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Persistent organic pollutants and pregnancy complications

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Abstract

We sought to investigate the relationship between maternal preconception exposures to persistent organic pollutants (POPs) and pregnancy complications, gestational diabetes (GDM) and gestational hypertension. Data from 258 (51%) women with human chorionic gonadotropin (hCG) confirmed pregnancies reaching ≥24 weeks gestation, from a prospective cohort of 501 couples who discontinued contraception to attempt pregnancy, were analyzed. Preconception concentrations of 9 organochlorine pesticides (OCPs) and 10 polybrominated diphenyl ethers (PBDEs) were quantified in serum. In separate multiple logistic regression models of self-reported physician diagnosed outcomes: GDM (11%) and gestational hypertension (10%), chemicals were natural log-transformed and rescaled by their standard deviation (SD). Models were adjusted for serum lipids, and then adjusted for age, body mass index, race, and smoking. Models were additionally adjusted for the sum of the remaining POPs in each chemical class. Women's serum concentration of PBDE congener 153 (PBDE-153) was positively associated with an increased odds of GDM per SD increase in log-transformed concentration, for unadjusted (OR = 1.36, 95%CI: 1.02–1.81), a priori adjusted (OR = 1.38, 95% CI: 1.03–1.86) and with the sum of remaining PBDEs (OR = 1.79, 95% CI: 1.18, 2.74) models. Our findings suggest that at environmentally relevant concentrations, maternal exposure to POPs prior to conception may contribute to increased chance of developing GDM.

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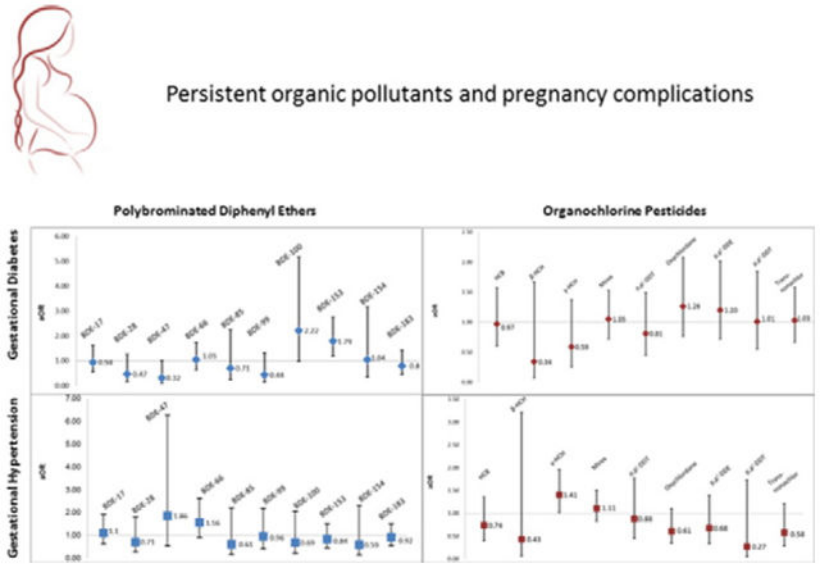
Graphical Abstract



Keywords

Gestational diabetes mellitus; Hypertension; Organochlorine pesticides; Polybrominated diphenyl ethers; Preconception

1. Introduction

Persistent organic pollutants (POPs) are of public health concern, given their long half-lives and the ability of lipophilic chemicals to bioaccumulate and biomagnify within food chains. Of particular interest are ubiquitous brominated and chlorinated POPs. Specifically, flame retardants and pesticides are two chemical classes that have been recognized as potential risk factors for adverse human health. Findings from animal studies have demonstrated that brominated flame retardants, polybrominated diphenyl ethers (PBDEs) (Nash et al., 2013) and hexabromocyclododecane (Yanagisawa et al., 2014) contribute to impaired lipid and glucose metabolism. Moreover, there is a growing body of epidemiological literature suggesting that exposure to various POPs, belonging to different chemical classes, is associated with an increased risk of adult onset diabetes (Taylor et al., 2013; Magliano et al., 2014), hypertension (Ha et al., 2009) and metabolic syndrome (Lim et al., 2008) among individuals in the general population. In spite of these findings, the extent to which POPs may contribute to common gravid diseases such as gestational diabetes mellitus (GDM) or hypertension is currently unknown. Both of these gravid complications are related to short- and long-term adverse health outcomes for women and their children and may contribute to the developmental origins of cardio-metabolic risk factors (Barouki et al., 2012; Yan and Yang, 2014). Early evidence suggested an inverse association between serum concentrations of multiple organochlorine pesticides (OCPs) measured during the third trimester and hypertension and preeclampsia (Savitz et al., 2014). Specifically, increasing levels of serum p,p′-dichlorodiphenyltrichloroethane (p,p′-DDT) was associated with being 20–60% less

