyrrell et al., 2013; Ye et al., 2008). These findings, in addition to ours, suggest that associations between SES and phthalate concentrations are highly variable and dependent on the metabolites and population in question.

Several limitations should be considered when interpreting these results. First, all analyses are based on phthalate measurements from a single urine sample taken in the second trimester of pregnancy. Phthalates are rapidly metabolized and excreted from the body and we were not able to control for sampling time or exposures prior to sampling. However, two studies have shown that a spot urine sample can be representative of phthalate exposure over a couple of days (Hoppin et al., 2002) or several months (Hauser et al., 2004). Second, we assume that phthalates have similar pharmacokinetic properties in all individuals, and that excretion rates do not vary. We know this is unlikely, but have attempted to minimize variability by correcting for urine concentration with specific gravity measurements and performing race-stratified multiple regressions. Lastly, we may be missing other potentially important predictive variables, such as dietary and PCP use habits. Future work will incorporate dietary information and additional sampling time points into the analysis. Major strengths of this study are its racially diverse population and relatively large sample size (n = 378). Our cohort consisted of 49% African American and 51% Caucasian women, providing a unique opportunity to examine racial disparities in phthalate concentrations.

5. Conclusions

In summary, we present phthalate concentrations in a racially diverse population of pregnant women in Charleston, SC. We found that phthalate concentrations were higher in women who were African American, less educated, single, had higher BMI, and/or low household income. Marital status was associated with phthalate concentrations in Caucasian women only, with greater concentrations in unmarried versus married women. Predictors of phthalate exposure varied by race, confirming significant racial and demographic variations in phthalate exposure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclaimer: Certain commercial equipment or instruments are identified in the paper to specify adequately the experimental procedures. Such identification does not imply recommendations or endorsement by NIST nor does it imply that the equipment or instruments are the best available for the purpose.

Abbreviations:

ANOVA	analysis of variance
BBzP	butylbenzyl phthalate
BMI	body mass index
CI	confidence interval

DBP	dibutyl phthalate
DEHP	di-2-ethylhexyl phthalate
DEHTP	di-2-ethylhexyl terephthalate
DEP	diethyl phthalate
DF	detection frequency
DiBP	diisobutyl phthalate
DINCH	diisononyl cyclohexane-1,2-dicarboxylate
DINP	diisononyl phthalate
DMP	dimethyl phthalate
DnBP	di-*n*-butyl phthalate
GM	geometric mean
GSD	geometric standard deviation
ICC	intraclass correlation coefficient
LOD	limit of detection
MBP	monobutyl phthalate
MBzP	monobenzyl phthalate
MEHP	mono(2-ethylhexyl) phthalate
MEHHP	mono(2-ethyl-5-hydroxyhexyl) phthalate
MEOHP	mono(2-ethyl-5-oxohexyl) phthalate
MEP	monoethyl phthalate
MiBP	monoisobutyl phthalate
MMP	monomethyl phthalate
MUSC	Medical University of South Carolina
NHANES	National Health and Nutrition Examination Survey
NIST	National Institute of Standards and Technology
PCP	personal care product
PVC	polyvinyl chloride
REF	reference group
SC	South Carolina

SD	standard deviation
SES	socioeconomic status
SG	specific gravity
SRM	standard reference material

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HIGHLIGHTS

- Phthalate metabolites are prevalent in pregnant women in Charleston, SC.
- African American women are exposed to more phthalates than Caucasians.
- Predictors of phthalate exposure vary by race.
- Age, BMI, education, & income are associated with phthalates in African Americans.
- Marital status was the only predictor of phthalate levels in Caucasians.

Table 1

Distributions of clinical and sociocultural characteristics overall and by race. Continuous variables are reported as median (interquartile range) and categorical variables are reported as n (%).

Clinical and demographic variables	Overall (n = 378)	African American (n = 186)	Caucasian (n = 192)	p-value
Age, years[a, i]	27.0 (8)	24.0 (8)	29.0 (7.5)	<0.001
BMI, kg/m^2 [b, i]	27.2 (8.5)	29.4 (9.8)	26.3 (6.4)	<0.001
Nulliparous[c, j]	153 (40.7)	60 (32.1)	93 (48.9)	<0.001
Ever smoker[d, j]	44 (11.7)	23 (12.4)	21 (11.1)	0.69
Used medication during pregnancy[e, j]	144 (40.0)	67 (38.1)	77 (41.8)	0.46
Used prenatal vitamins during pregnancy[f, j]	316 (88.3)	148 (84.6)	168 (91.8)	0.03
Used contraception before pregnancy[f, j]	68 (19.0)	26 (14.9)	42 (22.8)	0.06
Married or living as married[g, j]	197 (54.9)	44 (25.1)	153 (83.2)	<0.001
Education[f, k]				
< High School	40 (11.2)	28 (16.1)	12 (6.5)	<0.001
High School	75 (20.9)	57 (32.8)	18 (9.8)	
Some college	88 (24.6)	51 (29.3)	37 (20.1)	
College +	155 (43.3)	38 (21.8)	117 (63.6)	
Household income[h, k]				
< $25 000	90 (25.4)	70 (40.2)	20 (11.0)	0.03
$25 000 e $65 000	81 (22.8)	32 (18.4)	49 (27.1)	
> $65 000	89 (25.1)	5 (2.9)	84 (46.4)	
Don’t know	95 (26.8)	67 (38.5)	28 (15.5)	
Season of enrollment[k]				
Spring	88 (23.3)	46 (24.7)	42 (21.9)	0.66
Summer	124 (32.8)	64 (34.2)	60 (31.3)	
Fall	97 (25.7)	43 (23.0)	54 (28.1)	
Winter	69 (18.2)	33 (17.6)	36 (18.8)	
Year of enrollment[k]				

