Environment International 98 (2017) 89–95

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Full length article

Persistent organic pollutants in early pregnancy and risk of gestational diabetes mellitus☆

Marina Vafeiadi [a,*], Theano Roumeliotaki [a], Georgia Chalkiadaki [a], Panu Rantakokko [b], Hannu Kiviranta [b], Eleni Fthenou [a], Soterios A. Kyrtopoulos [c], Manolis Kogevinas [d,e,f], Leda Chatzi [a]

[a] Department of Social Medicine, Faculty of Medicine, University of Crete, Heraklion, Greece
[b] Department of Environmental Health, National Institute for Health and Welfare, Chemicals and Health Unit, Kuopio, Finland
[c] National Hellenic Research Foundation, Institute of Biology, Medicinal Chemistry and Biotechnology, Athens, Greece
[d] Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
[e] Hospital del Mar Research Institute (IMIM), Barcelona, Spain
[f] CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain

ARTICLE INFO

Article history:
Received 22 July 2016
Received in revised form 30 September 2016
Accepted 6 October 2016
Available online 12 October 2016

Keywords:
Gestational diabetes mellitus
Persistent organic pollutants
Polychlorinated biphenyls (PCBs)
Organochlorine pesticides
Pregnancy

ABSTRACT

Background: Persistent organic pollutants (POPs) are a group of diverse substances, including polychlorinated biphenyls (PCBs) and organochlorine pesticides that are resistant to biodegradation and ubiquitously present in our environment. Exposure to endocrine disrupting chemicals such as POPs has been linked to type 2 diabetes and metabolic disturbances in epidemiological and animal studies, but little is known about POPs exposure during pregnancy and the development of gestational diabetes mellitus (GDM). The purpose of this study was to determine the extent to which exposure to current low levels of different POPs in the first trimester of pregnancy is associated with GDM risk in 939 women from the "Rhea" pregnancy cohort in Crete, Greece.

Methods: Concentrations of several PCBs, dichlorodiphenyldichloroethene (DDE), and hexachlorobenzene (HCB) were determined in first trimester maternal serum by triple quadrupole mass spectrometry. We defined total PCBs as the sum of all congeners, nondioxin-like PCBs as the sum of PCB 153, 138, 170 and 180, and dioxin-like PCBs as the sum of PCB 118 and 156. Pregnant women were screened for gestational diabetes mellitus (GDM) between 24 and 28 weeks of gestation, and GDM was defined by the criteria proposed by Carpenter and Coustan. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using multivariable logistic regression models.

Results: Of the 939 women, 68 (7%) developed GDM. Serum concentrations of POPs were higher in women with GDM. Women in the medium and high tertiles of PCBs had 3.90 (95% CI: 1.37, 11.06) and 3.60 (95% CI: 1.14, 11.39) fold respectively higher odds of developing GDM compared to women in the lowest tertile of PCB exposure after adjusting for pre-pregnancy BMI and several other confounders. Odds of GDM for women in the medium and high tertiles of dioxin-like PCBs was 5.63 (95% CI: 1.81, 17.51) and 4.71 (95% CI: 1.38, 16.01) and for nondioxin-like PCBs 2.36 (95% CI: 0.89, 6.23) and 2.26 (95% CI: 0.77, 6.68) respectively. Prenatal DDE and HCB exposure were not significantly associated GDM risk.

Conclusions: These findings suggest that women with high PCBs levels in early pregnancy had higher risk for GDM. Further studies are needed to replicate these results and to evaluate potential biological mechanisms underlying the observed associations.

Abbreviations: AhR, aryl hydrocarbon receptor; BMI, body mass index; BDE-47, tetra-bromodiphenyl ether; CAR, constitutive androstane receptor; DDE, dichlorodiphenyl dichloroethene; DDT, dichlorodiphenyl trichloroethane; EDCs, endocrine disrupting chemicals; GDM, gestational diabetes mellitus; GWG, gestational weight gain; HCB, hexachlorobenzene; IOM, Institute of Medicine; LOQ, limit of quantification; PCBs, polychlorinated biphenyls; POPs, persistent organic pollutants; PXR, pregnane X receptor; SD, standard deviation; T2DM, type 2 diabetes mellitus; 95% CIs, 95% confidence intervals.