likely to develop gestational hypertension (ORs range: 0.4–1.0; p for trend = 0.002); findings were similar for beta-hexachlorocyclohexane (β-HCH). LikewiseSaunders et al. (2014), reported that women were 60% less likely to develop gestational hypertension per $\log_{10}$ increase in serum chlordecone concentrations measured during labor (OR = 0.4; 95% CI: 0.2, 0.6). However, a recent study with preconception quantification of serum perfluorooctanoic acid (PFOA) reported a 1.87-fold increase risk of GDM per 0.43 ng/mL increase in concentration (Zhang et al., 2015). This latter study is the only one known to us with preconception quantification of POPs and prospective follow-up of women throughout pregnancy to delivery. In light of emerging data on select POPs and gravid disease, we assessed serum OCPs and PBDEs in relation to prospectively ascertained GDM and gestational hypertension.

2. Materials and methods

2.1. Design and study population

The study population comprises women enrolled in the Longitudinal Investigation of Fertility and the Environment (LIFE) Study who became pregnant and delivered a live born infant. Briefly, the LIFE Study recruited 501 couples who were discontinuing contraception to try for pregnancy and who resided in 16 counties in Michigan and Texas between 2005 and 2009 (Buck Louis et al., 2011). Eligibility criteria were minimal: females aged 18–40 and males ≥18 years; in a committed relationship; no physician diagnosis of infertility/sterility; females had menstrual cycles between 21 and 42 days consistent with use of a fertility monitor to help achieve pregnancy; had not received injectable hormonal contraceptives in the past year which could delay the return of ovulation; and an ability to communicate in English or Spanish. Institutional review board approvals were obtained from all collaborating institutions; couples provided written informed consent prior to study participation.

2.2. Data collection

Upon recruitment, women completed in-person interviews to provide information on lifestyle and reproductive history. Standardized anthropometric assessments were performed by research assistants to measure body mass index (BMI) (Lohman et al., 1988) followed by the collection of blood specimens using equipment determined to be free of POPs. Women completed daily journals on lifestyle, menses and results of home pregnancy testing. Pregnant women completed daily journals through six weeks post-conception (80%) then monthly until experiencing either a pregnancy loss or delivery of a live born infant (82%). The pregnancy journals were designed to query women about their obstetrical courses relative to prenatal screening for maternal and fetal disorders including gravid diseases. Women reported any clinical diagnoses of GDM and/or hypertension starting at 9 weeks gestation based on women's last menstrual period. For the present analysis, GDM and gestational hypertension were defined as physician report high blood sugar and high blood pressure at ≥24 weeks of gestation, respectively; gestational time period was selected to comply with previously established screening guidelines for clinical assessment of GDM and gestational hypertension (ACOG, 2001; ACOG, 2002). Among the 347 hCG confirmed pregnancies, 272 women had a pregnancy lasting ≥24 weeks of gestation and complete

journals for analysis. Women with previous histories of diabetes (1%) and hypertension (3%) or prevalent disease at baseline were excluded; the final analytic cohort comprised 258 (95%) women.