Clinical and demographic variables	Overall (n = 378)	African American (n = 186)	Caucasian (n = 192)	p-value
2011	77 (20.4)	39 (21.0)	38 (19.8)	0.80
2012	122 (32.3)	60 (32.3)	62 (32.3)	
2013	113 (29.9)	58 (31.2)	55 (28.6)	
2014	66 (17.5)	29 (15.5)	37 (19.3)	

Characters represent missing observations.

[a] n = 1.

[b] n = 3.

[c] n = 2.

[d] n = 4.

[e] n = 19.

[f] n = 21.

[g] n = 20.

[h] n = 24.

[i] Mann-Whitney U test for difference by race.

[j] Chi-square test for difference by race.

[k] Cochran-Armitage trend test for difference by race.

Table 2

Limits of detection, detection frequency, and concentrations of urinary phthalate metabolites (ng/mL) during pregnancy in this study (n = 378) and in NHANES females from 2011 to 2012 (n = 1229).

Parent Phthalate	Phthalate Metabolite	LOD (ng/mL)	DF (%)	SG-adjusted GM[a] (95% CI)	Unadjusted GM[b] (95% CI)	NHANES'11 to '12[c] GM (95% CI)
DEHP	MEHP	0.35	95.8	3.13 (2.85−3.45)	2.65 (2.36−2.99)	1.24 (1.14−1.34)
DEHP	MEOHP	0.10	99.7	5.92 (5.48−6.42)	5.02 (4.50−5.62)	7.20 (6.77−7.66)
DEHP	MEHHP	0.10	100	7.49 (6.92−8.09)	6.34 (5.70−7.10)	4.71 (4.39−5.07)
DiBP	MiBP	0.17	100	11.3 (10.4−12.3)	9.57 (8.44−10.8)	5.52 (4.95−6.15)
DBP	MBP	0.95	98.4	16.1 (14.8−17.6)	13.7 (12.1−15.5)	7.14 (6.05−8.41)
BBzP	MBzP	0.10	98.4	11.2 (9.83−12.8)	9.47 (8.06−11.1)	4.27 (3.81−4.77)
DMP	MMP	0.34	93.7	2.27 (2.01−2.54)	1.92 (1.66−2.23)	[d]
DEP	MEP	1.00	98.9	55.5 (47.9−64.2)	47.0 (39.3−55.5)	37.7 (30.6−46.4)

LOD = limit of detection; DF = detection frequency; GM = geometric mean; NHANES = National Health and Nutrition Examination Survey.

[a] Values adjusted for specific gravity.

[b] values not adjusted for specific gravity.

[c] Centers for Disease Control (CDC) Fourth Report Updated, unadjusted values for females aged 6 + 2011–2012.

[d] Not calculated: proportion of results below limit of detection was too high to provide a valid result.

Table 3

Multiple linear regression associations between clinical and sociocultural factors with maternal urinary phthalate metabolites[a] in the overall population (n = 378).

