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Univariate predictors of maternal concentrations of environmental chemicals: The MIREC study

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ABSTRACT

Background: The developing fetus and pregnant woman can be exposed to a variety of environmental chemicals that may adversely affect their health. Moreover, environmental exposure and risk disparities are associated with different social determinants, including socioeconomic status (SES) and demographic indicators. Our aim was to investigate whether and how maternal concentrations of a large panel of persistent and non-persistent environmental chemicals vary according to sociodemographic and lifestyle characteristics in a large pregnancy and birth cohort.
Methods: Data were analyzed from the Maternal-Infant Research on Environmental Chemicals (MIREC) Study, a cohort of pregnant women (N = 2001) recruited over four years (2008–2011) in 10 cities across Canada. In all, 1890 urine and 1938 blood samples from the first trimester (1st and 3rd trimester for metals) were analysed and six sociodemographic and lifestyle indicators were assessed: maternal age, household income, parity, smoking status, country of birth and pre-pregnancy body mass index (BMI).
Results: We found these indicators to be significantly associated with many of the chemicals measured in maternal blood and urine. Women born outside Canada had significantly higher concentrations of di-2-ethylhexyl and diethyl phthalate metabolites, higher levels of all metals except cadmium (Cd), as well as higher levels of polychlorinated biphenyls (PCBs) and legacy organochlorine pesticides (OCPs). Nulliparity was associated with higher concentrations of dialkyl phosphates (DAPs), arsenic, dimethylarsinic acid (DMAA), perfluoroalkyl substances (PFASs) and many of the persistent organic pollutants. Smokers had higher levels of bisphenol A, Cd and perfluorohexane sulfonate, while those women who had never smoked had higher levels of triclosan, DMAA, manganese and some OCPs.
Conclusion: Our results demonstrated that inequitable distribution of exposure to chemicals among populations within a country can occur. Sociodemographic and lifestyle factors are an important component of a thorough risk assessment as they can impact the degree of exposure and may modify the individual's susceptibility to potential health effects due to differences in lifestyle, cultural diets, and aging.

1. Introduction

The developing fetus and pregnant woman are frequently exposed to a variety of environmental chemicals that may adversely affect their health (Fox et al., 2012). The *in utero* environment is a critical bridge to future health outcomes and environmental factors such as nutrition, environmental chemicals and other stressors can dramatically alter the development of the fetus (Grandjean et al., 2008; Newbold and Heindel, 2010). During pregnancy, increased blood volume, metabolism, renal perfusion and major changes to circulating hormones (essential elements and serum lipids) occur (Hansen et al., 2010, 2011; Soma-Pillay et al., 2016). These changes may have a substantial impact on absorption, distribution, metabolism and excretion of chemicals. Moreover, the fetus may be exposed to a complex chemical environment (up to 287 chemicals have so far been detected in human cord blood (Houlihan et al., 2005)) among which several cross the placenta (Stern and Smith, 2003) and enter the breast milk after delivery (Hites, 2004; Solomon and Weiss, 2002). Several of these environmental chemicals have been linked with adverse effects on health. For example, maternal urinary concentrations of various

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phthalates have been associated with increased oxidative stress markers in pregnant women (Ferguson et al., 2014, 2015a,b; Guo et al., 2014; Watkins et al., 2015). Oxidative stress plays a role in maternal and fetal morbidity (Gitto et al., 2002; Tabacova, 2000; Triche and Hossain, 2007), pre-eclampsia (Burton and Jauniaux, 2004; Guerby et al., 2015) and preterm delivery (Ferguson et al., 2015b). Moreover, ubiquitous exposure to environmental chemicals during pregnancy may disrupt hormones that regulate normal human reproduction and development (such as the endocrine system) (WHO and UNEP, 2013), increase the risk of adverse birth outcomes (Casas et al., 2015; Govarts et al., 2012), damage respiratory health (Gascon et al., 2014), increase obesity (Inadera, 2013), and neurotoxicity risk (Grandjean and Landrigan, 2014; Mone et al., 2004). Moreover, several environmental exposures and risk disparities are associated with different social determinants including socioeconomic status (SES) and demographic indicators (EPA, 1999; Sonneborn et al., 2008).