2.3. Measurement of serum POPs

Chemical measurements were performed by the Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention. Specifically, 9 organochlorine pesticides (OCPs): hexachlorobenzene (HCB); β-hexachlorocyclohexane (β HCH); γ-hexachlorocyclohexane (γ-HCH); oxychlordane; *trans*-nonachlor; 1,1,1-trichloro-2,2-di(4-chlorophenyl)ethane (p,p′ DDT); 1,1,1-Trichloro-2-2(o-chlorophenyl)-2-(p-chlorophenyl)ethane (o,p′ DDT); 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (p,p′ DDE,) and mirex; and 10 polybrominated diphenyl ether congeners (PBDEs): 17, 28, 47, 66, 85, 99, 100, 153, 154, and 183 were measured using isotope dilution gas chromatography-high resolution mass spectrometry using previously published standard operating procedures (Sjödin et al., 2004; Kuklenyik et al., 2005). All chemical concentrations were reported as nanogram pergram of serum (ng/g). The limits of detections (LODs) were in the low pg/g concentrations and varied per analyte and sample. The median LOD was used to quantify the detection frequency of serum chemicals. Serum lipids were quantified using commercially available enzymatic methods (Akins et al., 1989), and reported as total serum lipids (ng/g) using established methods based on individual components including phospholipids, triglycerides, total cholesterol, and free cholesterol (Phillips et al., 1989). Machine-observed values for all chemical concentrations were used in analysis to avoid introducing biases associated with substituting concentrations <LOD or automatically lipid adjusting concentrations (Lubin et al., 2004; Schisterman et al., 2005; Schisterman et al., 2006).

2.4. Statistical analysis

Univariate analyses were performed to assess the distribution of POPs and relevant covariates. Maternal characteristics were assessed by gravid disease status. Differences in characteristics between women with and without gravid diseases were assessed using independent *t*-test for continuous variables and Chi-square test for categorical variables. Distributional properties of chemicals were summarized as medians and interquartile range (IQRs). Missing chemical <3%) and lipid (<4%) data were imputed using Markov Chain Monte Carlo methods (Schafer, 1997) rather than performing a complete case analysis when the quantity of serum was insufficient for individual analysis to avoid biased point estimates of association (White and Carlin, 2010; Desai et al., 2011); for all other women, machine observed concentrations were analyzed in statistical models. Logistic regression models were used to estimate the unadjusted odds of physician diagnosed GDM and/or hypertension. All serum concentrations of POPs were natural log-transformed to account for the highly skewed nature of the exposure levels and rescaled by their standard deviations (SD) to aid in the interpretation of point estimates. For example, findings are interpreted as increased/decreased odds of diagnosis per standard deviation increase in each ln-transformed chemical concentration. For three OCPs (γ-HCH, Mirex and o,p′-DDT) and three PBDE congeners (17, 66, and 183) >80% of serum samples had concentrations below the LOD. Therefore, models were also run with these chemicals modeled dichotomously (above/below

LOD, range: 0.003–0.013 ng/mL), given that all values quantified as < LOD met all quality control requirements. Furthermore, this analysis was performed for the purpose of full data exploration, given the growing body of literature suggesting that endocrine disrupting chemicals may exhibit low-dose effects on the synthesis, secretion and metabolism of various thyroid hormones and insulin (Lee et al., 2011; Vandenberg et al., 2012). Multiple logistic regression models were adjusted for serum lipids (ng/g) and a priori specified covariates in light of limited data to inform model specification: age (years), BMI; race (white/non-white), and preconception smoking (yes/no). To assess the stability of findings, models were further adjusted for the arithmetic sum of the remaining log-transformed and rescaled POPs in each chemical class to account for serum concentrations of chemically similar compounds; chemicals were summed within subject and within imputation and reported in ng/g. All analyses were performed using SAS software (version 9.4; SAS Institute, Cary. NC).

3. Results

The cohort comprised mostly parous, non-Hispanic White women who were non-smokers. The mean age of participants was 29.7 ± 3.7 years, while mean BMI was 26.2 kg/m^2, respectively (Table 1). The prevalence of prospectively observed GDM and gestational hypertension was 11% (n = 28) and 10% (n = 27), respectively. No significant differences were observed in baseline maternal characteristics by gravid disease status although BMI was slightly higher among GDM women than non GDM.

The serum distributions of POPs are presented in Table 2 and reflect relatively low concentrations for women, as evident by many chemicals having more than half of the measured concentrations <LOD. Of the OCPs, p-p′-DDE serum concentrations were highest (overall median = 0.57 ng/g; IQR: 0.41, 0.78). Likewise, the PBDE congener with the highest serum concentration was BDE-47 (overall median = 0.11 ng/g; IQR: 0.06, 0.21). Serum median concentrations of POPs did not vary by maternal gravid condition status (Table 2).