Demographic factors	Overall $\beta_{adjusted}$[b] (95% CI)								
	MBP	MBzP	MEHP	MEOHP	MEHHP	∑DEHP[c]	MiBP	MEP	MMP
Age	0.03 * (0.01, 0.04)	−0.01 (−0.04, 0.01)	−0.01 (−0.03, 0.01)	0.00 (−0.02, 0.02)	0.00 (−0.02, 0.02)	0.00 (−0.02, 0.01)	0.02 (0.00, 0.03)	0.01 (−0.02, 0.04)	0.02 (−0.01, 0.04)
BMI	0.02 * (0.01, 0.04)	0.03 * (0.02, 0.05)	0.00 (−0.02, 0.01)	0.01 (0.00, 0.02)	0.01 (0.00, 0.02)	0.01 (0.00, 0.02)	0.01 * (0.00, 0.03)	0.02 (−0.01, 0.04)	0.01 (−0.01, 0.02)
Race	0.18 (−0.03, 0.38)	0.44 * (0.13, 0.75)	0.23 (−0.03, 0.49)	−0.14 (−0.35, 0.07)	−0.07 (−0.30, 0.15)	−0.05 (−0.26, 0.16)	0.41 * (0.21, 0.61)	0.62 * (0.26, 0.99)	0.31 * (0.03, 0.59)
Education	−0.11 * (−0.22,−0.01)	−0.11 (−0.26, 0.04)	−0.03 (−0.16, 0.10)	−0.03 (−0.14, 0.07)	−0.02 (−0.13, 0.08)	−0.03 (−0.14, 0.07)	−0.13 * (−0.23,−0.03)	−0.21 * (−0.40,−0.03)	−0.14 (−0.28, 0.00)
Marital Status	0.27 * (0.05, 0.50)	0.02 (−0.31, 0.35)	−0.02 (−0.30, 0.26)	0.21 (−0.02, 0.44)	0.20 (−0.04, 0.43)	0.14 (−0.09, 0.36)	0.19 (−0.03, 0.41)	0.27 (−0.13, 0.66)	0.29 (−0.02, 0.59)
Income (<25 K vs. >65 K	0.33 * (0.01, 0.65)	0.57 * (0.10, 1.04)	−0.23 (−0.62, 0.18)	−0.06 (−0.39, 0.26)	−0.11 (−0.45, 0.23)	−0.10 (−0.43, 0.22)	0.18 (−0.14, 0.49)	0.31 (−0.88, 0.26)	0.30 (−0.14, 0.73)
Income (25−65 K vs. >65 K)	0.20 (−0.05, 0.44)	0.38 * (0.02, 0.75)	−0.13 (−0.44, 0.18)	−0.01 (−0.26, 0.24)	0.00 (−0.26, 0.26)	−0.03 (−0.28, 0.22)	0.11 (−0.13, 0.34)	−0.09 (−0.53, 0.34)	0.15 (−0.19 0.48)
Income (don't know vs. >65 K)	0.36 * (0.04, 0.67)	0.42 (−0.04, 0.89)	0.08 (−0.31, 0.48)	0.04 (−0.28, 0.36)	0.02 (−0.32, 0.35)	0.06 (−0.26, 0.38)	0.10 (−0.21, 0.40)	−0.03 (−0.59, 0.53)	−0.03 (−0.45, 0.40)

* $p < 0.05$.

[a] Specific gravity-corrected, log-transformed values.

[b] Model mutually adjusts for age, BMI, race, education, marital status, and household income.

[c] Molar sum of DEHP metabolites (MEHP, MEOHP, MEHHP) in nmol/L.

Table 4

Multiple linear regression associations between clinical and sociocultural factors with maternal urinary phthalate metabolites[a] in African Americans only (n = 186).

Demographic factors	$\beta_{adjusted}$ [b] (95% CI) for African Americans								
	MBP	MBzP	MEHP	MEOHP	MEHHP	∑DEHP[c]	MiBP	MEP	MMP
Age	0.03 * (0.01, 0.05)	0.00 (−0.03, 0.03)	−0.01 (−0.04, 0.02)	−0.01 (−0.03, 0.02)	0.00 (−0.03, 0.02)	−0.01 (−0.03, 0.02)	0.02 (0.00, 0.05)	0.03 (−0.01, 0.07)	0.02 (−0.01, 0.05)
BMI	0.03 * (0.01, 0.04)	0.04 * (0.02, 0.06)	0.01 (−0.01, 0.03)	0.02 (0.00, 0.03)	0.01 (−0.01, 0.03)	0.01 (0.00, 0.03)	0.02 * (0.01, 0.04)	0.02 (−0.01, 0.05)	0.01 (−0.01, 0.04)
Education	−0.19 * (−0.33,−0.06)	−0.26 * (−0.42,−0.10)	−0.13 (−0.29, 0.04)	−0.06 (−0.18, 0.07)	−0.05 (−0.19, 0.10)	−0.07 (−0.20, 0.07)	−0.19 * (−0.32,−0.07)	− 0.27 * (−0.49,−0.05)	−0.13 (−0.31, 0.04)
Marital Status	−0.07 (−0.38, 0.23)	−0.17 (−0.55, 0.20)	−0.12 (−0.50, 0.26)	0.05 (−0.24, 0.34)	0.08 (−0.25, 0.40)	0.02 (−0.29, 0.34)	0.06 (−0.24, 0.35)	0.07 (−0.44, 0.59)	0.01 (−0.39, 0.41)
Income (<25 K vs. >65 K	0.80 * (0.02, 1.58)	0.16 (−0.80, 1.12)	0.15 (−0.83, 1.12)	0.60 (−0.14, 1.35)	0.53 (−0.30, 1.37)	0.49 (−0.31, 1.28)	0.12 (−0.63, 0.88)	0.57 (−0.75, 1.89)	1.00 (−0.03, 2.03)
Income (25−65 K vs. >65 K)	0.62 (−0.14, 1.37)	−0.02 (−0.95, 0.91)	0.23 (−0.72, 1.18)	0.53 (−0.20, 1.25)	0.51 (−0.30, 1.32)	0.46 (−0.31, 1.23)	−0.10 (−0.83, 0.64)	0.60 (−0.68, 1.88)	0.98 (−0.01, 1.98)
Income (don't know vs. >65 K)	0.87 * (0.09, 1.66)	0.01 (−0.96, 0.98)	0.36 (−0.63, 1.34)	0.80 * (0.04, 1.56)	0.73 (−0.12, 1.58)	0.69 (−0.12, 1.49)	0.06 (−0.71, 0.82)	0.88 (−0.46, 2.21)	0.88 (−0.17, 1.92)

