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Exposure to Endocrine-Disrupting Chemicals During Pregnancy Is Associated with Weight Change Through 1 Year Postpartum Among Women in the Early-Life Exposure in Mexico to Environmental Toxicants Project

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Abstract

Background: The postpartum period may be a vulnerable life stage for a woman's cardiometabolic health. We examined associations of exposure to common endocrine-disrupting chemicals (EDCs) during pregnancy with weight from delivery through 1 year postpartum among 199 women in Mexico City.
Materials and Methods: During each trimester of pregnancy, we collected a urine sample to assay bisphenol A (BPA), mono-*n*-butyl phthalate (MnBP), mono-isobutyl phthalate (MiBP), monobenzyl phthalate (MBzP), mono-3-carboxypropyl phthalate (MCPP), mono-2-ethyl-5-carboxypentyl phthalate (MECPP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethylhexyl phthalate (MEHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), and monoethyl phthalate (MEP). We calculated summary scores for di-2-ethylhexyl phthalate metabolites (ΣDEHP) and dibutyl phthalate metabolites (ΣDBP). We calculated the geometric mean of each EDC across pregnancy for use in the analysis. At delivery and three additional times during the first year postpartum, we measured the women's weight. We used mixed-effects linear regression models to estimate associations of each EDC with weight at delivery (kg) and weight change (kg/year) from delivery through 1 year postpartum. Covariates included urinary specific gravity, maternal age, parity, height, first trimester body mass index, and gestational age at enrollment.
Results: Mean ± standard deviation weight change during the first postpartum year was –0.49 ± 4.04 kg. The EDCs were inversely associated with weight at delivery, but positively associated with weight change through 1 year postpartum. For example, each interquartile range of urinary ΣDEHP corresponded with 1.38 (95% confidence interval: 0.44–2.33) kg lower weight at delivery and 1.01 (0.41—1.61) kg/year slower rate of weight loss. We observed similar associations for other EDCs.
Conclusions: Prenatal exposure to EDCs is associated with lower weight at delivery, but slower rate of weight loss through the first postpartum year.

Keywords: postpartum weight retention, endocrine disruptors, obesity, pregnancy

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Introduction

Endocrine-disrupting chemicals (EDCs), like bisphenol A (BPA) and phthalates, have been implicated in the development of obesity and metabolic risk.[1] Human exposure to these chemicals is ubiquitous, as they are found in food packaging materials, pesticides, and personal care items, among numerous other consumer products.[1] Exposure to these chemicals during vulnerable developmental stages, also known as sensitive periods, is particularly concerning, given the larger potential for exposures during these time frames to alter an organism's physiology and phenotype.[2,3]

Life course studies exploring sensitive periods for obesity and obesity-related disease have historically focused on life stages that coincide with rapid growth and/or hormonal fluctuation: *in utero* and infancy,[4] early childhood during the adiposity rebound,[5] late childhood around adrenarche,[6] and puberty.[7–9] However, the period of pregnancy—a time of rapid growth, physiological change, and hormonal fluctuation—within the context of women's health is a concept that has only recently received attention.[10–12] While there is a growing literature linking EDC exposure during gestation to a range of short- and long-term offspring health outcomes,[13–17] little remains known regarding consequences for maternal health.

In this study, we sought to investigate associations of exposure to BPA and nine phthalates during pregnancy with repeated measurements of weight from delivery through 1 year postpartum—a time frame during which a woman's weight status may serve as a bellwether for long-term obesity risk[18] and contribute to future cardiovascular and metabolic disease risk.[19] We carried out the analysis among 199 women in Mexico, a country afflicted by relatively high exposure to chemical toxicants[20] and exceptionally high rates of obesity and obesity-related disease.[21–23] We hypothesized that higher EDC exposure during pregnancy would be associated with higher weight at delivery after accounting for early pregnancy weight status, and slower rate of weight loss during the first postpartum year.