Maternal preconception OCP concentrations were not significantly associated with GDM, although ORs were elevated in adjusted models of oxychlordane (OR = 1.26; 95% CI: 0.76, 2.08) and p,p′-DDE (OR = 1.20; 95% CI: 0.72, 2.02) (Table 3). However, maternal serum concentration of BDE-153 was significantly and positively associated with GDM. Specifically, a 1 SD (0.20 ng/mL) increase in concentration was associated with a 37–79% increased odds of GDM in unadjusted (OR = 1.37; 95%CI: 1.02–1.84) and adjusted models that included the sum of remaining PBDEs (OR = 1.79; 95%CI: 1.18, 2.74). No other statistically significant associations were observed between other PBDE congeners. Nevertheless, there was suggested trend for a 2.22 times higher odds of GDM per one SD (0.09 ng/mL) increase in the serum concentration of BDE-100 after additionally adjusting for the sum of remaining PBDEs (OR = 2.22, 95% CI: 0.96, 5.17) (Table 3) and an inverse association between BDE-47 and adjusted odds of GDM (aOR = 0.32; 95% CI: 0.10, 1.01). No significant associations were observed for gestational hypertension with increasing preconception serum concentrations of OCPs or PBDE congeners. However, a 56% increased odds of gestational hypertension was observed for a 1 SD increase in ln-

transformed concentration of serum BDE-66 in the fully adjusted model; this finding was not significant (OR = 1.56; 95% CI: 0.93, 2.64).

For those chemicals with >80% of serum concentrations below the LOD, no significant associations were observed between preconception serum POPs and GDM (Supplemental material, Table 1). All the women with GDM and gestational hypertension had concentrations below the LOD for γ-HCH and Mirex, therefore dichotomous models of maternal POPs could not be performed. However, γ-HCH was significantly associated with gestational hypertension in the fully adjusted continuous model accounting for low-dose additivity of the remaining OCPs (OR = 1.41, 95% CI: 1.01, −1.96) (Supplemental material, Table 1). These results are placed in the context of 99% of γ-HCH samples having concentrations below the LOD.

4. Discussion

In the first epidemiologic study known to us to assess preconception concentrations of OCPs and PDBEs in relation to the development of gravid diseases, we observed that the odds of GDM were increased approximately 37–79% per 1 SD (0.20 ng/mL) increase in serum concentration of BDE-153 in unadjusted and adjusted models accounting for covariates and the sum of additional PBDEs, respectively. Still, we observed a suggestive inverse association between BDE-47 and odds of a GDM diagnosis, possibly a function of our relatively low chemical distributions relative to females in U.S. biomonitoring data (CDC, 2015) and a specific subsample of 100 pregnant women (Woodruff et al., 2011). This difference in serum concentrations of POPs may reflect our younger age distribution for the overall female biomonitoring data (12–60^{+} years) relative to ours (18–44 years). Also, our pregnancy cohort comprises mostly white, educated and married women whose household incomes were largely greater than the median household income during the course of LIFE Study (United States Census Bureau, 2005); all of which may explain lower exposure to the POPs under study.

Interpretation of all of our findings for preconception exposures and pregnancy related health endpoints in the context of the literature is challenged by the absence of similar studies with regard to quantification of chemicals prior to conception. Nevertheless, our findings do not support the statistically significant inverse associations between serum measurements of p,p′-DDT and β-HCH collected at approximately ≥27 weeks of gestation and gestational hypertension observed by Savitz et al. (2014), given that point estimates of association were in the same direction but did not reach statistical significance; potentially a sample size. Furthermore, differences in study design limit the direct comparison of our results with the Agricultural Health Study, a population in which the POPs under study were previously measured (Brock et al., 1998), which observed a significant twofold increased odds of developing GDM (adjusted OR 2.2 [95% CI 1.5–3.3]) among women who self-reported pesticide exposure (mixing or applying) during the first trimester of pregnancy (Saldana et al., 2007). However, we have noted that our significant findings were in general agreement with those reported in the previous study.