* $p < 0.05$.

[a] Specific gravity-corrected, log-transformed values.

[b] Model mutually adjusts for maternal age, BMI, education, marital status, and household income.

[c] Molar sum of DEHP metabolites (MEHP, MEOHP, MEHHP) in nmol/L.

Table 5

Multiple linear regression associations between clinical and sociocultural factors with maternal urinary phthalate metabolites[a] in Caucasians only (n = 192).

Demographic factors	$\beta_{adjusted}$ [b] (95% CI) for Caucasians								
	MBP	MBzP	MEHP	MEOHP	MEHHP	∑DEHP[c]	MiBP	MEP	MMP
Age	0.01 (−0.01, 0.04)	−0.04 (−0.08, 0.00)	−0.02 (−0.05, 0.02)	0.00 (−0.02, 0.03)	0.00 (−0.03, 0.03)	0.00 (−0.03, 0.02)	0.01 (−0.02, 0.03)	−0.02 (−0.07, 0.03)	0.01 (−0.03, 0.04)
BMI	0.01 (−0.01, 0.03)	0.02 (−0.01, 0.05)	−0.01 (−0.03, 0.01)	0.01 (−0.01, 0.03)	0.01 (−0.01, 0.03)	0.00 (−0.02, 0.02)	0.00 (−0.02, 0.02)	0.00 (−0.03, 0.04)	−0.01 (−0.03, 0.02)
Education	0.01 (−0.14, 0.17)	0.13 (−0.16, 0.41)	0.11 (−0.10, 0.32)	−0.01 (−0.19, 0.17)	0.00 (−0.17, 0.18)	0.01 (−0.16, 0.18)	−0.05 (−0.21, 0.12)	−0.13 (−0.44, 0.19)	−0.13 (−0.36, 0.10)
Marital Status	0.79 * (0.45, 1.12)	0.43 (−0.16, 1.01)	0.15 (−0.29, 0.58)	0.39 * (0.02, 0.76)	0.32 (−0.05, 0.69)	0.26 (−0.09, 0.62)	0.46 * (0.12, 0.80)	0.61 (−0.04, 1.26)	0.64 * (0.16, 1.11)
Income (<25 K vs. >65 K	0.24 (−0.21, 0.69)	0.70 (−0.09, 1.48)	−0.31 (−0.90, 0.27)	−0.12 (−0.61, 0.38)	−0.18 (−0.68, 0.31)	−0.18 (−0.65, 0.30)	0.11 (−0.35, 0.56)	−0.60 (−1.47, 0.27)	0.44 (−0.21, 1.08)
Income (25−65 K vs. >65 K)	0.16 (−0.10, 0.42)	0.42 (−0.04, 0.88)	−0.11 (−0.46, 0.23)	0.05 (−0.25, 0.34)	0.05 (−0.25, 0.34)	0.01 (−0.27, 0.29)	0.19 (−0.07, 0.46)	−0.16 (−0.67, 0.35)	−0.02 (−0.40, 0.35)
Income (don't know vs. >65 K)	0.17 (−0.22, 0.57)	0.52 (−0.18, 1.22)	0.23 (−0.29, 0.75)	−0.23 (−0.67, 0.21)	−0.20 (−0.64, 0.24)	−0.08 (−0.50, 0.34)	0.00 (−0.40, 0.40)	−0.29 (−1.07, 0.48)	−0.42 (−0.99, 0.15)

* $p < 0.05$.

[a] Specific gravity-corrected, log-transformed values.

[b] Model mutually adjusts for maternal age, BMI, education, marital status, and household income.

[c] Molar sum of DEHP metabolites (MEHP, MEOHP, MEHHP) in nmol/L.