☆ Conflict of interest and source of fundingThe authors declare they have no actual or potential competing financial interests associated with this manuscript.The Rhea project was financially supported by European Projects (EU FP6-2003-Food-3-NewGeneris, EU FP6. STREP Hiwate, EU FP7 ENV.2007.1.2.2.2. Project No 211250 Escape, EU FP7-2008-ENV-1.2.1.4 Envirogenomarkers, EU FP7-HEALTH- 2009- single stage CHICOS, EU FP7 ENV.2008.1.2.1.6. Proposal No 226285 ENRIECO, EUFP7- HEALTH-2012 Proposal No 308333 HELIX), MeDALL (FP7 European Union project, No. 264357), and the Greek Ministry of Health (Program of Prevention of obesity and neurodevelopmental disorders in preschool children, in Heraklion district, Crete, Greece: 2011- 2014; "Rhea Plus": Primary Prevention Program of Environmental Risk Factors for Reproductive Health, and Child Health: 2012-15).

* Corresponding author at: Department of Social Medicine, Faculty of Medicine, University of Crete, P.O. Box 2208, Heraklion 71003, Crete, Greece.
E-mail address: bafom@uoc.gr (M. Vafeiadi).

http://dx.doi.org/10.1016/j.envint.2016.10.005
0160-4120/

1. Introduction

Gestational diabetes mellitus (GDM), defined as glucose intolerance first recognized during pregnancy (Metzger and Coustan, 1998), is one of the most common medical complications of pregnancy and depending on the type of population and the diagnostic criteria used, it has been estimated that the total prevalence of GDM reaches almost 15%–20% (American Diabetes Association, 2014). Its prevalence is increasing and parallels the rising incidence of type 2 diabetes mellitus (T2DM) and obesity worldwide (Ben-Haroush et al., 2004; DeSisto et al., 2014; Wild et al., 2004). GDM increases the risk of development of type 2 diabetes in both mother (Bellamy et al., 2009) and child (Clausen et al., 2008; HAPO Study Cooperative Research Group, 2002), is associated with adverse short-term fetal outcomes, mainly with excessive fetal growth (Hiersch and Yogev, 2014; Mitanchez et al., 2014) as well as offspring long-term greater adiposity and adverse cardiometabolic health (Fraser and Lawlor, 2014). Maternal characteristics such as obesity, older age, and family history of type 2 diabetes mellitus are known to increase risk of GDM, but up to half of women with GDM do not have these classic determinants (Coustan, 1995), suggesting a role for environmental factors.

Persistent organic pollutants (POPs) include synthetic chemicals that were widely used as pesticides [e.g., dichlorodiphenyltrichloroethane (DDT), dichlorodiphenyldichloroethene (DDE), hexachlorobenzene (HCB)] and in industrial processes (PCBs), through most of the 20th century. POPs are of public health concern, given their long half-lives and their ability to persist, bioaccumulate and biomagnify through the food-chain. Although the use of these chemicals is presently banned (PCBs, HCB) or restricted (DDT) (Stockholm Convention on Persistent Organic Pollutants, 2009), because of their persistence in the environment, the general population is still exposed to these substances at low doses (Porta et al., 2008) and adverse health outcomes related to background levels of exposure are still a concern for the general population (WHO, 2010). Moreover, several of these compounds act as endocrine disrupting chemicals (EDCs) which can alter the normal function of endocrine systems in humans and wildlife (Diamanti-Kandarakis et al., 2009).

Experimental studies have shown that EDCs can alter beta cell function leading to insulin resistance (Hectors et al., 2011) and induce low-grade adipose tissue inflammation that accompanies the pathogenesis of metabolic diseases (Kim et al., 2012). POPs are hypothesized to increase risk of diabetes through modulation of glucose metabolism and also affect nuclear receptors [aryl hydrocarbon receptor (AhR), constitutive androstane receptor (CAR), and pregnane X receptor (PXR)], which increase chronic low grade inflammation, decrease mitochondrial function and fatty acid oxidation, and increase lipogenesis to ultimately produce insulin resistance syndrome (Lee et al., 2014; Ruzzin et al., 2010). Robledo et al. recently reviewed animal evidence to highlight the biological plausibility for an association between GDM and environmental chemicals (Robledo et al., 2016). Although adult epidemiological studies associate type 2 diabetes with exposure to environmental chemicals (Dirinck et al., 2014; Kuo et al., 2013; Lee et al., 2006; Lee et al., 2014; Taylor et al., 2013; Thayer et al., 2012) among individuals in the general population, studies focusing on the association with GDM are still very limited. To our knowledge, only four prospective studies have assessed the association between exposure to POPs and GDM (Jaacks et al., 2016; Shapiro et al., 2016; Smarr et al., 2016; Zhang et al., 2015). No associations were found between exposure to organochlorine pesticides (Shapiro et al., 2016; Smarr et al., 2016) and PCBs (Jaacks et al., 2016; Shapiro et al., 2016), while recent studies reported positive associations between serum perfluorooctanoic acid (PFOA) (Zhang et al., 2015) and polybrominated diphenyl ether (PBDE) 153 (Smarr et al., 2016) concentrations with GDM risk.