Materials and Methods

Study population

This study included participants from two of three cohorts comprising the Early Life Exposure in Mexico to Environmental Toxicants (ELEMENT) Project, a longitudinal cohort study of pregnant women and their offspring in Mexico City, MX. Study participants were recruited from public maternity hospitals in Mexico City between 1997 and 2004 during the first trimester of pregnancy. Details regarding recruitment and eligibility have been published.[24] In brief, the ELEMENT Project is composed of three cohorts comprising 2169 women enrolled during pregnancy, some of whom have been followed for more than 2 decades. The participants of this study were selected from a convenience sample of 250 women (sample size based on budgetary restrictions and availability of archived biospecimens for assays) who were part of a study exploring effects of EDC exposure during gestation on offspring health outcomes during peripuberty. Maternal and sociodemographic characteristics of these 250 participants are similar to those of the originally enrolled women, with the exception of older age at enrollment ($\sim$28 vs. $\sim$26 years) and higher proportion of single mothers ($\sim$30% vs. $\sim$9%). Of the 250 eligible women, we had data on urinary EDC concentrations during at least one trimester of pregnancy for 230. We further excluded 31 women missing data on weight at delivery and at least 1 additional weight measurement during the first postpartum year, leaving an analytical sample of 199 women with a decrease in sample size to 167 due to missing values for covariates included in multivariable models.

During pregnancy, the women participated at in-person research visits three times: at median 14 (''early pregnancy visit''), 25, and 34 weeks. At the early pregnancy visit, we measured the women's height and administered an interview-based questionnaire inquiring on sociodemographic and lifestyle characteristics, including smoking habits during pregnancy. During all three pregnancy visits, we collected a urine sample, which we used to assay EDC concentrations. At delivery and up to three additional times during the first postpartum year (for a total of four weight assessments), the women returned for in-person research visits where we measured anthropometry and collected information on breastfeeding practices and lifestyle habits.

Exposures: urinary BPA and phthalate concentrations

NSF International (Ann Arbor, MI) carried out all EDC assays using high-performance liquid chromatography and tandem mass-spectrometry methods described in detail elsewhere.[20,25]

We quantified concentrations of BPA, which was of interest due to its known endocrine-disrupting activities[26] and association with metabolic risk factors,[27] and eight phthalate metabolites, selected based on previously identified high detection in ELEMENT and relevance to other metabolic biomarkers,[14,20] including monoethyl phthalate (MEP), mono-isobutyl phthalate (MiBP), mono-*n*-butyl phthalate (MnBP), monobenzyl phthalate (MBzP), mono-3-carboxypropyl phthalate (MCPP), mono-2-ethylhexyl phthalate (MEHP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), and mono-2-ethyl-5-carboxypentyl phthalate (MECPP). Values below the limit of detection (LOD) were calculated as LOD/$\sqrt{2}$. We calculated a summary score for di-2-ethylhexyl phthalate metabolites (ΣDEHP) by adding the molar sums for MEHP, MEHHP, MEOHP, and MECPP. Likewise, we created a summary score for dibutyl phthalate metabolites (ΣDBP) as the molar sum of MnBP and MiBP. Urinary specific gravity, an indicator of urine dilution, was measured at the time of sample analysis using a handheld digital refractometer (Atago Co., Ltd., Tokyo, Japan).

In regression analysis, the exposures of interest were BPA, MBzP, MCPP, MEP, and ΣDEHP and ΣDBP (rather than individual metabolites that make up the summary scores to reduce the possibility of false positive findings) concentrations assessed during pregnancy. We natural log (ln) transformed each EDC and summary score variable due to non-normal distributions. In light of evidence that the geometric mean (rather than arithmetic mean, given the log-normal distribution of the EDCs) of urinary EDC concentrations across all three trimesters provides a more robust measure of exposure to quickly metabolized toxicants during pregnancy,[28,29] we examined the geometric mean of each EDC and summary score across all three trimesters, assessed by urine specimens collected during each trimester, as our primary exposure.