Evidence suggests that there are sociodemographic and lifestyle disparities in toxicant burden (Bravo et al., 2016) but the gradient may vary according to the specific chemical under study. Exposure to environmental contaminants varies with SES and lifestyle (Adler and Newman, 2002). Some studies have found that adopting a healthy lifestyle may be an option to reduce chemical exposure (Bai et al., 2015; Brantsaeter et al., 2016). Moreover, for pregnant women, variability of chemical exposures of individual mothers could be associated with lifestyle behaviors such as physical activity, vitamin D intake, coffee consumption and smoking exposure (Maitre et al., 2016; Martina et al., 2012). Housing quality is also poorer for low-SES families (Adler and Newman, 2002). Studies in developed countries found that individuals with high SES and smokers may be more frequently or more intensively exposed to environmental chemicals such as mercury (Hg), arsenic (As), caesium, thallium, perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), mono(carboxyoctyl) phthalate (MCOP) and benzophenone-3 (Tyrrell et al., 2013), pesticides (Cox et al., 2007) and polychlorinated biphenyls (PCBs) (Borrell et al., 2004). In addition to the amount or the duration of chemical exposures, the individual's or community's risk profile may influence their vulnerability to an exposure. For example, for certain health outcomes (e.g. asthma, cancer and diabetes) smokers and low SES (O'Neill et al., 2012) are more vulnerable to environmental chemicals than those who don't smoke and with high SES (Jemal et al., 2008; World Health Organization, 2002; Zheng and Land, 2012). As well, exposure profiles and levels of environmental chemicals in women vary both within and between countries (President's Cancer Panel, 2009). However, given the increasing globalization of chemical production (OECD, 2011) and the broad range of chemicals found in our environment (EEA, 2011), there is a need to examine the relationship between environmental toxicant burden and demographic parameters.

From a public health research perspective, it would be important to determine the contribution of variations in environmental exposures to social inequalities in health. Using results from the Maternal-Infant Research on Environmental Chemicals (MIREC) Study, our aim was to summarize the evidence regarding maternal levels of a large panel of persistent and non-persistent environmental chemicals and to determine if these levels vary according to sociodemographic and lifestyle characteristics in a large pregnancy cohort.

2. Methods

2.1. Study population

2.1.1. The MIREC study

The MIREC Study is a national-level pregnancy cohort. Of the 2001 pregnant women recruited, (mean age 32.2 years (SD 5.1)) from 10 cities across Canada between 2008 and 2011, 18 subsequently withdrew and asked that their data and biospecimens be destroyed, leaving 1983 participants (Arbuckle et al., 2013). Study participants were enrolled from the general population who were attending prenatal clinics (ultrasound, midwife and/or doctor's clinics) during the first trimester of pregnancy (6 to <14 weeks). Approximately 94% of study participants lived in an urban area according to postal forward sortation area codes (Ashley-Martin et al., 2015). At each pregnancy visit (corresponding to each trimester and at delivery) women completed questionnaires and provided both blood and urine samples. The questionnaires collected information on the participant's sociodemographics, current and previous pregnancies, smoking and lifestyle.

Research Ethics Board approval was obtained from all participating sites and Health Canada. Study subjects gave written informed consent. Additional details on study methods may be found in the published cohort profile (Arbuckle et al., 2013).

2.2. Measures

2.2.1. Environmental chemical exposure

Chemicals that were analyzed in the maternal blood and urine were chosen based priorities of the Government of Canada's Chemicals Management Plan and on a review of the literature to identify those with potential reproductive toxicity and whether valid biomarkers and laboratory methods were available (Arbuckle et al., 2013). In this article, we summarize results on chemicals with sufficient detection (at least 50%): 2 phenols (BPA: bisphenol A, TCS: triclosan); 7 phthalates metabolites (MBzP: mono-benzyl phthalate, MCPP: mono-3-carboxyypropyl phthalate, MEHP: mono-(2-ethylhexyl) phthalate, MEHHP: mono-(2-ethyl-5-hydroxyhexyl) phthalate, MEOHP: mono-(2-ethyl-5-oxohexyl) phthalate, MnBP: mono-n-butyl phthalate, MEP: mono-ethyl phthalate); 5 metals (As: Arsenic, Cd: Cadmium, Pb: Lead, Mn: Manganese, Hg: Mercury); 4 polychlorinated biphenyls (PCB 118, 138, 153, 180) and the mixture Aroclor 1260; 3 perfluoroalkyl substances (PFASs) (PFHxS: perfluorohexane sulfonate, PFOA: perfluorooctanoic acid, PFOS: perfluorooctane sulfonate); one polybrominated diphenyl ether (PBDE 47); 4 legacy organochlorine pesticides (Beta-HCH: β-hexachlorocyclohexane, DDE: dichlorodi-phenyldichloroethylene, oxychlordane, *trans*-nonachlor); 3 dialkyl phosphate metabolites (DMP: dimethyl phosphate, DMTP: dimethyl thiophosphate, DEP: diethyl phosphate) and 2 urinary arsenic species (ASAL: arsenocholine, DMAA: dimethylarsinic acid). In this study, all chemicals were measured in first trimester maternal plasma or urine except the metals which were measured in whole blood in both the 1st and 3rd trimesters. Chemical analyses of maternal blood and urine were carried out by the Institut national de santé publique du Québec (INSPQ), which is accredited by the Standards Council of Canada under ISO 17025 and CAN-P-43. The laboratory methods have been described in detail elsewhere (Arbuckle et al., 2014, 2016, 2015a,b; Ettinger et al., 2016; Fisher et al., 2016; Sokoloff et al., 2016). Aroclor 1260 was also calculated by INSPQ based on the sum of the wet weight concentration of PCB 153 and PCB 138 multiplied by a factor of 5.2 [(C153 + C138) × 5.2] (Health Canada, 2010).