Given the inconclusive results and because of the long-term consequences of GDM in both mother and offspring, it is important to better characterize the potential role that environmental chemicals may play in the development of glucose disorders during pregnancy. Using data from the Rhea mother-child cohort in Crete, Greece, this study sought to determine whether exposure to POPs during pregnancy was associated with increased risk of GDM.

2. Methods

2.1. The mother-child cohort in Crete (Rhea study)

The Rhea study prospectively examines a population-based sample of pregnant women and their children at the prefecture of Heraklion, Crete, Greece. Methods are described in detail elsewhere (Chatzi et al., 2009). Briefly, female residents (Greek and immigrants) who became pregnant during a period of one year starting in February 2007 were contacted and asked to participate in the study. The first contact was made at the time of the first comprehensive ultrasound examination (mean ± SD 11.96 ± 1.49 weeks) and several contacts followed the postpartum period. To be eligible for inclusion in the study, women had to have a good understanding of the Greek language and be older than 16 years of age. The study was approved by the ethics committee of the University Hospital in Heraklion, Crete, Greece, and all participants provided written informed consent after complete description of the study.

During the study period, 1765 eligible women were approached, 1610 (91%) agreed to participate and 1388 (86%) were followed-up until delivery. 1135 blood samples provided by the study participants were analyzed for POPs exposure. A cohort of overall 939 women, carrying and giving birth to a singleton, followed-up prospectively from early pregnancy to delivery that did not have a prior history of diabetes and with complete information on POP exposure and GDM was included in the present analyses.

2.2. Measurement of serum POPs

Maternal serum samples were collected at the first prenatal visit around the 3rd and 4th month of pregnancy, in 10 ml Silicone gel separator vacutainer (Becton Dickinson, UK), were centrifuged within 2 h from blood collection at 2500 rpm for 10 min and were then stored in aliquots at −80 °C until assayed. The POP analyses were performed in the National Institute for Health and Welfare, Chemical Exposure Unit, Kuopio, Finland with an Agilent 7000B gas chromatograph triple quadrupole mass spectrometer (GC-MS/MS). Pretreatment of serum samples for GC-MS/MS analysis has been described elsewhere (Koponen et al., 2013). Serum concentrations of six individual PCB congeners (IUPAC numbers: 118, 138, 153, 156, 170 and 180), HCB, p,p'-DDT and p,p'-DDE, and BDE-47 were determined. All the results were reported on volume basis and expressed in pg/ml serum, while samples bellow the limit of quantification (LOQ) were assigned the value 0.5 × LOQ. LOQ was 6 pg/ml for PCB118 and PCB 156; 10 pg/ml for HCB, p,p'-DDE, PCB138, PCB153, PCB170, PCB180 and BDE47, and 50 pg/ml for p,p'-DDT. We chose to use wet-weight levels for the POPs but adjusted for fasting maternal serum triglycerides [mean (±SD) = 128.9 (57.7) mg/dl] and cholesterol [209.2 (42.8) mg/dl] as continuous variables in all multivariable models to minimize potential biases associated with automatic lipid adjustment (Schisterman et al., 2005). Due to high percentages of samples below the LOQ, p,p'-DDT (64.7%) and BDE-47 (76.9%) were not used in the statistical analyses. The respective total PCB concentrations were calculated by summing the concentrations of individual PCB congeners, nondioxin-like PCBs as the sum of PCB 153, 138, 170 and 180, and dioxin-like PCBs as the sum of PCB 118 and 156.

2.3. Lipid analyses

Maternal fasting serum samples were collected during the first major ultrasound visit at or before week 15 of gestation (mean: 11.96 weeks, SD 1.49). Plasma triglycerides and total cholesterol