Outcome: maternal weight from delivery through 1 year postpartum

Starting at delivery and through 1 year postpartum, we measured the women's weight a median of four times on a digital scale to the nearest kg (BAME Mod 420; Catálogo Médico). We used these repeated weight measurements to assess differences in longitudinal weight trajectories with respect to the EDCs.

Data analysis

Before multivariable analysis, we examined univariate distributions of continuous variables and frequency tables of categorical and ordinal variables. We also assessed bivariate associations of *in utero* EDC exposure with key maternal and perinatal characteristics. Of particular interest was the relationship between EDC exposure and body mass index (BMI) at the early pregnancy visit as a proxy for weight status entering pregnancy (given evidence of a positive correlation between EDCs and excess adiposity[1]), and between EDC exposure and infant birth weight (since the size of the fetus accounts for a substantial portion of a woman's weight during pregnancy, which theoretically should not contribute to maternal weight gain that needs to be lost after pregnancy). These raw correlations are noteworthy, given that a woman's weight status entering pregnancy directly affects gestational weight gain, which in turn influences weight change in the postpartum period. This step, in conjunction with our *a priori* knowledge of determinants of maternal weight during and after pregnancy, informed covariate selection for multivariable models.

For the main analysis, we used mixed-effects linear regression models to explore the association of prenatal EDC exposure with weight at delivery and average annual weight change during the first year postpartum. The outcome of interest was repeated measurements of weight from delivery through 1 year postpartum and the independent variable was quartiles of each individual EDC, an indicator for time (calculated as months since delivery, then converted to decimal years for ease of interpretation), an EDC × time interaction term, random intercepts, and slopes for individual ID to account for correlations in the repeated measurements of weight. Because we did not note any nonlinear trends with quartiles of the EDCs, we entered the EDCs (ln-transformed BPA, MBzP, MCPP, MEP, ΣDEHP, and ΣDBP) into the models continuously and scaled to 1-interquartile range (IQR) to maximize power. In the multivariable models, the primary estimate of interest was the coefficient for the interaction term, which represents the average change in weight (kg/year) with respect to a given EDC. Given that, on average, women lost weight during the first postpartum year, a positive coefficient implies a slower rate of weight loss for the majority of the study sample per 1-IQR of each EDC. We chose this as the primary approach over evaluating associations of EDC exposure with weight at each time point separately or with change in weight between two specific time points for model efficiency—that is, if a participant only had weight data at delivery, but not at subsequent postpartum visits, her information still contributes to the estimation of standard errors in the mixed-effects model. We also considered the beta estimate for the main effect of each EDC, which in the face in the EDC × time interaction and after adjustment for early pregnancy BMI is interpreted as the effect of each EDC on the woman's weight at delivery, while holding early pregnancy weight status (a proxy for prepregnancy weight status[30]) constant. This estimate provides a sense of the relationship between EDC exposure and weight at the start of the postpartum period. *Nota bene*, we interpret these associations with caution, given constraints of our data (*e.g.*, lack of information of gestational weight gain and the potential variability in a woman's body composition during pregnancy) and unknown circumstances of delivery that could impact weight immediately after birth (*e.g.*, weight retained from intervenous administration of fluids).

After examining the unadjusted estimates, we accounted for a series of precision covariates, confounders, and potential mediators to control for bias and assess persistence of associations. In our basic model (Model 1), we adjusted for the geometric mean of urinary specific gravity across all three trimesters (precision covariate to control for variability in urinary EDC concentrations); maternal age at enrollment, parity, early pregnancy BMI, and height (confounders to the relationship between pregnancy EDC exposure and postpartum weight change); and gestational age at the early pregnancy visit (precision covariate to account for variability in timing of measurement of early pregnancy anthropometry). In Model 2, we further accounted for variables that may affect peripartum weight gain and/or retention (precision covariates for the outcome): maternal smoking habits during pregnancy (never, former, and smoked during pregnancy) and breastfeeding duration (<6 months vs. ≥6 months). Finally, in Model 3, we adjusted for the infant's birth weight (g, a confounder that serves as a partial proxy for gestational weight gain).

