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

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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.

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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. 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

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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unmarried versus married women. Results of this cross-sectional study provide evidence for significant racial and demographic variations in phthalate exposure.

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 phthalate 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