2.2.2. Maternal sociodemographic and lifestyle variables

Several sociodemographic characteristics were obtained from the questionnaire administered during the first trimester visit including: maternal age (18–24, 25–29, 30–34, and ≥ 35) and household income (≤$50,000, $50,001 to $100,000 and >$100,000 (CAD)), categorized according to the MIREC cohort profile (Arbuckle et al., 2013); parity: 0 previous births, 1 previous birth, and two or more previous births. Smoking status was coded as: current smoker or quit during pregnancy, former smoker, and never smoked. Pre-pregnancy body mass index (kg/m^2) was classified

Table 1
Study population.

Characteristic	Frequency	Percent
Maternal age group		
<25	139	7.01
25–29	459	23.15
30–34	709	35.75
35+	676	34.09
Household income[a]		
≤$50,000	347	17.49
$50,001–$100,000	786	39.64
>$100,000	757	38.17
Parity		
0	874	17.49
1	800	39.64
2+	307	38.17
Smoking status		
Current[b]	237	11.96
Former	542	27.36
Never	1202	60.68
Country of birth		
Foreign born	371	18.71
Canadian born	1612	81.29
Pre-pregnancy BMI		
Underweight to normal (BMI < 25)	1164	63.36
Overweight (25 ≤ BMI < 30)	404	21.99
Obese (BMI ≥ 30)	269	14.64

[a] Sum of percentages does not equal 100 because of missing values.
[b] Includes women who quit smoking during current pregnancy.

as: underweight to normal (BMI < 25), overweight (25 ≤ BMI < 30), and obese (BMI ≥ 30). A binary variable was assigned for the country of birth (born in Canada or outside Canada).

2.3. Statistical analyses

Geometric mean (GM) urinary and blood concentrations for each chemical with 50% of the data above the limit of detection (LOD) in all sociodemographic groups were calculated (Helsel, 2012). Statistical techniques to account for the left censoring induced by values below the LOD were applied, specifically parametric (maximum likelihood estimation) or nonparametric methods (Kaplan-Meier and the generalized Wilcoxon test) (Helsel, 2012). The GM from a lognormal random variable with left-censoring was calculated using the maximum likelihood method adjusted for specific gravity or total lipids as required. The specific gravity of each urinary concentration (or total lipids for each persistent organic pollutant, except the PFASs) was treated as a covariate in a linear model with the variable of interest (e.g. smoking, age, parity). For metals, since measurements were taken from the same mother in the first and third trimesters, a mixed model with left-censoring (Jin et al., 2011; Thiebaut and Jacqmin-Gadda, 2004) was implemented to properly account for the non-detects and the correlated nature of these contaminants. Details regarding the statistical analysis are presented elsewhere (Arbuckle et al., 2014, 2015a; Fisher et al., 2016). Hypothesis testing was performed under the null hypothesis of no difference in groups and a significance level of 1% ($\alpha = 0.01$) was assumed throughout.

3. Results

Demographic characteristics of the study population are provided in Table 1 and descriptive statistics for the chemicals analysed in Supplemental Table 1. Significant differences were observed in maternal chemical concentrations by categories of sociodemographic variables (Tables 2 and 3).

3.1. Maternal age

Maternal age was significantly associated with exposure to most metals and persistent organic pollutants (POPs). In contrast, the chemicals that were higher in younger women (age <25) compared to older age groups were BPA, MBzP, and PFHxS (Tables 2 and 3 and Supplemental Fig. 1).