Because maternal weight status entering pregnancy could differentially influence weight change during the postpartum period, we tested for an interaction between each EDC and early pregnancy BMI. None of the *p*-interactions was significant at alpha = 0.05, except for MEP ($p = 0.03$). However, given the large number of tests for interaction conducted (six EDC by early pregnancy BMI interactions), the statistically significant interaction for a single EDC could have been due to random chance, so we did not conduct further stratified analysis by the women's BMI.

In addition to the main analysis, we also carried out some sensitivity analysis. First, among 194 women with data on weight at delivery and at 1 year postpartum, we conducted a complementary analysis using linear regression models where weight change was the outcome of interest. The purpose of this analysis was to enhance interpretability, as it may be more intuitive to consider the difference in postpartum weight change per 1-IQR of each EDC, as opposed to the difference in annual rate of weight change. As with the mixed models, a positive coefficient implies a smaller amount of weight loss during the first postpartum year since the women in this study lost weight during the time frame of interest. Second, we assessed the impact of adjustment for maternal education, an indicator of socioeconomic status that could be a confounder. Inclusion of this variable did not change the results, so we did not include it in the final models for the sake of parsimony. Third, because EDC exposure is associated with gestation length,[31,32] which is associated with gestational weight gain and thus may influence postpartum weight change, we examined the influence of

Table 1. Background Characteristics of 199 Mothers in the Early Life Exposure in Mexico to Environmental Toxicants (ELEMENT) Project

	Mean ± SD or % (N)
Sociodemographic characteristics	
Age at enrollment (years)	27.87 ± 5.8
Marital status	
Single	29.8 (56)
Married/cohabiting	70.2 (132)
Education level	
<10 Years	37.2 (74)
10–12 Years	47.2 (94)
≥13 Years	15.6 (31)
Parity before index birth	
0–1	35.2 (70)
2–3	58.3 (116)
≥4	6.5 (13)
Smoked during pregnancy	
Yes	1.2 (3)
No	98.5 (196)
Breastfeeding duration	
<6 Months	36.7 (73)
≥6 Months	63.3 (126)
Calcium supplementation	
Yes	43.6 (82)
No	56.4 (106)
Maternal anthropometry	
Height (cm)	153.7 ± 5.4
Gestational week at first trimester visit	12.8 ± 4.4
Weight at the first trimester visit (kg)	61.2 ± 10.2
BMI at first trimester visit (kg/m^2)	25.9 ± 4.0
Weeks after delivery at 1 year postpartum visit	54.0 ± 3.4
Weight at 1 year postpartum (kg)	63.3 ± 11.2
BMI at 1 year postpartum visit (kg/m^2)	26.8 ± 4.3
Perinatal and infant characteristics	
Gestational age at delivery (weeks)	38.9 ± 1.54
Birth weight (g)	3154 ± 428

BMI, body mass index; SD, standard deviation.

adjustment for gestational age at delivery. Inclusion of this variable did not appreciably change the results, so we did not include it, given that it could be on the causal pathway between EDC exposure and postpartum weight change.

All analyses were carried out using SAS software (Cary, NC) or Stata software (StataCorp, LLC, College Station, TX).

Results

Mean ± standard deviation age at enrollment was 27.8 ± 5.8 years. On average, the women in this sample lost 0.49 ± 4.04 kg (range: −12.0 to 11.0 kg) during the first postpartum year. The majority (70.2%) of women were married or cohabiting. Additional background characteristics of the study sample are in Table 1.

Table 2 shows the distribution of BPA and nine phthalates, as well as ΣDEHP and ΣDBP, in native units ng/mL (*i.e.*, not ln transformed).