Findings from our analysis have been placed in the context of potential strengths and limitations regarding the measurement of preconception chemical concentrations. Given the long half-lives of the POPs under study, the uncertain timing of onset of gravid diseases, and previous findings suggesting that serum measurements of POPs vary during pregnancy as the result of biological changes occurring in pregnancy (i.e., changes in metabolism, expansion of blood volume), preconception concentrations may provide a more reliable estimate of exposure than a single measurement made at some point in pregnancy (Takser et al., 2005; Wang et al., 2009). On the other hand, the distributions of many chemicals under study were skewed to lower bounds leading to the potential for measurement error that may downwardly bias results (Richardson and Ciampi, 2003). Still, quantification of all chemicals was done in a blinded manner, and women were blind to their concentrations during follow up in the study. To this end, the distributions of exposures are not likely attributed to differential reporting of gravid diseases. Additionally, we recognize that the intentional exploration of individual chemicals, the result of extremely limited literature to help inform model specification, may present a potential limitation. We are aware of the recommendation by the National Academies of Sciences, National Research Council and other groups, to assess multiple chemicals in models of health outcomes (NRC, 2009); an approach that may not be as informative in our exploratory analysis of these individual chemicals and select gravid health outcomes. We did however, assume the potential for additivity and a priori chose to sum within chemical class as opposed to summing across chemical classes or using other means of data reduction. We also consider the role of chance in our findings given that p-values were not adjusted for multiple testing. Moreover, future assessment of serum POPs and gravid health would benefit from modeling chemical mixtures, based on a better understanding of shared mechanisms and/or chemical structure among POPs having strong signals of association with gravid conditions.

We also consider the comparability of disease prevalence in our cohort relative to other studies relying upon women's reporting of physician-diagnosed disease, and the potential limitations of our prospectively ascertained gravid disease outcomes. Prevalence of GDM was 11% for our cohort, an estimate that is slightly higher than the 9.2% prevalence of self-reported GDM in the U.S. Pregnancy Risk Assessment Monitoring System (PRAMS) 2007–2010 survey period of women 2–4 months postpartum, excluding those with self-reported prepregnancy diabetes (DeSisto et al., 2014). The prevalence of gestational hypertension in our cohort was 10%, which is within the 6–22% range generally reported in the literature (NHBPEP, 2000; ACOG, 2002). The slightly higher prevalence of GDM and gestational hypertension that we observed may be at least partly due to the fact that 47% of women in our cohort were overweight or obese upon entry into the study. However, we are unable to estimate innate GDM and gestational hypertension risks in the LIFE Study, given that specific variables (i.e., family history of diabetes) were not collected for our cohort. Potential limitations of our outcome measures include the fact that the women in our cohort were receiving prenatal care from various health care providers who may have used different methods for diagnosing and communicating gravid conditions, and the reliance on women's reporting of gravid diseases in monthly pregnancy journals tailored to clinical screening and guidance, intended to be completed following each monthly clinical prenatal visit. However, the similar recommended guidelines from the American Diabetes Association (ADA, 2004)

and the American College of Obstetricians and Gynecologists (ACOG, 2001) for the diagnosis of GDM were widely adopted during the conduct of the LIFE Study. Furthermore, we are aware that the use of self-reported history of diabetes to exclude GDM from undiagnosed diabetes detected during pregnancy may not be as precise as the use of a pre-conception fasting blood glucose test. Nonetheless, previous validation studies have reported good agreement between self-reported GDM and GDM data from medical records; GDM data in the multisite PRAMS cohort reported sensitivity as high 88% and specificity as high as 97% (Dietz et al., 2014). Still, while we recognize that these limitations could potentially result in GDM misclassification, but point estimates of association are not likely to be biased, given the prospective design and that self-reporting of diabetes history is not likely to be associated with serum POPs concentrations, which were unknown to our women.