3.2. Parity

In general, nulliparous women had higher geometric mean chemical concentrations than uniparous or multiparous woman (Tables 2 and 3 and Supplemental Fig. 2). This result was consistent for both persistent and non-persistent metabolites including MEP, DEP, DMP and DMTP, the PFASs, polychlorinated biphenyls (PCB 118, 138, 153, and Aroclor 1260), the legacy organochlorine pesticides, and total arsenic measured in blood (As) and speciated arsenic (DMAA) measured in urine. There was no evidence that the concentration of any chemical consistently increased with parity (Table 3).

3.3. Maternal smoking status

Significant differences by smoking status were observed for several chemicals. Surprisingly, for several chemicals (TCS, some OCPs, Mn and DMAA), non-smokers and former smokers had higher chemical levels compared to current smokers (Tables 2 and 3 and Supplemental Fig. 3), which may reflect an association between smoking status and one or more other variables. Currently smoking during pregnancy was associated with higher GM concentrations of BPA, Cd and PFHxS.

3.4. Country of birth

Maternal concentrations of phthalates (MEHP, MEOHP, MEHHP and MEP), metals (except Cd), PCBs and OCPs were higher in women born outside Canada. On the other hand, Canadian born participants had higher concentrations of MBzP, PFHxS, PFOS and PBDE 47 (Tables 2 and 3 and Supplemental Fig. 4).

3.5. Pre-pregnancy body mass index

Among obese mothers, chemical concentrations were higher for MBzP and PBDE 47 and lower for MEHP, DEP, DMTP, DMAA, Pb, Hg, PCBs, oxychlordane, and *trans*-nonachlor compared to non-obese mothers (Tables 2 and 3 and Supplemental Fig. 5).

3.6. Household income

Pregnant women from households with lower income had lower geometric mean (urine or blood) concentrations for TCS, MEHHP, DMAA, Hg, PFOA, PFOS, PCBs, *trans*-nonachlor and oxychlordane. On the other hand, higher concentrations of MBzP and Cd were present in women with lower incomes (Tables 2 and 3 and Supplemental Fig. 6).

4. Discussion

4.1. Main findings

Our results showed that, in the MIREC Study population, the distribution of environmental chemicals in maternal blood and urine varied according to their sociodemographic and lifestyle profiles. Regarding differential exposures to environmental pollution, significant relationships exist between SES and lifestyle characteristics and levels of exposure to environmental contaminants (Brulle

Table 2
Associations between Maternal Characteristics and Chemicals of Interest in Maternal Urine or Blood.

Chemical	Measure	Age Group	Parity	Never, Former, Current Smoker	Born Outside Canada	Pre-pregnancy BMI	Household Income
Phenols							
BPA	urine	–	NS	+	NS	NS	NS
TCS	urine	S	NS	–	NS	NS	+
Phthalates							
MnBP	urine	NS	NS	NS	NS	NS	NS
MBzP	urine	–	NS	NS	–	+	–
MCPP	urine	NS	NS	NS	NS	NS	NS
MEHP	urine	S	NS	NS	+	–	NS
MEOHP	urine	S	NS	NS	+	NS	NS
MEHHP	urine	S	NS	S	+	NS	+
MEP	urine	NS	–	NS	+	NS	NS
Dialkyl Phosphates (DAPs)							
DEP	urine	NS	–	NS	NS	–	NS
DMP	urine	NS	–	NS	NS	NS	NS
DMTP	urine	S	–	NS	NS	–	NS
Metals							
ASAL (speciated As)	urine	+	NS	NA	+	NS	NS
DMAA (speciated As)	urine	+	–	–	+	–	+
As	whole blood	+	–	S	+	NS	NS
Cd	whole blood	S	NS	+	NS	NS	–
Pb	whole blood	+	S	S	+	–	S
Hg	whole blood	+	NS	S	+	–	+
Mn	whole blood	NS	NS	–	+	NS	NS
Perfluroalkyl Substances (PFASs)							
PFHxS	plasma	–	–	+	–	NS	NS
PFOA	plasma	S	–	NS	NS	NS	+
PFOS	plasma	NS	–	NS	–	NS	+
Polychlorinated Biphenyls (PCBs)							
PCB 118	plasma	NA	–	S	+	–	+
PCB 138	plasma	+	–	S	+	–	+
PCB 153	plasma	+	–	S	+	–	+
PCB 180	plasma	+	NS	S	+	–	+
Arochlor 1260	plasma	+	–	S	+	–	+
Polybrominated Diphenyl Ethers (PBDEs)							
PBDE 47	plasma	S	NS	NS	–	+	NS
◦Legacy Organochlorine Pesticides (OCPs)							
Beta-HCH	plasma	NA	–	–	+	NA	S
DDE	plasma	+	–	–	+	NA	NS
Oxychlordane	plasma	+	–	S	+	–	+
Trans-nonachlor	plasma	NA	–	S	+	–	+