Supplementary Table S1 shows Spearman correlations of the EDC variables used in regression analysis (ln-transformed BPA, MBzP, MCPP, MEP, ΣDEHP, and ΣDBP) with maternal sociodemographic and perinatal characteristics. We noted a small positive correlation between early pregnancy BMI and the EDCs, ranging from 0.01 to 0.17.

Table 3 shows results from the analysis of EDC exposure during pregnancy with average weight change during the first year postpartum, which should be interpreted, while keeping in mind that women in this sample lost weight during the time frame of interest. All EDCs except MEP were significantly positively associated with weight change during the first postpartum year, at a magnitude ranging from ∼0.69 to ∼1.01 kg/year. The estimates were robust to adjustment for key confounders and potential mediators. Taking BPA exposure as an example, in Model 1 which accounted for the geometric mean of urinary specific gravity across all three trimesters, maternal age at enrollment, parity, height, early pregnancy BMI, and gestational age at the early pregnancy visit, each IQR increase in ln-transformed BPA exposure during pregnancy was associated with 0.69 (95% confidence interval [CI]: 0.08, 1.29) kg/year slower rate of

Table 2. Distribution of the Geometric Mean of Urinary Bisphenol-A (BPA) and Phthalates Across the Three Trimesters of Pregnancy Among 199 Mothers in the Early Life Exposure in Mexico to Environmental Toxicants (ELEMENT) Project

	Arithmetic mean ± SD (ng/mL)	*LOD*	*% >LOD*	*Minimum*	*25th*	*50th*	*75th*	*Maximum*
BPA	1.18 ± 0.91	0.40	76.1	0.40	0.58	0.89	1.31	6.90
MBzP	4.12 ± 3.86	1.00	91.6	0.22	1.69	2.77	4.89	20.89
MCPP	1.44 ± 1.17	0.20	99.8	0.20	0.63	1.01	1.98	6.02
MECPP	36.97 ± 25.68	0.10	100.0	2.24	20.38	30.56	45.64	172.39
MEHHP	21.91 ± 16.30	0.10	100.0	1.09	9.98	17.36	27.75	94.31
MEHP	5.96 ± 4.34	0.20	96.6	1.00	2.91	4.47	7.65	23.17
MEOHP	12.70 ± 9.66	0.20	91.0	0.62	5.94	10.40	15.95	59.22
MEP	225.72 ± 341.87	1.00	99.6	12.18	49.84	114.19	261.20	2283.49
MnBP	84.97 ± 84.54	0.50	99.6	4.36	28.32	54.34	107.23	467.46
MiBP	2.04 ± 3.47	0.20	77.9	0.20	0.53	1.07	2.26	32.42
ΣDEHP	78.53 ± 54.11			5.79	39.95	66.65	98.21	334.95
ΣDBP	84.56 ± 86.34			4.59	28.10	55.24	102.27	477.45

BPA, bisphenol A; DBP, dibutyl phthalate metabolites; DEHP, di-2-ethylhexyl phthalate metabolites; LOD, limit of detection; MBzP, monobenzyl phthalate; MCPP, mono-3-carboxypropyl phthalate; MECPP, mono-2-ethyl-5-carboxypentyl phthalate; MEHHP, mono-2-ethyl-5-hydroxyhexyl phthalate; MEHP, mono-2-ethylhexyl phthalate; MEOHP, mono-2-ethyl-5-oxohexyl phthalate; MEP, monoethyl phthalate; MiBP, mono-isobutyl phthalate; MnBP, mono-*n*-butyl phthalate.