Other important limitations include the potential for residual confounding given the exclusion of variables that are classically considered as confounders of the relationship between serum POPs and GDM (i.e., prior history of GDM). However we found that only 2% of the women in our cohort reported a prior history of GDM, which may be influenced by the inclusion of nulligravid women in the LIFE Study. Furthermore, we found that gravid condition and serum POPs did not vary by variables reflective of socioeconomic status (i.e., education, income) and were excluded from logistic regression models in an attempt to avoid overadjustment bias (Schisterman et al., 2009). Additionally, we recognize that information on other variables (i.e., dietary intake) was not collected among our study cohort and therefore was not included in regression models. Nevertheless, these limitations underscore the need for additional pregnancy cohort studies with preconception enrollment of women/couples to corroborate these findings.

In light of the study findings and associated strengths and limitations, the biologic plausibility needs to be considered. Primarily, mechanisms explaining the different directions of observed associations between BDE-47 and BDE-153 are obscure. Still, we consider that the difference in chemical structure (i.e., four vs six bromines) and exposure source (BDE-47 is found in the PentaBDE formulation, while BDE-153 is found in both the PentaBDE and OctaBDE formulations), may lead to differences in biotransformation of parent compounds once inside the human body and ultimately varied pharmacokinetics (Sjodin et al., 2008). Moreover, etiologic mechanisms and pathways have not been delineated for GDM in the context of POPs exposure. Nonetheless, PBDE congener 153 was associated with increased odds of GDM in our study and increased risk of diabetes in a dose response fashion among the general U.S. population (Lim et al., 2008), suggesting similar biologic pathways explaining POPs exposure as it relates to diabetes in both the gravid and general populations. Thus, animal studies of POPs and diabetes have suggested the activation of peroxisome proliferator-activated receptor alpha (PPARα) through interactions with the aryl hydrocarbon receptor (Remillard and Bunce, 2002), and insulin resistance (Ruzzin et al., 2010) as a primary mechanism for the effect of environmental chemicals on GDM. These findings are supported in human studies, where concentrations of serum POPs have been positively associated with measures of visceral and subcutaneous fat among those diagnosed as prediabetic or diabetic, when compared with those of normal glucose tolerance status (Dirinck et al., 2014). Likewise, in a prospective analysis of women with a history of GDM, levels of serum POPs measured at three months post-delivery or after ceasing

breastfeeding, were positively associated with insulin resistance markers assessed using homeostasis models; higher levels correspond to greater insulin resistance (Arrebola et al., 2015).

5. Conclusion

Our findings suggest that maternal exposure to PBDE congener 153 prior to conception may increase the odds of GDM in a cohort of women followed over sensitive windows of human reproduction, namely, peri-conception and pregnancy intervals. The findings for preconception serum BDE-153 and GDM are in the context of relatively low, serum chemical distributions. Still, these exploratory findings await corroboration and basic work that might inform potential mechanisms and elucidate the relationship between exposure to select POPs and gravid health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Abbreviations:

HCB	hexachlorobenzene
Beta (β)–HCH	beta (β)-hexachlorocyclohexane
γ-HCH	gamma (γ)-hexachlorocyclohexane
o,p′ DDT	1,1,1-Trichloro-2-2(ochlorophenyl)-2-(p-chlorophenyl)ethane
p,p′-DDE	1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene
p,p′-DDT	1,1,1-Trichloro-2-2(o-chlorophenyl)-2-(p-chlorophenyl)ethane
PBDEs	polybrominated diphenyl ethers
POPs	persistent organic pollutants
LOD	limit of detection
OCPs	organochlorine pesticides

LIFE Study	Longitudinal Investigation of Fertility and the Environment Study

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HIGHLIGHTS

- Detection of serum POPs varied by chemical (range: <1–99% below LOD).
- Low levels of preconception serum POPs was associated with gravid disease.
- PBDE #153 was associated with a 36–79% increased odds of gestational diabetes.

Table 1

Maternal characteristics by gravid condition status.

Characteristic	All (N = 258)	GDM (N = 28)	No GDM (N = 230)	p	HTN (N = 27)	No HTN (N = 231)	p
Age, years; mean (SD)	29.68 (3.70)	30.21 (2.87)	29.62 (3.79)	0.32	29.59 (3.82)	29.69 (3.69)	0.90
BMI, kg/m^2; mean (SD)	26.17 (6.29)	27.00 (4.65)	26.07 (6.46)	0.35	27.64 (4.74)	26.00 (6.43)	0.11
Parity, nulliparous; N (%)[a]	122 (47.3)	12 (42.9)	110 (47.8)	0.62	13 (48.1)	109 (47.2)	0.92
Race, non-white; N (%)	42 (16.3)	7 (25.0)	35 (15.2)	0.19	4 (14.8)	38 (16.5)	0.83
Smokers; N (%)	17 (6.6)	2 (7.1)	15 (6.5)	0.90	1 (3.7)	16 (6.9)	0.52

BMI, body mass index.

