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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

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