Abbreviations: **NA**: insufficient detection (>50% below LOD) in categories for analysis.
NS: not statistically significant ($p > 0.01$).
S: statistically significant overall but no consistent increase or decrease between geometric means (GMs) by categories ($p < 0.01$).
+: statistically significant overall ($p < 0.01$) and adjusted GMs increased across categories (e.g. as maternal age increased, GM PCB concentrations increased).
–: statistically significant overall ($p < 0.01$) and adjusted GMs decreased across categories (e.g. as parity increased, GM legacy organochlorine pesticides concentrations decreased).

and Pellow, 2006; Evans and Kantrowitz, 2002; Ringquist, 2005). As in previous studies, maternal age, parity, household income, smoking status, country of birth and pre-pregnancy BMI were found to be significantly associated with a number of chemicals. However, it may be difficult to build a standard sociodemographic profile for maternal environmental chemicals because of large differences in socioeconomic background within and between groups (Braveman et al., 2005; Hu et al., 2016). In addition, it is sometimes difficult to classify risk factors for maternal chemical concentrations into one socioeconomic characteristic, since concentrations vary according to the indicator of SES that is used (Braveman et al., 2005). Moreover, associations between socioeconomic status and maternal chemical concentration may be strongly influenced by the heterogeneity in socioeconomic determinants (Birch et al., 2000) and on the selection of confounding factors in the analyses. Also, there can be strong correlations among these sociodemographic and lifestyle factors.

We found specific maternal sociodemographic profiles to be associated with increased levels of a range of environmental chemicals. While one might expect to observe consistencies between associations between maternal chemical concentrations with maternal age and parity, this was often not the case in that opposite associations observed for DMAA, As, some PCBs, DDE, and oxychlordane. For those chemicals with longer half-lives such as PCBs, organochlorine pesticides, lower levels with increasing parity may be because of maternal transfer to the fetus and breast feeding infant. Moreover, the majority of As excreted in urine during pregnancy is of the methylated form, dimethylarsinic acid, and it is the major form that is transferred to the fetus (Concha et al., 1998; Rodrigues et al., 2015).

For the PFASs, we found only PFHxS concentrations to be lower in older mothers. Brantsaeter et al. (2013), Halldorsson et al. (2008) and Sagiv et al. (2015) found declining PFOA and PFOS concentrations with increasing maternal age. In contrast, Kato et al., Berg et al. and Sagiv et al. reported higher concentrations of PFOA, PFOS (Berg et al., 2016; Kato et al., 2011) and PFNA (Sagiv et al., 2015) for older women. Age-chemical concentration differences in pregnancy studies could also reflect differences in the sampling cohort

Table 3
Comparison of Geometric Mean Chemical Concentrations in 1st Trimester Blood or Urine by Sociodemographic Characteristics (μg/L).