SD, standard deviation.

p-Values are from *t*-test (continuous) and Chi-square (categorical).

[a]Parity is conditioned on gravidity.

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Table 2

Median and interquartile range (IQR) for lipid-adjusted serum chemicals by gravid condition status.

Chemical (ng/g, serum)	% < LOD	Overall (N = 258) Median (IQR)	GDM (N = 28) Median (IQR)	No GDM (N = 230) Median (IQR)	HTN (N = 27) Median (IQR)	No HTN (N = 231) Median (IQR)
OCPs[a]						
HCB	1.9	0.05 (0.04,0.06)	0.05 (0.04, 0.06)	0.05 (0.04, 0.06)	0.04 (0.04, 0.06)	0.05 (0.04,0.06)
β-HCH	58.5	<LOD (<LOD, 0.02)	0.013 (<LOD, 0.02)	<LOD (<LOD, 0.02)	<LOD (<LOD, 0.02)	<LOD (<LOD, 0.02)
γ-HCH	99.2	<LOD	<LOD	<LOD	<LOD	<LOD
Mirex	81	<LOD	<LOD	<LOD	<LOD	<LOD
o,p'-DDT	99.6	<LOD	<LOD	<LOD	<LOD	<LOD
Oxychlordane	17.1	0.03 (0.02, 0.05)	0.04 (0.03, 0.06)	0.03 (0.02, 0.04)	0.03 (0.02, 0.04)	0.03 (0.02, 0.05)
p,p'-DDE	0.8	0.57 (0.41,0.78)	0.60 (0.47, 0.97)	0.56 (0.38, 0.77)	0.57 (0.44, 0.68)	0.57 (0.39, 0.79)
p,p'-DDT	60.5	<LOD (<LOD, 0.02)	<LOD (<LOD, 0.02)	<LOD (<LOD, 0.02)	<LOD (<LOD, 0.014)	<LOD (<LOD, 0.02)
trans-Nonachlor	3.5	0.05 (0.03, 0.08)	0.06 (0.04, 0.09)	0.05 (0.03, 0.08)	0.04 (0.03, 0.06)	0.05 (0.03, 0.08)
PBDEs[b]						
17	84.9	<LOD	<LOD	<LOD	<LOD	<LOD
28	23.6	0.01 (0.003,0.01)	0.01 (0.004, 0.01)	0.01 (0.003,0.01)	0.01 (<LOD, 0.02)	0.01 (0.003,0.01)
47	1.2	0.11 (0.06,0.21)	0.13 (0.06, 0.19)	0.11 (0.06,0.21)	0.14 (0.05, 0.29)	0.11 (0.06,0.20)
66	86.8	<LOD	<LOD	<LOD	<LOD	<LOD
85	59.7	<LOD (<LOD, 0.004)	0.003 (<LOD, 0.004)	<LOD (<LOD, 0.004)	<LOD (<LOD, 0.004)	<LOD (<LOD, 0.004)
99	25.6	0.02 (0.01,0.04)	0.03 (0.01,0.04)	0.02 (0.01,0.04)	0.02 (0.01,0.04)	0.02 (0.01,0.04)
100	1.9	0.02 (0.01,0.04)	0.03 (0.01,0.04)	0.02 (0.01,0.04)	0.03 (0.01,0.06)	0.02 (0.01,0.04)
153	0.8	0.04 (0.02, 0.09)	0.03 (0.02, 0.10)	0.04 (0.02, 0.09)	0.05 (0.02, 0.11)	0.04 (0.02, 0.09)
154	62.4	<LOD (<LOD, 0.004)	0.003(<LOD, 0.005)	<LOD (<LOD, 0.004)	<LOD (<LOD, 0.004)	<LOD (<LOD, 0.004)
183	82.6	<LOD	<LOD	<LOD	<LOD	<LOD