Table 3. Associations of Each 1-Interquartile Range (IQR) Increment in Urinary Concentration of the Geometric Mean (Across All Three Trimesters) for Each Natural Log-Transformed Endocrine Disrupting Chemical (EDC) with Average Yearly Weight Change (kg/y) Through 1-Year Postpartum Among Mothers in the Early Life Exposure in Mexico to Environmental Toxicants (ELEMENT) Project

	β *(95% CI) for 1-IQR of each EDC*[a]							
	Model 0 (unadjusted)		*Model 1*		*Model 2*		*Model 3*	
	n = *199*		n = *167*		n = *167*		n = *167*	
	EDC main effect	*EDC × time*	*EDC main effect*	*EDC × time*	*EDC main effect*	*EDC × time*	*EDC main effect*	*EDC × time*
BPA (IQR: 0.92)	−0.82 (−3.04 to 1.40)	0.64 (−0.11 to 1.39)	−0.66 (−1.50 to 0.17)	**0.69 (0.08 to 1.29)**	−0.72 (−1.55 to 0.11)	**0.68 (0.07 to 1.29)**	−0.74 (−1.59 to 0.11)	**0.68 (0.07 to 1.29)**
MBzP (IQR: 1.21)	0.10 (−2.03 to 2.23)	**0.92 (0.16 to 1.68)**	**−1.23 (−2.08 to −0.38)**	**0.74 (0.09 to 1.39)**	**−1.19 (−2.03 to −0.34)**	**0.74 (0.08 to 1.39)**	**−1.23 (−2.09 to −0.36)**	**0.73 (0.08 to 1.39)**
MCPP (IQR: 1.08)	−1.61 (−4.06 to 0.84)	**0.98 (0.20 to 1.76)**	**−1.51 (−2.46 to −0.56)**	**0.79 (0.14 to 1.44)**	**−1.54 (−2.48 to −0.59)**	**0.79 (0.14 to 1.43)**	**−1.54 (−2.49 to −0.60)**	**0.79 (0.14 to 1.43)**
MEP (IQR: 1.67)	0.16 (−2.16 to 2.47)	0.63 (−0.21 to 1.46)	**−1.00 (−1.88 to −0.11)**	0.51 (−0.16 to 1.18)	**−0.92 (−1.81 to −0.03)**	0.5 (−0.16 to 1.17)	**−0.93 (−1.82 to −0.04)**	0.50 (−0.16 to 1.17)
ΣDEHP (IQR: 0.90)	−0.75 (−3.09 to 1.60)	**1.02 (0.30 to 1.73)**	**−1.38 (−2.33 to −0.44)**	**1.01 (0.41 to 1.61)**	**−1.38 (−2.32 to −0.44)**	**1.00 (0.40 to 1.61)**	**−1.43 (−2.39 to −0.47)**	**1.00 (0.40 to 1.61)**
ΣDBP (IQR: 1.34)	−0.16 (−2.53 to 2.21)	**0.98 (0.22 to 1.75)**	**−1.59 (−2.49 to −0.68)**	**0.79 (0.17 to 1.42)**	**−1.56 (−2.46 to −0.66)**	**0.79 (0.16 to 1.42)**	**−1.58 (−2.49 to −0.68)**	**0.79 (0.16 to 1.42)**

Model 1: Adjusted for geometric mean of urinary specific gravity across all three trimesters, maternal age at enrollment, parity, height, first trimester BMI, and gestational age at the first trimester visit. Model 2: Model 1 + smoking habits during pregnancy (never, former, and smoked during pregnancy), and breastfeeding duration (<6 months, ≥6 months). Model 3: Model 2 + offspring birth weight (g).

Bolded values indicate statistical significance at alpha = 0.05.

[a]Estimates are from a mixed-effects linear regression model where the explanatory variables include the EDC of interest, an indicator for time (decimal years), and an interaction between the two terms.

CI, confidence interval; EDC, endocrine-disrupting chemical; IQR, interquartile range.

weight loss. This association did not change after adjusting for smoking habits during pregnancy and breastfeeding duration (Model 2), or offspring birth weight (Model 3). We observed similar associations for MBzP, MCPP, MEP, ΣDEHP, and ΣDBP (Table 3).