Chemical	Age Group				Parity			Smoking status			Country of birth		Pre-pregnancy BMI			Household income		
	<25	25–29	30–34	≥35	0	1	>1	Current	Former	Never	Other	Canada	<25	25–29	≥30	≤50.000	>50.000–100.000	>100.000
Phenols																		
BPA	1.02	0.83	0.82	0.74*	0.85	0.78	0.75	1.01	0.81	0.77*	0.73	0.83	0.77	0.87	0.85	0.92	0.81	0.76
TCS	5.38	13.58	13.39	13.31*	15.48	13.95	12.25	8.83	10.97	14.41*	11.27	12.94	13.60	14.32	15.93	9.72	10.96	16.29*
Phthalates																		
MnBP	12.42	12.30	11.18	11.40	11.41	11.51	12.09	10.47	11.82	11.70	12.21	11.45	11.53	11.74	11.44	13.27	11.25	11.36
MBzP	6.75	6.21	5.01	4.57*	4.99	5.19	5.91	5.91	5.20	5.06	4.36	5.42*	5.01	5.11	6.28*	6.71	5.16	4.75*
MCPP	0.80	0.85	0.86	0.89	0.84	0.90	0.85	0.76	0.94	0.85	0.84	0.87	0.86	0.91	0.86	0.83	0.85	0.91
MEHP	1.84	2.49	2.17	2.24*	2.28	2.27	2.04	1.97	2.36	2.24	2.72	2.14*	2.42	2.20	1.84*	2.21	2.17	2.36
MEOHP	4.94	6.83	6.26	6.54*	6.43	6.48	5.97	5.46	6.76	6.40	7.18	6.21*	6.49	6.30	5.76	5.88	6.26	6.89
MEHHP	6.60	9.75	9.01	9.51*	9.06	9.44	8.71	7.62	9.71	9.21*	10.43	8.89*	9.25	9.16	8.41	8.28	8.95	10.04*
MEP	40.85	34.21	31.64	29.35	37.65	28.71	26.15*	39.67	31.37	30.79	41.1	30.15*	31.29	31.38	33.34	37.97	30.69	30.43
Dialkyl Phosphates (DAPs)																		
DEP	2.13	2.21	2.19	2.27	2.39	2.10	2.06*	1.99	2.29	2.22	2.35	2.19	2.33	2.09	1.90*	2.08	2.25	2.28
DMP	2.72	3.08	2.86	2.65	3.18	2.62	2.48*	2.48	2.75	2.93	3.43	3.10	3.27	2.96	2.97	3.27	3.19	3.11
DMTP	2.14	3.06	3.13	2.50*	3.57	2.39	2.17*	2.16	2.76	2.97	2.78	2.82	3.04	2.41	2.30*	2.75	3.48	3.13
Metals																		
ASAL (speciated As)	0.27	0.56	0.71	0.99*	0.82	0.62	0.67	–	–	–	1.38	0.60*	0.78	–	–	–	3.51	4.51
DMAA (speciated As)	1.76	2.18	2.38	2.45*	2.54	2.15	2.09*	2.00	2.32	2.37*	3.14	2.15*	2.44	2.24	1.89*	2.16	2.25	2.48*
As	0.59	0.67	0.71	0.77*	0.74	0.71	0.64*	0.63	0.75	0.71*	0.84	0.69*	0.73	0.71	0.66	0.68	0.71	0.73
Cd	0.26	0.20	0.20	0.22*	0.22	0.20	0.22	0.59	0.21	0.18*	0.23	0.21	0.22	0.21	0.20	0.26	0.21	0.19*
Pb (μg/dL)	0.54	0.54	0.58	0.67*	0.62	0.58	0.59*	0.63	0.63	0.58*	0.75	0.57*	0.62	0.56	0.55*	0.64	0.58	0.60*
Hg	0.26	0.41	0.55	0.79*	0.57	0.55	0.52	0.41	0.61	0.56*	0.91	0.49*	0.62	0.53	0.40*	0.42	0.51	0.68*
Mn	10.31	10.16	10.18	10.29	10.02	10.38	10.42	9.56	10.09	10.42*	11.00	10.05*	10.16	10.10	10.71	10.27	10.30	10.08
Perfluroalkyl Substances (PFASs)																		
PFHxS	1.29	1.10	1.06	0.91*	1.26	0.94	0.73*	1.19	1.05	0.99*	0.75	1.11*	0.99	1.09	1.09	0.93	1.00	1.00
PFOA	1.71	1.81	1.67	1.51*	2.22	1.35	1.17*	1.79	1.67	1.61	1.59	1.66	1.65	1.63	1.61	1.52	1.62	1.75*
PFOS	4.50	4.90	4.80	4.50	5.33	4.25	3.51*	4.42	4.56	4.59	4.14	4.67*	4.61	4.58	4.40	4.06	4.55	4.89*
Polychlorinated Biphenyls (PCBs) ($\times 10^{-2}$)[a]																		
PCB 118	–	–	–	–	1.60	1.40	1.19*	1.17	1.51	1.48*	1.98	1.35*	1.52	1.46	1.30*	1.24	1.39	1.65*
PCB 138	1.25	2.02	2.56	3.56*	2.76	2.57	2.16*	2.07	2.80	2.60*	4.24	2.31*	2.85	2.51	1.95*	2.11	2.47	3.01*
PCB 153	1.94	3.39	4.38	6.55*	4.73	4.47	3.82*	3.37	4.95	4.52*	7.94	3.92*	5.12	4.24	3.05*	3.48	4.26	5.34*
PCB 180	1.01	2.14	2.92	4.74*	3.04	3.06	2.68	2.10	3.37	3.04*	5.59	2.60*	3.57	2.74	1.79*	2.20	2.85	3.67*
Aroclor 1260	16.48	28.19	36.13	52.71*	39.03	36.70	31.18*	28.20	40.45	37.09*	63.47	32.45*	41.55	35.13	26.15*	29.12	34.96	43.54*
Polybrominated Diphenyl Ethers (PBDEs) ($\times 10^{-2}$)[a]																		
PBDE 47	4.57	5.07	4.10	4.00*	4.45	4.10	4.48	5.09	3.99	4.32	3.47	4.52*	3.84	4.52	6.27*	4.26	4.63	3.99
Legacy Organochlorine Pesticides (OCPs) ($\times 10^{-2}$)[a]																		
Beta-HCH	–	–	–	–	1.75	1.30	0.97*	0.99	1.45	1.51*	5.04	1.11*	–	–	–	1.32	1.30	1.62*
DDE	20.07	29.62	33.44	43.43*	39.02	32.67	27.10*	27.86	33.08	36.33*	84.01	27.97*	–	–	–	33.88	32.36	36.63
Oxychlordane	0.67	1.06	1.26	1.50*	1.37	1.18	0.99*	1.11	1.32	1.21*	1.36	1.20*	1.32	1.20	1.05*	1.06	1.17	1.41*
Trans-nonachlor	–	–	–	–	1.94	1.75	1.47*	1.54	1.87	1.79*	2.01	1.73*	1.94	1.72	1.48*	1.49	1.69	2.09*