HCB, hexachlorobenzene; β-HCH, β-hexachlorocyclohexane; γ-HCH, γ-hexachlorocyclohexane; o,p′ DDT, 1,1,1-Trichloro-2-2(o-chlorophenyl)-2-(p-chlorophenyl)ethane; p,p′-DDE, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene; p,p′-DDT, 1,1,1-Trichloro-2-2(o-chlorophenyl)-2-(p-chlorophenyl)ethane; OCPs, organochlorine pesticides; PBDE, polybrominated diphenyl ether; IQR, interquartile range; LOD, limit of detection. p-Values from Wilcoxon-Mann-Whitney tests were not statistically significant at $p < 0.05$ level.

[a]LOD for all OCPs was 0.013 ng/g, serum.

[b]LOD for PBDEs was 0.003 ng/g, serum, except for BDE-47 (LOD = 0.011 ng/g) and BDE-99 (LOD = 0.010 ng/g).

Table 3

Associations between maternal preconception serum POPs and gravid conditions.

Chemical	GDM (N = 28)		HTN (N = 27)	
	Model A OR (95% CI)	Model B OR (95% CI)	Model A OR (95% CI)	Model B OR (95% CI)
OCPs				
HCB	0.96 (0.63,1.46)	0.97 (0.60,1.57)	0.64 (0.37,1.11)	0.74 (0.40,1.36)
β-HCH	0.58 (0.17,2.01)	0.34 (0.07,1.67)	0.29 (0.04,2.15)	0.43 (0.06,3.21)
Oxychlordane	1.07 (0.73,1.56)	1.26 (0.76,2.08)	0.59 (0.35,1.01)	0.61 (0.34,1.10)
p,p'-DDE	1.11 (0.79,1.55)	1.20 (0.72,2.02)	0.62 (0.34,1.11)	0.68 (0.33,1.40)
p,p'-DDT	0.94 (0.60,1.48)	1.01 (0.55,1.85)	0.24 (0.05,1.11)	0.27 (0.04,1.73)
trans-Nonachlor	0.99 (0.67,1.46)	1.03 (0.67,1.58)	0.55 (0.28,1.07)	0.58 (0.28,1.21)
PBDE congeners				
28	0.81 (0.48,1.37)	0.47 (0.17,1.26)	0.80 (0.47,1.38)	0.71 (0.28,1.79)
47	0.83 (0.51,1.35)	0.32 (0.10,1.01)	0.98 (0.65,1.48)	1.86 (0.55,6.27)
85	0.94 (0.60,1.48)	0.71 (0.23,2.24)	0.83 (0.47,1.48)	0.61 (0.17,2.21)
99	0.78 (0.41,1.45)	0.44 (0.15,1.33)	0.91 (0.56,1.47)	0.96 (0.42,2.19)
100	1.15 (0.82,1.61)	2.22 (0.96,5.17)	0.85 (0.51,1.41)	0.69 (0.23,2.06)
153	1.37 (1.02,1.84)	1.79 (1.18,2.74)	0.81 (0.47,1.41)	0.84 (0.46,1.52)
154	0.99 (0.66,1.49)	1.04 (0.34,3.17)	0.84 (0.48,1.46)	0.59 (0.15,2.33)

HCB, hexachlorobenzene; β-HCH, β-hexachlorocyclohexane; γ-HCH, γ-hexachlorocyclohexane; o,p′ DDT, 1,1,1-Trichloro-2-2(o-chlorophenyl)-2-(p-chlorophenyl)ethane; p,p′-DDE, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene; p,p′-DDT, 1,1,1-Trichloro-2-2(o-chlorophenyl)-2-(p-chlorophenyl)ethane; OCPs, organochlorine pesticides; PBDE, polybrominated diphenyl ether; IQR, interquartile range; LOD, limit of detection; GDM, gestational diabetes mellitus; HTN, gestational hypertension.

Model A, multiple logistic regression models were adjusted for serum lipids.

Model B, multiple logistic regression models were adjusted for serum lipids, age, BMI, non-white race, smoking, and the sum of remaining chemicals in the relevant class of compounds.