The relationship between prenatal EDC exposure and delivery weight (the main effects for the EDCs) was, however, negative. Taking the example of MBzP in Model 1: each IQR of ln-transformed MBzP exposure during pregnancy corresponded with 1.23 (95% CI: 0.38–2.08) kg lower weight at delivery after accounting for the woman's weight status and stature (early pregnancy BMI and height) and other key confounders. This estimate was materially unchanged in Models 2 and 3 (Table 3). Taken in consideration with the MBzP × time interaction term ($\beta = 0.74$; 95% CI: 0.08–1.39 kg/year), these results suggest that exposure to EDCs during pregnancy is associated with lower weight at delivery (even after accounting for perinatal characteristics that might affect delivery weight like early pregnancy weight status, smoking habits, and fetal growth) and a slower rate of weight loss during the first postpartum year.

Supplementary Table S2 shows results from the complementary analysis where the outcome of interest was postpartum weight change during the first year. While results were not statistically significant, they are similar to those in Table 3: higher EDC exposure during pregnancy was associated with less weight loss during the first year after delivery.

Discussion

In this prospective study of 199 women in Mexico City, EDC exposure during pregnancy was associated with lower weight at delivery (0.7–1.6 kg lighter at delivery), and a slower rate of weight loss during the first year postpartum (0.6–1 kg/year slower rate of loss). These findings were not due to regression to the mean with respect to the women's early pregnancy BMI and were robust to adjustment for lifestyle and perinatal characteristics associated with weight change, including smoking habits and breastfeeding duration, as well as offspring birth weight.

Women in this cohort lost an average of 0.5 kg during the first postpartum year. Thus, the positive association between the EDCs and weight change during this timeframe corresponds with a slower rate of weight loss. These findings align with that of a recently published analysis in the ELEMENT cohort, wherein Rodriguez-Carmona et al.[33] found that higher exposure to MCPP during pregnancy corresponded with ~0.3 kg/year greater weight gain 8–10 years after delivery. Given that women typically lose weight during the first postpartum year, the slower rate of weight loss that we detected with respect to the EDCs is in line with the long-term weight gain detected by Rodriguez-Carmona et al.[33]

There are a number of mechanisms through which EDC exposure may impede weight loss during the postpartum period. One pathway involves disruption of activation of the peroxisome proliferator-activated receptors (PPAR), which is involved in a number of metabolic processes that may influence or co-vary with weight, including lipid oxidation, and fatty acid synthesis[34,35] and storage.[36] During pregnancy, specifically, PPARs (*e.g.*, PPAR-alpha, PPAR-beta, and PPAR-gamma) play a role in physiological processes like oxidative stress and inflammation,[37] the latter of which has been shown to modulate weight change.[38] EDCs may also influence key hormones during pregnancy, which may have residual effects in the postpartum period. In the Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) birth cohort, Johns et al.[39] reported an inverse association between MCPP and free triiodothyronine (T2), and a positive association between MBzP and thyroid-stimulating hormone (TSH) during pregnancy. While little is known of associations of these phthalates with thyroid hormones during the postpartum period, effects of EDCs on weight gain during pregnancy may also influence postpartum weight change through an influence on thyroid hormones.

While the association of pregnancy EDC exposure with slower rate of weight loss during the postpartum period supported our hypothesis, the fact that EDC exposure correlated with lower weight at delivery—even after accounting for early pregnancy BMI—was not expected, given the obesogenic mechanisms proposed for these chemicals.[40] A possible explanation is residual confounding by prepregnancy weight status—a variable that we do not have data on in this cohort, and insufficient adjustment for pregnancy weight gain proxied by birth weight in this study. Given the positive correlation between EDC exposure and early pregnancy BMI, it is likely that women who are more highly exposed to EDCs started pregnancy at a higher BMI, but gained less weight during pregnancy (as is the physiological expectation and recommendation[41,42]), and thus are of slightly lower weight at delivery. However, given that weight status entering pregnancy is a representation not only of a woman's environment and lifestyle characteristics but also of genetic predisposition,[43] these same women may also be prone to a greater degree of weight gain (or lower weight loss) following delivery. Regardless, we interpret these findings with caution based on the data available to us. Future studies with detailed information on prepregnancy BMI and gestational weight gain, in addition to postpartum weights, are required to interrogate these hypotheses.