Notes: Metals are based on both the 1st and 3rd trimester blood concentrations, estimated from a random intercept mixed model accounting for left-censored values. Urinary concentrations are specific gravity adjusted and POPs are lipid-adjusted except for the PFASs.

* p-value < 0.01.

[a] For the concordance of the table, polychlorinated biphenyls, polybrominated diphenyl ethers and legacy organochlorine pesticides concentrations have to be multiplied by 10.

time window (i.e. yearly trends in the availability of the chemicals) (Sagiv et al., 2015). Age trends of persistent organic pollutants could reflect year since peak emission, environmental persistence and biological half-life (Sagiv et al., 2015) (Quinn and Wania, 2012).

Similar to previous studies (Borrell et al., 2004; Calafat et al., 2008; Hightower and Moore, 2003; Sagiv et al., 2015), positive associations were observed between household income and TCS, PCBs, Hg and PFASs concentration whereas BPA (Nelson et al., 2012), metals (Pb and Cd) (Bushnik et al., 2010; Wang et al., 2016) and phthalates (such as mono-benzyl, mono-isobutyl, mono-*n*-butyl) (Tyrrell et al., 2013) appeared to decrease with increasing income in the general population. In the present study, we found only the metal Cd and the phthalate metabolite MBzP higher in the low income group. This could be due to the differences in lifestyle by household income. Mothers with high household income have a tendency to be non-smokers and to consume more fish which are associated with decreased Cd and increased Hg, respectively (Huisman et al., 2005; Verbeke and Vackier, 2005).

Higher PFAS, PCB and POPs concentrations were found to be associated with nulliparity in our study and that of others (Hardell et al., 2010; Nickerson, 2006; Patayova et al., 2013; Porpora et al., 2013; Sagiv et al., 2015). Lower concentrations with increasing parity is likely a function of placental transfer during previous pregnancies as well as deposition of these persistent chemicals in breast milk.

Our results showed that non-smoking mothers had higher concentrations of triclosan, some legacy organochlorine pesticides, and the metals Mn and DMAA than former or current smokers. In contrast, most previous studies have reported a linear positive association between smoking and PCBs, pesticides and metals (Bjerregaard et al., 2013; Butler Walker et al., 2006; Deutch and Hansen, 1999; Deutch et al., 2003). Moreover, smoking status is an important determinant of POP bioaccumulation (Deutch et al., 2003). Unlike some previous studies (Bjerregaard et al., 2013; Deutch and Hansen, 1999; Deutch et al., 2003), our finding may be due to the unmeasured confounders in our univariate observation of the maternal concentration characteristics (Wong et al., 2015).

We found consistently higher maternal concentrations for metals and POPs among pregnant Canadian immigrants than in Canadian born participants as have other Canadian studies (Foster et al., 2012). Curren et al. also reported higher concentrations of DDE and β-HCH in immigrant mothers compared to Canadian-born and Inuit mothers (Curren et al., 2015). Some of the disparities between country of birth and maternal chemical concentrations may result from exposures that occurred outside of Canada and may be explained by cultural habits, imported foods and lifestyle related to the country of origin (Muennig et al., 2011).