Strengths and limitations

Strengths of this study include the following: (1) our ability to prospectively explore associations of EDC exposure during pregnancy—a potential sensitive period for the development of obesity-related disease for women—with postpartum weight change; (2) the fact that we were able to examine associations not only with EDC exposure during a specific point in time during pregnancy but also across all of gestation; (3) availability of data on key covariates, precision variables (*i.e.*, timing of urine collection and weight measurement, and urinary specific gravity), and perinatal (*i.e.*, offspring birth weight) and lifestyle characteristics (*i.e.*, smoking habits, breastfeeding duration) that may account for variability in EDC exposure and weight; and (4) our longitudinal modeling strategy, which appropriately accounted for correlations among repeated assessments of maternal weight and efficiently leveraged the outcome data across multiple study visits.

This study also had several limitations. First, although we had information on infant birth weight as a partial proxy of gestational weight gain, gestational weight gain may be a confounder or a mediator to the associations of interest, given that gestational weight gain may be associated with EDC exposure, is a direct determinant of delivery weight, and is

inversely related to postpartum weight loss.[44] As such, we interpret our results, particularly those with respect to delivery weight, with caution. Second, we used early pregnancy weight (median 14 gestational weeks) in lieu of prepregnancy weight. However, a recent study found that weight during the first trimester was a valid proxy for prepregnancy weight.[30] Further, the investigators did not find systematic differences in weight gained by 12 weeks gestation with respect to prepregnancy weight status, suggesting that interindividual rank in weight gain is preserved and thus, use of weight assessed at 14 gestational weeks in our study likely did not introduce bias into estimates of association. Third, because EDCs have short half-lives, single measurements of urinary EDC concentrations may not accurately capture longer-term exposure. However, we evaluated EDC exposure based on average concentrations across all three trimesters, which is a more robust representation of exposure during pregnancy.[28,29] Fourth, we cannot discount the potential for reverse causation in the relationship between EDC exposure and weight since adipose tissue serves as a storage site for EDCs.[45] However, our prospective study design minimizes this possibility. Fifth, our sample size was relatively small and decreased with covariate adjustment. However, this did not hamper our ability to detect significant associations, and the drop in sample size due to missing covariate data did not appear to introduce selection bias, given the stability of estimates across multivariable models. Finally, given that ELEMENT comprised completely Hispanic participants residing in a low- to middle-income urban city, our results may not be generalizable to higher-income populations in other settings.

Conclusions

In this analysis of women in Mexico City, exposure to BPA and several phthalates during pregnancy was related to 0.7–1.6 kg (equivalent to 1.5–3.5 lbs) lower weight at delivery, and 0.6–1 kg/year (equivalent to 1.5–2 lbs/year) slower weight loss during the first year postpartum. Additional work is required to explore associations of prenatal EDC exposure with delivery weight, given constraints of our data. Regarding the relationship between EDC exposure during pregnancy and postpartum weight change, we note that the effect sizes were modest but slower postpartum weight loss may be of concern, given that women in this sample were already overweight at the early pregnancy visit (average BMI of $\sim 26\ kg/m^2$). Thus, identification of modifiable factors that impede postpartum weight loss and result in excess weight retention (which, in turn, can affect subsequent pregnancies) will unveil avenues for preventive intervention. Future studies are required to identify modifiable determinants of postpartum weight change, and to examine the efficacy of targeting such characteristics to optimize health, long-term women's health.

Author Disclosure Statement

None of the authors have any conflict of interests to disclose. No competing financial interests exist.

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Supplementary Material

Supplementary Table S1
Supplementary Table S2

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