Compared to other pre-pregnancy BMI categories, pre-pregnant obese women had lower concentrations of MEHP, DEP, DMTP, DMAA, Pb, Hg, PCBs, oxychlordane and *trans*-nonachlor, and higher concentrations of MBzP, and PBDE 47. Adipose tissue, as a storage compartment, can play a critical sequestering role in toxicokinetics of a variety of lipophilic pollutants such as phthalates and PCBs (La Merrill et al., 2013). For lipophobic contaminants, such as mercury, it is more difficult to explain our results. A possibility is that adipose tissue contains adipocytes, which are comprised mainly of lipid droplets (~95%), as well as stromal vascular cells with less lipid content (Lee et al., 2013). Moreover, like adipocytes, stromal vascular cells increase in size with increasing BMI, and may be a potential reservoir for lipophobic environmental contaminants (Rothenberg et al., 2015). Our results were similar to those found in previous studies (Caspersen et al., 2013; Loganathan and Kwan-Sing Lam, 2011; Wolff et al., 2007). Positive associations between PFASs (Brantsaeter et al., 2013; Sagiv et al., 2015), organochlorine pesticides and PCBs (Bachelet et al., 2011) and higher pre-pregnancy BMI have been shown in other studies. These inconsistencies may be due to the difference among studies in the degree of exposure to these chemicals in obese participants.

In comparison to other national surveys such as population-based Canadian Health Measures Survey (CHMS) (Health Canada, 2010) and the U.S. National Health And Nutrition Examination Survey (NHANES) study (Crinnion, 2010; Jones et al., 2010; Woodruff et al., 2011a), MIREC participants had lower geometric mean concentrations of phenols, phthalates, DDE and metals (lead and Mercury). Maternal *trans*-nonachlor and oxychlordane concentrations appear to be similar in MIREC to those found in the CHMS (Health Canada, 2010) and another Canadian study (Foster et al., 2012), and lower than that found in NHANES (Woodruff et al., 2011a). Consistency with other biomonitoring surveys in Canada (Rawn et al., 2012), in the MIREC maternal plasma samples, the predominant PCB congeners were 138, 153, and 180. Among the dioxin-like PCBs measured in MIREC, only PCB 118 was consistently detected in maternal plasma. PCB 118 concentrations were similar to those found in the CHMS (Health Canada, 2010) however, lower than other similar studies (Faupel-Badger et al., 2007; Foster et al., 2012; Ibarluzea et al., 2011). Compared to other large pregnancy cohorts, we found that MIREC participants had lower concentrations of PFASs for maternal age, parity, occupational status, prepregnancy BMI, smoking status in pregnancy and infant sex than in the Danish National Birth Cohort (Fei et al., 2007). PFOA concentrations in MIREC were similar to those reported in the Norwegian Birth Cohort (MoBa) (Gutzkow et al., 2012). On the other hand, MIREC pregnant women had higher levels of DDE and lower levels of PCBs for all SES and lifestyle factors than in the French CECILE study; however, both studies reported lower PCB concentrations with increasing BMI (Bachelet et al., 2011). Finally PBDE 47 concentrations in MIREC were notably lower than concentrations observed in pregnant women in the United States, NHANES (Woodruff et al., 2011b) and concentration of BPA and phthalate in MIREC tended also to be lower than those reported in Dutch (Snijder et al., 2013), Mexican (Harley et al., 2013a,b), Spanish (Casas et al., 2013) and American (Engel et al., 2009) pregnancy cohorts.

4.2. Strengths and limitations

A major strength of this study is the collection of biospecimens from a large pregnant population, the broad range of environmental chemicals studied, as well as the documentation of key information on important covariates that might affect exposures (Arbuckle et al., 2016).

Among the study limitations is the potential for selection bias as our sample is not representative of the Canadian population as a whole or of women giving birth in Canada (Arbuckle et al., 2013). Moreover, comparisons of results among biomonitoring studies should be interpreted carefully because differences in SES and lifestyle factors across countries and over time can occur and may also be indicative of time trends (National Research Council, 2006). Another limitation is that some observations may have been the result of chance from multiple statistical testing. Furthermore, we only considered the sociodemographic indicators individually, which precluded adjusting for the other indicators as well as testing for potential interactions between sociodemographic and lifestyle variables. Finally, we considered each chemical individually rather than studying interactions between chemicals. The sociodemographic profile associated with different chemical mixtures may be substantially different (Lokke et al., 2013).

5. Conclusion

In conclusion, maternal age, parity, smoking status, country of birth, and household income, were significantly associated

with most chemical exposures. Patterns and directions of associations were found to vary according to the maternal characteristic examined and the chemical studied. For example, foreign-born participants had significantly higher concentrations of phthalates, metals, PCBs and OCPs while multiparous participants had significant lower concentration of DAPs, PFASs, PCBs and OCPs. These factors are an important component of a thorough risk assessment as they can impact the degree of exposure and may highlight an individual's susceptibility to potential health effects due to differences in lifestyle, cultural diets, and aging.

Conflict of interest

None declared.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijheh.2017.01.001.

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